Research Article

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Preoperative Vitamin D Deficiency Is Associated With Higher Postoperative Complications in Arthroscopic Rotator Cuff Repair

Abstract

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From the Department of Orthopaedic Surgery, David Geffen School of Medicine at UCLA (Mr. Harada, Dr. Arshi, Dr. Fretes, Dr. McAllister, and Dr. Petrigliano) and the Department of Orthopaedic Surgery, Keck School of Medicine of USC (Mr. Formanek, Dr. Gamradt), Los Angeles, CA.

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JAAOS Glob Res Rev 2019;3:e075

DOI: 10.5435/ JAAOSGlobal-D-19-00075

Copyright © 2019 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of the American Academy of Orthopaedic Surgeons. This is an open access article distributed under the Creative Commons Attribution-NoDerivatives License 4.0 (CC BY-ND) which allows for redistribution, commercial and non-commercial, as long as it is passed along unchanged and in whole, with credit to the author. **Introduction:** Rotator cuff tears are one of the most common injuries worldwide, yet it is difficult to predict which patients will have poor outcomes after arthroscopic rotator cuff repair (RCR). The purpose of this study was to identify an association between preoperative vitamin D (25D) levels and postoperative complications in arthroscopic RCR.

Methods: From a national claims database, patients undergoing arthroscopic RCR with preoperative 25D levels were reviewed. Patients were stratified into 25D-sufficient (≥20 ng/dL) or 25D-deficient (<20 ng/dL) categories and examined for development of postoperative complications. Multivariate logistic regression was performed using age, sex, and Charlson Comorbidity Index (CCI) as covariates. From this, risk-adjusted odds ratios (ORs) were calculated comparing complications between the two groups.

Results: One thousand eight hundred eighty-one patients with measured preoperative 25D levels were identified; 229 patients were 25D deficient (12.2%). After adjusting for age, sex, and Charlson Comorbidity Index, 25D-deficient patients had increased odds of revision RCR (OR 1.54, 95% confidence interval 1.21 to 1.97, P < 0.001) and stiffness requiring manipulation under anesthesia (OR 1.16, 95% confidence interval 1.03 to 2.03, P = 0.035).

Conclusions: Vitamin D deficiency is associated with a greater risk of postoperative surgical complications after arthroscopic RCR and may be a modifiable risk factor. Further investigation on preoperative vitamin D repletion is warranted.

R otator cuff tears are one of the most common and costly injuries worldwide. Some studies estimate a prevalence of 20% to 34% in the asymptomatic general population with

incidence increasing to 64% in patients with shoulder pain.¹⁻³ As of 2002, these injuries accounted for over 4 million hospital visits and \$560 million dollars in surgical expenses.^{4,5}

Shoulder arthroscopy likely accounts for a notable portion of these expenses and remains the technique of choice for rotator cuff repair (RCR) given favorable, although variable, patientreported and functional outcomes. Despite these positive results, studies have found a number of preoperative risk factors for arthroscopic RCR failure, ultimately drawing into question which patients are surgically optimal candidates.⁶

Recently, 25-hydroxyvitamin D (25D) has become a popular topic of investigation because its benefits to musculoskeletal health are believed to extend beyond bone mineralization. Studies have found that 25D deficiency may be associated with decreased bone and soft-tissue healing, as well as dysregulation of inflammatory biomarkers.^{7,8} Some studies have also found that 25D may have a role in preventing postoperative surgical site infection (SSI) because it is believed to have a role in upregulating wound closure and the innate immune system.⁸ Specifically, 25D interfaces with the vitamin D receptor to transcriptionally upregulate epidermal stem cells, phagocytosis, and other antimicrobial peptides.8,9 Together, this may effectively the minimize risk of SSI and supports the notion that repletion of 25D may be a modifiable perioperative risk factor to minimize adverse outcomes in surgery.8,9 Interestingly, a previous study by Hegde et al¹⁰ in 2016 supports this hypothesis because they noted that 25D deficiency was associated with an increased risk of adverse postoperative complications after total knee arthroplasty. However, to date, no studies have examined what role perioperative 25D levels have on outcomes in arthroscopic RCR.

The purpose of this study was to further explore the benefits of 25D in

arthroscopic RCR by using a large administrative claims patient registry to examine the relationship between preoperative 25D levels and subsequent surgical complications. Given recent literature regarding the utility of 25D, it was hypothesized that low preoperative 25D levels would be associated with higher incidence of adverse outcomes after arthroscopic cuff repair.

Methods

The authors performed a retrospective study of administrative claims through the PearlDiver Patient Record Database (PearlDiver) to identify patients who underwent arthroscopic RCR. This commercially available database consists of roughly 20 million patient records from the nationwide health insurance provider, Humana. Diagnoses and procedures were queried using defined billing codes classified by the International Classification of Diseases, Ninth Revision (ICD-9), Current Procedural Terminology (CPT), and Logical Observation Identifiers Names and Codes.

Patients who underwent arthroscopic RCR between 2007 and 2016 were identified using CPT-29827 (arthroscopy, shoulder, surgical; with RCR), with identification of preoperative plasma 25D levels (Logical Observation Identifiers Names and Codes-1989-3) within the 90 days preceding the procedure. Those who were 25D sufficient $(\geq 20 \text{ ng/mL})$ were compared with those who were 25D deficient (<20 ng/mL) against a series of postoperative surgical complications using corresponding CPT codes (Table 1). 25D cutoffs were based on definitions established by the Institute of Medicine as criteria for

diagnosis and treatment with repletion.¹¹ Surgical complications included revision RCR, SSI requiring incision and drainage, arthroscopic débridement, revision to arthroplasty, and stiffness requiring manipulation under anesthesia (MUA). Patient demographics such as age (reported in 5-year groups), sex, geographic region, other medical comorbidities (using *ICD-9* codes), and Charlson Comorbidity Index (CCI) were also collected (Table 2). The CCI is a wellvalidated metric for 1-year mortality using 22 medical conditions.¹²

Inferential statistics comparing the baseline age, sex, regional, and comorbidity distributions of the two 25D-stratified cohorts was performed using chi-square analysis. A two-sided Student t-test was used to assess CCI between the two cohorts. Statistical significance was defined as P < 0.05. PearlDiver's statistics package was used to fit a multivariate logistic regression using age, sex, and CCI as covariates, and to calculate the adjusted odds ratios (ORs), 95% confidence intervals (CIs), and associated *P*-values for each surgical complication with 25D-deficient patients defined as the exposed group. All additional analysis was performed using SPSS version 21 software (IBM Corp).

Results

Between 2007 and 2016, 1,881 patients undergoing arthroscopic RCR had measured preoperative 25D levels in the Humana database (Table 2). Of these, 229 (229/1,881 = 12.2%) were found to be 25D deficient (<20 mg/dL). Both 25D-deficient and -sufficient groups were similar in distribution and had a median and mode age in the 65 to 69 years group (P =0.237) (Table 2). In addition, sex

None of the following authors or any immediate family member has received anything of value from or has stock or stock options held in a commercial company or institution related directly or indirectly to the subject of this article: Mr. Harada, Dr. Arshi, Dr. Fretes, Mr. Formanek, Dr. Gamradt, Dr. McAllister, and Dr. Petrigliano.

Complication Category	CPT Code	Code Description			
Revision RCR	CPT-29827	Arthroscopy, shoulder, surgical; with RCR			
I&D	CPT-11981	Insertion, nonbiodegradable drug delivery implant			
	CPT-23030	Incision and drainage, shoulder area; deep abscess or hematoma			
	CPT-23031	Incision and drainage, shoulder area; infected bursa			
	CPT-23035	Incision, bone cortex (eg, osteomyelitis or bone abscess), shoulder area			
	CPT-23040	Arthrotomy, glenohumeral joint, with exploration drainage, or removal of foreign body			
	CPT-23100	Arthrotomy, glenohumeral joint, including biopsy			
	CPT-23107	Arthrotomy, glenohumeral joint, with joint exploration, with or without removal of loose o foreign body			
Arthroscopic débridement	CPT-29820	Arthroscopy, shoulder, surgical; synovectomy, partial			
	CPT-29821	Arthroscopy, shoulder, surgical; synovectomy, complete			
	CPT-29822	Arthroscopy, shoulder, surgical; débridement, partial			
	CPT-29823	Arthroscopy, shoulder, surgical; débridement, extensive			
Arthroplasty	CPT-23470	Arthroplasty, glenohumeral joint; hemiarthroplasty			
	CPT-23472	Arthroplasty, glenohumeral joint; total shoulder (glenoid and proximal humeral arthroplasty)			
Stiffness requiring MUA	CPT-23020	Capsular contracture release (eg, sever type procedure)			
	CPT-23700	MUA, shoulder joint, including application of fixation apparatus (dislocation excluded)			
	CPT-29825	Arthroscopy, shoulder surgical; with lysis and resection of adhesions, with or without manipulation			

CPT = Current Procedural Terminology, MUA = manipulation under anesthesia, RCR = rotator cuff repair

distribution was equivalent between the two groups, as females comprised 66.8% and 63.8% of the 25D-deficient and -sufficient cohorts, respectively (P =0.373). Most cases were reported in the South geographic region (25D-deficient 80.3%; 25D-sufficient 81.4%). The 25D-deficient cohort had a higher comorbid rates of diabetes mellitus (P = 0.002), hypertension (P = 0.022), obesity (P = 0.006), and cerebrovascular disease (P = 0.036) (Table 3).

The most common complication after arthroscopic RCR was arthro-

scopic débridement (25D-deficient 24.0%; 25D-sufficient 28.7%), followed by revision RCR (25D-deficient 8.3%; 25D-sufficient 6.6%) and stiffness, requiring MUA (25D-deficient 4.8%; 25D-sufficient 3.8%) (Table 4). After adjusting for age, sex, and comorbidities using multivariate logistic regression, 25D-deficient patients undergoing arthroscopic RCR were more likely to undergo future revision RCR (OR 1.54, 95% CI 1.21 to 1.97, P < 0.001) and MUA for postoperative stiffness (OR 1.16, 95% CI 1.03 to 2.03, P = 0.035). Risks of postoperative SSI, arthroscopic débridement, and conversion to arthroplasty were not statistically significantly different between the two cohorts (Table 4).

Discussion

As shown, vitamin D deficiency is associated with increased postoperative complications in arthroscopic RCR. This finding comes in light of other studies highlighting the

Table 1

Table 2

Age, Sex, Region	Age, Sex, Regional, and CCI Distributions of Study Cohorts					
	Vitamin D Deficient (<20 ng/mL) N = 229	Vitamin D Nondeficient (≥20 ng/mL) N = 1,652				
Age						
Less than 40	4	13				
40-44	4	18				
45-49	12	42				
50-54	18	118				
55-59	33	183				
60-64	39	234				
65-69	45	460				
70-74	45	364				
75-79	20	158				
80+	9	62				
Sex						
Male	76	598				
Female	153	1,054				
Geographical region						
Midwest	31	189				
Northeast	2	12				
South	184	1,344				
West	12	107				
CCI						
Mean \pm SD	2.76 ± 3.05	2.46 ± 2.62				

CCI = Charlson Comorbidity Index

significance of 25D as a potential modifiable risk factor to limit muscle strains, improve fracture outcomes, promote articular cartilage health, and decrease postoperative complications in arthroplasty.^{10,13-16} Although mechanistically it is unclear how normalizing 25D can lead to improved outcomes in arthroscopy, addressing deficiency preoperatively is, in principle, a simple task and has the potential to improve clinical results at a relatively low cost. Further study is warranted to investigate what role preoperative normalization of 25D may have on decreasing rates of revision RCR and stiffness requiring MUA.

The role of 25D in human biology is constantly evolving, though with ample evidence to support bone, muscle, and calcium and phosphoregulatory mechanisms. Conversely, 25D's role in tendon-to-bone healing is poorly understood. Rotator cuff surgery heavily relies on this healing mechanism, and failure is often attributed to ineffective tendon-tobone repair. Some studies report as high as a 22% to 36% rate of recurrent tears after arthroscopic RCR.^{6,17,18} In turn, this has stimulated the need for augmentation of the procedure, with recent developments including dermal allografts and scaffolding to create more stable biomechanical constructs.^{19,20} Similarly, the role of supplementing 25D in these repairs is under consideration because it has been shown to mitigate the inflammatory milieu, with reports of improved healing in

animal models.²¹ Theoretically, this implies that a lack of 25D could promote an environment hostile to adequate repair and predispose the patient to increased postoperative complications. Irrespective, a deeper understanding of the biochemical role of 25D in facilitation of tendonto-bone healing is required to validate these conclusions and should be a target of future study.

As predicted, vitamin D deficiency was associated with a greater average CCI and associated medical comorbidities. Within the 25Ddeficient cohort, there were higher rates of obesity (P = 0.006), diabetes mellitus (P = 0.002), hypertension (P = 0.022), and cerebrovascular disease (P = 0.036) than in the 25Dsufficient group. In the current literature, 25D deficiency has been associated with each of these conditions, although its role in pathogenesis is still an active topic of debate. In the obese, 25D deficiency is thought to be diluted by body mass because some data have shown obese individuals have identical serum concentrations to nonobese after controlling for body size.22 This deficiency, whether dilutional or not, is thought to allow inflammatory processes in the metabolic syndrome, leading to damage of β -cells in the pancreas and cardiovascular dysfunction. This subsequently leads to an increase in insulin resistance and coronary, cerebral, and peripheral vascular diseases.²³ Notably, these comorbidities suggest that the 25D-deficient cohort inherently comprises a sicker population, and may confound why this group had more complications overall.

However, after controlling for these comorbidities, low levels of 25D were markedly associated with an increased need for RCR revisions. Re-tear or incomplete healing of the rotator cuff is common after RCR, although it may be of questionable clinical significance. Some studies

Table 3

Baseline Comorbidity Characteristics of Vitamin D-Stratified Cohorts

	Vitamin D Deficient (<20 ng/mL) (n = 229)			Vitamin D Nondeficient (≥20 ng/mL) (n = 1,652)	
Comorbidity	Ν	Frequency (%)	N	Frequency (%)	P Value
Diabetes mellitus	117	51.1	630	38.1	0.002
Hypertension	190	83.0	1,258	76.2	0.022
Coronary artery disease (CAD)	77	33.6	479	29.0	0.151
Nonischemic heart disease	35	15.3	181	11.0	0.055
Cerebrovascular disease	23	10.0	104	6.3	0.036
Peripheral vascular disease	62	27.1	395	23.9	0.296
Obesity	86	37.6	473	28.6	0.006
Body mass index (BMI) $>$ 30	47	20.5	291	17.6	0.283
Body mass index (BMI) > 40	17	7.4	94	5.7	0.298
Chronic obstructive pulmonary disorder (COPD)	47	20.5	288	17.4	0.253
Chronic kidney disease (CKD)	46	20.1	343	20.8	0.813
Chronic liver disease	23	10.0	135	8.2	0.340
Connective tissue disorder	33	14.4	194	11.7	0.247

Bolded values indicate statistical significance at p < 0.05.

Table 4

Frequency and Adjusted OR of Surgical and Medical Complications After RCR							
Postoperative Complications (at 1 Year)	Vitamin D Deficient (<20 ng/mL) (n = 229)		Vitamin D Nondeficient (≥20 ng/mL) (n = 1,652)		Adjusted OR (For Vitamin D		
	Ν	Frequency (%)	Ν	Frequency (%)	Deficient Patients) ^a	P Value	
Revision RCR	19	8.3	109	6.6	1.54 (1.21–1.97)	<0.001	
Arthroscopic débridement	55	24.0	474	28.7	1.11 (0.92–1.33)	0.295	
Stiffness requiring MUA	11	4.8	62	3.8	1.16 (1.03–1.03)	0.035	
Conversion to arthroplasty	3	1.3	18	1.1	1.16 (0.55–2.45)	0.703	
SSI with I&D	1	0.4	7	0.4	0.83 (0.21–3.34)	0.792	

CCI = Charlson Comorbidity Index, MUA = manipulation under anesthesia, OR = odds ratio, RCR = rotator cuff repair, SSI = surgical site infection ^a Adjusted OR derived from multivariate logistic regression with patient age, sex, and CCI used as covariates. Bolded values indicate statistical significance at p < 0.05.

note that the structural integrity of a RCR does not correlate with clinically notable differences in strength or pain, and patients will often report functional improvement despite failure to heal.²⁴⁻²⁸ As such, revision is often reserved for patients with persistent functional deficits or intolerable levels of residual pain.^{4,26,29} These outcomes, although likely multifactorial, could theoretically be affected by 25D deficiency. However, further investigation is required to determine how

25D is associated with the development of postoperative complications.

This study also found postoperative stiffness requiring MUA to be associated with 25D deficiency after controlling for age, sex, and comorbidities. Stiffness in the shoulder can be a direct result of postoperative inflammation because the upregulation of cytokines in an inflammatory response is thought to lead to myofibroblast-induced capsular hyperplasia and fibrosis. This subsequently decreases capsular volume and limits shoulder range of motion.³⁰ Although speculative, 25D may have a role in this pathogenesis secondary to its role in inflammatory regulation. Some studies have highlighted 25D's ability to inhibit myofibroblast activity, and it is thought that supplementation of this nutrient may have a role in preventing fibrosis and scarring.^{31,32} As such, the increased incidence of stiffness in the 25D-deficient cohort may be explained by uninhibited myofibroblast proliferation, leading to increased scarring and decreased mobility at the glenohumeral joint. Of note, previous studies estimate the prevalence of comorbid adhesive capsulitis in the diabetic population to be around 10% to 30%.33 Given the large incidence of diabetes in the study population, it is possible that this condition explains part of the increased incidence of postoperative shoulder stiffness as well. Although no clear etiology exists regarding the development of shoulder stiffness in diabetics, it is believed to also be related to chronic inflammation and increased fibroblast activity.34 Theoretically, by acting through similar mechanisms, this implies that diabetes and 25D deficiency might synergistically increase the risk of developing postoperative shoulder stiffness. Future study should aim to identify the role of 25D in this pathogenesis and determine whether supplementation can decrease the risk of this outcome.

Limitations

First, the PearlDiver database is less amenable to the study of patients on an individual level, and instead allows efficient analysis of larger groups. As such, ability to interpret and analyze patient-specific outcomes is likely inferior to that of chart review. Furthermore, data within PearlDiver is entirely driven by billing codes. As a result, entries may be subject to clerical error, miscategorization, or inconsistencies due subjective interpretation to of respective CPT or ICD codes. Similarly, given that the queried CPT and ICD codes were limited in detailing the specifics of a particular diagnosis or procedure, comparisons between severity of rotator cuff tear and different techniques for repair could not be accounted for in analysis. Next, some degree of selection bias was

likely also present because not all patients had preoperative 25D levels drawn. This likely means providers ordered this laboratory test in a cohort at greater risk for 25D deficiency, which may have skewed the observed results. This could imply that a large portion of the 25Dsufficient cohort may represent a receiving population adequate repletion, thus strengthening the argument that supplementation may mitigate the outcomes observed in the deficient group. Last, although beyond the scope of this study, these results do not comment on postoperative function or other subjective, patient-reported outcomes.

Conclusions

Among the patients scheduled for an arthroscopic RCR between 2007 and 2016, 12.2% were found to be deficient in 25D in the 90 days preceding surgery. This was associated with a greater risk of postoperative stiffness requiring MUA and need for future RCR revision. Although the role of 25D in the development of postoperative complications is unclear at this time, this study suggests the possibility that preoperative repletion could have a role in mitigating adverse outcomes. Further study should aim to investigate what role 25D supplementation may have on markedly reducing postoperative complications after arthroscopic RCR.

References

Levels of evidence are described in the table of contents. In this article, references 3, 7, 12, 13, 14, and 27 are level II studies. References 1, 6, 10, 22, 23, and 29 are level III studies. References 4, 5, 11, 15, 17, 18, 20, 24, 25, 26, 28, 30, and 33 are level IV studies. References 2, 8, 9, 16, 19, 21, 31, 32, and 34 are level V studies.

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