CLINICAL ARTICLE

Dynamic Spine Hyperflexion Is Related to Vertebral Compression Fractures in Postmenopausal Women

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Objective: Previous studies on osteoporotic vertebral fractures are usually based on the neutral posture of spine; however, the fractures are usually associated with the flexion posture of spine. Therefore, we aimed to ascertain the relationship between vertebral compression fractures and thoracolumbar hyperflexion Cobb angles (TLHCobb) and determine the clinical cut-off of the TLHCobb angle.

Methods: In this retrospective case–control study, TLHCobbs were collected from 154 postmenopausal women (67.45 ± 6.68 years) with vertebral compression fractures (study group) and 310 postmenopausal women (66.57 ± 8.22 years) without vertebral compression fractures (control group) from June 2017 to July 2019. Demographic data, clinical data, and quantitative computed tomography (QCT) findings were compared between the groups. Chi-squared tests, unpaired *t*-tests, and Mann Whitney U were used to assess the group characteristics and proportions. Logistic regression was used to examine the association between vertebral compression fractures and TLHCobb. The cut-off of the TLHCobb was determined by ROC curve and Youden's index.

Results: Fracture prevalence was higher in the higher TLHCobb study group than that in the control group [OR = 2.81 (2.15–3.67)] after adjusting for age, BMI, and QCT findings. TLHCobbs at and >20.05° were associated with an increased fracture prevalence and ORs of 2.79 (1.82–4.27) and 4.83 (3.24–7.20), respectively. TLHCobb, disk height (semiquantitative grading score) and QCT values differed between the study and control groups ($p < 0.001$ for all three). There were no significant differences in body mass index (BMI), or coronal TLCobb between the two groups.

Conclusion: There was an association between the prevalence of vertebral compression fractures and TLHCobbs in postmenopausal women, and a TLHCobb > 20.05° can be an indicator of vertebral fracture.

Key words: osteoporosis; postmenopausal women; thoracolumbar hyperflexion; vertebral fracture

Introduction

At present, it is a common clinical approach to screen the risk factors of osteoporotic fracture from imaging. On the other hand, thoracolumbar spine is the site with the highest incidence of spinal fractures.[1] Thus, it may be cost-effective to screen from the thoracolumbar spine in postmenopausal women.

The flexion posture is more common in low-energy spine injuries than the neutral posture.[2–4] Previous studies on osteoporotic vertebral compression fractures (OVCF) are usually based on the neutral posture of the spine; however, the fractures are usually associated with the flexion posture of the spine.[5–7] Spinal lateral radiography provides a method of assessing the risk of vertebral compression fracture in a neutral spine posture, but these lack an accurate posture imitation for vertebral fracture. In most falldown cases, the spine tends to move from a neutral posture to flexion or hyperflexion postures because of the joint action of the upper body, hip, and the center of gravity in front of the thoracolumbar segment. Therefore, spinal flexion posture on

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lateral X-ray of lumbar spine may have varying degrees of simulation of the spinal situation in these fractures.[8]

The thoracolumbar spine (T10–L2) is the junction of the lumbar and thoracic vertebrae. T11–L2, as a spinal transition region in anatomy and mechanics, has the highest incidence of vertebral deformity and fracture, particularly in women after menopause.[9] Hyperflexion and neutral lumbar X-rays provide two types of information: the thoracolumbar hyperflexion Cobb's angle (TLHCobb) and the range of forward flexion of the thoracolumbar spine. Lumbar hyperflexion X-ray may contribute to determining the risk of vertebral fracture, of which the TLHCobb, an indicator of the highest incidence of vertebral fracture, could be a radiographic reference for a vertebral compression fracture. Some studies suggested that excessive kyphosis of thoracolumbar spine is related to osteoporotic vertebral compression fracture, and there is Cobb angle threshold for clinical application.[5] However, the spinal neutral position used in these studies does not adequately reflect the risk of spinal hyperflexion in low-energy injuries. In this study, we aimed to (i) ascertain the relationship between vertebral compression fractures and TLHCobbs and (ii) determine the possible clinical TLHCobb cut-off degree.

Materials and Methods

With the approval of the Human Ethics Committee of Chinese PLA General Hospital (S2020034-05) and the informed consent of patients, a retrospective and single-center study was adopted. The medical records of postmenopausal women treated at Chinese PLA General Hospital from June 2017 to July 2019 were analyzed retrospectively.

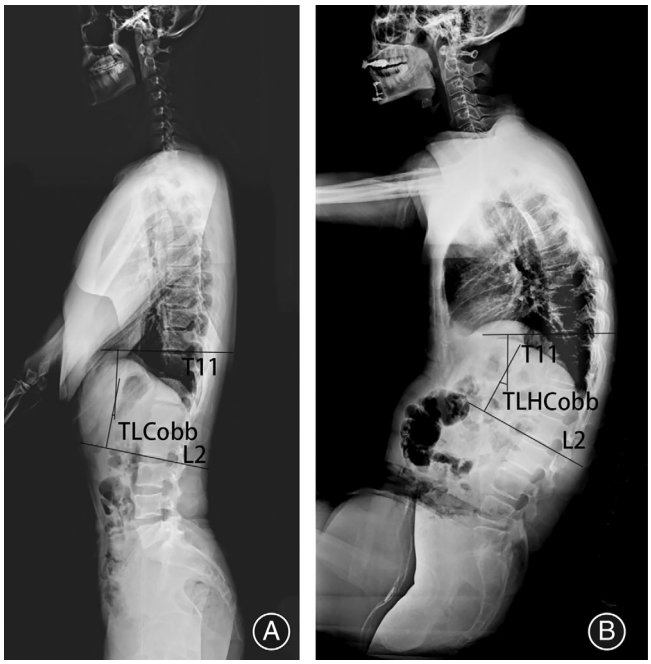

FIGURE 1 The relation of TLHCobb, TLCobb, and DTLCobb. DTLCobb is the difference between neutral spine posture in (A) and hyperflexion spine posture in (B): DTLCobb = TLHCobb.p-TLCobb.p

Inclusion and Exclusion Criteria

The inclusion criteria of study group (vertebral fracture group) were: (i) vertebral compression fracture of low energy (fall from standing height or a lower position and sneeze), (ii) first and only one vertebral body fracture, and (iii) treatment with vertebroplasty. The exclusion criteria were as follows: a tumor, spinal scoliosis (Cobb angle > 10°), and lack of information on standing and erect lumbar hyperflexion X-ray. The inclusion criterion of control group (non-vertebral fracture group) was age-matched (unpaired *t*-test, $p > 0.05$) patients without vertebral compression fractures, excluding patients with lumbar disc herniation, instability or spondylolisthesis, spinal tumors, ankylosing spondylitis, inflammatory spondylitis, congenital spinal deformity, spinal scoliosis (Cobb angle > 10°), and a previous history of osteoporotic fracture.

A total of 205 consecutive patients with a vertebral compression fracture were treated according to the inclusion criteria, of which 154 patients, with an average age of 67.45 ± 6.68 years, were included in the study group per the exclusion criteria. Altogether, 355 consecutive patients without vertebral compression fractures, of which 310 patients, with an average age of 66.57 ± 8.22 years, were categorized as the control group based on the exclusion criteria. Their information of age, body mass index (BMI; kg/m^2), radiographs of normal lumbar spine, normal lateral lumbar spine, lumbar spine flexion, and normal lateral thoracic spine were collected. The data on vertebral fracture site, TLHCobb, TLCobb, DTLCobb (the difference in the thoracolumbar Cobb's angle between the flexion and neutral postures, Figure 1), spinal osteoarthritis (OA) were recorded and calculated.

Radiological Examination

Data were obtained using Optima XR220amx (GE, Munich, Germany). Radiograph of normal lateral lumbar spine is taken in a standing position (SFE). Spinal imaging should be taken erect in the setting of non-trauma to give a functional overview of the lumbar spine. Ask the patient to cross their arms over their upper thorax. Radiograph of lumbar spine flexion is taken in the same way, at the last possible moment, instruct the patient to "bend forward" from the lower back, flexing their lower spine.

Bone Mass Density (BMD) Examination

BMD was measured using a QCTPRO2.0 workstation (Mindways Software Inc., Austin, TX, USA) and quantitative computed tomography (QCT) scans in a 16-slice spiral CT scanner (GE Discovery CT750 HD) with the following parameters: 120 kV, 125 mA, pitch 0.985, SFOV 500 mm, aperture 1.25mm, and table height 780 mm. BMD was

classified as normal (BMD > 120 mg/cm^3), osteopenia (80–120 mg/cm^3), and osteoporosis (BMD > 80 mg/cm^3) according to the criteria of the World Health Organization and the American College of Radiology (ACR). The maximal region of the cancellous bone was manually drawn in the middle cross-section of the vertebral body (Figure 2). The mean of two intact vertebrae in T12–L3 was selected to represent the density of the cancellous bone.[10] The density of the fractured vertebra before fracture was calculated by the mean density of the adjacent vertebrae (the upper and the lower of fractured vertebra).[11]

Vertebral Fracture Site

The site of vertebral fracture is recorded from radiographs of normal lateral thoracic spine and normal lateral lumbar spine.

TLHCobb, TLCobb, and DTLCobb

The TLHCobb is drawn by two lines parallel to the superior endplate of T11 and the inferior endplate of L2 on a hyperflexion lumbar radiograph. Accordingly, the thoracolumbar Cobb's angle is measured on a radiograph of lumbar spine flexion. The Cobb's angle formed on the ventral side is classified as positive, and on the dorsal side as negative.

TLHCobb is measured directly when vertebral compression fracture is not in T11 – L2. The TLHCobb with vertebral compression fracture in T11–L2 is retrospectively assessed by calculating the difference between the post-operation TLHCobb and the fractured-vertebral contribution to the post-operation TLHCobb.[5]

TLHCobb (pre-fractured) = TLHCobb (post-operation) – [Cobb(post-operation) – Cobb (unfractured mean)] (Figure 1).

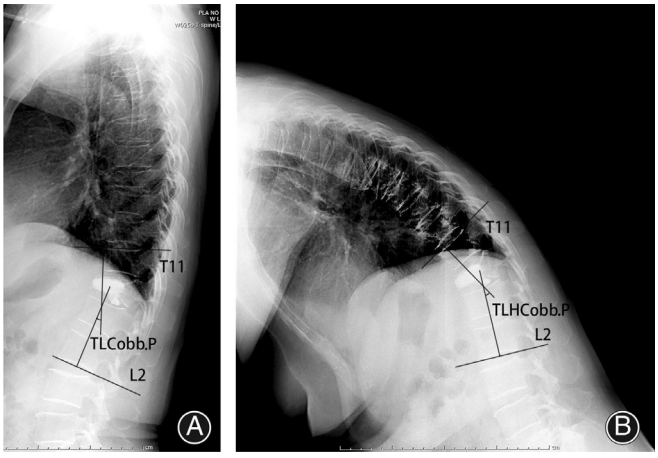

FIGURE 2 The measurement of BMD. The region of interest (ROI) in this study was defined as the largest volume of oval cylinder in the middle of the vertebral body in the sagittal, coronal, and axial positions. It has been found that this method could make the BMD value more stable and reduce the influence of hyperplasia and sclerosis in the vertebral body

The pre-fractured Cobb angle of the vertebral body is calculated on the average Cobb angle of the non-fractured vertebral body at the same position in the study group. The postoperative DTLCobb is collected (Figure 1).

Coronal TLCobb

Coronal TLCobb is recorded by two lines parallel to the superior endplate of T11 and the inferior endplate of L2 on a radiograph of normal lumbar spine. In this study, Cobb's angle greater than 10° was considered to affect the mechanical properties of the sagittal thoracolumbar spine.

Spinal Osteoarthritis (OA) Assessment

Spinal osteoarthritis (OA) includes disc narrowing (DSN) and osteophytes (OPH). Then, fourpoint scale: normal (0), mild (1), moderate (2), or severe (3) was used to evaluate DSN and OPH. Spinal osteoarthritis (OA) is defined as Grade 0 if both scores are normal; the Grade 1 with scores mild OPH or DSN; the Grade 2 with scores moderate or severe DSN or OPH. The interobserver reproducibility [k (95% CI)] assessed on radiographs by two trained orthopaedic doctors is 0.82 (0.66–0.95) and 0.67 (0.41–0.87) at the lumbar spine for DSN and OPH scores, respectively.

Parameters

Body Mass Index

Body mass index (BMI) is a value derived from the mass and height of a person.

Bone Mineral Density

A bone mineral density (BMD) test is the best way to measure your bone health.

Vertebral Fracture Site

Vertebral fracture site is the site of vertebral fracture in spine.

TLHCobb, TLCobb, and DTLCobb

The TLHCobb is the Cobb's angle of thoracolumbar in hyperflexion lumbar radiograph, accordingly, TLCobb is in lateral lumbar radiograph, and DTLCobb is the Cobb's angle range of thoracolumbar forword bending.

Coronal TLCobb

Coronal TLCobb is the Cobb's angle of thoracolumbar in normal radiograph.

Spinal Osteoarthritis (OA)

Spinal osteoarthritis (OA) is used to evaluate lumbar degeneration according to the suggestion of Sornay-Rendu *et al.*.[12]

Statistical Analysis

Data were analyzed using SPSS version 26 (IBM, Chicago, IL, USA). Descriptive statistics for continuous variables were expressed as means and standard deviations. Differences in

age, BMI, QCT findings, and Cobb angles between the two groups were assessed using chi-squared and unpaired *t*-tests. Differences in spinal OA, DSN, and OPH between the two groups were assessed with Mann–Whitney U test. The association between vertebral compression fracture and TLHCobb was examined using logistic regression analysis. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using multivariate logistic regression analysis of age, BMI, and QCT findings. The cut-off of the TLHCobb was determined by a receiver operating characteristic (ROC) curve and Youden's index.

Results

General Data and Baseline Characteristics

Despite the lack of differences in age, BMI, average Cobb angle and Coronal TLCobb in T11–L2 between the two groups ($p > 0.05$), the QCT values in the study group were lower than those in the control group ($p < 0.001$). The BMDs of the thoracolumbar spine were significantly different between the study and control group. Vertebral Cobb angles (T11, T12, L1, L2) were not significantly different between the two groups too (Table 1).

Vertebral Fracture Sites in the Study Group

There were seven T4 (4.5%), eight T5 (5.2%), 12 T6 (7.8%), 12 T7 (7.8%), 11 T8 (7.1%), 11 T9 (5.8%), eight T10 (5.2%), 17 T11 (11.0%), 20 T12 (13.0%), 22 L1 (14.3%), 12 L2 (7.8%), 10 L3 (6.5%), and four L4 (2.6%) compression fractures (Figure 3).

Spinal Osteoarthritis (OA)

Comparison of the spinal OA between the two groups Spinal OA Grade 1, 2 in the study group was significantly more prevalent than that in the control group, with OR = 1.59 (1.06–2.39). DSN was found to be different between the two groups with OR = 2.29 (1.54–3.40) and OPH was different from the study group to the control group with OR = 0.64 (0.50–0.82) (Table 2).

Comparison of TLHCobb, TLCobb, and DTLCobb between the Two Groups

When the two groups were combined and divided into mild, moderate, and severe subgroups according to the size of different TLHCobbs, the prevalence of vertebral compression fracture was found to be significantly associated with TLHCobbs. Cut-off values of 17.05° were determined by the ROC curve and Youden's index (Figure 4), with relevant OR = 2.81 (2.15–3.67), a sensitivity of 62. 3%, a specificity of 75.5%, an AUC of 0.754, and a 95% CI of 0.708–0.800. TLHCobbs were classified into mild (TLHCobb < 14.85°), moderate (TLHCobb 14.85–20.05°), and severe subgroups (TLHCobb > 20.05°). The fracture in both the moderate subgroup (BMD = 82.71 ± 9.25 mg/cm^3) and the severe subgroup (BMD = 49.05 ± 14.17 mg/cm^3) was significantly more prevalent than in the mild subgroup (BMD = 101.86 ± 13.16 mg/cm^3), with OR = 2.79 (1.82–4.27) and OR = 4.83 (3.24–7.20), respectively. DTLCobbs were 9.88 ± 2.79° in the mild subgroup, 7.81 ± 2.14° in the moderate subgroup, and 5.96 ± 2.62° in the severe subgroup.

TABLE 1 Baseline characteristics and research indices of study subjects (n = 464)

Variables	Study group (n = 154)	Control group (n = 310)	*p* value
Age (year)	67.45 ± 6.68	66.57 ± 8.22	0.218
BMI (kg/m^2)	25.15 ± 3.43	25.47 ± 3.00	0.302
Spinal OA [n (%)]	123 (79.87)	234 (75.48)	0.000
DSN	131 (85.06)	200 (64.52)	0.000
OPH	93 (60.39)	234 (75.48)	0.000
Cobb angles [(°), n]			
T11	5.53 ± 2.31 (137)	5.17 ± 2.55	0.165
T12	5.72 ± 2.40 (134)	5.30 ± 2.46	0.127
L1	5.74 ± 2.23 (132)	5.21 ± 2.61	0.068
L2	4.28 ± 2.40 (142)	3.89 ± 2.40	0.129
Average Cobb BMD (mg/cm^3), n	5.29 ± 2.34 (545)	4.89 ± 2.50	0.104
T11	66.06 ± 22.91 (137)	94.56 ± 22.71	0.000
T12	67.84 ± 23.79 (134)	92.80 ± 24.27	0.000
L1	71.20 ± 24.25 (132)	91.17 ± 25.93	0.000
L2	75.76 ± 25.63 (142)	89.29 ± 27.60	0.000
Average BMD	70.18 ± 23.99 (545)	91.95 ± 25.06	0.000
TLCobb angles (°)			
TLHCobb	20.00 ± 5.02	15.62 ± 4.18	0.000
DTLCobb	7.29 ± 2.83	8.42 ± 2.40	0.000
TLCobb	12.70 ± 6.84	7.19 ± 6.01	0.000
Coronal TLCobb	0.76 ± 3.75	1.06 ± 3.69	0.419

Abbreviations: BMD, bone mineral density; BMI, body mass index; DSN, disc narrowing; DTLCobb is the difference of thoracolumbar Cobb angle between hyperflexion posture and neutral posture; OA, osteoarthritis; OPH, osteophytes; TLHCobb, thoracolumbar hyperflexion Cobb angle.

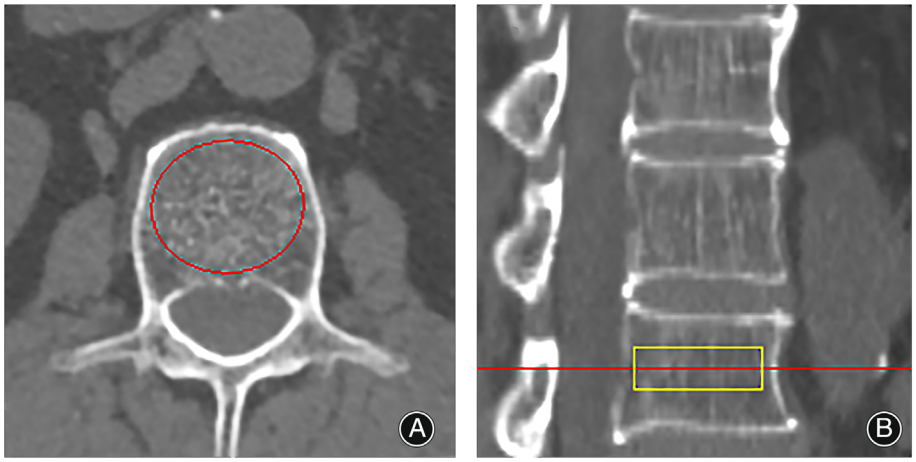

FIGURE 3 Vertebral fracture sites in the study group. Distribution of vertebral fractures in the study group

TABLE 2 Spinal osteoarthritis (OA) of study subjects (n = 464)

Variables [n (%)]	Study group (n = 154)	Control group (n = 310)
Spinal OA		
Grade 0, 1	41 (26.62)	204 (65.81)
Grade 2	113 (73.38)	96 (34.19)
DSN (fourpoint scale)		
0, 2	131 (85.06)	200 (64.52)
2, 3	23 (14.94)	110 (35.48)
OPH (fourpoint scale)		
0, 2	93 (60.39)	234 (75.48)
2, 3	61 (39.61)	76 (24.52)

Abbreviations: DSN, disc narrowing, OA, osteoarthritis, OPH, osteophytes.

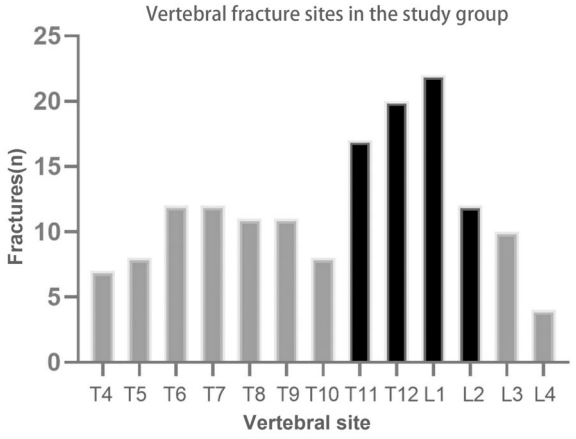

FIGURE 4 The ROC curve of TLHCobb, TLCobb, and DTLCobb. Receiver operating characteristic (ROC) analyses. ROC analysis to identify the Cut-off value of TLHCobb's and TLCobb's. TLHCobb's of 14.85° and 20.05° were determined using the ROC curve and Youden's index. The two lines showed the differences between TLHCobb's and TLCobb's. TLHCobb's presented the higher accuracy of detection than TLCobb's lines, Cut-off of 20.05° with a sensitivity of 46. 1%, a specificity of 86.1%, an AUC of 0.754, and a 95% CI of 0.708–0.800

Discussion

Previous fragile fracture and excessive spinal kyphosis have been accepted as the risk factors of osteoporotic fracture.[13] However, few studies have noted the association of the changes of posture during spinal fracture with the risk of OVCF. In our study, we found that the spine of most patients changed from neutral posture to flexion posture during low-energy spinal injury (Figure 5). The findings suggested that this posture change may be a factor contributing to the increased risk of OVCF in postmenopausal women. Our results show that there was a correlation between TLHCobb and OVCF incidence.

More DSN and Less OPH in the Fracture Group

The mechanical interactions of the disc and vertebrae indicate that the increased fracture risk of an osteoporotic spine segment may be slightly counterbalanced by the material consequences of disc degeneration. On the other hand, from the perspective of protection, OPH may become a positive factor against vertebral fractures as shown in Sornay-Rendu *et al.*'s study.[12] This finding could be verified in our study (OR = 0.64). However, disc degeneration and narrowing may eventually lead to changes in the risk of spinal fracture. In present study, DSN in the study group was more prevalent than in the control group, with more than 2.29 times the risk of vertebral fracture.

Significant Differences in TLHCobb, TLCobb, and DTLCobb between the Two Groups

Our study showed that the prevalence of fractures was related to the degree of TLHCobb. In postmenopausal women, the prevalence of fractures with relevant TLHCobbs of 14.85° to 20.05° or greater than 20.05° before injury was 2.8 or 4.8 times higher than that in fractures with TLHCobbs less than 14.85°, respectively. This increasing trend in the

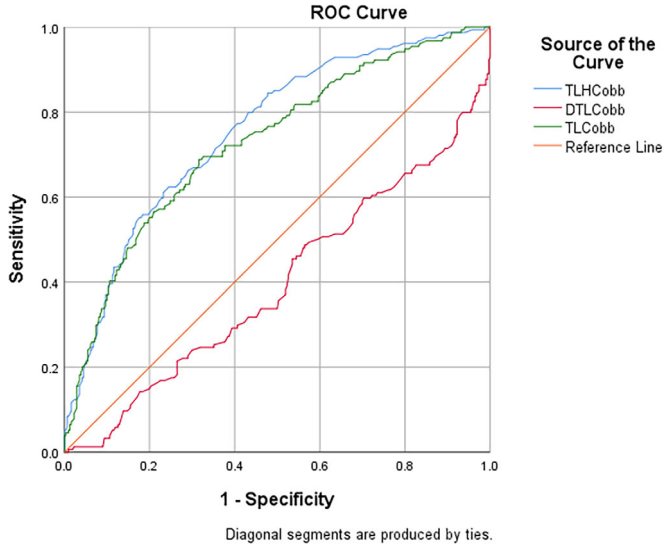

FIGURE 5 Posture changes during low-energy spinal injury. A neutral spine posture is relatively static and persistent (A). A dynamic and transient hyperflexion posture (B) under compression shows the stress process of most low-energy vertebral fractures. The TLHCobb is the key indicator for this process

prevalence of fracture could explain the increased risk of adjacent or other vertebral fractures due to increased kyphosis produced by anterior-wedge-deformed vertebra (no evident fracture plane or remembered injury).[14] Similarly, increased kyphosis caused by vertebral fractures could increase the risk of other vertebral fractures. Therefore, TLHCobbs can serve as radiographic references for vertebral compression fractures.[15]

In this study, a reduction in thoracolumbar motion range was observed in the osteoporotic fracture group. DTLCobbs tended to decrease from the mild subgroup ($9.88 \pm 2.79°$) to the moderate subgroup ($7.81 \pm 2.14°$) and the severe subgroup ($5.96 \pm 2.62°$). Spinal rigidity increases in the elderly population due to deterioration of the muscles, ligaments, intervertebral discs, and vertebral bodies.[16,17] The mobility decline of the lumbar spine and spinal inclination make people more susceptible to falls due to the altered biomechanical stability of the spine.[18] Therefore, decreasing the range of spinal motion could be suggested as a critical factor for predicting falls.[18]

Limitations

Our study with a small number of specific subjects was quick to conduct with regard to enrolling patients, reviewing patient records. Therefore, an obvious strength is that the research question can be addressed in a relatively short space of time. Furthermore, small studies often only need to be conducted over a few centres. Obtaining ethical and institutional approval is easier in small studies compared with large multicentre studies.

Some caution is advised in the interpretation of these data. This study was conducted in postmenopausal women treated in a comprehensive tertiary hospital. The generalizability of this information to other populations is unknown. First, the small sample size may not be enough to evaluate the association between OVCF and TLHCobb. Second, this study focused on the OVCF in postmenopausal women, without including the other parts (humerus, hip, and wrist).

Conclusions

Vertebral compression fractures are associated with TLHCobbs in menopausal women. The prevalence of vertebral fracture in osteoporotic women with TLHCobbs > 14.85° or 20.05° was 2.79 times or 4.83 times higher than in women with TLHCobbs < 14.85°, respectively. Therefore, a TLHCobb > 20.05° can be used as a high-risk marker of vertebral compression fractures. In the next step, multi-center study will be conducted to clarify the association and verify this high-risk marker. While TLHCobb is not widely available, our findings may prompt expansion of the clinical use of TLHCobb and provide the clue to develop new models for vertebral fracture prediction.

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Competing Interests

All authors declare that they have no conflict of interest.

Authors' Contributions

Zhirong Zheng, Wenhao Hu, Tian Tian, Weibo Liu, and Xiangyu Wang were three major contributors in writing the manuscript. All authors read and approved the final manuscript.

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