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Clinical Studies

Effect of vitamin D deficiency on surgical outcomes of degenerative cervical myelopathy

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ABSTRACT

Background: Due to its association with bone metabolic status and muscle strength/mass, vitamin D deficiency has the potential to affect neurological symptom recovery after surgery for degenerative cervical myelopathy (DCM). However, few studies have investigated the effects of vitamin D deficiency (serum 25(OH)D <20 ng/mL) on surgical outcomes in DCM patients. Herein, we investigated the prevalence of vitamin D deficiency in patients with DCM, and determined whether vitamin D deficiency affects surgical outcomes for DCM.

Methods: In this retrospective observational study we assessed the recovery rate 1 year after surgery in 91 patients diagnosed with DCM who underwent surgery. First, we analyzed the correlation between vitamin D levels and various background factors. Then, patients were divided into 2 groups according to vitamin D sufficiency, and univariate analysis was performed on vitamin D and surgical outcomes. Finally, Spearman correlation analyses were performed to identify factors correlated with recovery rate after surgery for DCM.

Results: The average Japanese Orthopedic Association score for the assessment of cervical myelopathy (C-JOA score) improved postoperatively. Age was positively correlated with vitamin D levels, and parathyroid hormone levels were negatively correlated with vitamin D levels. Among the 91 patients, 79.1% of patients were diagnosed with vitamin D deficiency. No significant differences in recovery rate were found between the vitamin D-deficient and vitamin D-sufficient groups. Finally, the Spearman correlation analysis showed a positive correlation between the preoperative C-JOA motor dysfunction score in the lower extremities and the recovery rate, while age demonstrated a negative correlation with recovery rate.

Conclusions: No association was found between vitamin D deficiency and clinical outcomes after surgery for DCM. The results of this study do not support the need to normalize vitamin D levels for achieving neurological improvements in patients with DCM.

Introduction

Vitamin D promotes calcium absorption in the intestine, thereby providing the calcium needed for bone calcification [1]. All cells that make up the skeleton (chondrocytes, osteoblasts, and osteoclasts) contain vitamin D receptors [2]. Vitamin D receptors are also present in the muscles [3], and vitamin D deficiency is associated with decreased muscle strength [4], and has been consistently associated with decreased muscle function and performance and increased disability [5]. In fact, a recent randomized controlled trial (RCT) demonstrated that supplementation

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with vitamin D and branched-chain amino acids (BCAAs) following lumbar spinal stenosis surgery significantly improved muscle strength when compared to the control group [6].

Regarding prior studies investigating the influence of vitamin D on the outcome of spine surgery, while 1 retrospective comparative study reported improved function and quality of life after lumbar spinal stenosis surgery with vitamin D supplementation [7], a recent RCT found that vitamin D and BCAAs supplementation did not improve clinical outcomes after surgery for lumbar spinal stenosis [6]. Given the expected improvement in neurological symptoms and muscle strength after surgery for degenerative cervical myelopathy (DCM) [8], we hypothesized that vitamin D deficiency may influence the improvement in neurological symptoms after surgery for DCM. However, few studies to date have yet investigated the effects of vitamin D deficiency (serum 25(OH)D <20 ng/mL) on surgical outcomes in patients with DCM. Thus, this study aimed to investigate the prevalence of vitamin D deficiency in patients with DCM and to determine whether vitamin D deficiency affects surgical outcomes for DCM.

Materials and methods

Study population

This study was approved by the institutional research ethics committee. The requirement for informed consent was waived due to the retrospective design and anonymization of patient data.

From August 2019 to August 2021, 132 consecutive patients diagnosed with DCM underwent surgery. The exclusion criteria were as follows: history of previous cervical surgery or renal failure (estimated glomerular filtration rate <35 mL/min/1.73m^2), and incomplete laboratory data or imaging results. Overall, 41 patients were excluded from the study. Demographic data, including age, sex, number of operated segments, and etiology of myelopathy were collected. Surgical indications and procedures (anterior decompression and fusion, anterior cervical disc replacement, laminoplasty, and posterior decompression and fusion) were determined based on the factors present in each patient, such as neurological status, presence of anterior compression, and spinal alignment.

Serum measurements

Blood samples were collected in an outpatient clinical setting before surgery. Serum 25(OH)D levels were measured to evaluate vitamin D deficiency. In this study, serum 25(OH)D level <20 ng/mL indicates vitamin D deficiency [9]. To evaluate patients' bone remodeling, we measured the following bone turnover markers: procollagen type 1 amino-terminal propeptide (P1NP) to assess bone formation and tartrate-resistant acid phosphatase 5b (TRACP-5b) to assess bone resorption [10]. These markers were used because they are less sensitive to diurnal variation, and are not affected by fasting or renal failure. Additionally, we assessed serum albumin as a nutritional status marker, hemoglobin A1c (HbA1c) as a glucose intolerance marker, calcium, estimated glomerular filtration rate, and intact parathyroid hormone (PTH).

We further investigated the relationship between vitamin D deficiency and other clinical factors, including age, sex, levels of operated segments, and nutritional status.

Outcome measures

Outcomes were assessed before and 1 year after surgery using the Japanese Orthopedic Association score for the assessment of cervical myelopathy (C-JOA score). The C-JOA score evaluates 6 categories of function, namely motor dysfunction in the upper and lower extremities, sensory function in the upper and lower extremities and trunk, and bladder function. These subscales are scored from 0 to 4, 4, 2, 2, 2, and 3, respectively, with a minimum score of 0, and an overall maximum score of 17 [11]. The recovery rate of the C-JOA score was calculated according to Hirabayashi's method using the following formula: recovery rate (%)=(postoperative C-JOA score−preoperative C-JOA score)×100 / (17−preoperative C-JOA score) [12].

Table 1
Baseline characteristics of patients and neurological outcomes

Characteristics	N = 91	Normal range
Age, years	66.1 ± 10.6	
Sex	Male 54 (59%)	
Albumin, g/dL	4.2 ± 0.3	4.0–5.0
Calcium, mg/dL	9.5 ± 0.4	8.5–10.2
HbA1c, %	6.1 ± 0.6	4.9–6.0
eGFR, mL/min/1.73m^2	71.9 ± 20.9	
Intact PTH, pg/mL	48.2 ± 20.5	10.3–65.9
P1NP, ng/mL	47.4 ± 22.3	Women 26.4–98.2 Men 18.1–74.1
TRACP-5b, mU/dL	387.5 ± 181.0	Women 120–420 Men 170–590
25(OH)D, ng/mL	15.9 ± 7.1	
Etiology	CSM 51 OPLL 40	
Surgical procedure	ADF 29 ACDR 2 LAMP 37 PDF 21 Anterior + posterior 2	
Preoperative C-JOA score	10.6 ± 2.8	
Postoperative 1 year C-JOA score	13.9 ± 2.3	
Recovery rate, %	49.5 ± 32.9	

Data are presented as mean ± standard deviation or n (%).
HbA1c, Hemoglobin A1c; eGFR, estimated glomerular filtration rate; PTH, Parathyroid Hormone; P1NP, procollagen type 1 amino-terminal propeptide; TRACP-5b, tartrate-resistant acid phosphatase 5b; CSM, cervical spondylotic myelopathy; OPLL, ossification of posterior longitudinal ligament; ADF, anterior decompresson and fusion; ACDR, anterior cervical disc replacement; LAMP, laminoplasty; PDF, posterior decompression and fusion; C-JOA, Japanese Orthopedic Association score for the assessment of cervical myelopathy

Statistical analysis

After assessing data normality with the Shapiro–Wilk test, we performed a Wilcoxon signed rank test to identify differences in the C-JOA score before and 1 year after surgery. The correlation between vitamin D levels and baseline variables was investigated using Spearman's correlation analysis. Subsequently, we used the Fisher's exact test or Mann–Whitney U test to compare the vitamin D sufficiency and deficiency groups. Additionally, the correlation between recovery rate and baseline variables was assessed using Spearman's correlation analysis. For all statistical analysis, JMP version 14 (SAS Institute) was used, except for power analysis, for which we used Stata 16 (Stata Corporation). P-values<.05 were considered significant. All data are presented as means ± standard deviation (SD).

Results

Patient demographics

A total of 91 patients were included in this study. The mean age was 66.1 years, and the mean serum 25(OH)D levels were 15.9 ng/mL (Table 1). The average preoperative C-JOA score was 10.6 points, which improved to an average of 13.9 points at 1 year postoperatively (p<.0001). The average recovery rate was 49.5% (Table 1).

Table 2
Spearman correlation analysis

	Vitamin D concentration	
Characteristic	ρ	p
Age, years	0.25	.02*
Albumin, g/dL	0.02	.84
Calcium, mg/dL	0.14	.18
HbA1c, %	0.01	.90
eGFR, ml/min/1.73m^2	−0.12	.26
Intact PTH, pg/mL	−0.27	.01*
P1NP, ng/mL	−0.04	.72
TRACP-5b, mU/dL	0.12	.25
Operated segments	−0.18	.11
Pre C-JOA score	0.02	.83
Pre C-JOA motor dysfunction in the upper extremities	0.10	.34
Pre C-JOA motor dysfunction in the lower extremities	0.10	.33
Postoperative 1-year C-JOA score	−0.01	.93
Recovery rate	−0.02	.87

HbA1c, hemoglobin A1c; eGFR, estimated glomerular filtration rate; PTH, parathyroid hormone; P1NP, procollagen type 1 amino-terminal propeptide; TRACP-5b, tartrate-resistant acid phosphatase 5b; C-JOA, Japanese Orthopedic Association score for the assessment of cervical myelopathy.
Correlation of baseline and operational variables with the vitamin D concentration.
ρ, Spearman's rank correlation coefficient.
* p<.05

Effect of vitamin D on surgical outcomes

Subsequently, we examined the correlation of blood vitamin D levels with background factors and outcomes. Age was positively correlated with vitamin D levels, and intact PTH levels were negatively correlated with vitamin D levels. However, the preoperative and postoperative C-JOA scores and recovery rate were not significantly correlated (Table 2).

Next, we divided patients into 2 groups according to their vitamin D levels. Of the 91 patients, 72 (79.1%) were diagnosed with vitamin D deficiency. Univariate analysis showed no significant differences between the 2 groups in terms of background factors, pre- and postoperative C-JOA scores, or recovery rate (Table 3).

Factors correlated with recovery rate after surgery for DCM

We subsequently conducted a Spearman correlation analysis to determine the factors correlated with the recovery rate in this cohort. The preoperative C-JOA motor dysfunction score in the lower extremities exhibited a positive correlation with the recovery rate, while age demonstrated a negative correlation with the recovery rate (Table 4). Additionally, we observed a tendency for albumin levels to correlate with the recovery rate (p=.05), whereas no other factors exhibited a significant correlation with the recovery rate.

Discussion

This study investigated the prevalence of vitamin D deficiency in patients with DCM, and further examined whether vitamin D deficiency affects surgical outcomes after surgery for DCM. In this study, 79.1% of patients undergoing surgery for DCM were diagnosed with vitamin D deficiency. In a previous prospective observational study, 71% of patients with cervical spondylotic myelopathy were vitamin D deficient [13]. In recent studies conducted on a cohort of healthy Japanese subjects, the prevalence of vitamin D deficiency was found to range from 52% to 54.1% [14,15]. DCM patients frequently experience gait disturbances, leading to reduced outdoor activities, and potentially increasing their vulnerability to vitamin D deficiency compared to individuals without the condition. Whether vitamin D supplementation helps prevent falls and fractures in the vitamin D-deficient group is debatable [16]. However, because patients with DCM have a higher risk of falls [17], it would be interesting to prospectively evaluate whether vitamin D supplementation in patients with DCM reduces falls.

Table 3
Univariate analysis

Characteristic	Vitamin D sufficient	Vitamin D deficient	p
No. of patients	19	72	
Age, years	69.0 ± 7.3	65.3 ± 11.2	.17
Sex	Male 12	Male 42	.80
	Female 7	Female 30	
Albumin, g/dL	4.2 ± 0.2	4.2 ± 0.3	.41
Calcium, mg/dL	9.6 ± 0.4	9.5 ± 0.3	.32
HbA1c, %	6.1 ± 0.5	6.1 ± 0.7	.31
eGFR, mL/min/1.73m^2	65.2 ± 19.8	73.7 ± 20.9	.08
Intact PTH, pg/mL	40.0 ± 50.4	50.4 ± 21.4	.07
P1NP, ng/mL	44.4 ± 17.1	48.2 ± 23.5	.40
TRACP-5b, mU/dL	393.6 ± 145.2	385.9 ± 190.1	.62
Etiology, n	CSM 10	CSM 41	.80
	OPLL 9	OPLL 31	
Surgical procedure, n	ADF 6	ADF 23	>.99
	ACDR 0	ACDR 2	
	LAMP 8	LAMP 29	
	PDF 5	PDF 16	
	Anterior + posterior 0	Anterior + posterior 2	
Operated segments	3.4 ± 1.4	3.8 ± 1.4	.38
Pre C-JOA score	10.9 ± 2.8	10.6 ± 2.8	.61
Postoperative 1-year C-JOA score	13.8 ± 2.1	13.9 ± 2.3	.79
Recovery rate, %	48.8 ± 28.3	49.7 ± 34.2	.79
Smoking, n (%)	2 (11)	11 (15)	.73

HbA1c, hemoglobin A1c; eGFR, estimated glomerular filtration rate; PTH, parathyroid hormone; P1NP, procollagen type 1 amino-terminal propeptide; TRACP-5b, tartrate-resistant acid phosphatase 5b; CSM, cervical spondylotic myelopathy; OPLL, ossification of posterior longitudinal ligament; ADF, anterior decompresson and fusion; ACDR, anterior cervical disc replacement; LAMP, laminoplasty; PDF, posterior decompression and fusion; C-JOA, Japanese Orthopedic Association score for the assessment of cervical myelopathy.
Association of baseline and neurological variables with vitamin D deficiency.
Data are presented as mean ± standard deviation or n (%).

Table 4
Spearman correlation analysis

	Recovery rate	
Characteristic	ρ	p
Age, years	−0.25	.02*
Albumin, g/dL	0.20	.05
Calcium, mg/dL	0.03	.75
HbA1c, %	−0.01	.91
eGFR, mL/min/1.73m^2	0.03	.74
Intact PTH, pg/mL	−0.03	.74
P1NP, ng/mL	0.08	.47
TRACP-5b, mU/dL	0.05	.65
Operated segments	−0.14	.20
Pre C-JOA score	−0.09	.40
Pre C-JOA motor dysfunction score in the upper extremities	−0.16	.13
Pre C-JOA motor dysfunction score in the lower extremities	0.25	.02*

HbA1c, hemoglobin A1c; eGFR, estimated glomerular filtration rate; PTH, parathyroid hormone; P1NP, procollagen type 1 amino-terminal propeptide; TRACP-5b, tartrate-resistant acid phosphatase 5b; C-JOA, Japanese Orthopedic Association score for the assessment of cervical myelopathy.
Correlation of baseline and operational variables with the recovery rate.
ρ, Spearman's rank correlation coefficient.
* p<.05

In the present study, no apparent association was found between vitamin D status and surgical outcomes following surgery for DCM. A previous prospective study reported that surgical outcomes in patients with DCM were worse in those with vitamin D deficiency [13], which is not consistent with the results of the present study. On the other hand, interestingly, both our study and the previous study showed a positive correlation between vitamin D levels and age [13]. It is worth noting that the cutoff for vitamin D deficiency in our study was 20 ng/mL, while the previous study used a cutoff of 30 ng/mL, which could have contributed to the disparity in results. In addition, there was a significant difference in age between the 2 groups in a previous study [13], and the possibility that this contributed to the results cannot be denied. Thus, a prospective, controlled study of whether vitamin D administration to patients with DCM and vitamin D deficiency or insufficiency would affect surgical outcomes should be conducted in the future.

In this study, intact PTH levels were weakly negatively correlated with vitamin D levels. Active vitamin D inhibits the synthesis and secretion of PTH [18]. PTH stimulates the kidney to produce active vitamin D; hence, the reduction in PTH secretion and production creates a feedback loop [18]. Indeed, consistent with our results, a negative correlation was found between serum PTH and vitamin D levels in the Japanese population evaluated in a prior cross-sectional study [19]. Interestingly, while patients with chronic spinal cord injury are known to exhibit bone loss, a higher percentage of patients with chronic spinal cord injury were vitamin D deficient [20]. Additionally, vitamin D and PTH were inversely correlated in patients with chronic spinal cord injury [21].

The higher prevalence of vitamin D deficiency in DCM patients compared to healthy individuals suggests the presence of underlying factors that may contribute to the trend toward mild secondary hyperparathyroidism in this patient population ($p=.07$). Consequently, these conditions could potentially enhance bone resorption, thereby increasing the likelihood of bone loss in patients with DCM. Due to their susceptibility to falls [17], DCM patients exhibit an increased risk of fractures, emphasizing the importance of assessing bone mass in this population.

In the present study, the preoperative C-JOA motor dysfunction score in the lower extremities exhibited a positive correlation with the recovery rate, while age demonstrated a negative correlation with recovery rate. A prior meta-analysis showed that elderly DCM patients are at an increased risk of perioperative complications [22]. In the present study, we observed a tendency for the postoperative recovery rate to decrease among patients with impaired walking function and elderly patients with DCM. Therefore, it may be advisable to consider surgical intervention before these conditions are reached. Prospective validation of this treatment strategy is also necessary.

This study has several limitations. First, this is a retrospective analysis, and the sample size may have been small. However, it is worth noting that the difference in recovery rate between the vitamin D-sufficient and vitamin D-deficient groups was minimal. This comparison holds little clinical significance, as the required sample size calculated based on the results of this study would require 19,096 patients in each group (alpha=0.05, power=0.80). Second, preoperative blood draws were conducted on an outpatient basis, and the time between blood draw and surgery was inconsistent. Therefore, the serum vitamin D levels and other parameters at the time of surgery may have changed since the time blood samples were collected. Further studies are required to address these limitations and validate our findings.

Conclusions

We found no association between vitamin D deficiency and clinical outcomes after surgery for DCM. Therefore, the study's results do not support the need to normalize vitamin D levels for achieving neurological improvements in patients with DCM.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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