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Clinical Research Article

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Lumbar Scoliosis in Postmenopausal Women Increases with Age but is not Associated with Osteoporosis

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Abbreviations: BMD, bone mineral density; DXA, dual-energy x-ray absorptiometry; FN, femoral neck; ICC, intraclass correlation; TH, total hip.

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Abstract

Context: The contribution of lumbar scoliosis to osteoporosis is unknown.
Objective: This work aimed to determine the prevalence and relationship of lumbar scoliosis to osteoporosis in aging women.
Methods: A cross-sectional analysis used dual-energy x-ray absorptiometry (DXA) scans of randomly selected groups of postmenopausal women (64-68, 74-78, and 84-88 years; N = 300 each) in a university teaching hospital from 2014 to 2019. Lumbar Cobb angle was tested for an association to femoral neck (FN), total hip (TH), and spine T score, age, weight, and ethnicity. Logistic regression tested an association between scoliosis (Cobb angle > 10°) and osteoporosis (T score ≤ –2.5). Available sequential DXA scans (N = 51) were analyzed for changes in Cobb angle using a linear mixed model of these longitudinal data.
Results: Osteoporosis and Cobb angle both increased with age: from 22% and 4.4 (SD = 7.8) respectively in 64- to 68-year-olds to 32.9% and to 9.7 (SD = 9.2) in women age 84 to 88 years. The prevalence of clinically significant scoliosis rose from 11.5% in the youngest group, to 27.3% and 39.4% in the age 74 to 78 and 84 to 88 cohorts, respectively. Cobb angle increased 0.7° per year of follow-up. After adjusting for covariates, there was no significant association between T scores at any site (TH, FN, or spine) and Cobb angle.

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Conclusion: Based on screening DXAs, the incidence and degree of lumbar scoliosis increases significantly in women between age 65 and 85 years. There was no association between the incidence of lumbar scoliosis and FN bone density.

Key Words: Cobb angle, aging, bone density

Despite the multitude of studies that guide the approach and treatment of postmenopausal osteoporosis, it is striking that an association with lumbar scoliosis—a common clinical entity afflicting the axial skeleton in the same age group [1]—has not been analyzed. During treatment of women for postmenopausal osteoporosis, studies reveal that lumbar spine bone mineral density (BMD) increases more rapidly than does hip density, and continues to increase in a sustained fashion when analyzed by serial dual-energy x-ray absorptiometry (DXA) exams [2-5]. However, quantification of BMD change at the lumbar spine is compromised in patients with spine deformities, particularly when an abnormal curvature in the coronal plane interferes with spine alignment [6, 7], and complicates monitoring of treatment. Moreover, that scoliosis may contribute to the appearance of vertebral fracture begs the question of whether scoliosis affects the diagnosis of osteoporosis.

Degenerative or de novo scoliosis in older adults is highly prevalent, estimated at 30% to 68% of adults [1]. Lumbar anatomical abnormalities are commonly recognized during review of bone density images from aging women, leading clinicians to discount spine DXA readings or to note that spine density is falsely elevated because of lumbar scoliosis or "sclerosis." Despite these truisms, few clinical studies in the bone field have attempted to quantify scoliosis, which, lacking an automated method, requires manual analysis. Moreover, individuals with scoliosis are routinely excluded from landmark osteoporosis trials that assess the efficacy of widely used pharmacologic therapies, exclusions based on imaging criteria, or diagnosis codes [8-10]. Frequent disqualification criteria includes patients with the presence of more than 2 nonevaluable lumbar vertebrae [11], focal sclerosis in the spine [4], or those designated as having bone diseases other than osteoporosis [12].

Importantly, it is unclear if postmenopausal osteoporotic patients have a higher prevalence of scoliosis than expected in an age-matched population. The literature gives clinicians little idea whether current treatments to prevent spine fragility fractures are efficacious in patients with scoliosis, or if osteoporotic treatments have any effect on scoliosis [13, 14]. Further, reliable distinctions between diagnosis of lumbar fractures due to osteoporosis and those due to adaptations to increasing lumbar curvature are currently lacking. In sum, the clinical ambiguity of spine BMD, which accompanies scoliotic spines [15], results in a confounding both of diagnosis and therapeutic treatment decisions relating to osteoporosis [16, 17].

We here aimed to determine the relationship between postmenopausal osteoporosis and a lumbar spine curve consistent with clinical scoliosis as defined by a Cobb angle greater than or equal to 10°. Randomly selected DXA scans conducted in postmenopausal women were used to study the association of bone density at the spine, femoral neck (FN), and total hip (TH) with lumbar Cobb angle. We present here that our analysis failed to detect a significant relationship between osteoporosis and lumbar scoliosis.

Materials and Methods

Study Design and Participants

A total of 900 women with density images and assessments captured in the University of North Carolina at Chapel Hill electronic medical record from 2014 to 2019 were randomly selected from assigned patient numbers recalling those who had received bone density scans. The patient population consisted of all women in our health care system and did not represent a subspecialty population. We focused on 3 age groups: 64 to 68 years (N = 300), 74 to 78 years (N = 300), and 84 to 88 years (N = 300). The age groups were selected to reflect the age of an initial baseline screening DXA in the United States (64 to 68 years), as well as DXA's performed in subsequent decades [18]. The institutional review board approved all aspects of this study.

Medical records of female patients having available DXA images were selected by a random number generator. Patient DXAs were analyzed with regard to ethnicity, weight, and T scores at 3 regions of interest. Height was not analyzed because it is inaccurately measured, or not measured at all, in radiology departments. Exclusion criteria included the presence of spinal instrumentation or absence of an available image (ie, performed at an outside facility where images were not available in our electronic health record). Cobb angle and osteoporosis at a single time point were assessed using the same scans. In a subset of 51 participants for whom more than one DXA was available, Cobb angle was determined in up to 7 sequential DXA exams.

Scoliosis Definition and Assessment

The Cobb angle is an accepted analysis of scoliosis severity and is determined by measuring the angle between the 2 maximally oppositely tilted superior vertebral end plate above and inferior end plate below the curve apex. Scoliosis was defined as a Cobb angle of 10° or more. Interpretation of Cobb scores in our study was completed by 2 independent readers (J.R. and J.S.). Intrarater agreement was high for continuous Cobb scores, with an intraclass correlation (ICC) of 0.92 (0.90-0.93), and for the dichotomous scoliosis definition ($\kappa = 0.79$; 95% CI, 0.76-0.82). Because of the high agreement, we used the mean Cobb score from both readers.

The reliability of Cobb angle measured from DXA scans was compared with Cobb angle assessed from other imaging modalities, which occurred within a 15-month window of the DXA scan. Twenty-nine patients had other imaging modalities available including lumbar x-rays, abdominal computed tomography scout films, and magnetic resonance imaging for comparison. Reliability was high, with an ICC of 0.92 (95% CI, 0.84-0.96), indicating substantial agreement between the measurements from different scans and validates the use of DXA scans in measuring Cobb angles, as performed by others [15].

Osteoporosis Definition and Assessment

Osteoporosis was assessed using data obtained from DXA scans. T scores were assigned for the spine, hip neck, and TH. A T score of less than or equal to –2.5 was defined as consistent with a diagnosis of osteoporosis at that site. Having a diagnosis of osteoporosis at any one site (spine, TH, or FN) was considered as a diagnosis of osteoporosis.

Statistical Analyses

Descriptive statistics for covariates according to osteoporosis status were computed. Covariates included age, race (White or non-White), and body weight. Age in years was also used in some analyses as groups: 64 to 68, 74 to 78, and 84 to 88. Continuous variables are presented as means ± SD, and categorical variables are presented as frequencies and percentages. Normality was assessed with the Kolmogorov-Smirnov test. All tests were 2-sided and considered statistically significant at the .05 level. Analyses were conducted using the statistical software package SAS version 9.4 (SAS Institute Inc).

A missing image or presence of hardware was present in 390 (43%) of participants who were randomly sampled (Fig. 1). Another 26 participants (3%) either had a missing Cobb angle reading from one reader or were missing covariates, for a final analysis sample size of 484 participants. For the assessment of an association between osteoporosis measures and presence of scoliosis, odds ratios (ORs) and 95% CI were calculated using logistic regression models for the presence of osteoporosis [19]. Covariates included age, weight, and race.

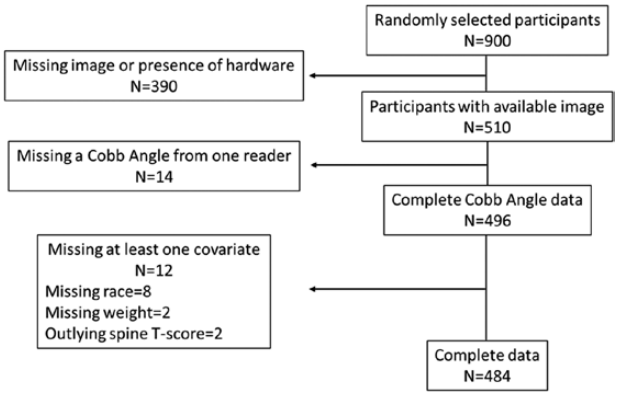

Figure 1. Flowchart for data acquisition.

The post hoc power analysis considered the power required to detect an arbitrary partial Pearson correlation (based on continuous variables as opposed to a categorical yes/no) at a .05 α level using Fisher z test. While our analysis had excellent power to detect a 0.30 correlation, it actually has substantial power throughout: Even with a threshold of 0.90, a 0.15 partial Pearson correlation could be detected with 0.830 power.

An additional longitudinal analysis was performed on a subset of 51 individuals in the data set, without regard to initial Cobb angle or to BMD, to gather information on with longitudinal progression of lumbar curvature. Individuals were entered in this analysis if 2 or more DXA images were available for analysis. A linear mixed model was used for repeated measures, assuming a within-subjects spatial power covariance structure due to unequal numbers of follow-ups and irregular follow-up times (SAS/STAT15.1 User's Guide; SAS Institute, 2018). A spatial power model is similar to an autoregressive model in that observations closer in time are more correlated than observations further apart, but it does not require the time between observations to be equal. This model can also accommodate missing data points due to an unequal number of follow-ups.

Results

Patient Demographics

Baseline characteristics of participants (n = 484) are reported in Table 1. The mean age of randomly sampled

Table 1. Descriptive characteristics (n = 484)

	Overall	Normal	Any osteoporosis	Normal	Hip neck osteoporosis	Normal	Total hip osteoporosis	Normal	Spine osteoporosis
		364 (75.2%)	120 (24.8%)	390 (83.2%)	79 (16.8%)	432 (92.3%)	36 (7.7%)	423 (87.4%)	61 (12.6%)
Age, y; mean (SD)	77.3 (8.22)	76.8 (8.08)	78.9 (8.47)[a]	76.7 (8.09)	79.5 (8.48)[a]	76.8 (8.16)	81.9 (7.30)[a]	77.2 (8.13)	78.5 (8.81)
Weight; mean (SD)	156 (35.0)	162 (35.1)	138 (28.2)[a]	160 (34.7)	133 (27.1)[a]	158 (34.8)	127 (23.2)[a]	158 (35.1)	139 (29.5)[a]
Non-White race (%)	101 (20.9%)	76 (20.9%)	25 (20.8%)	88 (22.6%)	11 (13.9%)	94 (21.8%)	5 (13.9%)	81 (19.1%)	20 (32.8%)[a]
Mean Cobb angle; mean (SD)	6.97 (8.60)	6.67 (8.45)	7.88 (9.00)	6.53 (8.59)	7.85 (8.02)	6.50 (8.42)	9.90 (8.96)[a]	6.98 (8.48)	6.93 (9.42)
Scoliosis (Cobb angle ≥ 10) (%)	122 (25.2%)	84 (23.1%)	38 (31.7%)	86 (22.1%)	28 (35.4%)[a]	98 (22.7%)	16 (44.4%)[a]	109 (25.8%)	13 (21.3%)

[a]*P* less than .05 (chi-square or Fisher exact *P* value for categorical variables; *t* test *P* values for continuous variables).

participants was 77 years, with age being higher in those with osteoporosis. A diagnosis of osteoporosis was present in 25% of the sample; body weight was significantly lower in those with osteoporosis. Those with spine osteoporosis tended to be non-White race. Scoliosis (Cobb angle ≥ 10°) was present in 25% of patients and was more frequently noted in those with hip osteoporosis.

Osteoporosis in a Postmenopausal Cohort

Osteoporosis at any region of interest (defined by a T score of ≤ –2.5) was found in 22% of the group age 64 to 68 years, increasing to 32.9% in the women in the 84- to 88-year-old group (Fig. 2). In all age groups, assignment of osteoporosis was more likely to be due to a low T score in the hip neck or spine, rather than in the TH. Osteoporosis diagnosed at any site was highest in women in the 84- to 88-year-old cohort, largely due to meeting criteria at the hip sites. Although hip density decreased during each decade for the hip, this was not true for spine density in the cross-sectional data.

Prevalence of Scoliosis Increases Significantly with Age

Cobb angle was measured to indicate the severity of scoliosis. We noted a higher mean Cobb angle in the older age groups: The mean angle was 4.4 (SD = 7.8) in the 64 to 68 age group and was 9.7 (SD = 9.2) in the 84 to 88 age group (Fig. 3A). The presence of a clinically significant Cobb angle (≥ 10°) was highest in the oldest age group; the prevalence in the 64 to 68 cohort was 11.5% (21 of 182), 27.2% in the 74 to 78 cohort (40 of 147), and 39.4% (61 of 155) in 84 to 88 cohort (Fig. 3B).

Association Between T Scores and Cobb Angle

The 64- to 68-year-old cohort was held to best represent individuals unselected for osteoporosis (screening recommendations), and was primarily used to test for a relationship between osteoporosis and scoliosis. Our analysis showed a nonstatistically significant decrease in TH T score, which is the most reliable measure of osteoporosis in patients with lumbar spine sclerosis, with increasing Cobb angle in this group, (P = .123) as shown in Fig. 4A, adjusted for weight and ethnicity. In the older cohorts no association was noted between TH T score (Table 2, Fig. 4A) and Cobb angle in any age group. Age-adjusted TH scores are shown in Fig. 4B, where all age groups were analyzed together (in these analyses, the P value is for the β coefficient, while an R^2 value < 0.05 would be significant for an association); this clarifies the lack of a measurable relationship between scoliosis and hip T score (R^2 = 0.174). As well, no association with Cobb angle in this age group was identified for T scores of the FN (Fig. 4C). Despite a statistical relationship in the spine (Fig. 4D), the clinical significance makes interpretation difficult in an area affected by scoliosis.

Association of Osteoporosis Measures with Clinically Significant Scoliosis

Table 2 presents results from logistic regression models that estimate whether presence of scoliosis is associated with osteoporosis measures. Unadjusted models found an association between scoliosis BMD at the FN and TH. However, after adjusting for age and weight these were no longer statistically significant. When stratified by age group there were also no significant associations noted.

Serial Dual-Energy X-Ray Absorptiometry in Available Patients

A subset of 51 patients with available serial DXA exams were analyzed for changes in Cobb angle with respect to age. The mean number of follow-up scans in this data set was 3.5 (SD = 1.4) and ranged from 2 to 7. At baseline the

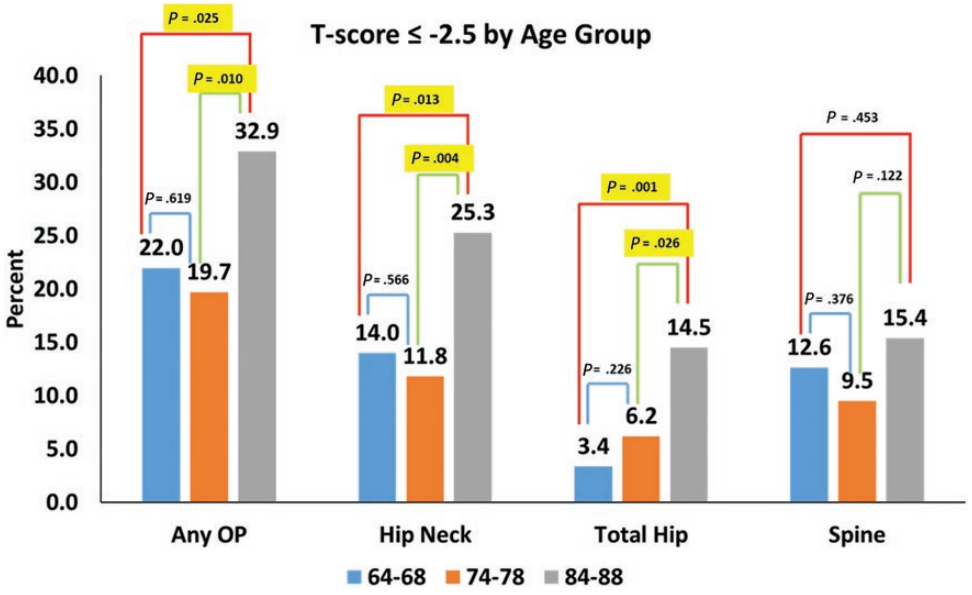

Figure 2. Osteoporosis by age group. Individuals randomly selected in mid-age ranges are shown. Osteoporosis at any site (T score ≤ –2.5, "Any OP") shown in the first bar set shows increased osteoporosis by age 84 to 88. The majority of the increase is due to increase at the hip neck, shown in the second bar (difference between 64 to 68 and 84 to 88, $P = .013$). Spine osteoporosis shows no significant increase across the age groups.

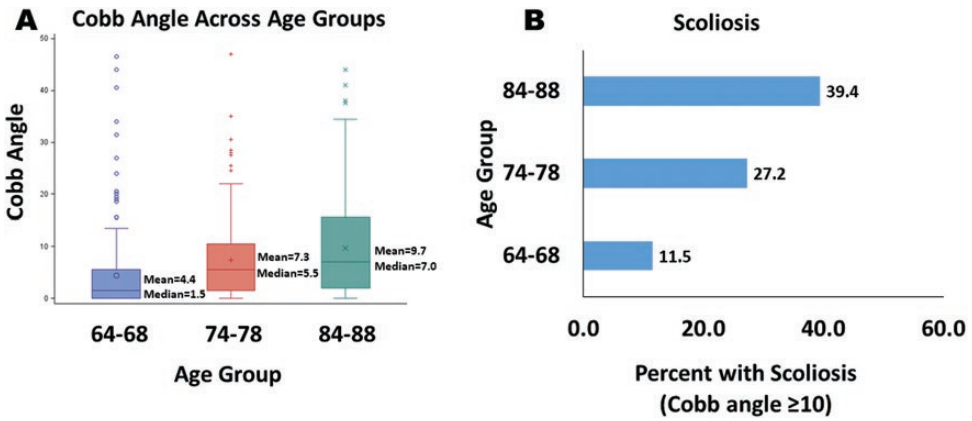

Figure 3. Cobb angle across age groups. A, Mean and median Cobb angles are shown for the selected age groups (64-65 vs 74-75: $P = .001$; 64-65 vs 84-85: $P \leq .001$; 74-75 vs 84-85: $P = .016$). B, Significant Cobb angle (≥ 10°) increases with age.

mean age was 73.6 (SD = 6.0) and a mean Cobb angle of 13.5 (SD = 8.9). The mean follow-up period was 4.5 years (SD = 3.4) and mean time interval between DXA exams was 4.4 years (SD = 3.5). Examination of the spaghetti plot in Fig. 5 reveals high variability in individual Cobb angles over follow-up scans. Increasing age was a statistically significant predictor of increasing Cobb angle, increasing 0.70 degrees for every year increase in age ($\beta = 0.70$; SE = 0.11, $P < .001$).

Discussion

Lumbar scoliosis complicates the analysis and treatment of osteoporosis. To discover whether lumbar scoliosis is associated with osteoporosis, we performed a cross-sectional analysis in postmenopausal women. The data set detected no association between lumbar scoliosis and osteoporosis at any region of interest within or across any age group. Our analysis further showed that lumbar scoliosis increased in prevalence and severity as women aged, so that nearly 40% of women in their ninth decade had clinically significant Cobb angles as defined by a lumbar curve greater than or equal to 10°. This suggests that such a high prevalence of lumbar scoliosis will affect the diagnosis of spinal osteoporosis in aging women.

Comparing across randomly selected samples from each decade of postmenopausal women, we found an expected age-dependent loss of bone density in the hip sites, leading to an increased diagnosis of osteoporosis. Twenty-two percent of women in their 60s met the

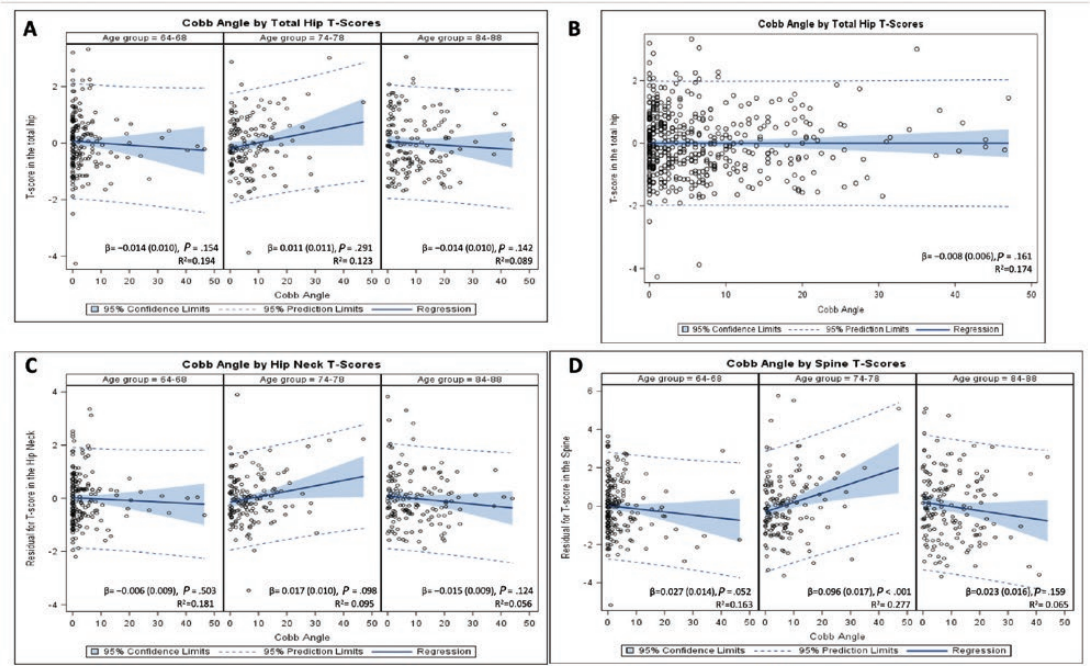

Figure 4. Cobb angle by T scores. A, There was no association of Cobb angle with total hip T scores within age groups or B, with groups combined adjusted for age and weight (R^2 = 0.174). Cobb angles for age and weight adjusted T scores of C, hip neck and D, spine.

Table 2. Odds ratios (95% CI) for association of scoliosis[a] with T score less than or equal to –2.5 (n = 484)

	T score ≤ –2.5 at any site (n = 484)		Fem neck T score ≤ –2.5 (n = 469)		Total hip T score ≤ –2.5 (n = 468)		Spine T score ≤ –2.5 (n = 461)	
	No	Yes	No	Yes	No	Yes	No	Yes
Scoliosis/No scoliosis	84/280	38/82	86/304	28/51	98/334	16/20	109/314	13/48
No adjustment	Ref	1.55 (0.98-2.44)	Ref	1.94 (1.15-3.26)	Ref	2.73 (1.36-5.46)	Ref	0.78 (0.41-1.50)
Adjusted age	Ref	1.34 (0.83-2.16)	Ref	1.63 (1.05-2.82)	Ref	1.99 (0.96-4.10)	Ref	0.68 (0.34-1.33)
Adjusted age and weight	Ref	1.04 (0.63-1.72)	Ref	1.17 (0.66-2.08)	Ref	1.36 (0.64-2.90)	Ref	0.54 (0.27-1.07)
Adjusted age, weight, and race	Ref	1.05 (0.64-1.74)	Ref	1.17 (0.66-2.07)	Ref	1.36 (0.64-2.91)	Ref	0.55 (0.27-1.10)

Abbreviations: Fem, femoral; Ref, reference.
[a]Scoliosis equals a Cobb angle greater than or equal to 10.

definition of osteoporosis, with a T score less than or equal to –2.5 at any of 3 surveyed sites. T scores in the hip neck progressed with increasing age, contributing to 33% of the 84 to 88 year group meeting criteria for a diagnosis of osteoporosis. Interestingly, osteoporotic T scores measured in the lumber spine region remained largely the same between all age groups, a point that our data suggest may be due to increasing prevalence of lumbar curvature. In the youngest age sampled, we found a wide spread of Cobb angles, yet only 11.5% was clinically significant. The proportion of clinically significant Cobb angles was 27.3% within 10 years, and 39.4% in the oldest cohort. Importantly, despite the correlation of age and osteoporosis, the advancing Cobb angle was not associated with T score at any site.

In the cross-sectional analysis, we assessed the lateral curvature of patients' lumbar spines by digitally measuring the Cobb angle on lumbar DXA images. Prior studies demonstrated that digital measurements of spine parameters—available on many reporting programs—are more precise than manual measurements [20], and that Cobb angles can be reliably measured from DXA radiographs [15, 21, 22]. We validated this methodology by comparing Cobb angles measured from DXA scans to those measured from other imaging modalities and found that interstudy reliability was high (ICC 0.92).

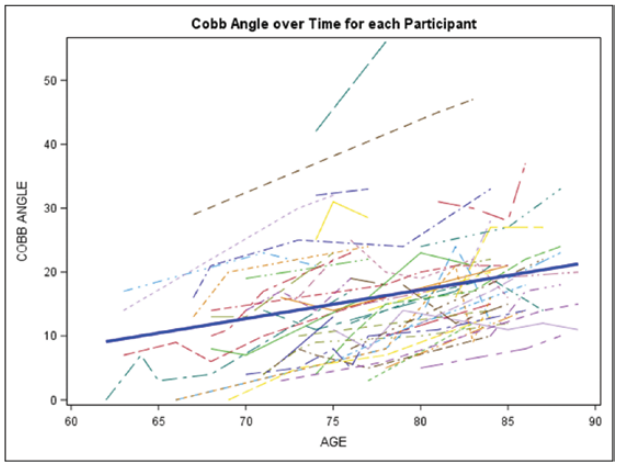

Figure 5. Cobb angle across time for individual patients.

Our study adds to the literature that suggests lumbar BMD values are significantly higher in patients with degenerative spinal disease [23]. While density in the lumbar vertebrae may be increased because of sclerotic remodeling of vertebral end plates, this increase does not necessarily infer less propensity to macroscopic or microscopic fracture [24]. As such, decisions regarding treatment response of spine osteoporosis are confounded by lumbar scoliosis, which interferes with the reliability of serial density scanning. We thus speculate that the failure of lumbar T scores to decrease along with hip density is at least partially due to aberrant increases in bone density associated with advancement of lumbar scoliosis. Indeed, the older a woman is, the more spine BMD may reflect age-related scoliosis. As such, T scores in the hip region represent more reliable data to predict fracture risk.

Patients with lumbar scoliosis are often excluded from clinical studies of osteoporotic treatments because sequential spine densities are unreliable and expected to be higher than actual measured areal bone density at the site of the patient's hip [25]. There is little formal guidance to overcome this challenge in clinical decision making, despite prevalent use of DXA and plain films to image the lumbar spine in osteoporosis patients [26]. Because vertebral fractures are more common in the postmenopausal population than hip fractures, obtaining an accurate assessment of this end point is critical and yet the medical literature has failed to address the knowledge gap of diagnosing compression fractures in the setting of scoliosis or answering whether these anatomically related entities are also mechanistically interrelated.

Many studies have shown that scoliosis increases with aging. As early as 1977, a large cross-sectional study showed that the prevalence of scoliosis in adults was higher than in school-aged children [27]. A review of DXA scans both from men and women found an increasing incidence of clinical scoliosis rising from 3% in individuals younger than 60 years to 21% in patients in their 80s [21]. Another large analysis of Cobb angles in older women found a 13% prevalence of clinical lumbar scoliosis, but age conferred only a small predictive effect [22]. Other studies show that Cobb angles increase in patients with scoliosis: Ten-year follow-up in adult scoliotic patients showed increased angle severity with advancing years [21, 28], with an average rate of lumbar curve progression of more than 3° per year [29, 30]. Our results confirm that the prevalence of scoliosis increases with advancing age. The prevalence of scoliosis was 11.5% (21 of 182) in the youngest group and 39.4% (61 of 155) in the oldest group. Among the patients with serial DXA scans (Fig. 5), Cobb angle increased an average of 0.70° for every year increase in age. Importantly, our subanalysis did *not* select for scoliosis or BMD, but rather for availability of serial DXA scans for analysis; as such, it would appear that many women with straight spines in their sixth decade acquire curvature as they age. Development of lumbar scoliosis mostly likely results from the combined effects of age-related degeneration of the vertebral body, facet joints, intervertebral discs, ligaments, and muscles. Intervertebral disc degeneration may lead to facet joint subluxation, which can cause remodeling of the posterior elements and result in segmental instability and scoliosis [31]. In individuals age 75 years followed for 10 years, degenerative changes, most commonly in the lumbar region, increased significantly in the subsequent 10 years [32], consistent with the advancing scoliosis that we report here.

It is unclear whether there is a causal relationship between osteoporotic vertebral compression fractures and spine scoliosis [33]. Healey and Lane investigated the association between scoliosis and vertebral compression fractures in a group of 50 older women with biopsy-proven osteoporosis with known compression fractures [34]. Nearly half of these women had clinically significant scoliosis, but compression fractures themselves did not lead to a curve because the posterior spinal elements are not disrupted in compression fractures. Another theory is that scoliosis does predispose patients to fractures, since vertebrae within scoliotic curve are subject to eccentric loading. This is supported by the fact that most compression fractures occur at the apex of the thoracolumbar or lumbar curves.

Our study is limited by the cross-sectional design, and by the inability to separate scoliotic changes in the lumbar spine from potential lumbar fractures. Despite this, the data are clear with regard to a lack of association between lumbar scoliosis and advancing hip osteoporosis at either the FN or total proximal density sites. We also did not examine thoracic scoliosis, or compare data in men, both subjects that we hope to study in the future, and hope that modifiers of scoliosis can be addressed in prospective studies. Another limitation is that many

comorbidities, influences of lifestyle, and medication history were not included in our analysis, and are likely to affect both the determination of osteoporosis and potentially the progression of scoliosis. Because ours was a retrospective study, an a priori power calculation was not performed. We did perform a post hoc power analysis for the partial correlation between lumbar scoliosis and osteoporosis while adjusting for 2 covariates—age and weight. Using an α of .05, a null correlation of 0, and our actual sample size of 300, analysis showed we had high power (> 99%) to detect even a weak partial correlation of 0.30. This supports our conclusion that an association between scoliosis and osteoporosis could not be identified.

Our analysis will help clinicians to answer their patients' questions regarding the discrepancy between spine and hip densities, etiology of their back pain, and speculation as to height loss during aging. Importantly, a majority of all fractures, including vertebral fractures, are not attributable to osteoporotic bone density [35], and this recent study also suggested that the magnitude of association between BMD and fracture risk decreases over time. Thus, although osteoporosis is clearly associated with risk of fracture, other risks, including falls and other morbidities of aging, predominate—and when our data reveal that the prevalence of scoliosis increases. In the future, the contribution of lumbar scoliosis, which will inherently alter mechanics of the spine, both to lumbar and thoracic fracture burden in older patients, will be an important area of investigation.

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Disclosures: The authors have nothing to disclose.

Data Availability: Some or all data sets generated during and/or analyzed during the present study are not publicly available but are available from the corresponding author on reasonable request.

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