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- Liz Olson: [00:04](#) I'm Liz Olson with the American Heart Association and know diabetes by heart. And, today we're here to answer your frequently asked questions on managing renal disease in patients with heart failure and type two diabetes. On our recent webinar on this topic, we took your questions and today we'd like to revisit some of the most frequently asked questions with our guest, Dr. Robert Eckel.
- Dr. Eckel, it's a pleasure to have you here today. How are you?
- Dr. Eckel: [00:28](#) Great, Liz, how are you doing?
- Liz Olson: [00:29](#) I'm very well, thank you. Can you tell our audience a little bit about your background?
- Dr. Eckel: [00:34](#) Right. Well, I've been at the University of Colorado medical school now for over 40 years. I'm now a Professor of Medicine Emeritus at the university. My appointments have been an endocrinology metabolism and diabetes, and in the division of cardiology, and I've had the privilege over my career to really mix basic science with clinical investigation. And, I've served the American Heart Association as a volunteer for many years, including being president in 2005 to 2006. And I just stepped down from being the media past president of medicine and science for the American Diabetes Association. So, I've had a wonderful career thanks to so many people, including the American Heart Association.
- Liz Olson: [01:15](#) That's a real pleasure to have you thank you for talking with me. I'd like to get started, how common is it for patients to have renal disease, heart failure, and type two diabetes all at once?
- Dr. Eckel: [01:27](#) Well, that's kind of the ugly triumvirate if you will. Certainly we know diabetes is very common up to 10 to 12% of the US population. We know congestive heart failure is an increasing entity that relates to poor outcomes and all patients with or without diabetes and chronic renal disease relates to both. But, if we look at patients as an outpatient who have heart failure, about 25% of them have diabetes, mostly type two, a bit of type one. Where if we looking at people in the hospital admitted to the hospital for symptoms or signs of congestive heart failure, about 40% of them have diabetes.

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And, when we get with the guidelines data, ultimately the coexistence of decreases in renal function is about one sixth of all patients with congestive heart failure and diabetes have EGFRs less than 30. And, 50% of patients with heart failure and diabetes have EGFRs less than 60 mils per minute. So, we're looking at really a common interaction between these three entities. Diabetes, heart failure, and chronic kidney disease.

- Liz Olson: [02:35](#) That's very interesting. So, how does this combination of comorbidities relate to, let's say the types of medications that can be prescribed, for example, hyperglycemics?
- Dr. Eckel: [02:45](#) There are a lot of glucose lowering medications out there, and we have a big list, including a multiplicity of insulin analogs and beyond. But, I think there are a couple of drugs we probably need to withhold in patients who have renal disease and heart failure. The [inaudible 00:03:01] as in stage two and beyond just [inaudible 00:03:06] should not be utilized. They're absolutely contra-indicated in three and four, but probably shouldn't be used even at stage two. Now, also another class of drugs that we need to be concerned about is some of the DPP four inhibitors have been shown to be associated with an increased risk for hospitalization, for heart failure. And then finally, I think Metformin has some limitations on its use. Typically we thought that before EGFRs less than 45 should not be consistent with Metformin administration, but now that's kind of dropped down to less than 30.

So, those three classes of drugs, I think, need to be reconsidered and you need to be specific for which DPP four inhibitor. Now, thinking beyond that, I think ultimately there are some new drugs that give a lot of promise in treating people with diabetes and chronic kidney disease with actually some evolving data that people even without diabetes with chronic kidney disease could benefit. And, those are two classes of drugs that are relatively new in the marketplace. The glucagon like protein receptor agonist, and also the SGLT two inhibitors. These two classes of drugs have shown promise both in modifying the natural history of kidney disease in patients with diabetes and some without now, and also heart failure, mostly in patients with diabetes, but also now some recent evidence from two different drugs indicating the benefit in people without diabetes.

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So, these are the two classes of drugs that I think really predominate our prescribing patterns and modifying beyond diabetes, just glucose control, but the natural history of congestive heart failure and chronic renal disease. Another issue that really needs to be considered as with age renal function diminishes in all of us with or without diabetes and with, or without congestive heart failure. So with age, I think there's another important consideration that that's not simply modified, but that needs to be assessed clearly in terms of the impact of how diabetes and heart disease reflects on kidney function.

And, I shouldn't need to mention to this crowd that people with congestive heart failure also can get chronic kidney disease with an incredible interaction between the kidney and the heart back and forth to modifying the natural history of both diseases. And, I think I should warn the audience when the creatinine ultimately goes up a little bit and people are being treated with RAS blockers, either an ACE inhibitor or an angiotensin receptor blocker. Don't stop the drug.

Now, if somebody's dehydrated and their creatinine is pre-renal and it's going up because they need to be hydrated, stop the drug until their creatinine corrects. But, even up to a 25 or 30% increase in creatinine and patients who were on RAS inhibitors should not be considered harmful. The medications should be continued to continue to protect the kidney and hopefully also lower the blood pressure.

Liz Olson: [05:59](#) For such a complex condition for the patient, it's obviously going to be a team effort. There's going to be a lot of players in the care of the patient but, I'm curious specifically, what role do endocrinologists and Nephrologists play in the care of these patients?

Dr. Eckel: [06:17](#) Well, Liz, as your question suggests, there's a tremendous amount of teamwork that relates to the care of patients with chronic kidney disease, diabetes, and a history of congestive heart failure. In terms of the endocrine nephrologist interaction, I think that needs to be determined on an individualistic basis, but the American Diabetes associated standards of metabolic care would indicate anyone with an EGFR less than 30, who is seen in the endocrine clinic, needs a referral to a nephrologist for further evaluation.

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And, I think we're all internists first. Endocrinologist, nephrologist, cardiologists. And, we need to think of other causes of renal disease, such as polycystic kidney disease, such as glomerulonephritis, such as obstructive uropathy. So, there are other causes of nephropathy in patients with diabetes that need to be assessed. And as internists, we should be able to start there, but when things get more confusing, when EGFR is quite low, like less than 30, ultimately the patient has heavy albuminuria that continues to progress. I think those patients should be referred from the endocrine practice to the nephrologist for further evaluation and advice on treatment going forward.

Now I should point out too, that Mike Blaha, Preventive Cardiologist at Johns Hopkins and I have been promoting the development of a new medical subspecialty called cardio metabolic medicine. And this class of physician, she or he's going to be able to assess this interaction between novelty diabetes and cardiovascular disease, but chronic kidney disease and now non-alcoholic fatty liver disease. So, this is the type of physician I think we need to train for the future actually for the present. But, the development of training programs I think is going to take time to happen. And ultimately I'm hopeful that within 10 or 15 years, the American Board of Internal Medicine is going to recognize such subspecialty training is very necessary and important to maintain the best health of our patients.

Liz Olson: [08:16](#) As patients become more aware of their condition and more literate in their condition and the various tests that will be asked of them and conditions that they need to monitor. I'd like for you to talk a little bit about why EGFR and albuminuria levels would be important to track for these patients.

Dr. Eckel: [08:38](#) Well, I think EGFR and your analyses to assess urinary protein spillage are commonly employed at very cheap, analytic tests to look at the metrics of kidney disease as they relate to diabetes, or even in the absence of diabetes. The urinalysis or urine albumin creatinine ratio is utilized to detect microalbuminuria. Now, microalbuminuria is not normal, but it's also something that is probably not kidney disease, but it's a marker of kidney disease to follow in some patients, not at all. So, what is it, if it's not kidney disease, it's really a leaky basement membrane. And,

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people with diabetes often with more long-standing diabetes have leaky membranes all over their body,

including the eye and the legs and other spaces of the body, other than the kidney. But, in the kidney, we can pick that up by measuring micro albumin in the urine. So, in other words, it's not kidney disease, but it's a marker of progressive kidney disease.

And, patients with microalbuminuria are more likely ultimately to develop macro albuminuria, which is defined as over 300 milligrams of urinary protein per day, than patients without microalbuminuria. And, I think another important thing about the urinalysis in patients with diabetes is now I'm going to throw this number out kind of vaguely, but around 10% of people with diabetes and diabetic kidney disease have no proteinuria. So some of these, and by the way, these are non hypertensive patients. We need to understand, that patients with diabetes are much more likely to be hypertensive and their risk of kidney disease, independent of proteinuria may exist.

So, that's a second group of people we need to understand the natural history of kidney disease. And even though they have diabetes, but they may not have proteinuria. But, a third-class is people have no proteinuria, have chronic kidney disease assessed by the EGFR, but have some red cells in their urine. Now, we used to think that red cells in the urine can't be diabetes, but ultimately are other causes such as glomerulonephritis, which needs to be mentioned in the differential diagnosis of chronic kidney disease. But, ultimately now it's been shown that patients with diabetes can have micro hematuria. In other words, they can have modest degrees of red cells in them urine without any other cause such as glomerulonephritis or other forms of kidney disease. Now, the EGFR is a assessment of renal function, which is related to microalbuminuria and macro albuminuria but may not be. So, we can again have patients progress with diminished renal function. Their EGFRs are falling, but do not have much proteinuria.

But, alternately we can see people with proteinuria who do not progress. So in other words, it's just another assessment

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now of renal function rather than simply the ability of the kidney to retain protein and not spill protein over the interval of observation. So, it's currently recommended patients with type one diabetes for more than five years, should have a urine checked for an albumin creatinine

ratio at least once a year. And, patients with type two diabetes, because they're typically older, should have a urine albumin correcting ratio checked every six months. So, these are kind of guideline related recommendations by the ASN. I think the Chronic Kidney Foundation and also the American Diabetes Association.

Liz Olson: [12:08](#) I'd like to think a little bit now about what kind of risk factor modifications should providers suggest to their patients for a condition that is inevitably going to progress?

Dr. Eckel: [12:22](#) Well, we're hopeful that it's not going to progress, but I think the kinds of risk factors that we ought to be thinking about is clearly hypertension is one. We know that more aggressive management of hypertension can protect the kidney and that's true of patients, with or without diabetes. So, we want to have optimal blood pressure control in these patients.

The other thing I think we need to think about is a choice of agents. And, I failed to mention earlier that the renin-angiotensin system is an important one to modify and patients with microalbuminuria should be treated with an ACE inhibitor or an ARB. But, other risk factors include excess body weight. Clearly weight relates to renal disease, independent of diabetes to a more modest extent than diabetes, but clearly weight reduction could be beneficial on the natural history of chronic kidney disease.

Smoking is also something else that we clearly need to eliminate, in the world actually, but particularly in people with diabetes and chronic kidney disease. So, this is another thing for the practicing physician to take into consideration when they're thinking about this relationship of chronic kidney disease in patients with diabetes.

Liz Olson: [13:33](#) From a health equity perspective, do we see more of a prevalence of these combined co-morbidities in any particular populations or age groups?

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- Dr. Eckel: [13:42](#) The data are increasingly replete and the idea that African Americans, Asian Americans, and also native Americans have a higher likelihood of developing chronic kidney disease than the Caucasian population. So, these are groups that we need to pay careful attention to in both screening and therapeutic approaches to modifying the natural history of their kidney disease.
- I should point out particularly in the African Americans, that that relationship may be partially explained by a higher prevalence of hypertension. We certainly see more hypertension in the black population than we do in the Caucasians and even the other two diverse populations. But nevertheless, all three populations appear to be at increased risk for kidney disease in the presence of diabetes.
- Liz Olson: [14:30](#) Final thought, how can providers improve health literacy around these concerns?
- Dr. Eckel: [14:35](#) Well, I think health literacy starts at the public level in general, where patients with diabetes need to have access to information that relates to the relationship between diabetes and kidney disease. And, hopefully the healthcare professional to whom they're seeing really up-to-date in terms of where the guidelines are at in terms of the assessment and management of the relationship between chronic kidney disease and diabetes.
- So, we need to have an awareness out there. I think increasingly guidelines by multiple professional organizations relate to this relationship and should be acknowledged and implemented in clinical practices of medicine and patients are being seen for type two diabetes. And Know Diabetes by Heart, it's been an incredibly important joint venture between the American Heart Association and the American Diabetes Association. I've been privileged to be part of this and thank all of the sponsors for supporting this very, very important program.
- Liz Olson: [15:31](#) Dr. Eckel, thank you so much for taking the time to speak with us today on such an important topic.



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- Dr. Eckel: [15:37](#) You're very welcome, Liz. It's been my pleasure.
- Liz Olson: [15:39](#) Today's podcast is made possible through the support of Know Diabetes by Heart. Founding sponsors, Boehringer Ingelheim Lilly and Novo Nordisk. And, national sponsors, Santa Fe, AstraZeneca and Bayer.
- I'm Liz Olson with the American Heart Association. Thank you for listening.