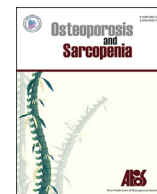




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Original article

Comparison of bone mineral density and vertebral fracture assessment in postmenopausal women with and without distal radius fractures



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ABSTRACT

Objectives: To compare bone mineral density (BMD) in Thai postmenopausal women with and without distal radius fracture, and to investigate the role of vertebral fracture assessment (VFA) in diagnosing osteoporosis after distal radius fracture.

Methods: A cross-sectional study was conducted in Thai postmenopausal women with and without distal radius fracture. BMDs of the femoral neck (FN), total hip (TH), lumbar spine (LS), and VFA were obtained within 2 weeks of injury. BMD were compared between groups. Participants were classified into osteoporosis, osteopenia or normal using BMD alone, and BMD plus VFA, where a mere presence of vertebral compression fracture indicated osteoporosis.

Results: Fifty postmenopausal women with distal radius fractures and 111 non-fracture postmenopausal women participated. The mean BMD was significantly lower at all sites in the fracture group (FN BMD 0.590 ± 0.075 vs 0.671 ± 0.090 , $p = 0.007$; TH BMD 0.742 ± 0.103 vs 0.828 ± 0.116 , $P = 0.009$; LS BMD 0.799 ± 0.107 vs 0.890 ± 0.111 , $P = 0.009$ in the fracture vs non-fracture group respectively). VFA increased the prevalence of osteoporosis from 16 (32%) to 23 (46%) in the fracture group, and 7 (6.31%) to 17 (16.22%) in the non-fracture group, with a number needed to treat 9.

Conclusions: Postmenopausal women with distal radius fractures had lower BMD. Incorporating VFA into diagnosis of osteoporosis increased the prevalence of osteoporosis in both fracture and non-fracture groups. Postmenopausal women aged 50 years or older with distal radius fracture are a good target for the investigation of osteoporosis.

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1. Introduction

Distal radius fractures are the most common upper extremity fractures that result from low-energy trauma. The incidence of distal radius fractures in each country varies with the population, race, culture, and economic status. A recent prospective study showed an incidence of 151 per 100,000 citizens in Taiwan, 76.9 per 100,000 in Japan, and 425 per 100,000 in Korea [1].

Osteoporosis is a disease of progressive bone loss and deterioration of bone microarchitecture with a resultant loss of bone

strength and increased risk of fracture [2]. In a large population-based cohort with 24 years of follow up, distal radius fracture was associated with an increased risk of spine and hip fractures [3,4]. Hence, distal radius fractures are commonly considered one of the osteoporotic fractures. Despite being common and associated with future fracture, physicians rarely investigate for osteoporosis in patients with distal radius fractures [5]. Furthermore, the Thai guideline for the management of osteoporosis does not include distal radius fractures as an indication to initiate anti-osteoporotic medication [6].

Nevertheless, the relationship between distal radius fracture and bone mineral density is still controversial, especially in the Asian population. While several studies from Western countries showed that the average bone mineral density (BMD) in postmenopausal women with wrist fracture were lower than those

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without fracture [6–10], such a difference was not replicated in other studies [11,12]. In a case-control study involving over 200 postmenopausal Asian women with distal radius fractures, the patients had lower hip BMD, while lumbar spine BMD and trabecular bone score (TBS), a parameter that possibly indicates bone microarchitecture, was found to be the same as age-matched controls [13]. Lee et al found lower hip BMD in Korean postmenopausal women aged 50–59 and 70–79, when compared to non-fractured women, while such a difference was not noted in women aged 60–69 [14]. The authors, therefore, concluded that the effect of BMD may be higher in patients in a certain age group, and recommended patients aged below 60 as a target for prevention of secondary osteoporosis.

To clarify the relationship between distal radius fracture and osteoporosis in the Thai population, we conducted a study to compare age- and site-related BMD in Thai postmenopausal women with and without distal radius fractures. We also investigated the role of additional vertebral fracture assessment (VFA) to increase yield to diagnose osteoporosis in postmenopausal women with wrist fractures. Finally, we explored the association between clinical risk factors and the presence of osteoporosis.

2. Methods

The study was approved by the Police General Hospital research committee (Ethical approval number Dh280642/61). Upon approval, a cross-sectional study was conducted in Police General Hospital from May 2018 to May 2020.

2.1. Recruitment of participants

In this cross-sectional study, we recruited postmenopausal women presenting at Police General Hospital emergency department or out-patient department with distal radius fractures from a low-energy trauma, which was defined as a simple fall from standing height or lower. Patients previously treated with anti-osteoporotic medication were excluded. We excluded women with diseases that contributed to secondary osteoporosis, including rheumatoid arthritis, hyperparathyroidism, hyperthyroidism, osteomalacia, surgical menopause before 45 years, chronic liver disease, malnutrition, hypogonadism, and malabsorption. Patients with skeletal malignancy, metabolic bone diseases, long-term use of oral steroids or other medical conditions that would affect bone quality were also excluded from the study. All fractured patients were enrolled in the Police General Hospital Fracture Liaison Service and received standard treatment.

The non-fracture group was randomly selected from postmenopausal women who visited the out-patient department during the same period for screening of osteoporosis with no history of fragility fracture. The same exclusion criteria also applied to the non-fracture group.

2.2. Biochemical investigation, dual energy X-ray absorptiometry, and vertebral fracture assessment

After informed consent was given, a venous blood specimen was obtained and sent for complete blood count (CBC), blood urea nitrogen (BUN), serum creatinine (Cr), calcium, phosphate, albumin, total alkaline phosphatase, 25-hydroxy vitamin D level, and intact parathyroid hormone level 2 weeks after the fracture occurred.

The BMD T-scores of the femoral neck (FN), total hip (TH) and lumbar spine (LS) were obtained from dual energy X-ray absorptiometry (DXA) scan performed within 2 weeks of fracture using a single DXA Hologic Horizon A (Marlborough, MA, United States) with reference values adapted for the Thai population. All

measurements were done in accordance with the recommendations from the International Society for Clinical Densitometry (ISCD) by a single certified densitometer technologist. The DXA was calibrated by the manufacturer and daily quality check was performed. The least significant change (LSC) of the DXA at our institution was 0.022 g/cm², 0.029 g/cm², and 0.027 g/cm² for the LS, FN, and TH BMD. The technologist regularly performed an in vivo precision assessment. VFA was also performed in the same session, using the same DXA model. A vertebral compression fracture (VCF) was defined as a collapse of more than 25% of vertebral body height [15]. When scoliosis was present, an X-ray of the spine was requested to detect VCF.

2.3. Sample size calculation

We calculated the sample size using a formula for testing 2 independent means. According to Lee OJ et al, the mean BMD \pm SD of Korean the female population 50 years of age or over was 0.753 \pm 0.11, while the mean BMD \pm SD of women with distal radius fracture was 0.662 \pm 0.08. The ratio between the fracture to the non-fracture group was 1:2 [14].

2.4. Statistical analysis

Demographic data were compared among groups using *t*-test for continuous variants and chi-square for dichotomous variants. Site-specific BMD were compared between the fracture and non-fracture groups using *t*-test. Subgroup analysis was also performed, dividing the participants into 3 age groups; 50–59, 60–69, and > 70 years of age.

Following the WHO criteria, the participants were classified as normal (BMD T-score \geq -1), osteopenia (BMD T-score between -1 and -2.5), or osteoporosis (BMD T-score \leq -2.5) using FN, TH, and LS BMD [2,16]. A presence of VCF marked the presence of osteoporosis regardless of BMD [6]. A number needed to treat (NNT) was calculated to demonstrate the benefit of VFA in the diagnosis of osteoporosis. Logistic regression analysis was performed to test the strength of association for clinical risk factors using osteoporosis as a dichotomous outcome. Multiple linear regression was performed to evaluate factors affecting site-related BMD. All statistical analysis was performed using STATA 16.1 (StataCorp LLC, College Station, TX, United States). A P-value of < 0.05 was considered statistically significant.

3. Results

Throughout the study, 50 postmenopausal women with distal radius fractures were recruited. The non-fracture group consisted of 111 postmenopausal women. The demographic characteristics of all 161 subjects are shown in Table 1. The fracture group was significantly older (66.14 \pm 8.27 vs 62.85 \pm 7.13, P = 0.006 respectively). The fracture group also had longer time since menopause (16.9 \pm 8.41 vs 13.94 \pm 8.29, P = 0.020 respectively). Participants with distal radius fractures also had higher serum intact parathyroid hormone level (74.53 \pm 4.48 pg/ml vs 60.02 \pm 3.37 pg/ml, P = 0.010). Weight, height, body mass index (BMI), the presence of hypertension, dyslipidemia, and type 2 diabetes mellitus were not significantly different. No participant reported smoking or alcohol consumption.

3.1. BMD

The mean FN, TH, and LS BMD of the participants, fracture group, and non-fracture group are shown in Table 2. The fracture group had a significantly lower BMD at all sites (FN BMD

Table 1
Baseline characteristics of the fracture group and the control group.

Characteristic	Fracture group (n = 50)	Control group (n = 111)	P-value
Age, yr	66.14 ± 8.27	62.85 ± 7.13	0.001*
Weight, kg	58.55 ± 1.31	58.03 ± 9.4	0.373
Height, cm	155.44 ± 5.38	155.7 ± 6.03	0.604
Body mass index, kg/m ²	24.23 ± 3.65	23.94 ± 3.66	0.319
Time from menopause, yr	16.9 ± 8.14	13.94 ± 8.29	0.020*
Serum 25-hydroxy vitamin D, ng/mL	24.6 ± 1.08	22.3 ± 1.05	0.930
Serum parathyroid hormone, pg/mL	74.53 ± 4.48	60.02 ± 3.37	0.010*
Hypertension	24 (48%)	37 (33.33%)	0.076
Dyslipidemia	14 (28%)	33 (29.73%)	0.823
Type 2 diabetes mellitus	6 (12%)	17 (15.32%)	0.578

*P < 0.05.

Table 2
Average site-specific BMD in cases and control groups.

Femoral neck			Total hip			Lumbar spine		
Fracture group (n = 50)	Non-fracture group (n = 111)	P-value	Fracture group (n = 50)	Non-fracture group (n = 111)	P-value	Fracture group (n = 50)	Non-fracture group (n = 111)	P-value
0.590 ± 0.075	0.671 ± 0.090	0.007*	0.742 ± 0.103	0.828 ± 0.116	0.009*	0.799 ± 0.107	0.890 ± 0.111	0.009*

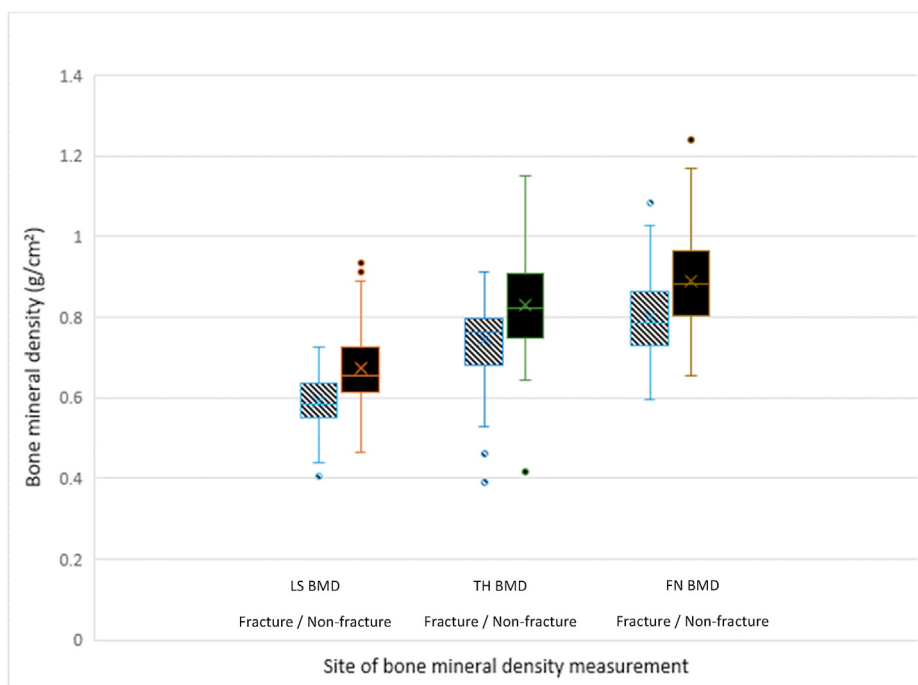
*P < 0.05.

0.590 ± 0.075 vs 0.671 ± 0.090, P = 0.0074; TH BMD 0.742 ± 0.103 vs 0.828 ± 0.116, P = 0.009; LS BMD 0.799 ± 0.107 vs 0.890 ± 0.111, P = 0.009 in the fracture vs non-fracture group, respectively). The distribution of site-related BMD in fracture and the non-fracture group is shown in Fig. 1. The participants were later stratified by age. The fracture group aged 50–59 years only had significantly lower FN BMD. The fractured patients aged 60–69 had lower BMD at all sites. FN and TH BMD in women 70 years of age or above were also found to be lower in the fracture group. While some remained statistically insignificant, the

fracture group had at least numerically lesser BMD in all sites measured in all age groups. The BMD of each age group are shown in Table 3.

3.2. Prevalence of osteoporosis diagnosed by BMD, and BMD with VFA

As demonstrated in Table 4, among 50 postmenopausal women in the fracture group, there were 16 (32%) osteoporosis, 32 (64%) osteopenia, and 2 (4%) normal patients. In the non-fracture group, 7



LS = lumbar spine, TH = total hip, FN = femoral neck, BMD = bone mineral density

Fig. 1. Distribution of site-related bone mineral density in fracture and non-fracture group, LS = lumbar spine, TH = total hip, FN = femoral neck, BMD = bone mineral density.

Table 3
Age-Stratified site-specific BMD in fracture and non-fracture groups.

Femoral neck			Total hip			Lumbar spine		
Fracture group	Non-fracture group	P-value	Fracture group	Non-fracture group	P-value	Fracture group	Non-fracture group	P-value
Age 50–59 years; fracture group n = 11, non-fracture group n = 36								
0.605 ± 0.055	0.690 ± 0.094	0.007*	0.780 ± 0.075	0.847 ± 0.117	0.083	0.858 ± 0.109	0.911 ± 0.125	0.207
Age 60–69 years; fracture group n = 24, non-fracture group n = 54								
0.588 ± 0.079	0.657 ± 0.088	0.002*	0.745 ± 0.099	0.813 ± 0.109	0.011*	0.766 ± 0.078	0.879 ± 0.093	< 0.001*
Age ≥ 70 years; fracture group n = 15, non-fracture group n = 21								
0.581 ± 0.083	0.676 ± 0.086	0.002*	0.718 ± 0.125	0.832 ± 0.132	0.015*	0.809 ± 0.131	0.880 ± 0.126	0.123

*P < 0.05.

Table 4
Percentage of patients classified as normal, osteopenia and osteoporosis based on bone mineral density, and bone mineral density plus vertebral fracture assessment.

Category	Classified by BMD		Classified by BMD plus VFA	
	Fracture group (n = 50)	Non-fracture group (n = 111)	Fracture group (n = 50)	Non-fracture group (n = 111)
Osteoporosis	16 (32%)	7 (6.31%)	23 (46%)	17 (15.32%)
Osteopenia	32 (64%)	69 (62.16%)	25 (50%)	60 (54.05%)
Normal	2 (4%)	35 (31.53%)	2 (4%)	34 (30.63%)

BMD = bone mineral density, VFA = vertebral fracture assessment.

(6.31%), 69 (62.16%), and 35 (31.53%) were classified as osteoporosis, osteopenia, and normal, respectively.

The additional interpretation of VFA in the categorization of patients increases the number of osteoporosis diagnosed in both groups. The fracture group contained 23 postmenopausal women with VCF. Seven (21.88%) formerly osteopenic patients were found to have a VCF. As a result, there were 23 (46%) osteoporosis, 25 (50%) osteopenia, and 2 (4%) normal in the fracture group. Among the non-fractured participants without osteoporosis, 10 (9.01%) showed VCF, turning 9 (13.04%) of the osteopenic group and 1 (2.86%) of normal postmenopausal women into osteoporotic patients, resulting in 17 (16.22%) osteoporosis, 60 (54.05%) osteopenia, and 34 (30.63%) normal BMD in the non-fracture group. Only 1 osteoporotic (1.00%) patient had VCF in the non-fracture group. An NNT of 9 was needed for VFA to increase the yield to diagnose osteoporosis. The re-categorization is also shown in Table 4.

We calculated the odds ratio for having distal radius fracture when VCF was present. The odds ratio was 3.354 (95% CI 1.190–9.382), P = 0.008. We also calculated the odds of being osteoporosis diagnosed by either low BMD or a presence of VCF. The odds ratio was 4.710 (95%CI 2.059–10.800), P < 0.001.

3.3. Association of clinical risk factors and osteoporosis

Using logistic regression analysis, we analyzed clinical risk factors that would influence BMD, which were distal radius fracture and several underlying diseases. As shown in Table 5, the distal radius fracture showed the highest strength of association with an odds ratio (95% CI) of 6.05 (2.38, 15.4). Other factors were found to be insignificant. Because chronic kidney disease (CKD) was only present in the non-fracture group, it was removed from the analysis.

Table 5
Association between clinical risk factors and osteoporosis.

Clinical risk factors	Odds ratio (95% CI)
Distal radius fracture	6.05 (2.38–15.4)
Hypertension	1.47 (0.61–3.53)
Type 2 Diabetes Mellitus	0.50 (0.10–2.29)
Coronary artery disease	2.4 (0.43–13.14)

3.4. Association of clinical risk factors and site-related BMD

We performed multivariable analysis adjusted by age to identify the factors that affected each site of BMD. The coefficient shows the change in absolute BMD value (g/cm²) when each variable was present with positive values contributing to higher BMD, while negative values contributing to lower BMD. For example, the coefficient of distal radius fracture toward LS BMD was 0.086, indicating that when distal radius fracture was present, the LS BMD decreased by 0.086 g/cm². Of all the factors, the presence of distal radius fracture, CKD, BMI and time since menopause affected LS BMD. The factors that affect FN BMD were distal radius fracture, age and BMI. For TH BMD, the factors affecting the BMD were the presence of distal radius fracture, age, BMI, and the presence of VCF in VFA. The aforementioned factors are demonstrated in Table 6.

4. Discussion

Osteoporosis, a disease of the bone characterized by loss of bone mass and degenerating bony microarchitecture, is commonly known to increase the risk of fractures [2,17]. The disease is asymptomatic and commonly detected when the patient finally suffers from fragility fractures. Common sites of fractures are the

Table 6
Multivariable analysis using multiple linear regression of statistically significant clinical factors and site-specific BMD, adjusted for age.

	Coefficient	Standard error	P-value
Lumbar spine bone mineral density			
Distal radius fracture	−0.086	0.019	< 0.001
Chronic kidney disease stage ≥ 3	0.087	0.008	0.015
Body mass index, g/cm ²	0.007	0.003	0.008
Time since menopause, yr	−0.002	0.001	0.037
Femoral neck bone mineral density			
Distal radius fracture	−0.081	0.016	< 0.001
Age, yr	−0.002	0.001	0.029
Body mass index, g/cm ²	0.009	0.002	< 0.001
Total hip bone mineral density			
Distal radius fracture	−0.067	0.019	0.001
Age, yr	−0.003	0.001	0.025
Body mass index, g/cm ²	0.016	0.002	< 0.001
Vertebral compression fracture	−0.052	0.023	0.027

hip, spine, proximal humerus, and distal radius. Certain factors increase the risk of osteoporosis, including early menopause (before 45 years of age or surgical menopause), low BMI, family history of fragility hip fracture, alcohol abuse, smoking, poor nutrition, lack of exercise, and poor mobility [17–19]. Certain medications such as thyroxine, anticonvulsants, and long-term corticosteroid use also contribute to skeletal fragilities.

A recent study in the northeastern part of Thailand found a prevalence of osteoporosis of up to 20% of 1935 postmenopausal women recruited [20]. The figure rose with age, making up about half of the population aged 70 years or older [21]. These surprisingly high numbers represents a remarkable disease burden in Thailand, and it is expected to upsurge as the population ages [20]. However, in this study, the prevalence of osteoporosis in the healthy non-fracture group was 6.31% when only BMD was considered. The apparent difference was possibly due to our exclusion criteria which excluded secondary osteoporosis, and healthy user selection bias as the non-fracture group also comprised healthy females who attended hospital for general check-up. Yet, to our knowledge, there has been no study about the relationship between postmenopausal osteoporosis and distal radius fractures in Thailand.

Until now, the well-studied relationship between BMD in Asian patients and distal radius fracture is limited to the Japanese and Korean female populations [14,22,23]. In this study, we assessed age- and site-related BMD and the prevalence of osteoporosis in Thai postmenopausal women with and without distal radius fractures.

The average age for distal radius fracture patients in our study was similar to previous studies. A large prospective study in Sweden found a mean age at fracture to be 65.4 ± 16.0 years [24]. Wrist fracture patients in another prospective cohort in Ireland had an average age of 67.8 years (range 60–86) [9]. The mean FN, TH, and LS BMD of the fractured participants were lower. When we stratified the subjects into 3 age groups, the fracture group had significantly lower age-, site-related BMD at most sites, except for TH and LS BMD in the 50–59 age group and only LS BMD in patients > 70 years which still showed a numerical reduction. Of note, FN BMD was lower in the fracture group in all age groups calculated, suggesting its usefulness in diagnosing osteoporosis in postmenopausal women with distal radius fractures.

Lill et al [10] performed a biomechanical test in 118 cadaveric forearms from elderly donors. The severity of distal radius fracture was found to increase with decreasing BMD. Stepwise regression analysis revealed that BMD, but not age, was significantly associated with ulnar variance and that ulnar variance was significantly associated with a radial inclination and dorsal angulation. Our study, however, included any pattern of distal end radius fractures from low energy trauma to avoid inter/intra-observer variation.

In our study, CKD stage ≥ 3 was identified in 8 participants, and was found to be related to higher LS BMD. The finding was inconsistent with general knowledge from many previous studies [25–27]. However, 7 out of 8 patients in our study had stage 3A to 3B CKD with a mean estimated glomerular filtration rate of $55.82 \text{ ml/min/1.73 m}^2$, while another participant was in stage 4. Surprisingly, the participants with CKD had a mean age of 61.38 years, which was younger than the mean age of our participants, and age is generally known to be an independent predictor of BMD [28]. These may explain the unusual association seen in our research.

Recently, new criteria for diagnosis of osteoporosis were suggested by the American Association of Clinical Endocrinologists (ACE) 2020 to include postmenopausal women with osteopenia

and a fragility fracture of the humerus, pelvis, and distal forearm [29]. This new update signifies the importance to evaluate and reduce future fracture risk in patients with fragility fractures, even when the BMD T-score is not in the osteoporotic range.

VFA increases the yield to diagnose osteoporosis by detecting silent vertebral fractures [30]. We used a standard cut point which is the vertebral wedge of at least 25% of the vertebral height. A patient with normal BMD would be classified as osteoporosis when a VCF was present. Of 50 wrist fracture patients undergoing VFA, nearly half had a silent VCF. As mentioned, adding VFA to DXA helped diagnose 18 more osteoporotic patients out of 161 and a number needed to treat (NNT) of 9 patients was calculated, indicating the usefulness of VFA in wrist fracture patients.

A study from the Canadian Radiologist Association showed that the vertebral fracture status was independent of bone density [31]. Instead, bone microarchitecture was an important parameter. Even in patients with normal bone density, a vertebral fracture was found in 18%. The author suggested BMD, together with VFA as a standard in osteoporosis testing with an NNT of 5. Many studies have shown good agreement between both methods, with very good sensitivities and specificities when using radiographs as a gold standard, especially for moderate and severe fractures [32–34]. Indeed, there is 1 report recommending the usage of VFA in postmenopausal women with osteopenia as a cost-effective method to identify patients to which treatment should be offered [35]. Therefore, although it is not formally proven, it would seem reasonable that the balance between costs and advantages is favorable.

To our knowledge, this is the first study in the Thai population comparing the BMD in patients with and without distal radius fracture which was commonly overlooked. Moreover, we highlight the importance of VFA and spinal assessment in the diagnosis of osteoporosis, so that clinicians in practice will request for BMD and also VFA in distal radius fracture patients. The Thai national guideline can be revised to include VFA in the investigation and treatment of osteoporosis. Furthermore, specific evidence in the Thai population is required by policymakers to change the Thai national policy and also reimbursement policy.

Our study had several limitations. First, the sample size was relatively small. However, the participation rates for both fracture and non-fracture groups were decent, allowing us to confirm and clarify the clinical data. Second, the fracture group was older than the non-fracture group, which may contribute to the lower BMD in the fracture group. However, after performing age-, and site-subgroup analysis, the difference in BMD remained significant. We also performed analysis of covariance to evaluate the effect of age on each site of BMD. Finally, the non-fracture group excluded secondary osteoporosis, and the non-fracture group also encompassed healthy females attending hospital for routine health check-up. These may contribute to a selection bias, explaining the relatively low prevalence rate of osteoporosis in our study, which may not represent postmenopausal women in the real-life setting. Therefore, future research in a community-dwelling population is required to further shed light on the topic.

5. Conclusions

Postmenopausal women with distal radius fragility fracture had lower hip and lumbar spine BMD than non-fracture women. Adding VFA into the diagnosis of osteoporosis increased the prevalence of osteoporosis in both fracture and non-fracture groups. We suggest that postmenopausal women aged more than 50 years with distal radius fragility fractures are a good target for the investigation and management of osteoporosis.

CRediT author statement

Tanawat Amphansap: Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Project administration. **Chayaphong Rattanaphonglekha:** Data collection, Investigation, Writing – original draft. **Jaruwat Vechasilp:** Conceptualization, Methodology, Validation, Visualization. **Nitirat Stitkitti:** Validation, Visualization. **Kamonchalat Apiromyanont:** Data collection and curation. **Atiporn Therdyothin:** Data curation, Writing – original draft, Writing – review & editing.

Conflicts of interest

The authors declare no competing interests.

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