Fracture thresholds in osteoporosis: implications for hormone replacement treatment

P J Ryan, G M Blake, I Fogelman

Abstract

The bone mineral densities of the lumbar spine and femoral neck were determined by dual energy x ray absorptiometry in 110 women aged 40–82 years (average 65 years) with spinal osteoporosis who had had at least one atraumatic vertebral compression fracture and in 1026 normal women aged 40–79 years (average 52 years). The women with osteoporosis showed a significant decrease in bone mineral density (BMD) at the lumbar spine and femoral neck compared with age matched normal women (sixth decade of life –26% spine, –23% femoral neck; seventh decade –26% spine, –16% femoral neck).

The fracture threshold, defined as the 90th centile of spinal BMD for women with osteoporosis, was 0.81 g/cm² at the lumbar spine and 0.656 g/cm² at the femoral neck. Five per cent of normal women aged 40–49 years, 20% aged 50–59 years, and 45% aged 60–69 years had a BMD below this threshold. To maintain the bones of women above the fracture threshold until the age of 70 years about 50% of postmenopausal women need hormone replacement therapy. However, if the BMD is to be kept above the fracture threshold for a woman's lifetime, e.g. until the age of 80–90 years, then most women will need treatment, though for various lengths of time depending on their initial BMD. Measurements of BMD in postmenopausal women currently help in identifying the risk of osteoporotic fractures but in the lifetime assessment of risk in a single subject they may have a more important role in deciding the duration of hormone replacement therapy.

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Bone mass cannot be substantially increased once osteoporotic fractures have occurred and at present the only viable approach to halting the growing epidemic of osteoporosis appears to be the prevention of bone loss. Consequently the measurement of bone mineral density (BMD) is being increasingly requested by doctors to assess a woman's risk of osteoporotic fracture. This part played by bone densitometry is supported by the recognition that bone mass is the most important determinant of bone strength with a relative risk of fracture increasing about twofold for every one standard deviation decrease in BMD.¹ In addition many studies have now shown that a single postmenopausal measurement predicts the risk of future fracture.^{2–4}

Although many issues need to be resolved before widespread screening by BMD measurements can be generally recommended,⁵ an increasing number of women wish to have the best possible advice on long term hormone replacement therapy and request measurements of their BMD. They are supported by a Royal College of Physicians report recommending that women aged about 50 years should have their BMD measured and oestrogen offered to those below a specific threshold.⁶ At present there is no agreement on the threshold levels of BMD identifying which women should be treated nor the length of treatment. The aim of this study was to examine BMD measurements in women with osteoporosis and normal women and from these to determine guidelines for treatment.

Methods

Bone mineral density was measured using a dual energy x ray absorptiometry system (Hologic QDR-1000) in 1026 normal white women aged 40–79 years (average age 52 years) referred for assessment of their risk of osteoporosis by doctors from London and the southeast of England. Women were not included as normal if they had a known secondary cause of osteoporosis, a menopause before the age of 40, a history of secondary amenorrhoea, use of steroids or hormone replacement treatment, a history of fractured spine, wrist or femur, or osteopenia detected radiologically as the reason for their referral. Bone mineral density was also measured in 110 women aged 40–82 years (average age 65 years) referred to an osteoporosis clinic with radiological confirmation of at least one atraumatic vertebral collapse.

Measurements of BMD were made at the lumbar spine and neck of femur. The spinal value was calculated as an average of the BMD from L1 to L4 and the femoral neck value was derived from a region of interest identified by the QDR-1000 software as a 1.5 cm band adjacent to the greater trochanter. Long term precision errors, estimated with daily BMD measurements using an anthropomorphic spine phantom, were 0.38% and the in vivo precision by four repeated measurements on three normal subjects over two weeks gave a coefficient of variation of 1.1% for the lumbar spine and 1.2% for the neck of femur. Two repeated measurements on the same day on 49 subjects with osteoporotic vertebral collapse gave a coefficient of variation of 1.6% for the lumbar spine and 1.2% for the femoral neck. Statistical analysis was performed using the paired *t* test.

Department of Nuclear Medicine, Guy's Hospital, St Thomas Street, London SE1 9RT, United Kingdom

P J Ryan
G M Blake
I Fogelman

Correspondence to: Dr P J Ryan.

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Table 1 Mean (SD) bone mineral density (BMD) (g/cm^2) of spine and neck of femur in normal women and women with osteoporosis

Age range (years)	Spinal BMD	Femoral BMD
50–59 (normal women (n=606))	0.934 (0.167)	0.750 (0.145)
50–59 (women with osteoporosis (n=29))	0.691 (0.110)	0.579 (0.091)
60–69 (normal women (n=109))	0.838 (0.149)	0.659 (0.136)
60–69 (women with osteoporosis (n=53))	0.622 (0.163)	0.556 (0.119)

Table 2 Numbers (per cent) of normal women with spinal or femoral neck bone mineral density (BMD) above the fracture thresholds

Age (years)	No above fracture thresholds	
	Spine	Femoral neck
40–44 (n=86)	80 (93)	82 (95)
45–49 (n=237)	216 (91)	207 (87)
50–54 (n=350)	292 (83)	311 (89)
55–59 (n=246)	171 (69)	184 (75)
60–64 (n=78)	48 (62)	44 (56)
65–69 (n=29)	16 (55)	15 (52)

Lumbar spine bone mineral density (BMD) (mean (SD)) for 1026 normal women aged 40–70 years plotted versus age and superimposed on a scatter plot of lumbar spinal BMD versus age for 110 women with osteoporosis.

Results

Table 1 gives the BMD results for the spine and femur in normal women and women aged 50–69 years with osteoporosis. There were only two women with spinal fractures in their fifth decade of life and three normal women in their eighth decade preventing an extension of the age range for comparison of the two groups. Spinal BMD was significantly decreased in the group with osteoporosis ($p < 0.001$) by -26% in women in the sixth and seventh decades. Femoral neck BMD was also significantly decreased ($p < 0.001$) by -23% in the sixth decade and -16% in the seventh decade.

A BMD fracture threshold has been defined as the 90th centile of BMD for the group with fractures.⁷ Using this definition the lumbar spine threshold was identified as $0.810 \text{ g}/\text{cm}^2$ and the femoral neck threshold as $0.656 \text{ g}/\text{cm}^2$ in the patients with osteoporosis.

The number and percentage of the 1026 normal women with spinal or femoral neck BMDs above the respective threshold values were calculated for five year age bands and are given in table 2. It is clear that there is an overlap in the spinal BMD values for the normal and osteoporotic groups. The figure shows a plot of spinal BMD results versus age for the group with osteoporosis with the mean (SD) values for the normal women superimposed.

We examined further the BMD of normal postmenopausal women with the same age of menopause, where known, but different chronological ages (tables 3 and 4). The average BMD weighted by age decreased by $0.006 \text{ g}/\text{cm}^2/\text{year}$ at the lumbar spine and femoral neck between six and 10 years (average eight years) and 11–15 years (average 13 years) after menopause. Assuming that bone mass decreases at the same rate after 11–15 years postmenopause as between six and 10 and 11 and 15 years, the average lumbar spine BMD would reach the spinal fracture threshold 18 years and the femoral neck threshold 15 years after the menopause.

Table 3 Mean spinal bone mineral density (BMD) (g/cm^2) of women with same age at menopause but different chronological ages

Age (years)	Years from menopause					
	1–5 years		6–10 years		11–15 years	
	No of women	Mean BMD	No of women	Mean BMD	No of women	Mean BMD
45–49	42	0.939	—	—	—	—
50–54	159	0.945	31	0.879	—	—
55–59	107	0.930	62	0.862	25	0.857
60–64	—	—	22	0.906	28	0.822
65–69	—	—	—	—	7	0.848

Table 4 Femoral neck bone mineral density (BMD) (g/cm^2) of women with same age at menopause but different chronological ages

Age (years)	Years from menopause					
	1–5 years		6–10 years		11–15 years	
	No of women	Mean BMD	No of women	Mean BMD	No of women	Mean BMD
45–49	42	0.731	—	—	—	—
50–54	159	0.769	31	0.718	—	—
55–59	107	0.751	62	0.714	25	0.701
60–64	—	—	22	0.710	28	0.657
65–69	—	—	—	—	7	0.673

Discussion

Many doctors want to know a woman's risk of osteoporotic fracture with a view to helping them make an informed decision regarding the use of long term hormone replacement treatment. At present, however, there is no consensus regarding appropriate advice. A Royal College of Physicians report suggested that hormone replacement therapy should be offered to women who have a BMD below a certain specified cutoff value.⁶ As the lifetime risk of hip fracture is about one in three it might be reasonable to offer hormone replacement therapy to women with the lowest 30% BMD.⁸ Hip fractures do not only happen to those with the lowest 30% of BMD, however, and furthermore the percentage of women who have spinal fractures, which can produce considerable morbidity, is probably higher than 30%.⁹

Another approach to the prevention of osteoporosis could be to maintain a woman's bone mass above the BMD threshold below which fractures occur. As can be seen from the figure, however, there is an overlap in the BMD of subjects with and without fractures and therefore no threshold can be chosen to completely separate the two groups. Furthermore whatever threshold is used increasing the threshold increases its sensitivity in identifying patients with fractures but at a cost of specificity, with a lower threshold having the reverse effect. A value of two standard deviations below young normal subjects has been proposed,¹⁰ however, though this is at about the 90th centile for spine and femoral neck BMD for crush fractures but at the upper 99th centile for femoral neck BMD for hip fractures. To overcome such regional differences it has been suggested that it should be defined with respect to a fixed upper axial BMD for the group of subjects with fractures, typically the 90th centile.⁷

Hormone replacement therapy is known to prevent loss of bone and to reduce fracture incidence in postmenopausal women.^{11 12} The phase of most rapid bone loss occurs in the first few years after the menopause and our data from women aged 40–69 years (tables 3 and 4) support those of others in showing that the age of menopause is a more important determinant of bone mass than chronological age.^{13–15} If bone mass is to be maintained at the highest level hormone replacement therapy should be introduced at the menopause, but it is not clear what percentage of subjects should be offered treatment. If we use the 90th centile of women with osteoporosis as the fracture threshold it is apparent (table 2) that less than 10% of normal women aged 40–44 years fall below it but this increases to 25–30% by the age of 55–59 years and to about 50% by 65–69 years. A case therefore exists to recommend hormone replacement therapy after the menopause to at least 50% of postmenopausal women. The data for BMD and years after the menopause (tables 3 and 4) show that the mean BMD will reach the

fracture threshold about 18 years after menopause at the lumbar spine and after 15 years at the femoral neck. This also implies that to keep their BMD above the fracture threshold by the age of 70 years, at least 50% of postmenopausal women will have to be treated.

For women aged 70–90 years further bone loss will have occurred. Estimates for normal rates of bone loss in the elderly have varied between 0.2 and 1%,^{7 16} but any further bone loss will mean that most women will eventually have a BMD below the fracture threshold. Therefore if the aim of treatment is to maintain women above the fracture threshold for life, then most will need hormone replacement therapy. This implies that for most women BMD measurements should be performed to assess the duration of hormone replacement therapy. For assessment of the risk of osteoporosis and which subjects require hormone replacement therapy, however, BMD measurements, though remaining useful, will have a decreased part to play. On the basis of data expressed in this paper it should be possible to generate tables showing the necessary duration of hormone replacement therapy based on age at menopause or, if unknown, the chronological age, BMD and life expectancy. Serial measurements of BMD would allow refinements to be made to these recommendations.

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