EPISODE 21: HEART FAILURE

Rita Kalyani, MD : Welcome to ***Diabetes Deconstructed***, a podcast for people interested in learning more about diabetes. I'm your host Dr. Rita Kalyani at Johns Hopkins. We developed this podcast as a companion to our Patient Guide to Diabetes website. If you want a trusted and easy to understand resource for diabetes or to listen to previous podcasts, please visit ***hopkinsdiabetesinfo.org***. On today's podcast, we are thrilled to welcome Dr. Edward Kasper, an E. Cowles Andrus Distinguished Professor in Cardiology and Professor of Medicine at the Johns Hopkins University School of Medicine, where he is also the director of outpatient cardiology and a specialist in heart failure. Welcome, Dr. Casper.

Edward Kasper, MD : Thank you for inviting me. It's a great honor.

RK: Thanks so much for being here. We're really excited to learn more about heart failure and diabetes. And I wonder if you could tell us, what is heart failure?

EK: So, heart failure is hard to define. But if you think about the heart as being just another muscle, it has certain metabolic needs. It needs oxygen, it needs food, and it needs to get rid of waste. And it's the circulatory system run largely by the heart that is in charge of making those things happen. Heart failure occurs when the heart is unable to meet the demands of the body. It has certain specific signs and symptoms and when we see that, this is a clinical diagnosis. We say a person has heart failure.

RK: What are some of the signs and symptoms that an individual might see if they have heart failure?

EK: Well, the symptoms are shortness of breath; that's the most prominent. Now we all get short of breath. If we go out and we run, we'll eventually get short of breath. But this is shortness of breath that occurs at a progressively lower and lower amount of exertion, until it can occur just moving about the room or even just getting out of bed. This is usually associated with swelling of the ankles, what we call peripheral edema. There may also be lightheadedness, a sense that your heart is racing or skipping beats, and you might even faint. All of these are some of the symptoms of heart failure. Some of the signs are swollen ankles. When you come and see a cardiologist or a doctor with your heart failure, they'll often spend an inordinate amount of time looking at the right side of your neck. You might wonder what they're doing with that. But they can get an estimate of what the abnormal pressures are within the heart by looking at the jugular vein on the right side of your neck. There might be some findings in the lungs. You can lose weight with heart failure. You can gain weight with heart failure. Appetite might be decreased. So, there's a whole constellation of signs and symptoms that we look for to say somebody has heart failure.

RK: So those are really good to know if you're concerned about having heart failure yourself to be aware of the signs and symptoms. When we say heart failure, does that mean that the heart has truly failed? That it's not working at all? Or does it mean that it's just not working as well as it should?

EK: Heart failure is an unfortunate term. I think we could have chosen better, although I'm not that old that I was involved in naming heart failure. But it's an unfortunate term. When you say the word heart failure to someone, they immediately think that like the car engine fails when it fails to start, or it stops, or it stalls out. But that's not what's happening with heart failure. The problem with heart failure is that the engine just isn't strong enough to move the car at the kind of speed and rate that you want it to go at. If the heart stops, then we call that sudden death, that's a different thing completely.

RK: That's important to make that distinction. So thanks for elaborating that heart failure really is more of a relative term as opposed to kind of the absolute cessation or stopping, if you will, of the heart at all. So heart failure is a type of heart disease. Is that right?

EK: Yes. So, it's one of many types of heart diseases. It is often the final common pathway. Coronary disease and heart attacks can lead to heart failure. Certain inflammatory disorders of the heart can lead to heart failure. Certain rhythm problems of the heart can lead to heart failure. In many ways, it's sort of where the heart ends up after a long period of time of problems. Now, there are acute episodes of heart failure where things happen – *POP!* – just like that. Usually, it's a more progressive disease.

RK: So, bringing it back to people with diabetes, how common is heart failure in people with diabetes? And can it occur at any stage of diabetes or who's at risk?

EK: It is very common in diabetics, and the flip side to that is that diabetes is very common in heart failure. It appears as if the two have an interaction between each other. It's a fascinating story. Now, some of this I think we all kind of understand, it's pretty easy to grasp the concept that since diabetes accelerates cholesterol plaques, it makes myocardial infarction more common; heart attacks more common. Heart attacks lead to weakening of the heart muscle. Heart muscle weakness leads to heart failure. I think we understand that. But there are also those patients who don't really have cholesterol blockages, who don't have heart attacks, who still ended up with heart failure, and who still have diabetes. The interesting flipside to that if you take someone with severe heart failure who has diabetes and the diabetes is difficult to control, one of the ways to make it easier to control it is to actually put in a partial artificial heart that takes over some of the work of the heart. With that, we often see an improvement in diabetic control. It's very clearly two systemic disorders: disorders that affect the whole body that interact and then you throw into that kidney dysfunction, which can be caused by diabetes and by heart failure. And you now have these three poles of vicious circles basically where each is affecting the other, which affects the other and that affects itself again and you just keep spinning in these bad circles.

RK: So it sounds like one can happen before the other or vice versa. In terms of diabetes and heart failure, it's really hard to know which one came first. But managing one helps the other condition. So managing diabetes can help the heart failure. Managing the heart failure can help with the diabetes. That's so interesting. I feel like I've been seeing or hearing more about heart failure in people with diabetes over the past few years. I don't know if that is because it's becoming increasingly recognized as a complication of diabetes or if we're truly seeing rising rates of heart failure. Do you have any insights into that?

EK: Well, we are seeing rising rates. Heart failure is often a disease of the aging. And so, as the population ages, we'll see more of those disorders that are associated with older cohorts. And heart failure is simply one of them. And diabetes is another one. Frankly, the older you get, the more likely it is that you'll have Type 2 diabetes. You see these sort of co- travellers perhaps on the same train of age.

RK: Who with diabetes is at risk for developing heart failure?

EK: I'd say almost anybody with diabetes is at risk for heart failure. There are certainly additive factors that go into this. If you've got diabetes and diabetes alone, your risk is probably two to four-fold higher than someone who doesn't have diabetes. If you add on top of diabetes, hypertension, and if you add on top of hypertension, high cholesterol, and these are things that often come with diabetes, then all of a sudden your risk might be four or five-fold that of someone who doesn't have diabetes, in terms of the development of heart failure. It's common and it is something that many patients with diabetes face.

RK: So how can someone with diabetes prevent getting heart failure?

EK: First and foremost, get good control of your diabetes. Follow the American Heart Association recommended guidelines for exercise and diet: get 30 minutes of walking in a day, seven days a week, follow a prudent low cholesterol, low fat, low sodium diet, take your medications faithfully. These are all the self-care sort of things that you can do that will help prevent the onset of heart failure.

RK: Do you see in your practice that people with diabetes whose blood sugars are not at their optimal targets are more likely to develop heart failure or not? You know, this is a question that comes up, for instance, with coronary heart disease. What is the role of high blood sugars in the development? Is it just that people with diabetes are at higher risk? Or is it that the high blood sugars actually make it more likely for you to develop heart failure?

EK: One of the problems in heart failure is that your volume overloaded and that's what causes the peripheral edema - there's too much water on board. You're kind of waterlogged and we can get into why the pathophysiology of that might be. If you're diabetic and your glucose is poorly controlled, now you're spilling lots of glucose in the urine. Glucose in the urine causes you to urinate more, which helps you to get rid of the extra fluid. You're sort of again in this cycle that may not be good in the long run. So sometimes, controlling blood glucose and glycosuria, the amount of glucose in your urine, may worsen heart failure for a period of time until you sort of catch up with the diuretics in order to get rid of the extra fluid that you're now no longer urinating away because

of all the glucose that's going out in your urine. You do have to be careful about patients, particularly when you start them on anti-diabetic medications, agents to control glucose, to make sure that you're not worsening their heart failure a little bit. That's a sort of risky time, and it requires some oversight.

RK: That's so interesting, because we think about certain medications, for instance, that might exacerbate or worsen heart failure symptoms. But the idea that lowering blood glucose initially also can lead to some changes in symptoms is an important thing for people to know about. Because they might think that by lowering their blood sugar, they're actually making things worse, where it's only a temporary or transient phase. Is that right?

EK: Yes, that's exactly right. You're going to get your blood glucose controlled, and eventually this will equilibrate out and it's important in the long run that glucose be controlled. You can't just live with a glucose of 300. I'm not an endocrinologist but even I know that. So step one, get the glucose under good control. Step two, keep a close eye on the patient for precipitation of heart failure or worsening of heart failure. And step three, take appropriate action. If you see that they're beginning to gain some weight, or their peripheral edema is getting worse or they're getting more short of breath, don't just ignore these cries for help.

RK: So in someone who develops heart failure and has diabetes, what are some of the treatments that you recommend or don't recommend that they be on for the heart failure, and then medications for diabetes that you should avoid that can make the heart failure worse?

EK: This is a terrific time for us because we now have quite effective therapy for heart failure. We're talking mostly here about heart failure with what we call reduced ejection fraction, meaning that the contraction of the heart is not as strong as it should be. There are basically four pillars of therapy. The first is a drug commonly known as Entresto, which is a combination of valsartan and sacubitril. The second is one of several beta blockers that have been shown to be of benefit in patients with heart failure such as metoprolol succinate, bisoprolol, or carvedilol. The third would be a mineralocorticoid receptor antagonists like spironolactone or eplerenone. The fourth and the most exciting, probably for an endocrinologist certainly, are the SGLT-2 inhibitors, which initially showed an improvement in the treatment of patients with diabetes, but now has been shown to not only benefit diabetics, but non-diabetics in terms of prevention of heart failure. You know, isn't this just terrific? The four pillars are what we try to get people on. These four pillars have been shown to improve survival and symptoms. To those four pillars for those people who are volume overloaded, you would add a diuretic pill that makes you urinate out excessive volume in order to improve shortness of breath and peripheral edema. Those are the four pillars that we normally are looking to try to get patients on. Unfortunately, all of them lower blood pressure to some degree or another so we usually start them kind of one at a time and slowly up-titrate them to we can get all the model for that. I think it's important if you get admitted with heart failure to the hospital to get on all four before you go home. It's harder to start these as an outpatient than it is to start them as an inpatient than simply up-titrate them as an outpatient. Numerous trials have shown that if you don't start it as an inpatient, it's less likely to be started as an outpatient.

RK: That's so interesting, and so exciting that there are so many options for treatment. The newer classes of diabetes medications, as you mentioned, are particularly exciting for us in diabetes and also the ability to coordinate care with cardiologists such as yourself because they not only lower blood glucose but really have had such overwhelming benefits for heart failure hospitalizations and heart failure outcomes. How commonly are you using these newer medications in your practice?

EK: Across the cardiology community, there has been a big push to try to get all of us comfortable in using these drugs in every patient with heart failure. I feel pretty comfortable at this point, but I have to admit that I was initially a bit hesitant. I'm feeling okay at this point, I don't see a large drop in glucose. One of the big concerns was [that] you were starting them on a medication that can lower blood glucose: “Am I going to be dealing with a lot of hypoglycemia?” And the answer to this was: “No. I have not seen an episode of hyperglycemia that I had to treat.” And there are certain side effects of a SGLT-2 inhibitors, including some infections in the private parts and the pictures of those are really quite scary. Thankfully, they don't occur very often.

RK: They are side effects definitely to look for. But I agree, I think that in practice, we often don't see them that much. And when we talk about the SGLT-2 inhibitors, we're talking about empagliflozin or Jardiance, canagliflozin or Invokana and dapagliflozin or Farxiga. And these medications, this class is so great for heart failure, and it's so great to hear that they're being used almost uniformly and whenever they can, and as soon as possible in patients with heart failure in your practice. For someone who has diabetes and is wondering, do I have heart failure? How is my heart working? How would they find that out? What would be the diagnostic tests? Or what would be the next steps for them to find out if their heart is working properly or not?

EK: The first step would be to speak with your primary care physician. That's first and foremost, the first line of screening if you will, and they're going to ask you about the signs and symptoms: "Do you have those? Do you have that?" [They will] do a complete physical exam, look at the neck veins, listen to the lungs, listen to the heart. If they find anything that is of concern, there will usually be both echocardiography done and a referral to a cardiologist. Echocardiography is just sonography of the heart itself. We're able to watch the heart in real time: moving, contracting, valves opening and closing. It's easy, it's relatively inexpensive, and it's painless. It can be done very quickly and then the visit with a cardiologist to help interpret the findings on the echocardiogram and put it all into context to come up with a care plan. So that's how I often see these things happening.

RK: And you had talked about a very common form of heart failure being that what's reduced ejection fraction. What does that mean? What is an ejection fraction? And what number do you usually look for as a cardiologist that might be worrisome on the echocardiogram.

EK: So the ejection fraction is an index of something called the stroke volume, which is the amount of blood that the heart pumps out with each heartbeat out of the left ventricle into the aorta, indexed to the amount of blood that's in the heart at the end of filling, which is the end of diastole. So it's stroke volume, over end diastolic volume. You would think that [the] number ought to be 100%. That we were all type A people or we wouldn't be doctors. You know, we never wanted to get anything less than 90% on any test. I mean, good Lord, if you could get a 98 [%], you'd want that better than a 92 [%]. But in this instance, 55% is considered normal. And if you stop back and think about it for a second, it makes sense. The Echo is done at rest, and you need some room to move upwards, when you get up and you start to do something. [When] you start to run your ejection fraction needs to go up, your heart rate and stroke volume goes up in order to provide more blood to exercising muscle. So 55%, we consider normal less than 50% or so we would consider reduced and realize that this is taking only a snapshot in time. Like most biological systems, it's not a standard straightforward line, and the ejection fraction goes up and down in waves. Today, it might be 55%. Tomorrow, it might be 45%. But in general, we're thinking less than 50% reduced ejection fraction, we had heart failure. I've divided this up into what we call mid-range, ejection fraction, and then low ejection fraction, which is really lower than about 40% or so.

RK: So on average, it sounds like it's the amount or the percent of blood volume that is really ejected or pumped out of the heart in relation to the amount of blood that is in the chamber of the heart, would you say?

EK: The left ventricle chamber at the end of its filling cycle, which is diastole. So remember, the heart is a simple pump that has two jobs. The first is to squeeze blood out and that happens in systole. That's the height number of the blood pressure 120 over 80 the 120 parts when the heart is squeezing. Then between each heartbeat, it has to relax and fill up. So if it does not relax well, it won't fill up well, and then it won't have enough volume to squeeze out appropriately. So you can get into heart failure by having an ejection fraction that's too low or a heart that's too stiff and doesn't fill appropriately between each systole. Each will lead to a decrease in the output of the heart, which will then be inadequate to supply the needs of the body. Then you will develop the signs and symptoms of heart failure.

RK: Heart failure is such a serious complication that can occur really in diabetes, you know, for all the reasons that you mentioned and the important role that the heart has in the body. In those who have progression of their heart failure, first of all, how commonly does that happen to most people have, let's say early stages and they stay stable? Or does it progress over time?

EK: If you'd looked at the older literature before these four pillars of therapy, you would say that about 50% within five years would progress to severe heart failure and maybe even more than that. These days, I think we are doing a lot better. The hope is that by getting people on these four pillars and by treating their diabetes and keeping a close eye on them, that we're going to get people to plateau and their ejection fraction to not just stabilize/not continue to fall, but actually to begin to rise again. And in some patients, we can get it to normalize. That's terrific when it happens [but] doesn't always happen. It's still a deadly disease. But on the other hand, it's much more treatable today than it ever was before. Much like diabetes early on, people with diabetes died. Without insulin, you are not going to live for very long. But with the development of insulin to that whole host of other drugs to manage this, the life span of diabetics is increasing and so has full lifespan of patients with heart failure.

RK: That's so amazing that some patients now can actually have improvement in their ejection fraction. It almost sounds like a reversal. Is that right? In some patients?

EK: Reverse remodeling.

RK: Reverse remodeling, that's great! Well, with all these new medications and the four pillars you mentioned it really sounds like there's so many more options for preserving lifespan and quality of life for people with heart failure. In those who still progress and have severe heart failure, at what point do you consider a heart transplant and what is that process like?

EK: There's really two options in our armamentarium for those who need advanced therapies. The first is left ventricular assist device (LVAD) which is a partial artificial heart, it's a pump that's implanted in the body. It has a drive line that sticks out of the body that's connected to the wall [for] electricity and works very well. Then the second is to replace the with a heart that works better. If you think of the heart as being a horse pulling a cart up a hill and your horses not doing well, you've got some options. The first is to unload the car - that's what we do with the medications basically. The second is to replace the horse with a new horse - that's heart transplantation. The third is to replace the horse with a tractor - which is the LVAD. People who are in this situation are the sickest of the sick. They usually are confined to the intensive care unit and usually the coronary care unit because outside of the coronary care unit, they just can't live. Their blood pressure is too low, they're too symptomatic, or they might need to be on intravenous medications. So we begin to think of these sorts of advanced therapies in people who are being repeatedly admitted to the hospital - people who you can never really get asymptomatic enough so that they feel comfortable in their daily life. Remember, I told you how these medications all tend to lower blood pressure. When you find yourself sort of backing off these medications repeatedly and they're tolerating less and less of this, that usually means that the heart muscle is getting weaker and weaker and weaker, just unable to generate a good blood pressure. And all of these are signs that make you think, “Okay, we have to start thinking that medicines aren't working here. And we have to think about something more advanced.”

RK: There are so many advances as well in heart transplant recently, not sure if you want to go into those details. But I know that in the past, it was always human to human transplant. Recently there has been some excitement about doing transplants from other animals. What do you think about that? Do you think that will have a future in heart transplant?

EK: Well, I certainly hope it does. Then the holy grail of transplantation we call this; animals to humans [transplantation] is called xenotransplantation. And xenotransplantation has always been sort of out there, in the future. Our colleagues over at the University of Maryland have done a truly wonderful job. They've shown that this is possible. And they've shown that they're able to get you know, 30-60 days survival where xenotransplants usually died within hours. So some of this was animal work; pigs into monkeys, dogs into pigs, but there had been other xenotransplants attempted in the world that failed within a matter of hours. To have it work and show that it was tremendous step up and I hope that this will be rapidly followed up by the further steps that will be necessary in order to make this a viable option for more patients. The problem is, of course, that we have a limited supply of donor hearts. You can't just use any old heart. It has to come from someone who usually died of a brain injury and whose heart is still functioning well. And that's not every person who dies.

RK: It seems like there’s been some really extraordinary milestones recently with xenotransplantation, but still some significant barriers to transplant as well with the limited donor supply.

EK: Yep, we do pretty well. I got involved in this fairly early on. In 1984, I was an intern in the hospital and I can remember being on the cardiology floor for the month and somebody was going for a heart transplant that night. The whole hospital had a certain buzz to it. People knew about this and there was real excitement. That's because it was fairly new and pretty rare, even still in 1984. These days, you know, it's kind of just another cardiac operation. It’s gotten pretty routine at this point and we can do them very well.

RK: That's fantastic. To think about how far we've come even in just 30-40 years is amazing and how far we'll go in the next 30-40 years in this field is really great. In terms of just some parting words, perhaps, for our patients or listeners, what would you say to them if they are worried or curious about whether they might be at risk or might have heart failure themselves? What would you recommend to them?

EK: My first recommendation would be [to] pay attention to your symptoms. Do you get short of breath when walking up a flight of stairs? If you do, do you find yourself parking really close to the mall or to stores because you have to sit down between your car and the entrance to the store? Do you find yourself gaining weight rapidly and your ankles are swollen? Do you find yourself short of breath at night that causes you to sit up and wakes you up at night? And if so, then first step [is to] see your primary care physician and probably get an echocardiogram [to] get a good look at the heart and from there on it's probably off to visit with a cardiologist.

RK: Well, thank you so much, Dr. Casper, for this really informative talk and insight into heart failure in people with diabetes. You know, I think it's often not as well recognized and it's increasingly now being acknowledged as something that people need to be paying attention to. And it's really so exciting to hear about the recent developments and more to come in the future as well. So thank you so much for taking the time today to speak with us.

EK: Thank you for asking me. It's been my pleasure and I hope our patients can benefit together.

RK: I'm Dr. Rita Kalyani, and you've been listening to ***Diabetes Deconstructed***, a companion podcast to the Johns Hopkins Patient Guide to Diabetes website which has all kinds of useful information about diabetes, including videos and animations a lifestyle and nutrition blog and a comprehensive diabetes glossary. For more information, visit ***hopkinsdiabetesinfo.org***.

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