Research

Our approach to osteoporosis screening and treatment needs to change

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Our understanding of and approach to osteoporosis is in the middle of a revolution. The prevailing view has been that the loss of ovarian estrogen production at menopause ushers in a period of bone loss. The loss is rapid for a few years and is then followed by a slower but constant rate of bone attrition. Bone density is usually measured by dual energy x-ray absorptiometry with the results expressed as a T score. The T score reflects the number of standard deviations above or below the density seen in young women. Women at risk for fracture are identified if their bone mineral density declines to or below a predefined threshold (e.g., a T score ≤ -2.5).[1] However, we are now realizing that bone loss begins before menopause and involves other hormones in addition to estrogen, and that measuring bone mineral density alone is an inefficient way of addressing the clinical burden of osteoporosis. These are some of the topics raised in this issue of *CMAJ* in the study by Berger and colleagues.[2]

The study by Berger and colleagues was conducted as part of the ongoing Canadian Multicentre Osteoporosis Study, which has defined the prevalence of osteoporosis in a large cohort of Canadian women and men. The authors examined how bone density changed over time and how the treatment of osteoporosis with antiresorptive agents affected those changes. Their main findings were that bone mineral density started to decline before the onset of menopause and that both men and women experienced an additional phase of accelerated bone loss from age 70 onward. Reassuringly, the use of antiresorptive therapy (predominantly hormone replacement therapy in this cohort) protected against bone loss over time.

The finding that bone loss began before menopause is supported by results from other recent studies.[3,4] Bone loss appears to occur in the inner trabecular bone rather than the outer cortex.[4] Since estrogen loss alone cannot account for the changes, interest has focused on other hormones whose levels change in early menopause. Hormones that have previously been thought to regulate only reproductive function, such as follicle-stimulating hormone and the activins and inhibins, have now been linked to important direct effects on bone density[5] and might account for this early loss. The acceleration in bone loss observed among elderly patients is not so well described and its origin is less clear. A progressive increase in the sensitivity of bone to endogenous glucocorticoids has been proposed as a cause of age-related bone loss,[6] but the decline in bone density might also reflect changes in body composition. Lean mass is an important determinant of bone density but tends to decline rapidly in old age.[7] Further analysis of the Canadian Multicentre Osteoporosis Study cohort should help to determine the cause of this loss.

Key points

- Bone loss in women begins before menopause and is accelerated in old age.
- Antiresorptive treatment helps to preserve bone density.
- The interval between bone density assessments can safely be increased to 5 years for many untreated women.
- Decisions about when to test and treat will increasingly focus on estimates of absolute fracture risk.

Although the change in bone density over time is clearly important, Berger and colleagues recognize that this is only one of many factors that will influence an individual's risk for fracture. The risk increases dramatically with age, and changes in bone density account for only a proportion of this increase. Aging is associated with complex changes in the size and shape of bones that can influence resistance to fracture.[8] More importantly, the risk of falls increases rapidly with age.

The most controversial aspect of the study by Berger and colleagues relates to the appropriate time intervals between densitometry measurements. The authors suggest that densitometry for most women can be repeated every 5 years rather than every 2–3 years, as recommended in current national guidelines.[1] This view is based on their finding that the average change in bone density over 2–3 years is small and

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comparable to the measurement error in the scanning technique. However, what we need to know is how frequently over 2–3 years women experience a decline in bone density that would influence management.

For women who are already receiving treatment for osteoporosis, it is debated whether they should have follow-up assessments of bone density at all, since changes in density as a result of therapy account for only a small component of the effectiveness of these medications.[9] If bone mineral density fails to increase following drug therapy for osteoporosis, this should not be taken as a failure of the drug to work. For women who are not taking osteoporosis medication, clinicians are likely to want repeat densitometry sooner among women whose bone density is close to the T-score threshold of –2.5. According to current guidelines, even a small change would lead to the initiation of treatment if the patient's bone density fell below this threshold.

However, this focus on the T-score threshold of –2.5 is changing. We are now more aware that a patient's bone density needs to be interpreted in the context of age, sex and other risk factors for fracture. New guidelines for the diagnosis and management of osteoporosis are attempting to incorporate these factors,[10] but to do this reliably requires large data sets that can examine the interaction of risk factors in individual patients. The latest and most sophisticated approach to combining these factors is the FRAX algorithm sponsored by the World Health Organization. This web-based application computes the 10-year fracture probability based on a patient's risk factors.[11] The FRAX data set is based on several large data sets from around the world, including the Canadian Multicentre Osteoporosis Study data.

It is likely that decisions on when to repeat densitometry will increasingly be based on how close a patient is to a treatment threshold determined by a fracture-risk algorithm. However, before this can be the case, the intervention thresholds need to be established using this technique. Until there is wide adoption of the risk score technique, clinicians will invariably continue the widely used but imperfect T-score threshold of –2.5. However, as Berger and colleagues suggest, individuals with T scores that are not close to this threshold and who have no additional risk factors for rapid bone loss, the interval between assessments of bone mineral density can safely be extended to 5 years.

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