Calcif Tissue Int (1990) 46:65–72

Calcified Tissue International

Clinical Investigations

Hip Fractures in Young Patients: Is This Early Osteoporosis?

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Summary. Hip fracture in patients under age 50 is rare, and is often not attributable solely to the energy of injury. Our aim was to determine if trabecular bone mineral density (BMD) is abnormal in young patients with hip fractures. We reviewed all hip fractures treated at our institution between 1979 and 1986 and contacted 20 patients under the age of 50 at the time of injury, all of whom wished to be studied. The mean age at the time of injury was 39 (range 24–47). Subjects were questioned for osteoporosis risk factors, classified by level of energy producing their injury, and then underwent quantitative computed tomography (QCT) bone densitometry of trabecular bone in the lumbar spine. Bone mineral density by QCT was below the mean for age in 90% of the patients, and was greater than 1 SD below the mean in 75%. Mean percentage BMD decrease from age-matched controls was 34% ($P < 0.005$) in women and 19% ($P < 0.005$) in men. There was an inverse correlation in the degree of BMD decrease and the energy level of injury. There was a direct correlation of the severity of BMD decrease and the cumulative number of osteoporosis risk factors. This investigation has found that 1–7 years following hip fracture, otherwise presumedly healthy young patients demonstrate a statistically significant decrease in spinal BMD from age/sex-matched controls. These data do not determine if osteopenia is the cause or the result of injury, nor do we wish to infer that measurement of bone density at one site can predict future fractures at other sites. However, as current thinking supports continuous age-related BMD decrease, this young group of patients with relatively low BMD for their age may be at increased risk for future development of more severe osteopenia. These findings suggest that the significance of hip fractures in young patients may currently be underestimated, and such patients may provide the unique opportunity for early identification of a group at increased risk for developing osteoporosis.

Key words: Osteoporosis — Hip fractures — QCT bone densitometry — Early detection — Young patients.

The social and financial impact of osteoporosis on the United States population continues to grow rapidly [1–4]. We are currently developing noninvasive screening methods and refinement of medical therapy. Several techniques of noninvasive bone mineral density (BMD) measurement are available, including radiographic photodensitometry, single- and dual-photon absorptiometry, computed tomography, and neutron activation [5, 6]. With continued improvement in these noninvasive modalities, early identification of patients at higher risk may facilitate timely treatment of the age-related decrease in bone density.

Proximal femur fractures are commonly seen with osteoporosis but are rare before age 50, comprising less than 10% of hip fractures in all age groups [7, 8]. In the past, much research has concentrated on the relation of risk factors and fracture incidence to BMD in postmenopausal women and

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Presented in part at the 35th Annual Meeting of the Orthopaedic Research Society, February 6–9, 1989, Las Vegas, NV, USA.

Table 1. Characteristics of patients in study group

	Male	Female	Total
No. patients	14	6	20
Age			
At time of study	41.7	41.2	41.4
At time of injury	38.9	38.2	38.6
Elapsed time to study	2.7	3.0	2.9
Race			
Black	4	0	4
White	10	6	16
Energy level of injury			
High	3	0	3
Medium	5	0	5
Low	6	6	12

elderly men. In this older population, clear correlations may be complicated by coexisting postmenopausal (type I) and senile (type II) osteoporosis [4, 9]. In the active young population, where the energy level of injury is often greater than that of a simple fall, the significance of proximal femur fractures as an early indicator of osteoporosis has not been well studied. The purpose of this investigation was to determine if young patients with hip fractures have abnormal trabecular BMD.

Materials and Methods

Patient Selection and Characteristics

We reviewed all hip fractures treated at our institution between 1979 and 1986. From 620 cases we identified 67 patients (52 male, 15 female) under age 50 at the time of injury. We contacted 20 patients (14 male, 6 female), all of whom wished to be studied (Table 1). Mean age at the time of injury was 39 years (range 26–47) and at the time of this study it was 42. There were 16 white and 4 black patients. Two fractures were transcervical and all others were sub- or intertrochanteric.

Patients were first classified by level of energy producing their injury (3-high, 5-medium, 12-low). High energy was considered to be produced by a fall from more than standing height (1 patient), or by a high-speed motor vehicle accident with associated pelvic, femoral, or tibial shaft fractures (2). Low energy level included falls from a standing height (9), and other low impact trauma (3). The medium energy category was assigned to low-speed motor vehicle accidents (3) and any injuries that were not clearly high or low energy (2 patients).

Patients were then questioned using a forced-choice questionnaire for underlying systemic disease, known calcium metabolism disorders, and the following osteoporosis risk factors: early menopause, low dietary calcium intake, cigarette smoking, alcohol and caffeine consumption, family history, sedentary life style, history of previous fractures (including childhood), use of antiseizure medication, race, and lean body habitus (<90% weight [10]). Patients were also questioned about calcium and estrogen supplementation. All patients had normal serum calcium, phosphorus, and alkaline phosphatase levels at the time of injury. One patient in the low energy subgroup had a history of cerebrovascular event and residual limb weakness, but the remainder had no history of significant disease. All but 2 patients were able to return to their pre-injury activity level.

To validate the use of a large published database of historical age/sex-matched controls, we obtained 50 normal volunteers from the general community to undergo QCT bone densitometry using the same protocol as the study patients. The normal volunteers denied history of back pain or surgery.

Bone Mineral Density Measurement

All patients were scanned during a 2-month period by the same technologist on a General Electric model 8800 CT scanner. Patients were scanned in the supine position with their hips flexed to straighten the lumbar lordosis and improve contact with the calibration phantom. A lateral scout image was used to position the gantry for four axial sections, one each through the midbody of L-1, L-2, L-3, and L-4. The 120 kVp sections were 10 mm thick and were oriented parallel to the vertebral endplates.

A region of interest (ROI) was generated over each axial section using commercially available software. A circular ROI was used to measure the attenuation value in each solution within the phantom, and an elliptical ROI was used for the vertebral body. The region was made as large as possible, excluding cortical bone and any areas of nonuniformity (i.e., vascular structures or areas of endosteal sclerosis).

The calibration phantom used has five tubes embedded in it which contain solutions of 50, 100, and 200 mg K_2HPO_4, water, and a fat-equivalent solution of ethanol (Imatron Inc., San Francisco, CA). A standard curve, which related the attenuation values for the phantom tubes in Hounsfield units to concentration of dipotassium hydrogen phosphate, was constructed by linear regression for each axial section. The attenuation values for the vertebral bodies were then interpolated and expressed as mg/cm^3 of an equivalent K_2HPO_4 solution.

Values for the four vertebral bodies were averaged to yield a composite value of BMD for each patient. In one patient, the value for a particular vertebral body was excluded from the average because it varied from the mean by more than 2 SD. In another patient, one value was excluded because there was obvious movement during the scan and poor fit of the standardization curve ($r < 0.997$).

Comparisons and Statistical Analysis

Comparison of the BMD of each study patient and normal volunteer was made to the mean of published controls of the same age and sex [11]. To facilitate analysis of data independent of patient age, the percentage decrease of BMD for each patient was calculated as

$$\%\ \text{BMD decrease} = \frac{\text{Age/sex-matched control mean—patient BMD}}{\text{Age/sex matched control mean}} \times 100.$$

Data analysis using percent BMD decrease yielded results comparable to calculations using the raw values of BMD decrease, however, the former is the mathematically preferable method as it corrects for the large variation in the absolute BMD values over a wide age range. Statistical linear regression and Spearman

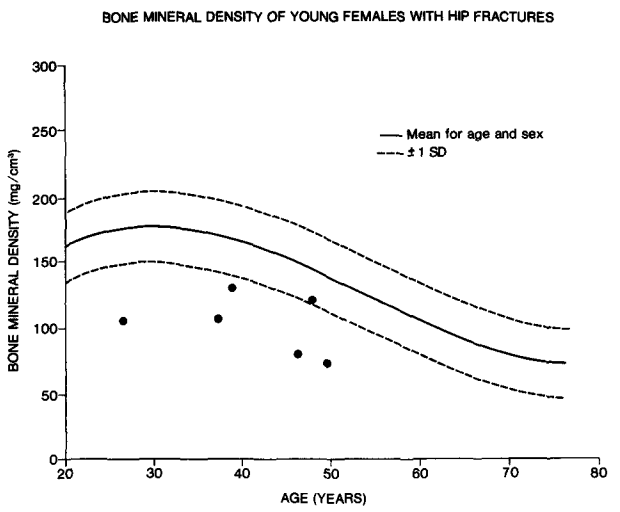

Fig. 1. Comparison of bone mineral density of young female patients with hip fractures to age-matched controls.

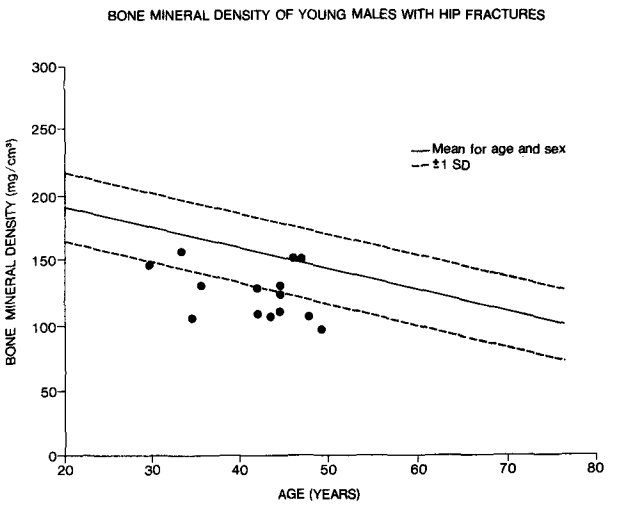

Fig. 2. Comparison of bone mineral density of young male patients with hip fractures to age-matched controls.

correlation coefficients were calculated using the SAS system to analyze trends in risk factors and energy of injury (SAS Institute Inc., Cary, NC).

Results

Bone mineral density determined by QCT was below the mean for age and sex in 90% of the patients (Figs. 1, 2) and was greater than 1 SD below in 75% of the patients studied. Mean percentage BMD decrease from that of age-matched controls was 34.2% ($P < 0.005$) in women, and 18.8% ($P < 0.005$) in men (Table 2). In contrast, the mean percent BMD difference of the 50 normal volunteers from the historical controls was 3.8% ($P > 0.05$).

There was a strong inverse correlation ($r = -0.66$, $P < 0.01$) in the degree of BMD decrease and the energy level of injury (Fig. 3). Mean percentage BMD decrease of the subgroup with low energy injury was 27.6% ($P < 0.005$) compared with 20.5 percent ($P < 0.005$) and 11.8% ($P < 0.025$) for the medium and high energy subgroups, respectively (Table 3). The apparent larger decrease in women was persistent even when comparing their decrease (34.2%, $P < 0.005$) to that of the men (20.9%, $P < 0.005$) in the same (low) energy level subgroup.

All patients studied had at least one of the surveyed risk factors for osteoporosis. The most common risk factors (Table 4) were non-black race 80%; history of previous fractures 70%; high caffeine intake (>4 cups coffee/day) 40%; significant cigarette smoking (>1 pack/day) 40%; and moderate alcohol consumption (>10 drinks/week) 25%. Sex was not considered a risk factor in this tabulation because

Table 2. Bone mineral density decrease and sex dependence

Patient subgroup	Mean % BMD decrease[a]	SEM[b]	95% confidence interval	*P* value
All females (N = 6)	34.2	5.1	20.8–47.6	<0.005
All males (N = 14)	18.8	3.2	11.7–25.9	<0.005
Males (low energy) (N = 6)	20.9	5.6	6.3–35.5	<0.005

[a] Mean percent change in BMD for each sex subgroup of patients from age/sex-matched control population mean
[b] Standard error of mean

BMD comparisons were made to sex-matched controls. Protective factors (estrogen and calcium supplementation) were subtracted from the number of risk factors to get a net risk factor number used for comparison with BMD. There was a strong positive correlation ($r = 0.67$, $P < 0.001$) of the severity of BMD decrease and the net number of osteoporosis risk factors (Fig. 4).

There was no correlation of BMD decrease with length of time from injury to scanning ($r = -0.30$, $P = 0.20$) or with age of patient ($r = 0.04$, $P = 0.86$). Analysis of the patients who were not contacted was as follows: mean age 38 years; sex 16 female, 31 male; energy of injury 8-high, 15-medium, 25-low; race 38 white, 9 black; mean time since injury 3.3 years.

Discussion

Many investigations, yielding variable results, have

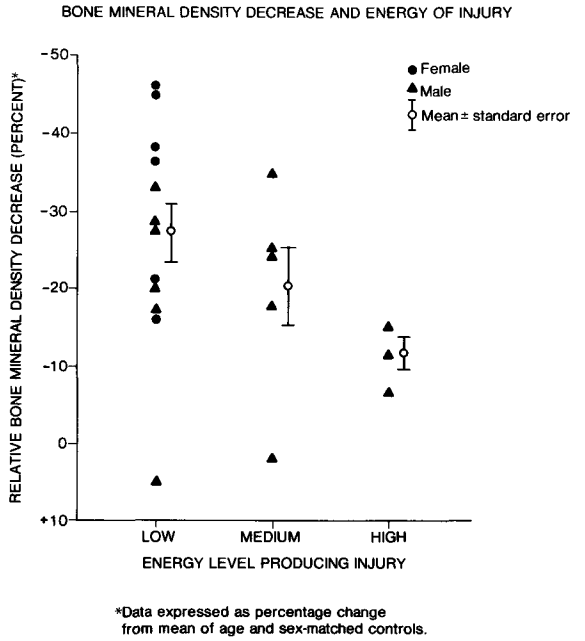

Fig. 3. Relationship of bone mineral density decrease (percent) from control population mean to the energy level producing the injury. Strong inverse correlation is evident.

Table 3. Bone mineral density decrease related to energy of injury

Energy level of injury	Mean % BMD decrease[a]	SEM[b]	95% confidence interval	*P* value
Low (N = 12)	27.6	4.2	18.3–36.9	<0.005
Medium (N = 5)	20.5	6.2	4.7–36.3	<0.005
High (N = 3)	11.8	2.4	1.4–22.2	<0.025
Low + medium (N = 17)	25.2	4.0	17.9–32.5	<0.005

[a] Mean percent change in BMD for each energy level subgroup of patients from age/sex-matched control population mean
[b] Standard error of mean

Table 4. Osteoporosis risk and protective factors in study group

Risk factors	No. patients
Race (non-black)	16
History of previous fractures	14
Cigarette smoking (>1 pack/day)	8
Caffeine consumption (>4 cups/day)	8
Alcohol consumption (>10 drinks/week)	5
Family history of osteoporosis	4
Sedentary life-style	3
Early menopause (surgical or natural)	2
Low dietary calcium intake	1
Slender build (<90% ideal weight)	1
Steroid, dilantin use	0
Protective factors	
Dietary calcium supplementation	4
Estrogen administration	1

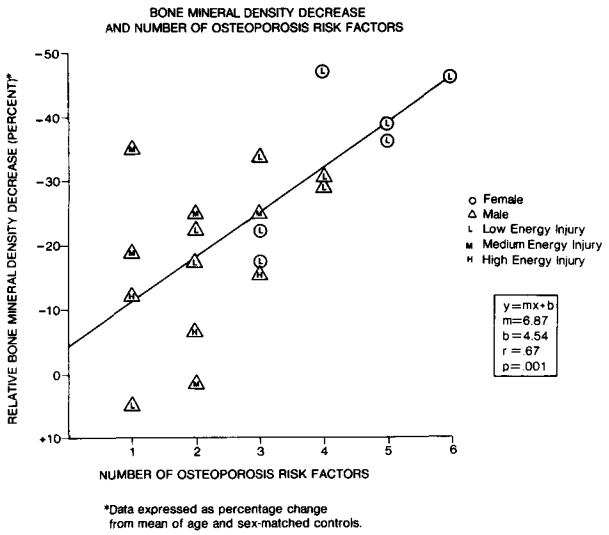

Fig. 4. Relationship of bone mineral density decrease (percent) from control population mean and the number of historical osteoporosis risk factors. Strong positive correlation suggests a cumulative association of risk factors with severity of bone mineral deficiency.

been undertaken in an attempt to correlate hip fractures with decreased BMD and osteoporosis [12–15]. The focus of most of these studies has been on the older population [7, 16, 17]. In young adults, the incidence of proximal femur fractures is extremely low [7, 18]; however, unlike in the older population, there is a male predominance [17, 19, 20]. In young patients the occurrence of hip fractures following moderate or severe trauma is not usually investigated on a pathologic basis. Accordingly, the significance of a hip fracture in a young adult and its relationship to the energy level of injury and to the BMD deserves consideration.

Quantitative computed tomography (QCT) has been widely utilized to selectively measure trabecular BMD with accuracy and precision [5, 6, 21–25]. Serial measurement of BMD has shown that the age-related rate of trabecular bone loss is eight times greater than that of cortical bone [26–28]. Accordingly, BMD measurement at sites composed of predominantly trabecular bone such as the vertebral body may be a more sensitive indicator of bone mass changes in osteoporosis [29–33]. However, the correlation of bone mass measured in the spine with bone mass or fracture risk at other sites is unreliable. Investigations in older patients and cadavers have generally shown a poor correlation between decreased spinal bone density and hip frac-

tures or femoral bone density [34–35]. In the present study, we analyzed this relationship in younger patients prior to significant "normal" age-related bone loss.

The results of our investigation using QCT densitometry indicated that most of the young patients following proximal femur fractures had low trabecular BMD of the lumbar spine. This BMD decrease was observed even in patients who sustained higher energy injuries. The strong inverse correlation of severity of BMD decrease with the energy level producing the injury is easily rationalized. A bone that is markedly weakened should require less trauma to reach its fracture threshold than a bone that is minimally weakened. The apparent greater BMD decrease in females may be related either to sex or to the fact that all the females studied were in the low energy subgroup. This issue is partially resolved by the finding that the sex difference persists when comparing the mean BMD decrease of males and females within the same (low) energy subgroup.

Many dietary, environmental, medical, and genetic risk factors have been associated with osteoporosis [1, 3, 4, 36–40]. Our risk factor survey did not attempt to validate individual risk factors, but rather to assess the prevalence of the more common established risk factors in young patients. The most common risk factor in our study group was the non-black race. A smaller decrease in BMD in the black patients was observed; however, definite correlations are difficult because of the small size of this subgroup. It has been suggested that the incidence of osteoporosis in the black population may be low because of racial differences in calcitonin and skeletal mass [41, 42].

Another common risk factor in our study population was a history of previous fractures. This issue is not frequently addressed in the literature; a few studies have reported the prevalence of previous fractures in patients with hip fractures and osteoporosis to be 33–68% [12, 33, 43, 44]. Although 55% of our study group had a history of one or more fractures, the number of fractures did not correlate with the severity of BMD decrease.

It is extremely difficult to quantify the relative weight of each risk factor [45, 46], and precise multivariate analysis in this size study would not be reliable. Instead, we attempted an approximate correlation of the cumulative effect of all risk and protective factors on the amount of BMD decrease observed in the study group. For this analysis the risk factors were assumed to have equal weight and the protective factors were assigned an equal but opposite weighting.

There was a strong correlation between the net number of risk factors and severity of BMD decrease. The data suggest that the risk factors may have a cumulative effect on the degree of BMD decrease. In addition, patients with higher energy injuries tended to have fewer risk factors.

The close relationship of risk factors, BMD, and energy level producing the fracture supports the concept of a dynamic BMD fracture threshold. Nordin [43] has previously shown that there is an increased risk of many types of fractures as bone density decreases, and that there is no true cutoff or fracture threshold. The failure point of a bone will depend on both its inherent strength and the energy of the deforming force applied. Injury is most often due to minor trauma in older patients because of their limited level of activity, and the energy factor may be assumed to be a constant. However, as the activity level of younger patients is usually more vigorous and variable, the potential for higher energy trauma is greater and the energy producing the injury is no longer constant. Therefore, a fixed BMD number representing the threshold for fracture is less meaningful in this younger population.

The potential inaccuracies of this study lie in the methods of data measurement and study design, in the control data used for comparison, and the effects of sampling error. Single-energy QCT has been shown to have an accuracy of 5–8% [8, 47] and a precision of 2–4% [48–50]. There has been much discussion about the degradation of accuracy in older patients because of the age-related increase in marrow fat content [51], and dual-energy scanning techniques have circumvented this effect [52]. In young patients (in the fourth and fifth decades), comparison of single- and dual-energy techniques failed to reveal a significant difference in BMD; therefore, single-energy was used in this study [8, 26]. For the purpose of this investigation, the absolute BMD of the patients was not as important as comparison to the BMD of a control population measured by the same technique. The accuracy and precision of the measurements in this study were optimized by use of a single technologist for all scans and a dedicated scanner. The short time period during which all the patients were scanned helped to minimize any long-term machine drift.

Because this was a partially retrospective cross-sectional study, the patients were scanned at times varying from 0 to 7 years following their injuries. Comparisons were made to control groups matching the patients' age at the time of scanning. It should not be assumed that osteopenia predisposed these patients to fracture. Alternatively, because of the time delay in some of the scans, the decreased BMD may have been the result of the injury and subsequent recovery process rather than the cause. If the later relationship was true, one might expect

to see a temporal correlation of BMD decrease and elapsed time since fracture. The data do not demonstrate such a correlation, and because young patients with hip fracture are rapidly mobilized, posttraumatic osteopenia was probably not a major influence. This issue can only be totally resolved by an investigation that obtains all scans at the time of injury.

Because of the small body of published evidence pertaining to the subject of this investigation and the ethical dilemma of irradiating young healthy controls when accepted control data is already available, this study was designed primarily to utilize the University of California, San Francisco historical age and sex-matched controls [11]. The UCSF control data were collected from 323 ambulatory volunteers with onset of low back pain syndrome using single-energy QCT. To validate use of this larger body of control data, we determined that the mean percent BMD difference of our 50 normal volunteers from the historical data was 3.8%. This difference was negligible and not of the order of magnitude capable of affecting our results.

Assuming the variation in BMD from an Eastern to a Western urban population is minimal, the major difference from our patient group was that only Caucasian or Asian patients were used as UCSF controls. However, the black population is known to have 2–8% higher bone mineral content [41, 53]. This phenomenon serves only to strengthen our findings as 20% of the study patients were black and would be likely to have a greater BMD decrease when compared to race-matched controls.

The 20 patients who were contacted for our study do not comprise all of the eligible young patients with hip fractures in the past 7 years at this institution. After careful review of the records of the remaining patients we could not contact, the subgroup we did study was not significantly different on the basis of age, sex, race, time since injury, or energy level of injury. The prevalence of risk factors in the unstudied group, however, could not be accurately evaluated. Another possible effect of sampling error could be that the patients who were available to be studied were sicker and more sedentary and those not contacted were healthier. Sufficient follow-up was available on 85% of the patients not contacted which documented progression to full weight-bearing activity. In addition, all but 2 study patients (90%) were able to return to preinjury activity level. There is no evidence to suggest that the subgroup of patients included in the study had significantly lower bone density than the unstudied subgroup on the basis of poor general health or lower activity level. We believe the statistically significant results of this investigation are real and were not substantially influenced by errors in measurement technique, study design, use of historical controls, or sampling error.

If one accepts the idea of continuous age-related BMD decrease, then the peak BMD achieved at a young age must play an important role in influencing which patients may ultimately develop symptomatic osteoporosis. In addition, there may be qualitative defects such as microfractures [24] or abnormal remodeling [54, 55] along with quantitative defects in bone structure. Increased rates of BMD loss will result in lower BMD at any given age. Therefore, patients with BMD in the low normal range for their age may be at increased risk for developing osteoporosis.

The majority of the young patients with hip fractures in this study had BMD in the lower "normal" range. From these data we cannot determine if this phenomenon was a predisposing cause of the fracture or actually a result of the injury. In either case, these patients may represent a group at higher risk for osteoporosis in later years as they continue to undergo physiologic age-related bone loss. Further investigation is necessary to determine if these patients' BMD will remain in the "low normal" range or drop further out of their age-specific normal range.

Conclusion

This investigation demonstrated that a group of presumedly healthy young patients following hip fracture had low vertebral trabecular BMD when compared to age and sex-matched controls. Osteoporosis risk factors had a cumulative association with increased severity of BMD decrease. Energy level of injury was inversely correlated with BMD decrease supporting a mutifactorial determination of fracture threshold.

As current thinking supports continuous age-related BMD decrease, such patients with low BMD at a relatively young age may be at risk for later development of severe osteopenia. Accordingly, we suggest that the significance of hip fracture in otherwise healthy young patients may currently be underestimated. These issues may prompt reconsideration of the definition of "normal" BMD and of "metabolically pathologic" fractures in young patients. Further studies of this nature will help increase our understanding of the pathogenesis of age-related bone loss and may facilitate early identification of a subgroup of patients who are at increased risk for osteoporosis.

Acknowledgments. The authors wish to thank Beth Saunders for

her valuable contribution to the statistical analysis and Carol Thomas for her technical assistance with the manuscript preparation.

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Received December 16, 1988, and in revised form June 6, 1989.