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Preoperative prealbumin and transferring

Relation to 30-day risk of complication in elective spine surgical patients

Erin Takemoto, PhD[a], Jung Yoo, MD[a], Sabina R. Blizzard, BA[a], Jackilen Shannon, PhD[b], Lynn M. Marshall, ScD[a,*]

Abstract

Summary of Background Data: There is growing interest in identifying nutritional biomarkers associated with poor outcomes of elective spine surgery. Prealbumin and transferrin are both biomarkers of nutritional status that can be obtained from clinical laboratories. However, associations of preoperative measures of these nutritional biomarkers across their range with risk of complications from spine surgery have not been fully investigated.

Objective: Determine associations of preoperative prealbumin and transferrin levels with 30-day risk of complication among elective spine surgery patients.

Study Design: Cohort study with preoperative prealbumin and transferrin collected as standard of care.

Outcome Measures: 30-day risk of medical complication.

Methods: Data were obtained from medical records of 274 consecutive adult patients ages ≥50 years who underwent elective spine surgery from June 2013 to June 2014. Prealbumin (mg/dL), serum transferrin (mg/dL), and preoperative factors were abstracted from medical records. Prealbumin and transferrin levels were categorized into quartiles and as below versus median or higher. The primary outcome measure was 30-day risk of medical complication, such as renal failure or infections. Associations of the biomarkers with outcome risk were assessed with chi-square tests and with risk ratios (RR) and 95% confidence intervals (CI) estimated with multivariable log-binomial regression.

Results: The 274 adults studied had a median prealbumin level of 27.4 mg/dL and a median transferrin level of 265.0 mg/dL. The 30-day risk of complication was 12.8% (95% CI: 8.8%–16.7%). Risk of complication did not vary by quartile for either prealbumin ($P = .26$) or transferrin ($P = .49$) and was not associated either with prealbumin (below median, RR = 1.1, 95% CI: 0.8, 1.5) or transferrin (below median, RR = 1.1, 95% CI: 0.8, 1.6).

Conclusions: Among adults undergoing elective spine surgery, the 30-day risk of complication was not associated with prealbumin or transferrin. Nutrition status, as measured by prealbumin and transferrin, does not appear to be associated with complication risk.

Level of evidence: Level III.

Abbreviations: ASA = American Society for Anesthesia, BMI = body mass index, CI = confidence interval, CV% = coefficients of variation, EMR = electronic medical record, RR = risk ratio, SD = standard deviation.

Keywords: adults, epidemiology, nutritional status, orthopedics, outcomes, postoperative complications, prealbumin, risk factors, spine surgery, transferrin

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[a] Oregon Health & Science University, School of Medicine Department of Orthopaedics and Rehabilitation, [b] Oregon Health & Science University, OHSU-PSU School of Public Health, Portland, OR.

[*] Correspondence: Lynn M. Marshall, Oregon Health & Science University, School of Medicine Department of Orthopaedics and Rehabilitation, 3181 SW Sam Jackson Park Road, Mail Code CB669, Portland, OR 97239-3098 (e-mail: marshaly@ohsu.edu).

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1. Introduction

Nearly 80% of the US population experience neck or back pain at some time during adulthood.[1–3] Together, back and neck pain comprise the second most common reason for physician office visits.[4–6] Adults with back or neck pain often elect surgical intervention and rates of spine surgery have substantially increased over the last 40 years, especially among older adults.[7–9] Because of increasing rates of surgery on increasingly older populations, higher complication rates may be expected. Understanding modifiable risk factors for the development of complications of spine surgery could facilitate presurgical interventions to reduce risk.[10]

Preoperative nutritional status reflects a patient's ability to successfully undergo a physically demanding surgical procedure, resist infection, and heal from surgical incisions.[11,12] Albumin, prealbumin, and transferrin are all nutritional biomarkers that are used clinically to assess overall nutritional status.[13–18] Prealbumin may be a more sensitive marker than albumin due to its shorter half-life and ability to reflect more immediate changes in nutrition.[14,16,19] Transferrin is also a sensitive and specific indicator of early iron deficiency that may serve as another important biomarker.[20] As surgery poses significant stress on the body and triggers a depletion of nutrients, we reasoned that nutritional status represented by prealbumin or transferrin could influence the development of complications following spine surgery.

The association of preoperative nutritional status as a potentially important modifiable risk factor for complications of spine surgery has not been fully investigated to date. Two small studies using convenience samples showed that low presurgical prealbumin level was positively associated with surgical site infection after spine surgery. However, inference from these studies is hampered by limitations including missing prealbumin levels for many potentially eligible patients, lack of assessment of the full range of prealbumin levels, and restricting the outcome to infection in a single surgical site.[21,22] Thus, further investigation is needed to determine the extent to which presurgical prealbumin or transferrin are associated with risk of any complications following spine surgery and whether there is evidence of a dose-response effect across the range of values for these biomarkers.

To more clearly determine the association of preoperative nutritional status with risk of complications following spine surgery, we used data from our academic medical center in which presurgical prealbumin and transferrin are obtained as a clinical standard on all patients undergoing elective spine surgery. We hypothesized that lower compared with higher levels of preoperative prealbumin or transferrin would be associated with an increased risk of complication within 30 days of surgery. We further hypothesized a dose-response such that complication risk would be reduced with successively higher levels of these nutritional biomarkers.

2. Materials and methods

Since 2013, the Oregon Health and Science University Spine Center surgeons have ordered prealbumin and transferrin to be measured among their surgical patients as a standard of care. We aimed to assess the first year of experience in obtaining these biomarkers in relation to spine surgery complications. At clinical laboratories, prealbumin is assayed using an immunoturbidimetric assay with a lower limit of detection of 3 mg/dL, and transferrin is assayed using quantitative immunoturbidimetry with a lower limit of detection is 10 mg/dL. Coefficients of variation (CV%) for the prealbumin assay range from 1.2% to 2.1% for intra-assay variation and from 1.9% to 2.2% for interassay variation. Intra- and interassay CV% for the transferrin assay are, respectively, 1.9% and 2.7%.

2.1. Selection of potentially eligible participants

We performed a retrospective cohort study using OHSU electronic medical records (EMR). The study procedures described here were approved by the Institutional Review Board. Potentially eligible patients were identified by systematically searching the EMR and billing systems for patients who met the following criteria: age at admission ≥ 50 years; elective cervical, thoracic, thoraco-lumbar or lumbar spine surgery by one of 4 primary spine surgeons; dates of service from 6/1/2013 through 6/1/2014; and preoperative blood work completed at the OHSU clinical laboratories.

Of the 442 patients identified from the initial query, we excluded 88 (19.9%) due to non-elective surgery, 69 (15.6%) for missing prealbumin or transferrin levels, 12 (2.7%) for multiple distinct surgeries in the study period, and 2 (0.4%) for missing follow-up. The remaining 274 patients comprised the analytic cohort (Fig. 1).

2.2. Ascertainment of serum measures, patient and surgical characteristics

Information on serum prealbumin, transferrin levels, patient demographic characteristics, and peri-operative factors was manually abstracted from EMRs for patients in the analytic cohort. Patient characteristics were gender, body mass index (BMI), marital status, current tobacco and alcohol use, American Society for Anesthesia (ASA) score, blood pressure, and history of spine surgery.[23] Peri-operative characteristics were number of vertebrae levels fused, surgical approach (anterior, posterior, anterior–posterior), estimated blood loss, blood transfusion use, length of hospital stay, and total anesthesia time.

Data on surgical complications were abstracted without knowledge of the presurgical information described above. Prior to abstraction, the authors created a list of 27 specific complications that were likely to occur following spine surgery (Supplemental Table 1, http://links.lww.com/MD/C856). Examples include wound problems (e.g., seroma, dehiscence), infections (e.g., urinary tract infection, pneumonia), morbidity (e.g., renal failure, pulmonary embolism) and mortality. A spine surgeon who was blinded to prealbumin and transferrin level then reviewed and adjudicated the list of complications abstracted from the records.

To assess reliability of the abstracting procedure, data were independently re-abstracted on a random sample of 10% of the initial cohort and compared to the original values. The percent concordance was 98%. Discrepancies were then reviewed and resolved.

2.3. Statistical analysis

Distributions of the primary independent variables, prealbumin and transferrin, were examined. Distributions of patient pre- and peri-operative characteristics were compared according to prealbumin and transferrin quartiles. One-way ANOVA or Kruskal–Wallis ANOVA were used to compare continuous variables and chi-square or Fisher's exact tests for categorical variables.

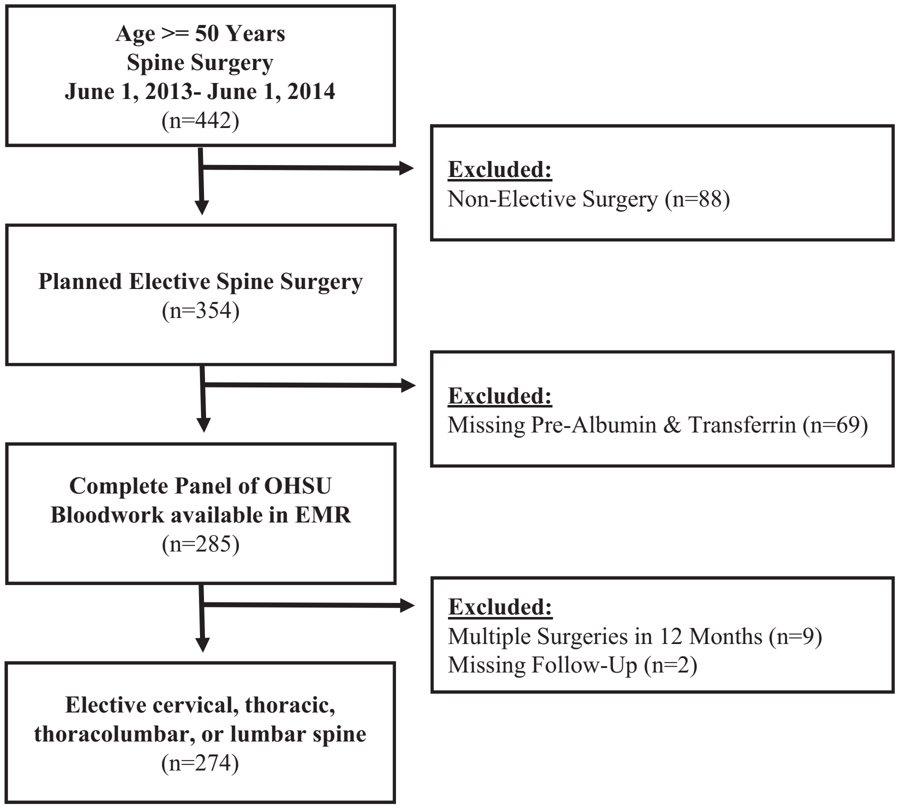

Figure 1. Creation of analytic cohort.

Frequency of complications was measured with cumulative incidence, a measure of risk for complication occurring during the 30-day postoperative follow-up period. The crude and adjusted relation between the biomarkers and risk of complications was assessed using chi-square tests and log-binomial regression, respectively. Risk ratios (RR) and 95% confidence intervals (CI) were computed as the ratio of the cumulative incidence in the group with lower biomarker values to the cumulative incidence in the group with higher biomarker levels. Risk ratios greater than 1.0 indicate increased risk of complication.

Variables assessed as confounders of the association between prealbumin, transferrin, and complication risk were gender, age, BMI, blood pressure, ASA score, history of previous spine surgery (Y/N), and number of levels fused. Variables were considered confounders if they changed the RR by >10%.[24] The final model included BMI, levels fused, gender, age, and ASA score. Lumbar, thoracic, and thoraco-lumbar surgeries may be more invasive than cervical surgeries, thus representing a unique patient population. To address this issue, we repeated the foregoing analyses after restriction of the analytic cohort to patients with lumbar, thoracic, and thoraco-lumbar surgeries. All analyses were performed using SAS software, Version 9.4 of the SAS System (Cary, NC).

3. Results

The analytic cohort was 46.4% women and the mean age (standard deviation, SD) was 64.0 (8.8) years. Mean (SD) prealbumin levels were 27.5 mg/dL (±5.6 mg/dL) and mean (SD) transferrin levels were 266.8 mg/dL (±43.8 mg/dL). Malnutrition is defined as prealbumin <15 mg/dL and transferrin < 170 mg/dL.[25,26] The prevalence of malnutrition was low, being 1.8% (5 patients) when defined as prealbumin <15.0 mg/dL (Fig. 2) and 0.3% (1 patient) when defined as transferrin <170.0 mg/dL (Fig. 3).

Distributions of patient demographic and preoperative characteristics were examined according to quartile of prealbumin (Table 1). Patients in the lowest prealbumin quartile were more likely to be male, and have a higher ASA score compared with patients in the highest quartile. Distributions of peri-operative characteristics varied little by quartile of prealbumin, with the exception that those in the lowest quartile tended to have 4 or more levels fused compared to those in highest prealbumin quartile (Table 2). When distributions of demographic, preoperative, and peri-operative characteristics were examined by quartile of transferrin, patients in the lowest compared with the highest transferrin quartile were more likely to be younger, female and have a lower BMI (Supplemental Table 2, http://links.lww.com/MD/C856). Distributions of peri-operative characteristics varied very little by quartile of transferrin (Supplemental Table 3, http://links.lww.com/MD/C856).

During the 30-day follow-up period, 35 patients experienced at least 1 postoperative complication, resulting in a cumulative incidence of 12.8% (95% CI: 8.8%, 16.7%). In quartiles 1 through 4 of prealbumin, respectively, the number (%) with complications were 6 (9%), 12 (17%), 11 (16%), and 6 (9%). In quartiles 1 through 4 of transferrin, respectively, the number (%) with complications were 6 (9%), 10 (14%), 7 (10%), and 12 (17%). Risk of complication did not vary significantly by quartile for either prealbumin ($P=0.26$) or transferrin ($P=0.49$). Thus, for the remaining analyses, we categorized prealbumin and transferrin as below the median (quartiles 1 and 2) and at or above the median (quartiles 3 and 4 together) to maximize

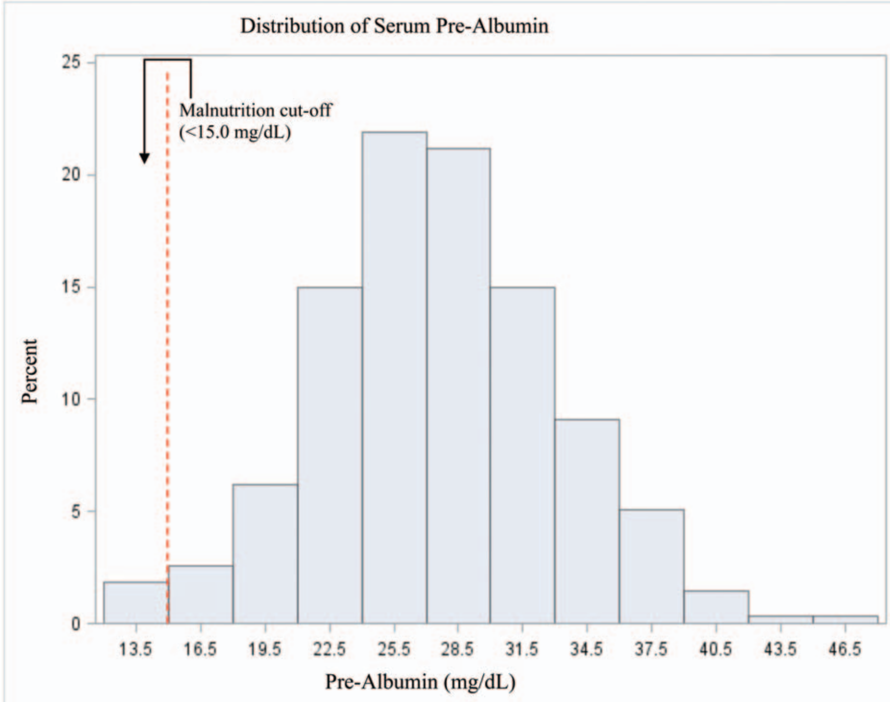

Figure 2. Distribution of serum prealbumin.

statistical power for the multivariable analyses. Accordingly, risk of complication was 12% in patients who had prealbumin levels above the median value and 13% in patients with levels below the median value. Risk of complication was 14% in patients with transferrin levels above the median value and in 12% in patients with levels below the median value.

Before and after adjustment for potential confounding factors, the association of low serum prealbumin with risk of complication

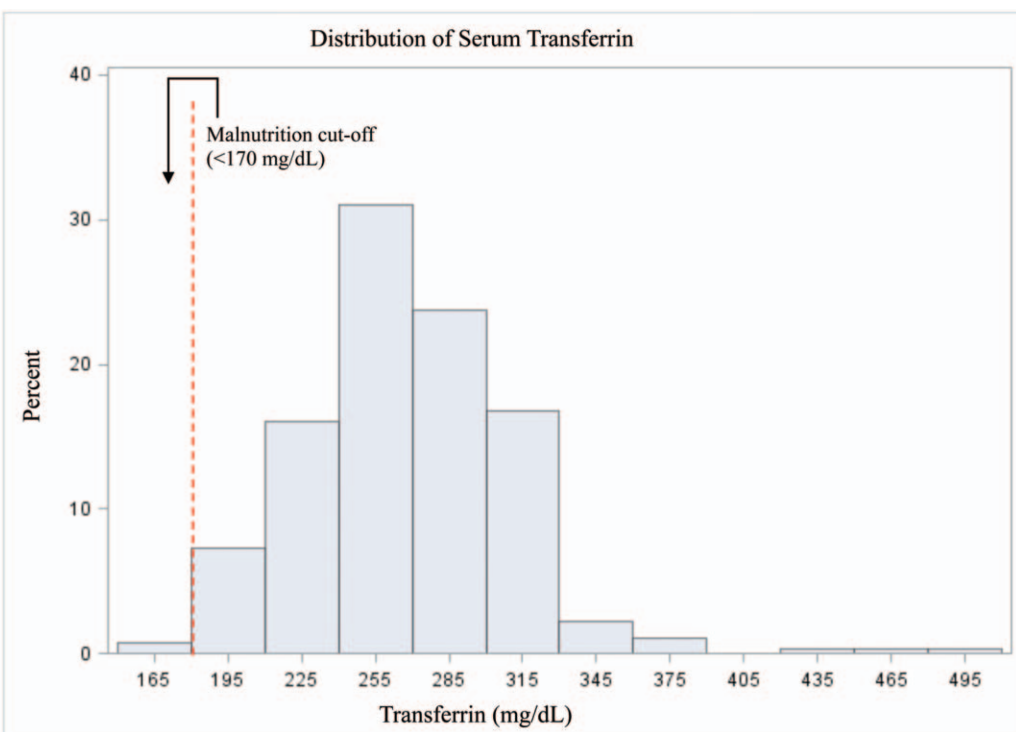

Figure 3. Distribution of serum transferrin.

Table 1

Distribution of demographic and preoperative characteristics among 274 adult elective spine surgery patients according to prealbumin (mg/dL) quartile 2013–2014.

	Quartile 1 12.9 - <23.8 mg/dL (N=67)	Quartile 2 23.8 - <27.4 mg/dL (N=69)	Quartile 3 28.8 - <30.8 mg/dL (N=68)	Quartile 4 30.8 – 47.9 mg/dL (N=70)	
Mean±SD in quartile	**20.6±2.8**	**25.6±1.0**	**28.9±1.0**	**34.6±3.2**	
Patient characteristic	**N (%)**	**N (%)**	**N (%)**	**N (%)**	***P*-value**
Age at surgery, years					
50–59	18 (19)	22 (23)	31 (32)	23 (24)	.43*
60–69	26 (26)	26 (26)	20 (20)	27 (27)	
70+	23 (28)	21 (26)	17 (21)	20 (25)	
Gender					
Male	48 (33)	40 (27)	33 (22)	26 (18)	<.01*
Female	19 (15)	29 (23)	35 (28)	44 (35)	
Marital status					
Single	22 (31)	19 (26)	16 (22)	15 (21)	.46*
Married/Domestic partner	44 (23)	48 (25)	47 (24)	55 (28)	
Current BMI, kg/m^2					
Normal	13 (26)	10 (20)	11 (22)	16 (32)	.44*
Overweight	21 (21)	22 (22)	30 (30)	27 (27)	
Obese	33 (27)	37 (30)	27 (22)	27 (22)	
Smoking status					
Not current smoker	33 (27)	25 (21)	28 (23)	35 (29)	.50†
Current smoker	7 (22)	2 (22)	8 (25)	10 (31)	
Former smoker	28 (23)	36 (30)	32 (27)	25 (21)	
Alcohol status					
No current use	35 (29)	26 (22)	33 (28)	23 (20)	.11*
Current Use	21 (18)	34 (30)	23 (20)	37 (32)	
Unknown	12 (28)	9 (21)	12 (28)	10 (23)	
American Society of Anesthesiologists' Score					
Scores 1 & 2	24 (18)	33 (25)	41 (30)	38 (28)	.03*
Scores 3 & 4	43 (31)	36 (26)	27 (20)	32 (23)	
Systolic blood pressure					
< 120 mm Hg	18 (25)	22 (31)	14 (19)	17 (24)	.73*
120–139 mm Hg	28 (25)	29 (25)	30 (26)	27 (24)	
≥140 mm Hg	21 (24)	18 (20)	24 (27)	26 (29)	
Previous spine surgery					
No	30 (22)	30 (22)	35 (26)	39 (29)	.43*
Yes	37 (26)	39 (28)	33 (24)	31 (22)	

* *P*-value using chi-square test.
† *P*-value using Fisher's exact test.
kg/m=kilogram per meter, mg/dL=milligram per decilitre, mm Hg=millimeter of mercury, N=number, SD=standard deviation.

was null (Table 3). Likewise, there was no evidence of a linear trend in the RR when we repeated the analysis using the prealbumin as a continuous variable (RR=1.0, 95% CI: 0.9, 1.1 (*P*-trend=.90) per 1 mg/dL increase in prealbumin). We also observed no association of low transferrin with the risk of complication (Table 4). Similarly, when we repeated the analysis using transferrin as a continuous variable the RR was 1.0 (95% CI: 0.99, 1.01; *P*-trend=.30).

We performed 2 sensitivity analyses. First, we compared the analytic cohort of 274 patients to the 69 who were missing prealbumin and transferrin. All preoperative and perioperative characteristics were compared between the 2 groups, and no characteristics significantly differed between the patient groups. For those patients missing these variables, the overall cumulative incidence of complication was 10.6% (95% CI: 1.8%, 19.5%), similar to that among the 274 patients comprising the analytic cohort. Second, when we also repeated the analyses restricting to patient's undergoing lumbar, thoracic, and thoraco-lumbar surgeries, the observed association of prealbumin and transferrin with risk of post-operative complications remained null (data not shown).

4. Discussion

This retrospective cohort study of 274 elective spine surgery patients aged 50 years and older provided new information on biomarkers of nutritional status in relation to 30-day risk of complications. First, we observed that <2% of this cohort had malnutrition, as defined by prealbumin and transferrin levels below 15.0 mg/dL and 170 mg/dL, respectively. The low prevalence of presurgical malnutrition supports examination of the entire range of nutritional biomarkers in relation to surgical outcomes. Second, contrary to our hypothesis, we observed no association of presurgical prealbumin or transferrin levels with 30-day risk of medical complications and no evidence of any dose-response reduction in risk with increasing levels.

We did observe that certain preoperative health and surgical characteristics indicative of poorer health were associated with being in the lowest quartiles of prealbumin. Patients with higher ASA scores, a preoperative measure of overall patient health, were more likely to be in the lowest quartiles of prealbumin. Additionally, patients undergoing procedures where more than 4 spinal levels were fused were also more likely to be in the lowest

Table 2

Distribution of peri-operative characteristics among 274 adult elective spine surgery patients according to pre-albumin quartile 2013–2014.

Patient characteristic	Quartile 1 (N=67) N (%)	Quartile 2 (N=69) N (%)	Quartile 3 (N=68) N (%)	Quartile 4 (N=70) N (%)	*P*-value
Number of levels fused					
No spine fusion	15 (22)	20 (29)	11 (16)	23 (33)	.05*
1 Level fusion	15 (17)	19 (22)	30 (34)	24 (27)	
2–4 Level fusion	20 (29)	19 (27)	17 (24)	14 (20)	
4+ Levels fusion	18 (38)	11 (23)	10 (21)	9 (19)	
Surgical approach					
Posterior only	48 (24)	52 (26)	47 (24)	51 (26)	.70‡
Anterior only	8 (25)	5 (16)	8 (25)	11 (34)	
Anterior–posterior	11 (25)	12 (23)	13 (30)	8 (18)	
Estimated blood loss					
Total mL (median)	400.0	350.0	300.0	300.0	.31†
Blood transfusion					
No	49 (22)	59 (26)	59 (26)	58 (26)	.15*
Yes	18 (37)	10 (20)	9 (18)	12 (24)	
Length of hospital stay					
Total days (median)	3.0	3.0	3.0	3.0	.18†
Anesthesia time					
Total hours (median)	4.4	4.4	4.2	3.8	.25†

* *P*-value using chi-square test.
† *P*-value using Kruskal–Wallis one-way analysis of variance.
‡ *P*-value using Fisher's exact test.
mL=milliliter, N=Number, SD=standard deviation.

prealbumin quartile, suggesting poorer overall health is associated with more advanced spinal pathologies and more complex procedures. However, control for these factors did not appreciably change our RR estimates. Thus, even though our descriptive data do support the relation between poor health and lower prealbumin, these factors did not negatively confound the associations between prealbumin level or transferrin level and 30-day complication risk.

To further examine the possibility of the patients with more complex spinal pathologies being different, we removed patients that had undergone surgery only on the cervical spine and repeated the analyses. However, the null association remained. These results provide further evidence that even among patients with spinal pathology requiring complex procedures, there is still no association between the nutritional biomarkers and the 30-day risk of complication.

This study extends prior research that reported a positive association of malnutrition using serum albumin (<3.5 g/dL) and postoperative complication risk following spine surgery.[27–30] The reasons that our findings differ from those of previous studies can only be hypothesized but we explore several potential possibilities. First, a substantially higher prevalence of malnutrition was present in the previous patient cohorts studied, ranging from 12% to 25% of the sample.[27–29] In the current analytic cohort, the proportion of patients with malnutrition was less than 2%. The 2 prior studies with the largest sample only obtained albumin measurements on less than 50% of the total patient population, ranging from 36.5% to 37.6% of the initial sample.[29,30] Incomplete data on the nutritional biomarkers introduces the potential for biased results. One possibility is that patients for whom presurgical albumin measures were ordered were sicker and therefore more likely to have complications than

Table 3

Risk ratios and 95% confidence intervals of complications within 30 days among adults undergoing elective spine surgery according to presurgical level of prealbumin.

	Prealbumin level	
Median, mg/dL	<27.4	≥27.4
Total N	136	138
N Complications (%)	18 (13%)	17 (12%)
Model	RR (95% CI)	
Unadjusted	1.0 (Referent)	1.0 (0.7, 1.3)
*Model 1	1.0	1.1 (0.8, 1.5)
†Model 2	1.0	1.1 (0.8, 1.5)

* Variables modeled are prealbumin level, transferrin level, body mass index (<30 kg/m^2, >=30 kg/m^2) and number of levels fused (no fusion, 1 level fused, 2–3 levels fused, ≥4 levels fused).
† Variables modeled include those in model 1 plus age group (50–59 years, 60–69 years, >=70 years), sex (female, male), and ASA score (1–2 points, 3–4 points).
CI=confidence interval, mg/dL=milligrams per decilitre, N=number, RR=risk ratios.

Table 4

Risk ratios and 95% confidence intervals of complications within 30 days among adults undergoing elective spine surgery according to presurgical level of transferrin.

	Transferrin level	
Median, mg/dL	<265.0	≥265.0
Total N	136	138
N Complications (%)	16 (12%)	19 (14%)
Model	RR (95% CI)	
Unadjusted	1.0 (Referent)	1.2 (0.6, 2.3)
*Model 1	1.0	1.1 (0.8, 1.5)
†Model 2	1.0	1.1 (0.8, 1.6)

* Variables modeled are prealbumin level, transferrin level, body mass index (<30 kg/m^2, >=30 kg/m^2) and number of levels fused (no fusion, 1 level fused, 2–3 levels fused, ≥4 levels fused).
† Variables modeled include those in model 1 plus age group (50–59 years, 60–69 years, >=70 years), sex (female, male), and ASA score (1–2 points, 3–4 points).
CI=confidence interval, mg/dL=milligrams per decilitre, N=number, RR=risk ratios.

patients with no presurgical albumin order. This type of selection bias, if it occurred, could lead to an overestimate of the malnutrition prevalence, as well as to a spurious association of malnutrition and complication risk. Data from our study showed that nearly 40% of patients undergoing fusion at more than 4 levels had prealbumin levels in the lowest quartile. This observation supports the possibility that lower average albumin levels would have been obtained in previous studies if albumin was preferentially obtained in those undergoing the most complex surgeries. Our study design minimized the possibility of selection bias, because prealbumin and transferrin were routinely ordered at the preoperative clinic visit for all patients undergoing elective spine surgery. Second, the previous studies have been small and limited to specific types of spine surgery. For example, Klein et al studied 74 patients undergoing elective surgery of the lumbar spine only, while Adogwa et al examined 136 patients undergoing spinal fusion.[27,28] The current study of 274 patients is considerably larger than samples used previously and includes a broad range of elective spine procedures utilized to treat symptoms and spinal pathology in patients presenting to a busy urban academic medical center spine practice. Finally, all previous studies[27–30] examined malnutrition defined by serum albumin (<3.5 g/dL); serum albumin, with a half-life of 20 days, reflects a longer-term measure of an individual's overall nutrition status. The current study utilized serum prealbumin and transferrin which may reflect more acute changes in recent dietary intake and nutrition status.

The results from our study are new compared to previous work demonstrating positive associations of prealbumin and transferrin with risk of postoperative outcomes in patients undergoing cardiac and gastric surgery.[31–33] The difference between our results and these previous works suggests that associations of nutritional status with risk of post-surgical complications depend on the patient population. Patients undergoing gastric or cardiac surgery may represent a less healthy population than elective spine surgery patients, especially if they require immediate or emergency cardiac or gastric surgery. The low prevalence of malnutrition in our patient cohort supports this reasoning.

There were several limitations to this study. Although the nutritional biomarkers were routinely obtained as standard of care, other variables, such as smoking status, were not consistently recorded. However, with the data available these variables were not found to confound the association between biomarker and risk of complication; it is unlikely that any of these variables are strong enough negative confounders to mask an actual association. Second, the ascertainment of complications was limited to those who returned to the specific institution for treatment or those who reported complications to their providers. It is possible that medical complications were treated elsewhere and were not captured, potentially underestimating the overall risk of any complication. However, the short follow-up period of 30-days minimized the possibility of patients leaving the area or seeking treatment elsewhere. Finally, generalizability of study results may also be limited given that our sample represents the experience of a single hospital in a large urban academic medical center.

Future studies should consider a larger sample size and a more diverse cohort of elective spine surgery patients, perhaps from multiple medical centers. Larger studies would enable the relation of prealbumin or transferrin levels to be examined in relation to specific types of complications, which appropriately have low overall frequency at any single institution. Additionally, a prospective cohort study in which independent and outcome variables are collected prospectively would be a more ideal design to examine associations of nutritional biomarkers and risk of complication. Finally, given the number of studies citing the positive association between serum albumin and the risk of complication, an additional study utilizing the same patient cohort to examine serum albumin's association with 30-day risk of complications could potentially add to the body of previously published studies. It is of interest to explore both this association of serum albumin with the risk of complication in this patient population as well as the discordance between serum albumin and serum prealbumin.

5. Conclusions

Low levels of prealbumin and transferrin are not associated with increased risk of postoperative complications following elective spine surgery. Additional work in large patient cohorts is needed to determine the association between these nutritional biomarkers and specific complications, such as wound infections, that may be closely related to recent nutrition status.

Author contributions

Conceptualization: Erin Takemoto, Jung Yoo, Jackilen Shannon, Lynn Marshall.
Data curation: Erin Takemoto, Jung Yoo, Sabina Blizzard, Lynn Marshall.
Formal analysis: Erin Takemoto, Sabina Blizzard, Lynn Marshall.
Funding acquisition: Jung Yoo.
Investigation: Erin Takemoto, Lynn Marshall.
Methodology: Erin Takemoto, Jackilen Shannon, Lynn Marshall.
Writing – original draft: Erin Takemoto, Lynn Marshall.
Writing – review & editing: Erin Takemoto, Jung Yoo, Sabina Blizzard, Jackilen Shannon, Lynn Marshall.
Erin Takemoto orcid: 0000-0001-7211-2704.

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