

EPISODE 32: DIABETES, PANCREATITIS & PANCREATIC CANCER

Dr. 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.

For today's podcast, we are pleased to welcome Dr. Michael Goggins. Dr. Goggins is a Professor of Pathology, Medicine and Oncology at the Johns Hopkins University School of Medicine. He opened the Pancreatic Cancer Early Detection Research Laboratory in 1999. He's an attending physician and gastroenterologist at Johns Hopkins Hospital, the Sol Goldman Professor of Pancreatic Cancer Research, and Director of Research in the Division of Gastroenterology and Hepatology. He is the PI (principal investigator) of the multicenter Cancer of the Pancreas Screening-5 or CAPS5 study supported by the National Cancer Institute through the Pancreatic Cancer Detection Consortium. He is also the principal investigator of an R01 grant (NIH Research Project Grant) to support evaluating markers of early pancreatic cancer, in addition to being principal investigator on multiple other grants. Welcome, Dr. Goggins.

Dr. Michael Goggins, MD: Thank you, Rita. Delighted to be here.

RK: Well, thanks so much for joining us today to talk about this important topic. We often hear about pancreatic cancer and how really life changing that diagnosis of pancreatic cancer can be. What is the link between pancreatic cancer and diabetes? This may not be something that many people are aware of. I wonder if you could tell us more about that.

MG: The link is bi-directional. In other words, pancreatic cancer and diabetes are connected in the same way as some patients with diabetes, long standing especially, are at increased risk of developing certain cancers. That is also true for pancreatic cancer. But in addition, the pancreas is where your insulin is produced and other hormones that control blood sugar. It's not surprising if the pancreas is not functioning properly, such as if you develop pancreatic cancer that can result in diabetes. You have people with long standing diabetes at a modestly increased risk of developing pancreatic cancer. And then you'll have people who develop pancreatic cancer who may develop diabetes.

RK: That's interesting. As you mentioned, both diabetes and pancreatic cancer have their origins in the pancreas. The organ that produces not only hormones, such as insulin, which we know is not as effective in people with diabetes or absent in people with Type 1 diabetes, but also pancreatic cancer, which is cancer of the pancreatic organ. Do you think that having diabetes is related to having cancer in the pancreas more so than someone who doesn't have diabetes?

MG: Yes, we think that some of the metabolic changes, especially with the long-standing diabetes associated with weight gain and insulin resistance, those factors associated with long-standing diabetes lead people to developing pancreatic cancer. Much in the same way we think that they can develop other cancers as well. Whether it's because of too much insulin or other mechanisms, it is considered an important metabolic cause of developing a variety of cancers, including pancreatic cancer.

RK: Now, you mentioned that people with diabetes are at an increased risk of many cancers, pancreatic cancer being one of them, of course, the one that we're focusing on today, but why the pancreas I guess, is the question? Why cancer in this organ? Is it long-standing diabetes, as you mentioned, just having diabetes for a long time? The inflammation related to diabetes? Do we know the mechanisms, you mentioned some of them such as obesity and other factors, but do we really know why there is this link between diabetes and pancreatic cancer? Or is that the million-dollar question?

MG: Well, it is a million-dollar question in terms of going from pretty well understood hypotheses to kind of having certainty about it. The evidence still would suggest that diabetes is a significant risk factor for pancreatic cancer, which has similar risk factors to many other cancers, such as smoking. If you have a family history of pancreatic cancer, you're more likely to develop pancreatic cancer, the more you smoke, and the longer you smoke, these [are] common risk factors. As you get older, you become more likely to develop pancreatic cancer as well. These are some of the main risk factors. In addition, in the pancreas, sometimes the pancreas gets injured and inflamed. Pancreatitis is a risk factor for pancreatic cancer, again, especially if it's long-standing, smoldering inflammation that occurs often over decades. So there are sort of common factors that involve multiple cancers and cancer-specific factors. Sometimes, like pancreatitis, which is thankfully not a common condition, can predispose.

In the clinic, we are focused on identifying risk factors that can lead us to suggest who should undergo screening, surveillance for pancreatic cancer if their risk is particularly high. Generally, that's based on having an extensive family history of pancreatic cancer or inheriting cancer, predisposing germline mutations. Those are the main factors that we're thinking about in relationship to pancreatic cancer and diabetes is part of that.

RK: It's interesting that you mentioned both factors that are general and related to pancreatic cancer and then those that might be more specific to diabetes, as you talked about. And you mentioned pancreatitis, I wonder if you could briefly describe what pancreatitis is and what role it might have and the relationship between diabetes and pancreatic cancer.

MG: Pancreatitis is by the name an inflamed pancreas. We consider pancreatitis as either an acute pancreatitis event or chronic inflammation. Acute inflammation of the pancreas is somewhat of a unique condition. The pancreas is designed to produce pancreatic enzymes as one of its main functions. The other one being producing the hormones. But much of the pancreas is involved in generating the pancreatic digestive enzymes that remain inactive in the gland until they are secreted into the gut. If they get activated within the pancreas, they'll digest your pancreas and cause tremendous inflammation sometimes. Usually, people who develop acute pancreatitis need hospitalization, very occasionally the ICU. It can be quite a serious condition. People will often heal from it, but that injury can sometimes lead on to what we call chronic pancreatitis. In other words, pancreatitis that recurs as either acute events or smolders, often causes ongoing pain, and may affect the long-term function of the gland. That injury to the to the pancreas, just like chronic inflammation elsewhere in the body, if that goes on for a long period of time, that's often decades and that can increase the risk of developing pancreatic cancer. Occasionally, people who develop acute pancreatitis: Well why do they develop it- There are reasons why that occurs: people have gallstones; they drink too much alcohol, you get an acute pancreatitis attack. Occasionally it is also something else, like pancreatic cancer has occurred or some other pancreatic neoplasm that has caused acute pancreatitis. But it's more in terms of pancreatic cancer, we're often thinking about chronic long standing pancreatic inflammation that will eventually lead to pancreatic cancer. Chronic injury will affect the gland not only sometimes the ability to produce the enzymes, but of course the ability to produce the hormones as well. So, people with long standing, chronic pancreatitis or a bad attack of acute pancreatitis will sometimes then go on to have diabetes as a result of their pancreas injury, their loss of the hormones - the islets that produce the hormones like insulin.

RK: Thanks for bringing that up. I think we often talk about the two major types of diabetes, Type 1 and Type 2 diabetes. But the kind of diabetes you're talking about, which is due to injury of the pancreas or inflammation such as pancreatitis, we are slowly, I think, recognizing pancreatogenic diabetes. A kind of diabetes secondary to diseases of the pancreas as being more and more common as we see other conditions such as cystic fibrosis and also in patients who have pancreatitis, like you mentioned, who develop diabetes later on. So, I appreciate you bringing that up. Because I think it's a type of diabetes, we often don't recognize as much as we should, and we're gaining more understanding. And you talked about the close link between diabetes and pancreatic cancer, diabetes, and pancreatitis, and pancreatitis and pancreatic cancer. It seems like it's a triad of some sort, is that right? That they're all really quite closely linked.

MG: They are quite closely linked. One of the areas of interest for how to use this information is recognizing the new onset diabetes. We just mentioned that you can have new onset diabetes after pancreatitis. That's an important consideration. What if you have new onset diabetes? Is that a signal for pancreatic cancer? And it can be and it's certainly a significant signal, in that the risk of having pancreatic cancer in someone who's developed new onset diabetes is initially high. In other words, when you develop new onset diabetes, you can generally assume correctly, that it's related to the common reasons why people develop diabetes in the population: they're overweight. They have the risk factors that we see that they're metabolically predisposed to developing. And it's kind of, I will say, a more of a usual pattern; we have the insulin-dependent type, and this adult-onset type, that we referred to, you have the pancreatitis type, but pancreatic cancer is there as well. Thankfully, it's not a very common cause of new onset of diabetes. It may be only one and a few hundred people who have a new onset of diabetes, who have it because of pancreatic cancer. And one question we're trying to better understand is: Who among the people who have new onset diabetes should be thought about as to whether or not they have pancreatic cancer? And should they have investigations and things like that? We know that they tend to present a little bit differently than the typical person who has new onset diabetes. They may be more likely to lose weight, for example, and there may be certain lab abnormalities that reflect that. We're trying to understand if you could detect pancreatic cancer earlier by identifying people who have new onset diabetes. That still is under investigation. While it may be helpful to do so, we want to be able to check pancreatic cancer, ideally at stage one. When a lot of people haven't yet developed pancreatic cancer, or who go on to have pancreatic cancer; at stage one, they often don't have any diabetes. That tends to be something we see as the cancer starts to grow and develop more, larger and affect the pancreas to a much greater extent. But it is an important question, it's under investigation.

RK: It is an interesting question that you bring up. I know that I have seen clinically some patients later in life diagnosed with pancreatic cancer, and then having the diagnosis of diabetes maybe just the year before or a few months before. And it does make you wonder if the new onset diabetes could have been a signal that there was something going on underlying, such as the cancer. And as you mentioned, the symptoms can be hard to disentangle from the typical symptoms of Type 2 diabetes, for instance, that's more common in adulthood. But I think the atypical factors that you mentioned, for instance, maybe someone who's not as obese or losing excessive amounts of weight, or doesn't have the family history, maybe doesn't belong to high-risk ethnicity, who really doesn't have risk factors for insulin resistance,

perhaps those patients should be considered to have further evaluation. At present, as far as I know, there's currently no recommendations for general screening of people with new onset diabetes who don't have the usual risk factors. But I'm curious as based on your research, what do you think? Do you think that people who don't have the usual risk factors for Type 2 Diabetes and are diagnosed later in life, let's say after the age of 70, do you think they should be screened for pancreatic cancer?

MG: Yeah, I don't think the evidence supports it yet, unless the clinician identifies certain additional factors, like we mentioned, the weight loss. I think there may become perhaps additional tests that are performed when someone is assessed as having new onset diabetes. Which means that they had a normal glucose, normal HbA1c, they were established as not having diabetes, and then at some subsequent period, labs are found and confirmed. And in terms of the pancreatic cancer window in that early period, the optimal period, in other words, if it's going to be pancreatic cancer, it is going to mainly be something that is emerging within that year. Even though you could sort of extend it out, sometimes people have looked at "Well, what is the incidence, three years after new onset diabetes diagnosis?" If it ever is going to have a utility, that little signal that there's something- Why did this person suddenly develop diabetes? It's in those first few months, certainly no longer than a year. In all likelihood, if you don't have pancreatic cancer emerge after a year, you probably don't have pancreatic cancer. But it's really, it's hard to say no to a question like that. But you have to put it into context, because again, it's only going to be one of every few hundred people. And that probably reflects, it would depend on the underlying prevalence of diabetes in the population. If you're in a high diabetic area, where there's a lot of the metabolic and familial factors, etc., that contribute to diabetes, well, then you could expect that that's going to be even rarer than in let's say you had a very healthy population. What this gets at is, in order to diagnose pancreatic cancer, the best way we do that currently is with imaging, you know, a CT scan, or some of the scans that we use when we're engaging in pancreatic surveillance, the MRIs of the pancreas or the endoscopic ultrasounds of the pancreas. So offering that to every person who developed diabetes is kind of low yield. We have to manage a lot of aspects of care when people develop diabetes at first. So, it's not quite at that point where we can say we should offer everybody, I'll say, a CT scan.

RK: It certainly would be a lot to do a CT scan on everyone diagnosed with diabetes, as you mentioned, but as you pointed out, there's a few per hundred that perhaps could benefit from further evaluation. We haven't talked about symptoms. Some symptoms of pancreatic cancer might be another way to alert the individual that perhaps they do need to be evaluated, with imaging or other tasks, for the possibility of pancreatic cancer. I wonder if you could talk briefly about the warning signs or symptoms that someone with diabetes should be on the lookout for, to alert them that they might need further evaluation for pancreatic cancer?

MG: Yes, for diabetes, it's the weight loss which we wouldn't anticipate, unexplained as opposed to intentional, that's one. People who develop pancreatic cancer will often develop abdominal pain, they may develop jaundice, they may develop back pain in their mid-back, sort of immediately behind where the pancreas is- in the upper abdomen and in the midline area, off slightly to the left, or similar to that in that epigastric area in the front of the abdomen. The abdominal pain, people of course can have other kinds of symptoms related to change in appetite, loss of appetite. The weight loss that we see is probably a combination of the change in appetite, but also maybe an element of the pancreas not working properly; not digesting food properly, in some cases, and so that's contributing to weight loss. Other classic [symptoms], we mentioned jaundice as well, your eyes go yellow, your skin goes yellow, your urine goes dark and sometimes your stool goes chalky white. And that would be a warning sign. Obviously, there are other causes for jaundice. Mood changes occur as well; some depression is a manifestation. We even see people developing blood clots occasionally, that's a warning sign. Unexplained blood clots can have other reasons, but pancreatic cancer is certainly one of them. Even clots along in the skin. Ideally, we would be able to identify patients mostly before they have symptoms. It's certainly helpful when you have symptoms to have early assessment. One of the things that we've understood with improvements in insurance coverage. We looked at this some years ago, it does appear that you're more likely to be diagnosed at an earlier stage of pancreatic cancer when you're insured. We suspect that that has something to do with just being able to access care when you have some concerning symptoms, more easily, more quickly. In the people who we have in our high-risk clinic based on their family history, where they have not just one first degree relative or parent, sibling, but multiple. Or they have some of the common cancer predisposing mutations that we commonly hear about; the breast cancer gene and BRCA2 and other BRCA genes and ATM and other genes like that. There we're, of course, wanting to detect abnormalities by scans before there are any symptoms. And when we see pancreatic cancer, in its early stages, especially stage one, which we will see. The majority people who develop pancreatic cancer under surveillance are stage one and they generally don't have symptoms. Some people who develop symptoms will have stage one pancreatic cancer, but often they don't. And so that's where we're really hoping for, but certainly it can help to be aware of the warning symptoms and to get care. The challenge is that some of them are nonspecific. And if you go to your primary care provider, and some of these have multiple causes. Some of them are more warning than others. If you develop a blood clot or you have jaundice, those are certainly significant symptoms. If you start losing weight, people don't always realize it. So, it is a challenge to use symptoms as your primary guide. But it is important to be aware of some of the warning symptoms.

RK: Yeah, thanks for going through those symptoms. I think it's important for people to be aware of but as you mentioned, you could have early stages of pancreatic cancer without symptoms and for those with known, what we call genetic risk or family history, who are actively

being followed to ensure that they don't develop the early signs, perhaps they may be individuals that don't have symptoms. But it sounds like for the vast majority of people who don't know that they have any increased risk they probably would first be alerted to being evaluated for pancreatic cancer by these symptoms so that's really good to know about. When we think about pancreatic cancer, I think many people think of late stages, serious complications. When we say pancreatic cancer, what are we really talking about? What are the types of pancreatic cancer? If you could just talk about them briefly. And we know it's a serious condition, but can it be treated once you're diagnosed? What's the prognosis when someone's diagnosed?

MG: Yes, most pancreatic cancers are the kind of exocrine ductal carcinomas, reflecting different cell types in the pancreas. You have the kind of the exocrine, where the pancreatic enzymes are made and the endocrine where you make your insulin and your other hormones like glucagon. There is another form, there's a neuroendocrine form of pancreatic cancer. There are even rarer types as well, reflecting the pancreas parenchyma, the acinar cancers. The vast majority of them, are these ductal adenocarcinomas and in the order of 95% or so, and they're the most serious kind. The challenge is that most people currently who are diagnosed present with advanced stage disease. Only 20% or so, who are diagnosed are diagnosed with a resectable cancer. A smaller percentage again are diagnosed with stage one. Stage one pancreatic cancer would mean the cancer is confined to the pancreas. Stage two, it means it has spread to local lymph nodes. Stage three is - to nearby organs. And stage four can be more extensively nearby or spread to other organs. And the management is understandably easier if it's confined to the pancreas where you can treat it with surgery. Nowadays, often, treatment begins with chemotherapy. The earlier the cancer is in its natural history, generally speaking, the easier it is for an oncologist to treat it. And so, the outcome very much depends on the stage. To a certain extent, certain cancers will be more sensitive to chemotherapy than others and some of them will even at an advanced stage can respond, with long-standing responses, to the chemotherapy or just occasionally immunotherapy. But most of the time, it's primarily if you're going to want surgery, and you're going to do better if you have a stage one or stage two, especially if you have stage one where it's confined to the lymph nodes. When we see people with stage one, pancreatic cancer, their long-term survival is really terrific, five-year survival- 80% plus 10-year survival, well over 60 percent. And we think these figures are slowly improving. Pancreatic cancer survival has been improving slowly over the last decade or so. Some of that is related to early detection. Some of its related to improvements in outcome. It's a deadly cancer, for sure. But if we get it at stage one in particular, people can do tremendously well. And we're still hoping that additional improvements in therapy will continue to make improvements in long-term survival for people with more advanced stage disease.

RK: Well, that's great to hear that outcomes can be good in the early stages of the disease. And it sounds like the key is to detect it early, as you talked about. And it sounds like much of your research is focused on early detection of pancreatic cancer. And I wonder if you want to talk about that research, just briefly, for those who are listening to understand what's coming down in the horizon. What's being looked at?

MG: Much of what we have done has been both the following of patients who are in high risk and undergoing surveillance and monitoring them carefully, ensuring that they get their scans, typically annually. That's for that small group of people who have these much higher risks than the average risk, even the risk of somebody with diabetes. The average risk of pancreatic cancer is a lifetime currently is 1 in 57 or some numbers such as that. If you have diabetes risk increases, some, it's still probably on the order of less than 1 in 40, or some number like that; it's still a relatively low number compared to many other cancers and many other problems that people with diabetes can suffer. The people who we follow in clinic often have a 10% roughly lifetime risk based on their more extensive family history and genetics. That's a lot of what we do and just following our cohort over a long period of time to show what the outcome is of surveillance, such as these stage one survival results. The research is focused on: Can we do better with adding blood tests to scans? Can you develop better scans? What is an optimal blood test? That's been quite a challenge because people need a blood test that isn't going to generate a lot of false positives, and yet is going to be able to detect the small early cancers. Blood tests haven't been used as a standard, as of yet, for our surveillance that we do in the clinic. Although we do have a clinical trial looking at one of our blood tests, but may become part of our standard in the coming years. We believe that will mainly be in the context of annual surveillance with scans, like your MRI scan, or your endoscopic ultrasound and then maybe in between having a blood test. Some of the blood tests that are used, that are being evaluated are for pancreatic cancer results, such as these DNA-based tests, that they may have a role as well. So, there's a lot of interest in trying to get these tests performing accurately enough. And the challenge for the blood tests is to be able to detect certainly for pancreatic cancer, small, highly curable cancer, not a cancer that we detect a little bit earlier, but not enough to cure, or at least have a reasonable shot of cure. So, in the clinic, the scans remain our mainstay of work. But for a lot of people, if you could do regular blood tests- if you missed a scan, but you could rely a little bit more on blood tests, that would be tremendous. And we've been making some progress there, I think. We want to be able to offer a good test to our patients. We're still evaluating, as I say, in a clinical trial.

RK: That was so exciting to hear about all the different research that you're doing. And I agree, having a blood test where you could detect your risk of cancer, that would be phenomenal, maybe a goal for the future. But really, it sounds like a lot of really neat things that that you and your colleagues are doing. So, congratulations, and thanks for sharing that with us.

You did mention about treatment for pancreatic cancer, and we won't go into the details of chemotherapy. But the surgery that can be necessary to treat pancreatic cancer can sometimes lead to diabetes itself as well, isn't that right? I wonder if you could talk about even if people who don't have diabetes initially, but have pancreatic cancer and then have surgery for pancreatic cancer, why would those people develop diabetes?

MG: Yes, we have to remove typically roughly half the pancreas and in pancreatic resection for cancer management. Sometimes, if somebody has a reduced reserve in their pancreas and their reduced ability to generate enough insulin, removing half the gland can induce diabetes when it wasn't present before. But actually, the opposite also happens. One of the things that happens when, we mentioned this earlier, that new onset diabetes associated with pancreatic cancer, the tumor affecting how the pancreas is functioning normally. And so, it's not unusual for people who have diabetes at the time of the pancreatic cancer for that diabetes to actually disappear once a tumor has been removed. We also see that as well. It just reflects the intricacies, as we started, between how we control our blood sugar with normal pancreas and how that can be affected by pancreatic cancer.

RK: Yeah, that's true, that perhaps shrinking the tumor may actually help in some people with diabetes, related to their pancreatic cancer. And I know clinically we often see in the hospital people who've had pancreatic surgery, such as the Whipple surgery, which is a type of pancreatic surgery, or just maybe even part of the tail of the pancreas removed, or we call it distal pancreatectomy, who then developed diabetes. And as you said, usually people who have low reserve or other risk factors, maybe they had prediabetes beforehand. And it is a type of diabetes such as the Pancreatogenic diabetes, we talked about related to pancreatitis where the management might be a little bit different. Often, we find that these patients need insulin, because they're not making insulin on their own with the absence of that tissue that's been resected. But nonetheless, if it cures or helps or pancreatic cancer, it's a necessary surgery. So, we have ways of managing the diabetes that occurs, post pancreatectomy for sure. One of the things we haven't talked about and has been a hot topic over the past few years, is some of the newer classes of medications for diabetes that have been approved and potential concerns that some of them may damage the pancreas in some way or lead to an increased risk of pancreatitis. I wonder if you could fill us in on some of the debates that have been out there and your thoughts?

MG: Yes, I agree. It's an important topic; the GLP-1 receptor agonists and the DPP-4 inhibitors that have shown such tremendous promise in diabetes control and weight control. And this was an early concern when the medications first came out, and thankfully the story has been quite reassuring. Some of the initial concerns about the medications included that they could induce pancreatitis, even that they could induce pancreatic cancer. This was something [that] was watched very closely in the early years. These drugs are now out in clinical use for a decade plus, and they were studied extensively in clinical trials trying to address this safety concern. Some of the reasons for that initial concern had to do with the rarity generally in the population of pancreatitis, pancreatic cancer, and also that while these drugs have an effect on the normal pancreas to a modest extent, it doesn't appear that they induce more pancreatitis or more pancreatic cancer as best we can tell. But it does appear as though that maybe these medications can affect the growth of normal pancreas tissue and that can affect the normal level of enzymes in the blood. There is a small increase in pancreatic enzymes in the blood, for example, in people on these medications. That's totally trivial. But when we go to diagnose people with acute pancreatitis, we use these blood tests. It's quite possible that many of the initial reports that looked at pancreatitis associated with these medications, they were either incidental, or in some level, this was a factor. We actually studied this in the pancreas tissue, a little bit to look at and see if maybe these medications might have a role. But we couldn't see, at a kind of a tissue level, any clear mechanism as to why these medications would promote pancreatic cancer. Many of the studies were done. Some of the initial studies were, like a lot of studies, maybe not optimally done. The bottom line is as to date, all the meta-analysis of clinical trials are not finding an increase in either pancreatitis or pancreatic cancer. I think this is going to be something to continue to be looked at. Especially the pancreatic cancer, because that is a problem that plays out over many years. But the initial concern was based on, for example for pancreatic cancer these kinds of adverse event reporting, so when someone takes a drug, and six months later, they have pancreatic cancer, which doesn't fit in any way with how cancer develops. So these were kind of like initial spurious associations. On the other hand, there's every reason to believe that perhaps these medications will have major benefits in terms of cancer reduction across multiple cancers because of their ability to control, whether it's the obesity and the high insulin, other negative aspects of having diabetes, also with metabolic syndrome, these medications are predicted to help. And so that's still going to take time to fully determine what those benefits versus risks are. But I think it's basically a nonstory. And so, people shouldn't be concerned about taking these medications for pancreatic cancer, or pancreatitis risk based on the current evidence, and I don't think that's going to change.

RK: It is a complicated story. But I agree. The bottom line is that some of these initial concerns, perhaps some are spurious. And, as you mentioned, people with diabetes already have a higher risk of pancreatitis. And so now to tease out whether it's a certain medication class...

MG: Yes.

RK:..such as the GLP-1 receptor agonists, or whether it's related to the underlying risk, or even other risk factors, that people even without diabetes [have]. It made it a bit more complicated to disentangle but by in large, I agree these agents have been in the market now for more than a decade and we're learning more and being more reassured regarding really no increased signal for pancreatitis that we're seeing in recent reports. But still, I think, it's an open question and one that we continue to follow for sure, with our patients.

Well, we've covered a lot of ground today, we've gone through a lot of great information and one of the questions that often comes up is how can I reduce my risk of developing this complication? What can I do to prevent from having in this case, pancreatitis, or pancreatic cancer? We know as you mentioned that it can be related to obesity. So, do you think keeping people at their target weight might be a way to best optimize their chances of not developing cancer or pancreatic cancer in particular? I wonder if you just have some parting words for our audience and what they can do to ensure that they continue to monitor their potential risk and reduce their own chance of developing pancreatic cancer in the future.

MG: No, not an easy question to address. On the pancreatitis side first, thankfully, pancreatitis is a relatively uncommon condition. One of the ways in which pancreatitis can develop in people with diabetes is through gallstone development, which is more common in people with diabetes, and can occur in people who undergo significant weight loss. For example, this was seen with bariatric surgery. Any significant major inducer of weight loss can result in, even with all its good benefits, will not infrequently cause gallstones, which only occasionally will cause pancreatitis, only very occasionally. But that's just something to be aware of. Management there can be helpful. In terms of pancreatic cancer, what we have are the SAMSA cancer prevention, screening, or an early detection of pancreatic cancer. And that's being aware mainly of your family history. Some years ago, we began looking at the prevalence of inherited variants in people who develop pancreatic cancer, and we generally find that across pancreatic and other cancer is that you're more likely to carry one of these deleterious variants than if you don't have one of these common cancers. And so the recommendation came along that if you have pancreatic cancer, then maybe you should be getting at least offered a gene test to look at your risk. And maybe often, since a family member may not be able to do that, when they develop pancreatic cancer, maybe their first relative as well. So, a small percentage of people with pancreatic cancer or their first relatives will have these significant gene mutations. And that then triggers changes in how you do your cancer prevention screening. And so being aware, both of your family history of pancreatic cancer and of whether it would be appropriate to one of these panel tests, is important. We have a very large family registry here called the NFPT, the National Familial Pancreas Tumor Registry. And so, we've been trying to identify new genes that are important in pancreatic cancer risk and studying families and understanding family history here at Hopkins. So that's something to be aware of, beyond that, is there an optimal diet? Is there an optimal exercise regimen? The evidence would point to, like it is for a lot of things, we need a lot better data on this. Your diet affects so many things; your gut microbiome, etc. We're trying to understand how these things affect pancreatic cancer risk. As best we can tell, a heart-healthy diet, and the exercise regimens and healthy sleep, patterns that contribute to so much health, whether it's diabetes or heart-healthy; we think based on risk factors may be helpful in reducing that risk. But it's not based on the kind of extensive data we would like. But we do think that is the optimal diet. As for kind of cancer prevention medications or other things, we had a vaccine trial, for example, we're not at a place where we can be offering cancer prevention type medications. When people have certain risks, we offer them long-term surveillance with imaging and maybe blood tests, would be a factor. But beyond that, it's these general health guidelines that you probably offer your patients every day.

RK: Yeah. Absolutely what you're talking about, it just reinforces that healthy behavior, smoking prevention, as you mentioned, another reason not to smoke. But so much that we don't know and hopefully we'll know more in the future about ways to prevent it. But for now, awareness and knowledge and communication with your healthcare provider for further surveillance, if needed. It sounds like those are the keys to ensure that you get the appropriate treatment if needed. Dr. Goggins, thank you so much for being with us today. We truly appreciate your expert insight and all the information you shared. Thank you.

MG: Thank you, Rita. My pleasure.

RK: I'm Dr. Rita Kalyani, and you've been listening to Diabetes Deconstructed. We've developed this podcast as a companion to our Patient Guide to Diabetes website. Our vision is to provide a trusted and reliable resource based on the latest evidence that people affected by diabetes can use to live healthier lives. For more information, visit hopkinsdiabetesinfo.org.

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