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ORIGINAL ARTICLE

Associations between ultra-distal forearm bone mineral density and incident fracture in women

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Abstract

Summary Bone mineral density measured at the ultra-distal forearm site was associated with any fracture, as well as distal radius fracture in women from a longitudinal cohort study.

Purpose Femoral neck (BMD_{hip}) and lumbar spine (BMD_{spine}) bone mineral density (BMD) are routinely used to assess fracture risk. More data are needed to understand how ultra-distal forearm BMD ($BMD_{UDforearm}$) may assist fracture prediction.

Methods Using a Lunar DPX-L, Geelong Osteoporosis Study women ($n = 1026$), aged 40–90 years, had BMD measured. Incident low-trauma fractures were radiologically verified. Using Cox proportional hazard models, hazard ratios (HR) were calculated for $BMD_{UDforearm}$ as a continuous variable (expressed as a one-unit decrease in T-score) and a categorical variable (normal/osteopenia/osteoporosis). Areas under receiver operating characteristics (AUROC) curves were calculated. Analyses were conducted for any fracture and distal radius fractures.

Results During 14,270 person-years of follow-up, there were 318 fractures (85 distal radius). In adjusted models, continuous $BMD_{UDforearm}$ was associated with any (HR 1.26;95%CI 1.15–1.39) and distal radius fractures (HR 1.59;95%CI 1.38–1.83). AUROCs for continuous $BMD_{UDforearm}$, 33% forearm($BMD_{33\%forearm}$), BMD_{hip}, BMD_{spine}, and FRAX without BMD were similar for any fracture ($p > 0.05$). For distal radius fracture, the AUROC for $BMD_{UDforearm}$ was higher than other sites and FRAX ($p < 0.05$).

In adjusted models, those with osteoporosis had a higher likelihood of any fracture (HR 2.12; 95%CI 1.50–2.98). For distal radius fractures, both osteopenia and osteoporosis had a higher risk (HR 4.31; 95%CI 2.59–7.15 and 4.81; 95%CI 2.70–8.58). AUROCs for any fracture were similar for categorical BMD at all sites but lower for FRAX ($p < 0.05$). For distal radius fractures, the AUROC for $BMD_{UDforearm}$, was higher than other sites and FRAX ($p < 0.05$).

Conclusion Ultra-distal forearm BMD may aid risk assessments for any distal radius fractures.

Keywords Forearm fracture · Fractures · Ultra-distal forearm bone mineral density · Women

Introduction

Bone mineral density (BMD) measured using dual-energy X-ray absorptiometry (DXA) at the femoral neck (BMD_{hip}) and lumbar spine (BMD_{spine}) are routinely used for assessment of fracture risk [1]. Individuals are considered to be at high risk for fracture if they have osteoporosis at the hip or spine, which is defined as a BMD T-score > 2.5 standard deviations below the young adult mean [2]. Osteopenia, or moderate bone deficit, is defined as a BMD T-score of < -1.0 and ≥ -2.5. Although measurements of BMD_{hip} and BMD_{spine} are recommended for fracture risk assessments, these are sometimes not available. This can be due to multiple reasons, such as hip arthroplasty, positioning difficulties, soft tissue calcification, degenerative changes of

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the lumbar spine, osteoarthritis, prior fracture, and obesity [2, 3]. In these cases, it is recommended to measure the BMD at the 33% forearm site ($BMD_{33\%forearm}$) [3]. Ultra-distal forearm BMD ($BMD_{UDforearm}$), however, is not used, even if it is available. However, the ultra-distal forearm site contains a significant amount of trabecular bone (50–70%) and may be useful for fracture risk predictions.

Measuring $BMD_{UDforearm}$ is quick, with a lower radiation dose [4], but more data are needed to understand how it may assist fracture prediction. $BMD_{UDforearm}$ has been associated with BMD at the hip and spine [4, 5]. Additionally, individuals with distal radius fractures have been reported to have lower BMD at the hip and spine [6]. Most studies investigating associations between $BMD_{UDforearm}$ and fractures have been cross-sectional, often comparing fracture cases with a control group.

Therefore, the aim of this longitudinal study was to investigate if $BMD_{UDforearm}$ is associated with any incident fracture, or distal radius fractures and compare with $BMD_{33\%forearm}$, BMD_{hip}, BMD_{spine}, and FRAX 10-year probability risk estimates [7].

Methods

Participants

Participants were from the Geelong Osteoporosis Study [8], a longitudinal cohort study situated in south-eastern Australia. Data for this study were drawn from the baseline assessment for women (1993–1997). At baseline, 1494 women aged 20–94 years participated. There were 1053 women aged 40–90 years, and of these, 1026 had ultra-distal forearm BMD measured. The age range of 40–90 years was selected in this study because fractures are most common in this group and is the age range used by the FRAX algorithm for fracture risk prediction.

Measurements

BMD at the non-dominant ultra-distal forearm ($BMD_{UDforearm}$), 33% forearm ($BMD_{33\%forearm}$), femoral neck (BMD_{hip}), and lumbar spine (BMD_{spine}) were measured using a Lunar DPX-L (Lunar; Madison, WI, USA). T-scores were also calculated for each skeletal site using the young normal reference range developed by the Geelong Osteoporosis Study for use in an Australian setting [9, 10].

Weight and height were measured to the nearest 0.1 kg and 0.001 m, respectively. Body mass index (BMI) was calculated as weight(kg)/height(m)^2. Biochemical data for serum albumin, serum calcium, and vitamin D were also obtained by analysis of blood samples collected after an overnight fast.

The majority of other measures included in this study were selected as they are included in the FRAX algorithm [7] and are well-known risk factors for fracture. Prior fractures were self-reported and excluded those of the face, skull, digits, and those occurring from high trauma. Radiological reports were used to confirm fractures where possible. The remaining measures were self-reported. Participants reported whether their parents had previously sustained a hip fracture. Smoking status was classified as current or not. Alcohol consumption was documented by self-report. High alcohol consumption was categorised as ≥ 30 g of alcohol per day. Secondary osteoporosis included type 1 diabetes, osteogenesis imperfecta, hyperthyroidism, premature menopause (< 45 years), chronic malnutrition, malabsorption, and chronic liver disease. These were self-reported except for malnutrition, which was classified as BMI < 18.5 kg/m^2, following a previously published method [11]. Participants also reported if they had fallen during the past 12 months and which medications they used, including glucocorticoids, bisphosphonates, hormone therapy, and calcium or vitamin D supplements. FRAX 10-year probability risk estimates without BMD for major osteoporotic fracture ($FRAX_{MOF}$) and hip fracture ($FRAX_{hip}$) were also calculated for each participant using the Australian version of FRAX [7].

Mortality was identified by data linkage with the National Deaths Index.

Incident fractures

Incident fractures were verified by examination of radiological reports from imaging centres across the region. Fractures of the skull, face, and digits were excluded. Those occurring by high trauma, such as a motor vehicle accident, were also excluded. Participants who sustained a distal radius fracture were also identified.

Statistical analyses

Continuous variables were presented using means and standard deviations (SD) or medians with interquartile range (IQR) as appropriate. Categorical variables were presented as n (%). Differences for participants with and without incident fracture were identified using two-sample t tests or Mann–Whitney tests for continuous variables and chi-square tests for categorical variables.

Scatterplots were generated to visualise the relationship between age and $BMD_{UDforearm}$ T-scores. This was also performed for T-scores at the other skeletal sites ($BMD_{33\%forearm}$, BMD_{hip}, BMD_{spine}). Another set of scatterplots was also generated to examine the relationship between T-score for $BMD_{UDforearm}$ and T-scores at the other skeletal sites.

Participants were followed from baseline to the date of the first fracture, date of death, or the end of the study period

(31 December 2016), whichever occurred first. Cox proportional hazard models were used for multivariable (adjusted) survival analysis. The following variables were tested in the models and were retained if $p < 0.05$: age, weight, height, prior fracture, parental hip fracture, smoking, alcohol consumption, secondary osteoporosis, rheumatoid arthritis, falls, glucocorticoids, bisphosphonates, hormone replacement therapy, calcium supplements, vitamin D supplements, serum albumin, calcium, and vitamin D concentration. Models for $FRAX_{MOF}$ and $FRAX_{hip}$ were adjusted only for falls, bisphosphonates, hormone replacement therapy, calcium supplements, vitamin D supplements, serum albumin, calcium, and vitamin D concentration because the other variables are already accounted for in FRAX. The analyses were performed for $BMD_{UDforearm}$ as a continuous variable, and also as a categorical variable, employing osteopenia (T-score < -1.0 and ≥ -2.5) and osteoporosis cut points (T-score < -2.5). For continuous BMD, hazard ratios from the Cox proportional hazards modelling were calculated to show the increase in fracture risk with a one-unit decrease in BMD T-score.

Additionally, areas under receiver operating characteristics (AUROC) curves were calculated for $BMD_{UDforearm}$, $BMD_{33\%forearm}$, BMD_{hip}, BMD_{spine}, $FRAX_{MOF}$, and $FRAX_{hip}$. In categorical analyses, cutpoints of $\geq 20\%$ and $\geq 3\%$ were used for $FRAX_{MOF}$ and $FRAX_{hip}$, respectively, according to US National Osteoporosis Foundation guidelines [12].

All analyses were conducted with two different incident fracture outcomes: (1) any fracture and (2) distal radius fractures only.

Analyses were completed using Stata (Version 17. StataCorp. 2017. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC) and Minitab (Minitab, version 19, State College, PA, USA).

Results

Descriptive statistics

During 14,270 person-years of follow-up, there were 318 participants who sustained at least one fracture. These first fractures were at the following skeletal sites: 84 spine, 22 rib, 14 pelvis, 1 clavicle, 3 scapula, 20 humerus, 12 forearm, 50 wrist, 3 carpal, 4 metacarpal, 42 hip, 7 femur, 2 patella, 8 tibia/fibula, 26 tarsal, and 20 metatarsal. There were also 85 participants who sustained a distal radius fracture (this may not have been their first fracture) during the study period. The median follow-up time per participant was 15.3 (IQR 7.3–20.6) years.

For the ultra-distal forearm site, 55.3% of women had normal BMD, 27.4% had osteopenia and 17.4% had osteoporosis. These proportions were similar to the lumbar spine, where 52.4%, 32.2%, and 15.2% of women had normal BMD, osteopenia, and osteoporosis, respectively. There were more women with osteopenia at the femoral neck (42.8%) compared to the ultra-distal forearm site, with a lower proportion having normal BMD (40.8%). However, the proportion with osteoporosis was similar (15.4%). For the 33% forearm site, the proportions were different; approximately half had normal BMD (49.6%), fewer with osteopenia (19.9%), and a higher proportion with osteoporosis (30.1%).

Most women with osteoporosis at the ultra-distal forearm site also had osteoporosis at the 33% forearm (94.9%). For women with osteopenia at the ultra-distal forearm site, only 40.2% also had osteopenia at the 33% forearm, while 42.3% had osteoporosis. However, most women with normal BMD at the ultra-distal forearm site also had normal values at the 33% site (81.1%).

Figure 1a shows that T-scores for $BMD_{UDforearm}$ decreased with increasing age. This is similar to the relationships observed for the other skeletal sites (Fig. 1b–d). Figure 2 shows the relationships between T-scores for $BMD_{UDforearm}$ and T-scores at the other skeletal sites. The relationship was greatest between $BMD_{UDforearm}$ and $BMD_{33\%forearm}$ ($R^2 = 0.7305$); however, $BMD_{UDforearm}$ was also associated with BMD_{hip} and BMD_{spine} ($R^2 = 0.4707$ and $R^2 = 0.4581$, respectively).

Table 1 shows the descriptive characteristics of the participants, stratified by incident fracture status. Women who sustained a fracture over the follow-up were older, weighed less, were shorter, and were more likely to have sustained a prior fracture or used glucocorticoids. Those who sustained an incident fracture also had lower BMD at the ultra-distal forearm, 33% forearm, femoral neck, and lumbar spine, as well as higher values for $FRAX_{MOF}$ and $FRAX_{hip}$. Interestingly, the relative difference for bone mineral density ($BMD_{fracture}$ / $BMD_{nofracture}$) between women with and without fracture was similar between all skeletal sites: 0.89, 0.92, 0.91, and 0.91 for $BMD_{UDforearm}$, $BMD_{33\%forearm}$, BMD_{hip}, and BMD_{spine}, respectively.

Continuous variables (BMD or FRAX)

In adjusted models where BMD was expressed as a continuous variable, lower BMD at all sites was associated with an increased risk of any incident fracture as well as distal radius fracture (Table 2). Higher FRAX values were also associated with an increased risk of any and distal radius fracture.

The AUROC values for $BMD_{UDforearm}$, $BMD_{33\%forearm}$, BMD_{hip}, BMD_{spine}, $FRAX_{MOF}$, and $FRAX_{hip}$ considered continuous variables were similar for any incident fracture (Table 3, Supplementary Fig. 1). For distal radius fracture, the AUROC for $BMD_{UDforearm}$ was higher than all other BMD and FRAX measures (Table 3, Supplementary Fig. 2).

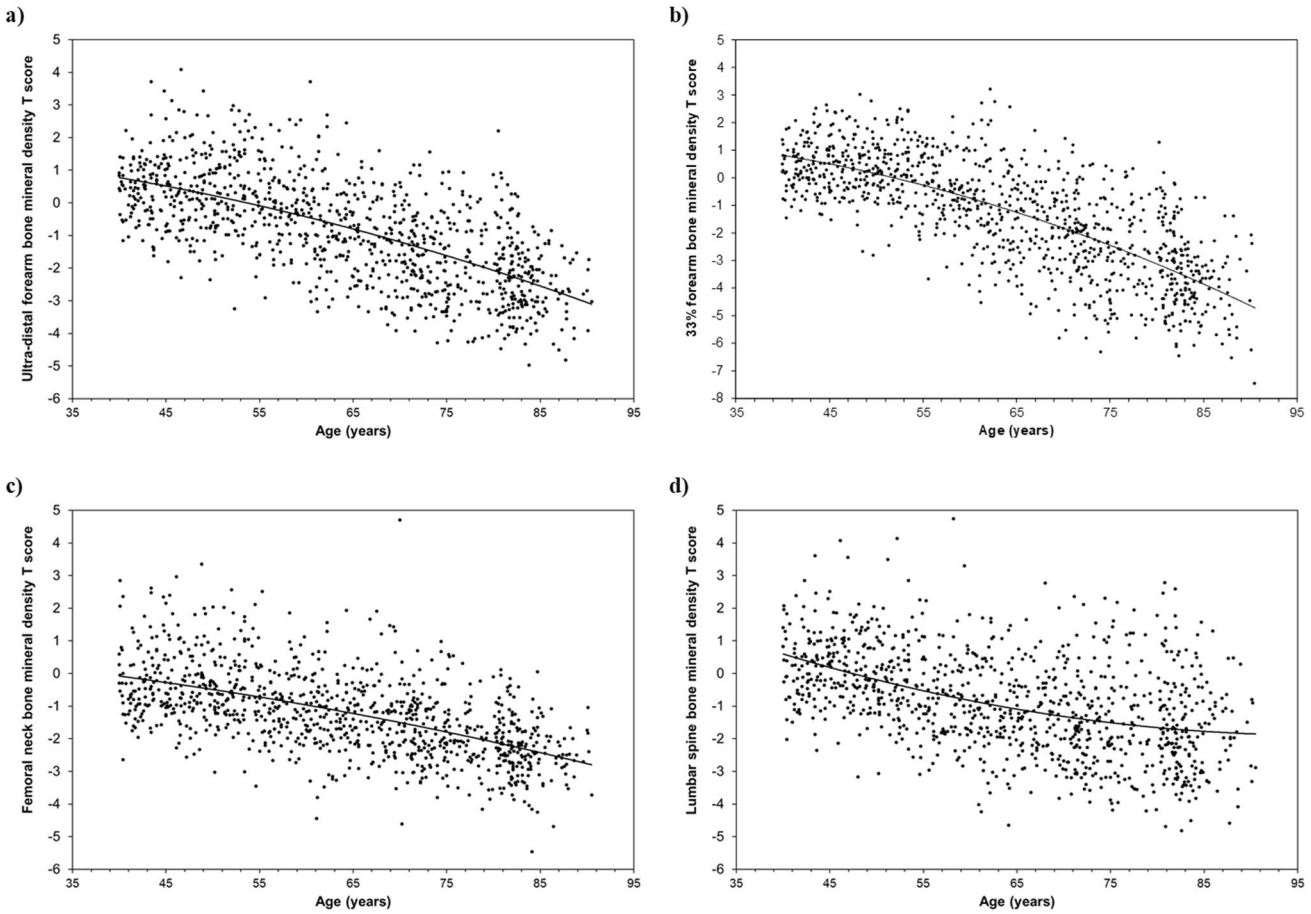

Fig. 1 Scatterplots showing age versus bone mineral density T-scores at the ultra-distal forearm (**a**), 33% forearm (**b**), femoral neck (**c**), and lumbar spine (**d**)

Categorical variables (BMD or FRAX)

In adjusted models where BMD was expressed as a categorical variable, women with osteoporosis at the ultra-distal forearm, femoral neck, or lumbar spine had a higher risk of any fracture (Table 2). Women with osteopenia at the femoral neck or lumbar spine also had a higher risk of any fracture. However, women with osteopenia at the ultra-distal radius site did not have an increased risk of any fracture. Osteopenia or osteoporosis at the 33% forearm site was not associated with any incident fracture. For FRAX scores, both $FRAX_{MOF} \geq 20\%$ and $FRAX_{hip} \geq 3\%$ were associated with a greater risk of any incident fracture.

Osteopenia or osteoporosis at all skeletal sites (except osteoporosis at the lumbar spine) as well as $FRAX_{hip}$ were associated with an increased risk of distal radius fractures (Table 2).

For any fracture, AUROC values were similar among the four BMD measures considered categorical variables (Table 3, Supplementary Fig. 3). However, AUROC values for $FRAX_{MOF}$ and $FRAX_{hip}$ were lower. For distal radius fractures, the AUROC value for $BMD_{UDforearm}$ was higher than all other BMD and FRAX measures (Table 3, Supplementary Fig. 4).

Discussion

In this study, $BMD_{UDforearm}$ was associated with any incident fracture, as well as with distal radius fractures. For any fracture, AUROCs for continuous $BMD_{UDforearm}$ were comparable with $BMD_{33\%forearm}$, BMD_{hip}, BMD_{spine}, $FRAX_{MOF}$, and $FRAX_{hip}$. When considered a categorical variable, AUROCs were similar for BMD at all skeletal sites, but AUROCs for $FRAX_{MOF}$ and $FRAX_{hip}$ were lower. For distal radius fractures, the AUROCs for both continuous and categorical $BMD_{UDforearm}$ were higher than for all other skeletal sites and FRAX. These results together suggest that $BMD_{UDforearm}$ could be useful in fracture risk assessment; $BMD_{UDforearm}$ performed similarly to the other skeletal sites for prediction of any incident fracture and was better for distal radius fractures.

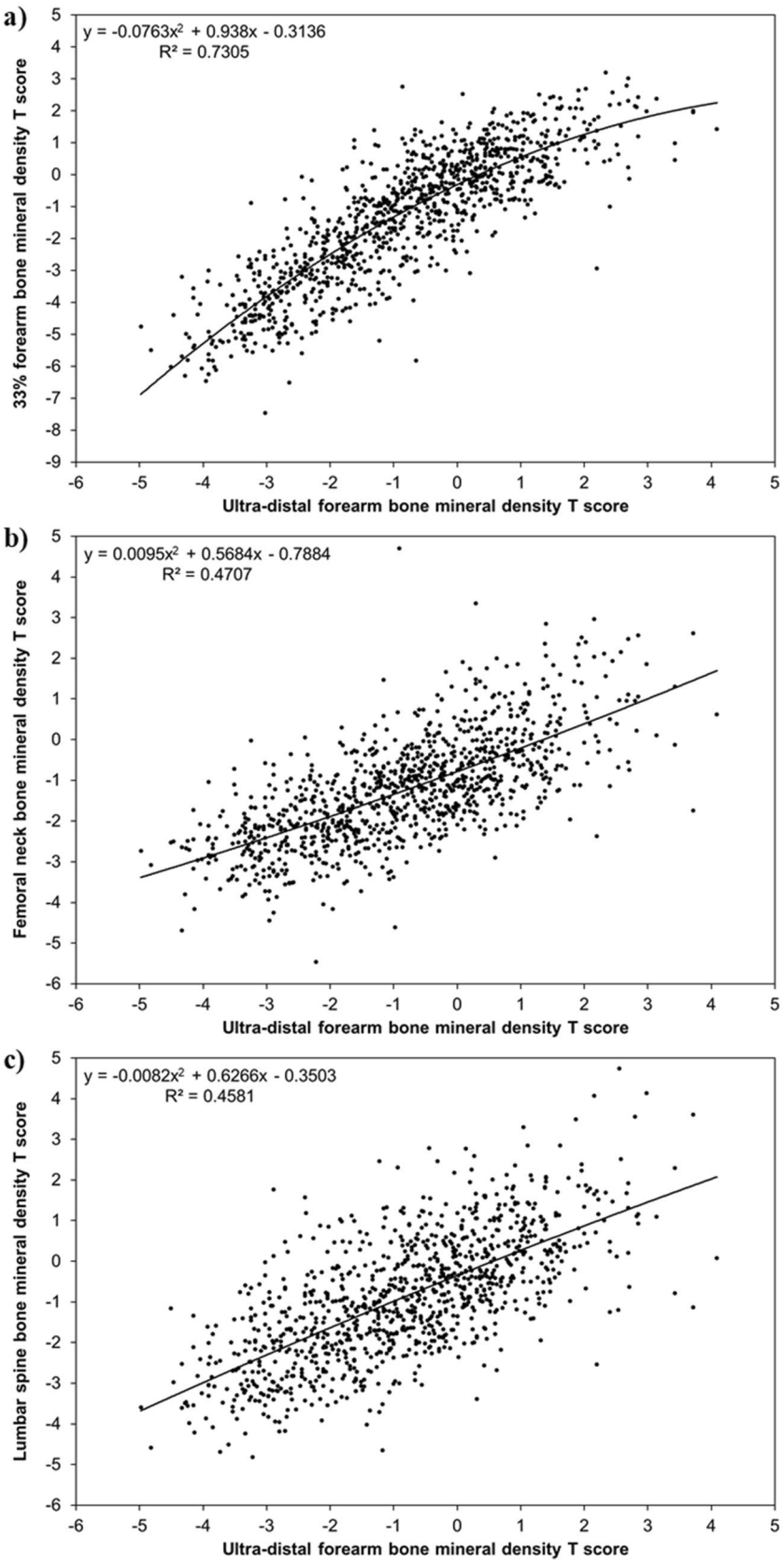

Fig. 2 Scatterplot showing the relationship between bone mineral density T-scores for ultra-distal forearm and 33% forearm (**a**), femoral neck (**b**), and lumbar spine (**c**)

Table 1 Participant characteristics. Data presented as mean ± SD or median(IQR), as appropriate

	No incident fracture ($n=708$)	Incident fracture ($n=318$)	p value
Age (years)	61.5 (50.2–74.6)	70.1 (56.7–78.8)	**< 0.001**
Weight (kg)	69.4 ± 14.5	66.8 ± 13.7	**0.006**
Height (cm)	159.5 ± 6.7	158.3 ± 6.3	**0.006**
Body mass index (kg/m^2)	27.3 ± 5.5	26.6 ± 5.0	0.062
Prior fracture	95 (13.4)	82 (25.8)	**< 0.001**
Parental hip fracture	39 (5.5)	23 (7.2)	0.398
Smoking	53 (7.5)	32 (10.1)	0.264
High alcohol consumption	4 (0.6)	3 (0.9)	0.547
Secondary osteoporosis	108 (15.3)	60 (18.9)	0.287
Fall in the past year	118 (16.7)	65 (20.4)	0.135
Medication use			
Glucocorticoid use	10 (1.4)	13 (4.1)	**0.012**
Bisphosphonate use	3 (0.4)	1 (0.3)	-
Hormone replacement therapy use	105 (14.8)	43 (13.5)	0.581
Calcium supplements	64 (9.0)	33 (10.4)	0.498
Vitamin D supplements	47 (6.6)	26 (8.2)	0.376
Biochemical data			
Serum albumin (g/L)	40.1 ± 3.3	39.8 ± 3.7	0.203
Serum calcium (mmol/L)	2.29 ± 0.114	2.29 ± 0.116	0.931
Vitamin D (nmol/L)	61 (44 − 83)	58 (40 − 80)	0.216
Bone mineral density (BMD)			
Ultra-distal forearm BMD (g/cm^2)	0.299 ± 0.070	0.265 ± 0.071	**< 0.001**
Ultra-distal forearm BMD T-score	− 0.593 ± 1.565	− 1.352 ± 1.577	**< 0.001**
33% forearm BMD (g/cm^2)	0.640 ± 0.107	0.590 ± 0.119	**< 0.001**
33% forearm BMD T-score	− 1.058 ± 1.904	− 1.950 ± 2.119	**< 0.001**
Femoral neck BMD (g/cm^2)	0.887 ± 0.165	0.807 ± 0.152	**< 0.001**
Femoral neck BMD T-score	− 1.031 ± 1.296	− 1.660 ± 1.201	**< 0.001**
Lumbar spine BMD (g/cm^2)	1.143 ± 0.203	1.042 ± 0.192	**< 0.001**
Lumbar spine BMD T-score	− 0.665 ± 1.506	− 1.414 ± 1.424	**< 0.001**
$FRAX_{MOF}$ without BMD	4.7 (1.6 − 9.7)	7.7 (2.8 − 16.0)	**< 0.001**
$FRAX_{hip}$ without BMD	1.3 (0.2–4.2)	3.0 (0.5–7.9)	**< 0.001**

Missing data: serum albumin $n=15$, serum calcium $n=16$, vitamin D $n=49$

$FRAX_{MOF}$: FRAX 10-year probability risk estimate for major osteoporotic fracture

$FRAX_{hip}$: FRAX 10-year probability risk estimate for hip fracture

Bold text indicates a significant difference between women who did and did not sustain a fracture over the follow-up period

This study also reported that the majority of women with either normal BMD or osteoporosis at the ultra-distal forearm site also had the same BMD category at the 33% forearm site. However, there were differences between the two sites for women with osteopenia at the ultra-distal radius site. Only ~ 40% of these women also had osteopenia at the 33% forearm site, and many had osteoporosis (~ 42%). Additionally, this study reported that categorical $BMD_{33\%forearm}$ (either osteopenia or osteoporosis) was not associated with any incident fracture, while women with osteoporosis at the ultra-distal forearm site did have an increased risk of fracture. These results suggest that $BMD_{UDforearm}$ may provide more useful information compared to $BMD_{33\%forearm}$. Further work is needed to replicate these findings in other studies.

In this study, FRAX scores for major osteoporotic fractures and hip fractures without BMD were included for comparison with $BMD_{UDforearm}$. In all analyses, any fracture or distal radius fracture, variables considered continuous or categorical, FRAX scores without BMD had lower AUROCs compared to BMD at the other skeletal sites, including $BMD_{UDforearm}$. We have previously reported that the Australian version of FRAX underestimates the risk of incident fractures in the Geelong Osteoporosis Study cohort [13]. Additionally, not all individuals can have FRAX scores

Table 2 Hazard ratios (95%CIs) for bone mineral density (BMD) at the ultra-distal forearm ($BMD_{UDforearm}$), 33% forearm ($BMD_{33\%forearm}$), femoral neck (BMD_{hip}) and lumbar spine (BMD_{spine}), as well as FRAX without BMD for major osteoporotic ($FRAX_{MOF}$) and hip ($FRAX_{hip}$) fracture; for any fracture ($n=318$) and distal radius fractures ($n=85$). Hazard ratios for continuous BMD show the increase in fracture risk with a 1 unit decrease in BMD T-score

	$BMD_{UDforearm}$	$BMD_{33\%forearm}$	BMD_{hip}	BMD_{spine}	$FRAX_{MOF}$	$FRAX_{hip}$
Continuous						
Any fracture	1.26 (1.15–1.39) $p<0.001$	1.21 (1.11–1.31) $p<0.001$	1.37 (1.21–1.54) $p<0.001$	1.23 (1.12–1.34) $p<0.001$	1.06 (1.05–1.07) $p<0.001$	1.06 (1.05–1.08) $p<0.001$
Distal radius fracture	1.59 (1.38–1.83) $p<0.001$	1.30 (1.17–1.45) $p<0.001$	1.50 (1.25–1.81) $p<0.001$	1.29 (1.09–1.52) $p=0.001$	1.04 (1.02–1.06) $p=0.001$	1.05 (1.02–1.08) $p=0.004$
Categorical						
Any fracture						
Osteopenia (or value ≥ 20% for FRAX)	1.30 (0.95–1.77) $p=0.102$	0.96 (0.67–1.36) $p=0.808$	1.59 (1.16–2.16) $p=0.004$	1.38 (1.05–1.82) $p=0.021$	*Value ≥ 20%*	*Value ≥ 3%*
Osteoporosis (or value ≥ 3% for FRAX)	2.12 (1.50–2.98) $p<0.001$	1.40 (0.98–2.00) $p=0.066$	3.04 (2.09–4.42) $p<0.001$	2.04 (1.48–2.82) $p<0.001$	3.35 (2.43–4.62) $p<0.001$	2.76 (2.18–3.51) $p<0.001$
Distal radius fracture						
Osteopenia (or value ≥ 20% for FRAX)	4.31 (2.59–7.15) $p<0.001$	2.34 (1.36–4.01) $p=0.002$	1.94 (1.17–3.22) $p=0.010$	1.85 (1.13–3.04) $p=0.015$	*Value ≥ 20%*	*Value ≥ 3%*
Osteoporosis (or value ≥ 3% for FRAX)	4.81 (2.70–8.58) $p<0.001$	2.77 (1.67–4.58) $p<0.001$	4.16 (2.28–7.59) $p<0.001$	1.48 (0.75–2.94) $p=0.261$	1.61 (0.77–3.37) $p=0.209$	2.50 (1.59–3.92) $p<0.001$

* Variables tested in the models: age, weight, height, prior fracture, parental hip fracture, smoking, alcohol consumption, secondary osteoporosis, rheumatoid arthritis, falls, glucocorticoids, bisphosphonates, hormone replacement therapy, calcium supplements, vitamin D supplements, serum albumin, calcium, and vitamin D concentration

Models for $FRAX_{MOF}$ and $FRAX_{hip}$ were adjusted only for falls, bisphosphonates, hormone replacement therapy, calcium supplements, vitamin D supplements, serum albumin, calcium, and vitamin D concentration because the other variables are already accounted for in FRAX

Table 3 Areas under receiver operating characteristics (AUROC) values (with 95%CI) for: bone mineral density (BMD) at the ultra-distal forearm ($BMD_{UDforearm}$), 33% forearm ($BMD_{33\%forearm}$), femoral neck (BMD_{hip}) and lumbar spine (BMD_{spine}), as well as FRAX without bone mineral density for major osteoporotic ($FRAX_{MOF}$) and hip ($FRAX_{hip}$) fracture; for any fracture ($n=318$) and distal radius fractures ($n=85$)

	$BMD_{UDforearm}$	$BMD_{33\%forearm}$	BMD_{hip}	BMD_{spine}	$FRAX_{MOF}$	$FRAX_{hip}$
Continuous						
Any fracture	0.630 (0.590–0.669)	0.623 (0.583–0.662)	0.641 (0.602–0.680)	0.630 (0.591–0.669)	0.615 (0.575–0.654)	0.615 (0.576–0.655)
Distal radius fracture	0.648 (0.590–0.705)	0.574 (0.511–0.637)*	0.583 (0.521–0.644)*	0.596 (0.538–0.655)*	0.552 (0.486–0.618)*	0.555 (0.491–0.620)*
Categorical						
Any fracture	0.619 (0.582–0.656)	0.597 (0.560–0.635)	0.629 (0.593–0.665)	0.612 (0.575–0.649)	0.546 (0.521–0.570)*	0.581 (0.546–0.615)*
Distal radius fracture	0.639 (0.582–0.696)	0.559 (0.498–0.621)*	0.581 (0.520–0.642)*	0.586 (0.525–0.647)*	0.507 (0.471–0.543)*	0.549 (0.491–0.607)*

* Asterisk indicates a significant difference ($p<0.05$) between $BMD_{UDforearm}$ and other BMD site/FRAX score

calculated, such as those outside the 40–90 year age range or the weight range of 25–125 kg. Thus, the inclusion of BMD in fracture risk prediction in an Australian setting can be useful, and $BMD_{UDforearm}$ may contribute to these assessments of risk.

The results of this longitudinal study are supported by data from other previous cross-sectional studies. One study reported that $BMD_{UDforearm}$ was better than BMD at the hip or spine or other clinical risk factors at discriminating between men (aged ≥ 50 years) with and without low trauma distal radius fractures [6]. This result is similar to our study in that $BMD_{UDforearm}$ had higher AUROC than BMD_{hip} and BMD_{spine} for predicting distal radius fractures.

In a retrospective case–control study including women aged ≥ 50 years, $BMD_{UDforearm}$ was better at discriminating those with distal radius fracture than BMD measured

at the hip or spine [5]. The authors did note, however, that T-scores for the ultra-distal radius site were lower than those at the hip or spine. If ultra-distal radius BMD was used on its own, this may result in a greater number of false positives for high fracture risk, and thus, the authors suggested that $BMD_{UDforearm}$ may be useful in combination with hip and spine BMD, not as an alternative.

In a case–control study that included Japanese postmenopausal women, BMD values at the ultra-distal forearm site were lower for those who had sustained a distal radius fracture; however, hip and spine BMD did not differ between the groups [14]. These results indicate that a reduction in BMD can occur at the forearm without a corresponding reduction at the hip or spine, and thus, measurement of $BMD_{UDforearm}$ could be useful for capturing individuals who may sustain a distal radius fracture, which consequently increases their risk for subsequent fracture.

Another cross-sectional study investigated correlations between $BMD_{UDforearm}$ with prior fracture, FRAX, and osteoporosis defined using hip and spine T-scores [15]. The study reported that $BMD_{UDforearm}$ was correlated with prior fractures, which remained statistically significant after adjustment for osteoporosis at the femoral neck, total hip or spine, and age. $BMD_{UDforearm}$ was also negatively associated with FRAX scores.

There is one longitudinal study that primarily aimed to investigate the ability of high-resolution peripheral quantitative computed tomography (HR-pQCT) to discriminate between postmenopausal women who had sustained a low trauma fracture over a follow-up of five years [16]. The study reported that trabecular and cortical volumetric BMD, as well as measures of bone microstructure, obtained at the forearm were able to predict incident fractures, independently of areal BMD at the femoral neck as well as FRAX. However, the authors also reported that including areal BMD at the ultra-distal radius site attenuated the associations, indicating that $BMD_{UDforearm}$ values captured some of the changes in trabecular and cortical volumetric BMD at this site. The authors suggested that since HR-pQCT is not widely available in clinical settings, $BMD_{UDforearm}$ may be a useful addition to fracture risk predictions.

This study has some strengths and limitations. One strength is that the study included women from a population-based study, and the participants were not selected on the basis of disease. There was also no loss to follow-up for the fracture outcome, as these data were obtained through examination of radiological reports across the study region. Data linkage with the National Deaths Index also provided objective mortality data for each participant. We also had additional variables such as weight, height, medication use, and falls that were included in the analyses. The follow-up time in this study was long – a median of 15.3 years. Some limitations of the study include a small number of distal radius fractures, which may have limited statistical power, particularly for women with osteopenia. It is also possible that some fractures were missed if they occurred outside the study region; however, these would be captured if a follow-up x-ray was conducted within the study region at a later date. Additionally, due to the small number of fractures, we were not able to investigate the performance of $BMD_{UDforearm}$ for predicting other major osteoporotic fractures such as those of the hip, spine, or proximal humerus. Some of the data were self-reported, but not the key variables within this study, specifically BMD, fractures, and mortality. Additionally, further studies are needed to determine if the same observations are also true for men.

Conclusion

Ultra-distal forearm BMD, considered as either continuous or categorical values, was associated with an incident fracture in women. For prediction of any incident fracture, AUROCs showed that $BMD_{UDforearm}$ performed similarly to all other skeletal sites, as well as FRAX without BMD. The AUROC values for the prediction of distal radius fractures were higher for ultra-distal forearm BMD than for all other skeletal sites and FRAX scores without BMD. This indicates that ultra-distal forearm BMD may have a role in fracture risk assessment, particularly for distal radius fractures or where it is not possible to obtain BMD measurements of the hip or spine. Additional studies are needed to confirm these results and to provide similar data for men.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00198-024-07041-4.

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Data availability Data are available upon reasonable request.

Declarations

Ethics approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Barwon Health Human Research Ethics Committee (project 92/01). Informed consent was obtained from all individual participants included in the study.

Conflicts of interest None.

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