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# To scan or not to scan? DXA in postmenopausal women

## ABSTRACT

Fracture is a major cause of morbidity and death in postmenopausal women. Dual-energy x-ray absorptiometry (DXA) measures bone mineral density, which helps in estimating fracture risk and in identifying those who may benefit from treatment. Although screening guidelines differ somewhat for postmenopausal women under age 65, in general, DXA is indicated if the patient has a high risk for fracture.

## KEY POINTS

Bone is lost with aging and declining estrogen and testosterone levels, particularly after menopause.

Advanced age, prior fragility fracture, and low T scores (< -3.0) are the greatest risks factors for fracture.

DXA is considered the therapeutic standard for measuring bone mineral density.

In younger postmenopausal women, guidelines recommend DXA only in those who have a substantial risk of fracture based on clinical factors.

A 56-YEAR-OLD WOMAN presents for a routine physical examination. Her last menstrual period was at age 51. She takes hydrochlorothiazide for hypertension and a multivitamin containing 400 mg of calcium carbonate plus 1,000 IU vitamin D<sub>3</sub> daily. On most days, she eats 2 servings of calcium-rich foods (6 oz yogurt and 1 or 2 servings of cheese). She has no personal or family history of osteoporosis or fracture. She exercises 3 times a week and has had no falls or imbalance. She drinks about 5 alcoholic beverages per week. Her weight is 140 lb (63.5 kg) and height is 5 ft 2 in (157.5 cm), giving her a body mass index of 25.6 kg/m<sup>2</sup>, stable from last year. She asks whether she should get a dual-energy x-ray absorptiometry (DXA) scan to check her bone mineral density (BMD) because many of her postmenopausal friends have done so.

Is DXA screening indicated in this patient?

## ■ BONE MINERAL DENSITY DECLINES WITH AGE AND MENOPAUSE

Most women achieve peak bone mass in their second or third decade of life, depending on skeletal site, with the most active bone formation occurring during childhood, adolescence, and young adulthood. Bone is lost with age and with declining levels of estrogen and testosterone, particularly after menopause, and low bone mineral density is associated with an increased risk of fracture.

Estrogen plays a key role in maintaining the balance between bone formation and resorption. Estrogen deficiency disrupts this balance, resulting in decreased bone formation and increased bone resorption.

The Study of Women Across Nations found that women may lose 5% to 10% of

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bone mineral density in both cortical and trabecular bones during late perimenopause and the first postmenopausal years.<sup>1</sup> As women age, this bone loss slows but continues at an average rate of about 0.5% to 1% per year.

Women with premature ovarian insufficiency or early menopause from natural or surgical causes experience more profound bone loss and are at higher risk of fracture during their life.<sup>2</sup>

Several other medical, genetic, and surgical conditions also either decrease peak bone mass or accelerate bone loss. These include medications such as glucocorticoids (> 5 mg for > 3 months) and lifestyle factors such as smoking and being underweight (ie, body mass index < 18 kg/m<sup>2</sup>). Rheumatoid arthritis and diabetes, particularly type 1 diabetes, also contribute to bone loss and increase the risk of fracture.<sup>3</sup>

The National Osteoporosis Foundation has published an extensive list of risk factors that can be shared with patients.<sup>4</sup> Advancing age, prior fragility fracture, and a T score below -3.0 are the strongest risk factors predicting future fracture.

### ■ OSTEOPOROSIS IS COMMON

According to data from the third National Health and Nutrition Examination Survey, more than 9.9 million Americans have osteoporosis (defined as a T score  $\leq$  -2.5), and an additional 43.1 million have osteopenia (a T score between -1.0 and -2.5), leading to more than 2 million fractures per year.<sup>5,6</sup> These osteoporosis-related fractures are a major cause of morbidity and death in postmenopausal women.

### ■ DXA SCREENING

DXA measures a patient's bone mineral density. Other screening tools exist, but DXA is considered the technical standard. Results are reported in absolute terms in g/cm<sup>2</sup> and also as a T score (the difference, in standard deviations, between the patient's value and the mean value for healthy 30-year-olds of the same sex) and a Z score (the difference between the patient's value and the mean value of people the same age, race, and sex).

The clinical purpose of a DXA scan is to

screen patients for low bone mass and osteoporosis. It also provides a surrogate measure of bone strength to help estimate fracture risk.

For example, a 10% loss of bone mass (equivalent to a 1 standard deviation decrease in the T score) in the vertebrae can double the risk of vertebral fractures. In the hip, a 10% loss of bone mass can cause a 2.5 times greater risk of hip fracture.<sup>7,8</sup>

For DXA to be an appropriate screening test, it must be able to detect disease (osteoporosis or osteopenia) at a stage when treatment (medication or lifestyle modification) can effectively reduce the serious consequences of the disease (eg, fracture). It must also be safe (this applies to both the test and the treatment), widely available, and inexpensive.

### ■ RECOMMENDATIONS FOR DXA SCREENING IN POSTMENOPAUSAL WOMEN

Several major medical societies strongly recommend DXA testing for women age 65 and older,<sup>3,9,10</sup> but the recommendations are not as clear for younger postmenopausal women, such as our patient. In general, however, women under age 65 should be screened if they have clinical risk factors for bone loss or fracture.

The US Preventive Services Task Force (USPSTF)<sup>9</sup> recommends DXA of the hip and spine if the 10-year predicted risk of major osteoporotic fracture according to the Fracture Risk Assessment Tool (FRAX)<sup>11</sup> without bone mineral density is 8.4% or greater. This is equal to the fracture risk of a 65-year-old white woman of mean height and weight without major risk factors for fracture.

The National Osteoporosis Foundation<sup>4</sup> and the International Society of Clinical Densitometry<sup>10</sup> both recommend DXA for postmenopausal women under age 65 and those in the menopausal transition who have clinical risk factors for fracture such as:

- Low body weight
- Prior fracture
- A disease or condition associated with bone loss
- Use of medications that cause bone loss, such as glucocorticoids.

DXA is also recommended in women being considered for pharmacologic treatment and to monitor treatment response.

**Most women achieve peak bone mass in their second or third decade of life**

TABLE 1

**Osteoporosis risk assessment calculators**

Risk factors used	FRAX <sup>12</sup>	Garvan <sup>23</sup>	OST <sup>24</sup>	SCORE <sup>25</sup>
Age	X	X	X	X
Sex	X	X	X	X <sup>b</sup>
Weight	X		X	X
Height	X			
Steroid use	X			
Prior fracture	X	X		X
Secondary osteoporosis	X			
BMD data	X <sup>a</sup>	X		
Race				X
Rheumatoid arthritis	X			X
Prior hormone therapy				X
Current smoking	X			
Hip fracture in parent	X			
Alcohol use	X			
Falls		X		

BMD = bone mineral density; FRAX = Fracture Risk Assessment Tool; HT = hormone therapy; OST = Osteoporosis Self-assessment Tool; SCORE = Simple Calculated Osteoporosis Risk Estimation

<sup>a</sup>Femoral bone (can calculate score without BMD); <sup>b</sup>Women only

### ■ WHY NOT SCREEN ALL YOUNGER POSTMENOPAUSAL WOMEN?

Because recommendations differ regarding DXA screening of postmenopausal women under age 65, patients are selected on the basis of their clinical risk factors other than bone mineral density. The USPSTF, as noted above, recommends basing the decision on the FRAX score without bone mineral density.

If a postmenopausal woman has a low clinical risk of fracture based on the FRAX score and the clinician's determination, DXA will not add any information to determine if she needs treatment. Therefore, women who recently went through menopause who are at low risk do not need DXA screening.

In addition, anyone who has already had

a fragility or low-trauma fracture (eg, fracture from falling from a standing height or less) as an adult should be evaluated for treatment of clinical osteoporosis. These patients do not need DXA screening because their risk of a subsequent fracture is 85%, regardless of bone mineral density.<sup>12</sup>

### Does DXA have side effects?

The USPSTF found only minimal harms from DXA screening.<sup>9</sup> They reported that patients had no increased anxiety or decreased quality of life associated with screening.

Radiation exposure from a DXA scan is low (typically 0.001 mSv, equivalent to 3 hours of background radiation). In comparison, a mammogram releases 0.4 mSv.<sup>13</sup>

Overall, DXA is a low-cost screening test

**Age, prior fragility fracture, and T scores below -3.0 are the strongest risk factors for future fracture**

for those who meet the criteria to be screened, but it should not be done in all early postmenopausal women.

### ■ FRAX IS A VALIDATED TOOL

FRAX<sup>11</sup> is a computer-based equation that uses clinical risk factors (and, if available, bone mineral density information) to estimate a patient's 10-year fracture probability. Although it has been validated in the general population, it has some limitations that may cause it to underestimate the fracture risk in postmenopausal women. Its use of yes-or-no responses can limit its clinical application. For example, a patient who smoked cigarettes for 10 years but has quit is considered a non-smoker in FRAX, even though their smoking history could have a substantial effect on their peak bone deposition and rate of bone loss.

Some experts suggest using one of the alternate risk calculators that include other variables to determine the risk of fracture.<sup>14</sup> Table 1 lists the risk variables used in each tool.

The Simple Calculated Osteoporosis Risk Estimate (SCORE) tool, for example, accounts for hormone therapy and race in its calculation, whereas FRAX does not. In addition, FRAX does not account for falls, which are a major contributor to fractures. Of note, except for FRAX, most of these risk calculators have not been validated in diverse populations and are not in widespread use. We recommend FRAX because it is an easy-to-use clinical tool and is used around the world, but with caveats, as mentioned above.

### ■ SHOULD OUR PATIENT UNDERGO DXA?

Our patient is a postmenopausal woman who went through menopause at an average age, does not smoke, has a normal body mass index, and has no personal or family history of osteoporosis or fracture. She consumes adequate calcium and vitamin D through supplements and diet. Based on her history and physical examination, we assume she achieved a normal peak bone mass before menopause and, thus, has a low risk for fracture. Her FRAX score, calculated without DXA screening, shows a 6% 10-year risk of major osteoporotic fracture, which does not meet the 8.4% threshold for DXA screening.

If she continues to get enough calcium, vitamin D, and exercise, and without any offending agents or conditions that accelerate bone loss, she has a low risk of fracture and a very low probability of needing treatment. If her clinical situation remains the same, she should undergo DXA screening at age 65.

In summary, clinicians can accurately assess the fracture risk in younger postmenopausal women (ie, before age 65) by performing a comprehensive history and physical examination and combining it with the FRAX tool without a DXA scan.

### ■ MANAGING LOW BONE MASS

More fractures occur in women with osteopenia than in those with osteoporosis because many more women have osteopenia, even though their fracture rate is lower.<sup>15</sup> Therefore, it is important to judiciously treat low bone mass in patients who meet the criteria for treatment based on their FRAX score and the practitioners' clinical judgment.

The trabecular bone score is an indirect measure of trabecular microarchitecture derived from DXA images of the lumbar spine. It provides information about bone quality. A score below 1.200 indicates degraded microarchitecture.

Using a trabecular bone score independently or in conjunction with a DXA scan or FRAX score can improve fracture prediction.<sup>16,17</sup> Also, FRAX can be adjusted for this score. More accurate evaluations of bone density and bone quality can help determine which patients with low bone mineral density need treatment.

The efficacy of treatment to reduce fracture rates in women at high risk of fracture but without a low T score ( $-2.5$  or below) has not been established. Most FDA-approved therapies are indicated for treatment based on bone mineral density.

### ■ EFFECTIVE AND EMERGING THERAPIES

For postmenopausal women who are candidates for pharmacologic treatment based on their fracture risk assessment, there are safe and effective FDA-approved options.

**If a woman is at low risk based on clinical factors, DXA will not add relevant information**

### Hormone therapy

Hormone therapy has been proven in the large Women's Health Initiative<sup>18</sup> and the Postmenopausal Estrogen/Progestone Interventions trial<sup>19</sup> to both prevent osteoporosis and reduce the incidence of fractures (such as vertebral and hip) compared with placebo. In the Million Women Study,<sup>20</sup> women who received hormone therapy had a significantly lower risk of any fracture than women who did not. Despite those results, hormone therapy is FDA-approved only for prevention of osteoporosis, not treatment. It is also recommended for menopause-related vasomotor symptoms and the genitourinary syndrome of menopause.

Candidates for hormone therapy are primarily women under age 60 who are fewer than 10 years past menopause; the risk-benefit ratio for older women is less favorable because of higher risks of heart disease and stroke.<sup>21</sup> It is important to engage the patient in an accurate, evidence-based discussion of the risks and benefits of hormone therapy.

Tissue-selective estrogen complexes can be appropriate options to reduce the fracture risk and prevent osteoporosis. These pair estrogens with selective estrogen-receptor antagonists or agonists, such as conjugated estrogen and bazedoxifene.

Selective estrogen-receptor modulators, such as raloxifene, are available in generic form. They may play a dual role of reducing risk of breast cancer and preventing or treating osteoporosis.

### Antiresorptives

The antiresorptive class of medications includes bisphosphonates (oral or intravenous) and denosumab, a subcutaneous monoclonal antibody; both are considered first-line treatment for women with osteoporosis. Denosumab is indicated for women (and men) with a history of fracture or who are at increased risk of fracture and cannot tolerate other therapies.

Although effective at reducing the incidence of fractures, antiresorptive therapies may increase the risk of osteonecrosis of the

jaw and atypical femoral fractures, especially with prolonged use. Fortunately, these are rare: the incidence rate with 10 years of denosumab use is 0.05%,<sup>22</sup> and only 0.001% to 0.01% with more than 4 years of oral bisphosphonate use.<sup>23,24</sup>

### Anabolic drugs

The anabolic drugs such as teriparatide, abaloparatide, and romosozumab build bone mass by stimulating osteoblasts more than osteoclasts. Abaloparatide was studied head-to-head against placebo and teriparatide for 18 months, after which patients received alendronate for 2 years; sequential treatment with abaloparatide followed by alendronate reduced the risk of vertebral, nonvertebral, clinical, and major osteoporotic fractures and increased bone mineral density.<sup>25</sup> Romosozumab, a humanized monoclonal antibody to sclerostin, is FDA-approved to treat women at high risk of fracture. It has a dual effect, stimulating bone formation and reducing bone resorption.

### CLINICAL BOTTOM LINE

Osteoporosis and osteopenia leading to fracture are major causes of morbidity and mortality in postmenopausal women. A DXA scan is considered the best tool to measure bone mass, which can be used to determine the risk of fracture and who may benefit from treatment.

For younger postmenopausal women (age 50 to 65), the need for a DXA scan is determined by a thorough history and physical examination, noting any risk factors that contribute to bone loss. A DXA scan is indicated if their fracture risk is high (ie, equivalent to that of a woman age 65 or older) based on a FRAX calculation without a bone mineral density measurement. If DXA is not indicated, clinicians should counsel women on ways to prevent bone loss and reduce fracture risks.

Conversely, women at the highest risk of fracture are those with a prior adult fragility fracture, regardless of T score. Evaluation and pharmacologic therapy should be strongly recommended in these cases. ■

**Antiresorptive drugs may increase the risk of osteonecrosis of the jaw and atypical femoral fractures, especially with prolonged use, but these are rare**

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