George Bakris: 00:04

Welcome. Thank you for joining this podcast on identifying and managing renal complications in patients with type 2 diabetes and cardiovascular disease. The purpose of this ongoing series is to reduce cardiovascular deaths, heart attacks, strokes and heart failure in people living with type 2 diabetes. It's based on the collaborative initiative between the American Heart Association and the American Diabetes Association, Know Diabetes by Heart™.

George Bakris: 00:31

This series is brought to you by funding sponsors, Boehringer Ingelheim and the Eli Lilly and Company, Diabetes Alliance and Novo Nordisk, and national sponsors Sanofi, AstraZeneca, and Bayer. I'm Dr. George Bakris, a nephrologist with expertise in diabetes-related kidney disease. I'm representing the National Kidney Foundation as a speaker for this podcast. Joining me is Dr. Peter McCullough, a cardiologist, who's also a board-certified internal medicine person as well.

George Bakris: 01:05

Peter, welcome, and thank you for joining me on this. Thank you to the audience for joining us. Hopefully, you will find this entertaining and enlightening. Let's start off with discussing kidney disease with type 2 diabetes. What's the epidemiology? I think a lot of people know a lot of this, but I want to go through it. Diabetes is by far the most common cause of kidney disease in the Western world.

George Bakris: 01:31

Interestingly, it is rapidly rising in Asia, specifically in Taiwan, where they've actually exceeded the incidence of diabetic kidney disease and end-stage kidney disease going onto dialysis. The reasons for this are unclear, but approximately one third of people with diabetes have kidney disease. Diabetes, as we said, is a leading cause of kidney failure. I think it's also important to know that we're living longer as a population and kidney disease is much more common in people age 65 and older, like about 38% of people have kidney disease.

George Bakris: 02:06

If you compare that to people that are younger, you're talking about 45 to 64, only 13%. Of course, younger people, younger than 44, only about 7%. Why is it important to manage kidney disease risk in a patient population? This is important. The risk factors that can be managed by family docs, primary care physicians, PAs, nurse practitioners are the same ones that are being managed by the specialist. I think it's underplayed and we really need to talk about this because there's a tremendous amount of effort that can be put in with doing what you're supposed to do anyway, but just monitoring for very specific risk factors.

George Bakris: 02:51

I'll just tell you what they are right now. This is no secret. Blood pressure, glucose, and lipids. Those three are critical and managing them is critical, not just for cardiovascular disease risk, but preserving the kidney. This has been shown in many, many studies, one long-term study going on 21 years from the Steno Diabetes group. This is very important information. I think it's also important to know that with diabetes, if you develop kidney disease, your cardiovascular risk dramatically increases.

George Bakris: 03:23

CV death risk increases almost fivefold when the estimated GFR goes below 45 and more than elevenfold when it goes below 30. This is what we're talking about. It's not just your GFR is falling and who cares. Your cardiovascular risk skyrockets. Now, the National Kidney Foundation and the American Diabetes Association clinical practice guidelines, which come out every year, they're updated every year, make a big, big deal about assessing kidney function in people with diabetes.

George Bakris: 03:57

They specifically focus not just measuring estimated GFR but measuring albumin and creatinine ratio. Very important. The recommendation is to do it annually. Now, there are certain limits for measuring albuminuria. A spot albumin and creatinine ratio is all you have to do. People think you have to do 24-hour urine, you don't. Some very basic rules. Less than 30 milligrams per gram of creatinine is normal. 30 to 299 is considered high albuminuria.

George Bakris: 04:32

That's the new terminology for what was microalbuminuria. If you have greater than or equal to 300, that's very high or macroalbuminuria. If that is present, even if your GFR is above 60, you are considered to have kidney disease. This is very, very important and albuminuria is not being measured. Peter, let me ask you, as a cardiologist, if we're talking about general cardiologist, do you see a value in measuring albuminuria?

Peter McCullough: 05:03

I certainly do. Published in circulation many years ago was an AHA scientific statement on the value of understanding albuminuria as a cardiovascular risk predictor, or at least an associated factor for cardiovascular disease. It has strong predictive abilities, not only for cardiovascular death, but also for the development of heart failure and importantly, in the renal space, progression to end-stage renal disease.

Peter McCullough: 05:34

The estimated GFR and the albumin/creatinine ratio can be organized in a two by two table as a heat map, if you will, showing really astronomical risks when the EGFR is low, let's say below 30, and the albumin and creatinine ratio is high, let's say over 300 milligrams per gram. Here, the standard Framingham

epidemiology is really blown out of the water with the cardiorenal epidemiology showing a manifold increased risk for these cardiovascular events.

Peter McCullough: 06:05

The estimated GFR is obtained through passive labs that patients have so many biochemistry panels that invariably we find these on the chart. The albumin and creatinine ratio takes effort. I think a major message of this podcast is to encourage cardiologists to make sure they fill in that part of the patient's profile and understand the albumin and creatinine ratio.

George Bakris: 06:28

Thank you very much for that. Let me further reinforce what you just said. There is a paper that will be coming out shortly. A very large paper that actually looked at microalbuminuria as a predictor of cardiovascular outcomes in a very large trial. Basically, showed that just like kidney disease progression, in kidney disease progression, you reduce albuminuria to slow progression. Here, the higher the baseline level, the greater the risk for cardiovascular events.

George Bakris: 06:59

We published ... And that's coming out soon, I believe in JACS, but I think it's important for the audience to know that. The other thing is, we published in 2014 in Diabetes Care, the whole concept that microalbuminuria is a cardiovascular risk marker. It's an inflammatory marker. It is the kidney's TRP. If you see that, that doesn't necessarily mean you have kidney disease. Means you're at risk for it and you definitely have some type of inflammatory process going on and it could be a whole bunch of things, but you need to pay attention to it.

George Bakris: 07:32

If you don't have it, it's a missing link. The old notion, you have microalbuminuria, you put them on an ACE and forget about it is garbage. It doesn't work like that. That has never been proven to be effective. Just because you're reducing it doesn't mean you fixed anything. You need to focus on risk factors. Microalbuminuria is definitely a risk marker without any question, but as Peter alluded to, and I mentioned, presence of kidney disease, especially when you get down to levels of GFR 45, is a clear risk factor that modifies cardiovascular outcomes.

George Bakris: 08:06

Now, to continue this and get back to some simpler things. We said, diabetes is number one. Number two, still as a cause of kidney failure is hypertension. Those two together account for 76% of everybody on dialysis today. The remaining diseases specifically, the next biggie on the list is polycystic kidney disease. That's a genetic disease. Then the rest fall off dramatically because they're glomerular diseases and they're not very common.

George Bakris: 08:35

I think it's important to note that if you're intervening, if you have a patient that say is 40 years old and has a GFR of 65, that is not normal for that person. Especially if they have albuminuria, that it's not normal. There have been trials through the years. The most recent trial, which really changes the whole landscape of treatment of diabetic kidney disease, is the CREDENCE Trial. This came out last year and I was privileged to be on the steering committee of this trial.

George Bakris: 09:07

It's the first trial since RENAAL and IDNT published in 2001 that looks at progression of kidney disease in people that have bona fide diabetic kidney disease. Shows in people with GFRs down to actually even a little bit below 30, you can slow progression of kidney disease with canagliflozin, which was the SGLT2 used dramatically. Of course, this is on top of ACE or ARB. It's not instead of. Very important trial.

George Bakris: 09:37

4,400 plus patients and high cardiovascular risk, 15% came in with heart failure. 5% came in with amputations. All of those people got benefit. We slowed progression of kidney disease by an additional 58% over what ACEs and ARBs do. Of course, the other SGLT2s have been looked at as well in less renally sick populations, but they also show a benefit, but it's-

Peter McCullough: 10:04

George, it's important to point out to qualify for the trial that patients did have diabetes and an albumin and creatinine ratio over 300 milligrams per gram. In fact, the average was about 800 getting into the trial.

George Bakris: 10:17

Actually, it was 927, but you're right. You're right. Thank you for bringing that up because I was just about the bridge and I was going to come to you because we showed tremendous cardiovascular benefit even in this group, which of course has a very high cardiovascular risk. The other trials with empagliflozin and the dapagliflozin also showed very good cardiovascular risk reduction and a benefit on slowing progression of kidney disease.

George Bakris: 10:42

Even though they were in much earlier stages in people that had micro or even normal albuminuria. Peter, I don't know if you want to opine on that a bit.

Peter McCullough: 10:51

Yes. Well, those other clinical trials clearly were at lower risk, actually lower risk for both heart disease and kidney disease. The EMPA-REG OUTCOME trial and the CANVAS trials program, as well as the large dapagliflozin trial. Importantly,

the consistency of effect was seen on heart disease more strongly for heart failure hospitalization and cardiovascular death. Then major adverse cardiovascular events, but most strongly driven through cardiovascular death.

Peter McCullough: 11:24

The thinking is that the cardiovascular death reductions are largely in those patients with heart failure or cardiomyopathy. These drugs probably don't have too much of an influence on atherosclerotic events, but clearly do with respect to myocardial events.

George Bakris: 11:40

To nail that point that Peter just made, the current ADA Clinical Practice Guidelines place SGLT2s as not quite mandatory, but almost mandatory with metformin in people that have advanced kidney disease or have heart failure. It's in the guidelines. This is not something that's just coming out of trial. Now, let's not forget that we have another new class of drugs to treat diabetes. The GLP-1 RAs and those drugs have a positive benefit, certainly on cardiovascular outcomes.

George Bakris: 12:14

There is a trial that is ongoing called the FLOW trial, looking at injectable semaglutide on renal outcomes. Now, that trial, and I'm also full disclosure on the steering committee of that, that trial will not be done until 2023. We're still recruiting or were before this epidemic. Again, there's evidence in the LEADER Trial with liraglutide that there may be some renal benefit from this group of drugs. I don't know if you want to talk about that Peter.

Peter McCullough: 12:41

Right. Well, the GLP-1 receptor agonist work by a very different mechanism in terms of the treatment for diabetes. The cardiovascular outcome trials and the approval trials did reduce the progression of worsening albuminuria and in general, trended towards favoring on hard renal end points, but not statistically significant. Because this form of treatment does not influence electrolytes or influence blood pressure, is in general well tolerated up to agonists has sufficient favorable data to also move forward in a very large cardiovascular outcomes trial called the SOUL trial.

Peter McCullough: 13:24

Additionally, this form of GLP-1 receptor agonist is available orally in the United States. Both SGLT2 inhibitors and GLP-1 receptor antagonists in general have favorable cardiovascular and renal outcomes, and also are approved to treat type 2 diabetes.

George Bakris: 13:44

That's excellent. Just to quickly summarize. We not only have the ACEs and the ARBs in people with established kidney disease that must be used for blood

pressure control, but now we have the SGLT2 inhibitors and the GLP-1 that primarily will give you benefits. The beauty of the SGLT2s have been shown to give you the benefit independent of glucose reduction. The CREDENCE Trial showed only a .2% change in hemoglobin A1c. Yet the benefit was seen all the way down to GFR of 30, where there was virtually no prediction that you would change glucose.

George Bakris: 14:24

I think you really need to think of the SGLT2s for sure as cardiorenal risk reducing drugs that have glucose lowering as a beneficial side effect, because yes, they came out as diabetes drugs. The reality is they are drugs for all seasons, and they help the kidney and the heart. The GLP-1 definitely are going to affect weight and they're going to affect the glucose. Again, as Peter nicely summarized, they definitely have benefits to help the kidney and the heart.

George Bakris: 14:52

The kidney we'll see when the FLOW trial is done, but certainly they're reducing inflammation by reducing albuminuria. Now, what do we really do? The ADA basically says in terms of optimizing slowing of progression of kidney disease at earlier stage. By the way, I'm not sure you know, but the recommendation to refer to a nephrologist is when the GFR is 30. If you have somebody with a patient of GFR 45 or 50, and you refer them to a nephrologist they're going to say, "Look, you know what to do, blood pressure, lipids, glucose. I have other things I have to do."

George Bakris: 15:28

You need to know that you really have a lot more power than you think and can have an impact. The recommendations for the ADA guideline are hemoglobin A1c, less than seven, ideally down to 6.5, blood pressure, less than 130/80. While they're a little softer on the cholesterol values, when you look at these long-term studies that have actually moved on cholesterol, you're talking about LDLs in the 70s.

George Bakris: 15:55

If you do that ... And a very nice paper that was published in Diabetologia in 2019, 21-year follow-up of the Steno Diabetes original population that was published in New England quite a number of years back, basically shows consistently over that time, a 20% absolute risk reduction and development of cardiovascular and renal events in a given patient. Very important. Cannot overemphasize that.

George Bakris: 16:23

Now, I want to just bring up metformin because metformin is still on the front lines. A lot of cardiologists have argued that it should be taken off because it hasn't really shown the benefits on cardiovascular or renal risk reduction. In

fact, it's dangerous if GFR falls too low and you keep using it. I wanted your thoughts on that Peter.

Peter McCullough: 16:44

I've adopted the viewpoint that if metformin does not have any GI intolerance in a patient and is well tolerated to continue it. I have to tell you George, if I have patients suffering, of which 15% or more do with some complaints regarding metformin, I do tend to change it out for an SGLT2 inhibitor.

George Bakris: 17:05

Yeah. That's fine. Listen, I'm not wedded to metformin. I think the audience should know that GFRs below 60 you have to cut the dose in half. You're going to lose some glucose lowering ability, so 500 BID. Then you can keep using it if they're on it, but you should not start it if the GFR is below 45. Whereas I just told you SGLT2s, you may not get the glucose benefit, but you're still getting cardiovascular benefit down to a GFR of 30.

George Bakris: 17:32

Actually, there's a paper we just submitted, it's in review, arguably down to a GFR of 25. I think it's important to understand that this is not just about glucose or blood pressure. These drugs have pleiotropic effects that definitely can affect other things. Now, one of the things I want to talk about, people are scared of the SGLT2s because everybody mentions SGLT2, you preassociate diabetic ketoacidosis. I want to just dispel that very quickly.

George Bakris: 17:59

The people, the only people at risk in the trial to develop diabetic ketoacidosis, were people that required insulin. They developed a GI illness and became volume depleted and they stopped their insulin, but continued, the SGLT2. Just like when you advise your patients to stop ACE inhibitors and ARBs if they develop a prolonged GI illness, you need to tell them to stop the SGLT2s for the different reason, but same kind of problem.

George Bakris: 18:28

That's it. Sulfonylureas, similar story. I think it's important to keep these concepts in mind. I know that they're new, but you need to keep them in mind. Peter, do you want to say anything about that before I move on to the next topic?

Peter McCullough: 18:42

I would just say, I know others disagree, but my practice pattern is I discontinue SGLT2 inhibitors, just like I do sulfonylurea and metformin when patients are hospitalized. I think there's too much going on in terms of patients being held NPO, getting diuretics and other things. Getting contrast procedures that I really think the drugs we're talking about today are ambulatory clinic outpatient drugs.

George Bakris: 19:10

That is an excellent point. Thank you for bringing that up, because I'm not sure who's disagreeing with you because I certainly am not. That's exactly what I do. I think that's a very important point. I'm going to move a little bit away to another pet peeve of mine. It's a pet peeve because we originally published this paper in 2000 and I'm still talking about it today, even though it's even in the guideline.

George Bakris: 19:30

That is, and Peter knows this well, if you start an ACE or an ARB, and especially if blood pressure gets controlled and the creatinine goes up, everybody stops it because they think they'd cause AKI. That couldn't be further from the truth. Let me just make a statement, and I want to go through some of this and get Peter's opinion as well. Number one, AKI means you have a 50% increase in serum creatinine that is sustained. Sustained. 50%, not at a bump from 1 to 1.2, that's not AKI.

George Bakris: 20:00

I think it's important to understand the definition first. Secondly, it's important to understand the concept that if somebody has not been treated well for hypertension and you're now treating them, I don't care what you're using. You're going to get a bump in creatinine. The kidney is a regulatory organ and it adjusts to its curving milieu. If you have somebody with a pressure of 200 and you bring them down to 130, trust me, you can use hydralazine the creatinine is going to go up.

George Bakris: 20:24

You haven't poisoned to kidney, it's readjusting. If you simply wait, it will come down. The difference that you need to know is look at the creatinine not a day later, but a week later. It's going to be up. How high is it going to be? If it's above 30%, well, then you can be a little concerned, but if it's below 30% and especially if potassium is okay, you've got nothing to worry about.

George Bakris: 20:46

In fact, long term there's excellent data, even in trial from The ACCORD that those people have better outcomes and they certainly are not at increased risk for cardiovascular. Peter, what are your thoughts about that?

Peter McCullough: 20:57

Yes. Unfortunately, I think we've done ourselves a bit of a disservice with using the term acute kidney injury for each and every instance that the BUN in creatinine are elevated. Because I can tell you it's been looked at fairly carefully now in heart failure when patients get intravenous loop diuretics or oral loop diuretics. In fact, there are no markers that are elevated indicating tubular injury, that these are transient hemodynamic adjustments that the kidneys are making in the drug milieu and with ACEs and ARBs.

Peter McCullough: 21:30

Now, even with other drugs, including SGLT2 inhibitors. We have to encourage doctors to be tolerant of elevations in BUN in creatinine as the body adjusts to these drugs, which over the long term have very favorable effects.

George Bakris: 21:45

Excellent. Excellent. I think it's important to keep in mind that these drugs are not magic. They are highly effective and pretty much mandated. Everybody with diabetes but that has albuminuria, the notion that you're going to use these drugs in normotensive people with no albuminuria or microalbuminuria, and you're going to be protected, has zero evidence to support it. Don't think of them as magic bullets. They're blood pressure lowering drugs that work by a specific mechanism and definitely will protect the kidney in advanced disease.

George Bakris: 22:18

Now, I think it's important, and I don't know how many of you manage nephrotic range proteinuria. We're talking about now three grams, four grams or higher. How do you get that down? ACEs and ARBs certainly work well. Adding diltiazem to it will give you an additional 20 to 40% reduction and adding spironolactone to that if the potassium can tolerate it, will give you, I've seen 80% reduction over the span of a couple of months. Very important to understand that.

George Bakris: 22:47

Now, one of the things that is important is we have potassium binders that I affectionately call enablers. A lot of these patients with advanced disease can't tolerate these drugs because of hyperkalemia. If you concomitantly give one of the two new potassium binders in very low doses, you can easily facilitate the use of maximal dose ACE or ARB or addition spironolactone. It's very doable. We've done it. There's trials going on now, outcome trials using this to prove the point. I think it's really important.

George Bakris: 23:20

There is a paper that was just published in JAMA Internal Medicine, literally within the last month and a very large database showing that stopping ACEs and ARBs prematurely in people with advanced kidney disease that actually are at cardiovascular risk actually increases cardiovascular event. You think you're doing them a favor because their creatinine went up, you've just increased their risk by stopping those drugs. It's very important to keep this in mind.

George Bakris: 23:45

Peter, let me ask you, what do you find are the biggest challenges with preventing or managing renal disease? I'm not talking now from the perspective of the nephrologist. I'm talking from the perspective of the cardiologist and even the intern.

Peter McCullough: 24:01

I still think George there's a large issue on recognition. In the published studies the patients themselves are only aware about 15% of the time that they have any form of kidney disease. The published studies of primary care doctors and other non-nephrology specialists show that their awareness is quite low. There still are a whole array of background things that are going on. Like use of nonsteroidal anti-inflammatory agents, no attention to sodium intake in the diet, things not being attended to in a way that we'd like to see.

Peter McCullough: 24:39

In fact, these patients may have repeated acute kidney injury with infections, nonsteroidal anti-inflammatory agents, nephrotoxic antibiotics, or iodinated contrast. I think all of this is going on behind the scenes. Before we know it, George, we have a patient who is now in your office with a hike serum creatinine, let's say over four, a GFR below 15, advanced proteinuria. Then we're asking you to really perform a miracle and pull this patient away from the progression to dialysis.

George Bakris: 25:12

Yeah. Absolutely. Correct. I think what's missing here, something very simple, is patient education. Of course, we don't have time, but without educating the patient we really can't expect them to really follow through. This is very important. Actually, to your point, there's a relatively recent paper. This was scary. There was a database analysis, but it showed that 40% of people, 40, 40% of people with stage four CKD, that means their GFR is below 30.

George Bakris: 25:43

They should be seeing a nephrologist if they're not, 40% of those people did not know they had kidney disease. I think the audience needs to know there's no symptoms. Hypertension is a silent killer. Kidney disease is a silent killer. You don't get symptoms of advanced kidney disease until you're literally ready to start dialysis. Even then you may not have them. You have to look at the numbers, you have to educate the patients.

George Bakris: 26:03

You have to empower the patients with the things that we've been telling you to basically slow progression of kidney disease. Because otherwise it just won't happen. It hasn't failed yet, you do not want the nephrologist to tell the patient, "By the way, did you know you have advanced kidney disease?" Because they're like, "Well, why didn't anybody tell me?" Which is what I've been hearing from patients for years. They're not understanding why their generalists didn't tell them.

George Bakris: 26:26

What I've been told by generalist is all they can do is write an ACE inhibitor and forget it. What we're trying to tell you is that's the wrong answer. You need to control the risk factors, just like you would for cardiovascular disease and the kidney will reap the benefit. As simple as that. Now, I have an answer to this. I'm going to say this through this next question, and then get your thoughts on this Peter. The question is, how do we overcome these barriers?

George Bakris: 26:50

I mean, it's not that physicians don't know this stuff. They know it, but it's not being transmitted. How can we fix this? What I've been told by many physicians is there's a bucket list that they have with check marks. What we want them to do, measure albuminuria, educate the patient with it. If it's not on that list, it's not happening because they don't have time and that's all they're getting paid. We can get Medicare to change. Of course, that's easier said than done. I don't know what other things you would do or even that. What are your thoughts?

Peter McCullough: 27:22

There are some examples, George, where some of these large integrated health systems have used electronic records to actually create warnings that go to patients and even crying patients who have had a precipitous decline in GFR and get them to nephrologist. I can tell you in my practice, I do have patients with end-stage renal disease. I'm proud to say I haven't had a single patient 'crash' into dialysis. Meaning that, no one had any advanced warning of this.

Peter McCullough: 27:52

End-stage renal disease does not have to be [inaudible 00:27:59] for every patient. They see nephrologist ahead of time. They get their vascular access lined up. I saw a patient this week who has coronary heart disease and heart failure but is now three years on dialysis. She is grateful that she's gotten good care and collaborative care among nephrology, cardiology and her primary care physician.

George Bakris: 28:11

I think that's the key is we need to have integrated care. In Ireland, I will tell you, and this has now been well over 10 years, there is a cardiorenal institute at the University of Cork. It is a single building and in this building is nothing but nephrologists and cardiologists. When the patient comes in, they are seen by both the nephrologist and cardiologist. If they need procedures, echo’s, etc., those are done. In fact, there's a dialysis unit downstairs.

George Bakris: 28:39

It's one building. They were a couple of nephrologists that lobbied the government over there to get the funding to do this. They're collecting data and the patients love it. I think this is really where we need to be going and change the reimbursement model for the patients actually. I couldn't agree more. I

want the audience to know ... I mean, we're giving you a lot of information. I want the audience to know in the few minutes that we have left that there are a number of resources.

George Bakris: 29:07

I know that the National Kidney Foundation has a lot of resources. In addition, to knowdiabetesbyheart.org, that's a website knowdiabetesbyheart.org, there are other resources that the National Kidney Foundation has. If you go to their webpage at nkf.org, there's patient portals. There's a tremendous wealth of information that you can find about this. I strongly encourage you to do this because the patients in my experience that have done the best are the patients that are well-educated and inquisitive and demand answers.

George Bakris: 29:42

I'm going to come back to you, Peter, for the final word. What do you think the big takeaway should be from this podcast in terms of management and prevention of kidney disease?

Peter McCullough: 29:54

George I'd finish and conclude by saying that I think every primary care and medical subspecialist, just like they have burned into their operational memory banks to assess for cardiovascular risk, they should also assess for the renal risk. They should know their patient's estimated GFR serum creatinine, as well as the albumin and creatinine ratio.

Peter McCullough: 30:17

They should integrate this information and understand that these new generation of antidiabetic drugs are wonderful for both the heart and the kidneys. They can set a course early and change the natural history of both heart and kidney disease in this at-risk population.

George Bakris: 30:33

I think that was well said. Very succinct. I think the concept needs to change here. Most of us grew up with the concept control sugar, control blood pressure, control lipid. I would say that that concept is good, but now we have drugs that are working in ways that we're not really sure they're working. These drugs lower sugar, yes, but they're protecting independent of lowering sugar, like the SGLT2s. How are they doing this?

George Bakris: 30:58

Well, we're trying to figure that out, but for sure we know it's not anything negative. These patients, the diabetic patients that are on the fringe of getting kidney disease or have kidney disease, their cardiovascular risk just skyrocketed. Plus, they're already in cardiovascular risk. They need full support. SGLT2s, GLP-1s add substantially to the already recognized regimen of ACEs and ARBs. Therefore, we need to be thinking of these drugs.

George Bakris: 31:28

By the way, these SDLT2s, they're not expensive. Canagliflozin and empagliflozin are both on the Medicare list. You can get them at very low prices. They need to be thought of in anybody that has high risk, because you're going to be hearing in about three or four months, the results of the DAPA-CKD study. Now, that's dapagliflozin in kidney disease. I will tell you that at least a third of those people, if not more, did not have diabetes and the study was stopped early for overwhelming efficacy.

George Bakris: 31:59

You know it's positive. The question is, are these drugs for everybody? Not just people with diabetes. Stay tuned. We'll see. For right now it's empowering the patient with knowledge to educating the patient. It's thinking outside the box to use these drugs to reduce cardiorenal risk. I want to thank Peter for your joining me and I want to thank you. Hopefully, you got something out of this, and the patients will be better served by it. Thank you very much for your time.