Int Surg 2016;**101**:367–374
DOI: 10.9738/INTSURG-D-16-00102.1

A Clinical Analysis of Vitamin D Status in Patients Before Spinal Surgery

Qingqing Li[1], Jianwei Zhang[1,2], Jian Chen[1], Jin Fan[1], Tao Jiang[1], Jian Yin[1], Wei Zhou[1], Lipeng Yu[1], Guoyong Yin[1]

[1]*Department of Orthopaedics, the First Affiliated Hospital with Nanjing Medical University, Jiangsu, China*

[2]*Department of Orthopaedics, the Third Affiliated Hospital with Nanjing University of Chinese Medicine, Jiangsu, China*

The goal of this paper was to study preoperative concentrations of vitamin D in patients undergoing spinal surgery and analyze relevant risk factors associated with vitamin D deficiency. Vitamin D plays an important role in maintaining normal functions of skeletal muscles, and vitamin D insufficiency or deficiency may affect outcomes of spinal surgery patients. A retrospective analysis was conducted on 503 patients undergoing spinal surgery in the First Affiliated Hospital with Nanjing Medical University from September 2012 to October 2013. Preoperative concentrations of serum 25-hydroxyvitamin D [25(OH)D] were measured. Normal vitamin D was defined as a serum 25(OH)D level $\geq$ 32 ng/mL, vitamin D insufficiency as $\geq$20 and $<$32 ng/mL, and vitamin D deficiency as $<$20 ng/mL. Relevant risk factors associated with vitamin D insufficiency and deficiency were analyzed. In 503 spinal surgery patients, rate of vitamin D deficiency and insufficiency was 71.4% and 23.9%. Rate of vitamin D deficiency in female patients was significantly higher than that in male ($P < 0.001$). Rate of vitamin D deficiency in patients with high body mass index ($P = 0.009$) or patients with smoking habit ($P < 0.001$) was much higher than other patients. Multivariate analysis demonstrated that female ($P < 0.001$), smoking ($P = 0.005$), and winter ($P = 0.001$) were potential risk factors for vitamin D deficiency. Screening preoperative vitamin D status and relevant treatment should be reinforced in spine surgery patients.

Key words: Vitamin D deficiency – Vitamin D insufficiency – Spinal surgery

Corresponding authors: Lipeng Yu, PhD, and Guoyong Yin, PhD, MD, Department of Orthopaedics, Jiangsu Province Hospital, The First Affiliated Hospital with Nanjing Medical University, 300 Guangzhou Road, Nanjing City, Jiangsu Province 210029, People's Republic of China.
Tel.: 025 83718836 6781; E-mail: yulipeng@hotmail.com; guoyong_yin@sina.com

Vitamin D, an important fat-soluble vitamin, plays an important role in maintaining normal functions of skeletal muscles. It primarily maintains homeostasis of calcium and phosphate metabolism in the body, and thus ensures normal mineralization of bones. 1,25-dihydroxyvitamin D3 [1,25$(OH)_2$ D3], the metabolite of vitamin D, is the most active form of vitamin D in the body and maintains homeostasis of bone formation and resorption by regulating the functions of osteoblasts and osteoclasts. Low levels of vitamin D ($\leq$9 ng/mL) will reduce the intestinal absorption of calcium, cause compensatory increases of parathyroid hormone, disrupt homeostasis of bone formation and resorption, and thus result in osteoporosis and osteomalacia disease, impair functions of skeletal muscles, and increase the risk of fractures and its associated kyphosis.[1–3]

In recent years, a large number of studies have shown that increased incidence of diseases associated with vitamin D deficiency has become a global issue.[4,5] Currently, approximately 10 million people worldwide have vitamin D insufficiency or deficiency.[5] The degree of deficiency is affected by many factors mainly including the duration of sunshine, dietary supplements, age, gender, race/ethnicity, etc. Since vitamin D levels are important for homeostasis of bone formation and resorption, vitamin D deficiency in orthopedic surgery patients has attracted more and more attention. A recent study showed that 43% of 723 orthopedic surgery patients had vitamin D deficiency,[6] whereas the rate of vitamin D deficiency in another study on 313 spinal surgery patients was 27%.[7] The incidence of vitamin D deficiency may substantially vary due to several reasons including living environment, physiological condition, lifestyle, etc.[4]Although there is controversy about the incidence of vitamin D deficiency in orthopedic patients, it has been confirmed that vitamin D deficiency affects surgical approach and prognosis of orthopedic surgery, especially spinal surgery. Studies have shown that vitamin D promotes fracture healing in humans.[8] Osteoporosis caused by vitamin D deficiency will result in reduced vertebral bone density, trabecular thinning, and reduced holding power of screws at bone interface. Complications of screw loosening and prolapse may occur in patients undergoing spinal fusion surgery due to factors associated with vitamin D deficiency, whereas adequate vitamin D levels are conducive to bone fusion after spinal fusion surgery by enhancing the stability of pedicle screws. Therefore, severe osteoporosis is a relative contraindication to a pedicle screw fixation surgery. Moreover, studies have shown that vitamin D deficiency affects the prognosis of patients with spinal surgery. An assessment of postoperative vitamin D status in female patients with spinal stenosis showed that patients with vitamin D deficiency had lower Oswestry Disability Index (ODI) score, and European Quality of Life-5 Dimensions (EQ-5D) scores compared with the other patients.[9] Therefore, preoperative vitamin D screening should be reinforced in spinal surgery patients and vitamin D should be replenished in case of vitamin D deficiency.

Previous research described already cannot accurately reflect the current situation of vitamin D deficiency in our country due to the differences in living environment, physiologic condition, lifestyle, etc. between foreign and domestic patients. Currently, no relevant research has been performed on preoperative vitamin D status in domestic spinal surgery patients. Vitamin D is critical for maintaining the normal functions of skeletal muscles, and its deficiency may influence the choice of surgical approach and outcomes. Therefore, it is very important to study the incidence of vitamin D deficiency in domestic spinal surgery patients, which is very helpful for spinal surgeons to make an early treatment plan for vitamin D deficiency and ultimately improve therapeutic efficacy of the surgery.

Materials and Methods

Patients

A retrospective analysis was conducted on 503 patients undergoing spinal surgery in the First Affiliated Hospital of Nanjing Medical University from September 2012 to October 2013. Preoperative concentrations of serum 25-hydroxyvitamin D [25 (OH) D] were measured and used for assessment of levels of vitamin D. Normal vitamin D was defined as a serum 25(OH)D level $\geq$ 32 ng/mL, vitamin D insufficiency as 25(OH)D $\geq$ 20 and $<$32 ng/mL, and vitamin D deficiency as 25(OH)D $<$ 20 ng/mL.[9] Spinal diseases in this study referred to those requiring surgical treatment and included cervical spondylosis, lumbar degenerative diseases (lumbar disc herniation, spondylolisthesis, and spinal stenosis), spinal fractures, osteoporotic vertebral compression fractures, and recurrent lumbar disc herniation and spinal tumors. This study was approved by the ethics committee in the First Affiliated Hospital of Nanjing Medical University and preoperative informed consent was signed by

Table 1 General medical data of patients

Total number of patients, n	503
Male, n (%)	228 (45.3)
Female, n (%)	275 (54.7)
Age (years)	58.2 ± 14.1
Level of 25[OH]D (ng/mL)	16.5 ± 7.9
Normal (≥32), n (%)	24 (4.8)
Insufficiency (20–32), n (%)	120 (23.9)
Deficiency (<20), n (%)	359 (71.4)
BMI (kg/m^2), n = 186	24.1 ± 4.6
Underweight (<18.5), n (%)	10 (2.0)
Normal (18.5–24.0), n (%)	236 (46.9)
Overweight (24.0–28.0), n (%)	214 (42.5)
Obese (≥28), n (%)	43 (8.5)
BMD (lumbar spine, g/cm^2), n = 206	0.878 ± 0.192
Normal (T ≥ −1.0), n (%)	70 (34.0)
Reduced bone mass (−2.5 < T < −1.0), n (%)	64 (31.1)
Osteoporosis (T ≤ −2.5), n (%)	72 (35.0)
Smoking history (male), n (%)	228
Yes	100 (43.9)
No	128 (56.1)
History of vitamin D supplementation, n (%)	503
Yes	31 (6.2)
No	472 (93.8)

BMI, body mass index.

each patient. Factors that may affect vitamin D levels were recorded including patients' age, gender, body mass index (BMI), bone mineral density (BMD), smoking history, history of vitamin D supplementation, season of admission, type of disease, etc. Taking into account different dietary habits and lifestyle of patients with different ages, subjects were divided into 3 age groups (18–50, 51–70, and ≥71 years of age). Subjects were also divided into 4 groups based on BMI criteria in China[10] including underweight (<18.5 kg/m^2), normal (18.5–24.0 kg/m^2), overweight (24.0–28.0 kg/m^2), and obese group (≥28 kg/m^2). Since smoking will reduce the absorption of calcium and thus increase bone loss,[11] smoking history 6 months prior to surgery was recorded. Preoperative BMDs and T-scores were recorded for patients who underwent dual-energy X-ray absorptiometry (DXA) before surgery. Preoperative scores according to neck disability index (NDI)[12] and ODI[13] were recorded for patients with cervical spondylosis and lumbar degenerative disease, respectively, to assess the degree of function obstacle.

Statistical analysis

All data were analyzed by SPSS software for Windows, version 19.0 (SPSS Inc, Chicago, Illinois). 25(OH)D concentrations (mean and standard deviation), rate of vitamin D insufficiency, and deficiency of all groups were analyzed. Potential risk factors (age, sex, BMI, BMD, smoking history, history of vitamin D supplementation, season, type of disease) were analyzed by univariate and multivariate regression models with serum 25(OH)D as the dependent variable and the factors aforementioned as independent predictors to determine risk factors independently associated with vitamin D insufficiency. OR, 95% confidence interval, and P value of each risk factor were recorded. $P \leq 0.05$ was considered statistically significant.

Results

Basic medical data of patients

A total of 503 patients were enrolled in this study including 275 females (54.7%) and 228 males (Table 1). The mean age was 58.2 ± 14.1 years, and 356 patients were over the age of 50 (70.8%). Mean BMI was 24.2 ± 2.9 kg/m with 214 overweight (42.5%) and 43 obesity patients (8.5%). Only 31 out of all 503 patients (6.2%) patients had history of vitamin D supplementation. A total of 101 patients (20.1%) had smoking history, which includes only 1 female smoker. Among 206 patients undergoing bone densitometry, 72 had osteoporosis, 64 showed osteopenia, and 70 were normal.

The number of cases in spring, summer, fall and winter were 113, 141, 161, and 88, respectively. The number of cases for each disease was as follows: 91 cases of cervical spondylosis, 228 cases of lumbar degenerative disease, 125 cases of osteoporotic vertebral compression fracture, 28 cases of spinal fracture, 21 cases of recurrent lumbar disc herniation, and 10 cases of spinal tumors.

Measurement of preoperative concentration of vitamin D

The mean value of preoperative 25(OH)D concentration was 16.5 ± 7.9 ng/mL, and the minimum and maximum values were 2.9 ng/mL and 49.2 ng/mL, respectively. Exactly 23.9% of 503 patients had vitamin D insufficiency, 71.4% had deficiency, and 4.8% were normal. 25 [OH] D concentration <9 ng/mL was observed in 86 patients, 9 to 20 ng/mL in 273 patients, 20 to 25 ng/mL in 73 patients, 25 to 30 ng/mL in 38 patients, 30 to 32 ng/mL in 9 patients, and ≥32 ng/mL in 24 patients.

Analysis of risk factors identified

The correlation between vitamin D deficiency with age, sex, BMI, BMD, smoking history, history of

Table 2 Univariate analysis of potential risk factors of vitamin D deficiency

	Normal, n (%)	Insufficiency, n (%)	Deficiency, n (%)	*P*
Age group (n = 503)				
18–50 years (n = 147)	10 (6.8)	31 (21.1)	106 (72.1)	0.364
51–70 years (n = 248)	8 (3.2)	66 (26.6)	174 (70.2)	
≥71 years (n = 108)	6 (5.6)	23 (21.3)	79 (73.1)	
Gender (n = 503)				
Male (n = 228)	19 (8.3)	72 (31.6)	137 (60.1)	<0.001
Female (n = 275)	5 (1.8)	48 (17.5)	222 (80.7)	
BMI (n = 503)				
Underweight (n = 10)	2 (20.0)	1 (10.0)	7 (70.0)	0.009
Normal (n = 236)	18 (7.6)	51 (21.6)	167 (70.8)	
Overweight (n = 214)	4 (1.9)	58 (27.1)	152 (71.0)	
Obese (n = 43)	0 (0.0)	10 (23.3)	33 (76.7)	
BMD (n = 206)				
Normal (n = 0)	2 (2.9)	20 (28.6)	48 (68.6)	0.577
Decreased bone mass (n = 64)	2 (3.1)	13 (20.3)	49 (76.6)	
Osteoporosis (n = 72)	0 (0.0)	15 (20.8)	57 (79.2)	
Smoking history (male) (n = 228)				
Yes (n = 100)	4 (4.0)	23 (23.0)	73 (73.0)	<0.001
No (n = 128)	15 (11.7)	49 (38.3)	64 (50.0)	
History of vitamin D supplementation (n = 503)				
Yes (n = 31)	5 (16.1)	6 (19.4)	20 (64.5)	0.009
No (n = 472)	19 (4.0)	114 (24.2)	339 (71.8)	
Type of disease (n = 503)				
Cervical spondylosis (n = 91)	3 (3.3)	20 (22.0)	68 (74.7)	>0.05
Lumbar degenerative diseases (n = 228)	10 (4.4)	51 (22.4)	167 (73.2)	
OVCFs (n = 125)	7 (5.6)	34 (27.2)	84 (67.2)	
Spinal fractures (n = 28)	1 (3.6)	8 (28.6)	19 (67.9)	
Spinal tumors (n = 10)	0 (0.0)	2 (20)	8 (80)	
Recurrent lumbar disc herniation (n = 21)	3 (14.3)	5 (23.8)	13 (61.9)	
Season (n = 503)				
Spring (n = 113)	1 (0.9)	21 (18.6)	91 (80.5)	0.001
Summer (n = 141)	6 (4.3)	41 (29.1)	94 (66.7)	
Fall (n = 161)	16 (9.9)	46 (28.6)	99 (61.5)	
Winter (n = 88)	1 (1.1)	12 (13.6)	75 (85.2)	
NDI (n = 91), ODI (n = 228)	41.9 ± 5.9	44.4 ± 6.3	51.5 ± 9.7	<0.001

BMD, bone mineral density; BMI, body mass index; NDI, neck disability index; ODI, Oswestry Disability Index; OVCF, osteoporotic vertebral compression fracture.

vitamin D supplementation, season, and type of disease (Table 2) was studied by univariate analysis. Results showed that no significant difference in vitamin D levels ($P = 0.364$) of patients among the 3 age groups. Female patients had a significant lower level of vitamin D compared with male patients ($P < 0.001$). BMI was correlated with vitamin D levels in that obese patients had significantly lower levels of vitamin D compared with nonobese patients ($P = 0.009$). Since there was only 1 female smoker in this study, the impact of smoking on vitamin D levels was analyzed in male patients. In 228 male patients, vitamin D levels of smokers were statistically lower than those of nonsmokers ($P < 0.001$). it was also revealed that patients with previous vitamin D supplementation had significantly higher levels of vitamin D compared with patients without history of supplementation ($P = 0.009$). No correlation between vitamin D levels and BMD or T scores of lumbar spine was identified in the analysis of 206 patients undergoing bone densitometry ($P = 0.316$). As shown in Fig. 1, the highest rate of vitamin D deficiency was observed in January (90.6%), and the lowest in September (44.8%). Additionally, the lowest level of vitamin D was observed in winter (13.0 ± 6.0 ng/mL), whereas the highest in fall (18.7 ± 8.9 ng/mL; $P < 0.05$). As shown in Fig. 2, patients in recurrent lumbar disc herniation group had the highest incidence of vitamin D deficiency (80%), followed by cervical spondylosis (74.7%) and lumbar degenerative disease group (73.2%). The lowest rate of vitamin D deficiency (61.9%) was observed in patients in spinal tumor group. Multivariate logistic regression analysis revealed that

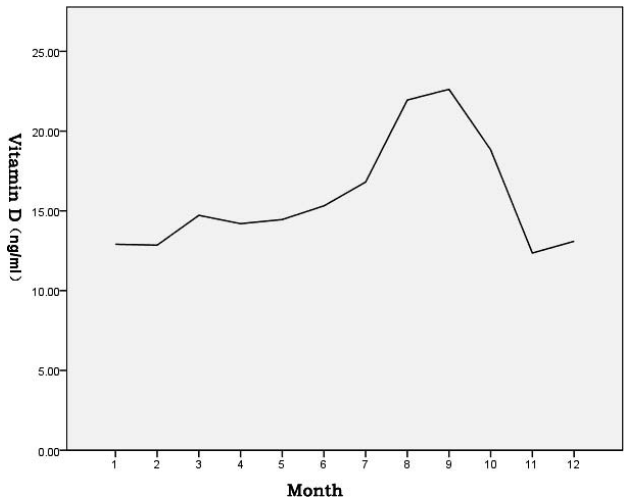

Fig. 1 Monthly mean value of vitamin D levels of different group.

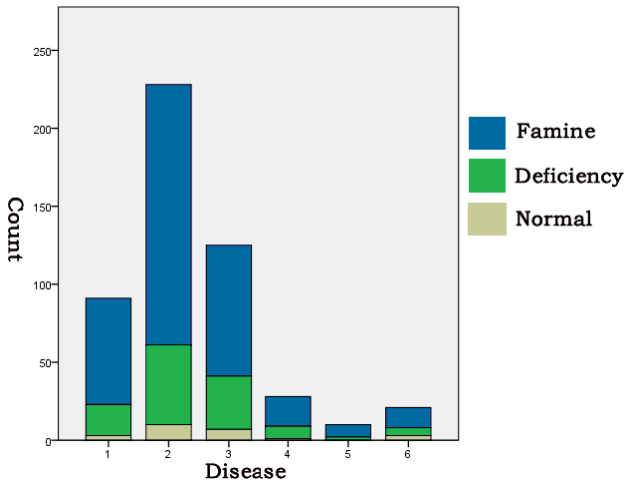

Fig. 2 Vitamin D status of patients with different type of diseases. Group 1, cervical spondylosis (n = 91); group 2, lumbar degenerative diseases (n = 228); group 3, osteoporotic vertebral compression fractures (n = 125); group 4, spinal fractures (n = 28); group 5, spinal tumors (n = 21); group 6, recurrent lumbar disc herniation (n = 10).

female, smoking history and winter were potential risk factors for vitamin D deficiency (Table 3).

Discussion

As an important fat-soluble vitamin, vitamin D is crucial for maintaining normal functions of skeletal muscles by maintaining homeostasis of calcium and phosphate metabolism in the body, and thus ensuring normal mineralization of bones.

Low levels of vitamin D (≤9 ng/mL) will reduce the intestinal absorption of calcium, cause compensatory rise of parathyroid hormone, lead to excessive absorption of bones, and thus result in osteoporosis and osteomalacia disease, impair functions of skeletal muscles, and increase the risk of fracture and its associated kyphosis.[1–3] Although research in other parts of the world has reported the incidence of vitamin D deficiency and its associated risk factors, no studies have been conducted on vitamin D status of spinal surgery patients in China. The current study investigated the vitamin D levels of 503 spinal surgery patients admitted in the First Affiliated Hospital of Nanjing Medical University. The rates of vitamin D insufficiency and deficiency were 23.9% and 71.4%, respectively. While no correlation was identified between vitamin D levels and age or BMD, factors including gender, BMI, smoking, vitamin D supplementation, and season were found to be related with vitamin D deficiency. Multivariate analysis suggested that being female, smoking, and winter were potential risk factors for vitamin D deficiency.

In a study of vitamin D levels in 313 patients with spinal surgery by Geoffrey E. Stoker *et al*, the incidences of vitamin D insufficiency and deficiency were 57% and 27%,[7] which were lower than those of this study. This may be associated with preoperative vitamin D supplementation in the research by Geoffrey E. Stoker, during which approximately 25% of patients had history of vitamin D supplementation. In contrast, a higher incidence of vitamin D deficiency in this study was probably due to a much lower rate of patients with preoperative vitamin D supplementation, suggesting that patients with vitamin D deficiency should be supplemented with vitamin D as soon as possible. Additionally, no significant difference was identified

Table 3 Multivariate regression analysis of potential risk factors associated with vitamin D deficiency (<20 ng/mL)

Risk factors	OR	95% CI	*P*
Gender			
Male	0.244	0.152–0.394	<0.001
Female	(Reference)		
Smoking			
Yes	2.270	1.264–4.078	0.006
No	(Reference)		
Season			
Spring	0.616	0.283–1.341	0.222
Summer	0.337	0.165–0.690	0.003
Fall	0.289	0.143–0.583	0.001
Winter	(Reference)		

between female and male groups in the research by Geoffrey E. Stoker, whereas this study showed that female patients had much lower levels of vitamin D compared with male patients ($P < 0.001$). Supplementation of calcium and vitamin D is often neglected in elderly patients due to the lack of attention on the prevention of osteoporosis in China. Moreover, reduced bone mass and severe bone osteoporosis are common in perimenopausal women with reduced estrogen levels due to recession of ovarian functions,[14,15] which might be the main reason for higher incidence of vitamin D deficiency of female patients compared with male patients in China.

The main way to get vitamin D for humans is by exposing to sunlight, during which 7-dehydrocholesterol (7-DHC) in the skin is converted to a precursor of vitamin D, and then is converted to vitamin D3 under the effect of ultraviolet light (mainly UVB).[16] The amount of vitamin D3 produced in the body depends on the latitude and sunshine hours received.[17]

In this study, the highest rate of vitamin D deficiency was observed in January (90.6%), and the lowest in September (44.8%). In addition, the lowest level of vitamin D was observed in winter (13.0 ± 6.0 ng/mL), whereas the highest was observed in fall (18.7 ± 8.9 ng/mL; $P = 0.001$). These results are similar to the findings in research of seasonal characteristics of vitamin D levels by Amy K. Kasahara *et al*, which shows that vitamin D levels of Americans reach the highest peak in late summer (August), and come to the lowest peak in late winter (February).[18] Both studies suggest that plenty of sunshine can increase levels of vitamin D in the body.

Previous research has proven that vitamin D levels are correlated with BMD. Clinical studies have shown that lumbar spine BMD of patients with osteoporosis caused by immunosuppression increases after a long-term $1,25(OH)_2D3$ treatment.[19] Animal experiments performed by Duque *et al* have demonstrated that $1,25(OH)_2D3$ dramatically increases BMD and bone mass of SAM P/6 mice by adjusting the balance between bone formation and resorption.[20] However, some other studies suggest that vitamin D levels are not correlated with BMD. A study of 206 patients performed by Kruavit has revealed no significant difference ($P = 0.577$) in mean lumbar spine BMD of vitamin D deficiency (0.869 ± 0.191 g/cm^2), insufficiency (0.898 ± 0.199 g/cm^2), and normal group (0.994 ± 0.082 g/cm^2).[21,22] In a study of menopausal women by O. Sahota *et al*, hip BMD of patients with vitamin D deficiency (≤30 nmol/L) and secondary hyperparathyroidism is lower than the other patients, whereas no significant difference in lumbar spine BMD has been identified among all patients.[23] The accuracy of lumbar spine BMD measurement is often affected by degenerative calcification and osteophyte formation around lumbar spine, and inflammatory changes of lumbar facet joints in elderly patients.[24] Moreover, in the study by Kruavit, patients with vitamin D deficiency and insufficiency are 154 (74.8%) and 48 patients (23.3%), respectively, whereas only 4 patients (1.9%) have normal levels of vitamin D. Such low proportion of patients with normal vitamin D levels may be another factor contributing to the conclusion that vitamin D levels are not correlated with lumbar spine BMD. Although the correlation between vitamin D levels and BMD remains controversial, it has been confirmed that vitamin D supplementation can increase BMD. Therefore, it is especially important for patients with osteoporosis to replenish vitamin D.

Among different groups of patients in this study, the group of recurrent lumbar disc herniation had the highest rate of vitamin D deficiency (80%), followed by a group of cervical spondylosis (74.7%) and lumbar degenerative disease (73.2%).

Previous study has shown that vitamin D can promote fracture healing in humans.[8] Vitamin D deficiency can cause osteoporosis and result in reduced vertebral bone density, trabecular thinning, and reduced holding power of screws at bone interface. Vitamin D deficiency may cause complications of screw loosening and prolapse in patients undergoing spinal fusion surgery, whereas adequate vitamin D levels are conducive to bone fusion after spinal fusion surgery by enhancing the stability of pedicle screws. Therefore, patients with vitamin D deficiency should be replenished with vitamin D, and the degree of osteoporosis of these patients should be systematically evaluated before surgery to choose an appropriate surgical approach.

Geoffrey E. Stoker *et al* found out that preoperative NDI and lumbar ODI scores were suitable indicators for vitamin D status.[7] Byung Ho Lee *et al* have shown that over 50% of patients with lumbar spinal stenosis exhibit vitamin D deficiency, and vitamin D levels are correlated with surgical outcomes (ODI and EQ-5D index). Such deficiency in vitamin D in these patients may be related to their limited outdoor activities.[8] In this study, NDI scores of 91 patients with cervical spondylosis and ODI scores of 228 patients with degenerative lumbar spine were measured before

surgery, and results have shown that increased NDI/ODI scores were significant correlated with vitamin D deficiency ($P < 0.05$).

The results of this study demonstrate that the incidences of preoperative vitamin D insufficiency (23.9%) and deficiency (71.4%) are very common in spinal surgery patients in China. Low levels of vitamin D may be related to lifestyle (sunshine duration, smoking, vitamin D supplementation) and reduced activity. Since vitamin D is very important for maintaining normal functions of skeletal muscles, vitamin D deficiency may influence the choice of surgical approach and prognosis. Therefore, preoperative screening of vitamin D in spinal surgery patients should be reinforced and patients with vitamin D deficiency should be subject to early intervention to facilitate prognosis and to reduce the incidence of long-term complications. Although this retrospective study may possibly have bias, and the prognosis of patients with vitamin D deficiency needs a long-term follow-up observation, the results of this study are still clinically significant.

Acknowledgments

This work was supported by National Natural and Science Foundation of China (81271988), Jiangsu Natural and Science Foundation (BK2012876). Lipeng Yu and Guoyong Yin contributed equally to this work. Qingqing Li and Jianwei Zhang contributed equally to this work.

References

1. Pfeifer M, Begerow B, Minne HW, Schlotthauer T, Pospeschill M, Scholz M. Vitamin D status, trunk muscle strength, body sway, falls, and fractures among 237 postmenopausal women with osteoporosis. *Exp Clin Endocrinol Diabetes* 2001;**109**(2):87–92
2. Gerdhem P, Ringsberg KA, Obrant KJ, Akesson K. Association between 25-hydroxy vitamin D levels, physical activity, muscle strength and fractures in the prospective population-based OPRA Study of Elderly Women. *Osteoporos Int* 2005;**16**(11):1425–1431
3. LeBoff MS, Hawkes WG, Glowacki J, Yu-Yahiro J, Hurwitz S, Magaziner J. Vitamin D-deficiency and post-fracture changes in lower extremity function and falls in women with hip fractures. *Osteoporos Int* 2008;**19**(9):1283–1290
4. Mithal A, Wahl DA, Bonjour JP, Burckhardt P, Dawson-Hughes B, Eisman JA. Global vitamin D status and determinants of hypovitaminosis D. *Osteoporos Int* 2009;**20**(11):1807–1820
5. Holick, MF. Vitamin D deficiency. *N Engl J Med* 2007;**357**(3):266–281
6. Bogunovic L, Kim AD, Beamer BS, Nguyen J, Lane JM. Hypovitaminosis D in patients scheduled to undergo orthopaedic surgery: a single-center analysis. *J Bone Joint Surg Am* 2010;**92**(13):2300–2304
7. Stoker GE, Buchowski JM, Bridwell KH, Lenke LG, Riew KD, Zebala LP. Preoperative vitamin D status of adults undergoing surgical spinal fusion. *Spine (Phila Pa 1976)* 2013;**38**(6):507–515
8. Doetsch AM, Faber J, Lynnerup N, Wätjen I, Bliddal H, Danneskiold-Samse B. The effect of calcium and vitamin D3 supplementation on the healing of the proximal humerus fracture: a randomized placebo-controlled study. *Calcif Tissue Int* 2004;**75**(3):183–188
9. Kim TH, Yoon JY, Lee BH, Jung HS, Park MS, Park JO. Changes in vitamin D status after surgery in female patients with lumbar spinal stenosis and its clinical significance. *Spine (Phila Pa 1976)* 2012;**37**(21):E1326–1330
10. LeBoff MS, Hawkes WG, Glowacki J, Yu-Yahiro J, Hurwitz S, Magaziner J. Vitamin D-deficiency and post-fracture changes in lower extremity function and falls in women with hip fractures. *Osteoporos Int* 2008;**19**(9):1283–1290
11. Qiao Z, Li-Xing S, Nian-Chun P, Shu-Jing X, Miao Z, Hong L *et al*. Serum 25(OH)D level and parathyroid hormone in Chinese adult population: a cross-sectional study in Guiyang urban community from southeast of China. *Int J Endocrinol* 2013;**2013**:150461
12. Krall EA, Dawson-Hughes B. Smoking increases bone loss and decreases intestinal calcium absorption. *J Bone Miner Res* 1999;**14**(2):215–220
13. Vernon H, Mior S. The Neck Disability Index: a study of reliability and validity. *J Manipulative Physiol Ther* 1991;**14**(7):409–415
14. Riggs BL, Melton LJ 3rd. The prevention and treatment of osteoporosis. *N Engl J Med* 1992;**327**(9):620–627
15. Gallagher JC. Moderation of the daily dose of HRT: prevention of osteoporosis. *Maturitas* 1999;**33** Suppl 1:S57–63
16. Holick MF, Frommer JE, McNeill SC, Richtand NM, Henley JW, Potts JT Jr. Photometabolism of 7-dehydrocholesterol to previtamin D3 in skin. *Biochem Biophys Res Commun* 1977;**76**(1):107–114
17. Heaney RP. The Vitamin D requirement in health and disease. *J Steroid Biochem Mol Biol* 2005;**97**(1-2):13–19
18. Kasahara AK, Singh RJ, Noymer A. Vitamin D (25OHD) serum seasonality in the United States. *PLoS One* 2013;**8**(6):e65785
19. Lips P, Duong T, Oleksik A, Black D, Cummings S, Cox D. A global study of vitamin D status and parathyroid function in postmenopausal women with osteoporosis: baseline data from the multiple outcomes of raloxifene evaluation clinical trial. *J Clin Endocrinol Metab* 2001;**86**(3):1212–1221

20. Duque G, Macoritto M, Dion N, Ste-Marie LG, Kremer R. 1,25(OH)2D3 acts as a bone-forming agent in the hormone-independent senescence-accelerated mouse (SAM-P/6). *Am J Physiol Endocrinol Metab* 2005;**288**(4):E723–E730
21. Kruavit A, Chailurkit LO, Thakkinstian A, Sriphrapradang C, Rajatanavin R. Prevalence of vitamin D insufficiency and low bone mineral density in elderly Thai nursing home residents. *BMC Geriatr* 2012;**12**:49
22. Kota S, Jammula S, Kota S, Meher L, Modi K. Correlation of vitamin D, bone mineral density and parathyroid hormone levels in adults with low bone density. *Indian J Orthop* 2013; **47**(4):402–407
23. Sahota O, Mundey MK, San P, Godber IM, Lawson N, Hosking DJ. The relationship between vitamin D and parathyroid hormone: calcium homeostasis, bone turnover, and bone mineral density in postmenopausal women with established osteoporosis. *Bone* 2004;**35**(1):312–319
24. Masud T, Langley S, Wiltshire P, Doyle DV, Spector TD. Effect of spinal osteophytosis on bone mineral density measurements in vertebral osteoporosis. *BMJ* 1993;**307**(6897):172–173