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Vertebral fractures in women aged 50 years and older with clinical risk factors for fractures in primary care

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ABSTRACT

Background: The identification of vertebral fractures (VFs) is important for decisions on fracture prevention. Vertebral fracture assessment (VFA) was shown to be a patient-friendly and valid method for detecting undiagnosed VFs in (Dutch) women. However, this has only been investigated in women seeking care at secondary or tertiary institutions.
Objective: To investigate the prevalence of previously undiagnosed VFs in women in Dutch primary care using VFA.
Study design: A total of 566 Dutch women aged 50 years and older (mean age, 69 years; SD = 8.4) with clinical risk factors (CRFs) for fractures volunteered for dual-energy X-ray absorptiometry (DXA) measurement and VFA. VFs were defined semi-quantitatively using Genant's method.
Results: One CRF was present in each of 130 women, 274 had two, and 162 women had more than two CRFs. In 120 (21%) of the women, previously unknown osteoporosis (T-score ≤ -2.5 SD) was diagnosed, and in 174 (31%), a previously undiagnosed moderate or severe VF was found. No osteoporosis was found in 130 (75%) of the women with a VF. Based on the outcome of DXA, 21% of the women were eligible for treatment, while the combination of DXA and VFA resulted in a total of 250 (44%) women requiring treatment.
Conclusions: The percentage of previously unknown VFs diagnosed by VFA in women aged 50 years and older with one or more CRFs for fractures in primary care is high. When only using BMD measurements, only half the women eligible for treatment would actually receive this. We recommend performing VFA in all women aged 50 years and older who are referred for DXA based on Dutch case finding criteria.

1. Introduction

During a person's lifetime, osteoporotic fractures affect one out of two women and one out of five men [1]. While society is faced with increasing costs resulting from fractures, individuals are affected by morbidity, mortality and decreased quality of life [2]. Patients at risk for osteoporotic fractures are mainly identified by the assessment of clinical risk factors (CRFs) and bone densitometry [3]. An important and independent risk factor for future fractures is vertebral fractures (VFs). Almost 20% of women who sustain a VF will suffer a further one the following year [4]. After a first VF, the risk of subsequent VFs is increased three to fivefold, and the risk of a non-VF (including hip fractures) is increased twofold [5]. Since only one in three VFs presents with acute signs and symptoms, accurate diagnosis requires imaging of the spine [6]. Spine X-rays are considered the gold standard [7]. Research has shown that a high percentage (21%) of undiagnosed VFs was identified in women in primary care using spinal radiographs [8]. Recently, another method of detecting VFs has been introduced: vertebral fracture assessment (VFA). This can be performed with the same device as Dual Energy X-ray Absorptiometry (DXA), and enables the combined assessment of bone mineral density (BMD) and VFs.

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Compared to spinal X-rays, the radiation dose is lower, leading to higher patient convenience and cost-effectiveness [9–11]. Comparable to the detection rate of VFs by spinal X-rays, VFA has proved to be a valid and patient-friendly technique for diagnosing VFs [10–12].

The identification of VFs is an important aspect of fracture prevention in primary care [8]. Therefore, the aim of this study is to investigate the prevalence of previously unknown VFs in women aged 50 years and older in Dutch primary care using VFA, and to discuss its impact on fracture risk management.

2. Methods

2.1. Subjects

Between September 2006 and June 2007, participants were recruited by means of advertisements in local newspapers and flyers left in Dutch general practices, which described a case-finding strategy according to the Dutch guidelines for osteoporosis, based on a list of CRFs for fractures with a risk-score per item (Table 1) [13]. Women aged 50 years and older with self-reported CRFs, who were not being treated for osteoporosis nor had suffered from a previously diagnosed VF, were invited for DXA and VFA assessment, which was covered by their health insurance. The invitation to participate was based on self-registration, regardless of risk score. However, only women with at least one CRF were eligible.

According to the Dutch guidelines from 2002, women with a *T*-score ≤ -2.5 SD and/or with one or more VFs were eligible for treatment [13]. A total of 629 women registered for participation. Two women were excluded due to being aged less than 50, 23 women failed to report at least one CRF for fractures, and ten women did not sign the informed consent. Furthermore, 28 women reported a history of VF. These women were excluded from the analysis for reasons of clarity. Therefore, analyses were carried out in 566 women (mean age, 69 years; SD = 8.4). The study was approved by the medical ethical committee of the Máxima Medical Centre Veldhoven, the Netherlands, and was carried out in accordance with the Declaration of Helsinki.

2.2. Measurements

During the appointment for BMD measurement and VFA, participants' clinical risk profiles were evaluated according to the Dutch guidelines for osteoporosis [13], including the following risk factors: long-term use of high doses glucocorticoids (>3 months > 7.5 mg prednisone equivalent/day), a previous history of fracture after age 50, age, a history of hip-fracture in a first-degree relative, low body weight (<60 kg), body mass index (BMI), and immobility (less than 15 min a day physical activity).

BMD and VFA were measured using a Hologic W DXA system. The DXA scans were obtained by one well-trained professional applying the standard procedures supplied by the manufacturer for scanning and analysis. Measurements made at the lumbar spine, total hip and left femoral neck were used for assessing BMD. In accordance with the World Health Organisation (WHO) classification [14], osteoporosis was defined as a *T*-score ≤ -2.5 SD, osteopenia as a *T*-score < -1.0 and > -2.5 SD, and normal BMD as a *T*-score ≥ -1.0 SD. Genant's semi-quantitative method was used to define VFs as mild (20–25% compression), moderate (25–40% compression), or severe (>40% compression) [15]. With radiography as gold standard, sensitivity and specificity of VFA, were reported to be 62.5–78.6 and 93.1 respectively, for the presence of one or more moderate or severe VFs [10]. Sensitivity increased with a higher prevalence of VFs [10]. Based on these findings, and the fact that moderate and severe VFs show the best predictive value for future fractures [10,16,17], we only considered moderate and severe VFs in this study. Mild vertebral compression was not considered a VF. Furthermore, a distinction was made in fracture site (thoracic spine or lumbar spine) and type of fracture (wedge, biconcave or crush).

Table 1
Dutch case-finding instrument for dual energy X-ray absorptiometry measurement: recommended if total risk score ≥4.

Risk factor	Score
Vertebral fracture	4
Long-term use of high-dose corticosteroids (>3 months; >7.5 mg/day)	4
Fracture after age of 50 years	4
Age >70 years	2
Age >60 years	1
Hip fracture in first-degree family member	1
Weight <60 kg	1
Immobility	1

2.3. Statistical analyses

Descriptive statistics were used to assess the rate of VFs, as was the consensus of fracture management based on DXA and VFA. Women with osteoporosis and those with ≥1 VFs were considered eligible for treatment. Chi-square, Student's *t*-tests and when appropriate with respect to skewed distribution of continuous data, Mann–Whitney *U* tests were used to assess statistical differences between women with and without VFs ($p < 0.05$). A multiple logistic regression analysis was performed to investigate the relevance of the number of CRFs present for unknown VFs, after controlling for age, BMI, the use of glucocorticoids, a history of previous fracture after age 50, hip fracture in a first-degree relative, and immobility. Statistical analyses were performed using the IBM Statistical Package for the Social Sciences (IBM SPSS Statistics) version 18.0.

3. Results

The characteristics of the population, including the results of DXA and VFA, are presented in Table 2. Of 7358 vertebrae, 267 (3.6%) were classified as unreadable, with 248 (93%) of the unreadable vertebrae located in T4–T6 and 19 (7%) from T7 to L4. Mild VFs were present in 44% of the patients without a moderate or severe VF, and in 64% of the patients who were classified as having a VF based on the presence of moderate or severe VFs. As for CRFs according to the Dutch guidelines: 54 women (10%) had used high doses of glucocorticoids for more than 3 months, 282 (50%) reported a history of fracture after age 50, 272 (48%) were aged >70 years, while a further 208 (37%) were aged 61–70 years. Hip fracture in a first degree relative was reported by 153 (27%) of the women and 119 (21%) weighed less than 60 kg. Furthermore, 100 (18%) women described their level of daily exercise as meeting the conditions for immobility. In total, 130 (23%) women met the criteria for one risk factor, 274 (48%) reported two risk factors, 141 (25%) fulfilled the criteria for three risk factors, 18 (3%) had four risk factors, and 3 (<1%) women fulfilled the criteria for five risk factors.

As presented in Table 2, 120 (21%) women, 44 with and 76 without VF, were diagnosed with osteoporosis based on the DXA measurement, and were thus eligible for treatment according to the Dutch guidelines. Based on VFA, 174 (31%) women had one (70%) or more (30%) moderate or severe VFs. Of these, 163 (94%) had a moderate fracture, while 11 (6%) had a severe fracture. One hundred and forty-one (81%) VFs were classified as wedge, 25 (14%) as biconcave, and eight (5%) as crush fractures. One hundred and thirty-five (78%) fractures were found in the thoracic spine and 39 (22%) in the lumbar spine. Considering fracture type, women with a wedge fracture were significantly younger compared to women

Table 2
Baseline characteristics, clinical risk factors and BMD in 174 women over 50 years with VF and 392 women without VF assessed by VFA.[a]

Characteristic	VF (n = 174) n (%)	No VF[b] (n = 392) n (%)	p	
			χ^2	Mann–Whitney U
Demographics				
Age	71.5 (52–91)	69.0 (50–89)		.002
BMI	27.1 (16.9–43.4)	26.0 (15.9–47.5)		.007
Fracture risk factors				
Use of glucocorticoids[c]	17 (10)	37 (9)	1.000	
Fracture after age 50	91 (52)	191 (49)	.488	
Age >70	96 (55)	176 (45)	.030	
Age 61–70	58 (33)	150 (38)	.304	
Hipfracture first-degree relative	39 (22)	114 (29)	.122	
Weight <60 kg	31 (18)	88 (22)	.256	
Immobility	23 (13)	77 (20)	.084	
Number of risk factors according to Dutch guidelines				
1	51 (29)	79 (20)	.023	
2	72 (41)	202 (52)	.032	
3	46 (26)	95 (24)	.650	
4	3 (2)	15 (4)	.291	
5	2 (1)	1 (<1)	.469	
Risk score	5.0 (1–12)	4.5 (1–11)		.549
BMD outcome				
Diagnosis[d]				
Normal BMD	55 (32)	149 (38)	.171	
Osteopenia	75 (43)	167 (43)	.985	
Osteoporosis	44 (25)	76 (18)	.141	
Lumbar spine				
BMD	0.91 (0.30–1.58)	0.92 (0.54–1.56)		.487
T-score	−1.2 (−4.5 to 4.9)	−1.1 (−4.7 to 4.6)		.715
Z-score	0.75 (−2.5 to 7.4)	0.80 (−2.8 to 6.9)		.933
Femoral neck				
BMD	0.66 (0.34–1.03)	0.69 (0.37–1.54)		.003
T-score	−1.7 (−4.6 to 1.4)	−1.5 (−4.3 to 6.2)		.002
Z-score	0.20 (−2.3 to 2.8)	0.20 (−2.3 to 8.5)		.078
Total hip				
BMD	0.82 (0.29 to 1.22)	0.85 (0.52–1.76)		.021
T-score	−1.00 (−5.3 to 1.6)	−0.80 (−3.5 to 6.7)		.016
Z-score	0.60 (−3.3 to 3.6)	0.60 (−2.3 to 7.5)		.179

BMI, body mass index; BMD, bone mineral density; VF, vertebral fracture(s); VFA, vertebral fracture assessment.
[a] Continuous data are presented as median (range).
[b] Including women with a mild fracture (in accordance with the semi-quantitative method of Genant).
[c] >3 months; >7.5 mg/day.
[d] Diagnosis based on BMD of the lumbar spine, femoral neck and total hip.

with a biconcave or crush fracture (Mann–Whitney U, p = .008). No significant differences were found in participant characteristics or CRFs with respect to fracture site (thoracic versus lumbar).

Of the 174 women with a VF, 44 (25%) were diagnosed with osteoporosis. Thus, using VFA, 130 women were eligible for treatment based on the presence of one or more VFs in addition to those identified by DXA measurement as having osteoporosis (Table 3). The total number of women eligible for treatment based on combined DXA (n = 120) and VFA (n = 130) was 250 (44%). Additional analyses showed that women with one or more VF were significantly older (Mann–Whitney U, p = .002), had a higher BMI (Mann–Whitney U, p = .007), showed lower BMD and T-scores of the femoral neck (Mann–Whitney U, p = .003 and Mann–Whitney U, p = .002 respectively), lower BMD and T-scores of the total hip (Mann–Whitney U, p = .021 and Mann–Whitney U, p = .016 respectively), and more often presented with one risk factor compared to the more common presence of two risk factors in women with no VFs (χ^2 = 6.4, df = 1, p = .011). Furthermore, with respect to the 130 women who were eligible for treatment by using VFA in addition to those identified by DXA measurement alone, the women with osteopenia had a significantly lower BMI (Mann–Whitney U, p = .009), and a lower BMD of the lumbar spine, the femoral neck and the total hip (Mann–Whitney U, p = <.001, Mann–Whitney U, p = <.001 and Mann–Whitney U, p = <.001 respectively) compared to the women with a normal BMD. According to the multiple logistic regression analysis, the number of CRFs did not significantly affect the risk of a VF, after controlling for age, BMI, the use of glucocorticoids, a history of previous fracture after age 50, hip fracture in a first-degree relative, and immobility (Table 4), However, BMI had a significant effect on the presence of a VF (OR = 1.23, 95% CI = 1.02–1.49).

4. Discussion

This study has shown a high percentage of previously unknown VFs (31%) in women aged 50 years and older (mean age, 69 years; SD = 8.4) with CRFs in primary care who volunteered for DXA and VFA after invitation. Of the women with a VF, 75% had no osteoporosis according to the WHO definition. Up until now, it was common practice, as advised in the 2002 Dutch guidelines, to evaluate the need for treatment for preventing fractures based on BMD outcome and in the presence of a VF, but there were no guidelines on how, when, and in whom to diagnose VFs [13]. Based on a T-score ≤ -2.5 SD of the femur or the lumbar spine, 21% of the women in our primary care study were eligible for treatment, while using VFA, 130 women were also identified, based on the presence of a VF. Thus, 250 compared to 120 women required treatment when VFA was added to the DXA, suggesting a more than two fold increase. This study emphasises the need for systematically performing VFA in women referred for DXA measurement in primary care patients.

Previous studies also reported a high prevalence of VFs (25–39%) in women aged over 50 years [6,18–20]. Jager et al. recently

Table 3
Baseline characteristics, clinical risk factors and BMD in 131 women over 50 years with VF assessed by VFA in addition to those identified by DXA measurement alone, with regard to normal bone mineral density and osteopenia.[a]

Characteristic	Normal BMD ($n = 55$) n (%)	Osteopenia ($n = 75$) n (%)	p	
			χ^2	Mann–Whitney U
Demographics				
Age	70 (52–91)	70 (54–90)		.294
BMI	29.0 (19.9–43.4)	27.2 (19.5–40.9)		.009
Fracture risk factors				
Use of glucocorticoids[b]	8 (15)	6 (8)	.366	
Fracture after age 50	26 (47)	42 (56)	.420	
Age >70	26 (47)	37 (49)	.956	
Age 61–70	21 (38)	29 (39)	1.000	
Hipfracture first-degree relative	13 (24)	19 (25)	.987	
Weight <60 kg	3 (5)	9 (12)	.333	
Immobility	8 (15)	13 (17)	.853	
Number of risk factors according to Dutch guidelines				
1	19 (35)	23 (31)	.781	
2	24 (44)	28 (37)	.587	
3	11 (20)	21 (28)	.401	
4	–	2 (3)	NA	
5	1 (2)	1 (1)	1.000	
Risk score	4 (1–10)	5 (1–12)		.458
BMD outcome				
Lumbar spine				
BMD	1.04 (0.30–1.58)	0.90 (0.78–1.26)		<.001
T-score	0.00 (−1.0 to 4.90)	−1.30 (−2.40 to 1.90		<.001
Z-score	2.00 (−0.60 to 7.40)	0.60 (−0.70 to 4.70)		<.001
Femoral neck				
BMD	0.75 (0.63–1.03)	0.65 (0.52–0.93)		<.001
T-score	−0.60 (−1.0 to 1.40)	−1.80 (−2.40 to 0.0)		<.001
Z-score	0.95 (−0.90 to 2.8)	0.20 (−1.60 to 1.90)		<.001
Total hip				
BMD	0.95 (0.82–1.22)	0.80 (0.65–1.13)		<.001
T-score	0.00 (−1.0 to 1.6)	−1.20 (−2.4 to 0.70)		<.001
Z-score	1.50 (−0.2 to 3.6)	0.55 (−1.0 to 1.9)		<.001

BMI, body mass index; BMD, bone mineral density; DXA, dual energy X-ray absorptiometry; NA, non applicable; VF, vertebral fracture(s); VFA, vertebral fracture assessment.
[a] Continuous data are presented as median (range).
[b] >3 months; >7.5 mg/day.

reported a prevalence of 20% VFs in Dutch women using VFA [12]. The higher percentage of VFs in our study could be explained by the fact that we only included women aged 50 years and older (mean age, 69 years; SD = 8.4), while Jager et al. included consecutive patients referred for BMD testing, and the 65% women in their study had a mean age of 54 years, range 18–94 years [12]. Our results suggest that the presence of VFs is not limited to women seeking care at secondary or tertiary institutions, but is also highly prevalent in primary care. This has also been reported by Netelenbos et al. who investigated the percentage of VFs in Dutch primary care women [8]. They included women aged over 60 years (mean age, 71 years) with no osteoporosis but with CRFs, and discovered VFs in 21% of the women. Compared to these results, we found a higher percentage of VFs in women with no osteoporosis (29%).

Table 4
Results of multiple logistic regression analysis in 566 women, dependent variable: vertebral fracture.

Variable	Odds ratio[†]
Age >70	1.41 (0.95–2.10)
BMI[a]	1.23 (1.02–1.49)
Use of glucocorticoids[b]	0.93 (0.45–1.93)
Fracture after age 50	0.97 (0.58–1.63)
Hipfracture first-degree relative	0.74 (0.41–1.32)
Immobility	0.56 (0.29–1.07)
Number of risk factors according to Dutch guidelines	1.07 (0.71–1.61)

[a] BMI was transformed into quartiles to compensate for skewness of the data: 15.93–23.53 ($n = 142$); 23.54–26.22 ($n = 142$); 26.23–29.54 ($n = 141$); 29.55–47.48 ($n = 141$).
[b] >3 months; >7.5 mg/day.
[†] Associations are presented as odds ratio (95% confidence interval).

This could be explained by the fact that Netelenbos et al. used a different set of CRFs to select the women for further examination [8]. Moreover, they used spinal radiographs to diagnose VFs. The rate of false positives could be higher in VFA compared to spinal radiographs, especially in the thoracic region, and therefore this could also in part be an explanation for the differences between the percentage of VFs in both Dutch populations [21]. However, a study to the accuracy of VFA in detecting moderate and severe VFs according to Genant's semi-quantitative method showed that the rate of false positives was low [10], which makes the difference in selection strategies a more likely explanation.

Furthermore, we found that women with VF had significantly lower *T*-scores at the total hip and the femoral neck of the hip than women without VF. However, no significant differences were found for the *T*-score of the lumbar spine. A possible explanation might be that a VF due to osteoporosis increases lumbar spine BMD and falsely suggests improved skeletal status [22].

Another notable finding is that, on average, women with VFs had a significantly higher BMI than women without VFs, while a reversed relationship has often been described [23]. However, Pirro et al. recently reported an increased risk of VFs in postmenopausal women with high BMI [24]. With respect to fracture type, women with a wedge fracture were younger compared to women with a biconcave or crush fracture. Our results are in line with the European Prospective Osteoporosis Study that reported an effect of age to increase incident fracture size. Furthermore subsequent fractures were reported to be significantly larger when the initial fracture was a biconcave or crush fracture [25].

Finally, the number of CRFs present did not affect the risk of VF in our research sample. According to tools such as the FRAX, which

have been designed to estimate fracture risk based on the presence of CRFs, fracture risk increases when more CRFs are identified. A possible explanation for our finding could be that the specific CRFs included in the Dutch case-finding method are not very sensitive for identifying subjects at high risk for fractures, since it has already been shown that this method is not very sensitive when selecting patients with osteoporosis [26]. However, the aim of this study was to asses the prevalence of unknown VFs in women aged 50 years and older in Primary care. The evaluation of the predictive value of case finding methods for identifying subjects with unknown VFs is beyond the scope of this paper.

This study has several limitations. Since the participants responded to advertising strategies and, according to the Dutch guidelines, only women with at least one CRF were included, a selection bias could have occurred. This could be reflected by the high number of corticosteroid users in the study population (10%), as well as the high number of patients with a history of fracture (50%). As a result, the prevalence of VFs in the current study may not be applicable to the general population. However, this was not the aim of the study. Despite this limitation, our results emphasise that previously unknown VFs are present in a substantial number of primary care women with CRFs, and that this finding is not limited to populations seeking care at secondary or tertiary institutions. A further limitation of this study is that the use of VFA is limited in the upper thoracic levels, due to overlying ribs and vascular structures. However, in this area, interpretation and image quality of radiographs are also diminished and the incidence of VF is less common [8]. Furthermore, we only investigated CRFs according to the Dutch guidelines. Several risk factors that are currently implemented in FRAX, a common used algorithm for fracture risk assessment, were therefore not included for fracture risk assessment in this study [27]. Age, long term use of high-dose corticosteroids, weight, a previous fracture and a hip fracture in a first-degree family member are incorporated in FRAX and the Dutch guidelines, but in different ways. FRAX uses age and weight as a continuous variable while the Dutch guidelines use a cut-off level (Table 1). Regarding corticosteroid use, FRAX implemented a smaller daily dose of corticosteroid use as CRF compared to the Dutch guidelines. Furthermore, the definition of a previous fracture and hip fracture in a first degree family member differ between both instruments. In addition to the Dutch guidelines, FRAX implemented CRFs such as current smoking, the presence of rheumatoid arthritis and secondary osteoporosis, three or more units of daily alcohol use and BMD. Considering the indications for VFA according to the International Society for Clinical Densitometry, historical height loss is another aspect which is lacking in the Dutch guideline [28].

From the present study, it can be concluded that the prevalence of previously unknown VFs diagnosed with VFA in women aged 50 years and older with CRFs in primary care, is unexpectedly high. When using BMD measurements only, only half the women eligible for treatment would actually receive this. We recommend performing VFA in all women aged 50 years and older who are referred for DXA based on Dutch case finding criteria.

Contributors

Martha van den Berg is the principle investigator and the main author of the manuscript. Victor Pop, Joop van den Bergh and Geraline Leusink are the supervisors of the principle investigator and responsible for the medical and scientific content of the manuscript. Noortje Verdijk, Piet Geussens and Esther Talboom-Kamp have contributed substantially to the intellectual content of the manuscript. All authors have read and approved the manuscript and agree with publication of their names.

Competing interests

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