Transcript Details

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Unmet Clinical Needs for Patients with T2D and Established CVD

Announcer

Welcome to ReachMD. The following program "The Unmet Clinical Needs for Patients with Type 2 Diabetes and Established Cardiovascuar Disease" is sponsored by Novo Nordisk.

Dr. Caudle

I'm Dr. Jennifer Caudle, and joining me to talk about unmet clinical needs for patients with diabetes and established cardiovascular disease is Dr. Mikhail Kosiborod. Dr. Kosiborod, welcome to the program.

Dr. Kosiborod

Good to be here.

Dr. Caudle

Well, we're excited that you're here. So, to start, let's level set the connection between diabetes and heart disease for our audience. What should we know about the burden of disease and morbidity and mortality rates for patients with coexisting diabetes and heart disease?

Dr. Kosiborod

Well, I think the first thing to point out is that diabetes is a major risk factor for developing cardiovascular complications, and it really doesn't matter which cardiovascular complication you look

at, whether it's myocardial infarction, stroke, risk of death, risk of developing heart failure. All of those cardiovascular complications are greater in people with diabetes than people without diabetes. And despite, unfortunately, all the advances in care that we've had over the past few decades, there is still that extra hazard of cardiovascular complications associated with diabetes.

Dr. Caudle
The outcomes, absolutely. That makes a lot of sense. Moving forward, though, given the high prevalence of heart disease in the general population already, are patients with diabetes actually at increased risk of developing cardiovascular disease—which you did kind of talk about this a little bit—or experiencing complications stemming from that? So, if you can maybe talk just a little bit more about that.

Dr. Kosiborod
Yes, there is no question. As I mentioned, if you have diabetes, the risk of every cardiovascular complication, whether it's atherosclerotic cardiovascular disease events like myocardial infarction, stroke, and dying from cardiovascular causes, is greater. Also, some events that may or may not be related to atherosclerotic disease progression, such as heart failure, is also greater. And what actual epidemiologic data shows is that if you look at the rates of cardiovascular complications in people with diabetes, overall over the past few decades, they have come down, with the exception of heart failure, perhaps, but certainly when it comes to myocardial infarction and atherosclerotic disease-type events, the risk of having those events in people with diabetes has come down over time. The risk of having those cardiovascular diseases in people without diabetes also has come down.

Dr. Caudle
So, you have talked a lot about the increased risk of cardiovascular events in patients with diabetes, so I am assuming that this increased risk must also negatively impact life expectancy by extension. What's the evidence to support this, though?

Dr. Kosiborod
Yes, and again, we have plenty of epidemiologic data showing that if you are a patient with diabetes, particularly if you're diagnosed at a relatively young age, diabetes will have an impact on your life expectancy, and there will, unfortunately, be on average life years lost due to diabetes, and most of those life years lost are actually because of cardiovascular complications. Again, front and center of this entire conversation is the fact that cardiovascular disease is the number one cause of death and disability in people with type 2 diabetes, and the number of years, the amount of that impact on life years lost actually is greater in younger patients, so patients that have diabetes diagnosed at a younger age compared to those diagnosed at an older age. So, it's really… Unfortunately, diabetes is

really impactful in a negative way, not just in terms of increasing cardiovascular risk and as complications, but actually reducing productivity and ultimately life years that are lost due to that. Of course, diabetes is not a rare disease, right? We probably can all think about somebody we know, either a family member or a friend or an acquaintance that has diabetes, and that, actually, really highlights why we are here talking about this, right?—

Dr. Caudle
Right, understood. You've really given us a clear sense of intrinsic links between diabetes and cardiovascular disease, but if we turn to clinical management, what are some of the key factors that are driving a paradigm shift to treat both more reflexively?

Dr. Kosiborod
I think the paradigm shift really is occurring in 2 areas. One is the way we think about the disease. What is type 2 diabetes? Traditionally, we have thought of type 2 diabetes as a sugar problem, right? Patients have elevated blood glucose and hemoglobin A1c, and that's how we diagnose the disease, right? I mean, that's what we actually measure to give somebody a diagnosis. So, it's perhaps natural that over the years we've thought that if we just control the blood glucose, if we just lower hemoglobin A1c to near-normal levels, we can ameliorate or even eliminate all of the complications that happen with diabetes, including cardiovascular complications, but it was, perhaps, somewhat of a naïve thought process, because if you actually think about what's driving the development of type 2 diabetes, a lot of patients with type 2 diabetes for many years, sometimes decades, have this issue with insulin resistance even before diabetes develops, and that's driven by obesity and visceral adiposity. So, just controlling glucose, by itself, you are really addressing a relatively small piece of the puzzle, not the entire picture.

Dr. Caudle
So, you talked about many of the cardiovascular outcomes trials. How do these even come about?

Dr. Kosiborod
Well, it's a great question, actually. Historically, a majority of these trials actually happened because of a change in the regulatory environment. So, at the end of 2008, FDA actually issued guidance to industry where the guidance actually said, "Look, if you're developing new agents for treatment of type 2 diabetes, you can't simply just show that they lower blood glucose and hemoglobin A1C. You have to demonstrate that they are also safe from a cardiovascular standpoint." The reason for that, actually, is there were lots of different reasons that that happened. One that many know about and frequently gets brought up is the controversy around rosiglitazone, TZD, one of the agents to treat type 2 diabetes. There was some controversy at the time about whether it's safe from a cardiovascular standpoint or

not, but it was actually much broader than that. the FDA really wanted to make sure that these medications don't just lower hemoglobin A1C, but at least you would have to demonstrate that at least they don't affect cardiovascular outcomes in a negative way, because these medications are going to be used for a long time, sometimes lifelong; they are going to be used in high-risk patients that either are at high risk for cardiovascular complications or already have cardiovascular disease. So, essentially their point was, "Look, you need to demonstrate to us, you need to convince us, in large, appropriately controlled, methodologically rigorous cardiovascular outcomes trials—you need to demonstrate to us that these agents are at least safe."

Dr. Caudle
Right, that's really interesting, and that makes a lot of sense. You've been talking about the data, the outcomes of these trials, etc., and what effect has all of this really had on practice guidelines?

Dr. Kosiborod
Right. Well, I mean, the first thing that I think is important to mention is that this guidance from the FDA really had a remarkable impact on just the amount of data and clinical research that has been generated in this field. For many years you had an occasional study here and there that was a large cardiovascular trial, but this was really an explosion where tens if not hundreds of thousands of patients subsequently have been enrolled in clinical trials with cardiovascular outcomes as a primary endpoint over the next decade, right? So, we're now 10 years after the guidance, and it's remarkable to see how much research and knowledge and impactful data has been generated, which again is the catalyst that fueled this entire paradigm shift that we are here to talk about. And, of course, the other impact of these very important data has been on the practice guidelines, not surprisingly, and the practice guidelines are now taking a similar approach to this paradigm shift that we've talked about. It's not just about hemoglobin A1c.

Dr. Caudle
Well, with these important updates in mind, I really want to thank Dr. Kosiborod for joining me and discussing the unmet needs for patients with type 2 diabetes and established cardiovascular disease. Dr. Kosiborod, thank you so much for being here.

Dr. Kosiborod
It's my pleasure.

Announcer
The preceding program was sponsored by Novo Nordisk. If you have missed any part of this discussion and to find others in this series, visit ReachMD.com/Type2Diabetes. This is ReachMD. Be Part of the Knowledge.

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