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Prevalent vertebral fracture on bone density lateral spine (VFA) images in routine clinical practice predict incident fractures

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ABSTRACT

Purpose: The predictive validity of vertebral fracture assessment (VFA) on bone density lateral spine images to identify prevalent vertebral fractures in routine clinical practice has not been established. Our objective was to estimate the associations of prevalent vertebral fracture identified on VFA images in routine practice with incident hip, all non-vertebral, major osteoporotic, and clinical vertebral fractures, using the Manitoba Bone Density database.

Methods: From 2010 onward, 9972 men and women (mean age [SD] 76 [6.9] years) had VFA images obtained at the time of bone densitometry that were interpreted for vertebral fracture by the clinicians reading the bone density tests. Definite and possible prevalent vertebral fractures, respectively, were identified in 1575 (15.8%) and 293 (2.9%) using a modified Algorithm Based Qualitative method. We ascertained incident fractures using Manitoba provincial health databases over a mean 2.8 (SD 1.7) years and used Cox proportional hazards models to estimate the associations of prevalent vertebral fractures with incident fractures.

Results: Compared to no prevalent vertebral fracture, those with definite prevalent vertebral fracture had higher hazard ratios for incident hip (HR 1.95, 95% C.I. 1.45 to 2.62), non-vertebral (HR 1.99, 95% C.I. 1.68 to 2.35), and clinical vertebral fracture (HR 2.68, 95% C.I. 1.69 to 4.23) adjusted for age, bone mineral density, body mass index, prior fracture, parental hip fracture, glucocorticoid use, alcohol use, smoking, and rheumatoid arthritis. These associations did not vary by FRAX fracture risk estimates or bone mineral density category.

Conclusion: Prevalent vertebral fractures identified on densitometric VFA images in routine clinical practice are strongly associated with incident fractures, and this study is the first to show this using *any* lateral spine imaging modality outside of research settings. These findings are strong evidence supporting the targeted use of densitometric VFA imaging among post-menopausal women and older men referred for bone densitometry.

1. Introduction

Osteoporosis defined as a bone mineral density (BMD) T-score of −2.5 or lower is recognized as an important indicator of high risk for osteoporotic fracture and an indication for pharmacologic fracture prevention therapy [1–3]. However, less than half of osteoporotic fractures occur in those with BMD below this threshold [4,5]. Prior fragility fractures at the hip or spine also predict future fractures, and are indications for pharmacologic fracture prevention therapy regardless of BMD according to many clinical guidelines [1,3].

However, two-thirds to four-fifths of vertebral fractures are not recognized clinically at the time of their occurrence [6–8], and require lateral spine imaging for their identification. Prevalent vertebral fractures identified on lateral spine radiographs are an indicator of bone fragility and high risk of subsequent fractures [9–11]. While the US National Osteoporosis Foundation has a guideline for screening spine radiography to identify those with clinically unrecognized vertebral fractures [3], this has not been widely embraced because of expense and radiation exposure, and uncertainty regarding the impact this has on subsequent fracture outcomes in clinical practice.

Densitometric thoracolumbar lateral spine images intended for vertebral fracture assessment (VFA) can be obtained at the time of bone densitometry (DXA) at very low cost and much less radiation exposure compared to standard radiography, and moderate to severe vertebral

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fractures can be identified on these images with high accuracy compared to standard radiographs [12,13]. Among older women referred for DXA, VFA imaging may increase the proportion of those identified as candidates for pharmacologic fracture prevention therapy beyond the bone density T-score ≤ -2.5 criterion by as much as 30% [14,15]. However, only one prospective study has shown that vertebral fractures identified on VFA images predicts subsequent fractures [16]. Moreover, no study has shown how well prevalent vertebral fractures identified with *any* lateral spine imaging modality predict incident fractures in routine clinical practice, outside of the context of a research study.

Since 2010 in Manitoba (Canada) VFA images have been obtained in older men and women referred for DXA meeting criteria based on age, BMD, height loss, and corticosteroid use, and assessed for prevalent vertebral fracture by the clinicians reading the bone density tests. Our primary objective was to estimate the association of one or more prevalent vertebral fractures with incident hip, non-vertebral, major osteoporotic, and clinical vertebral fractures, adjusted for age, BMD, and other clinical risk factors. Our secondary objective was to test whether the associations of prevalent vertebral fracture with incident fractures varies by BMD level or 10-year fracture risk estimated by FRAX with BMD [17,18].

2. Materials and methods

In the Province of Manitoba, health services are provided to virtually all residents through a single public health care system, and DXA services have been managed as an integrated program [19]. The program maintains a database of all DXA results, with a completeness and accuracy in excess of 99%, that can be linked with other provincial population-based computerized health databases through an anonymous personal identifier [20]. The study was approved by the Health Research Ethics Board for the University of Manitoba.

2.1. Study population

From the DXA database we identified 47,944 women and men age 50 years and older who underwent bone densitometry of the hip and lumbar spine between February 24, 2010 and March 30, 2015. Among these, 10,053 (21%) had VFA imaging performed at the time of the DXA test (Fig. 1). Indications for VFA were a T-score of ≤ -1.5 (at the lumbar spine, total hip, or femoral neck) plus; a) age $\geq$ 70 years; b) age 50 to 69 years and historical height loss (recalled young adult height minus current height) $>$ 5 cm, or measured height loss $>$ 2.5 cm, or corticosteroid exposure of $\geq$7.5 mg prednisone daily for at least 3 months over the past year. As has been done in other studies and clinical practices [21], bone densitometry technologists evaluated whether or not the person undergoing DXA had an indication for VFA, and proceeded accordingly. After excluding 77 individuals with poor quality VFA images and 4 with a pathologic or major trauma fracture, 9972 (93% women) were included in the analytic cohort (Fig. 1).

2.2. BMD measurements

Proximal femur and lumbar spine DXA scans were performed and analyzed according to manufacturer recommendations (Lunar Prodigy or iDXA, GE Healthcare, Madison WI). All instruments were monitored by a medical physicist through a rigorous quality assurance program [19]. The instruments used exhibited stable long-term performance (coefficient of variation $<$ 0.5%) with no significant between-scanner differences detected. Femoral neck T-scores (number of standard deviations [SD] above or below young adult mean BMD) were calculated from National Health and Nutrition Examination Survey (NHANES) III white female reference values [22], consistent with the World Health Organization standard [23]. For other skeletal sites, sex-matched reference values were used (NHANES III for total hip and manufacturer-specific for lumbar spine) [3].

2.2.1. Vertebral fracture assessment

Vertebral fracture assessment was performed on dual energy VFA images by the same physician (certified by the International for Clinical Densitometry [ISCD]) who also read the accompanying DXA scan. Based upon ISCD principles and informal review of the vertebral fracture literature, the readers agreed to use the following standardized VFA reporting process which was systematically captured in the Manitoba Bone Density database. All vertebrae from T4 through L4 inclusive were first assessed as to whether the image quality was sufficient to allow vertebral fracture adjudication. If the reading physician judged most vertebrae to be uninterpretable, the image was deemed to be of poor quality and not considered. For the remaining images, interpretable vertebrae were judged to be fractured if they exhibited endplate depression or cortical discontinuity or buckling; these criteria have been codified by others as the modified Algorithm Based Qualitative method [24,25]. This method posits that in the sagittal projection all vertebral fractures exhibit broad depression of the superior and/or inferior endplates toward the center of the vertebral body, or more rarely, just cortical buckling or discontinuity [26]. Vertebrae were considered definitely fractured if mABQ criteria for fracture were met and non-fracture causes of vertebral deformity (such as degenerative remodelling, Scheuermann's disease, Schmorl's nodes) were not a credible explanation of the image findings. Vertebrae clearly without endplate depression or cortical discontinuity or buckling were judged to be without fracture, and those for which the reader was unsure if these findings were present were judged to be uncertain (Fig. 2). VFA findings at the individual level were recorded as: a) one or more prevalent vertebral fractures definitely present, b) definitely not present, or c) possible prevalent vertebral fracture (usually with a recommendation for additional imaging). Vertebral level, number, or severity of fractures were not recorded in the database.

2.3. Covariate measurement and fracture probability calculations

The Canadian FRAX tool was calibrated using nationwide hip fracture and mortality data [27]. The Manitoba BMD Registry was not used in the creation or calibration of the FRAX tool. Ten-year probability of a major osteoporotic fracture (MOF) and hip fracture with femoral neck BMD was calculated for each subject using the Canadian FRAX tool (FRAX® Desktop Multi-Patient Entry, version 3.7). Briefly, prior fracture and other conditions required for calculating fracture probability with FRAX were assessed through a combination of self-report, hospital discharge abstracts (diagnoses and procedures coded using ICD-10-CA) and physician billing claims (coded using ICD-9-CM) as previously described [28]. Smoking status and parental hip fracture was ascertained at the time of DXA for every individual [28]. Rheumatoid arthritis was identified from hospital (1 or more) or physician codes (2 or more) during the 3 years prior to DXA testing. A proxy was used for high alcohol intake (alcohol/substance abuse diagnosis) over the same time frame; this method has been shown to provide prevalence and risk estimates similar to population-based estimates [28–30]. Prolonged corticosteroid use (over 90 days dispensed in the year prior to DXA testing) was obtained from the provincial pharmacy system [31]. FRAX predictions with the Canadian FRAX tool have been shown to agree closely with observed fracture rates in our cohort and in the general Canadian population [28,30].

2.4. Fracture outcomes

Hospital discharge abstracts and physician billing claims were assessed from the date of DXA and VFA imaging (index date) to March 31, 2015 for the presence of non-traumatic hip, clinical vertebral, forearm, humerus, and other fracture diagnostic codes using validated algorithms [32]. Fractures not associated with trauma codes were assessed through a combination of hospital discharge abstracts (using ICD-9-CM prior to 2004 and ICD-10-CA thereafter) and physician billing claims

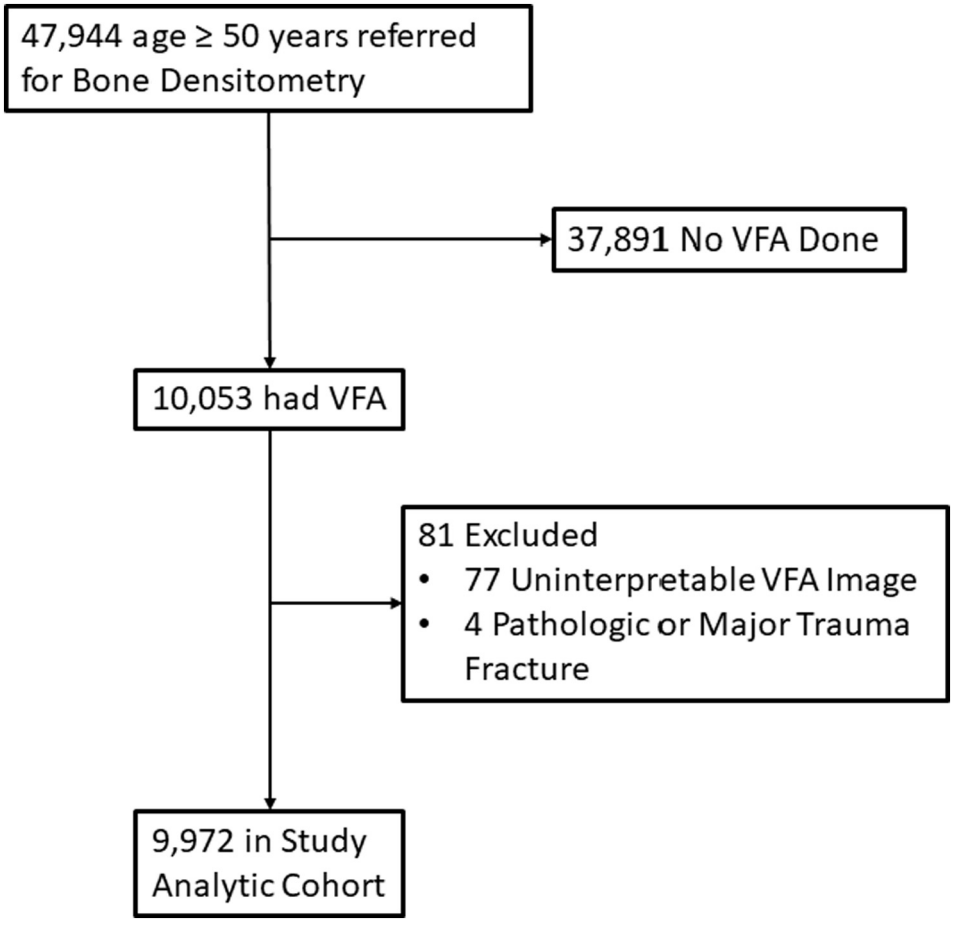

Fig. 1. Flow diagram for analytic cohort.

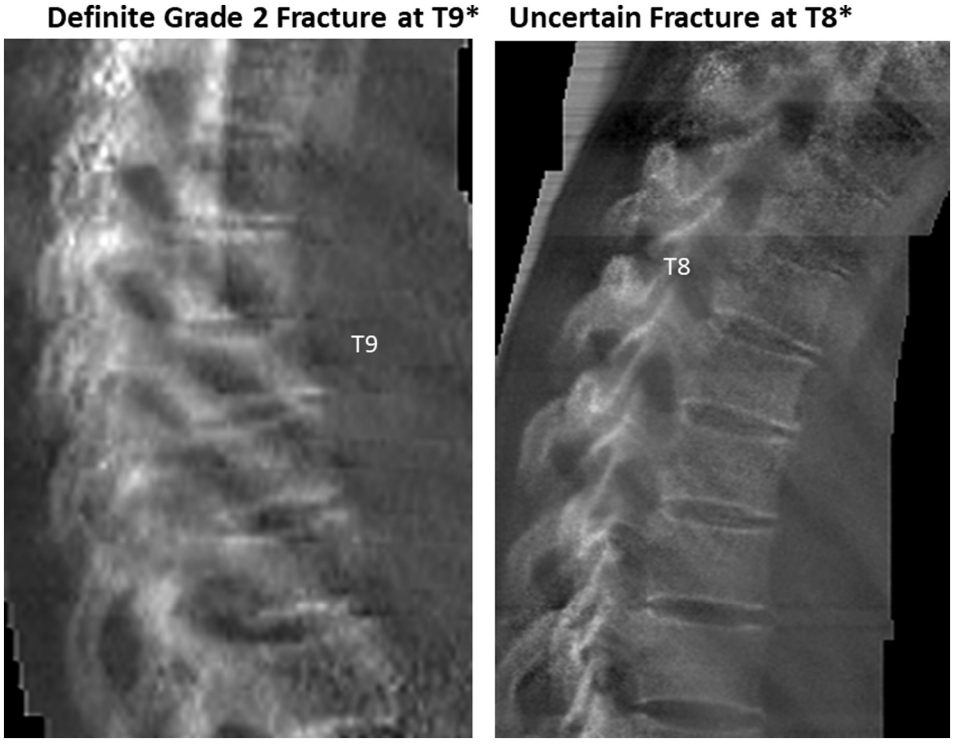

Fig. 2. Examples of definite and uncertain prevalent vertebral fractures.

Table 1
Baseline characteristics of analytic cohort (N = 9972) by prevalent vertebral fracture status on VFA images.

Characteristic	No prevalent vertebral fracture (N = 8104)	Definite prevalent vertebral fracture (N = 1575)	Uncertain prevalent vertebral fracture (N = 293)	p-Value[a]
Age, years (sd)	75.8 (6.7)	77.2 (7.9)	75.9 (7.7)	< 0.001
Sex female, n (%)	7660 (94.5)	1423 (90.3)	266 (90.8)	< 0.001
BMI, kg/m^2 (SD)	26 (4.9)	25.8 (4.5)	26 (4.6)	0.162
Prior fracture, n %	1633 (20.2)	584 (37.1)	83 (28.3)	< 0.001
Parental hip fracture, n (%)	1133 (14.0)	222 (14.1)	35 (11.9)	0.905
Current smoking, n (%)	610 (7.5)	147 (9.3)	24 (8.2)	0.015
Glucocorticoid use, n (%)	512 (6.3)	119 (7.6)	16 (5.5)	0.069
Rheumatoid arthritis, n (%)	272 (3.4)	69 (4.4)	7 (2.4)	0.044
High alcohol use, n (%)	13 (0.2)	5 (0.3)	S	0.186
Femoral neck T-score, (SD)	−2.0 (0.7)	−2.2 (0.8)	−2.1 (0.8)	< 0.001
Lumbar spine T-score, sd	−2.1 (1.1)	−2.5 (1.1)	−2.3 (1.2)	< 0.001
Total hip T-score, sd	−1.7 (0.8)	−2.1 (0.9)	−1.9 (0.9)	< 0.001
Minimum T-score ≤ −2.5, n (%)	3886 (48.0)	1035 (65.7)	152 (51.9)	< 0.001
MOF risk %[b] (sd)	16.3 (7.9)	19.9 (9.8)	17.5 (9.4)	< 0.001
Hip fracture risk %[b] (sd)	5.6 (5.8)	7.6 (7.3)	6.4 (7.6)	< 0.001
Osteoporosis treatment, n (%)	2831 (34.9)	800 (50.8)	123 (42.0)	< 0.001

S = suppressed due to small cell size.
[a] Definite vs no prevalent vertebral fracture.
[b] FRAX with BMD.

(using ICD-9-CM) [33]. Hip and forearm fractures were required to have a site-specific fracture reduction, fixation, or casting code to enhance specificity for an acute fracture event. To minimize potential misclassification of prior and incident fractures involving the same skeletal site, we required that there be no hospitalization or physician visit(s) with the same fracture type in the 12 months preceding an incident fracture diagnosis. There was no time restriction on prior and incident fractures involving different skeletal sites. Finally, since a vertebral fracture on VFA might be coded as a diagnosis attached to a subsequent clinical encounter, incident clinical vertebral fractures were considered only if the vertebral fracture code was associated with a clinical encounter (physician visit or hospitalization) that occurred 12 months or more after the VFA was performed. Non-vertebral fractures comprised all incident fractures that occurred at skeletal sites other than the spine, excluding those of the feet, hands, and face. Major osteoporotic fractures included hip, proximal, humerus, distal radius, and clinical vertebral fractures.

2.5. Statistical analysis

Baseline characteristics (ascertained at time of the DXA) of individuals with VFA positive for one or more vertebral fractures were compared to those with VFA negative for vertebral fractures using *t*-tests for normally distributed continuous variables, the Mann-U-Whitney test for continuous variables with non-normal distribution, and chi-square tests of independence for categorical variables. A Kaplan-Meier estimator was used to plot fracture-free survival as a function of follow-up time stratified by prevalent vertebral fracture status.

Cox proportional hazards models were used to estimate the association of one or more prevalent vertebral fractures vs no vertebral fractures with the following fracture outcomes; a) incident hip fracture; b) any incident non-vertebral fracture (excluding head/neck, hand/foot and ankle); c) incident major osteoporotic (incident hip, clinical vertebral, forearm, or humerus) fracture; and d) incident clinical vertebral fracture. Schoenfeld residuals were used to test that the proportional hazards assumption was not violated.

For each of these outcomes, we created four Cox models, adjusting for; a) age; b) FRAX with femoral neck BMD; c) individual risk factors as separate covariates (age, femoral neck BMD, prior fracture, parental history of hip fracture, smoking status, alcohol consumption, body mass index, corticosteroid use, rheumatoid arthritis); and d) aforementioned individual risk factors plus lumbar spine BMD and use of osteoporosis medications (bisphosphonates, calcitonin, systemic estrogen products, raloxifene, and teriparatide) for > 180 days in the year after DXA. FRAX scores were log transformed to account for a skewed distribution.

We also performed secondary analyses to test if the association of VFA-prevalent vertebral fracture with incident fractures varied by; a) BMD category (osteoporosis [T-score at a skeletal site ≤ −2.5], osteopenia [worst skeletal site T-score < −1.0 and > −2.5], or normal [all T-scores ≥ −1.0]); or b) FRAX with BMD 10-year fracture risk. Cox models were run including interaction terms of vertebral fracture status and FRAX with BMD major osteoporotic fracture risk score, and between vertebral fracture status and BMD category. Finally, since VFA images may have superior resolution when obtained on iDXA vs Prodigy Lunar densitometers, we also ran models including an interaction term of vertebral fracture status and densitometer type.

3. Results

3.1. Baseline characteristics

One or more definite prevalent vertebral fractures were identified in 1575 (15.8%), one or more uncertain fractures (without any definite vertebral fracture) in 293 (2.9%), and no vertebral fractures in 8104 (81.3%) individuals of the study analytic cohort. Those with a prevalent vertebral fracture were older, had lower BMD at all skeletal sites, had higher estimated 10-year risks of major osteoporotic and hip fractures by FRAX, were more likely to be male, more likely to have had a prior fracture, to be prior smokers, and to carry a diagnosis of rheumatoid arthritis (Table 1). Among 2562 with osteopenia (worst T-score < −1.0 and > −2.5) and intermediate 10-year risk (10 to 20%) of major osteoporotic fracture, 421 (16.4%) and 75 (2.9%) had, respectively, a definite or uncertain prevalent vertebral fracture. Over a mean follow-up period of 2.8 (SD 1.7) years, 226 (2.3%) had an incident hip fracture, 715 (7.2%) had an incident non-vertebral fracture, 552 (5.5%) had a major osteoporotic fracture, and 93 (0.9%) had an incident clinical vertebral fracture. Among those who ultimately did have an incident hip, non-vertebral, or major osteoporotic fracture, 32%, 29% and 28% respectively had a definite prevalent vertebral fracture on VFA at baseline.

3.2. Associations of prevalent vertebral fracture on VFA with incident fractures

Those with a definite prevalent vertebral fracture had moderate to

Table 2
Adjusted hazard ratios with 95% confidence intervals for incident fractures according to prevalent vertebral fracture status.

Outcome	Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]
Hip fracture				
VFA negative	Reference	Reference	Reference	Reference
VFA positive	2.47 (1.85, 3.28)	2.20 (1.65, 2.94)	1.95 (1.45, 2.62)	2.13 (1.51, 3.02)
VFA uncertain	1.54 (0.83, 2.84)	1.40 (0.76, 2.59)	1.32 (0.71, 2.44)	1.38 (0.67, 2.85)
Non-vertebral fracture				
VFA negative	Reference	Reference	Reference	Reference
VFA positive	2.33 (1.98, 2.75)	2.10 (1.77, 2.47)	1.99 (1.45, 2.21)	2.08 (1.71, 2.54)
VFA uncertain	1.37 (0.95, 1.90)	1.32 (0.92, 1.90)	1.27 (0.88, 1.83)	1.31 (0.86, 2.01)
Major osteoporotic fracture[e]				
VFA negative	Reference	Reference	Reference	Reference
VFA positive	2.28 (1.89, 2.76)	2.07 (1.71, 2.50)	1.95 (1.61, 2.37)	2.07 (1.65, 2.59)
VFA uncertain	1.52 (1.03, 2.25)	1.45 (0.98, 2.15)	1.41 (0.95, 2.10)	1.40 (0.89, 2.22)
Clinical vertebral fracture[e]				
VFA negative	Reference	Reference	Reference	Reference
VFA positive	3.00 (1.93, 4.68)	2.78 (1.77, 4.35)	2.68 (1.69, 4.23)	3.09 (1.85, 5.16)
VFA uncertain	1.98 (0.85, 4.61)	1.90 (0.81, 4.41)	1.93 (0.83, 4.51)	2.18 (0.85, 5.56)

[a] Adjusted for age.
[b] Adjusted for FRAX with BMD 10-year hip fracture risk (incident hip fracture) or FRAX with BMD 10-year Major Osteoporotic Fracture Risk (all other fracture outcomes).
[c] Adjusted for age, femoral neck BMD, prior fracture, parental history of hip fracture, smoking status, alcohol consumption, body mass index, corticosteroid use, and rheumatoid arthritis.
[d] Adjusted for Model 3 covariates plus lumbar spine BMD and current osteoporosis therapy.
[e] Excludes incident clinical vertebral fracture within the first year after baseline DXA plus VFA.

strong age-adjusted associations with incident hip (HR 2.47, 95% C.I. 1.85 to 3.28), non-vertebral (HR 2.33, 95% C.I. 1.98 to 2.75), major osteoporotic (HR 2.28, 95% C.I. 1.89 to 2.76), and clinical vertebral fractures (HR 3.00, 95% C.I. 1.93 to 4.68, Table 2). These associations were slightly attenuated after adjustment for FRAX with BMD or for clinical risk factors considered as separate covariates but remained moderately strong and highly significant. The associations were unaffected with additional adjustment for lumbar spine BMD and osteoporosis medication use, (Table 2).

Compared to individuals with no prevalent vertebral fracture, those with an uncertain prevalent vertebral fracture had modest but significant age-adjusted association with incident major osteoporotic fracture. The associations of uncertain prevalent vertebral fracture with all incident fracture outcomes were not significant after adjustment for FRAX with BMD 10-year fracture risks or additional clinical risk factors. Kaplan Meier plots showed fracture-free survival to be highest in those without prevalent vertebral fractures, intermediate for those with uncertain vertebral fracture status and lowest in those with a definite prevalent vertebral fracture for all incident fracture types (Fig. 3).

When interaction terms between prevalent vertebral fracture status and FRAX with BMD category entered into the models, there was no evidence that the association of prevalent vertebral fracture with incident fracture outcomes varied by FRAX with BMD risk score (p-values for interaction term 0.42, 0.25, 0.24, and 0.44, respectively, for incident hip, non-vertebral, major osteoporotic, and clinical vertebral fracture). Similarly, there was no evidence that the association of prevalent vertebral fracture with any fracture outcome varied by BMD category (interaction term p-values 0.84, 0.50, 0.59, and 1.00, respectively, for incident hip, non-vertebral, major osteoporotic, and clinical vertebral fracture). Finally, there was no evidence that the association of prevalent vertebral fracture differed according to DXA scanner generation (Prodigy vs iDXA, interaction term p-values 0.79, 0.30, 0.27, and 0.75, respectively, for incident hip, non-vertebral, major osteoporotic, and clinical vertebral fracture).

4. Discussion

Prevalent vertebral fractures are common among postmenopausal women and older men referred for DXA. Their presence on standard lateral spine radiographs in cohort studies are a marker of skeletal fragility and predict subsequent fractures. Vertebral fracture assessment can also be done with less expense, less radiation exposure, and greater convenience simultaneously with DXA [13,34–37]; these are all important features for a screening program for prevalent vertebral fractures to be feasible and cost-effective in the context of usual practice.

In this large cohort comprising all post-menopausal women and older men referred for DXA in the province of Manitoba, 21% had recognized indications for VFA lateral spine imaging, and a clinically meaningful proportion who had VFA imaging performed had one or more prevalent vertebral fractures, as has been noted in other studies [14,21]. Importantly, prevalent vertebral fracture identified on these lateral spine images were strongly associated with incident non-vertebral, hip, major osteoporotic, and clinical vertebral fractures, after adjustment for FRAX with BMD fracture risk, or for clinical risk factors considered as separate covariates. The strength of associations was similar to what has been demonstrated in cohort studies using standard lateral spine radiography in research settings to detect prevalent vertebral fractures [10,11,38–41], and the only study that has estimated the association of prevalent vertebral fracture detected with densitometric VFA with incident major osteoporotic fracture [16]. These associations were as strong in those with osteopenia or intermediate 10-year risk of fracture by FRAX (who are much less likely otherwise to be identified as candidates for fracture prevention therapy), as they were in those with osteoporosis by BMD criteria or high fracture risk by FRAX.

Ours is the first study to show that prevalent vertebral fractures, identified on *any* imaging modality in routine clinical practice outside of research settings, predicts subsequent fractures. This establishes the predictive validity of densitometric VFA imaging in clinical practice, and is strong evidence supporting its targeted use among post-menopausal women and men referred for bone densitometry. Importantly, while DXA tests are interpreted in many bone densitometry centers by non-radiologists, studies have shown that with modest training non-radiologists can interpret lateral spine radiographs and VFA images for vertebral fracture with a high level of accuracy compared to radiologists [42–44].

Two studies thus far have examined if VFA reports alter management of patients undergoing bone densitometry. Jager and colleagues reported that physicians, surveyed after receiving results of DXA test with VFA images, self-reported that identification of prevalent vertebral

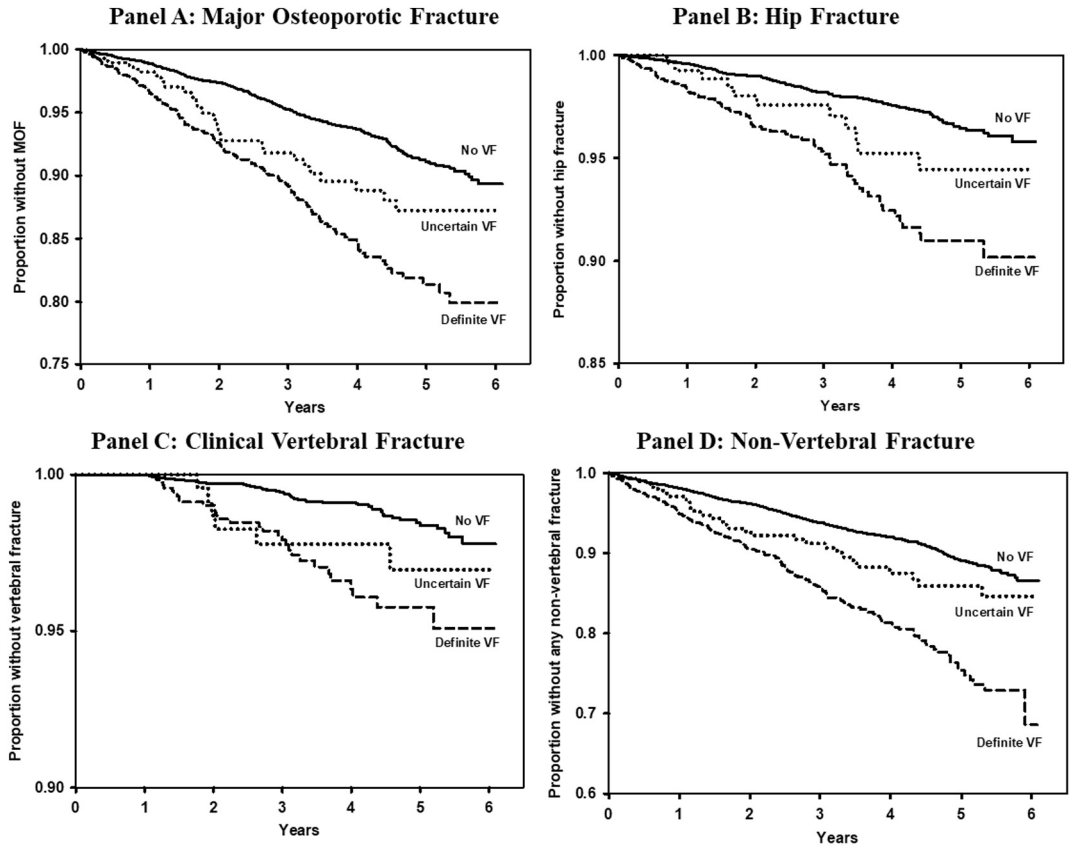

Fig. 3. Fracture-free survival for groups with definite prevalent vertebral fracture, uncertain prevalent vertebral fracture, and no prevalent vertebral fracture.

fractures influenced how they managed those patients 27% of the time [14]. Schousboe and colleagues noted that among patients with osteopenia (worst skeletal site T-score < -1.0 and > -2.5), those with one or more prevalent vertebral fracture on their VFA image had an odds ratio of 3.2 of being prescribed antiresorptive medication compared to those with a negative VFA after adjustment for age, sex, BMD, prior clinical fracture, and oral corticosteroid use [21]. Additional studies are needed as well regarding; a) the impact on *patient* fracture prevention behaviors including uptake of recommendations to commence and adherence to fracture prevention medication; and b) whether or not the use of VFA ultimately reduces incident fractures.

There are important strengths to our study. This is the largest longitudinal study to date of the association of prevalent vertebral fractures identified on any imaging modality with incident fractures in any setting (research or clinical practice) and is the sole study to date demonstrating the predictive validity of prevalent vertebral fracture on any imaging modality in clinical practice. The study population comprehensively captures post-menopausal women and men referred for bone densitometry in a substantial geographic region.

There are some limitations to our study as well. The VFA readers had no formal training in the mABQ method, their inter-rater reliability was not tested, and we did not have a standardized review process to ascertain the accuracy of the readings. However, any vertebral fracture ascertainment inaccuracy from this limitation would be expected to bias our results toward the null. It is possible that formal training in the mABQ method and central VFA reading review would yield more accurate ascertainment of prevalent vertebral fracture, and an even stronger association with incident fracture. Formal mABQ training is possible in clinical practice, but central reading review would be impractical.

We ascertained incident clinical fracture through administrative data, without confirmation with medical record or radiology report review. However, previous validation studies have shown that incident clinical fractures are ascertained with reasonable accuracy in the Manitoba Bone Density Registry [45,46]. Moreover, while there may be a low to modest level of misclassification of incident fracture status in our data, this would tend to bias our results toward the null. Hence, our results are robust to this limitation. The database only recorded whether or not one or more prevalent vertebral fractures were present, and did not capture the level, severity, and number of prevalent fractures. Hence we are unable to also confirm that the strength of association of prevalent vertebral fracture with incident fractures increases with the severity and number of prevalent vertebral fractures, as other have done [10,47]. The study population of Manitoba is largely Caucasian, and our results may not be generalizable to other ethnic groups or nationalities.

5. Conclusion

Vertebral fractures identified on bone density VFA images in clinical practice predict incident hip, non-vertebral, major osteoporotic, and clinical vertebral fractures. This study lends strong support to the incorporation of targeted VFA imaging at the time of bone densitometry to augment fracture risk assessment and identification of post-menopausal women and older men at high risk of fracture.

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Author roles

Study Design: JTS, WDL
Study Conduct: WDL
Data Analysis: WDL
Data Interpretation: JTS, LML, SNM, SD, MB, MA, WDL
Drafting Manuscript: JTS
Revising Manuscript Content: JTS, LML, SNM, SD, MB, MA, WDL
Approving Final Version of Manuscript: JTS, LML, SNM, SD, MB, MA, WDL

Conflicts of interest disclosure

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