



eLITERATURE REVIEW

eDiabetes Review Podcast Issue

Jointly presented by the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing

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VOLUME 1 – ISSUE 10: TRANSCRIPT

Featured Cases: Management Of Overweight And Obese Patients With T2DM

Our guest author is Clare J. Lee, Instructor of Medicine at the Johns Hopkins University School of Medicine in Baltimore, Maryland.

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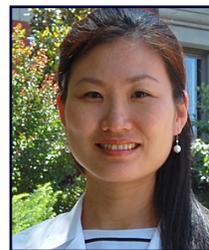
- Discuss how to counsel overweight or obese patients with type 2 diabetes on healthy lifestyle.
- Evaluate pharmacological options to treat obesity in patients with type 2 diabetes.
- Identify patients with type 2 diabetes and obesity who may benefit from considering bariatric surgery as a treatment option.

This discussion, offered as a downloadable audio file and companion transcript, covers the important topic of the management of overweight and obese patients with type 2 diabetes in the format of case-study scenarios for the clinical practice. This program is a follow up to the Volume 1, Issue 9 *eDiabetes Review* newsletter—Management of Overweight/Obese Patients with T2DM.

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Dr. Lee has indicated that her discussion will reference the use of liraglutide for weight loss, which is not currently approved by the FDA.

MEET THE AUTHOR



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Faculty Disclosure

Dr. Lee has indicated that she has no financial interests or relationships with a commercial entity whose products or services are relevant to the content of her presentation.

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- Clinicians do not appropriately intensify therapy as necessary to maintain glycemic control.
- Conflicting data about the safety of incretin agents may unduly deprive patients of treatment benefits.
- Clinicians are not aware of and/or are not implementing strategies to maximize the value of SMBG readings to improve patient outcomes.
- Clinicians do not adequately understand or treat to control CVD risk factors in their patients with T2D.
- Clinicians do not have a sufficiently current knowledge base to effectively consult patients about potential T2D therapeutic advances.
- Clinicians do not adequately counsel and treat their overweight/obese patients with T2D.

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MR. BOB BUSKER: Welcome to this eDiabetes Review Podcast.

Today's program is a follow-up to our newsletter issue on the *Management of Overweight and Obese Patients with Type 2 Diabetes*. With us today is that issue's author, Dr. Clare J. Lee, an instructor of medicine at the Johns Hopkins University School of Medicine in Baltimore.

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Learning objectives for this audio program include:

- Discuss how to counsel overweight or obese patients with type 2 diabetes on healthy lifestyle.
- Evaluate pharmacological options to treat obesity in patients with type 2 diabetes.
- Identify patients with type 2 diabetes and obesity who may benefit from considering bariatric surgery as a treatment option.

Dr. Lee has indicated that she has no financial interests or relationships with any commercial entity whose products or services are relevant to the content of today's presentation. She does note that her discussion today will reference the use of liraglutide for weight loss, which is not currently approved by the FDA.

I'm Bob Busker, managing editor of eDiabetes Review. And I want to thank you, Dr. Clare Lee, for joining us today.

DR. LEE: Thank you, Bob, it's my pleasure.

MR. BUSKER: In your newsletter issue, doctor, you reviewed some of the recent publications describing the evidence-based importance of managing obesity in patients with type 2 diabetes, and some of the ways clinicians can help their patients achieve weight loss. What I'd like to focus on today is how some of that new information can be incorporated into the clinician's current practice. So if you would, Dr. Lee, start us out by describing a patient.

DR. LEE: The patient is a 45 year old man with newly diagnosed type 2 diabetes who presents for further management. His hemoglobin A1c decreased from 7% at the time of diagnosis three months ago to currently 6% on a low carbohydrate diet. On exam, he is normotensive with BMI of 33 and central obesity.

MR. BUSKER: Just for clarity, doctor: this patient decreased his A1c by a full point without any type of pharmacotherapy?

DR. LEE: Yes. Often patients may surprise us by making an impressive improvement in their hemoglobin A1c at the time of diagnosis and shortly thereafter, because their hemoglobin A1c at the time of diagnosis may be related to completely uncontrolled diabetes. When they become aware of their diabetes, they realize they have to work on their lifestyle in the face of the new diagnosis, and they sometimes make quite an improvement without medication being involved.

MR. BUSKER: So sometimes just being told that they've got diabetes can motivate patients to begin making lifestyle change. How can the clinician use that initial motivation to educate the patient on how lifestyle choices can impact both glycemic and weight control?

DR. LEE: This is the perfect moment to congratulate him on his progress with his glycemic control, as he made a significant impact on his hemoglobin A1c just by diet alone. This is a clear demonstration that healthy lifestyle works on a chronic disease like diabetes, and given that diabetes is a lifelong endeavor, this would be a great opportunity to just drill in that important lesson that healthy lifestyle is the cornerstone of diabetes management.

This is also a great time to sit down with your patient whose diabetes is newly diagnosed to go over why we his glycemic control is important and why we are spending the time to discuss it, because studies have shown that good glycemic control makes a difference in long-term complications of diabetes. As we know, the diabetes-related complications are largely divided to macrovascular, such as heart attack and stroke, and microvascular, regarding retinal damage or kidneys or peripheral neuropathy damage.

These are the main points you want your patients to understand: that glycemic control will pay off in the long run by preventing these complications.

MR. BUSKER: So even though he got his A1c down — his BMI, as you described, is still 33 with central obesity. He is obese. So how would you counsel this patient about healthy nutrition?

DR. LEE: That's right, Bob. As you pointed out, his BMI is in the obese category, and that has a direct bearing on the diabetes. Being overweight can make the insulin work less well, as we all know, and cause insulin resistance. Therefore, we have to emphasize to this patient the importance of healthy nutrition and healthy lifestyle overall to address his obesity status.

Regarding healthy nutrition, we're talking about eating controlled portions; avoiding fatty fried foods; avoiding alcohol intake, as that has a lot of hidden calories packed in it; and most of all, avoiding sugary beverages, which are just easy calories to cut out that we don't need.

Exactly what types of diets should we emphasize in our patients with diabetes? Studies have looked at different types of diets, and basically the bottom line was, any diet that helps patients control their intake were effective, regardless of the types of macronutrient distribution. By macro nutrient distribution I mean diets emphasizing, for example, protein versus fat versus carbohydrates, regardless of what portions they recommended — any diet that helped people have some control over their intake paid off in the long run. So those are the types of approaches I would take, emphasizing overall lean protein, less fat and less carbohydrates, and essentially emphasizing that a nutritionist should be available to help with fine tuning patients' approaches to their diet.

MR. BUSKER: We know that one of the key reasons patients do not stick to their recommended diets is, very simply, that they become hungry. What kind of advice can a clinician offer them about that?

DR. LEE: That's a great point, Bob. Avoiding being hungry to the point where you make poor decisions, having some healthful snacks in between, definitely makes it easier to stick to a healthy diet. Healthy snacks can include fruits and vegetables that are easy to carry such as baby carrots, and also some nuts,

which are chock full of good nutrition, and also fiber that makes you less hungry between meals so that you don't fall into those traps that you can walk into.

A few easy points for the clinicians who are squeezed for time when you see these patients is talking about portion. Sometimes it's surprising how we're not aware of how much we eat, and just addressing portion size can be quite helpful. We can ask patients to go home and measure their intake of different types of foods by using a measuring cup, for example. That can be enlightening when they can bring those results back and discuss them with you at their next visit.

I can't emphasize enough the importance of cutting out easy calorie targets such as sugary beverages that could have a big payoff.

MR. BUSKER: We've talked about caloric intake; now let's look at the other side of a healthy lifestyle. Talk to us about energy output.

DR. LEE: A healthy lifestyle includes not only a healthy diet, but also physical activity. Often my patients ask what an exercise is, and I tell them it refers to a moderate intensity aerobic activity that causes your heart rate to go up ideally to 50% to 70% of the maximum heart rate. The general recommendation is that you strive to exercise at least 30 minutes every day and hope to achieve at least 150 minutes a week. This leads to an improvement in diabetes that patients can actually see through their blood glucose monitoring, because healthy lifestyle involving daily exercise helps with insulin resistance and ultimately makes your diabetes much easier to control. Sometimes with patients who are not yet on medications, this can help us to prolong the initiation of medications in people with diabetes.

MR. BUSKER: Thank you, Dr. Lee. And we'll return, with Dr. Clare Lee from Johns Hopkins, in just a moment.

SUSAN PORTER: Hello. I'm Susan Porter, clinical nurse practitioner and certified diabetes educator at the Johns Hopkins University School of Medicine. I'm one of the program directors of eDiabetes Review.

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MR. BUSKER: Welcome back to this eDiabetes Review podcast. I'm Bob Busker, managing editor of the program. Our guest is Dr. Clare Lee, from the Johns Hopkins University School of Medicine. And our topic is Management of Overweight and Obese Patients with Type 2 Diabetes.

We've been looking at how some of the new information Dr. Lee discussed in her newsletter issue can be applied in the exam room. So if you would, doctor, let's continue with another patient.

DR. LEE: Mrs. Jones is a 50 year old woman with type 2 diabetes and hypertension. She has had diabetes for 10 years and is currently taking metformin, sulfonylurea, and glargine, 30 units at bedtime. Her latest hemoglobin A1c was 10.2% and her BMI is 35.

MR. BUSKER: This patient — she's on two OADs, plus she's on insulin — and her A1c is still over 10 percent. And she's obese and she's hypertensive. That's a lot for the clinician to deal with. Where's the best place to start?

DR. LEE: Our first inclination as clinicians would be to change something about her medications and take action, but we have to hold back that urge and discuss why being on two oral medications and long-acting insulin made her hemoglobin A1c go off target.

A couple of pointers here: One is to discuss whether she is adhering to her diet, whether some challenges got in the way. Regardless of how much medication we are giving her, if she is not adhering to a low carbohydrate diet, that has to be the first thing we address before we make any changes in her medications.

We have to approach this delicately without passing judgment, and it's important to make her feel comfortable to share any challenges with you. It's also important to figure out whether there was a change in her body weight, because that can also

affect the overall insulin resistance and perhaps might be the underlying reason for her hemoglobin A1c being off target.

I'd make sure to address several other things for patients whose glycemic control remains off target. These include family history, recent illness, or steroid use, all of which can also adversely impact their overall glycemic control.

MR. BUSKER: Let me extrapolate a little bit. Let's say that you confirm that she's doing what she can with her diet, that she's adhering to her medication, that she is really giving this her best efforts. What changes in her medication regimen would you consider?

DR. LEE: Once we have confirmed that there aren't any oversights that could be complicating her diabetes care, we can review her medications and see if there is any room for adjustment.

One thing that I want our listeners to pay attention to is the fact that she's on sulfonylurea and insulin, which are perhaps adversely affecting her weight. Her BMI, after all, is in the obesity category of 35. So we can either adjust the doses of the preexisting medications or consider adding a new medication on top of those she's already taking. But overall, if we could reduce or eliminate the two medications that I mentioned to you, that could have an adverse effect on weight gain, that would be probably helpful for the patient.

So one medication that could perhaps help us to reduce or eliminate the weight gain promoting medications such as sulfonylurea and insulin, so we can consider some of the newer agents such as GLP1 agonists, DPP4 inhibitor, and SGLT2 inhibitor, all of these have the added benefit of being weight-neutral or slightly weight loss-promoting, which are probably helpful and encouraging for patients, including the one that we described to you before.

Regarding the GLP1 agonists, I want to spend a minute talking about liraglutide, which has received some attention recently. Given the FDA's favorable voting toward liraglutide being close to being FDA approval, we're now looking at a dose for weight loss of 3 mg instead of 1.8 mg that's currently FDA approved for diabetes management. A 3 mg dose seems to help with a body weight loss greater than 5% difference between the treatment arm and the

placebo arm. This is encouraging and something we need to consider. The good thing is, for patients with diabetes and obesity, liraglutide can help with both.

MR. BUSKER: I do need to reinforce that, at the time of this recording, the higher dose of liraglutide for weight loss has not been approved by the FDA. But let's talk about these newer agents in general, Dr. Lee. The GLP-1 receptor agonists, the DPP-4 inhibitors, the SGLT-2 inhibitors — how do you assess if a patient is a good candidate for any of these drugs?

DR. LEE: The GLP1 agonists and DPP4 inhibitors are great for diabetes control and slight weight loss, or being weight neutral. However, we do have to be mindful of some of the side effects that this class of medications can cause. The most common side effect is gastrointestinal, such as nausea or diarrhea, and some concerns have been expressed about pancreatitis with this class of drugs, although some of the follow-up studies have not shown any significant increase related to the use of this class of drugs and pancreatitis. This is still an area of concern.

Another option could be an SGLT2 inhibitor, which is one of the newest drugs on the block. It promotes glucose-wasting in the urine and can help us with a modest amount of weight loss and improvement in blood pressure as well. However, because we're losing glucose in the urine, this can predispose patients to urinary tract infection. I would be careful on prescribing this class of drugs to people who have a history of urinary tract infection.

MR. BUSKER: Now there are pharmacotherapies — most of them are relatively new — that are not necessarily used for diabetes but are indicated for weight loss. Give us a brief overview of those, if you would please.

DR. LEE: So we have several choices for medications that help us with weight loss and that may not necessarily have any impact on diabetes directly. For example, orlistat is a selective inhibitor of pancreatic lipase that blocks fat from being absorbed and as you can imagine, this can cause some gastrointestinal side effects related to fecal fat loss.

Lorcaserin is another drug which is a selective serotonin 2C receptor agonist, and a couple of things to keep in mind. Valvulopathy has been of concern with this class of drugs, but an extensive phase 3 study did not show any statistically significant increase in

valvulopathy. Overall it's a well-tolerated drug, although some of the common side effects include headache, nausea, dizziness, constipation. And I would be very careful about not prescribing this drug in those at risk of serotonin syndrome.

Next, phentermine-topiramate is a combination drug that reduces appetite, but it's important to keep in mind that topiramate is contraindicated in glaucoma and in pregnant women.

Next, naltrexone/bupropion has just recently been approved for treatment of chronic weight management by causing appetite suppression. There was a slight concern regarding elevation in blood pressure with this class of drugs. However, further studies did not show any significant elevation in blood pressure that would be clinically significant.

MR. BUSKER: Thank you, Dr. Lee. Let me ask you now to bring us one more patient, if you would, please.

DR. LEE: Mr. Smith is a 58 year old man with type 2 diabetes, sleep apnea, osteoarthritis, and hypertension. His diabetes was diagnosed five years ago, and he currently takes metformin and glipizide. His current hemoglobin A1c is 9% and his BMI is 45.

MR. BUSKER: Talk to us about counseling this patient — you want to improve his diabetes control, you want to improve his obesity — what are the initial steps you would take?

DR. LEE: Mr. Smith would benefit from the same sort of approach we discussed in the previous cases: emphasizing the importance of healthy lifestyle, especially healthy diet and regular physical activity. I would also review with him how successful he has been with sticking to his diet and his medications to understand his overall glycemic control. Particularly regarding his BMI, which is at a quite high of a level, I would want to understand whether he has made previous attempts at weight loss. That would include any diets or any commercial products he might have used, any attempts he might have made so I could try to understand what he's been through before.

I would definitely would use my colleagues in nutrition and physical therapy to help me to make healthy lifestyle available to him and also offer practical value to him that he can implement.

MR. BUSKER: You've talked about discussing his diet, his medication adherence, his prior attempts at weight loss, et cetera — but we see this patient is on metformin and a sulfonylurea, which are not going to help with weight loss. What would your thoughts be about changing his therapeutic regimen?

DR. LEE: Thanks for that point, Bob, I'm sure the listeners are wondering about the same, that his medications for diabetes do not seem to be maximized just yet before we talk about something as extreme as surgical therapy, for example, for diabetes and obesity. So as you pointed out, glipizide does tend to promote weight gain, so that is something that we can switch out to something that's less weight promoting. Metformin is a great drug so I would keep that, but we would consider, again, other medications such as GLP1 agonists or a DPP4 inhibitor, or SGLT2 which is new. But I actually put in the fact he has a history of sleep apnea, osteoarthritis, hypertension which together with type 2 diabetes qualify for comorbidities related to obesity.

He already suffers from several outcomes from obesity, and regardless of his treatment regimen for diabetes, this may be a good time for him to be aware of all the spectrums of treatments available for obesity.

MR. BUSKER: Included in that spectrum of available treatments would be surgical treatment of obesity. How would you discuss that with this patient?

DR. LEE: Mr. Smith has options of looking at surgical treatments for obesity. Under the NIH guidelines for bariatric surgery, anybody with a BMI greater than 40 or BMI greater than 35 with obesity-related comorbidities such as diabetes, hypertension, sleep apnea, and osteoarthritis would qualify for bariatric surgery. Because this is a surgical therapy, understandably a lot of patients may be timid to seriously consider this an option. However, between the clinician and the patient, this option should be at least presented within the full spectrum of available treatments, especially when patients are struggling with medical therapies or the treatment of obesity and diabetes in this case.

Among the surgical treatments available for weight loss, the roux-en-Y gastric bypass and sleeve gastrectomy have begun to show good efficacy in treating obesity and helping improve diabetes control.

MR. BUSKER: Doctor, tell us a little more about the efficacy of these procedures.

DR. LEE: A recent systemic review by Yip and colleagues show that at one year, the gastric bypass group had lost 72.5% excess BMI versus 66.7% in the sleeve group, and the gastric bypass group achieved diabetes remission in 76% versus 68% in sleeve group. These results are quite significant at one year, but we need more long-term results related to surgical weight loss and outcomes.

MR. BUSKER: And the benefits and risks of surgery to treat obesity plus diabetes?

DR. LEE: The benefit of bariatric surgery is, to date it's the most effective tool we have to treat obesity and diabetes. It causes substantial weight loss and brings in diabetes remission rates that are quite unmatched compared to medical therapies and lifestyle changes. It also brings improvements in other comorbidities such as sleep apnea, hypertension, and osteoarthritis.

The risks related to bariatric surgery include perioperative and postoperative complications such as anastomosis leak, perforation, bleeding, hernia, and late-onset complications including malabsorption, dumping syndrome, vitamin deficiency, and hypoglycemia. The overall mortality is quite low, under 1%, comparable to mortality from cholecystectomy and appendectomy.

MR. BUSKER: So assume that the patient is interested, he might consider bariatric surgery — what do you tell him about his odds of actually achieving diabetes remission?

DR. LEE: I'm sure the listeners are also wondering about that. Mr. Smith has had diabetes for approximately five years and is currently not on any insulin, and I purposely presented this case to raise the point that you do not necessarily have to wait until the diabetes is in the later stage to discuss bariatric surgery as an option. In fact, studies are beginning to show that patients who have had diabetes for a short time and are not on insulin may do better in achieving diabetes remission after bariatric surgery.

Ideally, we would have a risk calculator to be able to predict who will be able to achieve diabetes remission, but we do not yet have such a risk calculator. I'm sure a lot of research effort is going into answering that

question. However, overall we should be encouraged by the impressive outcome of diabetes improvements related to bariatric surgery.

MR. BUSKER: Thank you for today's cases and discussion, Dr. Lee. Let me ask you to look to the future for us now. What do you see as future tools and future methods of treating obesity in people with type 2 diabetes?

DR. LEE: Several tools on the horizon further our ability to address obesity and diabetes management. Foremost, the emergence of smart apps is quite exciting; I can't even keep track of all the apps available in the market. But apps are definitely becoming more available to our patients, which gives them the power to be better able to recognize calories and track and guide their physical activity. That hopefully will be a great tool for our patients to promote healthy lifestyles.

Next, we are excited to have different medication options for treating obesity and diabetes. As we mentioned, liraglutide and naltrexone/bupropion combination are some of the latest additions to our armamentarium to treat obesity and diabetes. We are expecting more developments in pharmacotherapy for obesity and diabetes.

Less invasive and endoscopic treatments are being developed to treat obesity, and they will also help us to further our menu to offer patients to treat obesity and diabetes.

MR. BUSKER: I do need to point out again that, as of the time of this recording, the injectable incretin liraglutide is not FDA-approved for weight loss. So, Dr. Lee, to wrap things up, I'd like to review today's discussion in light of our learning objectives. So let's begin: counseling overweight or obese patients with type 2 diabetes on healthy lifestyle.

DR. LEE: To promote a healthy lifestyle, we should start by understanding any barriers or challenges that our patients may face and then discuss the important aspects of healthy nutrition. That discussion should focus on plenty of vegetables and lean meat, and low carbohydrates and fat. We should also focus on the daily goal of at least 30 minutes of physical activity daily and sticking to this rule, because in the end this sort of healthy lifestyle will help us not only improve diabetes but also lower the risk of comorbidities related to obesity and the diabetes.

MR. BUSKER: And our second learning objective: pharmacologic options to treat obesity in patients with type 2 diabetes.

DR. LEE: We should recognize when to intensify pharmacotherapy for patients with obesity and type 2 diabetes. To achieve that, we should make sure that patients adhere to the medication and low carbohydrate diet. Once we recognize that the patient is unable to achieve glycemic control despite adhering to medical and diet, we should consider adding a medication or perhaps switching their current medication. As we discussed, medications such as sulfonylurea and insulin that may promote weight gain should be avoided when possible, while medications that may be weight-neutral or weight loss-promoting such as metformin, GLP1 agonist, DPP4 inhibitor, and SGLT2 inhibitor should be considered. In addition, medications specifically approved for weight loss should also be considered as an additional therapy.

MR. BUSKER: And finally: identifying patients with type 2 diabetes who may benefit from bariatric surgery.

DR. LEE: The clinician should be aware of patients who meet the NIH guidelines for bariatric surgery. The benefits of bariatric surgery include weight loss and diabetes remission, but the risks involve postsurgical complications, hypoglycemia, dumping, malabsorption, and vitamin deficiency.

MR. BUSKER: Dr. Clare Lee from the Johns Hopkins University School of Medicine, thank you for participating in this eDiabetes Review Podcast.

DR. LEE: Thank you so much for having me.

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