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Serum Levels of Albumin and Prealbumin Do Not Correlate With Nutrient Delivery in Surgical Intensive Care Unit Patients

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Abstract

Background: Serum albumin and prealbumin levels, may be more strongly associated with inflammation than with nutrient delivery. Their predictive value has not been extensively described in surgical intensive care unit (ICU) patients. *Methods:* We analyzed a registry of adult surgical ICU patients receiving enteral nutrition. Subjects with at least 1 serum albumin, prealbumin, or C-reactive protein (CRP) level were included. Demographic, nutrition, and clinical outcome data were collected. *Results:* A total 252 subjects were included. A subset had serial measurements: albumin (n = 194), prealbumin (n = 13), CRP (n = 9), white blood cell (WBC) (n = 131), and neutrophil–lymphocyte ratio (NLR) (n = 86). Serum albumin level was inversely correlated with all 3 inflammatory biomarkers (CRP, $\rho = -0.24$, $P < 0.02$; WBC, $\rho = -0.15$, $P < 0.001$; and NLR, $\rho = -0.26$, $P < 0.001$). Change in serum albumin level was inversely correlated with change in NLR ($\rho = -0.22$, $P = 0.044$) but not with CRP or WBC. Admission serum albumin level was significantly higher in nourished vs. moderately and/or severely malnourished patients (3.2 [2.7–3.7] vs. 2.7 [2.3–3.0], $P = 0.004$). Admission serum prealbumin level was significantly higher in nourished vs. moderately and/or severely malnourished patients (9 [7–12] vs. 4 [3–5], $P = 0.001$). Serum albumin level was inversely correlated with Charlson Comorbidity Index ($\rho = 0.20$, $P = 0.001$). Calorie and/or protein delivery in the ICU was not correlated with changes in serum albumin or prealbumin levels. *Conclusions:* In the ICU, initial serum albumin levels and serial trends are inversely correlated with inflammation. Although initial serum albumin levels are reflective of baseline nutrition status, neither serum albumin level nor serum prealbumin level trends correlate with calorie or protein deficits and should not be used to assess adequacy of nutrition delivery. (*Nutr Clin Pract.* 2018;33:419–425)

Keywords

inflammation; intensive care unit; nutrition assessment; prealbumin; serum albumin

Background

Malnutrition is widely prevalent in intensive care unit (ICU) patients and has long been recognized as an independent risk factor for increased complications, cost, length of stay (LOS), and mortality.[1,2] Yet, except extreme cases, diagnosing malnutrition is challenging and numerous methods have been proposed, including history and physical exam, anthropometric measurements, handgrip dynamometry, various scoring systems, and biomarkers. This multitude of methods without a clear "gold standard' illustrates the difficulty in diagnosing malnutrition in the ICU. Critically ill patients present additional challenges because of the inability to communicate (due to mechanical ventilation, delirium, or sedation), fluid resuscitation–related weight gain, and acute inflammation.

Serum albumin and prealbumin levels (also known as transthyretin) are commonly believed to be markers of nutrition status.[3] The negative association between serum albumin and prealbumin levels and clinical outcomes has been reported numerous times.[4-7] Lower serum albumin and prealbumin levels at operation or ICU admission have been correlated with higher risk of infection and mortality.[5,8] Additionally, serum prealbumin levels have been shown to decrease dramatically during postoperative starvation[9] and

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increase in response to nutrition therapy.[10] However, hepatic protein synthesis is influenced by non-nutrition factors and are thus unreliable as pure nutrition indicators, especially in the setting of acute inflammation.[11] Acute-phase reactants are proteins whose plasma concentrations increase (positive acute-phase protein) or decrease (negative acute-phase protein) at least 25% with inflammation. Serum albumin and prealbumin are negative acute-phase reactants, and their levels may be more reflective of decreased synthesis secondary to inflammation rather than nutrition status.[12-15] However, this is not always the case. The magnitude of inflammatory influence is unclear and may vary for individual patients. To further confuse the situation, inflammation itself is widely acknowledged to increase nutrition risk.[16,17] Patients with persistent inflammation commonly become malnourished secondary to prolonged catabolism. Yet, hepatic protein levels may respond to nutrition therapy with time when the inflammation is stable.

In some hospitals, it is common practice to measure serum albumin and prealbumin levels throughout the course of hospitalization, known as "nutrition labs," adjusting calorie and protein prescription according to the trend of these serum protein levels. Persistently low serum albumin and/or prealbumin levels may be interpreted as evidence of insufficient nutrient delivery and the prescription may be increased; conversely, rising serum albumin and/or prealbumin levels may reassure the clinician that the current nutrient prescription is sufficient. However, the validity of these assumptions has not been proven convincingly. Specifically, there is no strong evidence that increased nutrition intake in the hospital leads directly to increased serum albumin and/or prealbumin levels (after controlling for inflammation) or that increased levels are associated with improved outcomes.[18] The primary aim of this study is to examine the relationship between serum albumin and/or prealbumin levels and surrogate measures of inflammation: C-reactive protein (CRP), white blood cell (WBC), and neutrophil–lymphocyte ratio (NLR). Secondary aims are to: 1) examine the relationship between surgical ICU admission serum albumin and/or prealbumin levels with baseline nutrition status and chronic comorbid medical illness; 2) examine the correlation between serum biomarker trends and ICU nutrition delivery; and 3) examine the relationship between initial serum biomarker levels as well as serum biomarker trends with clinical outcomes.

Methods

This study was approved by our local Institutional Review Board (Massachusetts General Hospital). We performed a retrospective analysis of a registry of adult (age ≥ 18 years) surgical ICU patients receiving enteral nutrition (EN) (i.e., tube feedings) for >72 hours. Patients were excluded if they were taking oral nutrition, had an absolute contraindication for EN (e.g., bowel obstruction or proximal enterocutaneous fistula), were in a moribund state or had orders for limitation of life-saving interventions, had a previous ICU admission during the index hospitalization, or spent <72 hours in the ICU. Patients receiving concomitant parenteral nutrition (PN) were also excluded from this study. A registered dietitian specializing in critical care is routinely consulted within 24–48 hours for all patients initiating EN in the surgical ICU. The initial assessment includes an estimation of baseline nutrition status (although sometimes limited by inability to interview the patient), obtain an accurate baseline usual weight, and assess strength and functional status due to sedation, critical illness, or traumatic injuries. Patients were classified as nourished, moderately malnourished, or severely malnourished, based on the combination of known malnutrition risk factors, metabolic stress factors, and physical signs of malnutrition. Risk factors included inadequate nutrition intake prior to or during hospitalization, age, and comorbid illness; stress factors included physiologic status and current illness; physical signs of malnutrition included overt wasting of muscle mass or subcutaneous fat.[1]

Calories and protein were prescribed to target 25–30 kcal/kg/day and 1.0–1.5 g/kg/day based on actual body weight.[19] For obese patients (body mass index [BMI] >30), ideal body weight was used instead. To reach protein targets, additional supplementation was prescribed as Beneprotein (Nestlé, Vevey, Switzerland; whey powder 25 kcal/6g protein per packet) or Prosource liquid protein (Medline Industries, Mansfield, MA, USA; 60 kcal/15 g protein per packet). Calories received by propofol were accounted for in nutrition prescriptions. Indirect calorimetry was used infrequently at clinical discretion and, when available, results were used to adjust calorie prescription. Our standard surgical ICU practices for gastric residual volume, perioperative feeding, and initiation rate have been previously published.[20,21]

Demographic data collected included age, gender, weight, BMI, Acute Physiology and Chronic Health Evaluation (APACHE II) score, injury severity score (ISS) for trauma patients, Charlson Comorbidity Index (CCI), and baseline nutrition status. Nutrition data collected included the initiation of EN within 48 hours of ICU admission, calorie prescription (kcal/kg/day), protein prescription (g/kg/day), actual caloric delivery, actual protein delivery, and nutrition deficits. The daily calorie and protein deficits were calculated by subtracting the actual macronutrient delivery from the prescribed amount. Total ICU cumulative deficits were reported after 14 days of EN in the ICU or until progression to permanent oral intake, discharge from the ICU, or death, whichever occurred first. Serum laboratory tests recorded included albumin level, prealbumin level, CRP, WBC, and NLR. It is common practice in our ICU to measure serum albumin level, WBC,

and NLR at ICU admission, and repeat serum albumin level measurement weekly. There is no policy for routine prealbumin and CRP measurements, and these biomarkers were measured only at the clinician's discretion. Therefore, only a smaller subset of patients had multiple measurements with time. Clinical outcomes recorded included ICU LOS, hospital LOS, 28-day ventilator-free days (VFD), total complications, and in-hospital mortality. Complications included cardiovascular (atrial fibrillation, congestive heart failure, myocardial ischemia), gastrointestinal (abdominal distention requiring EN discontinuation, emesis, diarrhea), infectious (pneumonia, urinary tract infection, bacteremia, surgical site infection, or catheter-related infection), and wound-healing (anastomotic leak, wound dehiscence, decubitus ulcers).

Continuous data are summarized using mean with standard deviation or median with interquartiles. Spearman correlations coefficients (ρ) were used to summarize the relationship between serum laboratory values (serum albumin and prealbumin levels, CRP, WBC, NLR) using paired measurements taken within 3 days of each other. Baseline serum laboratory value was defined as the measurement closest to surgical ICU admission from all measurements obtained 2 weeks before surgical ICU admission to day 3 after admission. The rate of change was calculated by fitting a linear regression line for each individual using measurements from 2 weeks before surgical ICU admission to day 14 after admission or ICU discharge, whichever came first. The relationships between continuous variables were summarized using Spearman correlation coefficients. Wilcoxon rank-sum tests were used to compare serum laboratory values between groups. All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA). A 2-sided *P*-value of 0.05 or less was considered significant.

Results

The cohort included 252 subjects with at least 1 serum albumin level, prealbumin level, CRP, WBC, or NLR serum laboratory value. Demographic characteristics, nutrition data, and clinical outcomes for the entire sample are displayed in Table 1.

Table 1. Demographics, Nutrition Information, Inflammatory Biomarkers, and Clinical Outcomes.

Subject Data	N = 252
Age, years	61 (17)
Male gender (%)	173 (69)
Weight, kg	74.7 (18.0)
BMI	27.8 (6.8)
APACHE II	18 (8)
ISS[a] (n = 60)	30 (13)
CCI	4 (3)
Initial nutrition status (%)	
Not available	37 (15)
Nourished	189 (75)
Moderately malnourished	18 (7)
Severely malnourished	8 (3)
EN within 48 hours (%)	175 (69)
Calorie prescription (kcal/kg/day)	24.4 (5.3)
Calorie delivery (kcal/kg/day)	16.0 (6.3)
Protein prescription (g/kg/day)	1.5 (1.7)
Protein delivery (g/kg/day)	1.0 (1.0)
Day 3 caloric deficit (kcal)	2279 [1170–4140]
Day 3 protein deficit (g)	126 [63–229]
Day 7 caloric deficit (kcal)	3470 [1823–5830]
Day 7 protein deficit (g)	181 [71–313]
Total ICU caloric deficit (kcal)	3609 [639–6641]
Total ICU protein deficit (g)	111 [0–326]
ICU admission labs	
Serum Albumin Level (g/dL, reference range 3.5–5.2 g/dL) (n = 247)	3.0 [2.6–3.6]
Serum Prealbumin Level (mg/dL, reference range 20–40 mg/dL) (n = 58)	8 [5–11]
CRP (mg/L, reference range <0.5 mg/dL) (n = 49)	138.0 [79.5–223.3]
WBC (K/mL, reference range 4.0–10.5 K/mL) (n = 230)	12.2 [7.4–16.9]
NLR (reference range 0.78–3.53) (n = 209)	9.7 [5.0–20.2]
Hospital LOS, days	22 [15–38]
ICU LOS, days	12 [8–20]
28-day VFD	18 (9)
Total complications	2.2 (2.2)
In-hospital mortality	50 (20%)

Data are summarized as mean (SD) or median [interquartiles] for continuous variables.
APACHE II, Acute Physiology and Chronic Health Evaluation; BMI, body mass index; CCI, Charlson Comorbidity Index; CRP, C-reactive protein; EN, enteral nutrition; ICU, intensive care unit; ISS, injury severity score; LOS, length of stay; NLR, neutrophil–lymphocyte ratio; VFD, ventilator-free days; WBC, white blood cell.
[a]Only for the subset of trauma patients.

Primary Aim: Relationship Between Serum Albumin and Prealbumin Levels With Inflammatory Biomarkers

The correlations between all serum laboratory values (albumin level, prealbumin level, CRP, WBC, NLR) are summarized in Table 2. In pairs of measurements obtained within 3 days of each other, serum albumin level was negatively correlated with all 3 inflammatory biomarkers ($\rho = -0.24$, $P < 0.02$ for CRP; $\rho = -0.15$, $p < 0.001$ for WBC; and $\rho = -0.26$, $P < 0.001$ for NLR). Serum prealbumin level was measured less often, but showed the similar negative correlations with inflammation biomarkers. When limited to the measurements closest to ICU admission date, both serum albumin and prealbumin levels showed negative correlations with inflammation biomarkers.

Table 2. Spearman Correlation Coefficients From Paired Biomarker Measurements.

Biomarkers	Serum Prealbumin Level	CRP	WBC	NLR
Serum Albumin Level	0.14 (n = 118)	−0.24 (n = 102)	−0.15 (n = 671)	−0.26 (n = 504)
Serum Prealbumin Level	–	−0.28 (n = 42)	−0.04 (n = 87)	−0.17 (n = 61)
CRP	–	–	0.18 (n = 80)	0.15 (n = 48)
WBC				0.32 (n = 338)

CRP, C-reactive protein; NLR, neutrophil–lymphocyte ratio; WBC, white blood cell.

Table 3. Rate of Change Per Day From Serial Biomarker Measurements.

	N	Median [Q1, Q3]
ΔSerum Albumin Level, g/dL per day	194	−0.05 [−0.11, −0.01]
ΔSerum Prealbumin Level, mg/dL per day	13	0.55 [−0.60,1.03]
ΔCRP, mg/L per day	9	5.98 [−14.3, 0.17]
ΔWBC, per day	131	−0.13 [−0.61, 0.50]
ΔNLR, per day	86	0.06 [−0.79, 1.08]

Δ, change; CRP, C-reactive protein; NLR, neutrophil-lymphocyte ratio; WBC, white blood cell.

A smaller subset with serial measurements of serum albumin level (n = 194), serum prealbumin level (n = 13), CRP (n = 9), WBC (n = 131), NLR (n = 86) and the median rates of change is presented in Table 3. Rate of change in serum albumin level was negatively correlated with rate of change in NLR ($\rho = -0.22$, $P < 0.05$) but not with CRP or WBC. Rate of change in serum prealbumin level was not significantly correlated with rate of change in any of the 3 inflammation biomarkers.

Secondary Aims

Baseline nutrition status and comorbid medical illness. Admission serum albumin level was significantly higher in nourished patients compared with moderately and/or severely malnourished patients (3.2 [2.7–3.7] vs. 2.7 [2.3–3.0] g/dL, $P = 0.004$). Similarly, admission serum prealbumin level was significantly higher in nourished patients compared with moderately and/or severely malnourished patients (9 [7–12] vs. 4 [3–5] mg/dL, $P = 0.001$). Serum albumin level was negatively correlated with CCI ($\rho = 0.20$, $P = 0.001$). With the smaller sample size (n = 58), the negative correlation between serum prealbumin level and CCI did not reach statistical significance ($\rho = -0.17$, $P = 0.21$).

Nutrition adequacy. Changes in serum albumin level were not correlated with 3-day caloric deficit ($\rho = 0.10$, $P = 0.15$), 3-day protein deficit ($\rho = 0.01$, $P = 0.94$), 7-day caloric deficit ($\rho = 0.07$, $P = 0.32$), 7-day protein deficit ($\rho = -0.02$, $P = 0.81$), total ICU caloric deficit ($\rho = 0.02$, $P = 0.74$), or total ICU protein deficit ($\rho = 0.07$, $P = 0.31$). Similarly, changes in serum prealbumin level did not correlate with 3-day caloric deficit ($\rho = -0.04$, $P = 0.90$), 3-day protein deficit ($\rho = 0.00$, $P = 1.0$), 7-day caloric deficit ($\rho = -0.09$, $P = 0.78$), 7-day protein deficit ($\rho = -0.10$, $P = 0.76$), total ICU caloric deficit ($\rho = -0.11$, $P = 0.73$), or total ICU protein deficit ($\rho = -0.40$, $P = 0.20$). Figure 1 displays the scatter plots.

Clinical outcomes. Initial serum albumin level was negatively correlated with hospital LOS ($\rho = -0.16$, $P = 0.01$) but not with any other clinical outcomes. Serum prealbumin level was not correlated with hospital LOS, ICU LOS, 28-day VFDs, or total complications. Change in serum albumin, serum prealbumin, and CRP levels were not correlated with hospital LOS, ICU LOS, 28-day VFDs, or total complications. However, those who died in the hospital had slightly lower initial serum albumin level (median 2.9 vs. 3.1 g/dL, $P = 0.14$) and significantly lower rate of decrease (−0.03 vs. −0.05, $P = 0.034$).

Discussion

Despite accumulating evidence demonstrating their unreliability, serum albumin and prealbumin levels are still considered by many to be "nutrition markers," and it is common practice to measure them serially throughout the course of hospitalization to guide nutrition therapy. Our study has several important findings. First, we confirm the negative correlation between serum albumin level and CRP, WBC, and NLR at ICU admission. Similarly, serum prealbumin level is negatively correlated with CRP and NLR. Because serum albumin level and serum prealbumin level proteins are negative acute-phase reactants, it would be reasonable to assume that as the patient recovers from critical illness and the inflammation subsides, the CRP, WBC, and NLR levels would decrease while the serum albumin and prealbumin levels increase. We found this to be true for serum albumin level and NLR, but not with CRP or WBC. Rate of serum prealbumin level change was not significantly correlated with any inflammatory biomarker.

Second, we confirm that there is likely a link between serum albumin and prealbumin levels with baseline

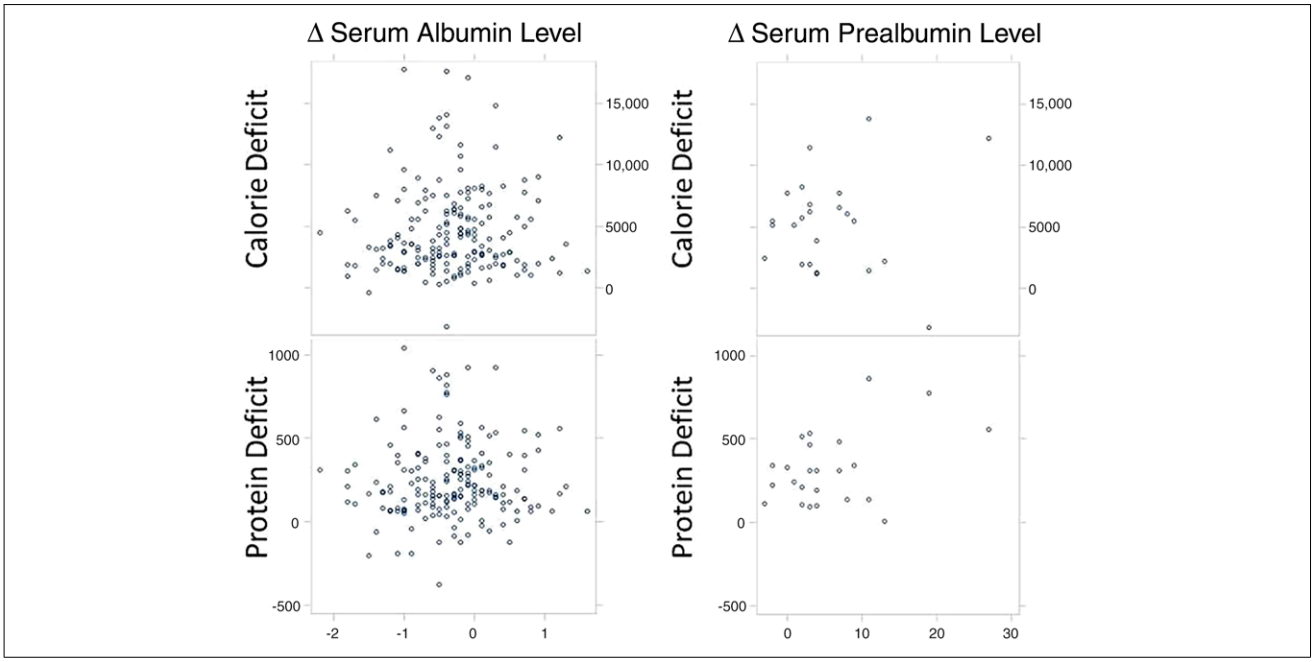

Figure 1. Correlation between change in serum albumin level and serum prealbumin level with calorie and protein deficit. Scatterplot demonstrates no correlation.

nutrition status, although this may be confounded by comorbid illness, as we also found a modest negative correlation between admission serum albumin level and CCI. Higher CCI (i.e., more comorbid medical conditions) was associated with lower serum albumin levels at admission.

Third, we were unable to discern any association between rate of change in serum albumin or prealbumin levels with the amount of calories or protein that the patient actually received during the first 2 weeks in the ICU. This directly undermines the utility of serial measurements of these biomarkers in the setting of acute critical illness. As Figure 1 demonstrates graphically, the relationship is seemingly completely random. Our data show that these trends lack content validity and, therefore, clinicians should not use trends in serum albumin or prealbumin levels to guide nutrition prescriptions during critical illness. Decrease in biomarker levels may deceive the clinician to inappropriately increase prescription (leading to overfeeding), while increase in biomarker levels may prevent recognition of underfeeding.

Finally, we confirm that baseline serum albumin levels are negatively correlated with hospital LOS, but not with any other clinical outcomes we examined. Initial serum prealbumin level was not correlated with any clinical outcomes.

Our findings are similar to those reported by others. In a study of 44 ICU patients receiving PN for >7 days, Lim et al. reported that changes in serum prealbumin levels did not correspond to nutrition therapy nor did they correlate with clinical outcomes.[22] Similarly, Davis et al. found that changes in serum prealbumin levels did not correlate with caloric delivery. Rather, change in CRP was a significant predictor of change in serum prealbumin level, suggesting that improvements in inflammation were responsible for increasing serum prealbumin level, rather than improving caloric intake.[23] We were unable to report a similar association in trends, possibly because of the limited sample size and the sporadic timing of repeat CRP measurements. In another study, Dennis et al. reported in elderly patients that changes in inflammatory markers (such as CRP and IL-6) accounted for 56% of the variance in serum prealbumin level change, while protein intake accounted for only 6%.[24]

Multiple investigations have reported that low serum albumin level at admission is a strong predictor for poor outcomes after elective surgery, emergency surgery, and traumatic injury. In a prospective observational study of 54,215 major non-cardiac surgery cases from the National VA Surgical Risk study, Gibbs et al. found that a decrease in serum albumin level from 4.6 g/dL to 2.1 g/dL was associated with an increase in mortality rate from <1%–29% and an increase in morbidity rate from 10%–65%.[6] The predictive power of serum albumin level for 30-day postoperative mortality was stronger than for American Society of Anesthesiology (ASA) class, disseminated cancer, and emergent operation.[25] While this study used very robust statistical methods on a very large sample size, their results may not be applicable to our patient population. The vast majority of their operations were electively scheduled and trauma operations were not included. Only cases with a

measured preoperative serum albumin level (average 6 days before surgery) were included. The overall mortality rate was low and most were not critically ill. While WBC was included in the list of variables investigated, other markers of inflammation such as IL-6 and CRP were not included. Subclinical inflammation may be confounding the serum albumin level–mortality connection; others have reported that after controlling for IL-6, the association between serum albumin level and mortality is no longer significant.[26]

For decades, low serum albumin level has been linked with malnutrition, mainly stemming from descriptions of kwashiorkor and marasmus published before elucidation of the link between inflammation, illness, and hepatic protein synthesis.[11] Indeed, it is now recognized that many patients with kwashiorkor and marasmus also suffer from chronic, subclinical inflammation, and this inflammation may explain the low serum albumin levels. This theory is supported by the observation that many patients with anorexia nervosa, a condition marked by severe malnutrition without concomitant inflammation, have relatively normal serum albumin levels. Thus, the basis for the link between serum albumin level and malnutrition may be flawed. The Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition have recently published updated guidelines for assessment of nutrition in critically ill patients.[27] Based on expert consensus, these professional societies do not recommend using "traditional" (i.e., serum albumin and prealbumin levels) nutrition indicators for assessment, due to lack of validation.[27] Our study suggests that while serum albumin and prealbumin levels may possibly reflect admission nutrition status, serial measurements are not useful for assessing nutrition adequacy. A causal relationship between increasing nutrition intake (while controlling for comorbid disease or inflammation) and increasing serum albumin level has yet to be convincingly demonstrated. Due to the multitude of other factors influencing serum albumin levels and its lack of construct validity and predictive validity, we question the concept of serum albumin level as a "nutrition marker" during acute hospitalization, especially in the setting of critical illness.[28]

Limitations

Our study has several limitations which must be discussed. Because of the retrospective study design, the correlation relationships we report as significant should be interpreted with caution because there may be confounding variables which strengthen or weaken the linkage. Likewise, lack of correlation does not imply that a relationship is nonexistent. Although there are no strict definitions, it is generally agreed upon that an absolute ρ value ranging from 0.5–1.0 is a strong correlation, 0.3–0.5 is a moderate correlation, and <0.3 is a weak correlation. Therefore, we acknowledge that, while statistically significant, the negative correlations between serum albumin level and the 3 inflammatory biomarkers were relatively weak, ranging from $\rho = -0.15$–-0.26. Similarly, the rate of change in serum albumin level was only weakly correlated ($\rho = -0.22$) with rate of change in NLR. Because serial measurements are not mandated in our clinical practice, repeat measurements were only available for some of the subjects, significantly decreasing our sample size. It is possible that a Type 2 statistical error exists, and we were simply unable to detect a significant association, especially for the serum prealbumin level trends. Additionally, we only collected in-depth nutrition information for up to 14 days of tube feeding in the ICU, and we only examined biomarker laboratory measurements that fell within the same time period. It is possible that had we been able to accurately estimate the adequacy of oral intake, or if we had continued to collect calorie and protein delivery beyond 14 days or beyond the ICU setting, a correlation relationship may have emerged. Because of the long half-life of albumin, it could be argued that improvements were not seen because of the relatively short time frame of our study. Next, we acknowledge that our estimates for the calorie and protein requirements are not based on strong evidence, although they generally conform with the recommendations from professional critical care and nutrition societies.[19] The exact amount of calories and protein "required" during the early phase of critical illness remains hotly debated and, therefore, the magnitude and clinical significance of our calorie and/or protein deficit remain unclear. Finally, our patient population was limited to surgical and trauma patients at an urban academic hospital, and our results may not necessarily be generalized to other settings. Despite these limitations, we feel that our results are meaningful and may help inform clinicians in their nutrition practice. Specifically, we recommend less reliance on serial serum albumin and prealbumin levels as markers of nutrition adequacy in acute critical illness.

Conclusions

Traditional biomarkers of nutrition status (serum albumin and prealbumin levels) may be reflective of baseline malnutrition and comorbid medical illness, but serum levels are confounded by concomitant acute inflammation. Changes in serum albumin and prealbumin levels during the course of ICU care are not correlated with calorie and protein delivery and should therefore not be used as an indicator of nutrition adequacy. Additional larger studies are required to confirm these findings.

Statement of Authorship

D. D. Yeh contributed to the conception and design of the research; D. D. Yeh, E. Johnson, and T. Harrison contributed to the acquisition of the data; Y. Chang contributed to the analysis of the data; D. D. Yeh, H. M. A. Kaafarani, J. Lee, P. Fagenholz,

N. Saillant, Y. Chang, and G. Velmahos contributed to the interpretation of the data; D. D. Yeh drafted the manuscript; D. D. Yeh, E. Johnson, T. Harrison, H. M. A. Kaafarani, J. Lee, P. Fagenholz, N. Saillant, Y. Chang, and G. Velmahos critically revised the manuscript, and agree to be fully accountable for ensuring the integrity and accuracy of the work. All authors read and approved the final manuscript.

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