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Thoracic kyphosis and rate of incident vertebral fractures: the Fracture Intervention Trial

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Abstract

Summary—Biomechanical analyses support the theory that thoracic spine hyperkyphosis may increase risk of new vertebral fractures. While greater kyphosis was associated with an increased rate of incident vertebral fractures, our analysis does not show an independent association of kyphosis on incident fracture, after adjustment for prevalent vertebral fracture. Excessive kyphosis may still be a clinical marker for prevalent vertebral fracture.

Introduction—Biomechanical analyses suggest hyperkyphosis may increase risk of incident vertebral fracture by increasing the load on vertebral bodies during daily activities. We propose to assess the association of kyphosis with incident radiographic vertebral fracture.

Methods—We used data from the Fracture Intervention Trial among 3038 women 55–81 years of age with low bone mineral density (BMD). Baseline kyphosis angle was measured using a Debrunner kyphometer. Vertebral fractures were assessed at baseline and follow-up from lateral radiographs of the thoracic and lumbar spine. We used Poisson models to estimate the independent association of kyphosis with incident fracture, controlling for age and femoral neck BMD.

Results—Mean baseline kyphosis was 48° (SD = 12) (range 7–83). At baseline, 962 (32 %) participants had a prevalent fracture. There were 221 incident fractures over a median of 4 years. At baseline, prevalent fracture was associated with 3.7° greater average kyphosis (95 % CI 2.8–4.6, $p < 0.0005$), adjusting for age and femoral neck BMD. Before adjusting for prevalent fracture, each 10° greater kyphosis was associated with 22 % increase (95 % CI 8–38 %, $p = 0.001$) in

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Compliance with ethical standards

Conflicts of interest None.

annualized rate of new radiographic vertebral fracture, adjusting for age and femoral neck BMD. After additional adjustment for prevalent fracture, estimated increased annualized rate was attenuated and no longer significant, 8 % per 10° kyphosis (95 % CI -4 to 22 %, $p = 0.18$).

Conclusions—While greater kyphosis increased the rate of incident vertebral fractures, our analysis does not show an independent association of kyphosis on incident fracture, after adjustment for prevalent vertebral fracture. Excessive kyphosis may still be a clinical marker for prevalent vertebral fracture.

Keywords

Vertebral fracture; Incidence; Kyphosis

Introduction

Age-related hyperkyphosis, an excessive anterior curvature in the thoracic spine, is common among older women and men, and is associated with substantial increase in morbidity and mortality. Longitudinal cohort studies have reported an increase in total number of fractures over 4 years [1], as well as an increase in non-spine fracture risk over 15 years among older women with hyperkyphosis [2]. Biomechanical analyses suggest that hyperkyphosis increases the load on vertebral bodies [3, 4], and may increase the risk of incident vertebral fractures in individuals with low bone mineral density (BMD), in particular when the spine is flexed during activities of daily living (ADL) [4, 5]. In addition, vertebral fracture contributes to hyperkyphosis [6–8]. Based on these observations, we speculate that hyperkyphosis may be a marker for a past vertebral fracture and a modifiable risk factor for incident vertebral fracture.

To our knowledge, there are no published studies that have examined whether hyperkyphosis is an independent risk factor for incident vertebral fracture. We used data from the Fracture Intervention Trial to assess the association of kyphosis with incident morphometric vertebral fracture over a median of 4 years among 3038 women 55–81 years of age with low baseline BMD.

Methods

Overview

The Fracture Intervention Trial (FIT) was a randomized, controlled multicenter trial among 6459 women with osteopenia or osteoporosis who were randomized to alendronate or placebo to test the efficacy of alendronate for reduction of risk of osteoporotic fractures [9]. Women randomized to the placebo arm of FIT, including women with and without radiographic vertebral fracture, were included in these analyses.

Subjects—Women included in FIT were required to be 55–80 years of age and post-menopausal for at least 2 years, live independently in the community, and have a bone mineral density (BMD) of the femoral neck 1.6 or more standard deviations (SD) below peak premenopausal femoral neck BMD (less than 0.68 g/cm²). Of the 3223 women in the placebo arm of FIT, 3038 women with complete data were included in our analyses. One

third of the women randomized to the placebo arm of the study had prevalent radiographic fractures at baseline.

Covariates—Baseline kyphosis angle was measured using a Debrunner kyphometer (Proteck AG, Bern, Switzerland), a protractor-like instrument. The ends of the device are placed over the spinous process of C7 superiorly and T12 inferiorly, and the protractor reads the kyphosis angle formed at the crotch of the two arms (Fig. Fig. 1) [6]. This measurement of kyphosis angle has excellent reliability and repeatability (intrarater and interrater correlation coefficients both 0.91) [10].

Vertebral fractures were assessed at baseline and follow-up using standardized digitization and semi-quantitative classification methods from lateral radiographs of the thoracic and lumbar spine. The determination of a fracture was made using a combined quantitative vertebral morphometry and semi-quantitative radiologic reading. At baseline, a technician triaged all scans into one of three categories: (1) definitely no fracture, (2) uncertain fracture/technically difficult film, or (3) at least one mild, moderate, or severe fracture. Vertebral morphometry was performed on all X-rays with suspected fractures using a six-point placement. A baseline morphometric vertebral fracture was defined if there was at least a 3 standard deviation reduction in anterior, mid, or posterior ratios compared with mean values that had been established using normative data [9]. Incident fractures were adjudicated at the follow-up visit and classified as a 20 % reduction in ratios and at least a 4-mm reduction in vertebral body height.

Baseline height was measured using a standard stadiometer protocol, and height loss (mm) was calculated compared to self-reported height at age 25. Bone mineral density at the hip and spine was measured using the QDR 2000 (Hologic, Inc., Waltham, MA, USA). Quality control measures have been detailed in other publications [11].

Statistical analysis—We used Poisson models with robust standard errors [12] to estimate the independent association of kyphosis with incident vertebral fracture (VF), using an offset to account for variations in trial follow-up and controlling for age and femoral neck BMD. Based on preliminary analysis using the Lowess smoother, we modeled the effect of kyphosis angle using a linear spline with a single knot at 36°. In addition to models with and without adjustment for baseline VF, we estimated the association of kyphosis with incident VF stratified by this factor, and tested for interaction. We also stratified on type (thoracic and lumbar) of incident vertebral fracture and adjusted for history of prevalent fractures by type.

Results

The mean age of our cohort was 68 (SD = 6.1) years, with a mean total hip BMD of 0.58 (SD = 0.06) g/cm² (Table 1). Mean baseline kyphosis was 48° (SD = 12) (range 7–83). At baseline, 962 (32 %) participants had a prevalent radiographic vertebral fracture. There were 587 participants with thoracic fractures, 208 with lumbar fractures, and 167 with both thoracic and lumbar fractures. Participants with a prevalent thoracic fracture had an average 5.5° (95 % CI 4.58–6.56) greater baseline Cobb angle of kyphosis, and those with prevalent lumbar fractures had a 1.1° (95 % CI –2.38 to 0.14) lower Cobb angle. A total of 221

participants experienced incident fractures over a median follow-up of 4.0 years (range 1.0–4.8), including 124 with incident thoracic fracture, 64 with incident lumbar fracture, and 32 with both; assessment of thoracic fracture was missing for 2 participants. The vertebral fracture incidence proportions increased linearly across quartiles of kyphosis (Table 2).

In the stratified analysis, the estimated effect for each 10° greater baseline kyphosis was 1.06 (95 % CI 0.93–1.22, $p = 0.39$) among women with a prevalent vertebral fracture at baseline. This effect was 1.17 (95 % CI 0.93–1.47, $p = 0.18$) among those without vertebral fracture at baseline (p value for interaction 0.48). Given no evidence for interaction, the groups with and without prevalent vertebral fracture were combined for all subsequent analyses. When we stratified on type of incident vertebral fracture, adjusting for prevalent fracture by type, the results were unchanged.

At baseline, prevalent radiographic vertebral fracture was associated with a 3.7° greater average kyphosis angle (95 % CI 2.8–4.6, $p < 0.0005$), after adjustment for age and femoral neck BMD, explaining about 4 % of the variation in kyphosis. Before adjustment for prevalent vertebral fracture, each 10° greater kyphosis above 36° was associated with a 22 % increase (95 % CI 8–38 %, $p = 0.001$) in the annualized rate of new morphometric vertebral fracture, controlling for age and femoral neck BMD (Table 3). After additional adjustment for prevalent vertebral fracture, the estimated increase in the new vertebral fracture rate was 8 % per 10° in kyphosis (95 % CI –4 to 22 %, $p = 0.18$). In this final model, prevalent vertebral fracture was independently associated with a 4.2-fold increase in the new vertebral fracture rate (95 % CI 3.1–5.5, $p < 0.0005$). Results were similar in a sensitivity analysis adjusting for lumbar spine rather than femoral neck BMD. Specifically, the estimated effect of each 10° in baseline kyphosis declined from 1.16 (95 % CI 1.02–1.31, $p = 0.19$) before adjustment for prevalent vertebral fracture to 1.05 (95 % CI 0.93–1.18, $p = 0.43$) after adjustment.

Discussion

In this analysis of 3038 women in the Fracture Intervention Trial, we found a statistically significant 22 % increase in the annualized rate of incident morphometric vertebral fracture for each 10° increase in kyphosis angle, after adjustment for age and BMD. However, after additional adjustment for baseline prevalent vertebral fracture, the estimated increase was only 8 % and no longer statistically significant.

Prevalent vertebral fracture is a well-established risk factor for incident vertebral fracture. In prior analysis in the FIT cohort, incidence of new vertebral fracture was 50 %, an average of 3.7 years follow-up among women with prevalent vertebral fractures and osteoporosis defined by BMD, compared to 9 % among women with no vertebral fracture and normal BMD [13]. Although unnecessary adjustment for history of the outcome can induce bias and/or reduce efficiency [14], we concluded that prevalent vertebral fracture should be regarded as a confounder in this analysis, and included it as a covariate in the fully adjusted model. Specifically, we hypothesized that past vertebral fracture is a likely cause of increased kyphosis [6, 7, 15] and independently linked to incident vertebral fracture through shared risk factors including a low body mass index, current smoking, low levels of daily

physical activity, and having a fall, as well as via direct causal effects [16]. Prevalent vertebral fracture likely is a surrogate for unmeasured confounders as well, such as parameters of bone strength that are not captured by DXA assessment. In the FIT cohort, prevalent vertebral fracture was strongly and independently associated with kyphosis angle and incident vertebral fracture. Accordingly, adjustment for prevalent vertebral fracture explained 60 % of the age- and BMD-adjusted association of kyphosis with incident vertebral fracture. While the 95 % upper confidence bound from the fully adjusted analysis remained consistent with a 22 % increase in the incident vertebral fracture rate for each 10° increase in kyphosis, we were no longer able to demonstrate a statistically significant independent effect.

Biomechanical analyses suggest that greater degree of kyphosis confers significantly more compressive load and shear force to the vertebral bodies compared to lesser degree of kyphosis [3]. Theoretically, this could increase the risk of vertebral fracture during activities of daily living (ADLs) in individuals with hyperkyphosis. We did not find that greater kyphosis predicted incident fractures, and it is possible that the spinal muscles adapt to hyperkyphosis to reduce the load. However, certain abrupt movements from coughing and flexion of the spine may confer risk of an incident vertebral fracture, in particular when there has been a past vertebral fracture and/or low bone mass, irrespective of the degree of kyphosis.

This study has several limitations. The participants were healthy post-menopausal women 55–80 years old with low bone mineral density, and the results cannot be generalized to other populations, including older men and women with normal bone density. In addition, reliability of the Debrunner kyphometer was assessed among 31 healthy volunteers, including 21 women and 10 men, with a mean age of 32 years (SD = 11) (range, 16–61), and may over-estimate the reliability of the measurements obtained among the older women with greater kyphosis in FIT. Finally, causal inferences based on observational studies must generally be advanced with caution. However, inferences about the independent effects of prevalent vertebral fracture and kyphosis angle on incident vertebral fracture are strengthened by the relatively weak correlation of these two potential causal antecedents. The weak correlation between prevalent vertebral fracture and baseline kyphosis made it possible to distinguish their effects statistically. Furthermore, by temporal ordering, we were able to exclude an effect of kyphosis that was measured at baseline on prevalent fractures that occurred earlier.

Conclusion

While greater kyphosis increased the rate of incident vertebral fractures, our analysis does not show an independent effect of kyphosis on incident vertebral fracture after adjustment for prevalent fracture. However, excessive kyphosis may still be a clinically useful marker for history of vertebral fracture, an easily identifiable signal that further investigation for possible vertebral fracture is indicated. Identifying underlying vertebral fractures, which frequently go undiagnosed, may be important for reducing incident vertebral fractures. Most vertebral fractures occur among those with low bone mineral density [17], thus recognizing that treatment may be indicated.

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References

1. Huang MH, Barrett-Connor E, Greendale GA, Kado DM. Hyperkyphotic posture and risk of future osteoporotic fractures: the Rancho Bernardo study. *J Bone Miner Res.* 2006; 21(3):419–423. [PubMed: 16491290]
2. Kado DM, Miller-Martinez D, Lui LY, et al. Hyperkyphosis, kyphosis progression, and risk of non-spine fractures in older community dwelling women: the study of osteoporotic fractures (SOF). *J Bone Miner Res.* 2014; 29(10):2210–2216. [PubMed: 24715607]
3. Briggs AM, van Dieen JH, Wrigley TV, et al. Thoracic kyphosis affects spinal loads and trunk muscle force. *Phys Ther.* 2007; 87(5):595–607. [PubMed: 17472956]
4. Briggs AM, Greig AM, Wark JD. The vertebral fracture cascade in osteoporosis: a review of aetiopathogenesis. *Osteoporos Int.* 2007; 18(5):575–584. [PubMed: 17206492]
5. Hayes WC, Myers ER. Biomechanical considerations of hip and spine fractures in osteoporotic bone. *Instr Course Lect.* 1997; 46:431–438. [PubMed: 9143985]
6. Ensrud KE, Black DM, Harris F, Ettinger B, Cummings SR. Correlates of kyphosis in older women. The Fracture Intervention Trial Research Group. *J Am Geriatr Soc.* 1997; 45(6):682–687. [PubMed: 9180660]
7. Ettinger B, Black DM, Palermo L, Nevitt MC, Melnikoff S, Cummings SR. Kyphosis in older women and its relation to back pain, disability and osteopenia: the study of osteoporotic fractures. *Osteoporos Int.* 1994; 4(1):55–60. [PubMed: 8148573]
8. Kado DM, Huang MH, Karlamangla AS, et al. Factors associated with kyphosis progression in older women: 15 years' experience in the study of osteoporotic fractures. *J Bone Miner Res.* 2013; 28(1):179–187. [PubMed: 22865329]
9. Black DM, Cummings SR, Stone K, Hudes E, Palermo L, Steiger P. A new approach to defining normal vertebral dimensions. *J Bone Miner Res.* 1991; 6(8):883–892. [PubMed: 1785377]
10. Ohlen G, Spangfort E, Tingvall C. Measurement of spinal sagittal configuration and mobility with Debrunner's kyphometer. *Spine.* 1989; 14(6):580–583. [PubMed: 2749372]
11. Black DM, Reiss TF, Nevitt MC, Cauley J, Karpf D, Cummings SR. Design of the Fracture Intervention Trial. *Osteoporos Int.* 1993; 3(Suppl 3):S29–S39. [PubMed: 8298200]
12. Zou G. A modified Poisson regression approach to prospective studies with binary data. *Am J Epidemiol.* 2004; 159(7):702–706. [PubMed: 15033648]
13. Cauley JA, Hochberg MC, Lui LY, et al. Long-term risk of incident vertebral fractures. *JAMA.* 2007; 298(23):2761–2767. [PubMed: 18165669]
14. Howards PP, Schisterman EF, Poole C, Kaufman JS, Weinberg CR. "Toward a clearer definition of confounding" revisited with directed acyclic graphs. *Am J Epidemiol.* 2012; 176(6):506–511. [PubMed: 22904203]
15. Kado D, Huang MH, Karlamangla AS, Cawthon P, Katzman W, Hillier TA, Ensrud K, Cummings SR. Factors associated with kyphosis progression in older women: 15 years experience in the study of osteoporotic fractures. 2011
16. Nevitt MC, Cummings SR, Stone KL, et al. Risk factors for a first-incident radiographic vertebral fracture in women > or = 65 years of age: the study of osteoporotic fractures. *J Bone Miner Res.* 2005; 20(1):131–140. [PubMed: 15619679]
17. Siris ES, Baim S, Nattiv A. Primary care use of FRAX: absolute fracture risk assessment in postmenopausal women and older men. *Postgrad Med.* 2010; 122(1):82–90. [PubMed: 20107292]

Fig. 1. Debrunner kyphometer device with the two ends of the device placed over the C7 and T12 spinous processes. The protractor reads the kyphosis angle formed at the crotch of the two arms

Table 1

Baseline characteristics

Baseline characteristic	Mean (SD or %)
Age (years)	68 (6.1)
Baseline kyphosis (°)	48 (12)
Vertebral fractures (<i>n</i>)	962/3038 (32 %)
Spine bone mineral density (g/cm ²)	0.82 (.14)
Femoral neck bone mineral density (g/cm ²)	0.58 (.06)
Height loss since age 25 (mm)	31 (31)

n number

Table 2

Crude new vertebral fracture incidence

Kyphosis angle by quartile	<i>n/N</i> (%)
7.0–40.0°	45/821 (5.4)
40.1–47.0°	43/704 (6.1)
47.1–55.5°	54/758 (7.1)
55.6–80.0°	79/755 (10.5)

Linear trend across quartiles: $p = 0.0003$ n/N number of incident vertebral fractures/number of participants in the kyphosis quartile

Table 3

Association of kyphosis angle with risk of new vertebral fractures

Kyphosis angle (per 10° > 36°)	IRR	95 % CI	p value
Model 1	1.18	1.05–1.34	0.006
Model 2	1.08	0.96–1.22	0.22
Model 3	1.09	0.96–1.22	0.18

Model 1: adjusted for age and femoral neck BMD; model 2: adjusted for age, femoral neck BMD, and baseline height loss; model 3: adjusted for age, femoral neck BMD, and baseline history of vertebral fracture