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Trabecular bone score and its association with Cobb angle kyphosis in older men: a cross-sectional study for the Osteoporotic Fractures in Men (MrOS) Study

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Abstract

Purpose: While vertebral fractures and low bone mineral density (BMD) contribute to kyphosis progression, it is unknown whether the trabecular bone score (TBS) may provide additional information on bone quality that could influence the degree of kyphosis. We hypothesized that degraded TBS would be associated with hyperkyphosis (HK) defined as a Cobb angle > 50°.

Methods: Using data from 1,997 participants of the Osteoporotic Fractures in Men (MrOS) study who had baseline TBS and Cobb angle kyphosis measured, we investigated whether men with degraded TBS were more likely to be hyperkyphotic, even after adjustment for BMD and prevalent vertebral fractures.

Results: Men were an average age of 74 ± 6 (mean ± SD) years with a mean kyphosis angle of 38.6 ± 11.5°, 295 (15%) were classified as hyperkyphotic, and 416 (21%) had degraded TBS. Compared with men with TBS > 1.2, men with degraded TBS were more likely to have HK (OR: 1.47, 95% CI: 1.06–2.06, p = 0.02) after adjusting for age, clinic, race, BMI, hip BMD and prevalent vertebral fracture. If spine instead of hip BMD was included in the model, the odds ratio decreased to 1.35 (95% CI: 0.97–1.89, p = 0.08).

Conclusions: Older men with degraded TBS are more likely to have HK not explained by underlying vertebral fractures.

Mini Abstract

Reema Patel, Jian Shen, Jeanne Nichols, John Schousboe, Gina Woods, Wendy Katzman and Deborah Kado declare that they have no conflicts of interest.

Hyperkyphosis (HK), or accentuated forward spinal curvature, commonly affects older people, although its causes are not completely understood. We tested whether a measure of bone quality, trabecular bone score (TBS), is associated with HK in 1,997 older men, and determined that men with degraded TBS were more likely to have HK.

Keywords

Hyperkyphosis; kyphosis; trabecular bone score; bone mineral density; vertebral fractures

Introduction

Hyperkyphosis (HK) is excessive forward curvature of the thoracic spine. There is no standardized, age-adjusted diagnostic criteria for defining HK, but the prevalence increases with age and is estimated to range from 20–40% among older individuals (age ≥60 years)[1]. Recent studies in men have defined HK as >50°[2]. The mean kyphotic angle in older men has been reported to be 44[3]. Multiple factors contribute to the progression of HK. Vertebral fractures, low bone mineral density, short vertebral height, degenerative disc disease, postural changes, muscle weakness, low body weight, and loss of elasticity of intervertebral ligaments have all been shown to potentially lead to early-onset HK[4,5]. Diagnosing and managing HK is important as it has been associated with multiple adverse health outcomes including thoracic pain, decreased pulmonary function, limited mobility, increased fractures, and increased mortality[1].

Trabecular bone score (TBS) is an indirect textural gray-level measurement derived from 2-D dual-energy X-ray absorptiometry (DXA) images of the lumbar spine using differential pixilation[6]. TBS has been shown to assess cancellous skeletal microstructure, an important factor of bone strength not captured by traditional DXA imaging and areal bone mineral density (aBMD)[7]. A low TBS value is associated with weaker bone microarchitecture, while a high TBS value is associated with stronger bone microarchitecture. TBS has been positively correlated with measures of volumetric bone mineral density (vBMD) and other parameters of trabecular microarchitecture, including, number of trabeculae, density, connectivity, and negatively correlated with distance between trabeculae[8–10].

Vertebral fractures and lower aBMD are risk factors for progression of kyphosis in older persons, but to our knowledge, correlations between TBS and measures of kyphosis, such as the Cobb angle have not yet been reported. TBS captures unique aspects of bone microarchitecture that could play an important role in the development of age-related HK.

The primary aims of this study were to examine cross-sectional associations between TBS and the degree of kyphosis as well as odds of hyperkyphosis, defined by >50° as measured by Cobb angle in older male participants of the Osteoporotic Fractures in Men (MrOS) Study.

Material and Methods

Study Design and Participants

A random sample of 2,344 participants were selected from the MrOS database (https://mrosonline.ucsf.edu/), which originally enrolled 5,994 ambulatory, community-dwelling men aged 65 or older (mean age 73.7 ± 5.9) from 2000 to 2002 in six different metropolitan regions in the United States (Birmingham, AL; Minneapolis, MN; Palo Alto, CA; Pittsburgh, PA; Portland, OR; and San Diego, CA)[11]. These men had both TBS and Cobb angle of kyphosis measured. Study participants on osteoporosis medication, corticosteroids, and hormone therapy (n=253), as well as participants with a BMI <15 or ≥35 kg/m^2 (n=99) were excluded, leaving a final number of 1,997 participants in the study.

Trabecular bone score measurement

The lumbar vertebrae, L1 to L4, were scored on anteroposterior (AP) spine Hologic fan beam DXA scans using TBS iNsight (Med-Imaps SASU, Merignac, France, version 2.1). Deformed vertebral levels were excluded[12]. Based on working TBS expert opinion and clinical relevance, TBS scores were categorized into three groups to differentiate bone micro architecture quality: degraded (TBS ≤1.2), partially degraded (1.2 < TBS < 1.35), and normal (TBS ≥ 1.35)[13].

Cobb angle of kyphosis measurement

Kyphosis can be measured using lateral spine radiographs to determine the angle of curvature of the spine, known as the modified Cobb angle, which is considered by many to be the gold standard for measuring kyphosis[1]. The modified Cobb method (refers to the Cobb angle measure used on sagittal instead of anterior-posterior radiographs) was used to assess the supine lateral spine radiographs taken of study participants[1]. An expert physician (John Schousboe, JS) used the SpineAnalyzer (Optasia Medical Ltd., Cheadle, UK) tool to place six quantitative morphometric points on the vertebral body corners and the endplate midpoints from T4 to T12. Perpendicular lines from the superior surface of T4 and the inferior surface of T12 were computerized and their intersection gave the kyphotic angle[1]. Because T1 to T3 typically are not easily seen on lateral spine radiographs, T4 and T12 were used as the cutoff points. In cases where T4 or T12 were not well visualized, the next bordering visible vertebrae was used for measurement. In line with recent studies, we defined HK as a Cobb angle >50 [2].

Vertebral fracture measurement

Vertebral fractures were identified from baseline lateral thoracic and lumbar spine radiographs, using the semiquantitative Genant method by an expert technician, Lisa Christiansen, and physician (JS). Prevalent vertebral fractures were defined as those with an SQ grade ≥ 2[14]. A vertebral deformity was defined as those with SQ ≥1, and included any mild vertebral deformity to the most severe vertebral fracture[14].

Other covariate measurements

Age, height, weight, body mass index (BMI), smoking status, alcohol intake, physical activity, and history of rheumatoid arthritis were obtained at the initial MrOS visit. Height was measured with a Harpenden stadiometer and weight was measured with an electronic scale or balance beam. BMI was calculated by dividing the weight (kg) by height (m^2). The participants self-reported whether they were current smokers, the number of alcoholic drinks they had per week, physical activity with the Physical Activity Scale for Elderly (PASE) questionnaire, and whether they had a history of rheumatoid arthritis[15].

Statistical analysis

Frequencies, means, and standard deviations were reported for characteristics of study participants. These characteristics were compared between participants with and without HK using T-tests for continuous and Chi-squared tests for categorical variables. Multivariate linear models were used to assess the association between lumbar spine (LS) TBS and the Cobb angle of kyphosis. Linear regression models were used to compare LS TBS between normal and hyperkyphotic groups. A logistic regression model was used to evaluate the OR and 95% CI of having HK according to TBS status. We evaluated potential confounding covariates by considering a list of factors that could be associated with TBS and kyphosis. In addition to the variables with known biologic plausibility, those factors that were significantly related to both TBS and kyphosis ($p < 0.10$) or just kyphosis were included in the multivariate models. Since it is likely that any vertebral deformity would contribute to worse kyphosis, in addition to prevalent vertebral fracture, any vertebral deformity was also included as a covariate in the multivariate models. Final reported models included age, race, enrollment site, BMI, prevalent vertebral fracture or vertebral deformity, and hip or spine BMD. All analyses were performed using SAS software (SAS Institute, Inc., Cary, NC, U.S.A.).

Results

The 1997 study participants had a mean ± SD age of 74 ± 6 years, BMI of 27 ± 3.2 kg/m^2, Cobb angle of 38.7° ± 11.5°, TBS of 1.28 ± 0.11, total hip BMD of 0.96 ± 0.14 g/cm^2, lumbar spine BMD of 1.17 ±0.24 g/cm^2, and T-score for total hip BMD of 0.11 ± 1.14. 89.7% were Caucasian, 3.5% were African-American, 3.1% were Asian, 2.4% percent Hispanic, and 1.2% were categorized as other. The overall distribution of the participants' Cobb angle measurements and lumbar spine TBS are shown in Figure 1.

The men were divided into two groups based on kyphosis status; 1702 (85%) were classified as having a normal degree of kyphosis (Cobb angle ≤50°) and 295 (15%) were classified as having HK (Cobb angle >50°). As shown in Table 1, those with HK were older, had lower BMI, lower BMD (hip and spine), more prevalent vertebral fractures, and lower lumbar spine TBS compared to those without HK.

Higher TBS was associated with lower Cobb angle, but the magnitude of correlation was low (correlation coefficient: −0.06, p=0.006). Higher TBS was associated with higher

lumbar spine BMD (correlation coefficient: 0.35, p<0.0001) and higher lumbar spine BMD was associated with lower Cobb angle (correlation coefficient: −0.12, p<0.0001).

Per standard deviation increase in TBS, there was a 0.83 degree decrease in kyphosis angle (95% CI: −1.4, −0.26; p=0.004). When adjusting for age, enrollment site, race, and BMI, this increased to a 1.14 degree decrease in kyphosis angle (95% CI: −1.76, −0.52; p=0.0003). However, further adjustment for hip BMD weakened the association (Cobb angle difference per SD −0.74, 95% CI: −1.44, −0.03; p = 0.04). The TBS association with Cobb angle lost significance in a model adjusted for age, site, race, BMI, hip BMD and vertebral deformity (Cobb angle difference per SD −0.65, 95% CI: −1.36, −0.05; p = 0.07). Substituting spine for hip BMD, in an age, site, race, and BMI adjusted model was also no longer statistically significant (Cobb angle difference per SD −0.36, 95% CI: −1.06, 0.34; p = 0.32). In models adjusted for age, site, race, BMI, spine BMD and including either vertebral deformity (Cobb angle difference per SD −0.27, 95% CI: −0.97, 0.43; p = 0.46) or prevalent vertebral fracture (Cobb angle difference per SD −0.26, 95% CI: −0.88, 0.37), p = 0.42) similarly attenuated the association between TBS and Cobb angle.

Fifteen hundred eighty one (79%) participants were classified as having normal or partially degraded TBS and 416 (21%) participants were classified as having degraded TBS (≤1.2). The normal and partially degraded TBS were collapsed into one group because these two groups had similar Cobb angles (mean 38.7 ± 0.5 vs. 38 ± 0.4, respectively) compared to the degraded TBS group (mean 40.2 ± 0.6). A degraded TBS increased the odds of having HK, even after adjustment for age, enrollment site, race and BMI (OR 1.73, 95% CI: 1.27, 2.35, p=0.0005). Results were somewhat attenuated with further adjustment for hip BMD (OR 1.5, 95% CI: 1.08, 2.09; p = 0.016). Still, after adjusting for age, enrollment site, race, BMI, hip BMD, and prevalent vertebral fractures, men with degraded TBS were at 1.47 times higher odds of having HK than those with normal or partially degraded TBS (95% CI: 1.06–2.06, p=0.02). When spine BMD was used in place of hip BMD, the odds ratio decreased to 1.39 and was no longer statistically significant (95% CI: 0.99, 1.93, p=0.055). In the model with spine BMD, the findings were similar if a more liberal vertebral deformity definition was used in place of prevalent vertebral fracture (OR 1.34, 95% CI: 0.96, 1.87; p = 0.088).

Discussion

We found that among older men, lower TBS is associated with worse kyphosis. However, the magnitude of the correlation coefficient was low and the linear association revealed a modest decrease in Cobb angle for per standard deviation increase in TBS. The association between TBS and Cobb angle appears to be confounded largely by effects on spine BMD. The decreasing associations seen after adjustments for hip BMD, prevalent vertebral fractures or progressive vertebral deformity, and spine BMD demonstrates aBMD accounts for some of the effect of TBS on kyphosis. Still, we found that compared to older men with normal or partially degraded TBS, those with degraded TBS are at significantly higher odds of having HK that is not explained by underlying prevalent vertebral fractures or vertebral deformity. Thus, these study findings suggest TBS captures other bone characteristics

beyond bone density that play a role in the progression of age-related kyphosis in older men.

Our study corroborated certain findings already reported in the current literature, including the strong evidence that low BMD and vertebral fractures are associated with baseline HK and progression of kyphosis[4,5]. A new finding of our study was the association between TBS and Cobb angle kyphosis. Though never studied before, we expected to find a negative correlation between TBS and HK based on previous studies showing TBS as a promising tool in combination with BMD to predict vertebral fractures, and the known associations among HK, BMD, and vertebral fractures. It was interesting to find a significant association that could not be explained by underlying prevalent vertebral fractures.

Several studies have shown that TBS scores are lower in postmenopausal women with a prior osteoporotic fracture compared to those without prior fractures, regardless of whether the BMD meets criteria for osteoporosis or osteopenia[16,17]. While less studied, similar findings have been demonstrated in men[18]. The OFELY study, a prospective study following a cohort of 560 white postmenopausal women, showed lumbar spine aBMD and TBS predicted fractures equally well, but 37% percent of fractures occurred in the lowest quartile of lumbar spine TBS, irrespective of BMD[19]. Furthermore, the OPUS study, a prospective study that examined the performance of TBS and aBMD in ambulatory European women, found that the combination of TBS and lumbar spine BMD had greater predictive power of vertebral fractures over lumbar spine BMD alone[20].

While vertebral fractures are commonly thought to be a major risk factor of HK, the Rancho Bernardo study revealed about two thirds of patients with severe HK do not have vertebral fractures[3]. This leaves a gap for other potential risk factors to play a major role. Our findings suggest non-fracture disruptions in skeletal microstructure, which are picked up by TBS, play a role in HK. Given these results, more routine use of TBS in patients with HK could provide a better understanding of the factors at play in kyphosis progression and allow for early targeted interventions.

A major strength of our study was the large, well-characterized cohort of participants evaluated. The men in this study were from geographically distant locations and not specifically selected for HK, allowing for a more generalizable sample. Moreover, to our knowledge, our study is the first to assess the association between TBS and HK.

There were some limitations of our study. One limitation was that TBS was measured on the lumbar spine, while kyphosis was evaluated on the thoracic spine. In theory, assessment of the microstructure of the thoracic spine would be better correlated with kyphosis. Moreover, the cross-sectional design of this study precludes determining if low TBS was present before development of HK in participants. Another limitation was that this study only evaluated men, thus the findings cannot be generalized to women. While about 10% of the MrOS study participants were ethnic minorities, this is not reflective of the diversity of the total US population, so the results should not be generalized to non-white patients.

Furthermore, this study only evaluated ambulatory, older community-dwelling men and cannot be applied to a sizable number of the older population that are mobility limited

and residing in care facilities. Lastly, it is possible that not all potential confounders were accounted for in our statistical analyses.

In summary, lower TBS is associated with a greater degree of kyphosis as measured by the Cobb angle in men. Men with degraded TBS are more likely to have HK not explained by underlying prevalent vertebral fractures. Based on these findings, we believe TBS can be used as a supportive tool in identifying unique aspects of bone microarchitecture that may contribute to age-related HK in older men.

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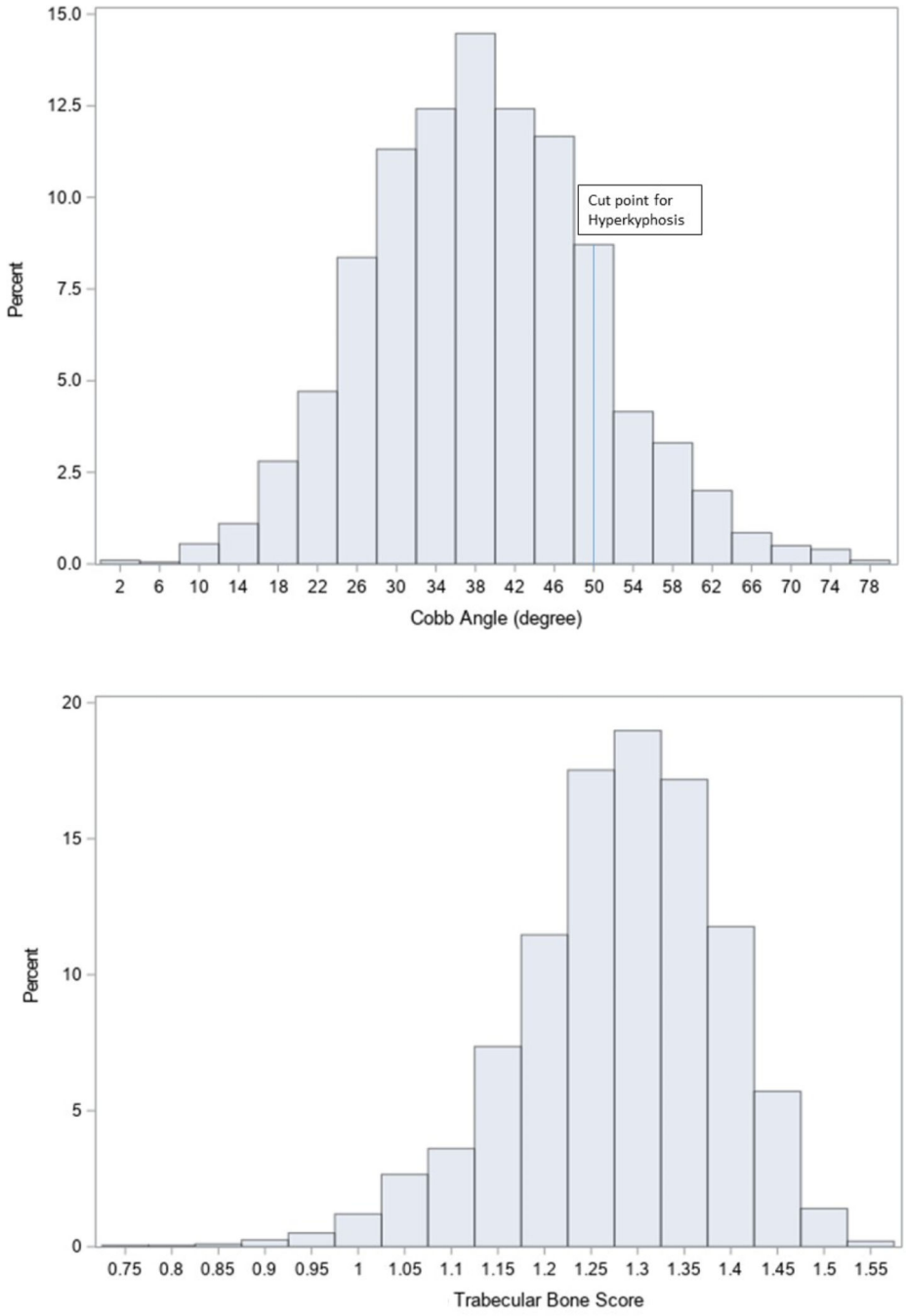

Figure.
Distribution of Cobb Angle Kyphosis and Trabecular Bone Score

Table 1.

Baseline Characteristics by Kyphosis Status

	Normal kyphosis (Cobb ≤50°) N = 1,702	Hyperkyphosis (Cobb >50°) N = 295	P-value
	N =1702	N = 295	
Age (years)	73.3±5.8	75.3±6.5	<0.0001
Height (cm)	174.3±6.9	174.4±6.3	0.81
Weight (kg)	82.4±11.7	81.3±11.4	0.14
BMI (kg/m^2)	27.1±3.2	26.7±3.1	0.05
Current smoker (N, %)	77 (4.5)	11(3.7)	0.64
Alcohol intake (# drinks/week)	4.8 ± 7.6	4.0 ± 6.4	0.10
Physical activity score	149 ± 69	148 ± 71	0.70
Prevalent vertebral fracture (N, %)	113 (6.6)	31 (10.5)	0.02
Rheumatoid arthritis (N, %)	83 (4.9)	11(3.7)	0.39
Total hip BMD	0.96±0.13	0.92±0.15	<0.0001
Lumbar spine BMD	1.18±0.24	1.12±0.23	<0.0001
Cobb angle of kyphosis	35.5 ± 8.9	57.1±6.1	<0.0001
Lumbar spine TBS	1.28 ± 0.11	1.26 ± 0.12	0.0002
Degraded spine TBS (N, %)	335 (19.7)	81 (27.5)	0.01

Mean (S.D.) or N (percentage) shown