ORIGINAL ARTICLE

Prevalence of non-fracture short vertebral height is similar in premenopausal and postmenopausal women: the osteoporosis and ultrasound study

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Abstract

Summary We observed similar prevalence of short vertebral height without endplate depression (SVH) in young women aged 20–39 years and older women aged 55–79 years. There was no association between SVH and low bone density. In older women, therefore, SVH may be largely long standing and not indicative of osteoporotic fracture.

Introduction Algorithm-based qualitative (ABQ) definition of osteoporotic vertebral fracture (VF) requires evidence of endplate fracture, and there is no minimum threshold for apparent 'reduction' in vertebral height. In older women, SVH without endplate fracture identified on baseline assessment may be long standing and unrelated to VF. If this is so, we would expect to see a similar prevalence of SVH in younger women. We aimed to compare the prevalence of pre- and postmenopausal women with SVH and the characteristics of women with and without SVH.

Methods We used the ABQ method to classify baseline vertebral images (DXA-based imaging) from 257 premenopausal and 1,361 postmenopausal women participating in the population-based Osteoporosis and Ultrasound Study. Images were classified as follows: normal (no VF, no SVH), SVH (no VF) or VF (with/without SVH in unfractured vertebrae). We compared proportions of women with SVH (chi-squared test) and compared age, height, weight and bone mineral density (BMD) by ABQ classification (two-sample t test/analysis of variance).

Results The prevalence of pre- and postmenopausal women with SVH was 37% and 33%, respectively ($P > 0.05$). Compared to women without SVH, premenopausal women with SVH were older ($P < 0.001$) and heavier ($P = 0.05$), and postmenopausal women with SVH were taller ($P < 0.05$), with higher spine BMD ($P < 0.01$). Postmenopausal women with VF were older ($P < 0.001$) and shorter ($P < 0.01$) with lower BMD ($P < 0.001$) than women without VF.

Conclusions Short vertebral height without endplate fracture is equally prevalent in pre- and postmenopausal women and not associated with low bone density.

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Introduction

Prevalent vertebral fracture is usually identified when vertebral height appears reduced by a pre-specified amount in comparison to expected appearances (visual assessment) or to normal reference values (morphometric assessment). However, true change in vertebral height can only be determined longitudinally; thus, we cannot always be certain that short vertebral height observed on baseline assessment is the result of a fracture. A qualitative visual approach, algorithm-based qualitative (ABQ) definition of fracture requires evidence of fracture at the vertebral endplate, with no minimum threshold for apparent reduction in vertebral height [1]. When vertebral height appears shorter than expected without evidence of endplate fracture, it is excluded as non-fracture short vertebral height (SVH). The appearance of SVH may be mainly due to long-standing normal or developmental variation and as such, we would expect to see similar appearances in younger people. In previous studies, we have found no significant association between SVH and low bone density in men or women over 50 years of age [2, 3], but have not previously performed these analyses in a younger population. Such studies have been difficult in the past, due to the radiation dose associated with spinal radiography, but we now have access to densitometric vertebral fracture assessment (VFA) which uses only a fraction of the radiation used in conventional radiography [4] and thus represents a low-risk alternative. We wished to test the theory that SVH is largely a long-standing variant by comparing the prevalence of SVH in younger and older women. The specific aims of this study were to (1) compare the prevalence of SVH in pre- and postmenopausal women and (2) compare the characteristics of women with and without SVH.

Methods

Study participants

We analysed vertebral images obtained from women participating in the population-based Osteoporosis and Ultrasound Study (OPUS). This was a prospective study based in five European centres, namely Aberdeen, Sheffield, Paris, Kiel and Berlin [5]. Baseline visits were attended by 463 premenopausal women, aged 20–39 years, and 2,374 postmenopausal women, aged 55–79 years. This report is based on the evaluation of vertebral images obtained at baseline in a subset of the full study population; these were obtained in Aberdeen (Department of Rheumatology, NHS Grampian in association with the University of Aberdeen, Aberdeen, UK), Kiel (Medizinishce Physik, Klinik fur Diagnostische Radiologie, Univesitats-klinikum Schleswig-Holstein, Campus Kiel, Kiel, Germany), Paris (Centre d'Evaluation des Maladies Osseuses, Service de Rhumatologie, Assistance-Publique, Hopital Cochin, Universite Rene Descartes, Paris, France) and Sheffield (Metabolic Bone Centre, Northern General Hospital, UK). Exclusion criteria for entry into the study were disorders that precluded valid quantitative ultrasound measurements or general inability to undergo the study examinations. UK women were recruited from local general practices, German women were randomly selected from government registers and French women were randomly selected from the registers of a complementary health insurance system. Women included in the current analysis had attended OPUS baseline visits between 1999 and 2001 for densitometric VFA. Women who attended the Berlin centre were not included in this analysis, due to problems in accessing baseline vertebral scan images. In total, 1,618 women were included in the current analysis; of these, 257 were premenopausal, and 1,361 were postmenopausal.

Vertebral imaging and bone density assessments

Baseline vertebral images were obtained in Sheffield, Paris and Kiel using a Hologic QDR 4500A densitometer (Hologic Inc., Bedford, MA). Aberdeen images were obtained using a Lunar Expert XL (Lunar, Madison, WI). The spine was imaged in the posterior–anterior and lateral projections between vertebrae T4 and L4. Bone density scans of the lumbar spine and hip were obtained by dual-energy x-ray absorptiometry (DXA) using the same devices. Areal bone mineral density (BMD) measurements were standardised and cross-calibrated across centres; these procedures were performed at the coordinating centre in Kiel.

Assessment of vertebral images

Hologic vertebral images were viewed using the Hologic Discovery analysis software version 12.0; GE Lunar vertebral images were converted to TIFF files and viewed in Adobe Photoshop version 5.0. Vertebrae T4 through L4 were assessed visually (LF) using the ABQ approach [1], and the researcher was blinded to the age and identity of each participant.

Vertebral images were categorised as follows:

(i)   Normal (no evidence of SVH or osteoporotic fracture)
(ii) SVH in one or more vertebrae (no evidence of osteoporotic fracture)

(iii) One or more vertebral fractures (with or without SVH in unfractured vertebrae)

Short vertebral height was identified when one or more heights (anterior, central or posterior) appeared short (compared to expected appearances for normal vertebral dimensions), without evidence of endplate fracture. Vertebral heights were not measured directly and 'shortness' of vertebral height in the absence of fracture was estimated visually. Short vertebral height was recorded as approximately ≥20% shorter or <20% shorter than expected for normal vertebral dimensions. We estimate that the minimum that can feasibly be observed by the naked eye equates to a threshold of around 15% shorter than expected, but this is likely to vary slightly according to visual acuity and image quality. Vertebral fracture was identified when the appearances were in keeping with endplate fracture, with or without fracture of the cortex [1]. When endplate depression was identified, the severity of fracture was also estimated subjectively. Fractures were recorded as mild if vertebral height appeared reduced by up to 25% compared to expected appearances, or moderate/severe if vertebral height appeared reduced by more than 25%.

Data analysis

The percent prevalence of women with SVH or vertebral fracture was calculated separately for pre- and postmenopausal women. The proportions of pre- and postmenopausal women with SVH were compared using the chi-squared test. Mean values for age, height, weight and BMD were compared in women classified as normal or SVH (two-sample t test); these analyses were performed separately in pre- and postmenopausal women. The mean values were also compared in women classified normal, SVH or vertebral fracture (one-way analysis of variance, ANOVA). Statistical analysis was performed using MedCalc® version 11.3.3.0 (MedCalc Software bvba). We used a threshold of $P < 0.05$ to indicate statistical significance.

Results

Prevalence of non-fracture short vertebral height and vertebral fracture

The prevalence of women with non-fracture SVH was similar in pre- and postmenopausal women (difference in proportions = 4.0%; 95% CI for the difference −2.5%, 10.7%; $P = 0.24$) (Table 1). The result remained similar when we included women from the fracture group who also had SVH in unfractured vertebrae (difference in

Table 1 Non-fracture short vertebral height and vertebral fracture in premenopausal and postmenopausal women

	Premenopausal (n=257)		Postmenopausal (n=1,361)	
	VF	No VF	VF	No VF
SVH	3 (1)	95 (37)	41 (3)	455 (33)
No SVH	5 (2)	154 (60)	54 (4)	811 (60)
Total	8 (3)	249 (97)	95 (7)	1,266 (93)

Results are presented as the number (per cent) of women identified with or without vertebral fracture (VF) and non-fracture short vertebral height (SVH). Vertebral images were acquired using the Hologic QDR 4500A or the Lunar Expert XL densitometer and were evaluated using the algorithm-based qualitative method [1]

proportions = 5.0%; 95% CI for the difference −3.5%, 13%; $P = 0.26$). Short vertebral height was predominantly characterised by short anterior height, with peaks in the vertebral level distribution of SVH in the mid-thoracic region and at the thoraco-lumbar junction (Fig. 1). The prevalence of women with vertebral fracture was significantly greater in postmenopausal compared to premenopausal women (difference in proportions = 4.0%; 95% CI for the difference 0.86%, 6.3%; $P = 0.02$) (Table 1). Among the women with both vertebral fracture and SVH in unfractured vertebrae, the majority of fractures (85%) were mild in severity: at least half of these (54%) had appearances in keeping with long-standing fracture. Approximately 10% of vertebrae could not be reliably assessed due to poor image resolution or obscuration of the vertebral endplates by artefacts.

Characteristics of women with short vertebral height

Premenopausal women

Premenopausal women with SVH (no fracture) were significantly older ($P < 0.001$) and heavier ($P < 0.05$) than premenopausal women classified normal (no SVH or fracture) (Table 2). When women with vertebral fractures were included in the within-group comparisons (ANOVA), the significant difference in age (normal/SVH) remained ($P < 0.01$), and there was a trend towards greater weight with SVH ($P = 0.065$). Women with vertebral fracture did not differ significantly from other premenopausal women in terms of any of the variables assessed in this analysis.

Postmenopausal women

Postmenopausal women with SVH were significantly taller ($P < 0.05$) and had higher lumbar spine BMD ($P < 0.01$) than women classified normal (Table 2). There was also a trend towards older age with SVH ($P = 0.05$). The differ-
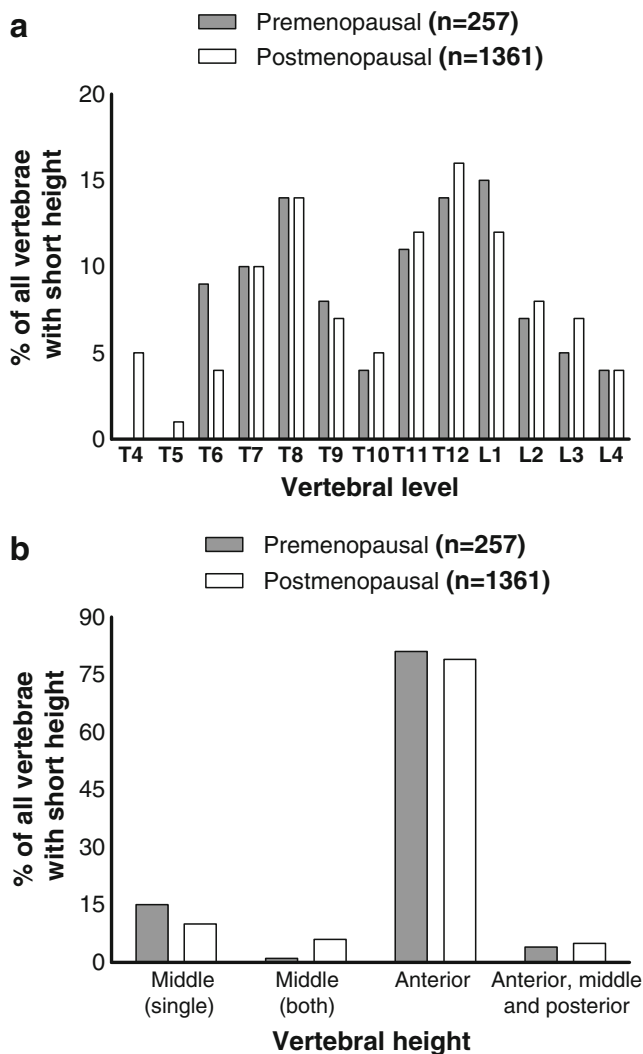
Fig. 1 Non-fracture SVH in pre-and postmenopausal women. Results are presented as **a** vertebral level-specific distribution of SVH and **b** height-specific distribution of SVH; for middle height, results are shown for vertebrae in which a single endplate or both endplates were identified as shorter than expected. Vertebral height was not measured, and a lower limit for SVH was not applied: we estimate the lowest threshold that can be visually detected without direct measurements to be approximately 15%

ences in height and lumbar spine BMD remained significant when women with vertebral fractures were included in the analysis (ANOVA). Women with vertebral fractures were significantly older ($P < 0.001$) and shorter ($P < 0.01$) and had lower lumbar spine and total hip BMD ($P < 0.001$) compared to women classified SVH or normal.

Discussion

We proposed that SVH without evidence of endplate fracture observed on baseline assessment in postmenopausal women is largely long-standing and unrelated to osteoporotic

fracture. We tested this theory by comparing the prevalence of SVH in pre- and postmenopausal women on DXA-based VFA. The prevalence of SVH was similar in both age groups and was not associated with low bone density in either age group. In contrast, the prevalence of vertebral fracture was significantly lower in premenopausal women.

The International Society for Clinical Densitometry (ISCD) position statement on VFA recommends that prevalent vertebral fracture is identified when vertebral height appears ≥20% shorter than expected. In addition, the ISCD guidelines suggest that the reader should also take the appearance of the endplate into account [6], and this has also been noted previously [7, 8]. Our results reinforce the importance of evaluating the endplate as well as vertebral height. Inexperienced readers, or those who have not undergone formal training in the diagnosis of vertebral fractures, might find this challenging and rely instead on the manufacturer's VFA quantitative analysis software for confirmation of fracture. Such an approach could lead to incorrect classification of SVH.

In both pre- and postmenopausal women with SVH, we predominantly observed short anterior height and peaks in the frequency of SVH in the mid-thoracic spine and at the thoraco-lumbar junction. Some researchers have proposed that wedging of the vertebral bodies increases with ageing, particularly in the thoracic region, but we observed a similar prevalence of short anterior height in both age groups. The evidence for non-fracture change in vertebral dimensions over life remains unclear; some studies suggest a decrease in vertebral height with ageing [9, 10], while others have not replicated these observations [11, 12]. Vernon-Roberts and Pirie described a decrease in intervertebral disc height with ageing [13], but there have been several reports of increases that reach a peak by ages 50 to 70 years [14–16]. Increased concavity of the lumbar vertebrae with age has also been reported [14, 16, 17]. The concept of bone 'creep' under lifelong loading has been proposed as an explanation for apparent changes in vertebral dimensions with ageing [18].

If non-fracture concavity does increase with age, this can be differentiated from osteoporotic fracture by careful observation of the endplate and the vertebral ring apophysis on the lateral projection [1]. In a true lateral projection, the unfractured endplate will appear superimposed on the vertebral ring and thus be indistinguishable from it. If the central endplate is depressed due to fracture, it will be imaged below the level of the vertebral ring, with the concavity extending between the inner anterior and posterior borders of the ring. The lines representing the vertebral ring will then be imaged very faintly and may be difficult to see, because the ring will no longer be superimposed on the endplate, and the reduced thickness of the structure when imaged in profile will provide poor attenuation of the x-ray

Table 2 Characteristics of premenopausal and postmenopausal women according to classification of vertebral images using the algorithm-based qualitative method

	Premenopausal (n=257)			Postmenopausal (n=1,361)		
	Normal (n=154)	SVH (n=95)	VF (n=8)	Normal (n=811)	SVH (n=455)	VF (n=95)
Age, years	30.7[****] (5.3)	33.2[****] (5.0)	32.1 (4.6)	65.9[*] (7.0)	66.7[*] (7.0)	69.8 (7.4)
Height, m	165.7 (6.6)	166.3 (7.4)	164.3 (8.3)	160.0[***] (5.9)	161.1[***] (6.6)	158.9 (5.7)
Weight, kg	64.5[**] (11.4)	68.5[**] (15.3)	66.0 (10.8)	67.9 (12.2)	68.5 (11.6)	66.3 (11.8)
BMD, g/cm^2						
Lumbar spine	1.151 (0.127)	1.182 (0.138)	1.161 (0.121)	1.033[***] (0.169)	1.061[***] (0.188)	0.968 (0.165)
Total hip	0.973 (0.126)	0.986 (0.136)	0.985 (0.080)	0.877[***] (0.139)	0.880[***] (0.140)	0.808 (0.148)

Results are presented as mean (SD) for women classified normal, short vertebral height (SVH) or vertebral fracture (VF). Means for women classified normal or SVH were compared within groups (pre- or postmenopausal) to women with vertebral fracture (two-sample t test; [*] P=0.05, [**] P<0.05, [***] P<0.01, [****] P<0.001). Vertebral images were acquired using the Hologic QDR 4500A or the Lunar Expert XL densitometer [1]

beam. The appearances may be less easy to interpret, however, when the projection is oblique or when there is scoliosis.

The age difference in younger women classified normal or SVH is difficult to explain and may be an artefact. Degenerative changes can give the appearance of short anterior vertebral height, when there is modelling and overgrowth of bone at the anterior surface of the vertebral body. The original anterior border may remain evident on a radiograph with good image contrast, but it may be less easy to determine on VFA due to the slightly inferior image resolution. Although we might expect degenerative changes to predominate in older women, degenerate intervertebral discs and vertebral osteophytosis have been reported in young women [19, 20]. We did not evaluate the reasons for SVH in this analysis, nor did we specifically exclude short vertebrae with the appearance of degenerative changes. However, we did ignore osteophytosis and 'lipping' in the determination of SVH, in keeping with the approach recommended for locating the endplates in quantitative morphometry [21].

There were some limitations to our analysis. Firstly, the subset of women studied did not represent all five participating centres in the OPUS study, due to difficulties in converting the Berlin GE Lunar images into a readable format within the allocated timeframe. However, the images from Aberdeen were acquired using a similar GE Lunar system, so our results may be applicable to images obtained by either GE Lunar or Hologic devices. Secondly, around 10% of vertebrae could not be reliably assessed by VFA, so the true prevalence of SVH or vertebral fracture in this study population could be higher. This was a low-risk study population, and we might expect to exclude a greater number of vertebrae from analysis when performing VFA in a high-risk population with lower bone density and greater prevalence of fracture. The ABQ method is a visual

method that does not employ direct measurements of vertebral dimensions. We believe that visual assessment is advantageous over morphometric analysis because it enables the expert reader to rule out non-osteoporotic deformities. However, the downside of this and other visual approaches is that the method is more subjective than the quantitative approaches. For this reason, it is essential that the visual assessments are conducted by appropriately trained and experienced readers. Other less experienced readers, therefore, could obtain different results on analysis of our dataset. Finally, there is no agreed gold standard definition of osteoporotic vertebral fracture, and all methods are subject to error. It is possible that some of the women identified as having short vertebral height without fracture represented false negative diagnosis by ABQ, particularly when vertebral height appeared more than 20% shorter than expected. However, on post hoc analysis of these women, we found no significant differences in lumbar spine BMD in either age group (two-sample t tests, P>0.44; data not shown). Total hip BMD was borderline lower in women with vertebral height ≥20% shorter than expected (0.877 g/cm^2 compared to 0.909 g/cm^2 in women with height <20% shorter than expected; P=0.05), but remained significantly higher than in women with vertebral fracture (P<0.0001).

In conclusion, short vertebral height without evidence of endplate fracture is equally prevalent in pre- and postmenopausal women and is not associated with low bone density.

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