J Bone Miner Metab (2003) 21:22–27

Journal of
Bone and
Mineral
Metabolism

Correlation between bone mineral density and intervertebral disk degeneration in pre- and postmenopausal women

Yoshiro Nanjo, Yasuo Morio, Hideki Nagashima, Hiroshi Hagino, and Ryota Teshima

Department of Orthopaedic Surgery, Tottori University, Faculty of Medicine, 36-1 Nishi-cho, Yonago 683-8504, Japan

Abstract The purpose of this study was to investigate the relationship between intervertebral disk degeneration and bone mass. Magnetic resonance imaging was performed to evaluate lumbar disk degeneration according to Thompson's classification (grades 1 and 2, normal disk; grades 3, 4, and 5, degenerated disk), and bone mineral density (BMD) in the lumbar vertebrae, radius, and calcaneus was measured by dual-energy X-ray absorptiometry for 90 women (22–74 years old). The relationship between the grade of intervertebral disk degeneration and the BMD (Z score) was analyzed in pre- and postmenopausal women. In premenopausal women, BMD was significantly higher at all measured sites in the degenerated disk group judged at the L5–S1 level than in the normal disk group ($P < 0.05$). In postmenopausal women, BMD was significantly higher at the anteroposterior L2–L4, lateral L3, and calcaneus in the degenerated disk group judged at the L2–L3 level than in the normal disk group ($P < 0.05$). BMD at the anteroposterior L2–L4 and calcaneus was significantly higher in the degenerated disk group judged at the L3–L4 level than in the normal disk group ($P < 0.05$). In conclusion, the BMD of not only the lumbar vertebrae but also the calcaneus and radius was mutually related to lumbar intervertebral disk degeneration from an early stage of degeneration.

Key words bone mineral density · dual-energy X-ray absorptiometry · intervertebral disk degeneration · magnetic resonance imaging

Introduction

Lumbar degenerative disk disease is a common age-related condition in elderly people that frequently causes low back pain or sciatica. In contrast to osteoporosis, this disease is reported to have high bone mineral density (BMD) in the lumbar vertebrae and other sites [1–6]. However, the relationship between the BMD of the vertebrae and intervertebral disk degeneration has not been established. In many of the reports that evaluated the correlation between BMD and intervertebral disk degeneration, most patients were postmenopausal women or elderly men, and degenerative disk diseases were evaluated using radiographs [1,3–6]. However, to elucidate the relationship between intervertebral disk degeneration and BMD, it is necessary to include patients with early stages of this disease in the study. Although it is difficult to detect early lumbar intervertebral disk degeneration by radiographs, magnetic resonance imaging (MRI) is reported to be useful in the evaluation of early changes in the degenerated disk [7,8].

To complement the information lacking in previous reports, we evaluated lumbar intervertebral disk degeneration using MRI in pre- and postmenopausal women. The purpose of this study was to investigate the relationship between the grade of degeneration and BMD in the lumbar vertebrae and appendicular bones.

Subjects and methods

The subjects were female patients who visited our department with a complaint of low back pain and/or leg pain between 1998 and 2000, and nurse volunteers at our hospital, a total of 90 subjects. The mean age of the subjects was 46.4 years (22–74 years old). Of the subjects, all 52 premenopausal subjects were nurse volunteers, and the mean age was 33.9 years (22–52 years old). Forty-two (80.8%) of the 52 nurse volunteers had experienced low back pain within the previous year. All the premenopausal volunteers had active daily lives without restrictions. All 38 postmenopausal subjects were consecutive patients with low back pain or leg pain or both, and the mean age was 63.4 years (49–74 years old). All the postmenopausal patients visited our hospital on foot

Offprint requests to: Y. Nanjo
Received: May 16, 2002 / Accepted: July 31, 2002

without any aids for walking, and had no history of being bedridden during 1 week before visits. Patients with spinal infectious disease, malignant bone tumor, and metabolic bone disease and individuals who had previously taken drugs affecting bone metabolism such as corticosteroid and therapeutic drugs for osteoporosis were excluded. Furthermore, patients with spondylolysis, lumbar spinal fracture, and spondylolisthesis at Meyerding [9] level 2 or higher were excluded. After the objective of this study was explained to the subjects and informed consent was obtained, the subjects underwent lumbar MRI and measurement of BMD.

Lumbar MRI

Using a 1.5-T superconducting imaging system (Magnetome H15; Siemens, Erlangen, Germany), lumbar MRI was performed at a slice thickness of 5 mm. Using mid-sagittal view T_2-weighted images (TR 4500 ms/TE 112 ms), degeneration of the L1–L2, L2–L3, L3–L4, L4–L5, and L5–S1 lumbar intervertebral disks was graded 1 to 5 according to Thompson's classification [8] by the first author (Y.N.) (Fig. 1). Two authors (Y.N. and H.N.) independently evaluated 20 randomly selected subjects. The concordance between two observers for disk degeneration grade was 0.547 (95%CI = 0.359–0.735). The first author evaluated the same subjects 1 week later, and the intraobserver error was 0.757 (95%CI = 0.562–0.952). Grades 1 and 2 were defined as normal disk (N) and grades 3, 4, and 5 were defined as degenerated disk (D). Scoring N and D as 0 and 1, respectively, the scores of L1–L2, L2–L3, L3–L4, L4–L5, and L5–S1 intervertebral disks were summed to calculate the disk degeneration score (DDS) (0–5 points).

Measurement of BMD

Using the dual-energy X-ray absorptiometry (DXA) method, the BMD of the various sites was measured. The BMD of the anteroposterior L2–L4 (AP L2–4), lateral L3 (Lat L3), and total body (TB) was measured using QDR-4500A (Hologic, Waltham, MA, USA). The BMD at the distal one-third of the radius (Radius) was measured using a DCS-600 (Aloka, Tokyo, Japan), and the BMD of the right calcaneus (Heel) was measured using heel scan DX 2000 (Kyoto-Daiichikagaku, Kyoto, Japan). The first author performed all BMD measurements. The coefficient of variation (CV) of the BMD was calculated from three measurements in five healthy adults, and the value was 0.6% for AP L2–4, 2.4% for Lat L3, 1.0% for Radius, 1.7% for Heel, and 1.0% for TB.

Statistical analysis

Because the age of the subjects ranged widely, from 22 to 74 years, the subjects were divided into pre- and postmenopausal groups. To eliminate the effects of age- and sex-related factors on raw BMD data, the results of each BMD measurement were compared with the *Z* score in age- and sex-matched Japanese controls from each of the these bone mineral measurement machines at each measured site [10]. The BMD was compared between the N and D groups at each lumbar intervertebral disk level using unpaired Student's *t* test. Furthermore, the correlation between DDS and BMD was analyzed using Spearman's rank correlation test. For statistical analysis, Stat View version 5.0 J (Abacus Concepts, Berkeley, CA, USA) was used, and $P < 0.05$ was considered significant.

Results

Characteristics of the subjects

The baseline characteristics of the pre- and postmenopausal subjects are shown in Table 1. There were no significant differences in body weight or body mass in-

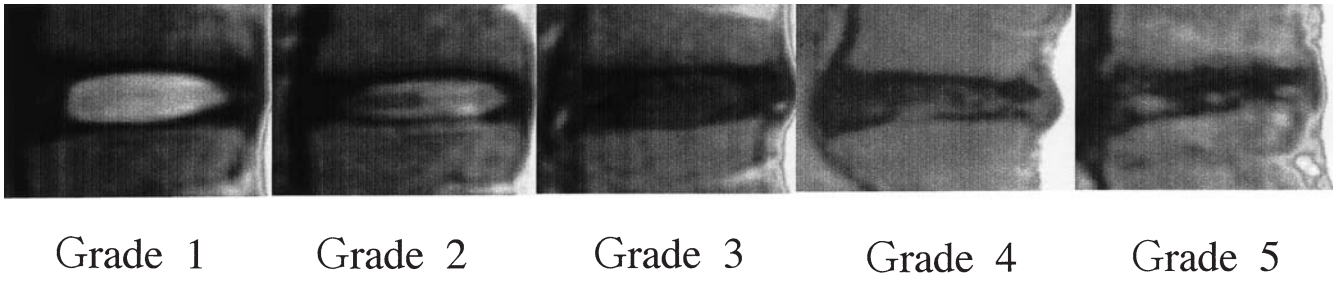

Fig. 1. Midsagittal view on T_2-weighted images of disks graded according to Thompson's classification. *Grade 1*, homogeneous, bright nucleus pulposus (NP) and homogenous dark gray annulus fibrosis (AF); *grade 2*, horizontal dark bands extended across the AF; *grade 3*, diminished signal intensity of AF and NP indistinguishable from AF; *grade 4*, further reduced signal intensity of NP and some bright and dark signals; *grade 5*, diminished disk height

Table 1. Baseline characteristics of the study population ($n = 90$)

	Premenopausal women	Postmenopausal women	*P*
Age (years)	33.9 (8.9)	63.4 (7.6)	<0.0001
Number (n)	52	38	
Weight (kg)	54.0 (8.1)	51.2 (5.5)	NS
BMI (kg/m^2)	21.7 (3.2)	22.1 (3.2)	NS
DD at L1–L2 (%)	3.8	21.0	
DD at L2–L3 (%)	1.9	39.5	
DD at L3–L4 (%)	7.7	63.2	
DD at L4–L5 (%)	36.5	84.2	
DD at L5–S1 (%)	40.4	71.1	
DDS (0–5)	0.942 (1.074)	3.316 (1.757)	<0.0001
AP L2–4 BMD (g/cm^2)	1.04 (0.14)	0.83 (0.13)	<0.0001
Z score	0.31 (1.21)	0.22 (1.21)	NS
Lat L3 BMD (g/cm^2)	0.79 (0.097)	0.62 (0.14)	<0.0001
Z score	0.99 (1.64)	0.76 (1.45)	NS
Radius BMD (g/cm^2)	0.67 (0.049)	0.53 (0.079)	<0.0001
Z score	0.023 (0.86)	0.39 (1.20)	NS
Heel BMD (g/cm^2)	0.87 (0.097)	0.75 (0.094)	<0.0001
Z score	0.42 (1.17)	0.49 (1.08)	NS
TB BMD (g/cm^2)	1.07 (0.08)	0.90 (0.090)	<0.0001
Z score	−0.046 (1.05)	−1.01 (0.94)	<0.0001

Values are means and values in parentheses are standard deviations; unpaired Student's *t* test; NS, not significant

Disk degeneration at L1–L2, L2–L3, L3–L4, L4–L5, and L5–S1 represents the incidence of degenerated disk

BMI, body mass index; DD, intervertebral disk degeneration; DDS, disk degeneration score; AP L2–4, anteroposterior L2–L4; Lat L3, lateral L3; Radius, distal one-third of the radius; Heel, right calcaneus; TB, total body

Table 2. Disk degeneration grade at each lumbar disk level in pre- and postmenopausal women

	Premenopausal women ($n = 52$)					Postmenopausal women ($n = 38$)				
Grade[a]	L1–L2	L2–L3	L3–L4	L4–L5	L5–S1	L1–L2	L2–L3	L3–L4	L4–L5	L5–S1
Grade 1	32	32	30	27	25	1	2	0	0	0
Grade 2	18	19	18	6	6	29	21	14	6	11
Grade 3	2	1	4	14	18	6	10	18	15	9
Grade 4	0	0	0	4	3	2	5	4	8	9
Grade 5	0	0	0	1	0	0	0	2	9	9

Values are numbers of the graded disk

[a] Disk degeneration grades were defined according to Thompson's classification [8]

dex (BMI) between the two groups. BMD was higher in the premenopausal group than the postmenopausal group. However, there were no significant differences in the *Z* score of the BMD at the measurement site AP L2–4, Lat L3, Radius, or Heel between the pre- and postmenopausal groups.

Evaluation of lumbar intervertebral disk degeneration by MRI

In the premenopausal group, grade 3 or higher lumbar intervertebral disk degeneration was observed in 3.8% (2/52) in L1–L2, 1.9% (1/52) in L2–L3, 7.7% (4/52) in L3–L4, 36.5% (19/52) in L4–L5, and 40.4% (21/52) in L5–S1. In the postmenopausal group, grade 3 or higher lumbar intervertebral disk degeneration was observed in 21.0% (8/38) in L1–L2, 39.5% (15/38) in L2–L3, 63.2% (24/38) in L3–L4, 84.2% (32/38) in L4–L5, and 71.1% (27/38) in L5–S1 (Table 2).

DDS was significantly higher in the postmenopausal group than in the premenopausal group (Table 1). In both pre- and postmenopausal groups, DDS was correlated with age. In the premenopausal group, DDS was correlated with BMI (Table 3).

Table 3. Correlations between disk degeneration score and bone mineral density

	Disk degeneration score	
	Premenopausal women	Postmenopausal women
Z score of AP L2–4 BMD	0.257	0.237
Z score of Lat L3 BMD	0.119	0.353*
Z score of Radius BMD	0.295*	0.356*
Z score of Heel BMD	0.362**	0.272
Z score of TB BMD	0.399**	0.093
Age	0.709**	0.376*
Body mass index	0.372**	−0.071

Values are Spearman's rank correlations
* $P < 0.05$, ** $P < 0.01$
AP L2–4, anteroposterior L2–L4; Lat L3, lateral L3; Radius, distal one-third of the radius; Heel, right calcaneus; TB, total body; BMD, bone mineral density

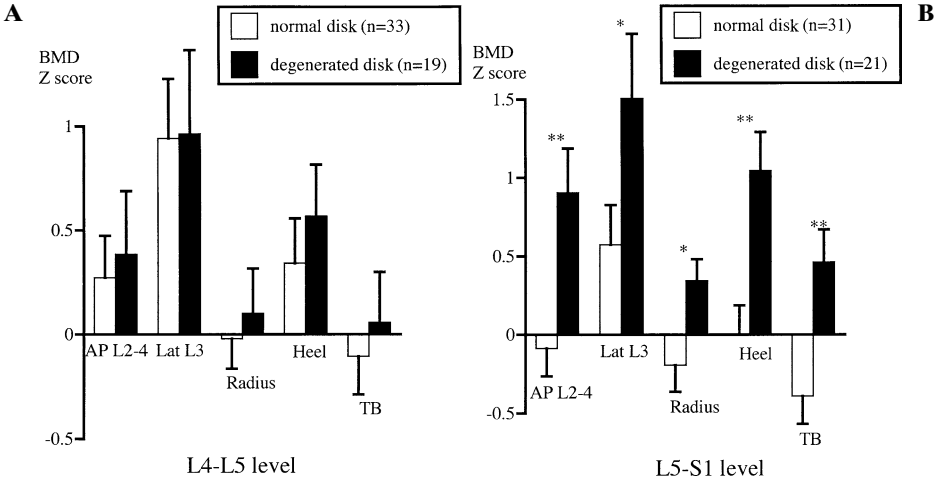

Fig. 2. **A** Relationship between L4–L5 intervertebral disk degeneration and bone mineral density (*BMD*) in 52 premenopausal women. **B** relationship between L5–S1 intervertebral disk degeneration and BMD in 52 premenopausal women. Each *bar* represents the mean; *vertical lines* represent standard error. Significance of differences was determined by unpaired Student's *t* test (*$P < 0.05$, **$P < 0.01$). Grades 1 and 2 were defined as normal disk and grades 3, 4, and 5 were as degenerated disk acording to Thompson's classification. *AP L2–4*, anteroposterior L2–L4; *Lat L3*, lateral L3; *Radius*, distal one-third of the radius; *Heel*, right calcaneus; *TB*, total body

Relationship between lumbar intervertebral disk degeneration and BMD in premenopausal women

BMD tended to be higher at all measurement sites in the D group judged at the L4–L5 level, compared to the N group, but the differences were not significant (Fig. 2A). There was no significant difference in BMI between the D and N groups.

BMD was significantly higher at all measured sites in the D group judged at the L5–S1 level, compared to the N group (Fig. 2B). The mean BMI were 23.5 and 20.5 (kg/m^2) in the D and N groups, respectively. The BMI was significantly higher in the D group than the N group ($P < 0.001$).

In the premenopausal group, DDS was positively correlated with the BMD at Radius, Heel, and TB (see Table 3).

Relationship between lumbar intervertebral disk degeneration and BMD in postmenopausal women

BMD was significantly higher at AP L2–4, Lat L3, and Heel in the D group judged at the L2–L3 level, compared to the N group (Fig. 3A). The BMD at AP L2–4 and Heel was significantly higher in the D group judged at the L3–L4 level, compared to the N group (Fig. 3B). There were no significant differences in the BMD between the D and N groups judged at the L1–L2, L4–L5, or L5–S1 level. There was no significant difference in BMI between the D and N groups judged at any intervertebral disk level.

In the postmenopausal group, DDS was positively correlated with the BMD at Lat L3 and Radius (Table 3).

Discussion

In most previous studies regarding the relationship between degenerative disk disease and BMD, the BMD of the lumbar vertebrae and other sites was higher in individuals with degenerative disk disease than the age-matched healthy individuals [1–6]. In these studies, most subjects were postmenopausal women or elderly men [1,3–6]. However, to discuss the relationship be-

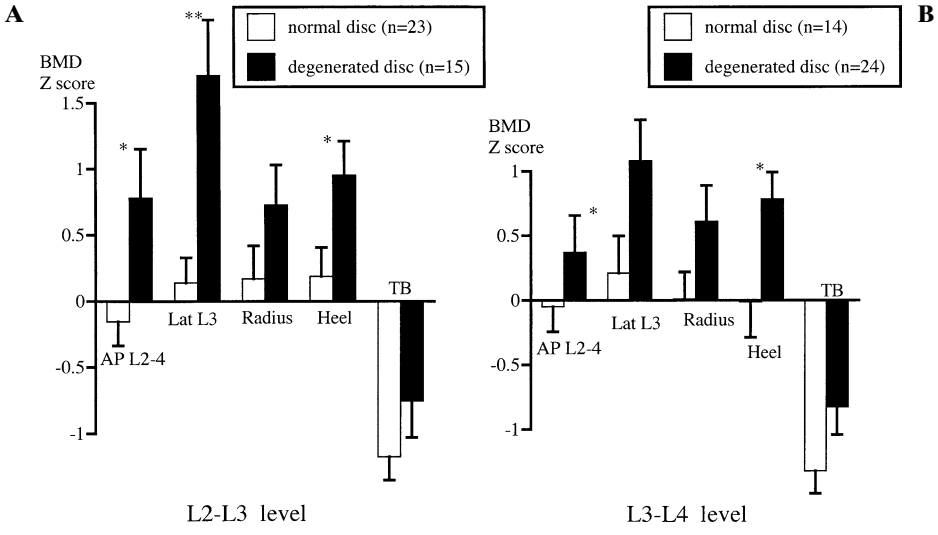

Fig. 3. **A** Relationship between L2–L3 intervertebral disk degeneration and bone mineral density (*BMD*) in 38 postmenopausal women. **B** Relationship between L3–L4 intervertebral disk degeneration and BMD in 38 postmenopausal women. Each *bar* represents the mean; *vertical lines* represent standard error. Significance of difference was determined by unpaired Student's *t* test ($*P < 0.05$, $**P < 0.01$)

tween intervertebral disk degeneration and BMD, it is necessary to include young people in the studies because lumbar intervertebral disk degeneration develops while patients are in their twenties [7]. In this study, in addition to postmenopausal women, premenopausal women aged 22–52 years were included. The premenopausal subjects were nurse volunteers at our hospital. The postmenopausal women were patients with low back pain or leg pain. The premenopausal women were 52 volunteers of which 42 had experienced low back pain within the previous year. In postmenopausal women, the *Z* score of total body BMD was lower, suggesting that the incidence of osteoporosis in postmenopausal women was higher than that in premenopausal women, perhaps because there was a difference in activity between the two groups. Several studies have reported that physical activity influences BMD [11,12]. Because the subjects were not homogeneous, a bias in subject selection might exist, which could be a limitation of the current study.

Radiographs have been used in many studies for the evaluation of intervertebral disk degeneration, but early intervertebral disk degeneration cannot be accurately detected by radiographs; thus, in this study, to detect early degeneration of the intervertebral disks, we used MRI, and the changes graded 3 or higher by Thompson's classification were judged as degeneration. It has been reported that in this classification the concentration of chondroitin sulfate in the intervertebral disk is markedly different between grades 2 and 3 and that grade 3 indicates early intervertebral disk degeneration [8].

In the premenopausal subjects, BMD was significantly higher at all sites in the D group judged at the L5–S1 level, compared to the N group, indicating that when lumbar intervertebral disk degeneration is severe, BMD is high not only in the lumbar vertebrae but also in other sites. Similarly, DDS was positively correlated with BMD at Radius, Heel, and TB. BMI was significantly higher in the D group than the N group, and DDS was positively correlated with BMI. Therefore, it is possible that obesity is involved in both intervertebral disk degeneration and BMD, as reported by Vogt et al. [13]. Higher BMDs and damaged disks may reflect different degrees of physical activity in the premenopausal subjects. However, the grades of degeneration and BMD were related to each other from the early stage of intervertebral disk degeneration in the current study. Furthermore, a significant correlation was observed between the BMD of the radius, which is a nonweight-bearing bone, and intervertebral disk degeneration, suggesting that a predisposing factor of systemic high BMD is involved in intervertebral disk degeneration. Thus, we consider that the higher spine BMD is not secondary to disk degeneration and that higher spine BMD may result from genetic tendency.

It has recently been clarified that a genetic factor is closely involved in intervertebral disk degeneration [14,15]. Stewart et al. reviewed studies regarding the relationship between osteoarthritis (OA) and BMD that were published between 1998 and 2000. They reported that in patients with spine and hip OA, BMD in the two sites was high, and that BMD for the knee was high in patients with knee OA. It is suggested that the vitamin D receptor (VDR) gene and insulin growth factor 1 gene are involved in OA and high BMD values [16]. Uitterlinden et al. has reported that a specific type of VDR genotype readily causes knee OA [17]. However, Huang et al. reported that there was no relationship between the VDR genotype and hip/hand/knee OA in Japanese [18]. A consensus has not been reached.

In the postmenopausal group, BMD was significantly higher at the AP L2–4, Lat L3, and Heel in the D group judged at the L2–L3 level and at AP L2–4 and Heel in the D group judged at the L3–L4 level than in the N group. DDS was positively correlated with the BMD of Lat L3 and Radius. Harada et al. evaluated lumbar intervertebral disk degeneration in postmenopausal women by MRI and reported that the ratio of intervertebral disk bulge from the posterior edge of the vertebral body was correlated with the BMD of the lumbar vertebrae and total body [19].

Our results indicated that intervertebral disk degeneration and BMD are associated with each other in premenopausal women as in postmenopausal women. However, although a significant difference in BMD between the D and N groups was observed at the L5–S1 level in the premenopausal group, it was observed at the L2–L3 and L3–L4 levels in the postmenopausal group. These findings may be due to the setting of the border between normal and degenerated disks on MRI. We set the border between grades 2 and 3 to detect early disk degeneration. These findings were consistent with the fact that intervertebral disk degeneration progresses from the lower to upper lumbar vertebrae with age [7].

Keller et al. reported that stiffness of the vertebral body is correlated with intervertebral disk degeneration [20]. Neumann et al. reported that there is interdependency among intervertebral disk degeneration, the BMD of the vertebral body, and the elastic modulus of the anterior longitudinal ligament [21]. Therefore, as vertebral BMD increases, vertebral stiffness increases and the role of the intervertebral disk in the shock-absorbing system also increases, resulting in an increase in stress on the intervertebral disk. Inversely, when vertebral BMD is low, the stiffness of the vertebra decreases and the vertebra plays a role with the intervertebral disks in the shock-absorbing system; thus, relative stress on the intervertebral disks may decrease. Thus, lumbar BMD and intervertebral disk degeneration may be associated with each other.

In conclusion, the BMD of not only the lumbar vertebra, but also the calcaneus and radius, was mutually related with lumbar intervertebral disk degeneration from an early stage of degeneration.

References

1. Jones G, Nguyen T, Sambrook PN, Kelly PJ, Eisman JA (1995) A longitudinal study of the effect of spinal degenerative disease on bone density in the elderly. J Rheumatol 22:932–936
2. Laitinen K, Välimäki M, Keto P (1991) Bone mineral density measured by dual-energy X-ray absorptiometry in healthy Finnish women. Calcif Tissue Int 48:224–231
3. Masud T, Langley S, Wiltshire P, Doyle DV, Spector TD (1993) Effect of spinal osteophytosis on bone mineral density measurements in vertebral osteoporosis. BMJ 307:172–173
4. Nuti R, Righi G, Martini G, Turchetti V, Lepore C, Doretti V (1988) Diagnostic approach to osteoporosis and spondyloarthrosis in post-menopausal women by total body dual-photon absorptiometry. Clin Exp Rheumatol 6:47–51
5. Reid IR, Evans MC, Ames R, Wattie J (1991) The influence of osteophytes and aortic calcification on spinal mineral density in postmenopausal women. J Clin Endocrinol Metab 72:1372–1374
6. Verstraeten A, Ermen HV, Haghebaert G, Nujs J, Geusens P, Dequeker J (1991) Osteoarthrosis retards the development of osteoporosis. Clin Orthop 264:169–177
7. DeCandido P, Reinig JW, Dwyer AJ, Thompson KJ, Ducker TB (1988) Magnetic resonance assessment of the distribution of lumbar spine disc degenerative changes. J Spinal Disord 1:9–15
8. Eyre D, Benya P, Buckwalter J, Caterson B, Heinegard D, Oegema T, Pearce R, Pope M, Urban J (1988) Intervertebral disc. In: Frymoyer JW, Gordon SL (eds) New Perspectives on Low Back Pain. American Academy of Orthopaedic Surgeons, Park Ridge, pp 191–195
9. Meyerding HW (1932) Spondylolisthesis. Surg Gynecol Obstet 54:371–377
10. Orimo H, Sugioka Y, Fukunaga M, Muto Y, Hotokebuchi T, Gorai I, Nakamura T, Kushida K, Tanaka H, Ikai T, Oh-hashi Y (1998) Diagnostic criteria of primary osteoporosis. J Bone Miner Metab 16:139–150
11. Goto S, Ishima M, Shimizu M, Kobayashi Y, Moriya H (2001) A longitudinal study for femoral neck bone mineral density increases in premenopausal caddies using dual-energy X-ray absorptiometry. J Bone Miner Metab 19:125–130
12. Kaneko M, Miyake T, Yokoyama E, Harano S, Toki T, Komine Y, Nozaki N, Nozaki S, Takeda N, Miyake M, Fukunaga M (2000) Standard radial bone mineral density and physical factors in ordinary Japanese women. J Bone Miner Metab 18:31–35
13. Vogt MT, Rubin DA, Valentin RS, Palermo L, Kang JD, Donaldson WF III, Nevitt M, Cauley JA (1999) Degenerative lumbar listhesis and bone mineral density in elderly women. Spine 24:2536–2541
14. Riggs BL, Nguyen TV, Melton LJ III, Morrison NA, O'Fallon WM, Kelly PJ, Egan KS, Sambrook PN, Muhs JM, Eisman JA (1995) The contribution of vitamin D receptor gene alleles to the determination of bone mineral density in normal and osteoporotic women. J Bone Miner Res 10:991–996
15. Videman T, Leppävuori J, Kaprio J, Battié MC, Gibbons LE, Peltomen L, Koskenvuo M (1998) Intragenic polymorphism of the vitamin D receptor gene associated with intervertebral disc degeneration. Spine 23:2477–2485
16. Stewart A, Black A (2000) Bone mineral density in osteoarthritis. Curr Opin Rheumatol 12:464–467
17. Uitterlinden AG, Burger H, Huang Q, Odding E, Duijn CM, Hofman A, Birkenhäger JC, Leeuwen J, Pols H (1997) Vitamin D receptor genotype is associated with radiographic osteoarthritis at the knee. J Clin Investig 100:259–263
18. Huang J, Ushiyama T, Inoue K, Kawasaki T, Hukuda S (2000) Vitamin D receptor gene polymorphisms and osteoarthritis of the hand, hip, and knee: a case-control study in Japan. Rheumatology 39:79–84
19. Harada A, Okuzumi H, Miyagi N, Genda E (1998) Correlation between bone mineral density and intervertebral disc degeneration. Spine 23:857–862
20. Keller TS, Ziv I, Moeljanto E, Spengler M (1993) Interdependence of lumbar disc and subdiscal bone properties: a report of the normal and degenerated spine. J Spinal Disord 6:106–113
21. Neumann P, Ekström LA, Kellar TS, Perry L, Hasson TH (1994) Aging, vertebral density, and disc degeneration alter the tensile stress-strain characteristics of the human anterior longitudinal ligament. J Orthop Res 12:103–112