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# Vitamin D Deficiency/Insufficiency Is Associated with Risk of Osteoporotic Thoracolumbar Junction Vertebral Fractures

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**Background:** The association between serum vitamin D level and vertebral fracture (Vfx) remains controversial. The purpose of this study was to determine whether serum 25-hydroxy vitamin D (25(OH)D) level is associated with osteoporotic thoracolumbar junction Vfx in elderly patients.





**Material/Methods:** From Jan 2013 to Dec 2017, this retrospective case-control study included 534 patients with primary osteoporotic thoracolumbar junction Vfx (T10–L2) and 569 elderly orthopedic patients with back pain (without osteoporotic Vfx) as controls. Serum 25(OH)D levels were measured and the association with osteoporotic Vfx was analyzed. Other clinical data, including BMI, comorbidities, and bone mineral density (BMD), were also collected and compared between these 2 groups.

**Results:** It was shown that 25(OH)D levels were significantly lower in patients with T10–L2 Vfx than in control patients. Among 534 Vfx patients, 417 (78.1%) patients showed grade 2–3 fracture. Serum 25(OH)D levels were significantly related to affected vertebral numbers and Vfx severities. The Vfx risk was 28% lower (OR=0.72, 95% CI 0.62–0.83) per increased SD in serum 25(OH)D. Compared with the 1<sup>st</sup> quartile (mean 25(OH)D: 29.67±6.18 nmol/L), the Vfx risk was significantly lower in the 3<sup>rd</sup> (mean 25(OH)D: 60.91±5.12nmol/L) and 4<sup>th</sup> quartiles (mean 25(OH)D: 103.3±44.21nmol/L), but not in the 2<sup>nd</sup> quartile (mean 25(OH)D: 45.40±3.95 nmol/L). In contrast, the Vfx risk was significantly increased in the 1<sup>st</sup> quartile (OR=1.87, 95% CI 1.42–2.45) compared with the 2<sup>nd</sup>–4<sup>th</sup> quartiles.

**Conclusions:** Vitamin D deficiency/insufficiency was associated with risk of osteoporotic thoracolumbar junction vertebral fractures in elderly patients.

**MeSH Keywords:** **Case-Control Studies • Osteoporosis • Spinal Fractures • Vitamin D Deficiency**

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 2630  6  2  38



## Background

Epidemiological studies have shown that vitamin D deficiency is a common nutritional disorder, especially in the elderly population [1]. Vitamin D plays an important role in increasing the intestinal absorption of calcium and phosphorus and thus helps to maintain a healthy musculoskeletal system [2]. Its deficiency can induce secondary hyperparathyroidism, leading to higher bone remodeling, increased osteoclastic activity, and consequently reduced bone strength [1–3].

Vitamin D insufficiency has been proven as a risk factor of hip fractures, while sufficient supplements of vitamin D plus calcium result in a reduction of hip fracture risk [4–7]. However, the association between serum vitamin D level and osteoporotic thoracolumbar vertebral fracture (VFX) remains controversial. Some studies reported there was no significant association between serum vitamin D level and osteoporotic thoracolumbar VFX [8–10]. Recently, 2 systematic reviews and meta-analysis based on randomized control trials also demonstrated that vitamin D supplementation alone or with calcium was not associated with reduced fracture incidence among community-dwelling adults [11,12]. In contrast, Maier et al. [13] reported that vitamin D insufficiency was a risk factor for fragile VFX, which was further supported by Zafeiris et al. [14], who found that hypovitaminosis D was a risk factor for VFX following kyphoplasty.

Osteoporotic thoracolumbar VFX, which frequently occurs at the thoracolumbar junction, are common diseases in elderly patients due to site-specific loading patterns [15]. However, few studies have focused on the relationship between serum vitamin D and osteoporotic VFX at the thoracolumbar junction region. The purpose of this study was to determine whether serum level of 25-hydroxy vitamin D (25(OH)D) is associated with primary osteoporotic thoracolumbar VFX (T10–L2 vertebrae) in elderly patients.

## Material and Methods

This was a retrospective, single-center, case-control study. The study protocol was reviewed and approved by the institutional review board and ethics committee of the Third Affiliated Hospital of Sun Yat-sen University, and informed consent were obtained from all included patients.

From Jan 2013 to Dec 2017, a consecutive series of patients admitted with osteoporotic vertebral fractures (VFX) were retrospectively assessed for eligibility. Enrolled VFX patients ( $\geq 50$  years old) were diagnosed as primary osteoporotic VFX at thoracolumbar junction (T10–L2) confirmed by subsequent X-ray images and BMD examination. Their serum 25(OH)D levels

were measured during hospitalization. In general, the mean age at natural menopause is approximately 49 years old for Chinese women [16,17]. Persons  $\geq 50$  years old with back pain were usually subjected to spine X-ray, BMD, and serum 25(OH)D test, and these patients without VFX were included as controls in this study.

Exclusion criteria were as follows: Patients with a high-energy traumatic VFX or a VFX beyond T10–L2 vertebrae; Patients with secondary osteoporosis or other diseases which could affect bone metabolism; Patients with a history of malignancy, severe hepatic diseases (serum alanine aminotransferase (ALT)  $> 3$  times upper limit) or renal diseases (serum creatinine (Cr)  $> 133$  mmol/L), gastrectomy or intestinal resection; and Patients who had regularly been receiving vitamin D, calcium, or corticosteroids treatment.

Clinical characteristics were collected by reviewing the electronic medical records or by telephone follow-up. These characteristics included sex, age, height, weight, body mass index (BMI), hospitalization date, and history of medication and comorbidities (e.g., hypertension, cardiovascular disease, pulmonary disease, liver disease, diabetes mellitus, rheumatoid disease) (Table 1).

The serum 25(OH)D was measured using ELISA method by IDS EIA kit (IDS, Boldon, UK), and serum calcium was examined by HITACHI 7060 Automatic Biochemical Analyzer (Hitachi, Japan). According to clinical guidelines of China [18], the UK [19], and Australia [20], we defined serum vitamin D status as follows: deficiency ( $< 30$  nmol/L), insufficiency (30–49.9 nmol/L), and sufficiency ( $\geq 50$  nmol/L).

BMD was examined at lumbar spine (L1–L4 vertebrae) and hip (femoral neck and total hip) using the Hologic Discovery dual energy X-ray absorptiometry system (Hologic, Bedford, MA). According to the World Health Organization (WHO) classification system, we defined osteoporosis as T-score  $\leq -2.5$ , osteopenia as  $-2.5 < \text{T-score} < -1$ , and normal as T-score  $\geq -1$ .

All the thoracolumbar spine X-ray films in posterior-anterior and lateral views were collected. These images were assessed for VFX and related spinal deformities (scoliosis and kyphosis). The severity of VFX was defined using Genant's semiquantitative method [21] as follows: 1) each image was assessed by 1 experienced spine surgeon (LM Zhang with  $> 10$  years of experience) and 1 experienced skeletal radiologist (YQ Zhu with  $> 10$  years of experience) to detect VFX in thoracolumbar junction (T10–L2); 2) According to Genant's scale, VFX severities were graded as following: a) Grade 1 (mild), a reduction in vertebral height of 20–25%; b) Grade 2 (moderate), a reduction of 26–40%; c) Grade 3 (severe), a reduction of over 40% (Figure 1). Thoracolumbar deformities were measured using

**Table 1.** Baseline characteristics of the included patients (n=1103).

Variables	VFx	Control	P-value	P-adjusted*
Number of patients n (%)	534 (48.4)	569 (51.6)	–	–
Female n (%)	426 (79.8)	434 (76.3)	0.168	–
Age (years)	68.05±9.72	66.84±9.99	0.120	–
Height (cm)	155.64±8.29	158.10±7.36	<0.001	–
Weight (kg)	54.27±10.35	57.09±10.38	<0.001	–
BMI (kg/m <sup>2</sup> )	20.81±3.55	22.58±3.66	<0.001	–
Hypertension n (%)	230 (43.1)	198 (34.8)	0.018	–
Cardiovascular disease n (%)	75 (14.0)	74 (13.0)	0.546	–
Pulmonary disease n (%)	69 (12.9)	84 (14.8)	0.409	–
Hepatic disease n (%)	53 (10.9)	106 (18.6)	<0.001	–
Diabetes mellitus n (%)	92 (17.2)	94 (16.5)	0.577	–
Rheumatoid disease n (%)	65 (12.2)	260 (18.7)	<0.001	–
25(OH)D (nmol/L)	54.53±28.11	64.56±40.90	<0.001	0.001
Season				
Summer n (%)	138 (25.8)	127 (22.3)		
Winter n (%)	117 (21.9)	125 (22.0)	0.386	0.089
Serum calcium (mmol/L)	2.41±2.71	2.30±0.14	0.343	0.728
Lumbar spine (M±SD)				
BMD (g/cm <sup>2</sup> )	0.65±0.14	0.79±0.17	<0.001	<0.001
T-score	–3.67±1.09	–2.38±1.48	<0.001	<0.001
Osteoporosis n(%)	463 (86.7)	292 (51.3)	<0.001	<0.001
Total hip (M±SD)				
BMD (g/cm <sup>2</sup> )	0.66±0.19	0.79±0.15	<0.001	<0.001
T-score	–2.28±1.12	–1.35±1.16	<0.001	<0.001
Osteoporosis n (%)	226 (42.3)	95 (16.7)	<0.001	0.041

VFx – vertebral fracture. Season, determined by the date of vitamin D examination: Summer, June–August; winter, December–January.

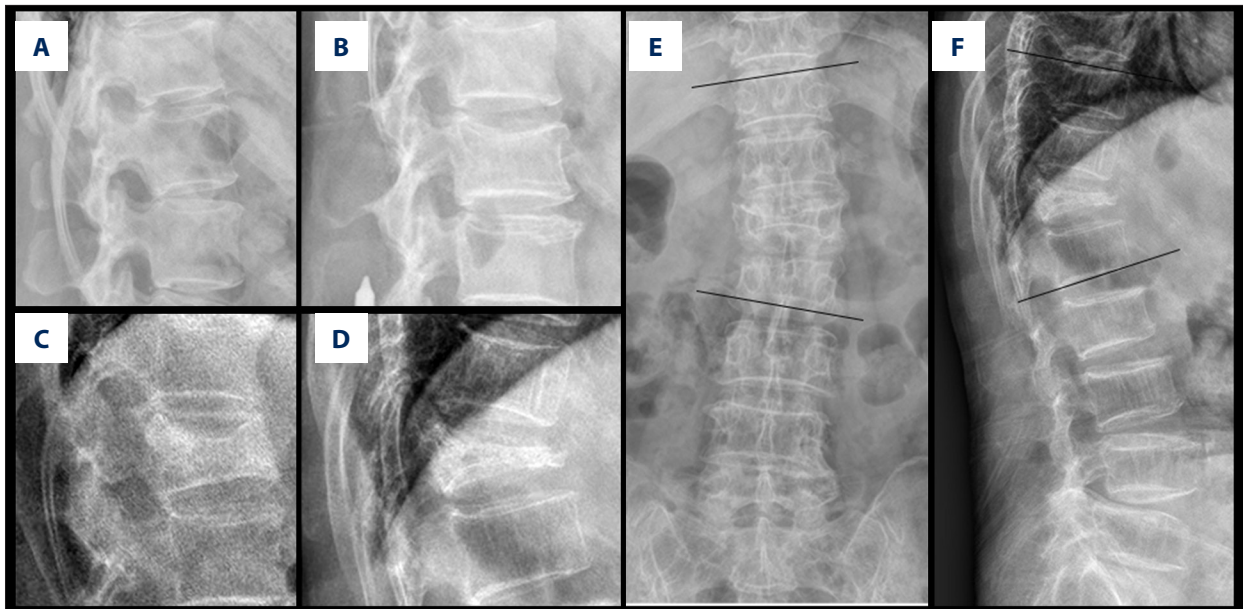
\* Adjusted by sex, age and BMI.

Cobb method and defined as follows: scoliosis – Cobb angle measurement greater than 10 degrees on coronal plane [22]; kyphosis – Cobb angle measurement greater than 15 degrees on sagittal plane [23] (Figure 1).

### Statistical analysis

Statistical analysis was performed using the SPSS software package version 19.0 (SPSS, Chicago, IL), and the results are presented as mean ±SD (for continuous variables) or frequencies (for categorical variables). The baseline differences between males and females were compared using the  $\chi^2$  test or *t* test, and were further adjusted for potential confounding factors

using an analysis of covariance (ANCOVA) or logistic regression analysis method. The association of vitamin D status with thoracolumbar VFx in females and males, fracture numbers, fracture grades, fracture locations, and spinal deformities were analyzed by using logistic regression analysis method, and they were also further adjusted for potential confounding factors. Each vitamin D measure was standardized, and the association of quartiles of serum vitamin D with VFx was analyzed by binary logistic regression analysis in different models. Finally, a receiver operating characteristic (ROC) curve was generated and the Youden index (Sensitivity+Specificity–1) was calculated for a range of cut-off scores. The cut-off value that corresponded to the highest Youden index was the optimal cut-off



**Figure 1.** Diagnosis of osteoporotic vertebral fractures and spinal deformities in thoracolumbar junction region. (A) Grade 0, normal vertebral shape; (B) Grade 1 (mild), a reduction in vertebral height of 20–25%; (C) Grade 2 (moderate), a reduction of 26–40%; (D) Grade 3 (severe), a reduction of over 40%. (E F) Thoracolumbar scoliosis (>10°) and kyphosis (>15°) measured at T10–L2 region on coronal and sagittal plane using the Cobb method.

**Table 2.** Prevalence of vitamin D deficiency/insufficiency in female and male patients.

	Female				Male				
	VFx (n, %)	Control (n, %)	P-value	P-adjusted*	VFx (n, %)	Control (n, %)	P-value	P-adjusted*	
25(OH)D (nmol/L)	<30	61 (14.3)	40 (9.2)	0.004	0.029	17 (15.7)	8 (5.9)	0.019	0.055
	30–49.9	162 (38.0)	142 (32.7)			38 (35.2)	42 (31.1)		
	≥50	203 (47.7)	252 (58.1)			53 (49.1)	85 (63.0)		

VFx – vertebral fracture. P-adjusted – adjusted by age and BMI.

value for serum vitamin D that was related with VFx.  $P < 0.05$  was considered statistically significant.

## Results

After assessment of osteoporotic VFx in thoracolumbar junction (T10–L2), 534 consecutive patients with primary osteoporotic VFx (Mean age  $68.05 \pm 9.72$ , 79.8% females) and 569 consecutive elderly orthopedic patients with back pain (mean age  $66.84 \pm 9.99$ , 76.3% females) were included in this study. The enrolled patients' demographics are shown in Table 1. The mean serum levels of 25(OH)D were significantly lower in patients with VFx than in control patients, which was  $54.53 \pm 28.11$  and  $64.56 \pm 40.90$  nmol/L, respectively (Table 1).

According to clinical guidelines [18–20], the enrolled patients were stratified into 3 groups: deficiency (<30 nmol/L), insufficiency (30–49.9 nmol/L), and sufficiency ( $\geq 50$  nmol/L). There was a significant difference in vitamin D deficiency/insufficiency between 2 groups, 278 (52.1%, VFx) vs. 232 (40.8%, Control), respectively. Low vitamin D status was significantly correlated with thoracolumbar junction VFx in both females and males, but it was not significant in male patients after age and BMI adjustment (Table 2).

Among 534 patients with thoracolumbar junction VFx, most of them (344, 64.4%) only had 1 affected vertebra, but 417 (78.1%) patients showed grade 2–3 fracture (Table 3). These VFx were mostly located at T12 (35.6%) and L1 (33.7%) vertebrae. There was a significant association between serum vitamin D levels and VFx numbers or severities, even after adjustment by sex, age, and BMI (Table 3). However, when the included

**Table 3.** Association of thoracolumbar junction vertebral fracture (VFX) or spinal deformities with serum vitamin D status.

Variables	25(OH)D level (nmol/L)			P-value	P-adjusted <sup>a</sup>
	<30	30–49.9	≥50		
Grade of VFX (n, %) <sup>b</sup>					
Normal	48 (8.4)	184 (32.3)	337 (59.3)		
Grade 1	17 (14.5)	45 (38.5)	55 (47.0)		
Grade 2	23 (15.1)	67 (44.1)	62 (40.8)		
Grade 3	38 (14.3)	88 (33.2)	139 (52.5)	0.001	0.024
Number of VFX (n, %)					
0	48 (8.4)	184 (32.3)	337 (59.2)		
1	52 (15.1)	133 (38.7)	159 (46.2)		
≥2	26 (13.7)	67 (35.3)	97 (51.1)	0.001	0.038
Location of VFX					
T10	9	12	19		
T11	4	21	29		
T12	23	71	96		
L1	31	72	77		
L2	11	24	35	0.394	0.403
Scoliosis of thoracolumbar spine (n) <sup>c</sup>					
–	108	337	525		
+	18	47	68	0.680	0.986
Kyphosis of thoracolumbar spine (n) <sup>d</sup>					
–	75	224	364		
+	51	160	229	0.630	0.636

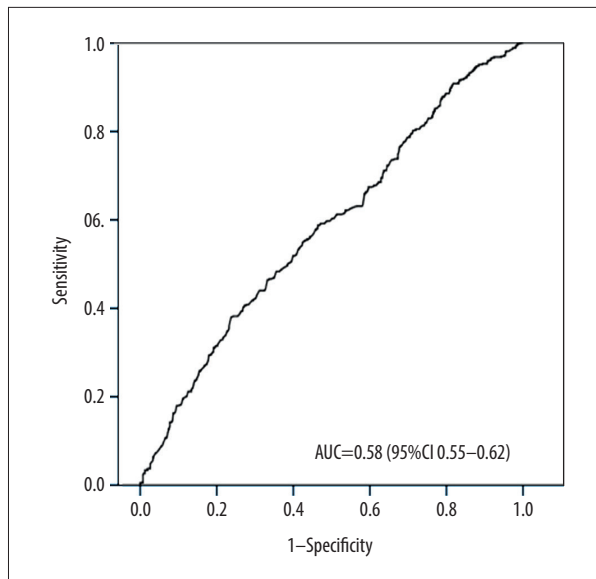
<sup>a</sup> Adjusted by sex, age and BMI; <sup>b</sup> grade of VFXs clarified as: Normal, absence of VFXs; Grade 1–3, reduction of vertebral height of 25%, 25–40%, over 40%, respectively. <sup>c</sup> ‘–’ – absence of scoliosis; ‘+’ – thoracolumbar Cobb angle more than 10 degree in the coronal plane. <sup>d</sup> ‘–’ – absence of kyphosis; ‘+’ – thoracolumbar Cobb angle more than 15 degree in the sagittal plane.

patients were divided into age groups per decade, the serum vitamin D levels were found to be associated with VFX only in the 60- to 80-year-old age group (Supplementary Table 1). When morphological features were assessed, serum vitamin D level was not related to fracture locations or local spinal deformities, including scoliosis and kyphosis (Table 3). Interestingly, although prevalence of osteoporosis was significantly different in the VFX and control group (Table 1), the serum vitamin D level was not associated with lumbar or total hip BMD in either group (Lumbar:  $p=0.88$  and  $0.69$ ; Total hip:  $p=0.76$  and  $0.83$ ; VFX and Control group, respectively) by using linear regression analysis adjusted by sex, age, and BMI.

The risk of thoracolumbar junction VFX was 28% lower (OR=0.72, 95% CI 0.62–0.83) per increased SD in 25(OH)D in the basic model (Table 4, Model 1). When adjusted by sex, age, BMI, and comorbidities, the magnitude of this protective effect

decreased slightly but was still maintained (OR=0.80, 95% CI 0.68–0.93, Table 4, Model 2). To eliminate potential confounding factors, the data were further adjusted by BMD and season, which demonstrated that the protective effect of vitamin D did not decrease (OR=0.79, 95% CI 0.67–0.94, Table 4, Model 3–4), indicating the protective effect of vitamin D was independent of BMD.

Data were subjected to quartile analysis. As shown in Table 4, the mean serum 25(OH)D level gradually increased from the 1<sup>st</sup> to 4<sup>th</sup> quartile: 1<sup>st</sup> quartile, deficiency; 2<sup>nd</sup> quartile, insufficiency; 3<sup>rd</sup> and 4<sup>th</sup> quartiles, sufficiency. The VFX risk was lower in those patients from the 2<sup>nd</sup> to 4<sup>th</sup> quartiles than that from the 1<sup>st</sup> quartile in both basic and adjusted models; however, it was only significant in the 3<sup>rd</sup> and 4<sup>th</sup> quartiles, but not in the 2<sup>nd</sup> quartile, indicating that serum vitamin D above 50 nmol/L can reduce the risk of VFX in elderly patients. To analyze the



**Figure 2.** Receiver operating characteristic (ROC) curves depicting the ability of serum vitamin D to predict osteoporotic vertebral fracture. AUC – the area under ROC curve.

VfX risk of 1<sup>st</sup> quartile, the 2<sup>nd</sup>–4<sup>th</sup> quartiles were used as referent, showing the VfX risk increased significantly in the 1<sup>st</sup> quartile and was maintained in all adjusted models (OR=1.65, Table 4). When the analysis was limited to the 60- to 80-year-old age groups, the VfX risk further increased to more than twice (OR=2.13, Supplementary Table 2).

To predict the diagnostic value of vitamin D for vertebral fracture, the serum vitamin D data were subjected to ROC curve analysis. The area under the ROC curve (AUC) was 0.583 (95% CI 0.55–0.62) and the cut-off value of vitamin D was 41.15 nmol/L (Figure 2).

## Discussion

We analyzed the association of serum vitamin D level with thoracolumbar junction (T10–L2) VfX in elderly osteoporotic patients. Our data showed that serum 25(OH)D level was significantly associated with thoracolumbar junction VfX, especially in elderly female patients, even after adjustment of lumbar BMD. These data suggest that low vitamin D could be an independent risk factor of thoracolumbar junction VfX.

The vitamin D insufficiency in VfX patients (52.1%, Guangzhou, latitude N 23°) was similar to that of Taiwanese postmenopausal osteoporotic patients [24] (49.5%, Taiwan, latitude N 22–25°) and Japanese postmenopausal women [9] (49.6%, Tokyo, latitude N 36°), but was significantly lower than in other studies from higher-latitude regions, such as in a German study [13] (89%, Mainz, latitude N 50°). Our data showed that vitamin D insufficiency in Control patients was 40.8%, slightly lower than that in other Asia-Pacific cities, such as cities in Japan 53.6% [25] and in Korea 59.1% [26], but higher than in regions in lower latitudes, such as Vietnam [27]. Therefore, the prevalence of vitamin D insufficiency in this study was similar to that in other elderly populations in the same latitude.

**Table 4.** Association of thoracolumbar junction vertebral fracture (VfX) with quartiles of serum vitamin D (OR, 95% CI).

Variables	25(OH)D (nmol/L)	VfX (n, Q%)	Model 1 <sup>a</sup>	Model 2 <sup>b</sup>	Model 3 <sup>c</sup>	Model 4 <sup>d</sup>
Per SD increase in 25(OH)D			0.72 (0.62–0.83) <sup>f</sup>	0.80 (0.68–0.93) <sup>e</sup>	0.79 (0.67–0.94) <sup>e</sup>	0.79 (0.67–0.94) <sup>e</sup>
Q1	29.67±6.18	168 (31.5%)	Referent	Referent	Referent	Referent
Q2	45.40±3.95	135 (25.3%)	0.62 (0.44–0.87) <sup>e</sup>	0.66 (0.44–0.98) <sup>e</sup>	0.70 (0.46–1.07)	0.70 (0.46–1.07)
Q3	60.91±5.12	121 (22.7%)	0.56 (0.40–0.78) <sup>f</sup>	0.59 (0.40–0.88) <sup>e</sup>	0.58 (0.38–0.89) <sup>e</sup>	0.58 (0.38–0.89) <sup>e</sup>
Q4	103.3±44.21	110 (20.6%)	0.44 (0.31–0.62) <sup>f</sup>	0.56 (0.38–0.83) <sup>e</sup>	0.54 (0.36–0.83) <sup>e</sup>	0.54 (0.36–0.83) <sup>e</sup>
P for trend			<0.001	0.017	0.021	0.021
Q2, Q3, Q4			Referent	Referent	Referent	Referent
Q1			1.87 (1.42–2.45) <sup>f</sup>	1.66 (1.20–2.30) <sup>e</sup>	1.65 (1.17–2.32) <sup>e</sup>	1.65 (1.17–2.32) <sup>e</sup>

OR – odd ratio. CI – confidence interval. Q – quartile of serum 25(OH)D. <sup>a</sup> Model 1 basic model without adjustment; <sup>b</sup> Model 2 adjusted for sex, age, BMI and comorbidities. <sup>c</sup> Model 3 adjusted for sex, age, BMI, comorbidities and lumbar spine BMD. <sup>d</sup> Model 4 adjusted for sex, age, BMI, comorbidities, lumbar spine BMD and season. <sup>e</sup>  $P < 0.01$ ; <sup>f</sup>  $P < 0.001$ .

Although low vitamin D levels is considered to be associated with hip or non-vertebral fractures, the relationship between vitamin D insufficiency and vertebral fracture is still controversial [7,11,12]. The present study, for the first time, focused on the thoracolumbar junction area where Vfx occur most frequently [15]. Our data demonstrated that vitamin D insufficiency was significantly associated with thoracolumbar junction Vfx in both female and male patients, but it was not significant in male patients after adjustment, which might be attributed to the sample size. These results were consistent with that from Maier et al. [13]. More importantly, our data found vitamin D insufficiency was significantly related to Vfx numbers and severities, indicating that patients with low vitamin D levels are more likely to suffer more severe fracture or re-fracture, which is supported by Zafeiris et al. [14], who found that hypovitaminosis D was a risk factor of subsequent Vfx after kyphoplasty. However, the association of vitamin D with Vfx was limited to 60- to 80- year-old patients, and was not found in the younger or older patients in this study. Multiple risk factors are attributed to low-energy vertebral fractures, among which age is one of the most important factors [28]. A prospective study based on postmenopausal southern Chinese women showed that the prevalence of Vfx increases remarkably with age (OR=1.60 for every 5-year increase); for example, 19% to 68% between 60 and 70 years to those  $\geq 80$  years, respectively [29]. Therefore, the low incidence of Vfx in the 50- to 60-year-old age group and the high incidence of Vfx in the  $\geq 80$ -year-old age group might be attributed to the lack of an association between vitamin D and Vfx in this study. However, well-control prospective studies are needed to verify our findings.

Bone loss and reduced bone strength are major causes of osteoporotic fractures in the elderly [30,31]. Interestingly, our study showed that serum vitamin D level was not related to BMD, and the reason for this phenomenon is still unknown. Vitamin D deficiency has been associated with muscle weakness and increased falling risk in elderly people [32,33], and supplementation of vitamin D reduced this risk and prevented fragile fractures [34,35]. In the present study, low vitamin D level was significantly associated with thoracolumbar Vfx, even after adjustment by age, sex, comorbidities, and BMD. Hence, our data demonstrated that low vitamin D level might be an independent risk factor of thoracolumbar Vfx.

To date, there is no universally accepted threshold of low serum level of vitamin D. The criteria defined by Holick et al. [1–3] were commonly used to diagnose vitamin D deficiency ( $< 50$  nmol/L) or insufficiency (50–75 nmol/L), which was adopted by the American Association of Clinical Endocrinologists [36], and also by Japan groups [37]. However, a report from the

Institute of Medicine showed that 50 nmol/L could be enough to meet the vitamin D demand in almost 97.5% of the population [38]; therefore, a threshold of 75 nmol/L might overestimate vitamin D insufficiency. In this study, we used thresholds of 30 nmol/L for deficiency and 50 nmol/L for insufficiency. When the data were subjected to quartiles analysis, the mean level of serum vitamin D was as follows: 1<sup>st</sup> quartile, deficiency; 2<sup>nd</sup> quartile, insufficiency; 3<sup>rd</sup> and 4<sup>th</sup> quartiles, sufficiency (Table 4). The Vfx risk was lower in the 3<sup>rd</sup> and 4<sup>th</sup> quartiles, but not in the 2<sup>nd</sup> quartile after adjustment. Furthermore, Vfx risk increased significantly, to nearly 2-fold, in the 1<sup>st</sup> quartile comparison with higher quartiles. The ROC curve analysis showed that the cut-off value of vitamin D was 41.15 nmol/L, but the AUC was only 0.58, indicating that a single biomarker of vitamin D deficiency alone was not enough to predict Vfx. Therefore, our data suggest that vitamin D deficiency is a risk factor of Vfx, and keeping vitamin D at  $> 50$  nmol/L might reduce the risk of thoracolumbar junction Vfx in elderly patients, but more prospective studies are needed to confirm this.

There were some limitations that should be acknowledged in this study. This was a retrospective case-control study, and enrolled patients were hospital patients rather than a community-based population, so the data might not have reflected the actual status in the general elderly population. Therefore, the present results need to be confirmed by prospective cohort studies with larger sample sizes.

## Conclusions

Serum level of vitamin D was significantly lower in primary elderly osteoporotic patients with thoracolumbar junction osteoporotic Vfx, and serum vitamin D status was significantly associated with primary osteoporotic Vfx, affected numbers of vertebrae, and severities of fracture, especially in female patients. Therefore, vitamin D deficiency/insufficiency was associated with risk of osteoporotic thoracolumbar junction vertebral fractures in elderly patients.

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## Conflict of interest

None.

## Supplementary Data

**Supplementary Table 1.** Association of thoracolumbar junction vertebral fracture (VFX) with serum vitamin D status (patients aged 60–80 y).

Variables	25(OH)D level(nmol/L)			P-value	P-adjusted <sup>a</sup>
	<30	30–49.9	≥50		
Grade of VFX (n, %) <sup>b</sup>					
Normal	22	82	161		
Grade 1	8	31	38		
Grade 2	16	52	35		
Grade 3	28	56	98	<0.001	<0.001
Number of VFX (n, %)					
0	22	82	161		
1	34	94	105		
≥2	18	45	66	0.008	0.014

<sup>a</sup> Adjusted by sex, age and BMI; <sup>b</sup> Grade of VFXs clarified as: Normal, absence of VFXs; Grade 1–3, reduction of vertebral height of 25%, 25–40%, over 40%, respectively.

**Supplementary Table 2.** Association of thoracolumbar junction vertebral fracture (VFX) with quartiles of serum vitamin D (OR, 95% CI) (patients aged 60–80 y).

Variables	Model 1 <sup>a</sup>	Model 2 <sup>b</sup>	Model 3 <sup>c</sup>	Model 4 <sup>d</sup>
Per SD increase in 25(OH)D	0.65 <sup>f</sup> (0.52–0.80)	0.67 <sup>f</sup> (0.53–0.85)	0.64 <sup>f</sup> (0.50–0.82)	0.64 <sup>f</sup> (0.50–0.82)
Q1	Referent	Referent	Referent	Referent
Q2	0.57 <sup>e</sup> (0.36–0.90)	0.59 (0.35–1.00)	0.6 <sup>f</sup> (0.35–1.04)	0.61 (0.35–1.05)
Q3	0.47 <sup>f</sup> (0.30–0.75)	0.47 <sup>f</sup> (0.28–0.79)	0.48 <sup>f</sup> (0.28–0.82)	0.49 <sup>f</sup> (0.29–0.84)
Q4	0.35 <sup>f</sup> (0.22–0.56)	0.37 <sup>f</sup> (0.22–0.63)	0.33 <sup>f</sup> (0.19–0.58)	0.33 <sup>f</sup> (0.19–0.58)
Q2, Q3, Q4	Referent	Referent	Referent	Referent
Q1	2.19 <sup>f</sup> (1.49–3.20)	2.12 <sup>f</sup> (1.38–3.25)	2.15 <sup>f</sup> (1.38–3.35)	2.13 <sup>f</sup> (1.36–3.32)

OR – odds ratio; CI – confidence interval; Q – quartile of serum 25(OH)D. <sup>a</sup> Model 1 basic model without adjustment; <sup>b</sup> Model 2 adjusted for sex, age, BMI and comorbidities. <sup>c</sup> Model 3 adjusted for sex, age, BMI, comorbidities and lumbar spine BMD. <sup>d</sup> Model 4 adjusted for sex, age, BMI, comorbidities, lumbar spine BMD and season. <sup>e</sup> P<0.05; <sup>f</sup> P<0.01.

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