Bone Mineral Density Testing in Premenopausal Women

When Should it Be Done?

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The Canadian Panel of the International Society of Clinical Densitometry recently published standards for the performance of densitometry in premenopausal women. It was recommended that women in the premenopausal period should only have bone mineral density (BMD) testing under specific circumstances (Table 1).

What is the cause of low bone density?

BMD in the young, healthy population follows a bell curve distribution. Approximately 15% of young healthy women have a T-score of < -1 (Figure 1). Of healthy women between the ages of 30 and 40, 0.5% have a T-score of -2.5 or less.

In the normal population, those individuals at the upper or the lower end of the normal bell curve may represent the normal variation in BMD; this may not be pathologic. It is necessary for physicians to evaluate individuals with low bone density and determine if it is secondary to an underlying skeletal or

Suzanne's case

Suzanne, 25, comes to your clinic concerned about her osteoporosis risk. She read about bone loss in young women with amenorrhea. She had her last period six months ago.

Menarche had been at the age of 12. Her periods had been regular until the age of 17. At that time, she had become conscious of her weight and had lost approximately 30 lbs over the course of 18 months. Following the weight loss, her periods became irregular. Her past medical history is otherwise unremarkable, with the absence of any thyroid, renal, or adrenal disease.

She is not taking any medications and is a lifelong non-smoker. She denies regular alcohol use, but has limited dairy intake due to lactose intolerance. She has had one fracture, which occurred of the forearm earlier this year.

On exam, she is found to be thin, with a weight of 90 lbs; her height is five feet. Exam is otherwise normal. In particular, the thoracic and lumbar spine are normal, with no evidence of deformity

For a followup on Suzanne, go to page 75.

Table 1

Indications for BMD testing in premenopausal women

- The presence of an identifiable cause of bone loss, including:
  - Glucocorticoid therapy
  - Premature ovarian failure (primary or secondary)
  - Diseases/conditions associated with bone loss
- Low-trauma fractures

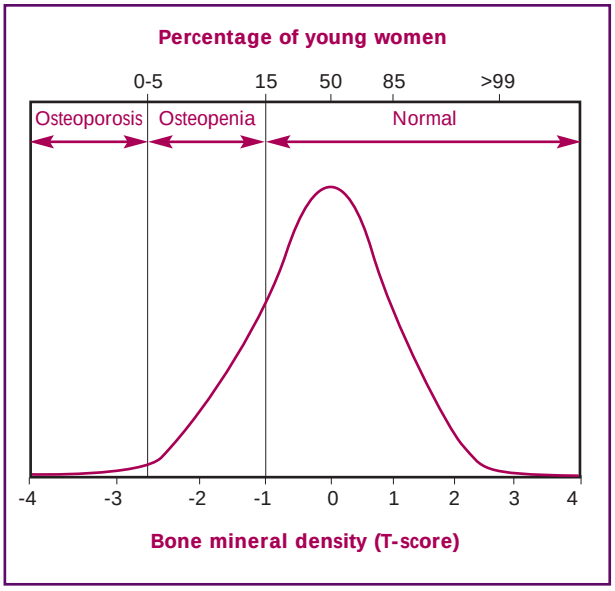

Figure 1. Distribution of BMD in healthy women aged 30 to 40 years.

systemic disorder or whether it is simply a manifestation of low peak bone mass. Low peak bone mass results from genetically determined peak bone density and environmental factors, such as exercise, dietary calcium intake, smoking, and alcohol consumption during the teenage and young adult years.

It is necessary to evaluate the premenopausal women with low bone density to ensure there are no secondary causes present (Table 2). It is also necessary to exclude common causes of low bone density and to ensure that the patient is truly estrogen-replete. The investigations recommended are listed in Table 3.

Prolonged amenorrhea is accompanied by estrogen deficiency and accelerated bone loss. Research indicates that menstrual status is an important factor in the achievement of peak bone mass and for the maintenance of BMD in women in the premenopausal period.

Elevations in follicle-stimulating hormone (FSH) of more than 20 mIU/L have been associated with increased bone turnover activity and progressive bone loss in the perimenopausal period. Therefore, a detailed assessment of menstrual status is necessary, as ovulatory disturbances are more frequently observed in premenopausal women with low BMD. Low BMD in a premenopausal woman is not associated with the same increase in fracture risk seen postmenopause.

Premenopausal women have a significantly lower risk of fracture even with falls, as they are younger and have normal bone structure and neuromuscular function. Premenopausal women are also estrogen-replete and do not have the increased rates of

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Table 2

Secondary causes of bone loss

Diseases/conditions

- Hypogonadism (primary and secondary)
- Primary hyperparathyroidism
- Thyrotoxicosis
- Hypercortisolism
- Growth hormone deficiency
- Osteomalacia
- Hypophosphatasia
- Mastocytosis
- Myeloproliferative disorders
- Connective tissue disorders
- Malabsorptive states
- Hepatic disorders (primary biliary cirrhosis)
- Inflammatory bowel disease
- Renal disease
- Hypercalciuria
- Osteogenesis imperfecta

Medicatons

- Glucocorticoids
- Thyroxine (excessive)
- Anticonvulsants (*e.g.*, phenytoin, phenobarbital)
- Heparin (long-term)
- Lithium
- Cytotoxic chemotherapy
- Gonadotropin-releasing hormone agonists
- Depo medroxyprogesterone acetate

bone turnover seen in post-menopausal women. Therefore, the risk of fracture in a young woman with low bone density is infinitesimally smaller than that of a post-menopausal woman. (Rates of bone turnover do not increase until women reach the peri-menopausal transition period, which begins two to three years prior to the onset of menopause.)

Table 3

Workup for low BMD in premenopausal women

Lab investigations

- Serum calcium (albumin corrected)
- CBC
- ESR
- Phosphate
- Magnesium
- LFTs
- TSH
- Creatinine
- Alk Phosphatase
- FSH
- Estradiol

24-hour urine collection

- For calcium, creatinine

Additional investigations

- 25-hydroxy vitamin D
- PTH
- Antigliadin antibodies
- Antiendomysial antibodies

BMD: Bone mineral density
CBC: Complete blood count
ESR: Eryhthrocyte sedimentation rate
LFT: Liver function test
TSH: Thyroid-stimualting hormone
Alk: Alkaline
FSH: Follicle-stimulating hormone
PTH: Parathyroid hormone

Making the diagnosis

BMD alone cannot be used to make a diagnosis of osteoporosis in premenopausal women. Osteoporosis can only be diagnosed in the presence of fragility fractures or confirmed by a bone biopsy. If low-trauma fractures are present, or if an individual is experiencing progressive bone loss, the patient should be referred to a specialty centre for additional investigations. In the premenopausal woman, it is necessary to evaluate BMD in comparison to age-matched peers, thus the Z-score should be used instead of the T-score and should not be weight adjusted.

Table 4
Lifestyle modifications to treat low bone density

- Weight-bearing exercise
- Maintaining a normal body weight; achieving a normal body mass index
- Adequate dietary calcium and vitamin D intake
- Smoking cessation
- Caffeine limitation
- Soft drink limitation
- Alcohol limitation

What are the treatment options?

It is important to remember that we currently do not have any data regarding the usefulness of bisphosphonates in premenopausal women with low BMD in the absence of glucocorticoid therapy. Women who have not been treated with glucocorticoid therapy and who are estrogen-replete may have bone turnover rates which are normal. Suppressing these further with a bisphosphonate may not be safe or effective in improving bone density or reducing fracture risk. This patient population is likely best served by a specialized metabolic bone clinic.

Antiresorptive therapy has not been evaluated in premenopausal women with low BMD in the absence of secondary causes of osteoporosis.

Antiresorptive therapy is of benefit in premenopausal women with secondary causes of bone loss, such as glucocorticoid use or primary hyperparathyroidism. It is important to remember that bisphosphonates have long-term skeletal retention and may be released from the skeleton several years after use.

Alendronate is a bisphosphonate that has been evaluated in premenopausal women with primary hyperparathyroidism. Alendronate has been shown to be effective in improving BMD in this population. Alendronate and risedronate, another amino bisphosphonate, are effective in improving BMD in glucocortoid-induced bone loss.

Antiresorptive therapy has not been evaluated in premenopausal women with low BMD in the absence of secondary causes of osteoporosis.

Lifestyle

Lifestyle modifications, including adequate calcium and vitamin D intake, should be encouraged in premenopausal women (Table 4).

Estrogen replacement

Those women who are estrogen deficient, either clinically or subclinically, may benefit from estrogen supplementation. Estrogen supplementation, either in the form of oral contraceptive pills (OCPs) or 17-beta estradiol in combination with a progestin, should be considered in order to prevent progressive bone loss. Estrogen supplementation is associated

with improvements in BMD in estrogen-deficient women. In women who are not estrogen-deficient, the role of estrogen supplementation is controversial.

Some evidence has shown that OCPs may exhibit a protective effect on premenopausal and post-menopausal women, while other trials have demonstrated a negative effect. Data from the Canadian Multicentre Osteoporosis Study indicated that OCP users had decreased BMD at the trochanter and spine in comparison to non-users. However, evaluation of this patient population indicated that prior to initiating OCP use, these women also had increased rates of smoking and alcohol use, and had a higher prevalence of menstrual irregularity in comparison to non-OCP users. Thus, prospective data is required to assess the effects of OCP on BMD in premenopausal women.

Lifestyle modifications, should be encouraged in premenopausal women.

In managing low BMD in premenopausal women, it is important to address nutrition and lifestyle modification. As well, it is necessary to treat the underlying cause of bone loss if a cause is identified.

A followup on Suzanne

Suzanne meets criteria for bone mineral density (BMD) testing, as she has been amenorrheic for six months and also has had a low trauma fracture.

Her BMD assessment indicates low BMD at the hip and the lumbar spine. Further evaluation is required.

A detailed history and physical should include a detailed menstrual history. It is necessary to investigate the cause of the amenorrhea and exclude secondary causes of bone loss.

Considering her decreased BMD, estrogen supplementation should be considered to prevent further bone loss. It is also necessary to emphasize lifestyle modifications, including adequate calcium and vitamin D intake and maintaining a normal body weight.

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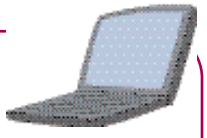
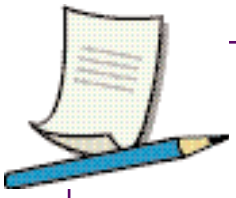


1. International Society for Clinical Densitometry: *www.iscd.org*
2. The Osteoporosis Society of Canada: *www.osteoporosis.ca*



Take-home message

How is osteoporosis diagnosed in premenopausal women?

- Ensure there are no secondary causes of low bone density.
- Exclude common causes of low bone density
- Ensure the patient is truly estrogen-replete.
- Under specific circumstances, BMD test should be performed, but can't be used alone to make an osteoporosis diagnosis.

What are the treatment options?

- Options include lifestyle modifications and estrogen replacement, if appropriate.
- Bisphosphonates can be used in glucocorticoid-induced osteoporosis.

Resources

1. Khan A,Bachrach L, Brown J, et al: 2004 Standards and guidelines for performing central dual-energy X-ray absoptiometry in pre-menopausal women, men, and children. J Clin Densitom 2004; 7(1): 51-63.
2. Lindsay R, Tohme J, Kanders B: The effect of oral contraceptive use on vertebral bone mass in pre- and post-menopausal women. Contraception 1986; 34(4):333-40.
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6. Khan AA, Syed ZA: Bone densitometry in premenopausal women: Synthesis and Review. J Clin Densitom 2004; 7(1):85-92.

Further references available—contact *The Canadian Journal of Diagnosis* at **diagnosis@st.ca**.

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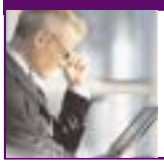

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