



VOLUME 3 - ISSUE 2

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Cardiovascular Outcomes in Type 2 Diabetes Management

After participating in this activity, the participant will demonstrate the ability to:

- Describe antidiabetic regimens that optimize cardiovascular benefits and reduce overall CV risk for patients with underlying CAD and PVD.
- Describe antidiabetic regimens that optimize cardiovascular benefits and reduce overall CV risk for patients with congestive heart failure.
- Describe antidiabetic regimens that optimize cardiovascular benefits and reduce overall CV risk for patients after an acute coronary syndrome or MI.

Guest Faculty Disclosure

Dr. Mathioudakis has disclosed that he has received consulting fees from GlucoMe and honoraria as a faculty lecturer for PriMed CME.

Unlabeled/Unapproved Uses

He has indicated that there will be no references to unlabeled or unapproved uses of drugs or products in today's discussion.

MEET THE AUTHOR



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Release Date:
December 28, 2017

Expiration Date:
December 27, 2019

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Podcast Transcript

DR. MATHIOUDAKIS: My pleasure, Bob. It's great to be back with you again.

MR. BUSKER: The current trend in diabetes management is moving from agents that show cardiovascular safety to those that have evidenced actual cardiovascular benefits. In your newsletter issue, you reviewed the key studies of the most commonly used noninsulin glucose-lowering agents, and described the importance of that data. Today I'd like to focus on how this new information can impact actual clinical practice. So please start with a patient scenario.

DR. MATHIOUDAKIS: This was a 59-year-old woman from Ghana I was seeing in initial consultation for type 2 diabetes. Her type 2 diabetes was diagnosed in 2014, so she has a relatively short duration of disease. She was initially treated in her home country with diet, but after a few months, because she was having persistent hyperglycemia, they put her on sulfonylurea gliclazide, which is not available in the United States. Three months after coming to the United States, before her initial visit here, her primary care physician switched the gliclazide to glyburide, which is available in the States, at 5 mg daily.

This patient had a history of some neuropathy, which developed shortly after chemotherapy treatment in 2017 for breast cancer. Two months after she stopped her chemotherapy in July of 2017, she started noticing some pain on the plantar aspects of her feet. She was evaluated by a podiatrist, who referred her urgently to a vascular surgeon; he was concerned about the way her toe looked. The vascular surgeon found gangrene in the fifth toe.

Her medical history was also notable also for stage 3 chronic kidney disease. She had a creatinine of 1.6 and a GFR of 38.

At the time of her initial visit with me, she had an essentially normal exam. The notable findings were a markedly elevated blood pressure of 196/82. She was a little overweight. She had a BMI of 29.3. And of course, she had the necrotic fifth toe, which was consistent with gangrene. She had absent pedal pulses on her left foot, the site of the gangrenous toe.

She underwent an angiogram of her left lower extremity, which confirmed that she had peripheral vascular disease. She was treated by the vascular surgeon with left superficial femoral artery drug-eluting stent and a left anterior tibial angioplasty, after which she was started on optimal medical therapy for PVD with aspirin, clopidogrel, and a statin.

Unfortunately, a couple of days later her gangrene progressed to wet gangrene, and she had to undergo a fifth toe amputation.

MR. BUSKER: A patient with PVD — peripheral vascular disease — as well as neuropathy and a gangrenous toe requiring amputation. What role do you think her diabetes played in the development of her initial foot ulcer

DR. MATHIOUDAKIS: We didn't have much of a history about her glycemic control at the time of her diagnosis three years earlier, but I suspect she had had longstanding hyperglycemia which clearly contributed to both microvascular disease in the form of her neuropathy and macrovascular disease in the form of her peripheral vascular disease. We know that the majority of diabetic foot ulcers are actually neuropathic ulcers, but a subset of these are due to the combination of ischemia from vascular disease and neuropathy, which was her case. It's interesting that she also received chemotherapy, which is known to contribute to neuropathy. So clearly the glucose played a big part in this, and potentially this could've been prevented had she been treated earlier.

MR. BUSKER: Let's talk about her treatment before she came to you. She was taking a sulfonylurea at the time of her initial diagnosis. What can you tell us about her glycemic control on this sulfonylurea, and your thoughts about this choice of medication as a first-line agent?

DR. MATHIOUDAKIS: She brought a log of her blood glucose readings on the glyburide 5 mg daily, and she had clearly uncontrolled blood glucose with average fasting readings around 197 and a wide range in the blood glucose from 150 to about 230. Her A1C in clinic was 8.1%, so clearly her diabetes was suboptimally controlled.

I was not a big fan of the glyburide in her case for several reasons. First of all, she was a woman with underlying chronic kidney disease. She had an estimated GFR of about 35 to 45, and the glyburide, and the agent, the sulfonylurea that she was put on, is renally cleared. So, if we were going to treat her with a sulfonylurea, that wouldn't be the right one to choose, and we might consider glipizide or glimepiride as the preferred agents because those two are cleared more by the liver,

and there's much less of a risk of hypoglycemia.

MR. BUSKER: Why do you think this patient was put on a sulfonylurea at the time of her diagnosis instead of being started on metformin?

DR. MATHIOUDAKIS: I suspect her primary care doc was concerned about her creatinine level, which had ranged from 1.4 to 1.6. Historically we've relied on the creatinine level for contraindications to this medication. But as we reviewed in the newsletter that accompanies this podcast, there's been a shift in the way we prescribe metformin in patients with renal insufficiency in recent years. We now focus more on the GFR and less on the serum creatinine as an absolute level.

In her case, her GFRs ranged from 35 to 45, so it's appropriate to continue metformin at half maximal doses with close monitoring of her renal function. Once the level goes below 30, though, metformin is contraindicated.

It's also worth noting, as we reviewed in the newsletter, that metformin is actually associated with reduced all-cause mortality in patients with chronic kidney disease. Patients who took metformin despite that historical contraindication had substantially better outcomes. So if we can use metformin as an insulin-sensitizing agent, I try to continue it until the very last minute.

MR. BUSKER: So when she came under your care, what did you decide to do about her antihyperglycemic regimen?

DR. MATHIOUDAKIS: Initially I switched her to metformin 500 mg once a day just for tolerability of GI side effects. We increased her to 500 mg twice daily after a week, and she was having significant hyperglycemia in part because of the diabetic foot ulcer and the related stress. It was clear to me that she would need something stronger than metformin monotherapy. In that context, sulfonylurea's a pretty strong agent. So I decided to replace the glyburide with a low dose of glipizide XL 2.5 mg daily and increased that to 5 mg because she was having sustained hyperglycemia.

MR. BUSKER: Instead of the sulfonylurea, why not choose one of the newer drugs — an SGLT-2 or a DPP-4?

DR. MATHIOUDAKIS: SGLT2 inhibitors are really an attractive option in patients like this woman who has peripheral vascular disease and potentially a higher overall risk of cardiovascular disease. The challenge in this patient is that one of the SGLT-2 inhibitors, canagliflozin, has been associated with increased risk of amputations. So I definitely want to avoid canagliflozin, and empagliflozin, the other drug in class, which has been shown to have favorable cardiovascular profile and has not been directly linked to increased amputation rate but — guilt by association — I would still be reluctant to use that in a patient with peripheral disease who has an active ulcer, until we have more studies about the safety of this class in terms of amputation. The FDA cautions against canagliflozin specifically in patients with active or high risk for ulceration.

The other thing that's important to note is that she had a GFR below 45, so empagliflozin, the SGL-2 inhibitor, is contraindicated in renal insufficiency, despite recent studies that have shown beneficial effects in preserving renal function in patients with GFRs in the 30 to 45 range. But for now, the product label of empagliflozin does preclude its use in that population.

DPP-4 inhibitors are a reasonable option. In fact, this woman started having some substantial hypoglycemia on even the low dose of glipizide, so I switched her to a DPP-4 inhibitor, linagliptin, 5 mg daily. I continued the metformin and — one thing to be aware of and was discussed in this newsletter — the DPP4 inhibitor, saxagliptin, has been associated with increased hospitalizations for patients with heart failure. But she had no underlying coronary disease and had normal cardiac function, so I wasn't concerned about for heart failure and thought a DPP4 inhibitor was a reasonable option.

MR. BUSKER: Thank you for that case and discussion. We'll return with Dr. Nestoras Mathioudakis from Johns Hopkins in just a moment.

MR. BOB BUSKER:

This is Bob Busker, managing editor of eDiabetes Review.

eDiabetes Review is a combination newsletter and podcast program delivered via email to subscribers. Newsletters are published every other month. Each issue reviews the current literature in areas of importance to clinicians treating patients with type 2 diabetes.

In the month following each newsletter, a case-based podcast discussion, like the one you're listening to now, is available to help translate that new clinical information into practice. These podcasts are also available as downloadable transcripts.

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Thank you.

MR. BUSKER: Welcome back to this eDiabetes Review podcast. Our guest is Dr. Nestoras Mathioudakis from the Johns Hopkins University School of Medicine. And we've been exploring how the focus on cardiovascular outcomes can impact current clinical practice when managing patients with type 2 diabetes. So, let's continue with another patient scenario.

DR. MATHIOUDAKIS: This was a 59-year-old man whose type 2 diabetes had been diagnosed 10 years earlier at the age of 49. He presented with classic hyperglycemic symptoms and was found to have a random blood glucose of 225. He was initially treated with metformin and shortly after starting the metformin, because he had been struggling with obesity, his primary care doctor started him on exenatide, a GLP-1 agonist, which he tolerated and did well with. But he wanted something a little more convenient than a twice daily injection, so he was switched to liraglutide, the other GLP-1 class, and did very well on that medication.

At the time of his initial visit he was taking metformin 1,000 mg twice a day, and maximum doses of liraglutide, 1.8 mg daily, and his A1C was 7.8%, a little bit above our target of 7%. His diabetic complications included coronary disease with mild systolic heart failure, mild peripheral neuropathy, and nonproliferative diabetic retinopathy.

On his exam he was morbidly obese, he had a BMI of 44 kg/m², and his blood pressure was above our target; it was 150/75. The remainder of his heart and lung exam was unremarkable. On his foot exam he had a mild vibratory sensory loss but normal movement, so just some very early neuropathy manifestations. He had 1+ edema but otherwise no overt signs of heart failure.

MR. BUSKER: No overt signs of heart failure, but obviously some underlying coronary artery disease. Talk to us about your approach to managing his CVD risk factors.

DR. MATHIOUDAKIS: His blood pressure was clearly not optimized. The goal should be less than 140/90, and even more recently there's been some new evidence to suggest less than 130/80 for patients like him who are at high risk for a CVD event. He was taking lisinopril 10 mg daily; I increased that to 40 mg daily and he had a good response. He was a nonsmoker and his lipid profile showed an LDL cholesterol of 93, HDL of 56, and triglycerides of 225, with a total cholesterol of 194. So in terms of his LDL, he'd already had coronary disease and had been taking a high dose statin, which I continued. I felt his triglycerides were elevated in the setting of uncontrolled diabetes and thought if we can get his A1C to target, his triglycerides will likely normalize as well. He was already taking aspirin, so the only other major cardiovascular risk factor we needed to address was his morbid obesity, with a BMI of 44, which is quite striking.

We had a lengthy discussion about bariatric surgery, and he was absolutely resistant to the idea of surgical intervention. But he was open to the idea of a medical weight loss program, so I referred him to our weight management center.

MR. BUSKER: What about improving his glycemic control? Which agents might you use to lower his sugar while reducing his risk of adverse cardiovascular outcomes?

DR. MATHIOUDAKIS: As we reviewed in this newsletter, we find ourselves at an exciting point in the management of diabetes. For the first time in decades, we finally have some agents to consider both for reduction of microvascular complications and also for macrovascular risk reduction. We discussed in this newsletter two SGLT-2 inhibitors, empagliflozin and canagliflozin, and we talked also about the GLP-1 agonist liraglutide, which has been shown to reduce CVD risk. Another GLP-1 agonist, semaglutide, has been shown to reduce CVD risk, but that's not yet commercially available in the US.

This gentleman was already taking a maximum dose of liraglutide, the GLP-1 agonist, which I encouraged him to continue in light of the new data about cardiovascular disease benefit. And because he was already taking a maximum dose of liraglutide and metformin and had an A1C above target, I recommended that he start an SGLT-2 inhibitor, empagliflozin 10 mg daily. In addition to its effects on blood glucose, for this patient I thought empagliflozin would be favorable for his weight and his blood pressure and his overall risk of cardiovascular disease. Landmark studies have shown a 14% reduction in composite risk of a major cardiovascular event.

We started him on that and I talked to him about the potential side effects of UTI and groin infection risk. And I do want to mention to your listeners that the combination of SGLT-2 and GLP-1 agonists has recently been shown to improve glycemic control and cardiovascular disease risk factors more than each drug alone.

The DURATION trial, which combined once weekly exenatide, a GLP-1 agonist, with dapagliflozin, the SGLT-2 inhibitor, found that 28 week A1C reductions were 2% in patients taking the combination of those two agents and the agents were safe when taken together.

The difference between SGLT-2s and GLP-1 receptor agonists in cardiovascular protection is that the SGLT-2s exert this

protective effect early via hemodynamic changes, whereas the GLP-1s take a little longer to work and are believed to work more via an antiatherogenic or antiinflammatory mechanism. Both drugs have reduced the risk and they also have favorable protective effects on renal function, reducing albumin excretion, decreasing the doubling time for serum creatinine, and slowing the time to end stage renal disease. So both are attractive options in a patient like this.

MR. BUSKER: Assuming that this patient was not on the GLP-1 receptor agonist, would a DPP-4 inhibitor have been an appropriate choice?

DR. MATHIOUDAKIS: This is a complicated question. We reviewed in this newsletter the association between DPP-4 inhibitors and congestive heart failure. The article that we reviewed was a very large meta-analysis of several clinical trials of the DPP-4s, and they found a very modest, nonsignificant trend toward an increased risk of heart failure in patients taking DPP-4 inhibitors, but that effect was driven largely by one of the drugs in class, which was saxagliptin.

The alogliptin trial showed a nonsignificant trend toward increased risk. Nonetheless, the FDA looked at the data from these two trials and was concerned enough to issue a safety warning about the risk of congestive heart failure for both of those drugs. This patient was on a GLP-1, which is a stronger drug, so I wouldn't stop that for a DPP4; but if you have a patient with congestive heart failure and it looks like a mild glucose lowering agent is needed, I would probably stay away from saxagliptin, the drug in a class that is found to have the increased risk, and maybe choose something like sitagliptin, which showed no safety signal in its clinical trial.

MR. BUSKER: I also want to ask you about metformin. You've kept this patient at 1000 mg a day. Is metformin helping to reduce this patient's cardiovascular risk? And what about the risk of lactic acidosis in a patient with potential heart failure?

DR. MATHIOUDAKIS: In the newsletter we reviewed a very interesting systematic review about metformin use in conditions that had historically been considered contraindications for metformin: heart failure, chronic kidney disease, and advanced liver disease. It turns out that not only is metformin not dangerous in those populations, it actually may be beneficial, particularly in heart failure and chronic kidney disease.

So in 2008 the FDA removed congestive heart failure as a contraindication to metformin use, and studies have shown that continuing metformin in somebody with congestive heart failure can reduce all-cause mortality and heart failure hospitalizations. So I generally continue metformin for patients with CHF.

The risk of lactic acidosis with metformin overall is extremely low and tends to occur in patients who have some other insult like sepsis or severe hypotension; but heart failure alone doesn't seem to confer much of a risk of lactic acidosis. So I'd generally continue metformin unless patients have a GFR below 30.

MR. BUSKER: Are there specific antihyperglycemic agents that you would want to avoid in this patient?

DR. MATHIOUDAKIS: I definitely would avoid sulfonylureas in a man with a BMI of 44 who is struggling to lose weight, and the only other class we might consider is thiazolidinediones. But this is a man who already has congestive heart failure, and we know those agents cause fluid retention and increased risk of heart failure. So that wouldn't be an attractive option.

MR. BUSKER: Thank you, doctor. Let's move on to one more patient scenario.

DR. MATHIOUDAKIS: This was a 57-year-old white male I was seeing in initial consultation for diabetes following a recent myocardial infarction. In late August of this year the patient presented with acute substernal chest pain that started while he was watching the Mayweather-McGregor boxing match at the local bar. He said he was really hyped up about the match, and this sent him to the local hospital where he was found to have a non-ST elevation MI. He had a cardiac catheterization which confirmed multivessel disease in his LAD, circumflex, and right coronary arteries.

The patient had a contrast allergy so, unfortunately, they could place cardiac stents. They were only able to give him enough contrast to do the angiography, so he was basically treated with maximal medical therapy. He was started on aspirin, ticagrelor (an anticoagulant), statin, beta blocker, and PRN nitroglycerin.

He had no history of diabetes, and during that hospitalization was found to have an A1C of 7.6% and some fluctuating blood glucose readings ranging from 130 to 240, although he told me that the reading of 240 was checked close to a meal. With newly diagnosed diabetes in the setting of an MI, he was discharged from the hospital on a regimen of glipizide 5 mg daily, which I stopped as soon as I saw him for reasons I'll talk about shortly.

He hadn't seen a physician in years, he had a family history of type 2 diabetes in his mother, and he remembered checking his glucose on her meter a year before and it was about 140. He worked the late-night shift in a bar/club, and he admitted to eating lots of bar food that was high in refined starches and engaged in very little exercise. Generally, he had a poor lifestyle.

On his exam he was normotensive with a blood pressure of 120/77, and had essentially a completely normal physical exam

including a foot exam and sensory exam.

MR. BUSKER: Boil it down for us, please. What's your initial impression of this patient?

DR. MATHIOUDAKIS: This is a man with undiagnosed diabetes who presents with an acute MI. Unfortunately, it seems as though this MI could have been prevented, had he been under better medical care in the previous years. I suspect that he had had prediabetes for years before developing overt diabetes and likely wasn't under good control and had a poor lifestyle contributing to his hyperglycemia.

We know that, despite improving statistics of mortality rates overall for our patients with diabetes, cardiovascular disease continues to be a big problem for our diabetic patients, who have a two- to four-fold increased risk of cardiovascular disease; CVD remains the leading cause of death for patients with diabetes.

MR. BUSKER: When you took this patient in under your care, what testing did you initially perform?

DR. MATHIOUDAKIS: We checked him for albuminuria, because that albuminuria confers an increased risk of cardiovascular disease in addition to renal impairment. He had an undetectable albumin level. I screened him for hepatitis C according to age guidelines, and I referred him to an ophthalmologist for his baseline retinal exam. He clearly needed to see our nutritionist, and I referred him immediately. He found that to be a very useful conversation, and he made some significant changes in diet.

MR. BUSKER: Let's focus on his glycemic control. Tell us about your thought process in selecting an antihyperglycemic agent for this post-MI patient.

DR. MATHIOUDAKIS: It was unclear to me why the patient was not started on metformin during his hospitalization with the MI. I suspect that the cardiology team was concerned about the contrast load they had just given him and they were worried that he could develop a nephropathy with the metformin, and that may be why they chose a sulfonylurea. But I really feel sulfonylurea is not an ideal choice in the setting of an acute MI, as some data suggests worse outcomes in patients treated with sulfonylureas after an acute myocardial infarction. Granted, most of these data come from older sulfonylureas like tolbutamide, and it's not clear whether our newer generation sulfonylureas like glimepiride, which are more selective for the pancreatic receptors over the cardiac receptors, have the same association with poor outcomes after an acute MI. But because some drugs in that class may be harmful, I'm concerned about using it in a man like him.

In addition, there's a greater potential for hypoglycemia after an acute MI, which is concerning in inducing stress on the heart and weight gain. So for many reasons, sulfonylureas have fallen out of favor as first or second line drugs. I started him on metformin 500 mg daily and advised him to increase it to 1,000 mg twice a day over four weeks. He had a beautiful response to metformin. He sent me a log of his blood glucose readings about a month later, they were largely between 70 and 120, and his A1C came down to 6.3%.

MR. BUSKER: What other antihyperglycemic medications might be beneficial for this patient? And when would you consider using them?

DR. MATHIOUDAKIS: As we reviewed in the newsletter, drugs from two classes have been shown to reduce major adverse cardiovascular events in patients with either underlying cardiovascular disease or at high risk for cardiovascular event: the SGLT-2 inhibitor class and the GLP-1 receptor agonists.

Within those classes, not all of the commercially available drugs have been tested or have been shown to have the beneficial results, but we expect within the next few years that most of these trials will be completed for all of the agents. In this patient's case I thought an SGLT-2 inhibitor would be my next go-to agent after metformin. I would select either empagliflozin or canagliflozin, as both of those drugs have been shown to be beneficial in cardiovascular disease risk reduction.

The patient had strong pedal pulses, normal sensation, and no underlying peripheral vascular disease, so that somewhat minimizes this concern of amputation risk with canagliflozin. But I would certainly educate him about the signs and symptoms of neuropathy and foot ulcers, since he did have some very early mild vibratory sensory loss on exam.

GLP-1 agonists would be another consideration, but for most patients with newly diagnosed diabetes, starting an injectable medication right off the bat is generally not appealing. And in this newsletter, we specifically discussed the role of a GLP-1 agonist, lixisenatide, after an acute myocardial infarction. They gave this medication to patients who had had an MI within the previous six months and found that although lixisenatide didn't improve outcomes in the post-MI period, it was not harmful; it showed a neutral effect, suggesting that GLP-1s are probably safe in the immediate post-MI setting. Lixisenatide is available in the United States alone and also in combination with the basal insulin glargine. I've found that the GLP-1 agonist alone is not widely marketed, but it is available.

Liraglutide was the other GLP-1 agonist we reviewed in this newsletter. It was shown in the LEADER trial to have favorable cardiovascular outcomes. Semaglutide, another GLP-1 agonist, was shown in the SUSTAIN trial to confer significant

cardioprotection. Semaglutide was approved for use in the United States, but it's not yet available.

So how do you decide between an SGLT-2 or a GLP-1 agonist? One thing to realize is that the time to benefit is likely to be much faster with SGLT-2 inhibitors since they seem to be mediating the risk reduction more by hemodynamic changes rather than by modification of atherosclerosis, probably blood pressure and weight, and other factors.

This patient had multivessel disease and he was already on maximal medical therapy, so I thought an SGLT-2 inhibitor would achieve the goal of CVD risk reduction faster than GLP-1. It's available orally, which is more convenient.

Of other oral agents, DPP-4 inhibitors are an option for a patient like this, but given the questionable signal about CHF with saxagliptin, if I were to pick a DPP-4 inhibitor I'd probably go with sitagliptin, which showed no signal about heart failure.

MR. BUSKER: Thank you, Dr. Mathioudakis, for sharing your insights in today's cases. Let's wrap things up now by reviewing today's discussion in light of our learning objectives. For patients with underlying CAD or PVD: selecting antidiabetic medications that optimize cardiovascular benefits while reducing overall risks.

DR. MATHIOUDAKIS: The first point is that while SGLT-2 inhibitors can reduce cardiovascular disease risk in high risk patients, and there does seem to be an increased risk of amputations with the SGLT-2 inhibitor canagliflozin. So, providers need to consider factors that could predispose patients to an increased risk of amputation in these patients, such as history of amputation, peripheral vascular disease, or neuropathy, or an active foot ulcer. The other main point is that metformin should be continued unless contraindicated based on renal function, given reduced all-cause mortality.

Another point we discussed was that the DPP-4 inhibitors seem to be neutral overall with respect to cardiovascular disease risk and would not be expected to improve peripheral vascular disease, and they don't increase the risk of amputation.

Finally, GLP-1 agonists are cardioprotective and are not associated with an increased amputation risk, so they would be a reasonable option to consider in a motivated patient who is willing to give injections.

MR. BUSKER: Our second learning objective: the same thing for patients with congestive heart failure — selecting antidiabetic medications to optimize cardiovascular benefits and reduce overall CVD risks.

DR. MATHIOUDAKIS: The first point is that the FDA has issued safety warnings for saxagliptin and alogliptin because of a potential increase in heart failure hospitalizations, so consider the use of those agents in that patient population. Metformin has been shown to reduce hospitalizations for heart failure, so it will always be appropriate to continue, as long as renal function is normal. SGLT-2 inhibitors have a favorable cardiovascular disease profile; they do not increase the risk of heart failure hospitalizations, and in fact may reduce it. And GLP-1 agonists have a favorable cardiovascular disease profile and do not increase the risk of heart failure hospitalizations.

MR. BUSKER: Finally: selecting antidiabetes medications for patients after an acute myocardial infarction.

DR. MATHIOUDAKIS: The first point is that sulfonylureas may be harmful in the postmyocardial infarction setting, and they really are not an ideal drug class for that patient population. The second point is that GLP-1 agonists and SGLT-2 inhibitors are safe to use in the post-MI setting. The third point is that if a DPP-4 inhibitor is used immediately after a myocardial infarction, we would favor the use of sitagliptin, which was not associated with increased heart failure admissions.

MR. BUSKER: Dr. Nestoras Mathioudakis from the Johns Hopkins University School of Medicine, thank you for participating in this eDiabetes Review podcast.

DR. MATHIOUDAKIS: It's been my pleasure, Bob. Thanks for having me again.

MR. BUSKER: To receive CME credit for this activity, please take the post-test at www.ediabetesreview.org

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eDiabetes Review is supported by educational grants from Merck & Co., Inc., NovoNordisk, and Sanofi.

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