

## Podcast 43: Diabetes and Bone Health

**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](http://hopkinsdiabetesinfo.org). Today, we are thrilled to welcome Dr. Kendall Moseley. Dr. Moseley is the Clinical Director of the Division of Diabetes, Endocrinology, and Metabolism; Medical Director of the Johns Hopkins Metabolic Bone and Osteoporosis Center; and Co-Director of the Johns Hopkins Multidisciplinary Parathyroid Clinic.

Dr. Moseley received her medical degree from Baylor College of Medicine in Houston, Texas, followed by internal medicine residency training at the Johns Hopkins Hospital. Upon completion of her endocrinology fellowship at Johns Hopkins, she joined the faculty in the Division of Endocrinology, Diabetes, and Metabolism of the Johns Hopkins University School of Medicine.

Dr. Moseley has a dynamic clinical practice and collaborations within the institution that focus on metabolic bone diseases, osteoporosis, hyperparathyroidism, vitamin D deficiency, atypical fractures, and skeletal survivorship. She is actively engaged in NIH-funded clinical and translational research involving the relationship between type 2 diabetes, osteoporosis, and aging.

She's additionally involved in research investigating mechanisms by which chronic disease states, such as malignancy, HIV, hepatitis C, and cystic fibrosis impact bone quantity and quality. Welcome Dr. Moseley.

**Dr. Kendall Moseley, MD:** Thank you so much, Dr. Kalyani, for having me today. I very much appreciate the ability to talk about type 2 diabetes.

**RK:** We are so thrilled to have you here and to talk about the condition that we don't give as much recognition to as we should in clinical practice, which is the relationship of type 2 diabetes to bone health. I wonder if you could start off by telling us—how does type 2 diabetes impact the bone?

**KM:** I think that that is an excellent question. It's funny when we think about bone disease and, particularly, osteoporosis or fracture risk—I think a lot of us have in our minds a picture of the typical person who's going to break a bone. These are individuals, men and women; we probably think about women more than we think about men, but believe it or not, both sexes can get osteoporosis. Women typically are on the smaller side. We might even describe them as being frail. They are thinner, they have lower muscle mass, and they may look a bit unsteady on their feet. Certainly, walking down the street, you see someone like that, maybe hunched over a little bit, and you would worry about their bone health and worry about their fracture risks.

As time has passed and we have looked at some of these large clinical trials, and we have really worked through some of the data, we realized that individuals who look absolutely nothing like that woman or that man that I just described are at risk. Individuals with type 2 diabetes needing oral therapies or insulin therapies are also at risk for fracture, and they aren't necessarily thin; they're not necessarily frail appearing. When we look at the data, there is this increased risk of fragility fractures. So, these are not something you would have after getting into a car accident or falling out of a two-story building. Rather, we are talking about fragility fractures—falling from standing height or less, slipping on ice and breaking your wrist, or falling backwards and breaking a bone in your back; sometimes even

silent fractures. We are seeing these more in individuals with type 2 diabetes, which has really given us pause to think about the mechanisms when we otherwise were not expecting it. It was a hidden complication of type 2 diabetes that is just now making it into commonplace knowledge.

**RK:** It does sound like, though it may be a hidden complication, a complication that can have tremendous consequences on mobility and movement. Fragility fractures, as you mentioned, we usually think of in older people, but can younger people with type 2 diabetes get this as well? Is this something that can occur across the lifespan?

**KM:** Absolutely. The toughest thing we have on our plates right now is the fact that we are not identifying this very often. Osteoporosis is a silent disease. Oftentimes we do not know our bones are thin until we fall, and we break a bone. We aren't necessarily screening individuals with type 2 diabetes for osteoporosis for the reasons I just mentioned, because they don't necessarily look like they might have osteoporosis. We are not capturing individuals until that first fracture occurs.

As we're thinking more and more about diabetes, and then bone disease as a complication of diabetes, I think we are starting to recognize it as a risk factor for fracture. When we do that and we go back and pore through some of the data, we're finding that, yes, individuals with diabetes—10 years are added to their bone life with a complication of type 2 diabetes. For example, a 55-year-old's bones are more like a 65-year-old's bones when you add on this layer of type 2 diabetes.

**RK:** Wow. It seems really important to recognize and even let people with type 2 diabetes know that they are at higher risk of bone disease. Why don't we talk about this more?

**KM:** I think it's important. I alluded to the screening, and one thing that we really struggle with in this population is that we have a lot of screening tests. In medicine and in diabetes, we've used things like hemoglobin A1C or fasting blood glucose oral glucose tolerance tests to make the diagnosis of diabetes in patients. In the osteoporosis world, where I live, our screening test for low bone density or osteoporosis is traditionally a scan called a DEXA (dual energy x-ray absorptiometry), a lot of words, which is why we call it a DEXA scan. We use a DEXA scan, which is basically a fancy x-ray where we look at the spine, we'd look at the hip, and generally the data that we get from those fancy x-rays gives us this diagnosis of osteoporosis.

It puts people on a curve based on standard deviations. That data is categorized as normal, osteopenia, or low bone density, or osteoporosis. The biggest challenge we face with type 2 diabetes, and this has now been described pretty thoroughly, is that bone mineral density testing in patients with diabetes is generally normal, if not more elevated than in individuals without diabetes of the same age.

We have a very difficult time screening people for bone disease, with osteoporosis, because our x-rays aren't working well enough. We're missing a lot of cases. This has generated a lot of talk as to what's really going on. If the bones look normal on these DEXA scans, on these fancy x-rays, but patients, men and women, are still breaking their bones, what's going on? Why are people breaking their bones despite this normal testing? We would ideally like to not have patients have a fracture before they come and sit in my clinic, and we need to talk about treating their bones. Ideally, we need better screening tests, and that's just under active investigation that's going on right now.

What do we think is going on? Why are people with type 2 diabetes breaking their bones? There are a lot of different thoughts, and there is no one right or wrong answer. Initially, some of the suspected causes, which are still suspected causes, would be things related to diabetes itself.

Maybe they are falling a little bit more; maybe blood glucose levels are dropping, and people are getting dizzy and falling to the ground, or maybe they have peripheral neuropathy, which is causing them not to be steady on their feet, or retinopathy, where you don't see as well and you're more likely to stumble and fall. Those things are not wrong; falls can be increased in individuals with type 2 diabetes mellitus. A lot of these big trials that we look at, where you filter out those risks, we are still seeing this 50 percent increased risk of hip fracture in people with diabetes compared to those without. There is up to a 25 percent risk of any osteoporotic fracture in people with diabetes compared with those without.

Thinking about that, maybe taking those off the table, there's still this risk. Is there a medication-related side effect that we're missing? We know that with too much insulin, you can have hypoglycemia, or with too much sulfonylurea, you can have hypoglycemia leading to falls. Thiazolidinediones (TZDs) are medications we don't use often clinically, but through a cellular mechanism, there can be some bone loss with those medications as well.

There was a bit of rumbling about a category of drugs called SGLT2 inhibitors a few years ago; due to a large clinical trial called the CANVAS Trial, it has been somewhat refuted as time has gone on. So we are using those medications more and more, but again, looking at these same large studies and filtering out patients on those medications, we are still seeing this increased risk. So medications are not the whole story.

What about diabetes complications? Bone is one of them, but there are other organ systems that can be impacted. Kidney disease can thin the bones. Any sort of vascular disease, our bones get a lot of very important nutrients from blood flow. If there's microvascular damage or macrovascular damage associated with diabetes, the bones inevitably will take a hit and don't get the nutrients they need, can thin, and become weakened. We talked about the eyes and fall risks, so again, we have to take that into account.

There can be some hormonal factors that we need to think about too. Vitamin D deficiency is more common in individuals with type 2 diabetes mellitus. There can be growth hormone deficiency and certainly insulin deficiency as time goes on with longstanding diabetes. Even gonadal changes—low testosterone, low estrogen, and our postmenopausal women—can impact the bones.

Then body composition—Dr. Kalyani, you've done a lot of work in this—looking at body composition as we age. We know we're going to lose muscle mass. We know we're going to gain fat mass, but that's particularly prominent in type 2 diabetes, where there's probably fat mass where you don't want it. This is inclusive of the bone marrow fat that can get into the bone marrow and cause changes in bone metabolism. Then loss of lean mass, not only contributing to falls, but bones really rely on lean mass. The push and pull of muscle against bone helps to generate healthy bone; keeping our bones active and rebuilding and remodeling is critical too. So many things at the outset are things we all suspected, and then a whole different category, which I'm happy to get into, is called bone quality, but I'll pause there.

**RK:** That was great to hear all the different factors that could really lead to changes in bone and affect bone health.

You mentioned many, including some medications that we use for diabetes, such as TZDs or thiazolidinediones; those include pioglitazone (Actos) or rosiglitazone (Avandia). Then also, the SGLT2 inhibitor, canagliflozin (Invokana), which there has, been a warning, on the package insert for that medication for potential risk of osteoporosis.

It is good to know about all of these risk factors; if you know that you're at risk, perhaps you can do something about that and be screened for it. I wonder if we could take a step back to talk about the definitions, because I know sometimes, they can get confusing. You mentioned osteoporosis; I've heard of osteopenia; you mentioned fragility fractures, and I know that there are other bone diseases that could also happen more commonly in people with type 2 diabetes. I wonder if you could briefly talk to us about what those diseases are and how they might be diagnosed.

**KM:** Starting with the easy ones, the DEXA scan will spit out a lot of numbers, but probably the ones we pay most attention to would be these things called T scores. A T score is comparing the patient against a 30-year-old. Why would we compare to a 30-year-old? We reach our peak bone mineral density as we age, by the age of 30. The best you're ever going to get, you'll have by the age of 30, and a T score is effectively a standard deviation.

A T score of anything greater than a -1 is considered normal bone density.

A T score of anything between -1 and -2.4 is considered low bone density or osteopenia.

Anything less than or equal to a -2.5 T score in a patient is considered osteoporosis.

It's important we label things, even though, as I'd stated at the outset, individuals with type 2 diabetes mellitus may have normal or low bone density; they can still break their bones. The critical piece of the definition is that those DEXA scores are completely out the window if someone's had a fragility fracture. I don't care if the bones are normal on DEXA; I don't care if they're in the osteopenia range, but if you've had a fragility fracture, your diagnosis is osteoporosis.

Sometimes this can be hard to demonstrate to patients: even though the numbers look great, you broke a bone, you're at risk of breaking future bones, and we need to do something about it. So that would be your spectrum of normal low bone density osteoporosis.

I mentioned osteomalacia, or softening of the bone. This is when we think about how our bones harden. Bones have different components to them: we've got the infrastructure of the bone, the strut work of the bone, keeping our house upright. But to really create good, strong bone, you have to have good minerals in the bone. I think about minerals as the cement of bone; these are things like calcium, phosphorus, and the collagen quality within the bone. Anytime you have deficits or deficiencies in calcium or vitamin D, that mineral, that cement, is soft, and that makes soft bone. You can see where, if there's any nutritional challenges, if there's any vitamin D deficiency, a lot of our patients undergo gastric bypass procedures or gastric surgery, where there may be challenges with getting those essential vitamins and minerals. When the cement just doesn't harden the way that we want it to, we call that osteomalacia, and you can have overlapping processes too. It's not that you fit into

one category or another; patients with kidney disease, all stages, can have alterations or changes in how their bones metabolize calcium, vitamin D, and phosphorus.

The kidneys are really important hubs for how we take in calcium, how we excrete calcium, how we convert inactive vitamin D to active vitamin D, and phosphate handling. As you can imagine, if you mess with that factory, with ongoing kidney disease, you can have abnormalities with all of those important vitamins and minerals for bone health. We can see a lot of changes in bone, ranging from lots of bone breakdown to very little bone breakdown to soft bone with kidney disease.

Then something we're seeing—I hope less of these days, as we've really focused in on glycemic control or glucose control in patients—is when we have longstanding vascular and nerve damage, particularly in the feet, we can see micro fractures and almost collapse of the feet. This condition is called Charcot joint or Charcot foot. This is generally in the setting of longstanding diabetes and some overlap of some of these other conditions mentioned.

**RK:** It does sound like there are a few conditions that could impact the bone where diabetes is involved. We talked a lot about osteoporosis and perhaps osteopenia, but it's really good to hear about the other conditions as they can all have significant impairments on mobility and quality of life.

I think what's sometimes frustrating for patients who develop fragility fractures is when they come into clinic and say, “But I had a normal bone density; my DEXA scan looked normal.” As you've mentioned, it can be hard to detect on the routine tests that we use for the general population. With DEXA, where we do see, if it's 2.5 standard deviations below the norm for a 30-year-old individual, we would call it osteoporosis, but for someone with type 2 diabetes, that might not be the case.

It seems it might highlight the role for ascertaining these other risk factors and screening for them. Is that right? Knowing the limitations of the usual tests that we have, how can we detect those who are at higher risk for these complications?

**KM:** That's a great question and certainly a clinical challenge that we all face. I think it all starts with just getting the word out that diabetes is truly a risk factor for bone disease and osteoporosis. I think a lot of us rely on screening tests to tell us what we need to do clinically. So, accepting that diabetes in and of itself is a risk factor, but then also looking at the whole profile, is there a kidney disease that's been ongoing? Are there medications that might be additionally thinning the bone?

A lot of patients, for example, develop diabetes in the context of other conditions, high-dose steroids for maybe a rheumatologic condition or an autoimmune condition. We know that steroids are hard on the bone for several different reasons, but that should go in the risk factor list in addition to diabetes.

So maybe now you have diabetes, maybe now you have a vitamin D deficiency, maybe now you have low testosterone levels associated with these disease processes, and then maybe you get a family history of multiple fractures, et cetera. What I find most helpful, in addition to just getting the screening test, is to put together a profile of diabetes. Then consider what other things we should be thinking about that ultimately should lead us to worry about fractures or not. Probably the most critical thing is that if there is a fracture, we call it a fragility fracture, if that's what it is, if we detect something incidentally on a CAT scan. Let's say you go for a CAT scan because you've got some chest pain or you think you have pneumonia, and there's a spine fracture on that CAT scan. That's not normal. But really

only about 20 to 30 of those actually make it into the chart as an osteoporotic fracture. They get ignored. It's important for us as physicians, providers, and health care workers to recognize these as real osteoporotic changes, real damage to the bone, and document it as such.

There are little changes that we can make to get a bit of a better sense of fracture risk, even after the DEXA scan. Some doctors will use something called a FRAX calculator. FRAX gives the physician or nurse practitioner an overall fracture risk; a 10-year overall fracture risk, this would be a risk to the spine, the pelvis, etc.

Then a 10-year fracture risk of the hip and using some of the data that comes out of that FRAX calculator. It helps us decide whether or not to start medication for a patient. We can make some adjustments to that calculator because diabetes is not included as a risk factor.

There are other things like age, smoking, steroids, and similar things, but we can make some adjustments to that calculator as simple as checking the box for rheumatoid arthritis. Even if a patient doesn't have rheumatoid arthritis, you could substitute rheumatoid arthritis for diabetes, and that counts then as a risk factor.

You can actually age a patient by 10 years. I had mentioned earlier that it's a 10-year accelerated risk if you have diabetes. Sorry if we make you 10 years older, but that gives us a more accurate representation of fracture risk. You're not taking that DEXA scan at face value. But it is tough, and it's something we all really struggle with, because by the time they make it to my clinic, usually there has been a fracture, which is, my goal is then to prevent future fractures. But on the front lines, where patients have a lot of different things that primary care providers need to address in the moment, unfortunately, osteoporosis risk slides to the bottom of the list.

**RK:** The FRAX score that you mentioned, which I know I've seen on reports for patients that get bone DEXA scans that I order, is reported as part of the readout. It sounds like diabetes should be considered a risk factor sometime in the future, so we don't have to make those educated tweaks to enhance or really give a better indicator of the FRAX score. Until we're there, until diabetes is formally included, it does sound like it's really a holistic assessment of both risk factors and using these different tools to inform clinical care. As you mentioned, people with diabetes are at higher risk of falls already; because of that too, they would be at higher risk in addition to the bone disease of developing a fragility fracture. Just to contrast that, the other type of fracture would be a traumatic fracture, is that right?

**KM:** That's right. So that would be falling from a two-story building or a car accident. If it sounds like anyone would have broken a bone in that circumstance, your 15-year-old child or a 25-year-old college kid, whatever the case may be, is this normal, or is this not abnormal? Sometimes we torture patients by trying to get down into every detail of how the fracture occurred. It is important to understand those fractures to decide if it's fragility versus traumatic, because that is going to dictate a lot of times, if you're going to start treatment and how deep a dive you go into workup for other causes of bone loss.

There are a lot of questions around fractures, but it absolutely should be part of the intake assessment in your endocrinologist's office or in your primary care doctor's office. If there is a history of fracture, that is a traumatic or a fragility fracture; those should be taken very seriously. To impress upon people how serious this is—it is like someone has had a heart attack and not getting the details of a heart attack. You want to know the details because you don't want there to be another event down the road. It is important to get the details and

treat them seriously because the worst-case scenario is there's another one on your watch, and the patient outcome is poor in those more common scenarios that we think about.

**RK:** It sounds like if you've had a fragility or a traumatic fracture in the past, detected incidentally on a radiographic scan, or you present to your healthcare provider with a fracture, that you're at a higher risk of a future one. Is that what you're saying?

**KM:** Absolutely two to three times higher within the first year. If you catch it, and you identify it as an osteoporotic fracture, it's important to intervene on that fracture to make sure there are not future ones. As you said at the outset, Dr. Kalyani, this is a very important disease.

That's the other thing, I probably even should have led with this, but osteoporosis is a big deal. We talk about numbers; we've just spent a lot of time talking about T scores and DEXAs and using all this sophisticated terminology, but why do we care about osteoporosis? In fact, in clinic, it's what I always lead with patients: why are we even talking about this?

Fractures, they're not fun; nobody wants to break a bone, but the problem with fractures is what lies down the road. These are things like pain, immobility, and the complications that come from pain and immobility. We think about blood clots, we think about weight gain, we think about loss of just the things you enjoy doing in life, loss of independence. Then in addition to all of those immediate issues, surgery, infection, risk, et cetera, a lot of times those things can culminate in increased morbidity and mortality. It's the mortality piece. For example, within the first year of a hip fracture, there's up to a 30% risk of death for patients, which is rivaling stroke data and heart attack data. We have to take these fractures very seriously because it's not just an inconvenience; it can be something that leads to someone's death at the end of the day. Unfortunately, a lot of our patients know people or have heard of people who've had a hip fracture, and then within the year, they're no longer with us.

Again, thinking about osteoporosis and bone disease in the same serious way that we think about heart attacks and strokes is very important; we need to get the word out that this is something we should be asking about, screening for, and treating if we identify these fragility fractures.

**RK:** Thank you for going over the "why do we care?" There are lots of reasons to care, and I know you and I have both seen, unfortunately, the devastating consequences after a hip fracture, a spine fracture. There can be a downward spiral, especially if you have other medical conditions or aren't able to bounce back as fast. It is a long road for some people to rehabilitate and get back to their baseline if they're able to, which is all the more reason to prevent these from happening in the first place.

Really what we're talking about here today includes quite a few risk factors that can lead to bone disease. I wonder, specific to diabetes, you've done a lot of research in this area too, but what about blood sugar levels and management of diabetes? How does that impact bone health? You mentioned bone quality before, so perhaps you can talk a little bit about that. What do we know about the role of glycemic management in protecting our bones?

**KM:** That is a great question because it's that next step in how we think about bone because I said at the outset, we're missing something. The fact that the bones look pretty darn good on DEXA scan, the amount of bone that we see on DEXA scan, is falsely reassuring. So, we feel good about the scan, but patients are still going out and breaking bones. That's bone quantity.

That's how much bone you have. It's that fancy x-ray that says you've got X amount of bone, and it looks sufficient.

The second step that we have to think about is bone quality. So not just how much bone you have, but how good is that bone? I use this comparator all the time; a lot of us have heard the story of *The Three Little Pigs*, and you have one pig, and he's got a ton of straw. It's a whole ton, but it's straw, and then you have another pig who's got a ton of brick. Both have tons of material, a ton of straw, and a ton of brick. They both build a house, but when the wolf comes along, which one do you want to live in? You want to live in the brick house. That's quality, right? Is it straw or is it stone? What we are speculating in the field, and there's been a lot more research going into it, is why might diabetic bones or people with diabetes in their bones—why might they be more like straw? Quantity looks pretty good, but not so great quality as opposed to stone.

What has happened? What are some of the factors contributing to that? This idea of bone quality has, depending on who you talk to, a million different definitions. There are different things we think about, so we think about how the bone is laid out. The architecture, or the microarchitecture, of the bone, the strut work, you peel back the drywall—what do the walls look like behind the scenes? Is it different in diabetes compared to those without diabetes? The answer is "yes." There are differences in microarchitecture; there are differences in how the hip bones are laid out, something called geometry. It's if you think about it in architectural terms, and now in engineering terms, the geometry of the bone is different; there's a point parameter that we look at; oftentimes it's how actively the bone is remodeling. Our bones are always building up and breaking down. They are not like rocks that we're walking around in; our bones have to renew and refresh themselves, like our skin. If we didn't shed the old skin and put in new skin, we'd look pretty gnarly. Bones are always remodeling. Is that recycling process and bone different in those with diabetes compared to those without? The answer is yes, diabetes impacts how actively and well bones rebuild and refresh themselves to keep them flexible. It's a lower rate of remodeling, so bone gets old and brittle as time goes on.

When we really look deep down inside the bone—even beyond that microarchitecture I just talked about, peeling back the drywall and looking behind the walls, really looking at the composition of the bone—that collagen, that mineral we talked about, is there something different about it that's disturbed with diabetes? The answer there too is yes. When looking at mineral content and looking at collagen formation, there are differences there in diabetes. In part, a lot of this may be due to advanced glycation end products (AGE) deposition. We're measuring it every time we get that hemoglobin A1C; these circulating AGEs. They actually do get deposited into the bone, and they can cause disruptions in or problems with how the bone is laid out, how flexible the collagen is, and how well the mineral is deposited within the collagen to harden. Those AGEs play a role in how strong bones are. That quality piece again, just like the beginning, there's a million different reasons why people with diabetes may not have perfect bones. There are quite a few reasons we're investigating actively as to why the quality of the bone might not be so great.

How does all of that translate into what we do about this? If we suspect that with longstanding disease, or as you have diabetes longer and longer, you have more problems with bone geometry. You have more problems with bone microarchitecture. You have more problems with bone remodeling. You have more problems with bone minerals, more problems with AGE accumulation, or deposits within the bone. You can imagine that the less severe your diabetes, the better glucose control you have, the fewer AGEs you have circulating, and the lower your hemoglobin A1C (or getting it down), the less damage can occur over time. Osteoporosis is not an overnight phenomenon. It happens over many years. So if you can slow that weakening of the bone with better glycemic control, keeping control



of your blood sugars, keeping a healthy active lifestyle, exercising, good nutrition, and calcium and vitamin D, you can see that at the end of the road, it's only going to be beneficial to the skeleton.

**RK:** I really like that analogy of *The Three Little Pigs* and the straw. When I think of a bushel of straw or a straw hut, you can imagine how easily it would fall compared to a ton of stone with a building or house, which would be more solid. I think that's a great way to think about the fact that even though there's a lot of building material, the building material has to be strong itself. You mentioned those AGEs, which are really just the circulating glucose sticking to proteins and sticking to areas in the body where it shouldn't. It sounds like the higher the glucose, the longer you've had diabetes, the more likely it is that higher glucose in the blood can stick to places where it shouldn't, such as the bone, and make it weaker. Underscoring again the importance of keeping those glucose levels at target, so that's really good to know.

You talked a little bit about the symptoms and signs of osteoporosis. I wonder if we could move now to talking about how people might know if they are having bone disease or a fracture. Then maybe talking a little bit about some of the treatments that we commonly recommend for people who have bone diseases.

**KM:** Osteoporosis is a really tricky one, Dr. Kalyani, because, again, like plaque building up in your arteries or brain issues, this is a silent disease. A lot of times patients will come in and they think that I'm going to be treating them for their knee pain or their shoulder pain or their back pain. I say, "Oh my gosh, I'm sorry you're having pain, but that's probably not osteoporosis because osteoporosis is generally silent with all of these changes happening underneath the surface of the bone until that fracture occurs." Then if there's a broken bone, you're going to feel that, although not all the time; 50% of vertebral fractures or spine fractures, we don't even know about until we get an image. There may have been an episode of some back pain a couple of months ago, and you don't know about it until you get a CT scan later, and there it is. So, osteoporosis in and of itself tends to be a silent disease.

Now sometimes we can develop thinning of the bone in diabetes and other conditions as well due to nutritional abnormalities. If you are not getting enough calcium, if you are not getting enough vitamin D, or if you have protein abnormalities or malnutrition in general, you can have side effects due to that. You can have softening of the bone and bone pain, particularly in your lower legs or in your upper legs. If you press on the surface of your bone, if it truly is soft, sometimes that is painful. I always press on the fronts of people's shins as a part of my physical exam. Some patients will actually jump, and sure enough, we'll get a vitamin D level or check their calcium levels, and those levels are elevated. That could be something that pops up every now and again with bone pain. I would say other symptoms of osteoporosis outside of a fracture are pretty limited. Sometimes patients have a risk for kidney stones that can thin the bones. If you're having back pain or blood in your urine, we look for kidney stones, but on the whole, it's tough. It's a very silent disease, so they don't come into my office again until oftentimes a fracture has already occurred.

**RK:** As you mentioned, it can be a silent disease. It sounds like more often than not, people might not have symptoms; is that right? And people really need to be screened.

**KM:** Yes, and that's the critical piece: screening. I'm thrilled that the American Diabetes Association is partnering with our bone groups to really work on incorporating bone health

into the guidelines. It's a thick guideline, but we have more than a word or two; we have this whole section now on bone disease and diabetes to try to raise awareness that this is part of the screening, much like you would think about cardiovascular health or ophthalmologic evaluations, getting your feet checked, your eyes checked, et cetera. You at least have to do a baseline bone density test and ask about fractures in that screening process because it is so asymptomatic.

**RK:** Do you think most people with type 2 diabetes should have a bone density or DEXA test at some point, and if so, when might you recommend it?

**KM:** Yes, that's a great question, and the answer is yes. It is definitely a risk factor; diabetes is a risk factor for bone disease. Whereas without any risk factors, it's generally recommended that women older than the age of 65 get a DEXA scan, men generally older than the age of 70 or so. With any one risk factor for bone disease or fracture, diabetes again being one of those, we generally are screening women around the time of perimenopause, when we're otherwise losing a lot of bone due to estrogen declines. Even men around the same age should at least have a screening bone mineral density test to know where the numbers are starting. Even earlier than that, if there's a fracture, that would prompt you to get the scan sooner, if there's a fragility fracture. Again, if we include diabetes now in the list, like we would rheumatoid arthritis or steroid use or family history of a hip fracture, we should be screening earlier than those 65 years of age for women and 70 years of age for men, it should be part of your initial assessment.

**RK:** One of the questions that I feel comes up sometimes, in clinical practice, is having a family member who's had a fracture and how that might increase someone's risk of having a fracture. I wonder if you could talk a little bit about that too.

**KM:** That's a good question, and in that FRAX calculator we were discussing earlier, it is included as one of the check boxes that you can select. Genetics are a huge component of bone health. Maybe 40% of our predetermined bone mineral density that we get again by the age of 30 is really a part of our genes. So if you have a family history of osteoporosis or a family history of fracture, maybe you didn't get to your peak bone mineral density by the age of 30. Maybe instead of getting to the 10th floor, you only made it to the 7th floor. That is something that should be discussed, in addition to other risk factors. It's not just diabetes—"Are you on steroids? Do you have a history of kidney stones or a family history of fractures?" These are all things that go into that melting pot of fracture risk assessment that ideally your primary care doctor is getting. But, when I hear a family history of fractures, particularly hip fractures, or a lot of patients will describe, "Mom just got shorter and shorter as she got older," or "Dad got shorter and shorter as he got older," or "They got that hook in their back." When I hear things like that, it really does make me wonder if maybe this person is at even more increased risk than I initially thought.

**RK:** Do some relatives confer higher risk? For instance, I know we often talk about maternal or having a history of fracture with your mother as something that we think about as a risk factor. But is there any relative who's had a fracture that confers higher risk, or do certain relatives make it more likely that you will?

**KM:** Yeah, it's mom and dad; they're first-degree relatives. This is one disease state where I feel like we do neglect men to some extent. We don't think about men as getting osteoporosis, but they absolutely do. So, either parent, if there's a history of fracture or, again, getting shorter with age or multiple fractures that are, again, fragile, not car accident-related, that should be considered. Then I always ask actually about brothers and sisters too, because sometimes we don't know our parents' history for whatever reason. Maybe there's adoption, or maybe there was an early passing of a parent, or they just didn't make it to the point in age where they may have had a fracture. But if I get a history of a brother or a sister who's had multiple fragility fractures, I take that into consideration as well. So it's any first-degree relative, although in the FRAX calculator it asks very specifically about parental history of hip fracture.

**RK:** That's really good to know and important to know the family history to know whether any of your first-degree relatives, parents, or siblings have fractures. Now, for those people who are listening and are interested in how they can prevent having bone disease, such as osteoporosis, and having fractures in the future—what are some lifestyle modifications or lifestyle measures they can take to optimize their bone health and really ensure that they have strong bones for their lifetime?

**KM:** As the first visit in my clinic comes to a close, it always comes out, "Hey, what's next? What do we do?" I always lead with what you, as a patient, can do to improve your bones. I can pull out my prescription pad until the cows come home, but it really is a partnership because it's not just about medication. It's about all of these other factors we've gotten into today.

Starting with a healthy lifestyle. I know that's a term that's very broad, but it is critical. These are things like exercise; we know the benefits of exercise to blood glucose control. Guess what? Exercise is really good for your bones too. We say resistance training, and that doesn't mean you need to go out and you need to get a gym membership and pump iron 8 hours a day. Resistance training can be. A 30-minute walk around the block on a nice day, and finally the weather is getting a little bit nicer so we can get outside a bit more. A nice walk around the block, exercise bicycles are great. Even elliptical trainers are great. Using the arms, there is so much free content now on the computer that you can get access to; you can go in, and you can use your search engine to look into osteoporosis or bone-building exercises, and you don't need a fancy gym membership. You maybe just need a couple of heavy cans at home that can give you the exercises you need. This includes even exercises for people who have functional limitations.

You can do things sitting from a chair; you can do things just with your legs, and you have to do things within your boundaries. But we generally recommend 3 to 5 days (a week) of 30-minute sessions of resistance training in some form. The only thing that really doesn't count is swimming. It's still good for your heart and other things, but swimming may not be as good for the bones because it doesn't provide that muscle against bone that we need to build healthy bone. Exercise is very important. In that same breath, it's interesting because for blood glucose control and really to optimize your blood sugars, make them the best that they can be. Weight loss is generally recommended in patients; if weight is contributing to glucose control, I always like to counter that with healthful weight loss.

In my world, if you lose too much weight too fast, you can also lose bone with that because really fast weight loss makes us lose lean mass. Again, Dr. Kalyani, you know all about this too, but when you lose a lot of lean mass or muscle mass really quickly, you can lose bone. We do have a special eye on individuals who undergo gastric sleeve procedures or

Roux-en-Y gastric bypass (RYGB) procedures. Just to make sure they're not losing bone, and unfortunately through studies, we know that they do. Prioritize healthful weight loss through exercise and healthful diets.

What can we do in our diets to really improve our bone health? Getting ample protein, you got to start there. Remember I said bones are made of collagen. Guess what? - Collagen is protein. So, you're depriving yourself of collagen; protein does not have to be meat. It can be plant-based as well. Intake adequate protein for someone of your height and your weight. As well as adequate calcium intake. Generally, for individuals at risk for osteoporosis, fracture, or bone loss, we recommend about 1200 milligrams of calcium total per day. Ideally, you get it through your diet. I think the cardiologist would prefer that. I know our heart specialists, our kidney specialists, would prefer that, but it is not always possible to get it through the diet. Sometimes patients are lactose intolerant, or they just don't like cheese, but there's plenty of other non-dairy sources out there, too, like fortified non-dairy milks, for example, where you can get calcium. Every once in a while, and certainly in my practice, you must oftentimes turn to a supplement, and there are calcium supplements out there that are well tolerated. But again, that 1200 milligram-a-day goal would be what you would strive for. Along with adequate vitamin D levels. The endocrine society would recommend a vitamin D level greater than about 30 nanograms per milliliter for patients at risk for fracture, which again, patients with diabetes are at risk. So, getting enough vitamin D, and that can range all across the board, Dr. Kalyani, and I'm sure you've seen it too. Some patients need 2,000 a day, some patients need 5,000 a day and some patients need prescription strength. So really that would be something to work on with your provider to decide exactly how much you need to meet that 30 nanograms per milliliter threshold.

As far as other things with lifestyle, guess what? I'm going to be yet another doctor telling you, please don't smoke; please don't drink too much; please do try to avoid toxins that might otherwise harm the rest of your body too. Then don't neglect those other areas of your health. We said kidneys can affect the bone and vascular damage can affect the bone. This is—I know it's annoying—I'm adding one more thing to think about, right? With all of the other pieces of this complicated disease state puzzle, I'm adding one more and saying we have to think about your bones. But guess what? In treating all those other things, hopefully you've been doing as best you can. You're ultimately going to do good by the bone as well. Managing your blood pressure, managing your cholesterol, and taking good care of your kidneys—all of those things, at the end of the day, will trickle down and have a good impact on bone health too.

**RK:** I think it's great to hear about a variety of ways that people can choose—whether it's through exercise, which they should definitely exercise, or also through different types of foods and maintaining adequate intake of protein and calcium and vitamin D—to keep their bones strong. With the addition then of not drinking and not smoking.

What about the consumption of sodas or the consumption of sugar-sweetened beverages? How do they, or do they, affect the bones in any way?

**KM:** They're not the best, right? I think sugar. It tastes good. I love a good gummy bear every now and again. But, no, it's not good for bone health.

It's not just carbonation. There is a lot of information out there about carbonation and its impact on bone health, which is not the best data. I find that the problem with sugary sodas, and sugary drinks in general, is they tend to replace more healthy choices. Instead of having a glass of almond milk, if you reach for a sugary beverage instead, you're depriving yourself of the nutrition that might otherwise come from that glass of almond milk.

Then again, getting back into this discussion of those high blood sugars and then what that does with these advanced glycation end products (AGEs) that then go and accumulate in the bone, causing increased fat production within the body, and that is bad for bone health.

There are a lot of downstream effects of all of that sugar too, which have immediate and long-term effects on bone health and bone strength. I know it tastes good, and no one is saying never, but at the end of the day, the less you drink sugary drinks, or carbonated beverages with lots of sugar in them, probably the better off you'll be. This is not only from the diabetes standpoint, Dr. Kalyani, but certainly from the bone standpoint as well.

**RK:** Yeah, it definitely can have wide-ranging benefits to moderate or reduce sugar-sweetened beverage consumption. I think the point that you made about weight loss is really important because we do often, knowing that obesity is a risk factor for type 2 diabetes, talk about weight loss with many of our patients with diabetes. As you mentioned, it can have potentially adverse effects in both the muscle and the bone. Knowing that ahead of time is important to counteract potential adverse effects by doing exercise, by ensuring that nutrients are in the diet to protect the bone as well. The post-bariatric bypass population, or those who undergo weight loss surgery, certainly are at the highest risk, wouldn't you say, of those bone deficiencies?

**KM:** They are, and we have the data to show that not just with DEXA but also using some more sophisticated imaging techniques. I think what we're all struggling with is, beyond the immediate weight and bone loss, the long-term benefit of those surgeries: Does it still outweigh the skeletal question marks that we have, and can your bones regain strength over time?

We don't know the answers to that. I think, again, it's why that nutritional counseling piece, not only prior to the surgeries but also ongoing nutritional support following the surgery, is very important. So that the vitamin D levels don't drop and there's adequate calcium intake. We know there's malabsorption with a lot of these surgeries where the body just doesn't absorb nutrients as well as it should, either because the stomach is a fraction of its original size or because the intestines have been rerouted and you're not supposed to absorb things any longer, but really continuing to partner with someone educated in nutrition to prevent some of that inevitable bone loss that will occur.

One thing I do want to circle back to, because I'll kick myself later if I don't bring it up, is another reason that exercise and maintenance of muscle mass are so important: so that we prevent falls. I have spent so much time, probably more recently than ever, feeling like I'm surrounded by people who fall. My father is a "faller"; my mother-in-law was a "faller." So, I'm always thinking about these things. My father has had type 2 diabetes for over 20 years now, and so he's got a whole host of complications with neuropathy and vascular issues. He now falls, and I worry every day about him taking a tumble. You better believe I'm all over him about doing his physical therapy and eating his protein and continuing to strengthen his muscles so that he doesn't topple and so that his bones aren't challenged. People fall, and they don't always break bones, but I say, "Listen, stop testing your bones. Let's just not fall to begin with." So not only exercise, but glucose control to the point where your blood sugars are well controlled, but not too low either. We know we fall when we get woozy, and certainly my dad has had a couple of those episodes too. Avoiding the low blood sugars too, because that can get patients into trouble as well.

**RK:** Thank you for sharing that. The scenario you described with your father, unfortunately, I think is more common than we realize, and he, of course, benefits from your expertise in this area, but the link between falls and fractures can't be underscored and then you add

diabetes to that. It's almost like a triple threat. Perhaps those who do fall or feel unsteady on their feet should think a little bit more about protecting their bone health. Wouldn't you say, because of that risk?

**KM:** Absolutely. Not to terrify people, I don't want people to feel like they're *Humpty Dumpty* out there. We don't want to wrap anyone in bubble wrap before they go outdoors, but just to be mindful of it. Frankly, if it motivates you to take that extra walk around the block or to go to that physical therapy session that your provider's been recommending out of concern that maybe you are a fall risk—if that's the motivator that you need—then by all means, take this talk that we've had today and use it as yet one more reason why you should be exercising.

**RK:** I fully agree. I can't underscore the importance of prevention. We focused a lot today on talking about the prevention of bone disease and how to diagnose bone disease. I don't think we need to go into large detail about the treatments that are available, but I wonder if you could just say a few words about how good the treatments are that are out there and what people should do if they're interested in getting diagnosed or identified for this and potentially getting treated.

**KM:** Yes, absolutely. This is where the prescription pad comes into play beyond lifestyle and diet and exercise and what have you. Sometimes we must pull out our prescription pad; if there's been a broken bone and we're worried about future broken bones, we're going to be more inclined to do that. Or if the numbers don't look so great on the DEXA scan, or if there are so many risk factors we worry about, we're waiting too long before we prescribe a medicine. You're right, Dr. Kalyani; there's a whole buffet line now of osteoporosis medications that we use, ranging from pills that patients can take once a week or once a month. There are infusions, where you get an IV and you get a treatment once a year, which can be pretty convenient for patients. There's injection therapy that's given twice a year and even bone-building medications. In some patients, a lot of the pills and infusions and injections really prevent the bones from breaking down, and they're our go-to medications in a lot of situations. But if we're really worried about patients and patients, maybe there have been multiple fractures, or their numbers may actually be low, or there are other things at play. We may turn towards a category of medicines that really build the bones back up again. That part of the decision-making process is highly individualized. It involves looking at a lot of different factors, ranging from other diseases that may be on the list to other medications to patient preference.

I find that the most important thing is that I can recommend daily injections. One of the bone-building medicines is a daily injection, but you may be tired of daily injections, or maybe you're not on insulin, and you have no intention of starting daily injections if you don't have to. That's where the partnership comes into play and talking about shared goals, because medicines are only successful if you actually take them. So again, that part of it does come to pass sometimes if there's been a broken bone or progression of osteoporosis, and they all work.

We've had some studies looking at the effectiveness of these different types of osteoporosis drugs in individuals with type 2 diabetes, and we know they do work to prevent fractures. So, beyond that, it's just a matter of coming up with the right drug or drugs, and if they don't work, sometimes we must pivot and try something else. There are lots of options out there, again, in addition to the calcium, the D, and the lifestyle interventions, because it's always a teamwork approach to really optimizing and improving bone health and strength.

**RK:** Dr. Moseley, this has been such an informative discussion. I know I've learned a lot, and I'm sure our listeners have learned a lot, too, about the higher risk of bone diseases in people with type 2 diabetes, some of the challenges of diagnosing bone diseases using some of the routine measures, such as the dexamethasone and bone test, and really the importance of screening for risk factors, including family history and other lifestyle factors and other medical conditions that might raise someone's risk of having bone disease, and then knowing that if medication is needed, it's reassuring to know that they are effective often in preventing a fracture.

I wonder in parting if you have any last words for our listeners who, after hearing this discussion, are empowered to really try and do their best to preserve their bone health. What would you recommend that they do as next steps?

**KM:** This, just listening to this podcast and learning about this, is the most important step. As I have stated, part of what I like to do most is get the message out there that this is something we should be thinking about: bones, bone strength fractures in people with type 2 diabetes, that it is a more recently recognized complication of diabetes that sits on that list with eyes and feet and heart and kidneys.

Bones are now on that list too. By understanding that we have to now consider bones as patients, we can go to our providers and say, "Should we maybe talk about my bone health? Should we maybe screen me for my bone density to see if there's anything that we need to maybe intervene upon?" I think that that's very important.

Educating patients so they can maybe go and educate their providers a little bit more. And I think it's again, one more reason, in understanding the importance of bone health and its association with type 2 diabetes. It's one more thing to motivate patients to do all of those elements that really are critical for improving blood glucose levels or blood sugar levels: the diet, the exercise, and healthy lifestyle choices. We're all working towards the same goal. Luckily, there's so much overlap with what patients can do to improve their health with bones, heart, kidneys, and overall wellness. I think that, very luckily, it's just one more motivator for them to make the right choices in life.

**RK:** Dr. Moseley, thank you so much again for your time today and sharing your expertise. We truly appreciate it.

**KM:** Thank you so much, Dr. Kalyani.

**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.

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We love to hear from our listeners. The email address is [hopkinsdiabetesinfo@jhmi.edu](mailto:hopkinsdiabetesinfo@jhmi.edu).

Thanks for listening. Be well and see you next time.

