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Osteoporosis in CKD: Closing the Gaps in Diagnosis and Treatment

Announcer:
You're listening to *On the Frontlines of Osteoporosis* on ReachMD. And now, here's your host, Ryan Quigley.

Ryan Quigley:
Welcome to *On the Frontlines of Osteoporosis* on ReachMD. I'm Ryan Quigley, and joining me to discuss his recent review that examined the link between osteoporosis and chronic kidney disease, or CKD for short, is Dr. Charles Ginsberg. He is an Associate Professor in the Department of Medicine at the UC School of Medicine and a board-certified nephrologist at UC San Diego Health. Dr. Ginsberg, thanks for being here today.

Dr. Ginsberg:
Thanks so much for having me. I've been looking forward to this. It should be fun.

Ryan Quigley:
Absolutely, me as well. So to start us off, Dr. Ginsberg, what motivated you to write this review and really nail down this relationship?

Dr. Ginsberg:
I've been studying bone health in patients with kidney disease since I was a medical student at Washington University, so I've been in this field for a long time. And as I've gone from medical student through my training and now into faculty, I've seen how prevalent bone disease is amongst our patients with kidney disease, especially in women with kidney disease, yet how frequently this disorder not necessarily gets mismanaged, but just gets ignored. So I think this is a problem that frequently gets punted, and raising awareness about the fact that we have treatment options and we do need to address this is really important. And that's kind of what led me to write this review.

Ryan Quigley:
Now you mentioned the review. Can you walk us through the biggest things that you discovered about osteoporosis and how it affects people with advanced kidney disease?

Dr. Ginsberg:
Yeah, I think there's a few salient points that I'd highlight. So firstly, osteoporosis in patients with kidney disease is extremely prevalent to the point that some studies suggest that about a quarter of women in the United States with osteoporosis actually have kidney disease. So this is a very widespread problem and is probably massively underdiagnosed—not only because we don't know our patients have osteoporosis, but we also don't know our patients have kidney disease.

I think other important points are despite some old research, we've learned that you can reliably diagnose osteoporosis with your standard DEXA scan for bone density in our patients with kidney disease. There are a lot of treatment options out there, and they can be prescribed safely so long as we properly investigate, do your patients have osteoporosis? What's causing their osteoporosis? How related is it to their kidney disease?

And finally, I think that maybe the most important thing that I would like to transmit to my colleagues is ask your patients about their bone health. Ask them if they fractured. Sometimes that's the easiest way to get the ball rolling; your patients don't think to tell their kidney doctor that they broke a bone, but they should.

Ryan Quigley:
Now there's one thing I want to ask you about your review: you referred to the bone biopsy as the gold standard. What did you find that reinforces its value or perhaps even limits it?

Dr. Ginsberg:
So unfortunately, one of the main drivers of osteoporosis in patients with kidney disease is abnormalities in something called bone turnover, which is how fast you build and break down bone. This is far more of an issue in kidney patients than the general population with osteoporosis. While we have blood testing that can tell you what people's bone turnover abnormalities are, they're not very accurate. And the only way we know definitively what someone's bone turnover is with a bone biopsy. The treatments for osteoporosis all affect bone turnover: some increase turnover, and some decrease turnover. But if you get their underlying turnover wrong, you might choose the wrong therapy. So if somebody has low turnover and you give a drug that slows turnover, that's probably going to make things worse.

That's what's nice about the biopsy: it has about 98 percent accuracy to tell your patients what exactly their turnover abnormality is as opposed to if you rely on biomarkers, you're probably closer to 80 percent. The main limitation of biopsy is getting it. It's an invasive procedure. It's relatively painless, but it's generally done in an OR, although in some settings, it has been done in a clinic visit, but generally, it's done in an OR. It requires anesthesia and a pathology site to read the biopsies, and there's only a handful of those in the United States. For example, at UCSD, we do biopsies. There are maybe 10 places in the country that do something like that. We send it to UCLA to read it because they're the site on the West coast that does it. So setting up those relationships are critical and can be difficult, especially for small practices to set up all the contracts to get this done. I think that's the biggest limitation.

Ryan Quigley:
For those just tuning in, you're listening to *On the Frontlines of Osteoporosis* on ReachMD. I'm Ryan Quigley, and I'm speaking with Dr. Charles Ginsberg about his review, which focuses on bone health and chronic kidney disease.

So, Dr. Ginsberg, we just touched on some of the recommendations clinicians can utilize when diagnosing osteoporosis and CKD patients, but now let's talk about management. Specifically, you talked about using anabolic drugs for low bone turnover. What did you find that suggests that these might be a good option even in dialysis patients?

Dr. Ginsberg:
There've been a number of studies in the United States and some big ones in Europe—I believe Belgium is the most prominent place—where they've looked at the frequency of bone turnover abnormalities in patients with kidney disease, and what they find is that low bone turnover is actually very common in patients with kidney disease, especially kidney transplant patients.

We don't have good trials that target specific bone turnover type, i.e., we don't have a trial that says, "Hey, let's take patients with low bone turnover and give them an anabolic drug." The drugs were generally just given to everybody. We know how these drugs work. And so if you have osteoporosis because your osteoblasts don't build bone anymore, giving a drug that doesn't tell the osteoblast to build bone isn't going to solve the problem.

And that's what anabolics do: they tell your osteoblast it's time to build bone. If you give them a drug that says don't resorb bone like an osteoclast inhibitor or a bisphosphonate, it isn't getting at their underlying issue, and for complicated reasons, it may actually worsen it. So to some extent, these recommendations are based on our understanding of physiology because it's really hard to do the clinical trials that we really would want to do. But considering how prevalent the low turnover is, it only makes sense that we should be stimulating bone turnover in those patients. Anecdotally, we've done this a lot, and we've seen really good results. Our patients tolerate the drugs really well because they're not nephrotoxic—unlike some other osteoporosis medications—and their bone density improves. So as long as they don't mind injections, which many of our patients are on anyway with diabetes and insulin, it's generally well tolerated, and we get good results. So it's always nice when they have low turnover. It's easier to treat, I find.

Ryan Quigley:
Now, just a quick follow up to that question, you mentioned that trials in that realm are not non-existent, but a bit limited. What are some of the limitations keeping those from taking place?

Dr. Ginsberg:
Yeah, so if you wanted to do a clinical trial based on bone turnover and you were depending on biopsy, you'd have to get a lot of people

to agree to do a biopsy, which a lot of people aren't willing to do. And then once you did the biopsy, I don't know if it would be ethical to randomize somebody not to an anabolic if you found they had low turnover. I certainly wouldn't let somebody give me an anti-resorptive if the biopsy tells me to do something else. So it's hard to design a trial around a rare procedure that's going to strongly dictate the therapy you need. It's kind of like the old 'we don't have any clinical trials proving parachutes help skydivers' because once somebody goes up on the plane, they're probably going to expect to have that parachute. Maybe that's a little bit extreme compared to what I'm saying, but if I had a biopsy that told me this is probably the best drug based on your physiology, I really wouldn't want to let anybody randomize me to do anything else. And so I think it's very hard to do those kinds of trials in the space.

Ryan Quigley:
Yeah, it's a very high-risk endeavor, so that totally makes sense to me. Now what did you learn about fracture risk in CKD patients that you think some providers might not realize yet?

Dr. Ginsberg:
So looking at the fracture risks in CKD, there's actually a nice linear relationship where as kidney function gets worse, your fracture risk rises. So in early CKD, fracture rates are probably about two times the general population. When you get to dialysis, it's more like four times the general population.

So when you think about, say your 80-year-old grandmother with osteoporosis and think, oh, I really don't want her to break her hip. If you imagine she was on dialysis, that risk would now be four times as high, and that means that's a major contributor to their morbidity. If you look at mortality rates in elderly dialysis patients who have a major fracture, like a hip fracture, probably over one in four are going to die within a year. Maybe even close to 50 percent. So the consequences of a fracture are so catastrophic in that patient population that it's not something we can just say, well, your endocrinologist is going to handle that because they're probably not going to be as well attuned to the other complexities of dialysis as we as nephrologists are. So it really is a bit of a tag-team approach where you really have to address the problem and then work with your colleagues to come up with a solution and not just say, well, I guess you're stuck because you're on dialysis.

Ryan Quigley:
Now, Dr. Ginsberg, based on everything you found or that you've reviewed, what are the next steps for improving how we diagnose and treat osteoporosis in people with chronic kidney disease moving forward?

Dr. Ginsberg:
The thing that's most easy to tackle is improving biomarkers and imaging because as we've talked about, biopsy has been around for longer than I've been alive, and less and less people seem to be doing it every year. So I don't think there's any world where this is going to become widely utilized. I would love it if it was, but you know, I'm being realistic. But there are improvements in how we're studying biomarkers and blood testing to tell us about underlying bone turnover. There's been advances in imaging using high-resolution CT scans and potentially bone MRI that can tell us more about what's happening on the bone micro architecture.

Combining that with blood tests, maybe we won't get to the bone biopsy gold standard, but we might get really close where we have 90-95 percent ability to know what's happening accurately in the bone, and then we can make treatment decisions based on that. So I think where the next steps lie is improving our diagnostics and not just saying, "Hey, this person's high risk; this person's low risk," but "This person's high risk, and this is why they're high risk."

Ryan Quigley:
Well, as those comments bring us to the end of today's program, I want to thank my guest, Dr. Charles Ginsberg, for joining me to share his insights on the management of osteoporosis and chronic kidney disease. Dr. Ginsberg, it was great speaking with you today.

Dr. Ginsberg:
Thank you so much for having me. This was fun.

Announcer:
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