

Prevalence and Clinical Correlation of Vitamin D Inadequacy in Traumatic Hip Fracture among Elderly Patients

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Abstract

Introduction: High prevalence of vitamin D deficiency has been described in more than 1 billion people around the world, especially in Middle-East and Asia. In Thailand, the largest study of vitamin D status in normal population (N=2641) identified overall 45.2 percent of vitamin D inadequacy in normal population. However, there was no study focusing on Vitamin D inadequacy in traumatic elderly patients. The purpose of this study is going to define the prevalence of vitamin D inadequacy in traumatic hip fracture among elderly patients and to identify a clinical correlation.

Materials and Methods: A prospective study of elderly patients (more than 60 years old) with low energy trauma who underwent orthopaedic surgery at Phramongkutklao Hospital between the period of January 2016 and December 2016. All hip fracture patients underwent orthopedic surgery were collected for demographic data, comorbidities including Charlson Comorbidity Index. Primary outcome was to identify a prevalence of vitamin D inadequacy (<30 ng/ml) and vitamin D deficiency (<20 ng/ml) in hip fracture underwent orthopedic surgery. Secondary outcome was to define association of demographic data, comorbidity with vitamin D level. Additionally, comparison the ambulatory status and mechanical failure between normal vitamin D and vitamin D inadequacy

Results: The serum 25(OH)D levels for this study was normally distributed, with a mean of 25.0±12.2 ng/ml in all patients, Prevalence of vitamin D inadequacy was 70.5 percent (n=103) and the prevalence of vitamin D deficiency was 37.7 percent (n=55). There was no significant difference of ambulatory status between vitamin D inadequacy and sufficient vitamin D groups (p=0.958). Additionally, there was not different in mechanical failure between groups (4.5% and 0%, p=1.000).

Conclusion: Vitamin D inadequacy is so common in traumatic elderly patients. We should raise attentiveness among physician to determine vitamin D status. Public health strategy should add knowledge about diet, supplements or adequate sun exposure to elderly population. Vitamin D inadequacy did not affect the outcome including time to union and ambulatory status at 1 year follow up.

Keywords: Vitamin D; Fractures; Patients

Introduction

Vitamin D plays a vital role not only in making our bones strong and it is important in bone mineralization and maintenance of bone quality through the regulation of calcium and skeletal homeostasis, but also it maintain our immune system, reproductive system, musculoskeletal system and integumentary system in all ages and races [1]. The minimum level of 30 ng/ml is necessary in older adults to minimize the risk of fractures due to falls [2,3]. High prevalence of vitamin D deficiency has been described in more than 1 billion people around the world, especially in Middle-East and Asia [4] and it has been seen in all races, age groups and ethnic background [2]. There are a few data demonstrating a screening for vitamin D deficiency in asymptomatic adults or during pregnancy [5,6] while most experts agree that it is not necessary to perform broad screening of serum 25(OH)D levels in the general population or during pregnancy [5,7].

Systematic review and meta-analysis identified prevalence of Vitamin D inadequacy in traumatic patient, they found that 70% of all fracture patients and 73% of fragility fracture (age more than 50 years old) have Vitamin D level less than 30 ng/ml⁴. In Thailand, there are several studies demonstrating the prevalence of vitamin D deficiency. Soontrapa S. et al. [8] found that 66.3 percent of elderly Thai women in Khonkaen province have Vitamin D deficiency [25(OH)D level <35 ng/ml] while the largest study of vitamin D status in normal population (N=2641) identified overall 45.2 percent of vitamin D inadequacy in normal population [9]. However, there was no study focusing on Vitamin D inadequacy in traumatic elderly patients. So, the purpose of this study is going to define the prevalence vitamin D inadequacy in traumatic hip fracture among elderly patients.

Materials and Methods

Subjects

We performed a prospective study of hip fracture among elderly patients (more than 60 years old) with low energy trauma who underwent orthopaedic surgery at Phramongkutklao Hospital between the period of January 2016 and December 2016. After approval by our institutional review board and got informed consent from patients/first degree relatives, study subjects needed to obtain serum 25(OH)D at the time of admission, prior to surgery. Patients with high risk for Vitamin D inadequacy (Serum creatinine more than 2md/dL, mal absorption

syndrome, post gastrectomy, active liver disease, acute myocardial infarction, anorexia nervosa and steroid dependency), pathological fracture and multiple sites of fracture were excluded. Finally, 146 elderly patients were recruited in this study. We also further randomly investigated a serum 25(OH) vitamin D level in 146 normal elderly populations without any fracture for the control group.

Laboratory Studies

Serum Calcium, phosphorus, and albumin levels were measured with use of standard automated laboratory method at our hospital. Vitamin D level was identified by using "chemiluminescent immunoassay" on Roche property Asset No. 9006102 model cobase 601 for detect total serum 25-hydroxyvitamin D. This machine can interpret level 3.00-70.00 ng/ml (if less than 3 ng/ml, it's interpret 3 ng/ml and if more than 70 ng/ml, it's interpret 70 ng/ml). Vogeser et al. compared reliability of this machine with gold standard (liquid Chromatography - Tandem Mass Spectrometry) and they found that this machine was appropriate for hospital [10].

Background Data

Patients demographic and background that may be the risk factors for Vitamin D inadequacy were collected by researcher. Variables included age, sex, height and body weight for calculate body-mass index (BMI), location of fracture, ambulatory status before fracture, history of previous fracture, timing of sun exposure per day, timing from fracture to surgery and comorbidities for calculate Charlson Comorbidity Index [11]. Age was further categorized into three groups (sixty to sixty-nine, seventy to seventy-nine and more than 80 years) to investigate their potential effects on serum Vitamin D level. Body-mass index was grouped into two groups: less than 30 kg/m² and equal or above 30 kg/m².

Outcome Measures

Our primary objective was prevalence of vitamin D inadequacy (less than 30 ng/ml) and vitamin D deficiency (less than 20 ng/ml) in traumatic hip fracture among elderly patients.

Secondary objectives were association of demographic data (age, gender, BMI) and vitamin D level. We also identified an association between Charlson Comorbidity Index (CCI), preoperative albumin, ambulatory status before fracture, history of previous fracture, timing of sun exposure per day, timing from fracture to surgery, length

of hospital stays with vitamin D level. We also followed patients for 1 year to find an association between ambulatory status at 1 year, time to union and failure of implants with vitamin D level (sufficiency and inadequacy groups).

Statistical Analysis

Primary outcome was analyzed by prevalence (number and percentage) of Vitamin D inadequacy (less than 30 ng/ml) and deficiency (less than 20 ng/ml) in overall population.

In secondary outcomes, univariate and multivariate logistic regression models were used to assess the independently relative risk for vitamin-D inadequacy in each potential risk factor (age group, sex, body-mass index, preoperative albumin, ambulatory status before fracture, history of previous fracture and timing of sun exposure per day, timing from fracture to surgery, length of hospital stays).

Independent t-test was used for Charlson Comorbidity Index while chi-square test was applied for preoperative albumin, history of previous fracture and timing from

fracture to surgery. Ambulatory status before fracture, ambulatory status at 1 year, and failure of implant were analyzed by Fisher's exact test was used. The association of sun exposure per day, length of hospital stays, Charlson Comorbidity Index, time to union and vitamin inadequacy was analyzed by Mann-Whitney U test. All parameters were performed with use of two-tailed tests. The level of significance was set at p-value less than 0.05.

Results

Baseline Characteristics

A total of 146 patients participated in this study, 24.7% (n=36) were men and 75.3% (n=110) were women (Table 1). Ages ranged from 60 to 100 years; with a mean age (and standard deviation) were 78.8±8.9 years. The average body-mass index was 22.0±4.3 kg/m². Almost of our population (97.9%, n=143) was not obesity (body-mass index less than 30 kg/m²). According to pre-fracture status, these patients can walk independently approximately 60% (n=88) and they had no previous history of fracture (85.6%, n=125).

Characteristics	Male (n=36)	Female (n=110)	Total (n=146)
Age ---yr	78.0 ± 8.2	79.1 ± 9.1	78.8 ± 8.9
BMI ---kg/m ²	23.0 ± 4.6	21.6 ± 4.1	22.0 ± 4.3
Vitamin D -- ng/ml	25.6 ± 12.6	24.5 ± 12.1	25.0 ± 12.2
CCI --- total	4.7 ± 1.4	4.8 ± 1.5	4.8 ± 1.5
Albumin ---g/dL	3.7 ± 0.4	3.7 ± 0.5	3.7 ± 0.5
Previous fx --- no. (%)			
No	31 (86.1)	94 (85.5)	125 (85.6)
Yes	5 (13.9)	16 (14.5)	21 (14.4)
Pre-fracture status --- no. (%)			
Independent	25 (69.4)	63 (57.3)	88 (60.3)
Gait aid	11 (30.6)	45 (40.9)	56 (38.3)

Table 1: Baseline characteristics of the study populations (divided by gender).

* Plus-minus values are means ± SD, fx means fracture

CCI means Charlson Comorbidity Index

%=percentages of each parameter divided by each column

Prevalence of Vitamin D Inadequacy

The serum 25(OH)D levels for this study was normally distributed, with a mean of 25.0±12.2 ng/ml in all patients, 25.6±12.6 ng/ml in male, 24.5±12.1 ng/ml in female, and minimum and maximum values of 3.0 and 66.89 ng/ml (Table 1). Prevalence of vitamin D inadequacy (<30 ng/ml) was 70.5 percent (n=103) (Table

2) and the prevalence of vitamin D deficiency (<20 ng/ml) was 37.7 percent (n=55).

Vitamin D Associated with History of Previous Fracture

Those patients with previous history of fracture was not significantly higher rate of vitamin D inadequacy

comparing to those without previous history of fracture (57.1% vs 42.9%, $P=0.168$, respectively)

Vitamin D Associated with Timing of Sun Exposure and Time from Fracture to Surgery

The average median time of sun exposure (Table 2) was 15 minutes a day (minimum, maximum=0,4 hours) in vitamin D inadequacy group while it was 30 minutes a day (minimum, maximum=0,5 hours) for sufficient

vitamin D group, which were significantly different between both groups ($p<0.001$).

Timing from fracture to surgery, the former group was significantly higher rate of waiting for surgery more than 1 week comparing to the latter group (77.8% vs 22.2%, $p=0.013$). However, total length of hospital stay was not significantly different between both groups (mean 14 days, p -value=0.604).

Factors	Vit. D < 30 ng/ml	Vit. D ≥ 30 ng/ml	P Value
Age --- yr			0.042
Total --- no. (%)	103 (70.5)	43 (29.5)	
60-69 ---no. (%)	22 (88.0)	3 (12.0)	
70-79 ---no. (%)	31 (64.6)	17 (35.4)	
≥ 80 --- no. (%)	50 (69.9)	23 (30.1)	
Gender			0.487
Male ---no. (%)	24 (66.7)	12 (33.3)	
Female ---no. (%)	79 (71.8)	31 (28.2)	
BMI -- kg/m²			0.557†
< 30 ---no. (%)	100 (69.9)	43 (30.1)	
≥ 30 ---no. (%)	3 (100.0)	0 (0)	
CCI --- total	4.75 ± 1.76	4.83 ± 1.26	0.736¥
Albumin --- g/dL			0.164
< 3.5 ---no. (%)	24 (80.0)	6 (20.0)	
≥ 3.5 ---no. (%)	79 (68.1)	37 (31.9)	
Previous fx			0.168
No ---no. (%)	90 (72.0)	35 (28.0)	
Yes ---no. (%)	12 (57.1)	9 (42.9)	
Previous fx status			0.615†
Independent ---no. (%)	60 (68.2)	28 (31.8)	
Gait aid ---no. (%)	41 (73.2)	15 (26.8)	
Bed ridden ---no. (%)	2 (100.0)	0 (33.3)	
Timing of sun expose# -- hour/day	0.25 (0-5)	0.5 (0-4)	<0.001‡
Timing from fracture to surgery			0.013
< 7 days ---no. (%)	33 (58.9)	23 (41.1)	
≥ 7 days ---no. (%)	70 (77.8)	20 (22.2)	

Table 2: Baseline characteristics of the study populations (divided by Vitamin D status).

* Plus-minus values are means ± SD., CCI means Charlson Comorbidity Index, †Fisher's exact test, ¥Independent t-test, Chi-square test, and ‡ Mann-Whitney U test for other P Value, # Timing of sun exposure shows in median (minimum-maximum), P value <0.05 considered statistical significance; 44% of all patients had sun exposure less than 0.25 hour/day

Vitamin D Correlated with Ambulatory Status at 1 Year, Time to Union and Failure of Fixation

We follow up this population for 1 year after fracture; eight patients were died while six patients were loss of follow-up. Finally, 132 patients were included for further

analysis (Table 3). Even though most of them can ambulate by single cane (72.0%, $n=95$), only 20.0% ($n=19$) can ambulate independently at one year follow up which was significantly different comparing to pre-fracture status (60.3%, $n=88$).

Association of vitamin D and ambulatory status, there was no significant difference of ambulatory status between vitamin D inadequacy and sufficient vitamin D groups ($p=0.958$). Generally, displaced femoral neck fracture subgroup treated by primary hemiarthroplasty cannot evaluate for bone union including clinical union and radiographic union while time to union was measured in subgroup of intertrochanteric fracture treated by proximal femoral nail anti-rotation (PFNA) fixation and they were further divided into clinical union and radiographic union. Mean time of clinical union and radiographic union were also not significantly different

between both groups (4 weeks vs 6 weeks, $p=0.741$ and 10.5 weeks vs 10 weeks, $p=0.566$, respectively). Furthermore, in cases of fixation failure, we also focused only on intertrochanteric fracture (65 cases) that underwent PFNA fixation. Although two-third (67.7%, $n=44$) of this group had vitamin D inadequacy, only 2 cases had implant failure (PFNA blade cutout-both of them were in group of Vitamin D inadequacy). Additionally, there was comparable rate of fixation failure between vitamin D inadequacy and sufficient vitamin D groups (4.5% vs 0%, $p=1.000$).

Factors	Vit. D < 30 ng/ml	Vit. D \geq 30 ng/ml	P Value
Ambulatory status at 1 year			0.958†
Independent ---no. (%)	14 (14.7%)	5 (13.5%)	
Cane (single/tripod) ---no. (%)	69 (72.6%)	26 (70.3%)	
Walker ---no. (%)	10 (10.6%)	5 (13.5%)	
Bedridden ---no. (%)	2 (2.1%)	1 (2.7%)	
Time to union --- weeks			
Clinical union	4 (2-30)	6 (3-18)	0.741‡
Radiographic union	10.5 (4-38)	10 (8-22)	0.566‡
Failure of implant fixation			1.000†
No ---no. (%)	42 (95.5%)	21 (100%)	
Yes ---no. (%)	2 (4.5%)	0 (0%)	

Table 3: Univariate analysis of ambulatory status at 1 year after fracture, time to union and failure of implant fixation according to Vitamin D status.

†Fisher's exact test, ‡Mann-Whitney U test

P value <0.05 considered statistical significance. %=percentages of each parameter divided by each column.

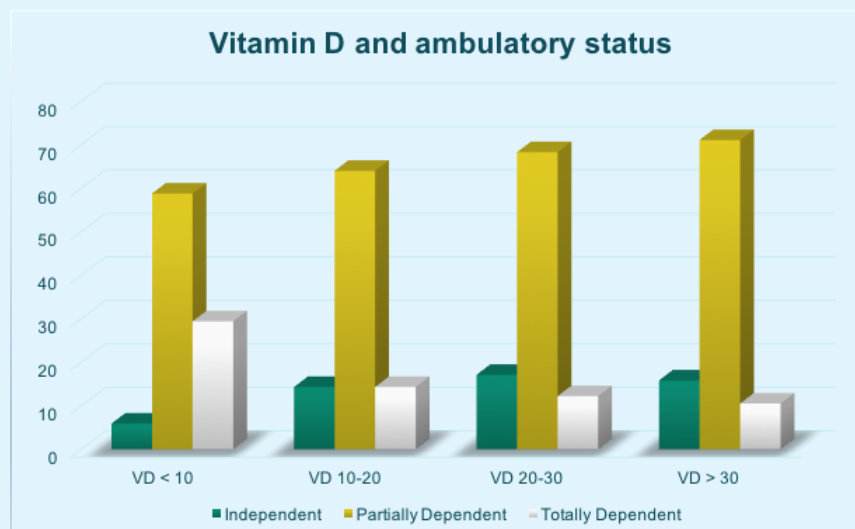


Table 4: Analysis of ambulatory status at one year follows up among each subgroup of vitamin D inadequacy and sufficient vitamin D level.

Totally Dependent (wheel chair until bed ridden; white color box) was 29.4%, 14.3%, 12.2%, and 10.5% for vitamin D level <10, 10-20, 20-30, and >30 ng/ml, respectively.

Vitamin D in Normal Elderly Population

One hundred and forty six vitamin D levels were randomly obtained and they were classified into 3 age groups (60-69 years, 70-79, and ≥80 years). Mean serum vitamin D level was 31.4, 32.9, 34.8 ng/ml, respectively. Mean serum Vitamin D level was higher in male than female in all age groups (Table 4).

Discussion

The purpose of this study is going to define the prevalence vitamin D inadequacy in traumatic hip fracture among elderly patients and to identify a clinical correlation of the vitamin D level. This study evaluated vitamin D status in traumatic elderly patients in Bangkok, Thailand, which is located in the central region of the country. The findings show that 70.5 percent have vitamin D inadequacy (less than 30 ng/ml). This value is almost the same as Vitamin D status in traumatic elderly patients according to systematic review and meta-analysis by Sprague S, et al. [4] which 73% of fragility fracture (age more than 50 years old) had vitamin D level less than 30 ng/ml. The prevalence of vitamin D inadequacy in our study was high that was comparable with Sprague's studies even though our patients live in tropical zone that should not have low vitamin D level. This may be explained by sedentary life style, almost elderly patients with hip fracture in our country are not only retired from work, but they also have low activity level preoperatively. Moreover, lack of vitamin D supplement in regular food especially in milk (only calcium supplement) and some patients (44 percentages) had sun exposure less than 0.25 hour.

Previous study by Chailurkit L, et al. [11] identified the largest vitamin D status in normal population in Thailand (n=2641, age 14-98 years): overall population had 45.2 percentages of vitamin D inadequacy, particularly Bangkok is the highest rate of this problem (64.6%). However, they have not demonstrated vitamin D status of traumatic hip fracture in elderly patients. Our study firstly identified the vitamin D level in hip fracture among elderly patients and we found a high prevalence of vitamin D deficiency in men that was compatible with previous study [12]. The association between gender and Vitamin D inadequacy was varied, some studies show

higher percentage in women (very low serum 25(OH)D levels have been reported in the Middle East especially in women because of clothing habits while the others was common in men) [13]. However, the prevalence of vitamin D inadequacy was comparable between male and female in our study (66.7% vs 71.8%, p=0.487).

Charlson Comorbidity Index (CCI) was high in hip fracture. Some data suggested that CCI more than 2 was higher risk for vitamin D inadequacy (Relative risk = 16.8) [14]. The relationship between vitamin D inadequacy and obesity is still unknown, our study was not shown an association of them because we had low proportion (2.1 percent) of patients with obesity (BMI more than 30 kg/m²).

Length of hospital stay in this study was not different between groups, agreed with Gumieiro DN, et al. [15] that serum Vitamin D level was not associated with length of hospital stay after hip fracture while Maier GS, et al. [16] found that length of stay in multivariate analysis was significantly higher rate associated with low Vitamin D levels (p-value=0.002). However, the latter study collected the data from elective cases of hip or knee arthroplasty.

Not surprising, timing of sun exposure was strongly significant difference between two groups (p-value less than 0.001). Timing from fracture to surgery was significantly longer in group with vitamin D less than 30 ng/ml (p-value 0.013). Further analysis found that population in group of vitamin D inadequacy tend to have higher rate of anticoagulant usage (such as aspirin and clopidogrel) that had to stop before surgery, and they had higher rate of medical problem that needed to be stabilized before surgery.

When we followed up these population for 1 year, someone died, someone loss to follow up. Only 132 patients were completed follow up. Even though one year-ambulatory status was not different in both groups, almost of them dependently required gait aid for ambulation. Sixty-one percent of population can walk independently before fracture versus only twenty percent can walk independently after fracture at 1 year follow up. In the fixation group, union rate (clinical/radiographic union) was not significantly different. When focus on fixation with PFNA of hip legion, two cases of PFNA blade cutout was found, both of them occurred in group of vitamin D inadequacy. The association between fixation failure and vitamin D status was not found because of very low rate (2 out of 65) of fixation failure. The other

reason why there was no difference in fixation failure between groups because successful fixation mainly required proper surgical technique rather than vitamin D level.

Our study had several limitations. Firstly, a disproportionately large number of our patients were urbanized because most of them live in Bangkok. Given the predisposition of lower sun exposure when compared to population in rural area. Secondly, serum vitamin D levels were measured during various seasons. It is possible that seasonal variation may have affected the findings of this study. To solve this uncertainty, further study about individuals varies in their physiologic responses to sunlight and serum vitamin D levels in different seasons should be done. As above-mentioned in limitations, so we need further studies to define the precise extent of vitamin D inadequacy in the orthopaedic surgery patient.

Conclusion

Vitamin D inadequacy is so common in traumatic hip fracture among elderly patients. We should raise attentiveness among physician to determine vitamin D status. Public health strategy should add knowledge about diet, supplements or adequate sun exposure to elderly population. Vitamin D inadequacy did not affect the outcome including time to union and ambulatory status at 1 year follow up.

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