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Insights for Postmenopausal Osteoporosis Patients at Very High Risk of Fracture

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Here's your host, Dr. Jennifer Caudle

Dr. Caudle
This is ReachMD, and I'm your host Dr. Jennifer Caudle. Today, our program will focus on how we can manage postmenopausal osteoporosis patients who are at a very high risk of fracture. And joining me for this discussion is Dr. Felicia Cosman, who's a well-known osteoporosis clinician and researcher, and is Professor of Medicine Emerita at Columbia University Vagelos College of Physicians and Surgeons in New York.

Dr. Cosman, welcome to the program.

Dr. Cosman:
Thank you, I'm looking forward to our discussion today.

Dr. Caudle:
Well, I am as well. And if we start with some background, can you tell us about some common predictors of fracture in postmenopausal women?

Dr. Cosman:
Of course. In patients who have not had a fracture, both bone mineral density, or BMD for short, and age are key predictors of the risk of fracture. For example, the data from the Study of Osteoporotic Fractures indicate that 5-year risk of vertebral fracture increases with advancing age and declining BMD in white women 65 years or older.

The most important predictor of subsequent fracture risk is prior history of fracture, and the recency of fracture is of critical importance. In an analysis of Medicare claims data with over 350,000 women with a first fracture, the risk of subsequent fracture was particularly high in the first 2 years after the first fracture occurred. On average, 10% of these women with a first fracture had another fracture within 1 year, and 18% had another fracture within 2 years. In fact, 35% of all subsequent fractures during 5 years of follow-up occurred within one year after the initial fracture. There was also significant variability of risk based on the site of the first fracture; it was highest after fractures of the spine and pelvis.

Vertebral fracture defined radiographically is also a major predictor of subsequent fracture. In the placebo arm of a 3-year clinical trial of postmenopausal women with osteoporosis, risk of future vertebral fractures increased with the number of prevalent vertebral fractures as well as the severity of vertebral fractures. Approximately 36 percent of women with 3 or more prevalent vertebral fractures experienced new vertebral fractures at 3 years. And approximately 38 percent of women with the most severe grade of prevalent vertebral fracture experienced a new vertebral fracture during this timeframe.

Dr. Caudle:
Thank you for that. And now, with those predictors in mind, what are the current diagnostic criteria for osteoporosis in postmenopausal women?

Dr. Cosman:
In 2020, the American Association of Clinical Endocrinologists, or AACE, published their Clinical Practice Guideline for the Diagnosis

and Treatment of Postmenopausal Osteoporosis. According to this guideline, osteoporosis can be diagnosed based on bone density T-score of minus 2.5 or lower at the lumbar spine, femoral neck, proximal femur, or ⅓ radius. Additionally, osteoporosis can be diagnosed clinically in the presence of a low-trauma spine or hip fracture, regardless of BMD. Patients with low bone mass, defined as T-score between minus 1.0 and minus 2.5, may be diagnosed with osteoporosis if there is a history of proximal humerus, pelvis, or distal forearm fracture or high fracture probability indicated by a FRAX score.

AACE Guidelines also recommend stratifying risk as either high or very high risk for fracture. Patients considered at Very High Risk of Fracture include those with recent fracture within the past 12 months, multiple fractures, or a very low T-score (such as less than minus 3.0) even without a fracture. In addition, a fracture occurring while on approved osteoporosis therapy, fractures on drugs causing skeletal harm, a high risk for falls, and a very high FRAX score are other criteria that qualify as having a very high risk of fracture. The Endocrine Society defines very high risk differently – they specify multiple or severe spine fractures and or fractures in patients who also have a T-score at the hip or spine of -2.5 or below. In my view, all of these patients should be considered at very high risk for fracture.

Dr. Caudle:
Dr. Cosman, in addition to identifying patients with these criteria, what else should clinicians include when assessing their patients' fracture risk? What does risk assessment actually look like in clinical practice?

Dr. Cosman:
Beyond medical history and BMD, vertebral imaging tests should be performed in many women to determine if there are vertebral fractures present. These fractures are often subclinical or completely asymptomatic and yet are still highly predictive of subsequent fracture risk. So, it's important for our audience to know that vertebral fracture assessment, which consists of conventional, lateral, thoracic and lumbar spine X-ray imaging, and/or vertebral fracture assessment, or VFA, using DXA, is recommended for high-risk individuals. This includes:

- All women 65 years and older with a T-score of minus 1.0 or below
- Postmenopausal women with a fracture at age 50 or older
- Postmenopausal women with 1.5 inches or more of height loss from peak height or 0.8 inches or more of recent height loss
- Recent or ongoing long-term glucocorticoid treatment, or
- Medical conditions associated with bone loss, such as hyperparathyroidism

Dr. Caudle:
So, Dr. Cosman, now that we have a better understanding of the factors that increase the risk of fracture, as well as the current guidelines on diagnosing osteoporosis and assessing risk, let's shift our focus to treating these patients at very high risk of fracture. What is the treatment landscape in this population?

Dr. Cosman:
I'm so glad we're talking about this because unfortunately, treatment rates of osteoporosis in postmenopausal women have consistently remained low. For instance, in the last decade, less than 10% of women aged 50 years and older have received treatment for their osteoporosis. And despite the high risk of experiencing a subsequent fracture, treatment rates following an initial fracture remain extremely low. A retrospective observational study evaluating treatment patterns in women 50 and older after they experienced an incident fracture, found that treatment rates were only 11 percent at 2 years post fracture. Treatment rates using anabolic or bone-forming agents were particularly low in these recent fracture patients.

Dr. Caudle:
So then given this critical gap in treatment, can you tell us about the current recommendations for treating osteoporotic patients at very high risk of fracture?

Dr. Cosman:
Patients at very high fracture risk need to rapidly reduce their fracture risk and build new bone. Anabolic agents stimulate new bone formation and for that reason, anabolic therapy is usually recommended as initial therapy by multiple medical societies for these very high risk patients. For comprehensive information about treatment recommendations please consult the respective medical society publications. Most recently, the joint 2024 position statement from the American Society for Bone and Mineral Research and Bone Health & Osteoporosis Foundation recommended anabolic therapy as initial treatment for many patients at very high risk for fracture. This includes those with prior vertebral, pelvic, or hip fractures—regardless of timing. Moreover, fractures at other sites such as humerus, radius, and tibia should be considered for initial anabolic therapy if they occurred recently or even remotely especially if T-score is below -2.5. In addition, postmenopausal women who have a very low T-score even without fracture should receive anabolic treatment first.

For patients at very high fracture risk, whether or not they have had a previous fracture, treatment goals are to rapidly reduce fracture risk and build new bone. As I mentioned just a few moments ago, anabolic agents, which stimulate bone formation, reduce fracture risk faster and to a greater extent than antiresorptive agents, which inhibit bone breakdown. We know that the sequence of anabolic first followed by antiresorptive treatment improves BMD more than antiresorptive first followed by anabolic treatment. In fact, studies show that patients with very low T-scores have a greater likelihood of normalizing BMD if anabolic therapy is chosen first.

Dr. Caudle:
Well, considering the low rates of osteoporosis treatment and the critical role of selecting appropriate initial therapy, I have one final question for you today, Dr. Cosman. How can primary care providers help address the unmet needs of this high-risk population?

Dr. Cosman:
I think it's important to remember that ultimately, the goal of osteoporosis management in patients at very high risk of fracture is rapid risk reduction.

Given the long-term, trusted relationship primary care providers have with their patients, they are uniquely positioned to identify and manage individuals at very high risk for osteoporotic fracture. Through a comprehensive medical history, and proactive screening to identify very high-risk patients, treatment with appropriate therapies, and referral to a specialist or Fracture Liaison Service, when appropriate, primary care providers can play an important role in closing the treatment gap in this patient population and ultimately reducing fractures and their consequences.

Dr. Caudle:
As those final comments bring us to the end of today's program, I want to thank my guest, Dr. Felicia Cosman, for joining me to share best practices for managing osteoporosis patients who are at a very high risk of fracture. Dr. Cosman, it was great speaking with you today.

Dr. Cosman:
Thank you so much for having me.

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