

Vertebral body bone mineral density in patients with lumbar spondylolysis: a quantitative CT study

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PURPOSE

Spondylolysis is known to be a part of a disease process, which describes a defect in the pars interarticularis of vertebra. We aimed to use quantitative computed tomography (QCT) to measure vertebral body bone mineral density (BMD) in patients with lumbar spondylolysis and compare it with readings in controls.

METHODS

Forty symptomatic patients with lumbar spondylolysis aged 18–52 years and 40 matched controls of same sex and approximate age (± 2 years) were included in the study. Measurements of BMD were performed by QCT analysis for each vertebral body from T12 to L5 and mean BMD was calculated for each case.

RESULTS

Of 40 patients, 22 (55%) demonstrated L5 spondylolysis, 14 (35%) L4 spondylolysis, three (7.5%) L3 spondylolysis, and one (2.5%) L2 spondylolysis. Spondylolisthesis was found in 29 patients (73%). Patients with spondylolisthesis were significantly older than patients without spondylolisthesis (42 ± 6.9 vs. 37.2 ± 5.4 , $P = 0.024$). Mean BMD value of the patient group was significantly lower than that of the controls (105 ± 24 mg/cm³ vs. 118.7 ± 25.6 mg/cm³, $P = 0.015$). Subgroup analysis of 19 patients and 19 controls under the age of 40 revealed that the mean BMD value of the patients was significantly lower than that of the controls in the younger age group as well (108.7 ± 23.5 mg/cm³ vs. 130 ± 25.8 mg/cm³, $P = 0.009$).

CONCLUSION

This study demonstrated that patients with spondylolysis had significantly lower mean vertebral body BMD compared with controls.

Spondylolysis is known to be a part of a disease process, which describes a defect or stress fracture in the pars interarticularis of the vertebra (1). It is a relatively common cause of low back pain among child and adolescent athletes resulting from biomechanical stresses on a congenitally weak or dysplastic pars interarticularis in the form of chronic low grade trauma such as repetitive flexion, extension, and rotation, and shear forces exerted at the lumbar spine (2, 3). Bilateral spondylolysis may lead to spondylolisthesis.

Spondylolisthesis is the term used to describe forward translation of one vertebra over the adjacent vertebra. It is divided into five types according to its etiopathogenesis (4). Dysplastic spondylolisthesis (type I) is a consequence of congenital abnormality of the facet. Spondylolysis is not initially present, but may originate secondary to listhesis. Isthmic spondylolysis (type II) describes a lesion in pars interarticularis. Subtypes are defined as Type II-A (lytic) when there is a fatigue fracture of pars articularis and Type II-B when pars is elongated as a consequence of repeated microfractures and healing. Degenerative, traumatic, and pathologic spondylolisthesis are classified as types III, IV, and V, respectively. It is reported that spondylolysis with or without spondylolisthesis is present in 5%–8% of adults, yet the accurate prevalence is not well known because of varying data in the literature (2, 3).

Spondylolysis and spondylolisthesis may present a wide clinical spectrum from an asymptomatic incidental finding to a source of back pain and disability (5). Spondylolisthesis more than 25%, spondylolysis or listhesis at the level of L4 vertebrae, and early disc degen-

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eration at the level of the spondylolisthesis were described as common radiologic features of symptomatic patients (6). Patients with refractory pain from spondylolysis despite appropriate conservative management, progression of spondylolisthesis to Grade II or higher, and persistent pain despite appropriate conservative management of a Grade I spondylolisthesis without evidence of progression are candidates for spinal surgery.

The etiopathogenesis of spondylolysis is still not fully understood (7). Theories based on dysplastic/congenital, traumatic, or other factors such as Looser zone in osteomalacia are being discussed. A better understanding of the etiopathogenesis of spondylolysis is needed to allow formulating evidence-based management and prevention of the disease.

Quantitative computed tomography (QCT) is a three-dimensional nonprojectional technique to detect "real" bone mineral density, avoiding some pitfalls and overlying structures or disease (e.g., aorta/soft-tissue calcifications, osteoarthritis) (8, 9). This study aimed to investigate vertebral body BMD in patients with lumbar spondylolysis by using QCT and compare the findings with those of healthy controls. To our knowledge, this is the first study in the literature to investigate vertebral BMD in this particular group of patients using QCT.

Methods

Patients

Ethics committee of our institution approved this retrospective study. Forty symptomatic patients with lumbar spondylolysis at any level with or without accompanying spondylolisthesis were randomly selected from our database between January 2012 and December 2015. Because age is an im-

portant determinant of BMD, patients aged 18–52 years were included in the study (10). Controls without spondylolysis or spondylolisthesis of the same sex and the same approximate age (± 2 years) were matched to the patients included in the study. Control cases were selected from picture archiving and communication system of our radiology department randomly out of patients admitted to the emergency room due to other reasons unrelated to low back pain. Patients and controls who had earlier spinal surgery, vertebral fractures, scoliosis, systemic disorder related to bone metabolism, known malignancy, renal failure, and postmenopausal women were excluded from the study since BMD would be affected. Computed tomography (CT) images of patients and controls with any artifacts were also excluded.

CT imaging and measurement of BMD

CT imaging without contrast medium was performed by either 16-slice or 64-slice multidetector CT scanner (Brilliance 16 or Brilliance 64, Philips Medical Systems). Spinal column CT scanning parameters were as follows: 120 kVp; 120 mA; beam pitch, 0.688; slice thickness, 0.75 mm. Axial scans were reconstructed with 1.0 mm slice thickness and 0.75 mm reconstruction increment to obtain sagittal plane images. Sagittal reconstructed images were evaluated to determine spondylolysis and to detect accompanying spondylolisthesis. The level of spondylolysis, existence and grade (I to IV) of spondylolisthesis were recorded.

All CT images were transferred to a workstation (Philips Extended Brilliance Workspace V3.5.0.2254) for further QCT analysis. A radiologist with 12 years of experience performed the QCT analysis. The measurements of BMD were recorded for each vertebral body one by one from T12 to L5, and the mean BMD of each case was calculated. Another radiologist with 18 years of experience conducted an independent measurement of 20 of the patients to test interobserver coefficient of variation (CV).

The trabecular BMDs (mg/cm^3) were measured by phantomless QCT technique. An approximately 2.5 cm^3 region-of-interest (ROI, with a thickness of 1 cm and an area of 2.5 cm^2) was drawn by using hands-free tracing tool and located in the trabecular bone of the corpus vertebrae. Posterior venous plexus and degenerative sclerotic areas were not included in the ROI. Total volume measured was about 2.5 cm^3 . We used our

standard QCT BMD protocol by measuring CT number of fat and muscle areas for calibration on the same slice according to the guidelines set by the manufacturer (Fig.). The described technique presented satisfactory reproducibility in a previous study and has been shown to be accurate and sufficiently precise for clinical utility (11).

Statistical analysis

The intra- and interobserver CVs of QCT BMD measurement were analyzed. Continuous data are expressed as the mean \pm standard deviation (SD) or median (min–max), and categorical variables are expressed as percentages. Test of normality of the variables were performed using Kolmogorov-Smirnov and Shapiro-Wilk tests. Thus, BMD values of patients and controls were compared using independent samples *t* test. Correlation analysis was performed by Pearson correlation coefficient. BMD values of each vertebral level from T12 to L5 of the patients were also compared with those of controls. Subgroup analyses of the cases under the age of 40 were performed for continuous and categorical variables using independent samples *t* test and chi-squared test, respectively. Mann-Whitney *U* test was used for comparison of age between the subgroups according to presence of spondylolisthesis. A two-sided *P* value <0.05 indicated statistical significance. Statistical analysis was performed using the SPSS 20.0 for Windows statistical software (IBM Corp.).

Results

Of 40 patients, 12 (30%) were male and 28 (70%) were female. The male-female ratio of the patients was 0.4. Control subjects were sex and age-matched. The mean ages of patient and control groups were 40.7 ± 7.1 and 41.0 ± 6.9 , respectively (range, 18–52 years). Of 40 patients, 22 (55%) demonstrated L5 spondylolysis, 14 (35%) demonstrated L4 spondylolysis, three (7.5%) demonstrated L3 spondylolysis, and one (2.5%) demonstrated L2 spondylolysis. The intra- and interobserver CV of QCT BMD measurement was satisfactory (5.1% and 5.9%, respectively).

A negative correlation was determined between the age and BMD value of the control group ($P < 0.001$, $r = -0.636$), while there was no correlation between the age and BMD value of the patient group ($P = 0.394$, $r = -0.138$).

Patients had significantly lower mean BMD values compared with the controls ($105 \pm 24 \text{ mg}/\text{cm}^3$ vs. $118.7 \pm 25.6 \text{ mg}/\text{cm}^3$, *P*

Main points

- Bone mineral density (BMD) values of controls were negatively correlated with age, while there was no correlation between the age and BMD values of the patient group.
- BMD of the patients with spondylolysis was significantly lower than the controls.
- Among subjects <40 years of age, the mean BMD value of the patients was significantly lower than that of the controls.
- The mean BMD value of patients with spondylolisthesis was significantly lower than that of the controls.

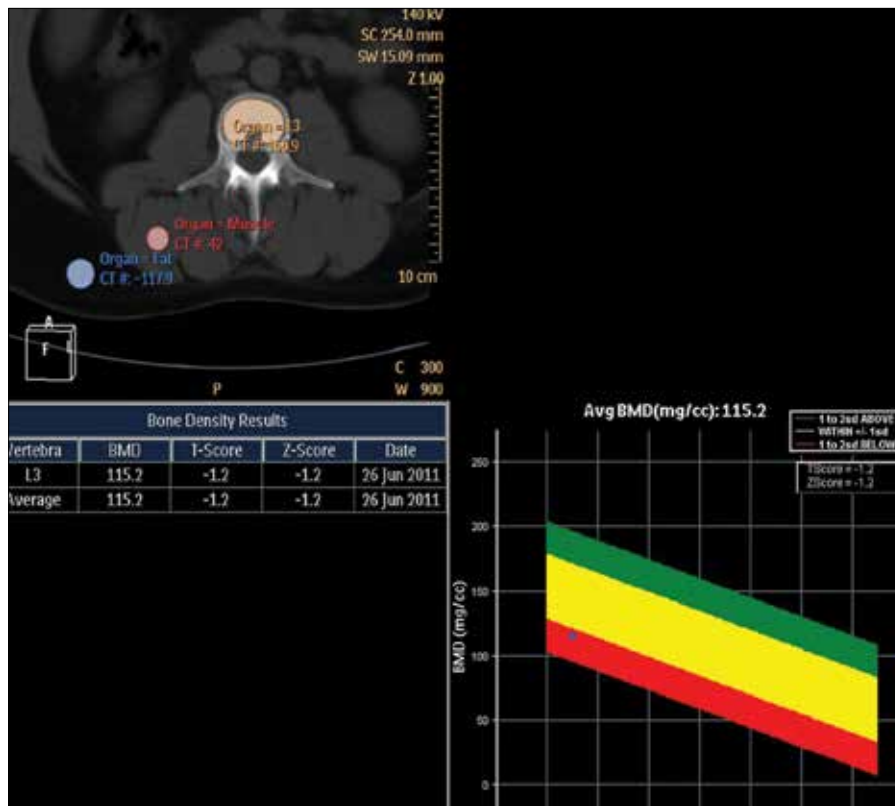


Figure. Measurement of bone mineral density (BMD) by using quantitative computed tomography (CT). Regions of interest of L3, muscle, and fat are shown with their CT readings in yellow, pink, and blue color, respectively. BMD was calculated as 115.2 mg/cm³ in this example.

significantly lower than that of the controls (105.8 mg/cm³ [83.8–182.6 mg/cm³] vs. 131.6 mg/cm³ [63.8–158.2 mg/cm³], $P=0.009$).

Twenty-nine of these patients (73%) also demonstrated spondylolisthesis on CT. Age was significantly different between patients with and without spondylolisthesis (42±6.9 years vs. 37.2±5.4 years, $P = 0.024$). Patients with spondylolisthesis had significantly lower mean BMD value compared with age-matched controls (103.5±25.9 mg/cm³ vs. 117.7±27.1 mg/cm³, $P = 0.046$). Of 29 patients with spondylolisthesis, 8 (28%) were male, 21 (72%) were female. There was no statistically significant difference in sex of the patients with or without spondylolisthesis ($P = 0.589$).

Out of 29 patients with spondylolisthesis, 21 (72%) were grade I and 8 (28%) were grade II. The grade of spondylolisthesis was significantly correlated with patient age ($P = 0.010$, $r=0.401$). Out of 21 patients with grade I spondylolisthesis, 14 were female and 7 were male, while out of 8 patients with grade II spondylolisthesis, 7 were female and one was male. Statistically significant difference was not detected between the grade of spondylolisthesis and sex ($P = 0.262$).

Discussion

Our results showed that BMD of patients with spondylolysis was significantly lower than the controls. Since it is known that breaking strength of bone is linearly related to its mineral content we speculate that lower BMD could be a predisposing factor in the etiopathogenesis of spondylolysis.

In recent studies the association between BMD and spinal problems including spondylolisthesis, intervertebral disc degeneration, and osteoarthritis was investigated but vertebral BMD alteration in patients with spondylolysis has not been studied yet (5, 12–14). Besides, most of these studies were conducted using dual X-ray absorptiometry (DXA) and found conflicting results. The vast majority of the studies on spinal arthropathy and disc degeneration suggest that increased mineral density of spinal and appendicular bones plays a role in etiopathogenesis (13–17). On the contrary, a few studies demonstrated that low spinal BMD is associated with degenerative changes in the lumbar spine (18, 19).

Vogt et al. (12) used DXA to investigate the association between BMD and lumbar spondylolisthesis in elderly white women. They reported that BMD at axial and ap-

	Patients (n = 40)	Controls (n = 40)	P
Age (year), mean±SD	40.7±7.1	41.0±6.9	
Male to female ratio	28/12	28/12	
Spondylolisthesis, n (%)	29 (73)	N/A	
Grade 1	21 (72)	N/A	
Grade 2	8 (28)	N/A	
BMD (mg/cm ³)			
T12	110.8*	126.9	0.007
L1	110.3	118.5	0.572
L2	101.4	117.9	0.009
L3	97.4	112.7	0.009
L4	100.5*	114.9	0.020
L5	110.7**	121.3	0.539
Overall mean	104.0	118.7	0.015

*Measured in 39 patients; **measured in 38 patients.
QCT, quantitative computed tomography; BMD, bone mineral density; N/A, not available; L, lumbar; T, thoracic.

= 0.015). However, there was no statistically significant difference in BMD values at L1 and L5 levels between patient and control groups ($P = 0.572$ and $P = 0.539$, respectively). Mean BMD, BMD of each vertebral level,

and demographic features of patient and control groups are given in the Table.

Subgroup analysis of 19 patients and 19 controls under the age of 40 revealed that the mean BMD value of the patients was also

pendicular sites was higher than in those with no listhesis at L3-L4, was similar at L4-L5, and was lower at L5-S1. Using DXA, He et al. (5) investigated the potential risk factors of lumbar spondylolisthesis and suggested that higher spinal BMD is associated with higher prevalence of spondylolisthesis. Contrary to their work, in the current QCT study, we found significantly lower BMD values in patients with spondylolisthesis than in controls. We suggest their results could be influenced by degenerative changes in the vertebral column of elderly patients, which may have developed over time due to spondylolysis and may have led to false BMD results. Furthermore, evaluation of BMD in elderly people by using DXA may lead to confusion and false BMD measurement because of high body mass index and atherosclerotic vascular calcifications related to aging. Thus, this study is performed by QCT, which is largely independent of degenerative changes of the spine (20). Even so, BMD values of one patient at T12, one patient at L4, and two patients at L5 levels were not included in the analysis because of noticeable sclerosis of vertebral body due to osteoarthritis. We suggest that there would still be an invisible but measurable sclerosis due to degeneration of the vertebral column related with the process.

Contradictory results of previous researches and our study raise the question of whether lower BMD value of our patient group could be a cause or a result of spondylolysis. Herein, subgroup analysis showed that mean BMD value of the patients under the age of 40 was significantly lower compared with the controls in spite of the small number of patients. This finding supports our hypothesis that BMD of this particular group of patients is lower despite their younger age.

In the current study, BMD values of controls were negatively correlated with age. Similarly, a previous study in the normal population showed that annual total BMD loss was 0.74% in women between 30 and 80 years of age and 0.33% in men (21). However, such a correlation was not observed in patients with spondylolysis included in this study. Considering that the grade of spondylolysis is correlated with age, we suggest a process starting with spondylolysis that leads to progressive spondylolisthesis and induces degenerative sclerosis. Therefore, there was no correlation between the age and BMD values of the patient group.

We found no statistically significant difference in BMD of L5 vertebrae between patients and controls, even though it was lower in the patient group. According to our hypothesis, degenerative changes and shear stress affected mostly L5 vertebrae and gave rise to increase in BMD since spondylolysis and listhesis were mostly detected at this level.

The major strength of this study is that it is the first one to use QCT to demonstrate vertebral BMD changes in patients with lumbar spondylolysis. DXA is today's established standard for BMD. It is a common method used in the clinical setting for monitoring bone strength in humans (22). Thus, most of the studies investigating the association between BMD and vertebral column diseases such as spondylolisthesis, degenerative and postoperative changes have been performed with DXA. However, it measures the mass and areal BMD of large volumes of bone tissue. It also has some disadvantages due to its projectional nature including sensitivity to aortic calcifications, degenerative and osteoarthritic changes. In the recent years, dynamic contrast-enhanced magnetic resonance imaging, magnetic resonance spectroscopy, and diffusion-weighted imaging have been investigated for their potential diagnostic value in evaluation of bone strength and osteoporosis by means of bone marrow fat composition (23–25). Still, the findings of these studies need further corroboration in larger series (23). On the other hand, QCT provides true volumetric measurement of trabecular BMD without being affected from vascular calcification, body size, or morphologic variability. Unlike DXA, QCT BMD measurement is less influenced from misleading factors such as osteophytes and subchondral sclerosis, because it assesses trabecular bone only. Thus, this study was performed by QCT as a more novel method to quantify the distribution of BMD within different levels of spine as it relates to bone strength.

Another strength of this study is the age range of patient and control groups because most of the previous studies included elderly patients. We suggest that age limitation set in this study helped us to eliminate the BMD changes related to aging.

Our study has several limitations. First, we did not know the BMD of the patients before spondylolysis, which would definitely prove our hypothesis. Second, we did not know age of the patients when spondylolysis occurred to correlate with BMD. Third, our study has a small sample size with un-

balanced male/female population. Fourth, two different CT scanners were used for imaging the spine. Even though phantomless technique has been shown to be an accurate and useful method to assess BMD (23–25), variable CV values may be another limitation (CV was 5.1% and 5.9% for intra- and interobserver assessments, respectively).

In conclusion, this study demonstrated that the vertebral body BMD values of the patients with spondylolysis are significantly lower than that of the controls.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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