



Preoperative Vitamin D Deficiency is Associated with Postoperative Functional Recovery and Complications after Hip Fracture Surgery

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Background: Low concentrations of vitamin D are considered one of the risk factors for hip fracture and are associated with worse outcomes. The purpose of this retrospective study was to compare vitamin D deficient group and vitamin D sufficient group and assess the association preoperative vitamin D deficiency and postoperative walking ability after hip fracture surgery. **Methods:** Between January 2014 and January 2020, 1,029 elderly patients with hip fracture (243 in men and 785 in women) were measured preoperative serum 25-hydroxy-vitamin D3 levels. Among 1,029 elderly patients, 702 patients were classified as Vitamin D deficient group (<20 ng/mL). Outcome parameters for functional recovery were the length of the hospital stay and KOVAL score, and those for complications were delirium, pneumonia, and thromboembolism. **Results:** The mean length of the hospital stay in the vitamin D deficient group was significantly longer than in the vitamin D sufficient group (27.7 ± 17.8 vs. 2.9 ± 11.8 days; odds ratio [OR], 1.03; 95% confidence interval [CI], 1.02-1.05; $P=0.001$). The mean postoperative KOVAL score in the deficient group was significantly higher than in the sufficient group (4.0 ± 2.1 vs. 3.1 ± 1.9 days; OR, 1.21; 95% CI, 1.11-1.32; $P=0.001$). Vitamin D deficiency was significantly associated with a higher risk of delirium and pneumonia in deficiency group. **Conclusions:** Preoperative vitamin D deficiency in hip fractures patients was associated with prolonged duration of hospital stay and decrease of postoperative ambulatory status, and may increase the risk of delirium and pneumonia. Therefore, it is necessary to evaluate the preoperative vitamin D level and recommend vitamin D supplementation in elderly patients with a high probability of hip fracture.

Key Words: Hip fractures · Postoperative complications · Recovery of function · Vitamin D

INTRODUCTION

Hip fracture is one of the most serious injuries in elderly patients that leads to physical function decline, loss of independence or at times even death.[1,2] The worldwide number of hip fractures was 1.26 million in 1990, which is expected to increase to 4.5 million in 2050.[3] The medical cost of treatment for hip fracture is increasing and comparable to other common disease such as cardiovascular disease. The other social cost including social isolation, poor quality of life, disability, and mortality is probably greater.[4]

Although most hip fractures require acute surgery, which increases the surgical and medical complications in elderly patients.[5] Moreover, up to half of the patients lose their pre-injury level of mobility, leading to functional disability and high rates of mortality.[6,7] The important goal of hip fracture treatment in elderly patients is to attenuate the risk of inability to walk and mortality. There are several risk factors associated with functional recovery and complications following hip fracture surgery.[8] Thus, the understanding of these risk factors is important to increase the ability to walk and decrease the postoperative complications.

Vitamin D has an important role in maintaining bone health, bone mineralization and resorption via calcium and skeletal homeostasis.[9] Elderly patients with hip fractures have lower levels of vitamin D due to poor dietary intake and reduced exposure to sunlight.[10] Low vitamin D level (serum 25-hydroxy-vitamin D [25(OH)D] <20 ng/mL) is considered a risk factor for fall, hip fracture and in turn associated with worse outcomes.[11-13] However, the effect of vitamin D on postoperative functional recovery and complications after hip fracture has not been completely understood. A few studies have reported an association between preoperative vitamin D level and postoperative functional recovery or postoperative complications after hip fracture.

The purpose of this retrospective study was to compare vitamin D deficient group and vitamin D sufficient group and assess the association preoperative vitamin D deficiency and postoperative walking ability after hip fracture surgery.

METHODS

This study was approved by the Institutional Review Board (ethics committee). Due to the retrospective nature of the study, the need for informed consent was waived.

1. Patients

A total of 1,097 patients admitted with hip fractures between January 2014 and January 2020 were assessed. The inclusion criteria were (1) hip fracture (femoral neck, intertrochanteric, subtrochanteric fracture) requiring surgery; (2) >65 years at the time of surgery; and (3) available preoperative serum 25(OH)D level. The exclusion criteria were

(1) <1 year of follow-up period (N=64); and (2) metabolic bone disease or secondary hip fracture due to tumor (N=4). Thus, 1,029 patients (243 in men and 785 in women) were analyzed for the study. The patients were divided 2 groups according to preoperative Vitamin D levels (serum 25[OH]D level <20 ng/mL). Among 1,029 patients, 327 patients were classified as vitamin D sufficient group, and 702 patients were vitamin D deficient group.

2. Biochemical analysis

The blood sample was drawn on admission day before surgery. Preoperative serum vitamin D level was quantified by 125 radioimmunoassay (DIAsource ImmunoAssays SA, Louvain-la-Neuve, Belgium) for determining the levels of 25(OH)D₂ and 25(OH)D₃. The combined concentration of 25(OH)D₂ and 25(OH)D₃ was considered as the preoperative vitamin D level. The deficiency was defined as serum 25(OH)D level <20 ng/mL in accordance with the National Academy of Medicine.[12]

3. Functional assessment

Postoperative functional recovery was assessed on the basis of the duration of the hospital stay and preoperative and postoperative KOVAL scores. The length of hospital stay was calculated from the admission day until discharge and included the surgical treatment and rehabilitation procedure. Ambulatory ability was assessed with KOVAL score (1, independent community ambulator; 2, community ambulator with cane; 3, community ambulator with walker/crutches; 4, independent household ambulator; 5, household ambulator with cane; 6, household ambulator with walker/crutches; and 7, nonfunctional ambulator). The scores were evaluated at the final follow-up period.

4. Postoperative complication

The postoperative complication included delirium (symptomatic transitory psychotic syndrome), pneumonia, thromboembolism, and surgical site infection during follow-up periods.

Pneumonia was defined if any of the following criteria were met: antibiotics treatment, postoperative chest radiograph with infiltration or diagnosis by a physician. Delirium was indicated based on the Diagnostic and Statistical Manual of Mental disorders, fifth edition, which included: (1) disturbance un attention and awareness; (2) disturbance

develops acutely and the severity tends to fluctuate; (3) at least one additional disturbance in cognition; (4) disturbance are not better explained by pre-existing dementia; (5) disturbances not occurring in the context of a severely reduced level of arousal or coma; (6) evidence of an underlying organic cause or cause. Thromboembolism included deep vein thrombosis and pulmonary embolism and was diagnosed by the presence of blood clots in lung or leg vein.

5. Statistical analysis

Continuous data are presented as means and standard deviation and categorical data are shown as frequency or proportions. While student's *t*-test was used for continuous data, χ^2 test was employed for categorical data. Logistic regression analysis was performed to adjust for potentially confounding variables (age, gender, body mass index [BMI], bone mineral density [BMD]). Odds ratio (OR) and 95% confidence interval (CI) are reported. All analyses were performed using SPSS for Windows (version 24.0; IBM Corp., Armonk, NY, USA), and *P*-value less than 0.05 was considered to be significant.

RESULTS

1. Baseline characteristics

In elderly 1,029 hip fracture patients, the mean age was 80.3 ± 7.2 years (range, 65-101), and 785 (76.3%) were women. Fractures were at the femoral neck ($N=436$, 42.4%), intertrochanteric ($N=563$, 54.7%) and subtrochanteric ($N=30$, 2.9%) region. With 20 ng/mL as the threshold for deficiency, 702 patients (68.2%) had vitamin D deficiency. There was no difference in baseline characteristics (age, gender, BMI, underlying disease, BMD, fracture type) between the vitamin D deficient and the sufficient group (Table 1).

2. Postoperative functional recovery

The mean length of hospital stay was 25.6 ± 16.4 days

(range, 9–63). The mean duration of hospital stay in the vitamin D deficient group was significantly longer than that in the sufficient group (27.7 ± 17.8 vs. 20.9 ± 11.8 days; OR, 1.03; 95% CI, 1.02-1.05; $P=0.001$) (Table 2).

The mean preoperative KOVAL score was 2.4 ± 1.9 (range, 1–7). The mean score in the deficient group was higher than that in the sufficient group. However, this was not statistically significant (2.6 ± 1.9 vs. 2.0 ± 1.6 ; $P=0.801$) (Table 2).

The mean postoperative KOVAL score was 3.7 ± 2.0 (range, 1–7). The mean score in the vitamin D deficient group was significantly higher than in the sufficient group (4.0 ± 2.1 vs. 3.1 ± 1.9 days; OR, 1.21; 95% CI, 1.11-1.32; $P=0.001$) (Table 2).

3. Postoperative complications

Delirium and pneumonia were found to be significant postoperative complications with preoperative vitamin D

Table 1. Patient's demographics

	Total	Vitamin D deficient group	Vitamin D sufficient group	<i>P</i> -value
No. of patients	1,029	702	327	
Age	80.3 ± 7.2	81.3 ± 7.2	79.6 ± 7.3	0.791
Gender				
Male	244 (23.7%)	172 (24.5%)	72 (22.0%)	
Female	785 (76.3%)	530 (75.5%)	255 (78.0%)	0.327
BMI	22.3 ± 3.7	22.2 ± 3.7	22.2 ± 3.3	0.150
BMD	-2.7 ± 1.1	-2.8 ± 1.1	-2.6 ± 1.1	0.688
Underlying disease				
HTN	617 (60.0%)	427 (60.8)	190 (58.1)	0.300
DM	303 (29.4%)	216 (30.8)	87 (26.6%)	0.609
COPD	26 (2.5%)	19 (2.7%)	7 (2.1%)	0.164
CKD	83 (8.1%)	59 (8.4%)	24 (7.3%)	0.141
Fracture type				
Femur neck	436 (42.4%)	299 (42.6%)	137 (41.9%)	
Intertrochanteric	563 (54.7%)	382 (54.4%)	181 (55.4%)	
Subtrochanteric	30 (2.9%)	21 (3.0%)	9 (2.8%)	0.559

The data is presented as number (%) or mean \pm standard deviation. BMI, body mass index; BMD, bone mineral density; HTN, hypertension; DM, diabetic mellitus; COPD, chronic obstructive pulmonary disease; CKD, chronic lung disease.

Table 2. Postoperative functional recovery

	Total	Vitamin D deficient group	Vitamin D sufficient group	<i>P</i> -value	OR (95% CI)
Length of hospital stay	25.6 ± 16.4	27.7 ± 17.8	20.9 ± 11.8	0.001	1.03 (1.02-1.05)
Preoperative KOVAL score	2.4 ± 1.9	2.6 ± 1.9	2.0 ± 1.6	0.801	
Postoperative KOVAL score	3.7 ± 2.0	4.0 ± 2.1	3.1 ± 1.9	0.001	1.21 (1.11-1.32)

OR, odds ratio; CI, confidence interval.

Table 3. Postoperative complications

	Total	Vitamin D deficient group	Vitamin D sufficient group	P-value	OR (95% CI)
Delirium	209 (20.3%)	162 (23.1%)	47 (14.4%)	0.046	1.52 (1.01-2.31)
Pneumonia	47 (4.6%)	41 (5.8%)	6 (1.8%)	0.016	3.82 (1.29-11.34)
Thromboembolism	30 (2.9%)	25 (3.6%)	5 (1.5%)	0.123	2.41 (0.79-7.34)
Surgical site infection	5 (0.5%)	4 (0.6%)	1 (0.3%)	0.882	

OR, odds ratio; CI, confidence interval.

level. The 209 patients (20.3%) developed delirium during the hospital stay. Vitamin D deficiency was significantly associated with a higher risk of delirium, with 162 patients (23.1%) in the deficient group and 47 patients (14.4%) in the sufficient group (OR, 1.52; 95% CI, 1.01-2.31; $P=0.046$) (Table 3).

The 47 patients (4.6%) developed pneumonia during the hospital stay. Vitamin D deficiency was significantly associated with a higher risk of delirium, with 41 patients (5.8%) in the deficient group and 6 patients (1.8%) in the sufficient group (OR, 3.82; 95% CI, 1.29-11.34; $P=0.016$) (Table 3).

It was seen that vitamin D deficiency was associated with a higher risk of thromboembolism. In all, 30 patients (2.9%), 25 (3.6%) in vitamin D deficient group and 5 (1.5%) in vitamin D sufficient group developed thromboembolism during a hospital stay. However, this was not statistically significant (OR, 2.41; 95% CI, 0.79-7.34; $P=0.123$) (Table 3).

DISCUSSION

Vitamin D has an important role in maintaining bone health, bone mineralization and resorption via calcium and skeletal homeostasis.[9] We compared functional outcomes between vitamin D deficient and sufficient groups in 1,097 patients with hip fractures. The principal findings in this study demonstrated that preoperative vitamin D deficiency is associated with increased duration of the hospital stay and reduced ability to walk after hip surgery in elderly patients.

In this study, the postoperative KOVAL score in the vitamin D deficient group was significantly higher than in the sufficient group. These findings are in line with previous studies. Hao et al. [8] reported that low preoperative vitamin D level (serum 25[OH]D < 12 ng/mL) was associated with a lower rate of walking without human assistance at 30 and 60 days follow-up after hip fracture surgery in geriatric patients. Liu et al. [13] reported that low preoperative

vitamin D level (serum 25[OH]D < 20 ng/mL) was associated with poor functional outcome (Barthel index) in postmenopausal women after hip fracture surgery. Although the etiology of poor walking ability in patients with vitamin D deficiency is not clear, several studies report that vitamin D in humans is a positive correlation with muscle strength.[14,15] It has also been documented that skeletal muscle requires an optimal level of vitamin D for maintaining the muscle structure and function [16] and that vitamin D deficiency causes atrophy of type II muscle fiber, loss of muscle mass, and muscle weakness.[17] Consequently, the loss of muscle mass was associated with disability in elderly and increase the risk of fall.[16] Although there are controversies about whether supplementation of vitamin D improves muscle strength and mobility, we believed that it is necessary to evaluate the preoperative vitamin D level and prescribe vitamin D in elderly patients with high probability of hip fracture.

In this study, we found that preoperative vitamin D deficient group had a higher risk of delirium than preoperative vitamin D sufficient group. Several studies have reported the association between vitamin D deficiency and delirium. Torbergsen et al. [18], reported that 51% of hip fracture patients had delirium and the concentration of vitamin D (25[OH]D) was lower than controls in their case-control study. Ingstad et al. [19] reported that 21% of the preoperative vitamin D deficient group and 15% of preoperative vitamin D sufficient group were diagnosed with delirium. The risk of delirium was significantly high in vitamin D deficient group (OR, 1.48; 95 CI, 1.04-2.12; $P=0.03$). It has been hypothesized that chronic stress and inflammation in brain are involved in the pathophysiology of delirium.[20] Vitamin D and its receptors play an important role in exerting anti-inflammatory and anti-oxidant effects in brain cortex and hippocampus, which are crucial regions for cognition and neuroimmune modulation.[21] Therefore, the delirium in vitamin D deficient patients may be due to increased in-

flammation in brain.[19]

We also found that preoperative vitamin D deficient group had a higher risk of pneumonia than preoperative vitamin D sufficient group in hip fracture patients. There have been no studies associating preoperative vitamin D deficiency and pneumonia after hip fracture surgery. In a meta-analysis, Zhou et al. [22] reported an association between vitamin D deficiency and an increased risk of community-acquired pneumonia. Vitamin D may play an important role in the occurrence of pneumonia by binding to the vitamin D receptor which can promote the expression of antibacterial peptides that inhibit bacterial and viral infections. [23] However, vitamin D deficiency results in a decrease of vitamin D receptors. Consequently, the inflammation cannot be controlled, leading to injury of pulmonary tissue and subsequently pneumonia.[24] The pulmonary epithelial cells can convert the inactive vitamin D into its active form thereby stimulating the expression of antibacterial peptides.[25] Thus, the deficiency of vitamin D has been associated with increase in inflammation, lung injury as well as severe pneumonia. It has been documented that vitamin D supplements may reduce the occurrence and severity of pneumonia.[22]

This study had several limitations. First, this study was designed as a retrospective study. Therefore, the possibility of insufficient data collection and selection bias cannot be excluded. Second, the evaluation of vitamin D levels was performed at admission after fracture and may thus not accurately reflect pre-injury vitamin D status. Third, we did not evaluate the levels of parathyroid hormone and vitamin D receptors, which may have affected the functional outcome. Fourth, we also did not evaluate the sarcopenia, which may be associated with vitamin D. Lastly, as this was a single-center study, future large, multi-centered and prospective study are warranted.

In conclusion, preoperative vitamin D deficiency in hip fractures patients was associated with prolonged duration of hospital stay and decrease of postoperative ambulatory status and may increase the risk of delirium, pneumonia and thromboembolism. Therefore, it is necessary to evaluate the preoperative vitamin D level and prescribe vitamin D supplements to elderly patients with a high probability of hip fracture.

DECLARATIONS

Ethics approval and consent to participate

This study conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Institutional Review Board.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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