

EPISODE 34: DIABETES & STROKE

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.

Today, we are pleased to speak with board certified cerebrovascular neurologist, Dr. Michelle Johansen, who will be speaking to us about diabetes and stroke. Dr. Johansen is an associate professor of neurology at the Johns Hopkins University School of Medicine and associate faculty in the Bloomberg School of Public Health. Dr. Johansen focuses her research on the heart brain connection, specifically with regard to stroke etiology in order to allow earlier diagnosis and ultimately prevention of embolic stroke. Dr. Johansen has already established a relationship between cardiac markers of health and brain changes in her patients at Johns Hopkins, as well as large community-based population studies. She also has been recognized for her work in understanding the vascular contributions to impaired cognition in patients with heart disease. She's the inaugural Guy McCann associate professor of neurology. Welcome Dr. Johansen.

Dr. Michelle Johansen, MD, PhD: Hi Rita. Thank you so much for having me.

RK: We are so excited to have you on the podcast today. I wondered if you could start off by just telling us what is a stroke and what are the different types of strokes? .

MJ: Sure, I'm glad that you started with this question because a lot of people know a lot about disease states, for example, a heart attack. If you went out on the street in Baltimore and you said, "What's a heart attack?" most people would be able to describe to you in some form or another what a heart attack is. But a lot of people struggle with a stroke. And even when we do a great job educating our patients after they've had a stroke, when they come back to see us in clinics, sometimes they're still not sure what a stroke is.

A stroke is normally thought of as, "cessation of blood flow to a specific part of the brain for a period of time." That's the simplest way to think about it. That can happen as a result of a clot that embolizes and goes to the brain and causes stroke, most commonly being a cardiembolic stroke, and that's the area that I do research in.

It can come from some of the very small blood vessels of the brain that get damaged over time. For example, in diabetes, those are small vessel strokes are called lacunar disease; that's another type of stroke. It can come from plaque that builds up in the carotid artery, for example, and that can break loose and go to the brain.

That's an example of a large artery stroke. Those are the big three buckets. Then we have strokes that are called cryptogenic strokes where we're not quite sure of the cause. And there have been other subsets that have come out from that, for example, "ASSUS" -symbolic stroke of unknown source, you can have strokes that are in the venous system.

So, you can have clots in the veins of the brain and that can lead to a venous stroke. You can have dissections, which are tears in the blood vessel wall. Those can lead to strokes. You can have strokes in the setting of cancer or infection. These are the different, some of the simple big buckets that we think about stroke, but not all stroke is the same, and that's why it's really important to figure out what caused the stroke.

RK: Wow, it seems like there's so many different, kinds of strokes and different ways that blood flow to the brain can really be affected and contribute to a stroke. How common are strokes in the general population?

MJ: Sure, we talked a lot about ischemic stroke and I'm focusing on ischemic stroke because this is for patients who have diabetes and ischemic stroke is the most common type of stroke for people who have diabetes. But there's also bleeding types of strokes. For example, hemorrhagic strokes are where people have brain bleeds. You can have subarachnoid hemorrhage, which is where you have rupture of an aneurysm and that results in blood in the brain.

We're very proud of the fact that in the United States now stroke is the fifth leading cause of death. It used to be much higher than that, but across the world globally, stroke is still the second leading cause of death, but is a huge, massive public health problem and normally falls right behind cardiac disease across the world. And then here in the States, now it's below accidental trauma and some other types of deaths.

But stroke is a massive problem and there's certain things that we can do about it to prevent a stroke, particularly within a certain period of time after someone has acute onset of stroke symptoms. If they get themselves to an emergency room, there's things that we can do about it in a very acute period of time.

RK: It sounds like, it's quite common, unfortunately, as a source of early death or morbidity in many parts of the world. And though it's gotten better in the United States, it sounds like it's still one of the top five causes. How is stroke related to diabetes? I feel like we talk a lot about diabetes and heart disease and cardiovascular risk factors. How do strokes relate to the risk of cardiovascular disease in people with diabetes?

MJ: Yeah, I think it's a continuum. I think that you can think about diabetes causing cardiovascular risk, what's in results in stroke. But I think you can also think about diabetes probably having a direct mechanism besides just vascular risk that leads to damage to those small blood vessels in the brain.

As you know, diabetes is a complex disease and diabetes is associated with lots of other vascular risk problems and normally come in pairs like high blood pressure. People who have diabetes are, tend to have higher rates of obesity certainly have higher rates of heart failure, those sorts of things. And all of those can cause strokes, but. There has been data to suggest that those high glucose states that diabetics experience are not good for the structures of the brain. Diabetes in and of itself, even though it's paired with those other risk factors, is known to be an independent risk factor for stroke. And that's through that high glucose concentration, it's not good for anything. And that includes the blood vessels and structures of the brain. When we do PET scans looking for cancer, people usually ignore the brain. And the reason for that is because PET scans use glucose or a glucose-based tracer, and the brain is constantly running on glucose. It takes it up. It's important to think about what that high state of glucose throughout your body is doing, particularly when you're thinking about stroke and stroke risk factors.

RK: What I recall, glucose is a very important energy source in the brain. Is it not?

MJ: That's exactly right. that's why when you're doing scans of the brain, you can certainly use PET for the brain. Absolutely. But my point being that glucose is such a high energy source and your brain is constantly drawing energy. That's why it's so sensitive to perturbations or loss of oxygen. You can restart somebody's heart. You can transplant a kidney, but for the brain within seconds, when you have clots or whatever else is causing lack of blood flow to the brain, you have instantaneous damage and instantaneous dying of brain parenchymal tissue.

RK: Sounds like all the more reason to really notice the symptoms promptly given how acutely or how suddenly these symptoms can occur.

Just before we move on to talking a little bit more about treatment, you talked about risk factors such as high blood glucose, which clearly in people with diabetes, we work to lower, to individualize targets, to reduce many complications. And it sounds like for stroke as well, really keeping the glucose at target can, can really help reduce the risk of adverse impacts on the brain. What other cardiovascular risk factors can contribute to stroke in people with diabetes? How about high blood pressure and high cholesterol?

MJ: Yeah, Rita, that's a podcast in and of itself. And there have been books and papers and I mean, we could fill my whole office with research in this area. The very short answer to that question is that absolutely – yes. So high blood pressure can cause stroke, obesity, like I already said. If you are doing behavioral things that led to the diabetes in the first place, if you are drinking alcohol, if you are eating too much fatty foods, therefore leading to high cholesterol, if you, and then also high triglycerides, if you have lack of physical activity, all of those things that I'm sure you've talked about before on your podcast that are cardiovascular risk factors or risk factors for stroke.

RK: And how much more common are strokes in people with diabetes versus without diabetes?

MJ: The proportion of patients who have strokes are certainly higher among those that have cardiovascular risk. And because diabetes is so tightly linked to cardiovascular risk, then we know that stroke is much higher among people who have diabetes compared to those that don't. Like you said, pulling out the absolute, increase risk for someone who has diabetes is a little tricky because it's obviously dependent on the patient who's sitting in front of you. And a lot of those risk factors go together. You talk about metabolic syndrome in the field of diabetes all the time, but we know that the proportion of patients who have, for example, lacunar artery disease and have lacunar strokes, almost all of them have diabetes. Very specific to some stroke mechanisms, but just globally with regards to stroke, diabetes, patients who have diabetes, much, much higher risk of having a stroke compared to those who do not.

RK: Yeah, we definitely talk about the higher risk of the micro- and macrovascular complications as we talk about complications in the small blood vessels and then the large blood vessels of the body and certainly just like the heart, the brain is one. We probably don't screen for as well as we should in our own primary practices or even in our endocrine practices, but certainly one

that can cause, as you said, suddenly acute morbidity and acute symptoms as well. Are there certain locations in the brain you talked about lacunar strokes for those who may not be familiar with what part of the brain that is? I wonder if you could talk about whether there are certain parts of the brain where people with diabetes may be more likely to have strokes.

MJ: Yeah, I would honestly say that probably all parts of the brain are open for discussion for someone with diabetes and the reason for that is because, it depends on the risk and the contribution of the risk to the patient sitting in front of you.

MJ: Diabetes is associated with lots of things. If someone has diabetes, and they also smoke and are obese, then chances of having damage to the small blood vessels of the brain, which are deep structures, are higher. As a result of that, you can get strokes in the brainstem, and you can get strokes in those deep structures in the brain, and they usually control motor function on one side of the body and sensory function on one side of the body. They're referred to as pure motor strokes or pure sensory strokes. That's a very simplified overview of that. Patients with diabetes, however, can also have other things that can cause strokes. Patients with diabetes can have poor cardiac function, which can predispose them to atrial fibrillation. They can end up with a cardioembolic stroke just like anybody else. Patients who have diabetes can have high cholesterol, eat the wrong kinds of foods, which is what led to the diabetes in the first place, and also smoke and then end up with plaque in the carotid artery and have a large artery stroke. That's why stroke is not just cut and dry. It's not because someone has diabetes, they're going to have this kind of stroke. It all interplays together. But if you want to think about lacunar, those small vessel disease strokes, which patients with diabetes certainly have a high risk for those, would tend to affect the deeper structures of the brain and or the brainstem. And the brainstem is important for cranial nerves. It's important for the way your eyes move, for example, your swallowing capability. All of those important structures are in the brainstem. Even though the blood vessels themselves may be small and feed a smaller area of the brain, those strokes can also be very devastating.

RK: Wow. That's so interesting to hear about how many different parts of the brain can be affected.

And then also those deep brain, that the brainstem strokes that you talked about too, that are much more common in people with diabetes. Talking now about the signs and symptoms of stroke, what should a person with diabetes be aware of as a warning sign for a stroke?

MJ: There are the warning signs and symptoms of stroke all localized to the area of the brain that the patient is having the stroke. If you have a stroke going on and the part of the brain that is responsible for your speech, then you're going to have a condition called aphasia where you have problems with your language.

If you're having stroke in the part of the brain that controls your face, then you're going to have weakness on the contralateral or opposite side normally, if it involves a cortex or ipsilateral side, if it involves the brainstem, which is the same side of the face. All of those things are how we localize the lesion, which is what we teach our neurology residents to do, which means a patient is sitting in front of you, if you're a good neurologist, you should be able to do a physical exam and tell me exactly where that stroke is happening.

Because if you use your physical exam and do a good neuro exam, we can figure it out, which is unbelievable, and one of the reasons why I love neurology so much. If we're thinking about specific to patients who have diabetes.

The signs and symptoms that I teach for stroke are the signs and symptoms that everybody should know. There's a little mnemonic that I use. It's called BE FAST. And the emphasis there is on time. As soon as you notice anything that's not quite right, you don't want to sit around and wait. Now people say the lines at the emergency room are horrible. I understand that. But if you say the word stroke, they will quickly get you to an evaluation because they realize once again, there are things we can do within a short period of time.

So what are those signs and symptoms? If you have weakness of one side of your body, your face and your arm particularly, can also involve your leg. If you have lack of sensation on one side of your body, face, arm, and leg. If you have difficulty getting your words out. If you have sudden loss of vision, particularly part of your vision, and it's in the same side of your vision in both eyes, That is concerning for stroke, or if you have loss of only vision in one eye, that's concerning for stroke. If you have balance problems, meaning all of a sudden it was like you got hit by a train and you can no longer walk, that's concerning for stroke. If you have difficulty getting up out of a chair, you feel so profoundly dizzy, you have a headache, you have nausea, vomiting, unlike anything you've ever experienced before.

That's concerning for stroke. that's a way that we think about signs and symptoms of stroke. And it's also involvement of those cranial nerves like I talked about before. Stroke is pretty hard to miss. Normally what people think is, "Oh, I just hope that it would get better." They have weakness on one side and just something is wrong, but I just hope that it would get better. And that's where the delays come in getting treatments.

RK: That's really interesting. Some of the signs and symptoms you described. It could happen with other conditions as well, but it's that suddenness, it sounds like, of the symptoms and signs and the fact that it doesn't go away, the numbness like you talked about.

MJ: Certainly things can present like a stroke, but stroke is different in that it normally only involves one side of the body. If you have spinal cord problems and you have back problems, you're going to have weakness in both of your legs. If you have some sort of neuropathy problem, you're going to have numbness and tingling, carpal tunnel, usually involving both of your wrists from typing, for example.

Stroke is unique in that it normally lateralizes only to one side. There's very few things that cause you to have weakness in one side of your face and one arm. That's pretty distinctive of stroke. Especially if you're not sure, get evaluated because people will be able to figure it out if you're having a stroke or not. And even if they're not sure. The things that we do for you are normally very safe in people who have stroke mimics. Let's say you have a horrible headache, but you have a history of migraines. It's unlike your typical migraine. You're seeing things in your vision. You're not quite sure what's going on. Get evaluated because if we do something like give you an IV thrombolytic, which is a very strong blood thinner we can give to patients within a certain amount of time after the onset of symptoms, normally those patients are fine, even if it does turn out to be a migraine.

RK: That's really helpful to have that tip that it's the unilaterality or the asymmetry really on the one side that is a real big tip off that it could be a stroke and that, even if it's a mimic, like you said, it's a migraine or something else that the treatments are relatively safe, even just to be assured that it's not a stroke and to present to the emergency room. Among people with diabetes, are there certain individuals that are at higher risk of stroke, for instance, longer duration of diabetes people who have higher blood sugars or A1C or, for instance, I saw a person in my clinic just the other day who came in with a very high blood pressure that she had not known 190 over 130. And we started talking about the symptoms of stroke to be aware of just with that high level, what, what are the risk factors among people with diabetes who would be at higher risk for stroke?

MJ: In general, like we talked about before, if people who have diabetes are more likely to develop heart disease, as a result of that, that would make them higher risk. There's been literature to show that the more vascular risk factors that you have, they kind of stack on top of each other, the higher your overall risk of stroke. And some of those risk factors act together and they sort of have a kindling effect, which I'm sure you've educated your diabetic patients about a lot. The connection between diabetes and stroke obviously relates to how your body handles glucose. Clearly somebody who is a raging diabetic, poorly controlled, that patient is going to have much more risk of having damage to blood vessel structures because the body cannot keep up with that glucose that's floating around in the body.

In order to kind of think about how you would lower your risk of stroke, in general, you would want your A1c to be lower. Patients who have lower A1c's normally is going to have a lower average blood glucose for the past however many months. That's a good thing. Blood pressure for patients who have diabetes should be absolutely normal intensive, less than that 140 over 90 and even that target has started moving down. Cholesterol should be well controlled for patients who have diabetes. Nobody should be smoking. That doesn't matter if you're a diabetic or not. Thinking through all those things that we normally recommend for patients just to prevent stroke anyway, are the things that you would absolutely emphasize for somebody who has diabetes.

RK: Are there any differences across different sexes, men versus women, across different ethnicities, or even age? Is it only in older age that we'd see strokes, or could it occur at any age?

MJ: Yes, yes, and yes, once again, that's a whole topic in and of itself. Patients who are older age are normally at higher risk because age is an indicator of risk.

The older you get, the more likely you are to be on multiple medications, the more likely you are to not be meeting your exercise target, the more likely you are to have gained some weight, the more likely you are to have multiple vascular risk factors just as a result of being older. But we know that while age is a good moniker for how healthy someone is, that we always see the exceptions to the rule.

You have your patient who comes to clinic who's 42 years old who looks like they're 80 and you have your 80 year old who comes to clinic who acts like they're 30. Age is just sort of a moniker for risk. Risk is what really matters. Men and women do vary, with regards to the way that you think about vascular risk, meaning some risk factors track more with women. Unfortunately, there are more women who are obese than men. But that doesn't necessarily mean that men or women are at higher risk of stroke. We do know that more women are living with stroke, but we also know that more women live longer. There's a lot of research going on in estrogen and how that contributes to stroke. We know that when women who are

supplemented with estrogen, that hormone replacement therapy, we stopped doing that because that increased risk for cardiovascular disease and stroke. There's a lot of research going on in that area about how hormones, et cetera, modify stroke risk. But in general, regardless of whether or not you're a man or a woman, your signs and symptoms of stroke are pretty much going to be the same. Now, sometimes women have more subtle signs and symptoms, but those are the same signs and symptoms you should know for stroke. Stroke is no respecter of persons. It does not matter what race you are. There are some conditions that march along with race. For example, just like we talk about sickle cell being predominantly in African Americans or in people of African ancestry. Obviously that's a unique risk factor for stroke, just like someone who's from Northern European ancestry. We can have inheritable genetic diseases that predispose us to having stretchy blood vessels. Sometimes disease states march along with race, but stroke is no respecter of persons. While there may be some differences between things just based on risk factors, it doesn't matter who you are or where you're from. You can have all the money in the world and have a stroke. You can have no money in the world and have a stroke, and that's why it's such an important disease to recognize.

RK: That's really important to emphasize and thank you for going through that. Really anyone, it sounds like with diabetes, could be at a higher risk for stroke. Understanding the factors that can increase your risk are important, but really it could impact anyone of any background.

If a patient goes to the emergency room with concerns of a stroke, maybe signs and symptoms that they or a family member noticed that seem concerning for a stroke, what are usually the next steps for diagnosing stroke? What kind of tests are done? And then what are the usual treatments that are done in the hospital?

MJ: That question has three parts. If you want to invite me back three more times, we can talk through them in appropriate detail, but if you have any doubts go to an emergency room and they will treat you according to your symptoms. So once again, as a neurologist, you should not have to need an image. You should not have to have any additional tests. You should be able to make a clinical diagnosis of stroke based on the patient sitting in front of you. That's what we always did for years and years before we got super fancy and started MRI'ing everybody. I just gave a lecture this morning to a wonderful group of neurologists in Zambia. They do not have the resources that we have in the United States and in Europe. They have to figure these things out clinically. The first thing that should happen if you arrive to an emergency room is they should quickly say, Oh, you're looking like a stroke. And you should have a rapid evaluation, either by an emergency room physician or an internal medicine physician or neurologist, and they will activate an alert. That alert says all hands on deck. People come running from everywhere to do very quick evaluations of you to see what your signs and symptoms are. If you meet certain criteria on a score that says this is looking like a stroke, we're automatically going to start talking to you about treatment, even before we do any of the tests, because once again, it's a clinical diagnosis. Frequently you'll get a head CT, which is a CAT scan. That's a rapid evaluation to make sure there's no blood in the brain. That would be a contraindication or an exclusion from me administering an IV medication that is a clot busting medication either called IV tissue plasminogen activator, or now we have a newer one called tenecteplase that will bust up clots in the brain and enable blood flow to be restored to the brain. There are certain things that we rapidly evaluate for, "Are you on a blood thinner? If you're on a blood thinner, I can't give you another blood thinner. Do you have blood in the brain? That's a contraindication. Have you had recent major surgery that if you were to bleed from that site would be catastrophic?" There's a whole list of things that we go through. "Are your platelets zero?" Those things we always evaluate for, but we don't rely on an image or a test to say, "aha, you have stroke."

Once again, it is a clinical diagnosis. After we sort of go through a rapid evaluation to decide whether or not we're going to treat you with a thrombolytic, then we start looking at the blood vessels. We look at the blood vessels because, there are procedures now called thrombectomies, or mechanical thrombectomies, where there is a guide wire and a wire that you can see using x ray technology, using an angiogram is what we call it, where you can thread this wire up through an artery in the groin or going into the radial artery in your wrist. We can go all the way up into the brain and we can actually pull the clot out. If I give you a medication that's a clot busting medication, the clot does not resolve, your symptoms are not getting better. Or even if I can't give you that clot busting medication, you still may be eligible for this procedure. It really started coming to fruition around 2015 and it has exploded now. We have even more research supporting how efficacious this procedure is. And once again, we can only do it for certain patients within a certain time window. The reason time matters so much for stroke, is because if the brain dies off, that brain becomes a nasty wet sponge, which means it is very sensitive to perturbations in blood flow and it likes to bleed and the tissue is damaged, beyond repair. Your body is constantly trying to save the brain. The brain is the number one organ that your body is trying to save. But once it goes past a certain point, your body can't do anything to save it anymore. That's why time really matters and why these procedures we can only do to a certain point, because past that point we may actually cause more harm than good.

If there's already irreparable tissue damage in the brain, and I go up with a catheter to retrieve a clot, that could actually cause more problems. All of these things are rapidly evaluated when you come to an emergency room. And then after that acute period

is over, then do we start looking and doing more testing for what's going on with your heart, what's going on with your blood profile, have you been ill, and all those other things. That happens after that acute time period, because we recognize, as clinicians, that there's a time period that if you miss it, it's gone.

RK: That's neat to hear about all the newer ways to really treat a stroke and also the thrombolytics as well, and all the options that are available if presenting or coming to the hospital in a timely manner, when you say that time is important, are we talking about minutes? Are we talking about hours? Could you give us a sense of that window knowing that it might vary?

MJ: Every minute counts, literally every minute counts because we have shown that neurons die in minutes. Now, when we're talking about treatment windows, standard treatment window for giving an IV thrombolytic is about three hours. In certain patients, we can go out to four and a half hours and then pass out; I can't give you a thrombolytic anymore. For the thrombectomy procedure, we can now go out to even about 24 hours after the onset of symptom, but I do not recommend that. The faster you get to me, the better your outcomes are for both the thrombolytic and the thrombectomy procedure.

RK: That's really important for our audience to hear that really every minute counts. I liked how you summarize that, that even though some of these procedures can be done within a few hours for even up to a day, it sounds like the sooner the better. And getting to the hospital is the most important thing. After someone has been treated for a stroke, clearly it depends on when they presented and where the stroke is and how big the stroke is. But what is the recovery like? Do most people can even make the statement to most people recover from strokes or what does the long term outlook look like?

MJ: That is a hard question to answer with a generic statement, because like you said, it is a stroke by stroke. Literally every single patient, it depends. It depends on how much stroke burden there is, meaning how big the stroke is. The bigger the stroke, the worse you do. It depends on what structures of the brain were involved. Some of them have other areas of the brain that can also do that function. Some of them, there's only one area of the brain that does that function. And if it's damaged, it's much harder to recuperate from. Things like motor recovery, while it can be absolutely devastating, you can work on walking and you can work on using your arm again and the assist device that we have for those types of things are better than someone who can't talk. If you're cognitively impaired as a result of a stroke, that impacts everything, including your motor recovery. And the burden from that stroke may be a tiny little lesion, but it may hit an area of the brain. That's imperative for the way that you think and process and make decisions. I would argue that even though that stroke burden is not large, they may look okay, if they're impaired and cannot talk to you, that's pretty devastating.

RK: Yeah, for sure. To affect an area of the brain that impacts speaking or impacts walking, those are major parts of our day to day quality of life. Do people recover function ever?

MJ: A hundred percent. I'm a big believer in neuroplasticity. I'm a big believer in rehabilitation. There are lots of people doing rehab. I work here at Johns Hopkins and we have lots of neat research things that are going on, constantly trying to get people to a state of a hundred percent. Most patients never reach a hundred percent, but they can get pretty darn close. They can get 99.999 percent there. And they'll come to you and say, Hey, Dr. Johansson, when I'm tired and sick, I don't feel like myself again. Some of my stroke symptoms start coming out. But no one would guess in a million years that they've ever had a stroke. Absolutely, people do recover completely from a stroke. But once again, it depends on the severity, it depends on how big the stroke was, and it depends their vascular risk factors. If you know someone who is otherwise completely healthy and runs and just happens to have atrial fibrillation, they're going to do much better. And a diabetic who's obese, who has a large waist circumference, who's smoking, chewing tobacco, high triglycerides, that patient is not going to recover as well.

RK: Well, it's really encouraging to hear about the possibility for recovery and the ability of the neurons, to grow again, to grow back, to do the function they did before, but again, on a case by case basis, it sounds like in terms of the ability for functional recovery, but still encouraging that that is possible. When we talk about prevention, when we take a step back now and we talk about how can we prevent strokes, and you already talked about, the cardiovascular risk factors, the high blood pressure, the cholesterol, the smoking, really getting those at target, not smoking at all. What about lifestyle such as diet and exercise? We talk about that all the time for people with diabetes. How does that impact the risk of stroke?

MJ: Oh, 100%. I am a huge believer in that. When patients come to see me, I love stroke and I love stroke neurology for a couple of reasons. I love the acuity of it. I love taking care of really sick patients. I love taking care of patients in an ICU, but I also love the long term aspects and counseling of it. I love seeing patients back in clinic that I've seen for years and years and years and, asking me how I'm doing and how things are going and getting to hear their stories. Partnering with people to set goals is something that I try to do on a pretty regular basis. In other words, thinking about how you can set specific goals that are measurable and attainable and realistic and have a time component to them, that S.M.A.R.T. Goal acronym, is really imperative in patients who've had strokes because these are things that they have established. These are habits that are incredibly hard to break. Smoking is one of the most addictive habits that we know. And now they are maybe even devastated from a stroke and slightly depressed. We know depression increases after stroke. And now I'm going to come to them and say, quit smoking, which is the one thing that gives them comfort during a day. That's incredibly challenging. that goes to really partnering with your patient. Giving them hope, never false hope, but hope that they can actually make a decision and change meaningfully and then emphasizing what the American Heart Association, what the American Stroke Association recommends. At least 30 minutes, five days a week of cardiovascular exercise. We are all busy, but it does not matter how busy you are. You can find 30 minutes in your day to get up and move around, to get your heart rate up, and those sorts of things are imperative. Small changes to diet, you may not be able to lose 50 pounds in two weeks, but you can say this week I am going to try to only have one soda this whole week. That's my goal for this week. And then the next week you can say, I'm going to try to not have any sodas at all next week. And then the week after that, you can say, well, I didn't, I actually didn't even really miss those sodas. I feel better now because I got rid of some of the caffeine. This week I am going to try to fill in the blank. So small little pieces to sort of lead them to these goals. Because if you say, "Don't smoke, maintain a healthy diet, exercise every day, limit alcohol, learn to manage stress." I love it that we just throw these things at patients and they walk out, "oh my gosh, how am I going to do this?" We know from trying to make changes ourselves. I'm trying to make a change and do something more productive with the amount of time that I have. I have written that out. I have put it in my phone. I have an alert set for me, right, to remind me that this is something that I am trying to do on a daily basis. if I have to do that with something small, these are things that have been going on for years for patients. Counseling is imperative, as well as emphasizing how imperative it is for their health. This is not just, well, quit smoking because you should. Quit smoking because you have to, you've already had a stroke, your risk of having another one is higher.

RK: Yeah, it's so true. I think all those things you mentioned, all the different factors that can contribute to stroke, it can be overwhelming to think about them all together, but if you break it down to small steps that are attainable on a week by week basis, you can see incremental gains over time. That's so important. And it sounds like the lifestyle modifications, which we recommend for diabetes in general, particularly apply if you will, for stroke as well, in terms of reducing the stroke risk. I wonder if you could comment on any specific medications for diabetes that might've been found either to increase risk or decrease risk in stroke. For instance, I, have come across studies that have looked at pioglitazone or Actos. I'm not sure if that's something that you could comment on, but from what I recall, that they may have protective effects in diabetes. Could you comment on specific medications?

MJ: Sure, no, I'm happy to. You probably know a lot more of the recent literature regarding some of the newer agents that are coming out. Obviously, I'm seeing a lot more patients who are getting placed on GLP-1 RA such as Ozempic (semaglutide) who are trying to lose weight. So, in general, I think the easy answer is the better control of your diabetes, the lower your stroke risk is going to be. I am not aware of any medications that are used for diabetes that increase stroke risk. That's excellent news. Patients who have hemoglobin A1c lowering on some of the newer agents as well as the ability to lose weight, for example with Ozempic, all of those things are going to help them get to where they need to be to lower their stroke risk; we're all on board with that. We work very closely with our endocrinologists at Hopkins to really have a conversation about what's going on. And I appreciate that because sometimes those medications may help my stroke patients get to their goals. I know there's a lot of discussion about who should be on these agents, allocation of agents, resource, et cetera. And as time goes on, as time goes on, there's going to be a lot more data out about what these agents look like for stroke prevention. I anticipate a time when a lot more people are going to be on these types of agents.

Other medications that we use, good old aspirin, still works. Aspirin is wonderful when it comes to secondary prevention of stroke, meaning you've had a stroke, then therefore you're on an aspirin. We use other antiplatelet drugs like Clopidogrel, which is Plavix, Brilinta (ticagrelor), there's other drugs that we use that are antiplatelet drugs in particular cases. We are big fans, I am particularly a big fan of statins and the power of statins. Some of the newer lowering agents that are coming out are also very helpful for getting patients cholesterols to where they need to be. And then finally, anticoagulation if there's an indication- Apixaban, Rivaroxaban, Dabigatran, Edoxaban even Coumadin. All of those things may be useful given the

specific etiology of the stroke, for example, an atrial fibrillation to decrease risk going forward. Once again, all depending on the mechanism and the patient sitting in front of you.

RK: That's encouraging to hear of the role that some pharmacotherapies can have as well, and as you talked about the newer treatments, the SGLT2 class of medications and the GLP1 receptor agonist class, specific agents in those classes that have demonstrated benefits in reducing heart attacks and stroke, but I think it is true that they're probably all lumped together in those studies looking specifically at stroke as an outcome. We probably do need more data, I would think. Would you agree?

MJ: Oh yeah, absolutely. I know I was just at the scientific sessions, which is a big cardiology conference, giving a talk. And some of the drug reps were there and they were talking about how there are trials that are going to come out, looking at some of these agents specifically with regards to stroke risk. Like you said, stroke, unfortunately, in my view, gets lumped in with a lot of other cardiac endpoints. But it's really nice when they focus numbers on stroke because sometimes we don't have enough numbers of patients who have strokes in those populations to get to meaningful outcomes. But looking at some of those drugs in the future going forward, particularly with regards to stroke risk, is going to be very interesting.

RK: Yeah, I agree. And thanks for talking about aspirin. Sometimes old is best and definitely in people with a history of heart disease or stroke or peripheral vascular disease to be on aspirin. What are your thoughts on aspirin as a primary prevention of people who haven't had a history of stroke to reduce the risk?

MJ: Right now, unless you have another indication, okay, and lots of people with diabetes have other indications. But if we're just talking about a purist person. Who doesn't have another indication for aspirin for primary prevention of stroke, there is no evidence. It used to be everybody got thrown on an aspirin and we realized that the risk of bleeding was too high for primary prevention of stroke.

So I'm talking about someone who has had a stroke and also has diabetes, then absolutely aspirin would be indicated in that person. There's some maybe literature coming out about how aspirin might help with cognition in older people. All of that is very soft yet. For primary prevention, there's no evidence for aspirin. For secondary prevention, meaning they've had a stroke, then we do advocate for aspirin.

RK: Yeah, definitely that risk of bleeding that you can see with aspirin, especially in older ages, I think in the studies have been found to be one of the harms, if you will, of using aspirin as prevention in terms of hemorrhagic stroke, having bleeding in the brain. So it's interesting how much our practices have changed over time from really giving aspirin to many people to now narrowing it to a very specific population of people at higher risk. Of, of stroke and heart disease. What about low blood glucose? Can that put people at risk for stroke?

MJ: Normally hypoglycemia is not thought of as a contributor to stroke. I will say that patients who are hypoglycemic can mimic having a stroke. If you have hypoglycemia, you can get behavioral changes. You can be sort of loopy and out of it. Your speech can sound slurred. You may have a sort of loss of consciousness and a fall that could be attributed to a stroke. Hypoglycemia can be considered a stroke mimic.

But once again, if I treat someone who has low blood glucose by accident, let's say now everybody has. finger stick point of care glucose testing in the emergency room, you get an answer in seconds. Chances of me giving a thrombolytic to someone who only has hypoglycemia is pretty rare, but even if I do do it, once again, I've told you that the literature supports that patients who have stroke mimics like hypoglycemia, if we think they're having a stroke and we give them a thrombolytic, they normally do just fine. So you should still go to the emergency room.

RK: Well, that's definitely reassuring. Dr. Johansen, it's been so great to hear all about strokes and prevention and treatment and people with diabetes. I wonder if you have some parting words for our listeners who are concerned about the risk of stroke. What would you say to them in terms of the top things they can do today?

MJ: Obviously the point of this podcast is not to terrify anybody. We don't want to say that just because you have diabetes, you're going to have a stroke tomorrow. That's not the goal here. But the goal is to think about stroke as a condition that you never want to get to. If you have an opportunity to do a better job of controlling your diabetes today, to prevent a stroke in the future, use stroke as a motivating factor. That would be the first thing I would say. The second thing is know the signs and symptoms of stroke, just as we've already discussed on the podcast. And then the third thing is be your own advocate. If you're not feeling well and there's something going on, tell somebody right away, that way you can get help right away. Sometimes, I

hear so many patients who say, “Oh, well I thought it was my diabetic neuropathy.” No, no. If there’s something that’s completely different than what you’ve experienced before, then you should act on that and take that seriously. And come in and be evaluated, because worst case scenario, we turn you away and say you haven’t had a stroke. And I would say that’s actually a good outcome.

RK: Dr. Johansen, thank you so much for sharing your expertise and really underscoring the importance of being aware of the signs and symptoms and alerting those around you and seeking immediate help. It sounds like they’re definitely preventable, but having the knowledge is imperative to prevention. So, thank you so much for being here with us today.

MJ: All right. Thank you so much.

RK: I’m Dr. Rita Kalyani, and you’ve been listening to Diabetes Deconstructed. We 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. Thanks for listening, be well, and see you next time.