Current Criteria for Hip Fracture Risk Assessment – Are We Missing Something?

Elena Segal MD[1], Chaim Zinman MD[2,4], Batia Raz MD[3] and Sophia Ish-Shalom MD[1,4]

[1]Metabolic Bone Diseases Unit, [2]Department of Orthopedic Surgery, and [3]Endocrine Laboratory, Rambam Medical Center, Haifa, Israel
[4]Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

Key words: bone density, hip fracture prediction, risk factors

Abstract

Background: Hip fracture rates are increasing worldwide, and the risk for a second hip fracture is high. The decision to administer antiresorptive treatment is based mainly on bone mineral density and/or a history of previous osteoporotic fractures.

Objectives: To evaluate the contribution of BMD, previous fractures, clinical and laboratory parameters to hip fracture risk assessment.

Methods: The study population included 113 consecutive hip fracture patients, aged 72.5 ± 9.4 years, discharged from the orthopedic surgery department. BMD was assessed at the lumbar spine, femoral neck and total hip. The results were expressed in standard deviation scores as T-scores – compared to young adults and Z-scores – compared to age-matched controls. Plasma or serum levels of parathyroid hormone, 25-hydroxyvitamin 3 and urinary deoxypyridinoline cross-links were evaluated.

Results: We observed T-scores ≤-2.5 in 43 patients (45.3%) at the lumbar spine, in 47 (52.2%) at the femoral neck and in 33 (38%) at the total hip. Twenty-eight patients (29.5%) had neither low BMD nor previous osteoporotic fractures. Using a T-score cutoff point of (-1.5) at any measurement site would put 25 (89%) of these patients into the high fracture risk group. Mean DPD level was 15.9 ± 5.8 ng/mg (normal 4–7.3 ng/mg creatinine). Vitamin D inadequacy was observed in 99% of patients.

Conclusions: Using current criteria, about one-third of elderly hip fracture patients might not have been diagnosed as being at risk. Lowering the BMD cutoff point for patients with additional risk factors may improve risk prediction yield.

IMAJ 2007;8:35–38

Hip fractures account for about 10% of all fractures, and a much greater proportion in the elderly [1]. The rate of hip fracture is increasing by 1–3% annually [2]. The annual hip fracture rate in the United States, estimated at 1.7 million in 1990, is expected to reach 6.3 million by 2050 [3]. In Israel, 6000 hip fractures occur yearly [4]. About 8% of these patients sustain repeat hip fractures during the first post-fracture year [5]. The frequency of two hip fractures in the course of an individual's life could reach 20% [6].

Mortality from a hip fracture is 10–20% and half the fracture survivors are left with a longstanding disability [7]. Identification of patients at risk for hip fracture is extremely important. The World Health Organization criteria for the diagnosis of osteoporosis are a bone mineral density T-score ≤-2.5 at any measurement site or a history of previous osteoporotic fracture. These are usually the decisive factors for the administration of fracture prevention treatment.

BMD = bone mineral density
DEXA = Dual Energy X-ray Absortiometry

Patients and Methods

Patients

The study group comprised 113 elderly hip fracture patients, 87 women and 26 men (mean age 72.5 ± 9.4 years) who were hospitalized during 1 year in the orthopedic surgery department. A detailed medical history of each patient was obtained, including individual and family fracture history, concomitant diseases and current drug treatment. Patients suffering from malignant diseases and metabolic bone diseases, patients with dementia and patients taking glucocorticoids or bisphosphonates were excluded from the study.

Laboratory evaluation

Serum calcium, inorganic phosphate, creatinine, albumin, and liver enzymes were assessed, using standard laboratory techniques (Hitachi 747™, Roche). 25-hydroxyvitamin D3 was assessed by ^{125}I-radioimmunoassay (DiaSorin, Stillwater, Minnesota, USA), intact parathyroid hormone by IRMA (Nichols Institute Diagnostics, CA, USA), and deoxypyridinoline cross-links level in second morning urine by Pyrilinks-D ELISA (Metra Biosystems, Mountain View, CA,USA).

BMD measurements

Dual energy X-ray absorptiometry analysis was performed 3–6 months after hospital discharge. BMD measurements of the lumbar spine (L2-L4), femoral neck and total hip of contralateral leg were performed using DEXA (Lunar DPX scanner, Madison, WI, USA). BMD results were expressed in comparison to young adults (T-scores) and in standard deviation scores compared to age-matched controls (Z-scores).

Statistical analysis

Analysis was performed using the SPSS statistical software version 11.5 (SPSS Inc., Chicago, USA). Chi-square test (Fisher's exact test when appropriate) was used to examine differences between groups in categorical variables, and *t*-test for continuous variables.

Results

Twenty patients (18%) reported previous low trauma osteoporotic fractures. There was no difference in the previous fractures between patients with T-scores ≤-2.5 and those with T-scores >-2.5. The data are presented in Table 1.

BMD L2-L4 T-scores ≤-2.5 were observed in 43 patients (45.3%): 39 women (53%) and 4 men (18%). Significantly more women than men had T-scores ≤-2.5 at the spine (P = 0.004). Femoral neck T-scores ≤-2.5 were observed in 47 (52.2%); of them 38 (56%) were women and 9 (41%) men. The difference was not statistically significant. Total hip T-scores ≤-2.5 were observed in 33 (38%); 29 women (45%) and 4 men (18%), $P < 0.03$.

Twenty-eight patients (29.5%) – 18 women and 10 men (32% of all women and 45.5% of all men) – had neither a history of previous osteoporotic fractures nor BMD measurement results consistent with osteoporosis. Using a cutoff point of T-score -2.0 in at least one measurement site put 16 of these 28 patients (57%) into the high fracture risk group. Using a T-score cutoff point of -1.5 at any measurement site put 25 (89%) of patients into the high fracture risk group.

Eighty-eight patients (95%) had increased DPD levels (range 4–32.9, mean ± SD 15.85 ± 5.77). Thirty-eight patients (33.6%) were vitamin D deficient [25(OH)D3 serum level ≤ 10 ng/ml], 29 (25.7%) were vitamin D insufficient [25(OH)D3 serum level 10–15 ng/ml] and 46 (39.8%) had vitamin D serum level > 15 ng/ml. Forty-five patients (39.8%) had 25(OH)D3 levels between 15 and 30 ng/ml, defined now as vitamin D inadequacy. One patient (0.9%) had 25(OH)D3 level above 30 ng/ml. Comparative characteristics of hip fracture patients with and without low BMD and/or previous osteoporotic fractures are presented in Table 2. Patients with lowest BMD and patients with a history of previous osteoporotic fracture had significantly higher DPD levels ($P < 0.001$).

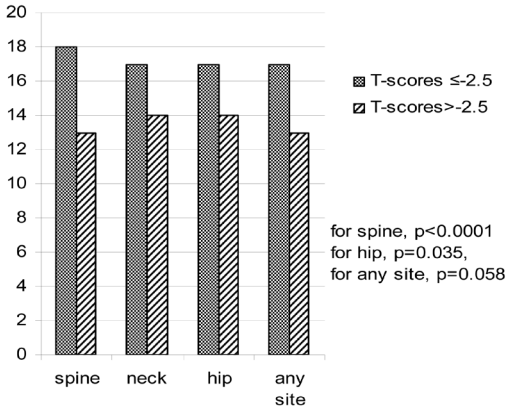

Figure 1. DPD level in hip fracture patients

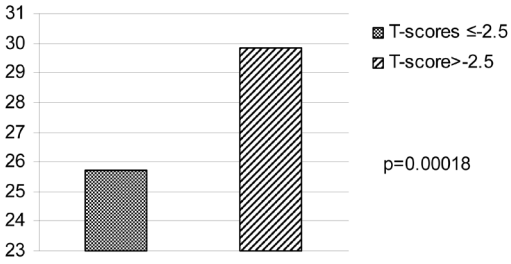

Figure 2. BMI in hip fracture patients

DPD = deoxypyridinoline cross-links
25(OH)D3 = 25-hydroxyvitamin D3

Table 1. Previous osteoporotic fractures in elderly hip fracture patients

		Hip		Vertebral		Wrist		Humerus		Two fractures
	No. (%)	T≤–2.5	T>–2.5	T≤–2.5	T>–2.5	T≤–2.5	T>–2.5	T≤–2.5	T>–2.5	
Men	4 (15.4)	0	1 (3.8)	1 (3.8)	0	1 (3.8)	0	1 (3.8)	0	2 (7.6)
Women	16 (18.3)	0	0	1 (1.2)	1 (1.2)	6 (6.9)	5 (5.8)	1 (1.2)	2 (2.4)	3 (3.6)
Total	20 (17.8)		1(0.9)	2 (1.8)	1(0.9)	7 (6.3)	5 (4.5)	2(1.8)	2(1.8)	5 (4.5)

Table 2. Comparative characteristics of hip fracture patients with and without low BMD and/or previous osteoporotic fracture

	Neither low BMD nor fracture (n=28)	Low BMD and/or fracture (n=85)
Men	10 (35.7%)	15 (18%)
Women	18 (64.3%)*	70 (82%)
Age	51-88 (70.2 ± 10.0)	50-90 (73.2 ± 8.8)
Family history of fracture	2 (7.14%)	9 (10.5%)
Smoking	6 (21.4%)	13 (15.2%)
BMI	28.5 ± 3.99	27.2 ± 4.8
25(OH)D3 serum level	13.1 ± 4.3	12.8 ± 5.9
DPD	12.4 ± 4.6**	16.9 ± 6.1
Impaired vitamin D status 25(OH D3 < 15 ng/ml	15 (60%)	48 (56%)
Cardiovascular diseases	21 (75%)	53 (62.7%)
Gastrointestinal diseases	2 (7.1%)	10 (11.7%)
Renal diseases	2 (7.2%)	3 (3.5%)
Diabetes mellitus	9 (32.1%)	20 (23.9%)

* P = 0.06, ** P < 0.001

Only two patients had DPD levels within the reference range. Higher DPD levels were observed in patients with lower BMD T-scores [Figure 1]. Patients with lower BMD T-scores at any measurement site had lower body mass index [Figure 2]. The T-score cutoff point, which included 92% of the patients in the high risk group, was -1.2.

Discussion

Fractures of the femoral neck are currently one of the most serious healthcare problems facing the aging population [8]. The estimated lifetime risk for a hip fracture is 15.6–17.5% in women and 5.2–6.9% in men [9]. The diagnosis of osteoporosis and the estimation of a fracture risk in the primary care setting are currently based mainly on bone densitometry results and history of previous low trauma fractures. Femoral neck BMD measurement was found to predict osteoporotic fracture [10]. BMD accounts for the great majority of bone strength and is the current gold standard for the diagnosis of osteoporosis, as well as for predicting fracture risk. Sensitivity of BMD measurements in fracture risk

prediction in the elderly remains controversial, and while lower BMD has been found to be associated with an increased risk for hip fracture prior to age 70, a considerable overlap in BMD between hip fracture patients and controls was observed after the age of 70 [11]. Comparable osteoporotic indices in cases and controls were previously observed [12]. BMD accounts for up to 85% of the variance in bone strength [13] and exhibits a continuous association with strength, such that with each standard deviation decline in BMD, the risk of fragility fracture approximately doubles [14].

High bone turnover is considered to influence bone quality and increase the risk for fractures [14]. Persistently elevated bone turnover throughout menopause is associated with structural decrements. It cannot be measured routinely and non-invasively and testing is used mostly in research applications [15]. However, the sustained high levels of bone turnover after menopause, when the rate of bone resorption consistently exceeds bone formation, do lead to progressive declines in BMD and deterioration of microarchitecture. This process results in the irreversible loss of structural elements and accounts for much of the increase in fracture risk with advancing age observed among untreated women. Significant associations between high bone turnover and increased risk of fracture have been reported in some, but not all studies [16]. Although neither BMD nor bone turnover is a perfect predictor, there are no useful alternatives, at present, for either the researcher or the clinician [15].

An increase in DPD in our patients could be partially explained by a recent hip fracture; however, we observed higher DPD levels in patients with lowest BMD or with a history of previous fractures. It may support the postulation that higher bone turnover may increase bone loss and bone fragility (multiple fractures)

In the Rotterdam study, the risk of hip fracture was shown to increase 13-fold from age 60 to 80; decrease in bone density associated with age contributed a 1.9-fold increase in risk in women and 1.6 in men [17], and it was found that 85% of the rise in risk of fracture in both men and women was attributable to factors other than BMD. The fracture threshold of BMD T-score (-2.5) does not change through life, but it is well known that age is a strong and independent predictor of hip fracture [17] and was found to be a better predictor than BMD [18].

Patients with multiple risk factors are at greater risk for hip fracture. Previous low trauma fractures, family history of severe osteoporosis, vitamin D status, smoking status, BMI, propensity to falls due to several concomitant diseases, and long-term use of benzodiazepines, anticonvulsants and ingestion of large amounts of caffeine [19] increase the risk of hip fracture. Older age, previous self-reported fracture after age 50, maternal history of hip fracture after age 50, greater height at age 25, impaired cognition, slower walking speed, nulliparity, type 2 diabetes mellitus, Parkinson's disease, and depth perception each independently predicted a 1.17 to 1.83-fold increase in hip fracture risk, whereas each standard deviation decrease in hip BMD was found to be independently associated with a 1.84-fold increase in risk [20].

In the OFELY Study in postmenopausal women with osteopenia, an association was found between low BMD, increased bone turnover markers, prior fracture, and an increased risk of fracture in the subsequent 10 years [21]. Assessment of additional risk factors may play an important role in identifying subjects at high risk of fracture who could not be adequately detected by BMD measurement alone and who may benefit from therapeutic intervention. In our study, patients with low BMD and/or previous osteoporotic fractures and patients with so-called non-osteoporotic BMD and/or without previous fractures had the same rate of vitamin D deficiency, the same BMI, age and smoking status; the difference in the number of previous fractures between the groups was not significant. Family history of osteoporosis was equally frequent in both groups. DPD was higher in the low BMD group. An almost twofold increase in hip fracture rate was observed in diabetics [22]. We found a higher, but non-significant, rate of diabetes in the patients with hip fractures and normal BMD. This observation illustrates the higher fracture risk in diabetics, regardless of BMD measurements. Furthermore, we found a higher rate of cardiovascular disease in the normal BMD group. It can be concluded then that patients with diabetes and ischemic heart disease deserve special attention in terms of fracture prevention. Our hip fracture patients with normal, osteopenic or osteoporotic BMD had the same characteristics, with only a slightly higher rate of concomitant diseases.

The evidence that bone density predicts fractures is based on epidemiologic studies of large populations. Clinicians treat individuals, and in this context, the confidence with which bone density can be used to predict fracture in an individual is arguably negligible [23]. According to Miller et al. [24], previous fracture was found to be the strongest predictor of fracture in 1 year. The classification algorithm [24] for identifying women with osteopenic BMD T-scores between -1.0 and -2.5 includes previous fracture, BMD T-scores less than -1.8, poor health status and poor mobility. Yet again, one-third of our patients had never suffered from a fracture before they sustained a hip fracture, and we did not observe any significant difference in the general health of these patients compared with the rest of the group. While trying to identify additional risk factors for hip fractures, aside from BMD, that could help to identify persons at high risk, we actually found that about one-third of patients at risk could have easily been missed.

According to Siris et al. [25], within 1 year after BMD measurement, 82% of osteoporotic fractures occurred in women with peripheral T-scores higher than -2.5; 67% had T-scores greater than -2.0, and only 18% of fractures occurred in women with osteoporotic T-scores. Even using the NOF (National Osteoporosis Foundation) guidelines to treat patients with T-scores of $\leq$- 2.0 or $\leq$1.5 with prior osteoporotic fracture, family history of fracture, low body weight or smoking, only about half of the fractured patients described in this study would have been treated.

Using a higher BMD cutoff point may help identify persons at risk for hip fracture. It is widely believed that the most reli-

BMI = body mass index

able BMD measurement for predicting fracture risk at any given skeletal site is one made at the fracture site itself. For the hip, the data are consistent with a linear relationship, and suggest that measurements made at other sites provide no additional information about fracture risk above and beyond that provided by hip BMD itself.

The decrease in bone density associated with age makes a limited contribution to the exponential increase in the risk of hip fracture with age. For effective prevention, high risk groups need to be identified. Age, BMI, gender, height, the use of a walking aid, cigarette smoking, concomitant diseases, and laboratory evaluation [25(OH)D3 serum level in particular, that warrants a different specific therapeutic intervention, such as vitamin D replenishment until adequate serum levels are achieved] are not included in clinical hip fracture risk assessment and are not considered acceptable criteria for reimbursement of fracture risk-reducing treatments.

Conclusions

About one-third of the elderly hip fracture patients in our study had "non-osteoporotic" bone densitometry results and no previous osteoporotic fracture, and might have been missed using currently applied criteria for fracture prevention treatment.

Hip fracture risk assessment should probably include numerous factors: non-skeletal disorders such as diabetes, coronary artery disease and others that may increase the propensity to fall, vitamin D status, and possibly bone turnover assessment. Quantitative assessment based on a combination of these and other factors with established risk assessment thresholds is not yet available and are currently being developed by the WHO committee. For the time being, physicians should be more attentive to the presence of these factors and broaden the indications for therapeutic intervention (for example, vitamin D replenishment until adequate serum levels are achieved) for the elderly with "non osteoporotic" BMD values.

References

1. Eastell R, Reid DM, Compston J, et al. Secondary prevention of osteoporosis: when should a non-vertebral fracture be a trigger for action? QJM 2001;94:575–97.
2. Cummings SR, Melton LJ. Epidemiology and outcomes of osteoporotic fractures. *Lancet* 2002;359:1761–7.
3. Cooper C, Campion G, Melton LJ. Hip fractures in the elderly: a worldwide projection. *Osteoporosis Int* 1992;2:285–9.
4. Givon U. Consensus conference on the treatment and rehabilitation of hip fractures in the elderly. *IMAJ* 1999;1:131–6.
5. Bischoff HA, Solomon DH, Dawson-Hughes B, Wang PS, Avorn J. Repeat hip fractures in a population-based sample of Medicare recipients in the US: rates, timing and gender differences. J *Bone Miner Res* 2001;16:S1:291.
6. Dolk T. Influence of treatment factors on the outcome after hip fractures. *Upsala J Med Sci* 1989;94:209–21.
7. Meunier PJ. Epidemiology and prevention of hip fractures. In: Proceedings of the Conference on ILAR Congress of Rheumatology, Singapore, 1997;XIX:65–8.
8. Marks R, Allegrante JP, Ronald MacKenzie C, Lane JM. Hip fractures among the elderly: causes, consequences and control. *Aging Res Rev* 2003;2:57–93.
9. Boonen S, Broos P, Dequeker J. Age-related factors in the pathogenesis of senile (type 11) femoral neck fractures. An integrated view. *Am J Orthop* 1996;25:198–204.
10. Melton LJ, Crowson CS, O'Fallon WM, Wahner HW, Riggs BL. Relative contribution of bone density, bone turnover, and clinical risk factors to long-term fracture prediction. J *Bone Miner Res* 2003;18:312–18.
11. Cummings SR. Are patients with hip fractures more osteoporotic? Review of evidence. *Am J Med* 1985;78:487–94.
12. Fitzpatrick P, Kirke PN, Daly L, et al. Predictors of hip fracture and mortality in older women. *Irish J Med. Sci* 2001;170:49–53.
13. National Osteoporosis Foundation. Osteoporosis: review of the evidence for prevention, diagnosis, and treatment and cost-effectiveness analysis. *Osteoporos Int* 1998;8(Suppl 4):S1–88.
14. Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. *Br Med J* 1996;312:1254–9.
15. Miller PD, Hochberg MC, Wehren LE, Ross PD, Wasnick RD. How useful are measurements of BMD and bone turnover? *Curr Med Res Opin* 2005;21:545–54.
16. Garnero P, Hausherr E, Chapuy MC, et al. Markers of bone resorption predict hip fracture in elderly women: the EPIDOS prospective study. J *Bone Miner Res* 1996;11:1531–8.
17. De Laet CE, van Hout BA, Burger H, Hofman A, Pols HA. Bone density and risk of hip fracture in men and women: cross sectional analysis. *Br Med J* 1997;315:221–5.
18. Burger H, de Laet CE, Weel AE, Hofman A, Pols HA. Added value of bone mineral density in hip fracture risk scores. *Bone* 1999;25:369–74.
19. Cummings SR, Nevitt MC, Browner WS, et al. Risk factors for hip fracture in white women. Study of Osteoporotic Fractures Research Group. N *Engl J Med* 1995;332:767–73.
20. Taylor BC, Schreiner PJ, Stone KL, et al. Long-term prediction of incident hip fracture risk in elderly white women: study of osteoporotic fractures. J *Am Geriatr Soc* 2004;52:1479–86.
21. Sornay-Rendu E, Munoz F, Garnero P, Duboeuf F, Delmas P. Identification of ssteopenic women at high risk of fracture: the OFELY Study. J *Bone Miner Res* 2005;20:1813–19.
22. Schwartz AV, Sellmeyer DE, Ensrud KE, et al. Study of Osteoporotic Features Research Group. Older women with diabetes have an increased risk of fracture: a prospective study. J *Clin Endocrinol Metab* 2001;86:29–31.
23. Wilkin TJ, Devendra D. Bone densitometry is not a good predictor of hip fracture. *Br Med J* 2001;323:795–9.
24. Miller PD, Barlas S, Brenneman SK, et al. An approach to identifying osteopenic women at increased short-term risk of fracture. *Arch Intern Med* 2004;164:1113–20.
25. Siris ES, Chen YT, Abbott TA, et al. Bone mineral density thresholds for pharmacologic intervention to prevent fractures. *Arch Intern Med* 2004;164:1108–12.

Correspondence: Dr. S. Ish-Shalom, Metabolic Bone Diseases Unit, Rambam Medical Center, P.O. Box 9602, Haifa 31096, Israel.
Phone: (972-4) 854-2584
Fax: (972-4) 854-3416
email: e_segals@rambam.health.gov.il