Prealbumin as a Serum Biomarker of Impaired Perioperative Nutritional Status and Risk for Surgical Site Infection after Spine Surgery

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Abstract

Introduction Impaired perioperative nutritional status has been shown to be an important predictor of surgical morbidity and is the earliest marker of nutritional deficiency. No study, however, has examined serum prealbumin as a surrogate marker of nutritional status in patients undergoing spine surgery.

Methods We performed a retrospective review of all patients who developed a postoperative deep wound infection after undergoing spine surgery at the University of Pittsburgh Medical Center from January 2008 through December 2011. Demographics, preoperative diagnosis, type of surgery, perioperative serum prealbumin level, time to infection, number and type of debridement procedures, and length of hospital stay were recorded.

Results A total of 83 patients had prealbumin levels available at the time of presentation of infection. Mean patient age was 56 years, and 71% were women. Surgical treatment for the infection required between 1 and 13 debridements, and 21 (25%) of the 83 patients who had instrumentation placed at the time of the initial surgery required removal of their instrumentation. Inpatient hospitalizations were extended by an average of 13 days. Prealbumin levels were below normal in 82 (99%) of the 83 patients; levels were < 7 mg/dL in 24 patients, between 7 and 11 mg/dL in 32 patients, and between 11 and 19 mg/dL in 26 patients.

Conclusions All patients except one who developed postoperative deep wound infection after spine surgery had serum prealbumin levels in the malnutrition range at the time of presentation. The current study suggests serum prealbumin levels may be an inexpensive screening biomarker for nutritional status and risk stratification for postoperative infection after spine surgery.

Keywords
- perioperative nutrition
- spine surgery
- prealbumin
- transthyretin
- surgical site infection

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Introduction

Malnutrition has been associated with increased risk of perioperative infection, longer hospital stays, and worse outcome after surgery in a variety of patient populations.[1–7] The relationship of nutritional status to outcome has been most extensively investigated in the gastrointestinal surgery literature, where the recognition that malnutrition has significant negative effects on surgical outcome has resulted in trials of preoperative nutritional supplementation (Drover et al, verbal discussion at a department lecture).[2,3,5,6,8–14] Early studies used serum albumin concentration as a gauge of nutritional status, but this marker has fallen out of favor due to several shortcomings including its long serum half-life (20 days) and its variability secondary to factors such as hydration status and renal function.[15–18] Transthyretin, also known as prealbumin, is a protein produced predominantly by the liver that has one of the highest proportions of essential-to-nonessential amino acids of any protein in the body, making it a distinct marker of visceral protein synthesis.[15,19] Furthermore, prealbumin has a short half-life of 1.9 days, making it an early indicator of changes in nutritional status and thus a preferred marker for studies linking malnutrition to outcome after surgery.

Although malnutrition is especially prevalent—and problematic—in patients with gastrointestinal malignancy, poor nutritional status is not limited to these patients. Furthermore, infectious complications after surgery stand out as a significant, and potentially avoidable, burden on hospital resources. The development of a surgical site infection, particularly deep wound infections, after spine surgery has significant consequences for patients and the health care system at large. Postoperative spinal wound infections generally lead to longer in-hospital lengths of stay, higher costs, and the potential for reoperation. Moreover, these complications are known to decrease patient satisfaction and increase patient morbidity and mortality.[20–24]

An audit of surgical site infectious complications occurring after spine surgery performed at our hospital was undertaken to test the hypothesis that impaired perioperative nutritional status, as indicated by decreased serum prealbumin level, is associated with infection after spine surgery. There are limited data in the literature regarding the use of prealbumin as a marker of nutritional status as it relates to outcomes following major spinal surgery.

Methods

With approval from the University of Pittsburgh institutional review board (IRB PR008120394), all patients who developed a wound infection after undergoing spine surgery at UPMC Presbyterian Hospital between January 2008 and December 2011 were identified by querying the hospital's Infection Control database. The electronic medical record was reviewed for each patient, and patient demographics, type of surgery, type of infection, interval between surgery and the development of infection, treatment, hospital length of stay, and perioperative serum prealbumin levels were recorded.

Over the 48-month span, $>$ 8,000 spine surgeries were performed; of those, 148 patients (1.9%) were treated for a postoperative surgical site infection. Perioperative serum prealbumin levels were available for 84 patients. One patient was excluded because her infection was related to an intraoperative esophageal injury, leaving 83 patients in the study group (►**Table 1**). Patients' ages ranged from 19 to 85 years (mean: 56 years). Preoperative diagnoses included symptomatic degenerative lumbar stenosis, tumor, traumatic thoracolumbar fracture, deformity, and syringomyelia. Sixty-nine patients underwent instrumented fusion, two patients underwent noninstrumented fusion, 11 patients underwent decompression alone (for tumor, hematoma, or stenosis) and one patient underwent laminectomy for placement of a cervical syringopleural shunt. Surgeries spanned 2 to 10 levels (median: 5; interquartile range: 3).

Prealbumin levels were obtained on readmission to the hospital at the time patients presented with a wound infection, prior to operative debridement. Nutritional status was subsequently categorized based on the prealbumin values described by Bernstein and colleagues.[25] Patients with prealbumin levels $<$ 20 mg/dL were considered malnourished. Patients were then subcategorized into three groups: mild malnutrition (prealbumin 11–19 mg/dL), moderate malnutrition (prealbumin 7–10 mg/dL), and severe malnutrition (prealbumin $<$ 7 mg/dL).

Results

Patients presented with a wound infection between 7 and 345 days after surgery (median: 19; interquartile range: 14). The mean age of patients who presented with infection was 56 years, compared with a mean patient age of 53 years among those patients who did not develop an infection. Mean initial operative time for patients who presented with infection was 2.85 hours compared with 2.65 hours among those patients who did not develop an infection. Eighteen of 83 patients had a comorbid condition associated with an elevated risk of malnutrition, and these included malignancy with or without chemotherapy, diabetes mellitus, chronic pulmonary disease, vascular insufficiency, and rheumatoid arthritis on immunosuppressive medications. All surgical site infections were deep to the lumbodorsal fascia, and all demonstrated bacterial growth on cultures obtained from the deep wound tissue. In 12 patients, treatment consisted of a single operation in which the wound was irrigated, debrided, and closed. In 71 patients, treatment consisted of serial debridements (range: 2–13) with placement of a negative pressure wound dressing, followed by definitive wound closure. In four patients, the wound was allowed to heal by secondary intention with biweekly irrigation and debridement followed by replacement of a vacuum-assisted closure device. One patient's infection was treated with placement of a pigtail catheter into a perinephric abscess. Twenty-one patients underwent removal of instrumentation as part of the infection treatment. Hospital length of stay was extended by between 5 and 60 days (median: 13; interquartile range: 16). In all patients, intravenous antibiotic therapy was

Table 1 Patient characteristics

Age, y[a]	55.8 (19–85)
Sex, % female	71.4
Diagnosis, *n* (%)	
Stenosis	56 (67.5)
Trauma	8 (9.6)
Tumor	7 (8.4)
Deformity	7 (7.1)
Hematoma	4 (4.8)
Syringomyelia	1 (1.2)
Spinal level, *n* (%)	
Occipitocervical Cervical	2 (2.4) 17 (20.5)
Thoracic	5 (6.0)
Thoracolumbar/-pelvic	8 (9.6)
Lumbar	51 (61.4)
Procedure, *n* (%)	
Instrumented fusion	69 (83.1)
Noninstrumented fusion Decompression alone	2 (2.4) 11 (13.3)
Shunt	1 (1.2)
Number of levels[b]	5, 3 (2–10)

[a]Mean (range).
[b]Median, interquartile range (range).

administered, based on the specific recommendations of the Infectious Disease service. All of the infections were successfully eradicated, and all wounds eventually healed. Infection characteristics are summarized in ►**Table 2**.

Overall, 82 of the 83 patients had a prealbumin level below the normal range of 20 to 40 mg/dL: 24 patients had a prealbumin < 7 mg/dL; 32 had a prealbumin level of 7 to 10 mg/dL, and 26 patients had a prealbumin level of 11 to 19 mg/dL (►**Table 2**). Following their presentation with a deep wound infection and concomitant nutritional impairment, all patients received some form of nutritional supplementation. Patients who demonstrated the capacity for being able to supplement their caloric intake by mouth received protein shakes and nutritional supplements containing Arginaid (Nestle Health Science, Florham Park, New Jersey, United States) with meals. The remaining patients underwent placement of a nasoduodenal feeding tube and were administered tube feeds. Serial prealbumin levels were followed on an outpatient basis, and supplemental nutrition continued until prealbumin levels normalized. All patients in this study maintained follow-up, and no patient developed an additional delayed wound infection.

Table 2 Infection characteristics

Interval to diagnosis of infection, d[a]	19, 14 (7–345)
Incremental hospital length-of-stay, d[a]	13, 16 (5–60)
No. of surgical debridements[a]	2.0, 4 (0–13)
Perioperative nutritional status (prealbumin, mg/dL)[b]	
Normal ($\geq$20)	1 (1.2)
Mildly impaired (11–19)	26 (31.3)
Moderately impaired (7–10.9)	32 (38.6)
Severely impaired (< 7)	24 (28.9)

[a]Median, interquartile range (range).
[b]Number (%).

Discussion

The association of postoperative infectious complications with impaired nutritional status has been previously demonstrated in the gastrointestinal surgery literature, and malnutrition is increasingly being recognized as a common problem in hospitalized patients.[1–7,11,15,26,27] However, the link between impaired nutritional status and increased risk for surgical site infections has been sparsely studied among patients undergoing spine operations. In a recent study by Schoenfeld et al[28] of $>$ 5,800 spinal fusion patients obtained from the National Surgical Quality Improvement Program, the authors found that those with a low serum albumin level were at increased risk of developing a wound infection. Of note, no studies to date have explored the association between spine surgical site infections and serum prealbumin levels; prealbumin is a more optimal marker of nutritional status.

This relationship between nutritional status and spine surgical site infection is especially noteworthy because of the significant implications of this complication for patients, who often require one or more additional surgeries and potentially require removal of instrumentation and long-term intravenous antibiotic therapy, and for the health care system, which must bear the significant additional cost of treating these complications.[25] Although hospital-wide programs to reduce infection have traditionally focused on improving antisepsis policies and procedures, comparatively little effort has been directed toward optimization of patient nutritional status, despite convincing preliminary data that nutritional status is a modifiable risk factor for postsurgical infection. Indeed, several trials of nutritional supplementation in the general surgery, gastrointestinal surgery, cardiothoracic surgery, and head and neck surgery populations have yielded clinically and statistically significant reductions in infectious complications and hospital length of stay. Although preoperative nutritional screening is practiced by some spine surgeons—particularly, in patients undergoing elective deformity surgery—routine screening is not widely performed.[29] The identification of a serum marker of nutritional status that would allow surgeons preoperatively to stratify a patient's risk for developing a deep wound infection after spine surgery has the potential to reduce the incidence of this troublesome and costly complication of spinal surgery, and it would enable patients and their surgeons to optimize their nutritional status before and after spine surgery.

Our observation that 99% of patients who developed postoperative deep wound infections had a prealbumin level consistent with impaired nutritional status is significant for several reasons. First, although the importance of adequate nutrition for wound healing has long been appreciated, the association between impaired nutritional status and wound infection has been understudied in the spinal neurosurgery literature. Second, if borne out by the results of an ongoing prospective investigation at our institution, the identification of prealbumin as a strong, reliable predictor of the development of a surgical site infection after spine surgery will provide spine surgeons with a screening tool to identify at-risk patients prior to surgery. Ultimately, these results should empower surgeons, patients, and hospitals to actively improve surgical outcome through the implementation of simple and inexpensive programs of perioperative nutritional supplementation.

It is important to note that the current study suffers from several shortcomings. First, the study was retrospective in design and therefore subject to the typical sources of confounding and bias associated with retrospective investigations. Furthermore, prealbumin levels were only obtained in patients who developed a wound infection, precluding any calculation of the actual risk conferred by low prealbumin. Additionally, prealbumin levels were not available for all patients who developed a wound infection, which raises the question of whether malnourished patients who developed an infection were more likely to have a prealbumin level drawn than were well-nourished patients who developed an infection.

Finally, our results are also confounded by heterogeneity in the times at which perioperative prealbumin levels were drawn. This is problematic because prealbumin is generally felt to behave as a negative acute-phase reactant, with levels decreasing in times of stress.[15,19,25,30] In the initial phases of the stress response, catabolic processes predominate and there is a net loss of nitrogen while available amino acids are diverted preferentially toward the synthesis of positive acute-phase reactants such as C-reactive protein, complement proteins, and fibrinogen.[15,19,25,30–33] Prealbumin levels typically reach a nadir within 3 to 5 days after the initiation of acute injury, coincident with the peak of nitrogen urinary excretion.[30] Prealbumin levels have also been shown generally to decline during the course of hospitalization due to a variety of factors including nausea, unpalatable food offerings, and periods of imposed fasting.[7] As a consequence, the prealbumin levels reported in this study, having all been obtained in the setting of infection and, in some cases, in the setting of recent surgery, may not provide a true measure of patients' nutritional status due to the negative effects of the stress response. Of note, the response of prealbumin levels under conditions of systemic stress is complex and remains incompletely understood, with some investigators advocating that prealbumin no longer be regarded as a negative acute-phase reactant but rather as an active participant in the second wave of the stress response.[30]

Conclusions

Malnutrition has been shown to correlate with risk of infectious complications after intra-abdominal surgery, and prealbumin is emerging as the preferred marker for measurement of nutritional status. We have identified a high incidence of impaired nutritional status, as indicated by decreased prealbumin level, in patients who developed a deep wound surgical site infection after spine surgery. Prospective evaluation of preoperative serum prealbumin levels in determining outcome after elective spine surgery will provide further insights, and a trial of perioperative nutritional supplementation in at-risk patients is warranted.

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