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骨髓血流灌注與骨質密度的相關性—性別,年齡與老化的影響

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共同主持人：劉華昌

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Tiffany Ting-Fang Shih, MD
Hwa-Chang Liu, MD, PhD
Chee-Jen Chang, PhD
Shwu-Yuan Wei, BS
Ling-Chun Shen, BS
Pan-Chyr Yang, MD, PhD

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Abbreviations:
BMD = bone mineral density
ROI = region of interest
SD = standard deviation

[1] From the Departments of Medical Imaging and Radiology (T.T.F.S., S.Y.W., L.C.S.), Orthopedics and Biomedical Engineering (H.C.L.), and Internal Medicine (P.C.Y.), National Taiwan University Hospital and National Taiwan University College of Medicine, 7 Chung-Shan South Road, Taipei 100, Taiwan; and Department of Medical Research, National Taiwan University Hospital (C.J.C.). Received September 18, 2003; revision requested December 2, 2003; final revision received February 20, 2004; accepted March 11. Supported by grant NSC 91–2314-B-002–395 from the National Science Council, Taiwan. **Address correspondence to** P.C.Y. (e-mail: *pcyang@ha.mc.ntu.edu.tw*).

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Author contributions:
Guarantors of integrity of entire study, T.T.F.S., P.C.Y.; study concepts and design, T.T.F.S., H.C.L., P.C.Y.; literature research, T.T.F.S.; clinical studies, T.T.F.S., H.C.L., S.Y.W.; data acquisition, T.T.F.S., L.C.S., C.J.C., S.Y.W.; data analysis/interpretation, T.T.F.S., C.J.C.; statistical analysis, C.J.C.; manuscript preparation and editing, L.C.S., T.T.F.S., C.J.C.; manuscript revision/review, T.T.F.S., H.C.L., P.C.Y.; manuscript definition of intellectual content and final version approval, P.C.Y., T.T.F.S.

Correlation of MR Lumbar Spine Bone Marrow Perfusion with Bone Mineral Density in Female Subjects[1]

PURPOSE: To prospectively assess lumbar spine bone marrow perfusion at dynamic magnetic resonance (MR) imaging and correlate perfusion with bone mineral density (BMD) in female subjects.

MATERIALS AND METHODS: BMD measurement and dynamic MR imaging of the lumbar spine were performed in 69 female subjects (mean age ± standard deviation, 57 years ± 11). Subjects were stratified into premenopausal ($n = 19$) and postmenopausal ($n = 50$) groups, with the latter group including both women who were ($n = 13$) and women who were not ($n = 37$) receiving hormone replacement therapy. BMD (in grams per square centimeter) was measured with dual energy absorptiometry in the lumbar spine. Peak enhancement ratio, measured with time–signal intensity curves calculated from dynamic MR image data, represented bone marrow perfusion. Peak enhancement ratio was compared with age and BMD by using linear regression analysis and Pearson correlation.

RESULTS: A significant positive correlation was found for BMD with peak enhancement ratio of lumbar vertebrae among all subjects ($n = 69$, $r = 0.63$, $P < .001$), all postmenopausal women ($n = 50$, $r = 0.50$, $P < .001$), and postmenopausal women without hormone replacement therapy ($n = 37$, $r = 0.61$, $P < .001$). However, the correlation between BMD and peak enhancement ratio was not significant ($P > .05$) in premenopausal women ($n = 19$) or postmenopausal women receiving hormone therapy ($n = 13$). Both BMD and peak enhancement ratio were inversely correlated with age ($P < .001$, Pearson correlation). Pearson partial correlation coefficient for peak enhancement ratio and mean in all subjects, with control for inverse correlation with age, was significant ($r = 0.63$, $P < .001$).

CONCLUSION: Significant correlation was found between the peak enhancement ratio of vertebral bone marrow and BMD in postmenopausal female subjects. This result may suggest a vascular component in the pathogenesis of osteoporosis.

An association of decreased vascular blood flow with osteoporosis has been described previously (1). In patients with peripheral vascular disease of the lower extremities, mean bone mineral density (BMD) was reported to be significantly lower in the more severely affected limb than in the less severely affected limb (2). In an epidemiologic study of elderly women with osteoporosis, diminished BMD was found to be associated with increased risk of death from stroke (3,4). These reports are highly suggestive of a relation between ischemia and bone metabolism. An association may exist also between vascular defect in the intraosseous microenvironment and osteoporosis. In a histomorphometric study by Demmler et al (5), the numbers of arterial capillaries and sinuses per unit area were found to be reduced in osteoporotic bone. Burkhardt et al (6) also showed diminution of bone marrow capillaries in patients with geriatric and primary osteopenia. The involvement of a vascular component in the pathogenesis of osteoporosis, however, may be multidimensional and protracted over time.

There is no direct evidence of a link between BMD and blood flow in bone or bone marrow in humans. Kita et al (7) used an ex vivo hydrogen washout method to measure

bone marrow blood flow in rabbits and found that decreased bone marrow blood flow was related to histologic changes with increased age. Dynamic magnetic resonance (MR) imaging with contrast enhancement has proved useful for evaluating bone marrow perfusion (8,9). There were strong correlations between MR image data and microsphere blood flow measurements in a dog model (8). MR imaging is commonly used for evaluating musculoskeletal neoplasms and monitoring their response to chemotherapy (10,11). It also has been useful in the differential diagnosis of benign and malignant compression fractures of the spine (12). In a previous study, we demonstrated the use of dynamic MR imaging for evaluation of vertebral bone marrow perfusion and proved that the latter varied significantly according to differences in age and sex ($P < .05$). A significant decrease in bone marrow perfusion was found in women older than 50 years, and a less substantial decrease was found in men of the same age (13). In addition, the incidence of osteoporosis in women is significantly increased after menopause (14,15). Postmenopausal women also have increased risks for cardiovascular disease or stroke (16,17). Thus, the purpose of our study was to prospectively assess lumbar spine bone marrow perfusion at dynamic MR imaging and to correlate perfusion with BMD in female subjects.

MATERIALS AND METHODS

Subjects

All subjects were women referred from the orthopedics and osteoporosis clinic by one investigator (H.C.L.). History of malignancy and previous spinal surgery were excluded through oral questioning by a research nurse. The orthopedic surgeon then performed a physical examination of the subject at the outpatient clinic to rule out major spinal deformities, such as scoliosis of more than 5° or kyphosis of more than 15°–20°, which were criteria for exclusion. If the subjects fit the criteria, they were invited to participate in the research project. The study was sponsored by a grant from the National Science Council, Taiwan, and was approved by the Institutional Review Board of the National Taiwan University Hospital. All subjects were given information about the procedures for BMD measurement and contrast material–enhanced MR imaging of the lumbar spine, and signed informed consent was obtained prior to their participation.

A total of 79 female subjects (age range, 30–75 years) were consecutively enrolled during a 4-month period (from July to October 2002). Subjects were excluded if lumbar vertebral body compression was present and associated with low signal intensity on T1-weighted images. Subjects with compression fractures depicted as areas of iso- to hyperintense bone marrow signal on T1-weighted images were not excluded, because they were considered to have fatty regeneration of bone marrow in the collapsed vertebra. Such findings suggested the chronicity of compression fracture and might be related to osteoporosis. Subjects with acute fracture identified on the basis of medical history and clinical presentation were excluded from the study. Altogether, 10 subjects were excluded: One had a compression fracture in the L2 vertebra with low signal intensity on T1-weighted turbo spin-echo images and reported back pain of more than 1 month in duration, which indicated subacute vertebral fracture. Two subjects had a history of hyperparathyroidism, five had technical failure during the rapid injection of the MR contrast agent, and two were excluded because of ambiguous menstrual history (one subject was in the perimenopausal period less than 1 year after the last menstrual cycle, and the other subject had undergone hysterectomy). A total of 69 subjects (mean age ± standard deviation [SD], 57 years ± 11) were included in the analysis.

Nineteen of the subjects were premenopausal (age range, 32–54 years; mean age, 46 years ± 5; age distribution: 32–40 years [$n = 3$], 41–45 years [$n = 7$], 46–50 years [$n = 5$], and 51–54 years [$n = 4$]). The remaining 50 subjects were postmenopausal (age range, 46–75 years; mean age, 62 years ± 9; age distribution: 46–50 years [$n = 4$], 51–55 years [$n = 12$], 56–60 years [$n = 6$], 61–65 years [$n = 9$], 66–70 years [$n = 11$], and 71–75 years [$n = 8$]). Thirteen of the postmenopausal subjects had received hormone replacement therapy for more than 6 months; the type and dosage of medication and the exact duration of therapy, however, were not recorded in the medical history. Each subject underwent both BMD and MR bone marrow perfusion measurements of the lumbar spine. The two measurements for each subject were performed within a 2-week interval.

BMD Measurements

BMD was measured with dual energy absorptiometry by one of the authors (L.C.S.) by using a fan-beam bone densitometer (QDR-4500A; Hologic, Waltham, Mass). Instrument quality control of our bone densitometer is performed at least 5 days per week. The precision error of BMD measurements on anteroposterior projections of the lumbar spine was less than 0.01 g/cm^2. BMD was measured from L1 to L4 on anteroposterior projections, and the mean of the values measured at these four levels was considered to represent BMD for anteroposterior projections in each subject. BMD was measured also from L2 to L4 on lateral projections, and the mean of measured values at these three levels was considered to represent BMD for lateral projections in each subject.

MR Measurements of Bone Marrow Perfusion

MR imaging of the spine was performed by using a 1.5-T superconducting system (Magnetom Vision Plus, H-SP; Siemens Medical Solutions, Erlangen, Germany) and a phased-array spinal coil. A routine T1-weighted turbo spin-echo sequence (repetition time msec/echo time msec, 600/12; turbo factor, 3; section thickness, 4 mm; field of view, 28 cm) was applied in the midsagittal plane from the level of T11 to the sacrum. T1-weighted images of the spine were evaluated by a musculoskeletal radiologist (T.T.F.S.) for areas of abnormal bone marrow signal intensity that might indicate compression fracture, neoplasm, or infection, all of which were criteria for exclusion from the study. One subject was excluded, as mentioned before, because of an area of abnormal low signal intensity seen on T1-weighted images, a finding indicative of subacute vertebral fracture due to compression.

Dynamic contrast-enhanced MR imaging was then performed in the midsection of the vertebral body (section thickness, 10 mm; field of view, 28 cm), from T11 to the sacrum. A slightly oblique angle was used for dynamic imaging to avoid flow artifacts from the abdominal aorta. A turbo fast low-angle shot gradient-echo pulse sequence (repetition time msec/echo time msec/prepulse inversion time msec, 8.5/4.0/160; flip angle, 10°; matrix, 72 × 128) was used. The acquisition time was 0.89 second with an 0.11-second delay. A total of 100 dynamic images were obtained within 100 seconds (1 frame per second) in each subject.

An injection of gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) containing 0.1 mmol of gado-

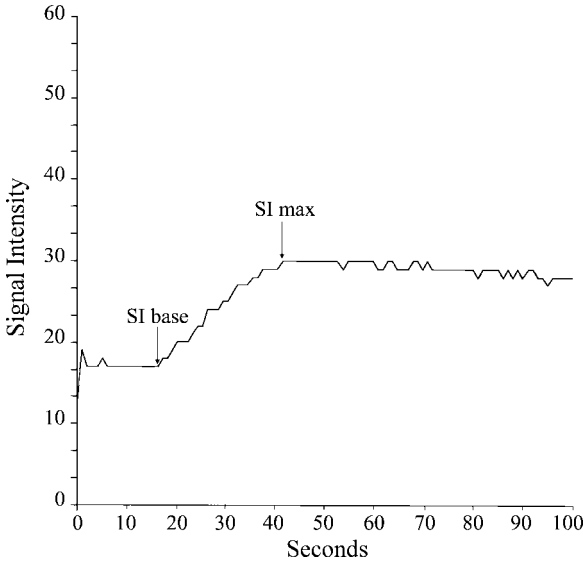

Figure 1. Time–signal intensity curve plotted with data from dynamic contrast-enhanced MR imaging of L3 in a 41-year-old female subject shows signal intensity change during 100 seconds of acquisition time. After peak contrast enhancement (*SI max*), which occurred about 40 seconds after the start of contrast medium injection and imaging (first rapidly rising phase), signal intensity remained relatively stable (equilibrium phase). *SI base* = mean signal intensity at baseline.

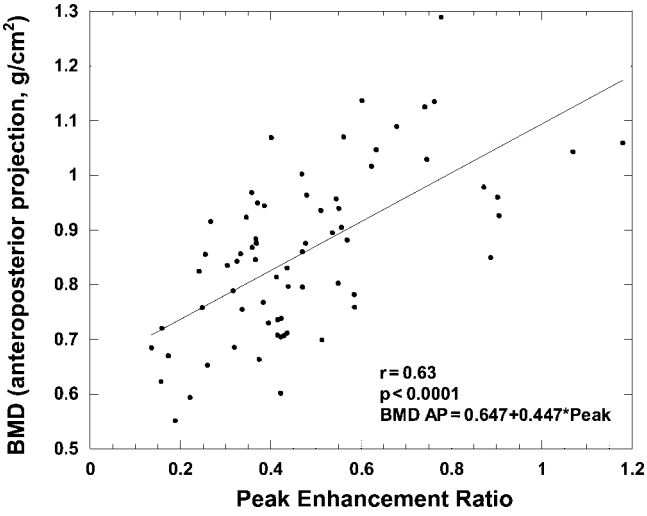

Figure 2. Scatterplot and regression line show positive correlation between mean BMD (anteroposterior projections) and mean peak enhancement ratio in the lumbar spine in all 69 study subjects.

linium per kilogram of body weight was administered manually at a constant injection rate of approximately 2.0 mL/sec, with a total injection time of 5–8 seconds, through a 21-gauge intravenous catheter previously inserted in the right antecubital vein. The contrast medium injection was immediately followed by a 20-mL saline flush administered at the same injection rate. Dynamic imaging was started when the injection of the contrast medium commenced.

Data Analysis

Signal intensity values were measured in operator-defined regions of interest (ROIs). The musculoskeletal radiologist (T.T.F.S., with 14 years of experience) and senior MR technologist (S.Y.W., with 9 years of experience) placed the ROIs together in consensus. The ROIs were placed, with the aid of a cursor and a graphic display device, along the border of high-signal-intensity bone marrow on T1-weighted images and covered the entire bone marrow of each vertebra. One vertebral body was covered by one ROI measurement. The ROIs ranged in area from 2.1 to 3.5 cm^2 (mean, 2.62 cm^2 ± 0.46). The ROI was measured separately for each of five lumbar vertebrae (L1 through L5) in each subject. The signal intensity values derived from the ROI measured in each vertebral body were then plotted against time to obtain a time–signal intensity curve (Fig 1) for each vertebral body. The baseline value for signal intensity (SI_{base}) on a time–signal intensity curve was defined as the mean signal intensity from the first three images. The maximum signal intensity (SI_{max}) was defined as the maximum value of the first rapidly rising part of the time–signal intensity curve. The time to peak contrast enhancement was defined as the time between SI_{base} and SI_{max}. After the peak, which usually occurred about 40 seconds after the start of injection, the time–signal intensity curve entered an equilibrium phase that lasted about 30 seconds. The total 100-second imaging time encompassed both the first rapid rise in the curve and the early equilibrium phase. In our study, the SI_{base} and SI_{max} were measured only from the first rapidly rising curve. For the semiquantitative analysis, the peak enhancement ratio was calculated for each ROI as $(SI_{max} - SI_{base})/SI_{base}$. Because of a statistically significant correlation observed between peak enhancement ratio and age in our previous study (13), we used the peak enhancement ratio to represent bone marrow perfusion. The peak enhancement ratio for each vertebra was derived from the time–signal intensity curve for that vertebra. The mean of the peak enhancement ratios for the five vertebrae was used to represent bone marrow perfusion for each subject.

Statistical Methods

Descriptive statistics, including the mean, median, and SD of continuous variables such as BMD from anteroposterior and lateral projections and peak enhancement ratio from dynamic MR imaging, were calculated separately for all subjects and for premenopausal and postmenopausal women with and without hormone replacement therapy. Comparisons were made by using the two-sample Wilcoxon rank sum test. Comparisons between age and BMD measured with dual energy absorptiometry and peak enhancement ratio measured with dynamic MR imaging were made by using Pearson correlation analysis. Partial correlation coefficients also were derived for peak enhancement ratio and BMD (anteroposterior and lateral projections) with adjustments for age. The correlation between BMD measured with anteroposterior projections and peak enhancement ratio of the lumbar vertebrae was analyzed. All statistical analyses were performed by one senior statistician (C.J.C.). Regression analysis of the data was performed by using the general linear model and correlation procedures provided in a statistical software package (SAS/STAT, version 8.1; SAS Institute, Cary, NC). *P* values less than .05 were considered to indicate statistically significant differences.

TABLE 1
Summary of Descriptive Statistics for All Subjects and for Pre- and Postmenopausal Groups

Parameter	All Subjects (n = 69)			Premenopausal Subjects (n = 19)			Postmenopausal Subjects (n = 50)			P Value for Comparison between Pre- and Postmenopausal Subjects
	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	
BMD (g/cm^2)										
Anteroposterior projections	0.86	0.86	0.15	0.99	0.98	0.13	0.81	0.81	0.13	<.01
Lateral projections	0.64	0.61	0.10	0.75	0.76	0.08	0.61	0.59	0.07	<.01
Peak enhancement ratio	0.47	0.42	0.21	0.70	0.62	0.21	0.39	0.38	0.14	<.01

TABLE 2
Summary of Descriptive Statistics for Postmenopausal Subjects

Parameter	Subjects Receiving Hormone Replacement Therapy (n = 13)			Subjects Not Receiving Hormone Replacement Therapy (n = 37)			P Value
	Mean	Median	SD	Mean	Median	SD	
BMD (g/cm^2)							
Anteroposterior projections	0.81	0.80	0.08	0.81	0.81	0.14	.85
Lateral projections	0.60	0.58	0.07	0.61	0.60	0.08	.94
Peak enhancement ratio	0.46	0.41	0.16	0.36	0.37	0.13	.04

RESULTS

Descriptive statistics for BMD measured with anteroposterior and lateral projections and for peak enhancement ratio at dynamic MR imaging in the 69 female subjects are summarized in Tables 1 and 2. In accordance with the definitions established by a working group of the World Health Organization on the basis of bone mass measurements in postmenopausal Caucasian women, osteoporosis is defined as a BMD level more than 2.5 SDs below the mean for young adult women (T score, −2.5 or lower), and osteopenia is defined as a BMD level between 1.0 and 2.5 SDs below the mean for young adult women (T score, higher than −2.5 and lower than −1.0). A normal BMD level is no more than 1 SD below the mean for young adult women (T score, −1 or higher) (18).

Table 1 shows descriptive statistics for the 69 subjects stratified into premenopausal (n = 19) and postmenopausal (n = 50) groups. Statistically significant differences were found in BMD (both anteroposterior and lateral projections) and in peak enhancement ratio between premenopausal and postmenopausal women, as follows: BMD for anteroposterior projections was 0.99 g/cm^2± 0.13 versus 0.81 g/cm^2± 0.13 and for lateral projections was 0.75 g/cm^2± 0.08 versus 0.61 g/cm^2± 0.07, and peak enhancement ratio was 0.70 ± 0.21 versus 0.39 ± 0.14, for premenopausal and postmenopausal women, respectively (P < .01 for all three comparisons).

Table 2 shows the same descriptive statistics for the 50 postmenopausal women stratified into two subgroups: those who were (n = 13) and those who were not (n = 37) receiving hormone replacement therapy. The peak enhancement ratio was significantly higher in the group receiving hormone replacement therapy than in the group not receiving such therapy (0.46 ± 0.16 vs 0.36 ± 0.13; P < .05), whereas there was no significant difference in BMD (anteroposterior projections, 0.81 g/cm^2± 0.08 vs 0.81 g/cm^2± 0.14, P > .05; lateral projections, 0.60 g/cm^2± 0.07 vs 0.61 g/cm^2± 0.08; P > .05).

Scatterplots and regression lines for correlation of BMD (anteroposterior projections) with peak enhancement ratio are shown in Figures 2–4. BMD showed a significant positive correlation with peak enhancement ratio for all subjects (n = 69, r = 0.63, P < .001) (Fig 2), for all postmenopausal women (n = 50, r = 0.50, P < .001) (Fig 3, *B*), and for postmenopausal women not receiving hormone replacement therapy (n = 37, r = 0.61, P < .001) (Fig 4, *B*). The difference in slope between the two lines (Figs 3, *B,* and 4, *B*) was not statistically significant. The data for postmenopausal women who were receiving hormone replacement therapy, however, did not show a statistically significant correlation (n = 13, r = 0.28, P = .36) (Fig 4, *A*). The difference in slope between the two lines in Figure 4 (*A,* postmenopausal women receiving hormone replacement therapy; *B,* postmenopausal women not receiving hormone replacement therapy) was statistically significant (P = .026). The data for premenopausal women also showed no statistically significant correlation between peak enhancement ratio and BMD (n = 19, r = 0.32, P = .18) (Fig 3, *A*).

The effect of age on these parameters was assessed by using Pearson correlation analysis (Table 3). The peak enhancement ratio at dynamic MR imaging and the BMD for anteroposterior and lateral projections decreased significantly with increasing age (P < .001). Because of the high correlations of both peak enhancement ratio and age with BMD, a partial correlation analysis of peak enhancement ratio with BMD was performed with age as the controlling variable. The resultant Pearson partial correlation coefficient was 0.63 for anteroposterior projections (P < .001) (Table 4). The results of multiple linear regression analysis indicated that, with control for the age effect, the BMD for both anteroposterior and lateral projections was positively correlated with the peak enhancement ratio (P < .001), and, thus, that peak enhancement ratio was an important predictor of BMD.

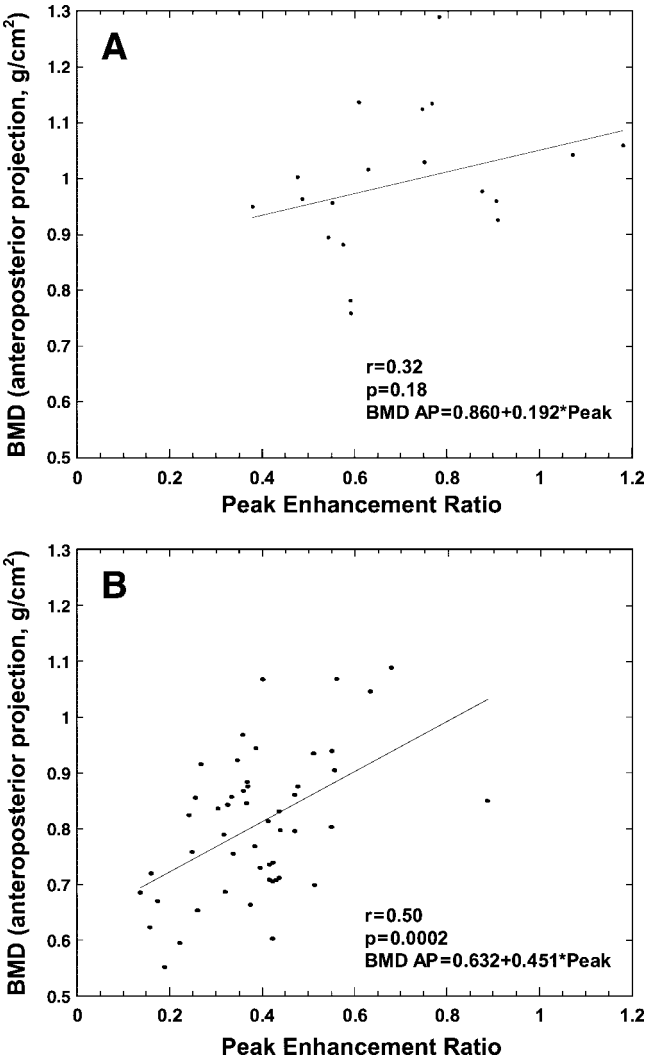

Figure 3. Scatterplots and regression lines for comparison of mean BMD (anteroposterior projections) with mean peak enhancement ratio in the lumbar spine show, *A,* no correlation in premenopausal subjects, and, *B,* strong correlation in postmenopausal subjects.

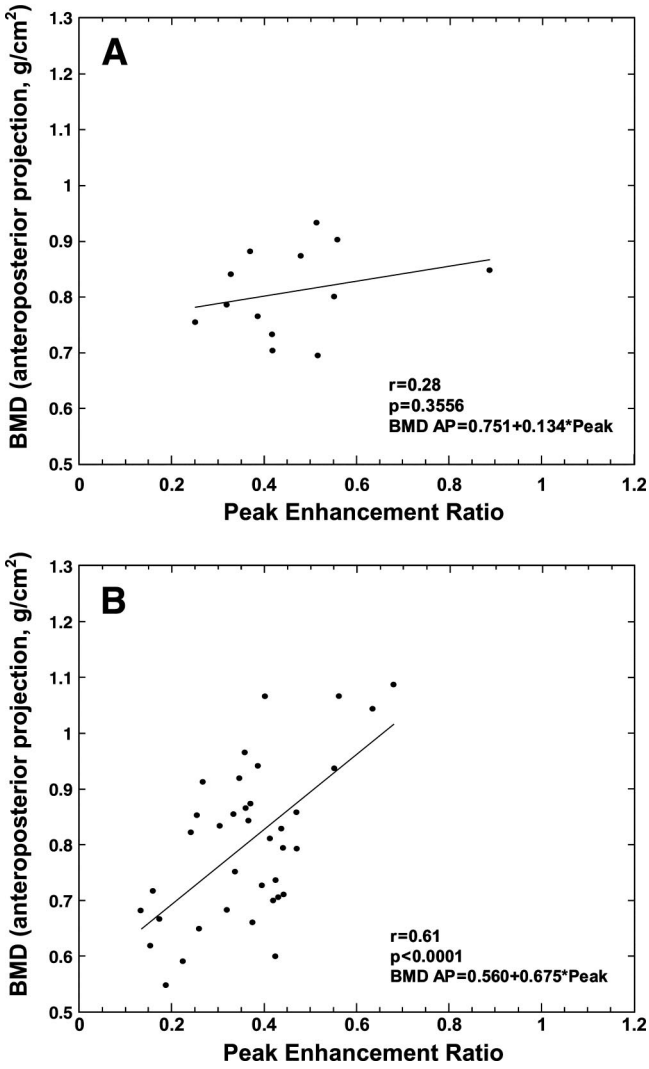

Figure 4. Scatterplots and regression lines for comparison of mean BMD (anteroposterior projections) with mean peak enhancement ratio in the lumbar spine in postmenopausal subjects show, *A,* no correlation in the group receiving hormone replacement therapy, and, *B,* strong positive correlation in the group not receiving such therapy.

DISCUSSION

The pathogenesis of osteoporosis is complex and multifactorial. The underlying mechanism is still not fully understood but may include genetic background, hormonal status, nutrition, and other factors. BMD is known to be correlated with age and sex. BMD in the spine decreases by about 20% in Caucasian women between 40 and 70 years of age, with a continued but slower decrease thereafter (14,15,19). Values reported for BMD in the lumbar spine in Chinese women are similar to those reported for the Caucasian population (20). It has been hypothesized that osteoporosis is caused by disturbances of blood circulation in bone; reduced arterial blood supply or reduction of extravascular fluid pressure may provoke an increase in osteoclastic activity and, thus, osteoporosis (21). Histomorphometric studies also showed that skeletal blood flow was independently correlated with the corrected apposition rate, an index of the work rate of osteoblasts, in each multicellular unit of bone. Thus, skeletal blood flow may be associated with bone turnover, and low vascularization is considered a sign of diminished vitality in bone (22,23). Both atherosclerosis and osteoporosis are common in the elderly. Many previous studies have shown an association between atherosclerotic cardiovascular disease (hence, vascular compromise) and the severity of osteoporosis. This association was most evident in postmenopausal women, who had increased risks for cardiovascular disease or stroke (16,17), as well as for osteoporosis (14,15). Boukhris and Becker (24), in a population study, demonstrated a positive correlation between the prevalence of osteoporosis and aortic calcification. Jensen et al (25) proposed that vascular compromise due to arterial calcification might lead to bone loss. Subsequent studies showed that women with aortic calcification had significantly lower bone density compared with those without such calcification (26,27) and that coronary calcium scores in postmenopausal women were significantly higher in those with osteoporosis than in the control group (28). In a study by Kiel et al (29)

TABLE 3
Pearson Correlation Coefficients for Comparison of Peak Enhancement Ratio and BMD with Age for All Subjects

Correlation Parameter	Peak Enhancement Ratio	BMD	
		Anteroposterior Projections	Lateral Projections
Coefficient	−0.62	−0.57	−0.58
P value	<.001	<.001	<.001

TABLE 4
Pearson Partial Correlation Coefficients for Comparison of BMD with Peak Enhancement Ratio for All Subjects, with Control for Age

Correlation Parameter	BMD	
	Anteroposterior Projections	Lateral Projections
Coefficient	0.63	0.71
P value	<.001	<.001

that covered a 25-year period, women with the greatest magnitude of bone loss also demonstrated the most severe progression of abdominal aortic calcification. Vogt et al (30) also reported that a lower ankle-brachial pulse index was associated with increased bone loss in the hip and calcaneus. The parameters used to represent vascular compromise in those studies, however, reflect the severity of atherosclerosis or blood flow change only in large and medium-sized vessels and not in the small arterioles that nourish the bone; these parameters, therefore, provide only indirect evidence of a vascular component in the pathogenesis of osteoporosis. In this study, we evaluated bone marrow perfusion and BMD in the lumbar spine in female subjects. We demonstrated a significant correlation between MR bone marrow perfusion (presented as peak enhancement ratio) and BMD in female subjects. Both the peak enhancement ratio and BMD were inversely correlated with age ($P < .001$), and a significant positive correlation was found between BMD and the peak enhancement ratio in the lumbar spine ($P < .001$).

Time–signal intensity curves derived from dynamic contrast-enhanced MR images were used to represent perfusion in bone and bone marrow lesions (8–13,31). The semiquantitative assessment of time–signal intensity curves can be performed by using parameters such as slope or maximum value of enhancement. Mainly tissue vascularization and perfusion determine the first-pass (wash-in phase of) time–signal intensity curves. After the first pass, capillary permeability and interstitial space components that contribute to the characteristics of the curve yield a further rise, a plateau, or a downslope, which represent a further increase in contrast medium influx, a state of equilibrium, or an early washout phase, respectively. Rise or decline in the second part of the curve, however, varied within a very small range. The first-pass part of the time–signal intensity curve (from SI_{base} to SI_{max}) was considered to indicate the influx of contrast medium from the arterial capillaries into the extracellular space of the vertebral body. In this study, we calculated the peak enhancement ratio from this part of the time–signal intensity curve. As mentioned earlier, there was a high correlation between the dynamic MR data and the microsphere blood-flow measurement (8). Hawighorst et al (31) used the relative signal intensity enhancement ratio to present the time–signal intensity curve of the spine. The relative signal intensity enhancement also was used to normalize the signal intensity–time data, for differentiating between benign and malignant breast lesions (32) and vertebral lesions (12). Chen et al (13) demonstrated that the peak enhancement percentage of vertebral bone marrow, but not the enhancement slope, decreased significantly with increasing age. In the present study, we also used the peak enhancement ratio to represent bone marrow perfusion. In evaluating the blood perfusion of bone marrow within the vertebral body, we included the small vessels and sinusoidal capillaries, myeloid and other cells, marrow fat, and trabeculae but did not include the cancellous cortical bone. We use the general term "bone marrow perfusion" to represent blood perfusion in the bone marrow cavity, not in cortical bone. In the vertebral bone marrow, contrast enhancement is influenced by macrovascular (paired segmental arteries and intravertebral small arterioles) and microvascular (arterial and sinusoidal capillaries) factors and by the concentration of contrast agent in the extravascular extracellular compartment. When the circulation to the vertebral bodies is impaired, the volume of blood flow to the bone marrow may be decreased, in which case the concentration of contrast material in the bone marrow also will be decreased. The peak enhancement ratio should be regarded as the outcome of a complex process that includes blood inflow and outflow, vascular permeability, and the equilibrium of contrast agent between the intravascular and interstitial spaces but does not include factors related to intracellular-extracellular interaction or to bone metabolism at the cellular level.

A positive correlation was found between peak enhancement ratio and BMD of the lumbar spine in female subjects ($r = 0.63$, $P < .001$), a finding that indicates a possible connection between decreased bone marrow perfusion and osteoporosis. Other common causes also may exist for osteoporosis and decreased blood perfusion, such as atrophy or degeneration of tissue that occur with aging. Our data also showed an inverse correlation of peak enhancement ratio and BMD with age ($P < .001$). After statistical adjustment for age (Pearson partial correlation with control for the age variable), the peak enhancement ratio retained its correlation with BMD ($r = 0.63$, $P < .001$). These findings indicate that the peak enhancement ratio has an important influence on BMD. Since the bone acts as a closed chamber, we presume that the blood perfusion in the intraosseous environment of the vertebra plays an important role in bone trabeculation. Because our study involved data collected over a cross-sectional period, however, our results support a hypothesis of correlation but not of causation between low MR bone marrow perfusion and low BMD. Further studies performed with follow-up of women over a longer time (longitudinal series) may provide results that support a hypothesis of causation.

The correlation between peak enhancement ratio and BMD is influenced by menopausal status; a significant correlation was observed in our study in postmenopausal subjects ($r = 0.50$, $P < .001$) but not in premenopausal subjects ($r = 0.32$, $P > .05$). In previous studies (14–17,28), an association was found between osteoporosis and atherosclerosis in postmenopausal women, in whom these conditions are prevalent, but not in premenopausal women. BMD measurements in premenopausal women in our

study revealed osteopenia, as defined in accordance with World Health Organization criteria (a T score between −1.0 and −2.5), in only three subjects. The remaining 16 subjects had normal BMD. The small number of premenopausal women in our study population might have contributed to the lack of a correlation.

Results in the 13 postmenopausal subjects who were receiving hormone replacement therapy did not indicate a correlation between BMD and bone marrow perfusion ($r = 0.28$, $P > .05$). Although bone marrow perfusion was higher in the group receiving hormone replacement therapy than in postmenopausal women not receiving such therapy (0.46 ± 0.16 vs 0.36 ± 0.13, $P < .05$), there was no difference in BMD between the two subgroups. We postulate that the effect of hormone replacement therapy on the vascular system may precede any effect on BMD. Small sample size and inadequate history of hormone replacement therapy, however, limit our ability to generalize on the basis of these study results. Further investigation is needed to determine the effect of hormone replacement therapy on bone marrow perfusion and BMD.

Other systemic diseases commonly seen in elderly women, such as diabetes mellitus and hypertension, may contribute to the severity of vascular disease. Patients with diabetes mellitus often also have either microvascular disease (eg, retinopathy, nephropathy) or macrovascular disease (eg, peripheral vascular or cerebrovascular disease) (33). The results of research concerning an association between diabetes and osteoporosis, however, are controversial. Young patients with type I diabetes had low BMD, whereas older patients with type II diabetes had normal or increased BMD. Factors other than vasculopathy, such as hyperglycemia, may also influence BMD in diabetic patients. In this study, we focused on the effect of bone marrow perfusion on BMD, not the possible influences of systemic disease such as diabetes or of cardiac output on blood perfusion in vertebrae. Cigarette smoking has been shown to play an important role in vasculopathy and osteoporosis and to be positively correlated with stroke mortality for both sexes, with the predominant effect in women (34). A statistically significant association was found between current smoking and the rate of bone loss in elderly women (35). Browner et al (3,4), however, reported that the association of BMD with stroke was not confounded by smoking. In Taiwan, the prevalence of cigarette smoking in July 2001–June 2002 among adult women was about 7.8% and was much lower among women older than 50 years, according to the annual statistical information compiled by the Department of Health. Thus, we did not investigate smoking as a factor in the correlation between bone marrow perfusion and BMD.

The influence of marrow fat content on BMD measurement was another limitation of this study. An increase in the number of fat cells in marrow is accompanied by a corresponding reduction in the numbers of arterial capillaries and sinuses per unit area (5). The influence of vertebral fat on the accuracy of quantitative CT attenuation measurements was mentioned previously (36,37). A change of 50% in the bone marrow fat content will change the BMD of an average-sized vertebra by 5%–6% at dual energy absorptiomety (38). Although both techniques are influenced by marrow fat content, the BMD measurements with both techniques are highly correlated with the chemically determined bone mineral mass (39). BMD in our study was measured with dual energy absorptiometry in anteroposterior and lateral projections. Although quantitative CT may provide more accurate BMD measurement in the highly trabeculated bone in the centrum of the vertebra, quantitative CT results in general are similar to those from dual energy absorptiometry in the lateral projection. In our study, MR data from both projections showed correlations with approximately the same level of statistical significance. We chose the anteroposterior projection data for linear regression analysis of BMD with MR peak enhancement ratio because they best matched the World Health Organization criteria.

In conclusion, we calculated the peak enhancement ratio at dynamic MR imaging of the lumbar spine as a measure of vertebral bone marrow perfusion in female subjects. Both BMD and bone marrow perfusion were inversely correlated with age, and a significant positive correlation was found between BMD and bone marrow perfusion in postmenopausal women. These results may suggest a vascular component in the pathogenesis of osteoporosis.

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