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Original Article

Relationship between 25-hydroxy Vitamin D level and surgical site infection in spine surgery

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Received: 25 February 2024
Accepted: 25 April 2024
Published: 24 May 2024

DOI
10.25259/SNI_135_2024

Quick Response Code:

ABSTRACT

Background: 25-hydroxy Vitamin D (25[OH]D) level has been shown to have antimicrobial and wound healing effects in animal models. Low preoperative 25(OH)D has been shown to correlate with surgical site infection (SSI) in thoracolumbar spine surgery.

Methods: This study involved 545 patients undergoing thoracolumbar spine surgery from 2012 to 2019 at an academic medical center. We evaluated the serum 25(OH)D level (i.e., adequate level = level 30–60 ng/dL), along with SSI, body mass index, and smoking status. Statistical analysis was done using bivariate analysis with Fisher's exact, Wilcoxon rank-sum test and multivarible logisitic regression analyses.

Results: We included 545 patients in the study, and there were no statistical differences in the average preoperative 25(OH)D between SSI and non-SSI groups. The average 25(OH)D in the non-SSI group was 31.6 ng/dL ± 13.6, and the SSI group was 35.7 ng/dL ± 20.2 ($P = 0.63$).

Conclusion: SSI rates following thoracolumbar spine surgery were not affected by preoperative 25(OH)D levels.

Keywords: Fusion, Laminectomy, Spine, Surgical site infection, Vitamin D

INTRODUCTION

Surgical site infection (SSI) following spine surgery can range from 0.2% to 16.7%.[6,7] Despite the importance of this topic, the current understanding of risk factors still needs to be improved.[8] In adult orthopedic surgery patients, the prevalence of Vitamin D hypovitaminosis has been noted to be 43%, likely increasing the rate of SSI.[1,4] SSI was defined as a deep SSI needing irrigation and debridement.[10] This study investigated whether low preoperative 25-hydroxy Vitamin D (25[OH]D) levels increased the risk of postoperative SSI following thoracolumbar spine surgery.

MATERIALS AND METHODS

With IRB approval, we evaluated Vitamin D levels in 545 patients undergoing thoracolumbar spine surgery (2012–2019) surgical procedures performed by one fellowship-trained orthopedic

spine surgeon at a single academic center. The primary outcome of the study was the presence of SSI within 12 months of surgery (SSI group and non-SSI group).

Antibiotic protocol

All patients received preincisional antibiotics (cephalexin without penicillin allergy). During surgery, we utilized a solution containing povidone-iodine and normal saline irrigation of the wound while, followed by placement of intrawound vancomycin powder (i.e., above/below fascia lumbar/thoracic fusions 2 g, 1 g for lumbar laminectomies, and 250 mg for microdiscectomies).[4,5,9]

Most preoperative 25(OH)D levels were obtained within 30 days of surgery [Table 1]. In our institution an adequate 25(OH)D was identified as 30-60 ng/dL. Greater than 60 ng/dL was identified as potentially harmful. Low 25(OH)D or deficiency (<20 ng/dL) and insufficient (21–29 ng/dL) levels were also defined.[3] Multiple other variables were studied [Tables 2 and 3].

Statistical analysis

Bivariate analysis (i.e., using Fisher's exact test and Wilcoxon rank-sum test) compared characteristics between non-SSI and SSI cohorts. We also utilized multivariable logistic regression analyses [Tables 2 and 4].

RESULTS

The average 25(OH)D in the non-SSI group was 31.6 ng/dL ± 13.6, and 35.7 ng/dL ± 20.2 in SSI group (p=0.63) [Table 1].

Of 545 patients who met the inclusion criteria, the SSI rate was 1.65% (nine patients) [Table 5].

The SSI group had a higher proportion of smokers, 33.3%, versus 20.9% in the non-SSI group ($P = 0.29$) [Table 5]. Most of the SSI group was identified as the American Society of Anesthesiologists (ASA) class 3 or 4 (62.5%), whereas most of the non-SSI group was identified as ASA 1 or 2 (53.6%, $P = 0.29$) [Table 5]. There was no statistical significance in infection rates for revision compared to nonrevision surgeries ($P = 0.61$) [Table 5].

Culture data

Six patients' cultures grew single Gram positives (i.e., *Bacillus* species or Methicillin-sensitive *Staphylococcus aureus* [MSSA]) or Gram-negatives (i.e., *Enterococcus faecalis*, *Proteus mirabilis*) or two *Pseudomonas* species. Three patients' cultures were polymicrobial and included *Staphylococcus epidermis*, *Bacillus* species, *Micrococcus* species; *Enterococcus faecium*, *Escherichia coli*, *Klebsiella pneumoniae*; *P. mirabilis*, diphtheroid species.

Table 1: Bivariate analysis of Vitamin D data in non-SSI and SSI groups.

	Non-SSI (*n*=536), %	SSI (*n*=9), %	*P*-value
25(OH) D (ng/dL) (mean±SD)	31.6±13.6	35.7±20.2	0.63
25(OH) D			
<20 ng/mL deficiency	21.7	33.3	0.041*
20–29 ng/mL insufficiency	27.9	11.1	
30–60 ng/mL adequate	46.8	33.3	
>60 ng/mL potentially harmful	3.6	22.2	
Season			
Winter: December–March	32.7	44.4	0.51
Spring: April–May	12.9	22.2	
Summer: June–August	26.7	22.2	
Fall: September–November	27.8	11.1	

*P<0.05 is significant, SSI: Surgical site infection, SD: Standard deviation, 25(OH) D: 25-hydroxy vitamin D

Table 2: Multivariate logistic regression model using EOM guidelines.

Units	Multivariate OR (95% CI)	*P*-value
25(OH) D level		
<20 ng/dL deficiency	Ref	
20–29 ng/dL insufficiency	0.26 (0.021–3.07)	0.282
30–60 ng/dL adequate	0.12 (0.013–1.04)	0.054
>60 ng/dL potentially harmful	1.59 (0.13–19.21)	0.714
Gender		
Male	Ref	
Female	9.45 (0.91–97.94)	0.060
Age		
Years	1.08 (1.00–1.17)	0.053
BMI		
Kg/m²	1.08 (0.96–1.22)	0.201
Surgery		
Thoracolumbar/thoracic	3.11 (0.38–25.19)	0.287
Diagnosis		
Deformity	2.36 (0.24–23.48)	0.465
Diabetes		
No	Ref	
Yes	3.70 (0.55–24.88)	0.178
Rheumatoid arthritis		
No	Ref	
Yes	13.09 (0.81–211.10)	0.070

BMI: Body mass index, EOM: Endocrine Society, CI: Confidence interval, OR: Odds ratio, 25(OH) D: 25-hydroxy vitamin D

Multivariable analysis

We did not find a significant association between preoperative 25(OH)D levels and an increased risk for postoperative SSIs.

Table 3: Multivariate logistic regression model using IOM guidelines.

Units	Multivariate OR (95% CI)	*P*-value
Gender		
Male	Ref	
Female	7.84 (0.79–77.99)	0.079
Age		
Years	1.06 (0.99–1.14)	0.080
BMI		
Kg/m²	1.08 (0.96–1.21)	0.215
Surgery		
Thoracolumbar/thoracic	3.52 (0.48–26.05)	0.217
Diagnosis		
Deformity	3.04 (0.36–25.77)	0.307
Diabetes		
No	Ref	
Yes	3.68 (0.56–24.27)	0.176
Rheumatoid arthritis		
No	Ref	
Yes	5.99 (0.45–80.38)	0.177
25(OH) D level		
<12 ng/dL deficiency	Ref	
12–20 ng/dL insufficiency	0.64 (0.046–8.98)	0.743
20–50 ng/dL adequate	0.13 (0.01–2.00)	0.143
>50 ng/dL potentially harmful	0.29 (0.014–5.96)	0.423

BMI: Body mass index, CI: Confidence interval, OR: Odds ratio, 25(OH) D: 25-hydroxy Vitamin D, IOM: Institute of medicine

Table 4: Multivariate logistic regression model using Vitamin D as a continuous variable.

Units	Multivariate OR (95% CI)	*P*-value
Gender		
Male	Ref	
Female	6.34 (0.71–56.86)	0.099
Age		
Years	1.05 (0.98–1.12)	0.151
BMI		
Kg/m²	1.10 (0.98–1.23)	0.098
25(OH) D		
ng/dL	0.99 (0.93–1.05)	0.729
Surgery		
Thoracolumbar/thoracic	3.28 (0.41–26.54)	0.265
Diagnosis		
Deformity	3.06 (0.34–27.16)	0.316
Diabetes		
No	Ref	
Yes	4.25 (0.69–26.04)	0.117
Rheumatoid arthritis		
No	Ref	
Yes	6.01 (0.48–75.39)	0.164

BMI: Body mass index, CI: Confidence interval, OR: Odds ratio, 25(OH) D: 25-hydroxy Vitamin D

However, the odds of SSIs were lower among those with higher 25(OH)D levels (except for the potentially harmful group) [Table 1]. We did not identify a statistical difference in SSI rates based on gender, age, surgery, smoking status revision surgery, diagnosis, diabetes mellitus, rheumatoid arthritis and 25(OH)D, and other factors identified in multivariable logistic regression analyses [Tables 2-4].

Table 5: Bivariate analysis of patient characteristics in non-SSI and SSI cohorts.

	Non-SSI (*n*=536), %	SSI (*n*=9), %	*P*-value
Gender			
Male	50.4	11.1	0.02*
Female	49.6	88.9	
Age (years)	56±15.6†	64±7.5	0.07
BMI	31.6±6.5†	34.8±9.6	0.36
Race/ethnicity			
African-American	17.2	22.2	0.78
Hispanic	3.2	0	
Asian	0.8	0	
Native American	0.4	0	
White	78.5	77.8	
Smoking			
No	79.1	66.7	0.29
Yes	20.9	33.3	
Diabetes			
No	92.5	77.8	0.15
Yes	7.5	22.2	
Rheumatoid arthritis			
No	97.6	88.9	0.21
Yes	2.4	11.1	
ASA			
1 or 2	53.6	37.5	0.29
3 or 4	46.4	62.5	
Diagnosis			
Degenerative	81.6	66.7	0.084
Deformity	5.2	33.3	
Tumor	3.2	0	
Trauma	10.1	0	
Surgery type			
Lumbar discectomy	33.6	33.3	0.052
Lumbar posterior spinal fusion	37.3	33.3	
Lumbar laminectomy	21.3	0	
Thoracolumbar/ thoracic fusion	7.8	33.3	
Revision surgery			
Yes	12.69	0.00	0.61
No	87.31	100.00	

*$P<0.05$ is significant, except for revision surgery. $P<0.299$ is significant, †Mean±Standard deviation, SSI: Surgical site infection, BMI: Body mass index, ASA: American Society of Anesthesiologists

DISCUSSION

We evaluated the role of preoperative 25(OH)D levels regarding the incidence of SSI following 545 thoracolumbar operations;

Table 6: Studies relating to SSI in the orthopedic surgery patient population and their outcome measures.

Study	Design	Population	Sample Size	Variable evaluated	Study findings
Bogunovic *et al.*	Retrospective cohort	Patients scheduled for orthopedic surgery	723	Serum vitamin D level.	It is common for patients undergoing orthopedic surgery to have low serum Vitamin D levels.
Donnally III *et al.*	Retrospective cohort	Patients who underwent lumbar spinal fusion	150	Pre and postoperative Vitamin D levels	Pre and postoperative Vitamin D levels were not significantly associated with risk of pseudarthrosis, revision surgery, hardware failure, or 1-year VAS pain score after lumbar spine fusion surgery.
Holick *et al.*	Systematic review	_	_	Serum 25-hydroxyvitamin D	There is not sufficient evidence to recommend screening individuals who are not at risk for vitamin D deficiency.
Mesfin *et al.*	Case-control	Patients undergoing spine tumor surgery	151	Protocol to reduce SSI	Betadine irrigation and intrawound vancomycin powdered a significant decrease in SSI rates following spine tumor surgery.
Onishi *et al.*	Retrospective cohort	Spinal surgery patients	323	Two methods to reduce SSI	Normal saline irrigation after 90 s of 1% PVP-I pooling every 1.5 h was associated with a reduction in the incidence of deep SSI.
Ravindra *et al.*	Prospective study	Elective spinal fusion patients	133	Serum Vitamin D level	Serum Vitamin D levels may affect nonunion rate and time to fusion.
Schimmel *et al.*	Case-control	Spinal fusion patients	171	Risk factors for SSI	Patients who had had a previous spinal surgery are a high-risk group for infection compared with those who never had surgery.
Stoker *et al.*	Retrospective cohort	Spinal fusion patients	313	Serum Vitamin D level	It is common for patients' spinal fusion to have abnormal serum Vitamin D levels.
Ter Gunne and Cohen	Retrospective cohort	Spine surgery patients	3174	Risk factors for SSI	A prior SSI, diabetes, and obesity all increased the risk of SSI
Zajonz *et al.*	Prospective cohort	Patients with PPI after total hip and knee arthroplasty	240	Postoperative 25 OH Vitamin D3 and calcium levels	Acute PPIs of the hip and knee joints show significantly reduced calcium and 25 OH Vitamin D3 levels compared with chronic infections.

SSI: Surgical site infection, PPI: Periprosthetic infections, PVP-I: Povidone-iodine, VAS: Visual analog scale

9 (1.65%) patients developed deep SSIs needing irrigation and debridement. There was no statistically significant difference in average preoperative 25(OH)D between non-SSI and SSI groups (P = 0.63), including multivariable analyses. We did not identify a higher risk of SSI in patients with higher body mass index, smoking, diabetes mellitus, rheumatoid arthritis, or ASA class. Donnally *et al.* performed a single-center retrospective study of 150 patients to investigate the relationship between 25(OH)D deficiency and outcome after lumbar spinal fusions.[2] They found no correlation between 25(OH)D and postoperative pseudarthrosis, revision, and instrumentation complications at 1 year [Table 6].

In contrast, Ravindra *et al.* examined the association between perioperative 25(OH)D and nonunion rates in elective spine surgery patients. They demonstrated that insufficient 25(OH)D was associated with prolonged time to fusion and a lower fusion rate.[6] Stoker *et al.* analyzed the prevalence of 25(OH)D in 313 patients undergoing spinal fusion at a single institution; 57% of the patients had 25(OH)D <30 ng/dL and 27% with levels <20 ng/dL [Table 6].[8] In our study, the SSI group had a higher deficiency distribution <20 ng/dL than the non-SSI group (P = 0.041). Although our study did not identify a statistically significant correlation between 25(OH)D level and surgical infection rate, the odds of SSIs were lower among those with higher 25(OH)D (except for the potentially harmful group).

CONCLUSION

Our study showed no significant differences in preoperative 25(OH)D levels between non-SSI and SSI groups undergoing 545 patients with thoracolumbar surgery.

Ethical approval

The research/study was approved by the Institutional Review Board at the University of Rochester, number STUDY00000497, dated 2015.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

Addisu Mesfin MD: Speaker fees Depuy, Grant Nuvasive, Lodging/travel Medtronic.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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How to cite this article: Liu S, Sulovari A, Joo P, Thirukumaran C, Benn L, Mesfin A. Relationship between 25-hydroxy Vitamin D level and surgical site infection in spine surgery. Surg Neurol Int. 2024;15:173. doi: 10.25259/SNI_135_2024