RESEARCH ARTICLE

# Prospective Study Investigating the Prevalence and Evolution of Malnourishment in the Acute Orthopaedic Trauma Patient

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## Abstract

**Background:**Orthopaedic trauma surgeons believe that nutritional status is important. The primary aim of this study was to prospectively investigate the prevalence and progression of malnourishment in orthopaedic trauma patients and determine when and what labs should be ordered. The secondary aim was to determine if malnourished patients had increased complications.

**Methods:** Prospective cohort study of orthopaedic trauma patients at a Level I trauma center. Assessment of nutritional status over the hospital course was performed using the Rainey MacDonald nutritional index (RMNI) and nutritional laboratory markers on admission, day 3, day 7, and 6 weeks post-op.

**Results:** 98 patients were enrolled and included. On admission, 60%, 41%, and 38% of patients were malnourished based on albumin, prealbumin, and RMNI values, respectively, with 31% in severe acute-phase response (APR) as determined by CRP. By day 3, a significant increase in the percent of malnourished patients was noted based on the laboratory markers, 85%, 90%, and 80%, respectively, with 70% in severe APR. On day 7, values stabilized at 74%, 89%, 69%, with 56% in severe APR. At six weeks, malnourishment persisted in 13%, 19%, and 12% of patients, with 4% in severe APR. Older patients demonstrated a greater depression of nutritional markers throughout the hospital stay.

**Conclusion:** The prevalence of malnourishment, based on serum nutritional markers, in the presence of acute orthopaedic injury is substantial, and it continues to rise during the acute hospital stay. Recommend obtaining prealbumin or albumin levels on hospital day 3 to assess nutritional status.

**Level of evidence:** II

**Keywords:** Complications, Nutrition, Malnourishment, Orthopaedic trauma, Nutritional status

## Introduction

When surveyed through the Major Extremity Trauma Research Consortium, 75% of orthoapedic traumatologists believed that nutritional status was very important in regard to the final outcome of patients. 88% of the surgeons perform laboratory screening, but a majority are uncertain about what specific labs to obtain and when to obtain them. 42% think it is important to trend laboratory markers and 50% are unsure if labs should be drawn at multiple points.

The World Health Organization cites malnutrition as the greatest single threat to the world's public health (1).

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Traditionally, malnutrition was associated with poverty in third world countries, but we know this disease is not limited to these populations. Malnutrition is a highly prevalent disease in acute hospital settings, with a rate of 20 to 50% in developed countries (2). It has been shown to be associated with poor clinical outcomes in surgical patients. Patients with poor nutritional status have higher infection rates, impaired wound healing, depression of the immune response, longer lengths of stay, increased muscle loss, increased recovery time and increased mortality (2-5).

Malnutrition, as described by Kinosian, is an imbalance between dietary intake and the patient's energy requirements (6). Trauma patients have a 15 to 25% increase in energy requirements, which may grow to 100% if the infection is present (7). These patients may present with inflammatory, hypermetabolic, and/or hypercatabolic conditions, which are increasingly identified as factors leading to malnutrition (8-11). Patients with low baseline risk of malnutrition, when left unrecognized and unaddressed, may experience a rapid decline in nutritional status (8-14). Overweight or obese adults who experience a major traumatic event may develop undernutrition that requires and can benefit from intensive nutrition intervention (12-14). These patients are often suffering from reduced oral intake due to nausea and multiple surgeries and are frequently placed on intravenous fluids alone for the majority of their hospital stay. It is not surprising that patients fall far short of the nutritional support needed to meet their increased energy demands. The incidence of malnutrition in hip fracture patients ranges from 6-78% in the orthopedic literature and is identified as the most financially costly co-morbidity associated with this patient group (15-17).

### *Rationale*

To our knowledge malnutrition has not been studied specifically in a large group of orthopaedic trauma patients. While there is no gold standard to assess nutritional status in trauma patients, simple hematologic markers have been used previously to diagnose malnutrition in hip fracture patients including albumin, prealbumin, transferrin, and total lymphocyte count (18-21). Incorporating albumin and transferrin, a negative Rainey MacDonald nutritional index (RMNI) value was previously reported to be significantly associated with longer hospitalization and higher rates of septic complications (22). The more negative the RMNI value the more malnourished the patient. The chosen laboratory markers are relatively inexpensive and readily available in most hospitals.

We undertook a prospective study to better determine the evolution of malnutrition in the acute orthopedic trauma patient and its role in postoperative outcomes. This data would potentially help us determine when and what labs should be obtained during the acute hospital stay. Our hypothesis was that the degree of malnutrition would significantly worsen during the acute hospital stay based on laboratory markers.

All subjects gave informed consent to participate in the study and the study was approved by the Institutional Review Board.

## Materials and Methods

After institutional review board approval was obtained, 105 orthopaedic trauma patients admitted to Orthopaedics as the primary team at a Level I regional trauma center over an eight month period were enrolled in the study. Of note ICU patients were not included because they are not on the Orthopaedics primary team. All patients were identified at the time of hospital admission and were entered into the prospective database. Exclusion criteria included: age less than 18, patient lacking capacity to consent with no family members present during admission, and non-English or non-Spanish speaking patients.

Subject demographic (age, gender, height, weight, BMI) and clinical (date of admission, dates of operation, date of discharge, 6-week follow-up, type of orthopaedic injury, surgery performed, co-morbidities, and occurrence of nutritional consultation) data were recorded and entered into a confidential database. The co-morbidities recorded were a history of hypertension, diabetes, HIV infection, smoking, substance abuse, and hepatitis. The markers applied to assess nutritional status included albumin (ALB), prealbumin (PAB), transferrin (TRA), CRP, and vitamin D. Serum laboratory markers were obtained on admission, hospital day 3, hospital day 7 (if not discharged), and at 6 weeks post-surgery (if malnourished on discharge). Vitamin D levels were obtained on admission and 6-week follow-up. Nutritional status was determined using the Rainey MacDonald nutritional index (RMNI). The RMNI was calculated as follows: $RMNI=(1.2 \times ALB) + (0.013 \times TRA) - 6.43$(23). Values considered representative of suboptimal nutrition were ALB <3.5g/dL, PAB <18mg/dL, TRA <180mg/dL, and vitamin D <32ng/mL, while a serum CRP level of >10mg/L was considered indicative of acute-phase response.

We assessed apparent trends and effects of demographic and clinical characteristics on four nutritional markers (ALB, PAB, CRP, and RMNI) using regression analyses treating admission levels as an explanatory factor. That is, we adjusted for admission levels (as in an analysis of covariance). These analyses allow the change (decrease or increase) in markers to differ according to baseline. Due to a pattern of heterogeneity of variance, CRP was analyzed on a logarithmic scale. The other three markers were modeled in the original units of measurement. The demographic factors were Age, Sex, Injury Severity Score (ISS), and BMI.

The research proposal was approved by the committee on research ethics at the institution in which the research was conducted in accordance with the Declaration of the World Medical Association (www.wma.net) and informed consent from human subjects was obtained as required.

## Results

Out of 103 total patients enrolled, 5 patients were excluded because they did not get appropriate lab results

**Table 1. Baseline demographic and clinical data**

| | N=98 |
|---|---|
| **Sex (M:F)** | 51:47 |
| **Age (range)** | 49 ± 17y (18-91 y) |
| **Body height (cm)** | 172.8 ± 13.0 |
| **Body weight (kg)** | 87.0 ± 28.9 |
| **BMI (kg/m$^2$)** | 28.4 ± 8.1 |
| **Mean no. of pre-fracture comorbidities** | 0.9 ± 1.1 |
| **Type of orthopaedic injury, no. cases (%)** | |
| Femur fracture | 22 (22.5%) |
| Tibia fracture | 33 (33.7%) |
| Ankle fracture | 18 (18.4%) |
| Humerus fracture | 6 (6.1%) |
| Forearm fracture | 9 (9.2%) |
| Pelvis fracture | 6 (6.1%) |
| Acetabular fracture | 17 (17.3%) |
| Other | 26 (26.5%) |
| **Musculoskeletal injuries requiring >1 surgery, no. cases (%)** | 32 (32.7%) |
| **Patients receiving nutrition consults (%)** | 39 (40.2%) |
| **Median length of hospital stay in days (Range)** | 6 (2-48) |
| **Infections, no. cases (%)** | 9 (9.2%) |
| **Median ISS (Range)** | 7 (4-26) |

drawn on hospital day 3. As a result, 98 orthopaedic trauma patients were included in the final analysis. There were 51 males and 47 females with a mean age of 49±17 y (18-91 y). All patients had at least one orthopaedic surgery procedure during the acute hospital stay. The median hospital length of stay was 6 days. Baseline demographic and clinical data are summarized in [Table 1].

Nutritional marker levels trended downward during the hospital stay reaching their nadir at hospital day 7, with 89% of patients being malnourished based on prealbumin levels on day 7 [Table 2]. These values trended toward correction by 6-week follow-up with significant improvement from the admission labs. CRP levels increased from admission to a peak at hospital day 3, with a decline at the 6-week follow-up.

Nutritional trends are reflected in the percent of subjects malnourished based on lab markers, as seen in [Table 3]. The proportion of subjects malnourished increased dramatically between admission and hospital day 3 regardless of criteria. Admission values compared to day 3 were 60% vs 85% for albumin, 41% vs 90% for prealbumin, and 38% vs 80% using the RMNI. Globally, the nutritional markers were slightly less indicative of malnutrition from day 3 to 7. A large decrease in the percent of patients being malnourished from day 7 to 6 week follow-up. However, 13.0%, 19%, and 12% of patients remained malnourished based on ALB, PAB, and RMNI, respectively at six weeks. Similar trends were seen in the percent of patients in acute-phase response; with an increase from admission to HD3 and a continual decrease until 6-week follow-up. All patients were in APR (CRP>10mg/dL) at HD3, with 70% in severe APR as defined by the upper quartile of our study group's admit CRP levels. 81% of patients had abnormal Vitamin D levels on admission, improving slightly to 70% seen at 6 weeks.

**Table 2. Mean Nutritional Marker Levels at Each lab draw**

| Marker | Admit | Hospital Day 3 | P-value (Admit to HD3) | Hospital Day 7 | P-value (HD 3 to HD 7) | 6 week Follow-up |
|---|---|---|---|---|---|---|
| ALB (g/dL) | 3.3 | 2.9 | $9.5 \times 10^{-11}$ | 2.8 | 0.23 | 4 |
| PAB (mg/dL) | 19.3 | 12.2 | $2.6 \times 10^{-25}$ | 10.7 | 0.67 | 26.7 |
| TRA (mg/dL) | 205 | 167 | $2.9 \times 10^{-6}$ | 171 | 0.71 | 245 |
| RMNI | 0.253 | -0.62 | $2.9 \times 10^{-11}$ | -0.81 | 0.48 | 1.71 |
| CRP (mg/L) | 40.4 | 104.6 | 1.6 x 1$^{0-1}$3 | 72.6 | 0.11 | 3.8 |
| Vit. D (ng/mL) | 21.1 | | | | | 22.7 |

**Table 3. Malnutrition prevalence at each lab draw**

| % Malnourished based on | Admit | Hospital Day 3 | Hospital Day 7 | 6 Week Follow-up |
|---|---|---|---|---|
| ALB (<3.5g/dL) | 60.2 | 84.9 | 73.9 | 12.9 |
| PAB (<18mg/dL) | 41.2 | 89.7 | 89.1 | 19.4 |
| RMNI (<0) | 38.1 | 79.8 | 68.9 | 11.5 |
| % In severe acute-phase response (CRP>61.65mg/L) | 30.6 | 69.8 | 55.8 | 3.7 |
| % Vitamin D abnormal (≤32ng/mL) | 81.9 | | | 70.0 |

Sixty-nine percent of patients were under the age of 60 and 31% of patients were aged 60 years or greater (senior patients). Anthropometric and laboratory nutritional measurements for these two groups are presented in [Table 4]. The senior patients trended towards a lower median BMI which is not statistically significant, and this group had more female patients (63 vs. 41). Both groups had similar rates of malnourishment on admission with similar median laboratory nutritional markers. Vitamin D levels for senior patients were higher than for patients less than 60 years on admission and were notably higher at 6-week follow-up.

The regression analyses of day 3 nutritional marker levels compared to admission levels in demographic and clinical covariates confirm the statistical significance of the changes in these nutritional markers, adjusting for age, sex, ISS, and BMI. In fact, the only patient characteristic that is significantly related to the levels of these nutritional markers is age, with older patients showing greater depression of ALB, PALB, and RMNI. The coefficients of Sex, ISS, and BMI in the linear regression models were not significant and there was no evidence of interaction with marker levels at admission.

Tables 2 and 3 and makes clear the statistical

**Table 4. Laboratory Nutritional Measurements**

| Nutritional variable | Under 60 years n=68 Median | 60 years and older n=30 Median | *P-value* |
|---|---|---|---|
| **BMI** | 27.4 | 26.4 | 0.705 |
| **CRP (mg/L)** | | | |
| Admit | 40.40 | 40.85 | 0.827 |
| HD3 | 104.55 | 119.40 | 1.000 |
| HD7 | 72.60 | 86.90 | 0.656 |
| 6WK | 4.00 | 2.70 | 0.766 |
| **Albumin (g/dL)** | | | |
| Admit | 3.30 | 3.30 | 0.854 |
| HD3 | 2.90 | 2.80 | **0.042** |
| HD7 | 2.75 | 2.25 | 0.314 |
| 6WK | 4.00 | 3.95 | 0.537 |
| **Prealbumin (mg/dL)** | | | |
| Admit | 19.30 | 19.65 | 0.774 |
| HD3 | 12.20 | 12.20 | 0.943 |
| HD7 | 10.65 | 9.25 | 0.314 |
| 6WK | 26.70 | 26.75 | 0.766 |
| **Transferrin (mg/dL)** | | | |
| Admit | 205.00 | 196.00 | 0.706 |
| HD3 | 167.00 | 163.00 | 0.695 |
| HD7 | 171.00 | 147.00 | 0.236 |
| 6WK | 244.50 | 219.50 | 0.133 |
| **RMNI** | | | |
| Admit | 0.25 | 0.25 | 0.947 |
| HD3 | -0.62 | -0.96 | 0.062 |
| HD7 | -0.81 | -1.91 | 0.542 |
| 6WK | 1.71 | 1.58 | 0.764 |
| **5-OH vitamin D3 (ng/mL)** | | | |
| Admit | 19.10 | 25.50 | 0.114 |
| 6 weeks | 19.70 | 42.90 | **.011^1**2 |

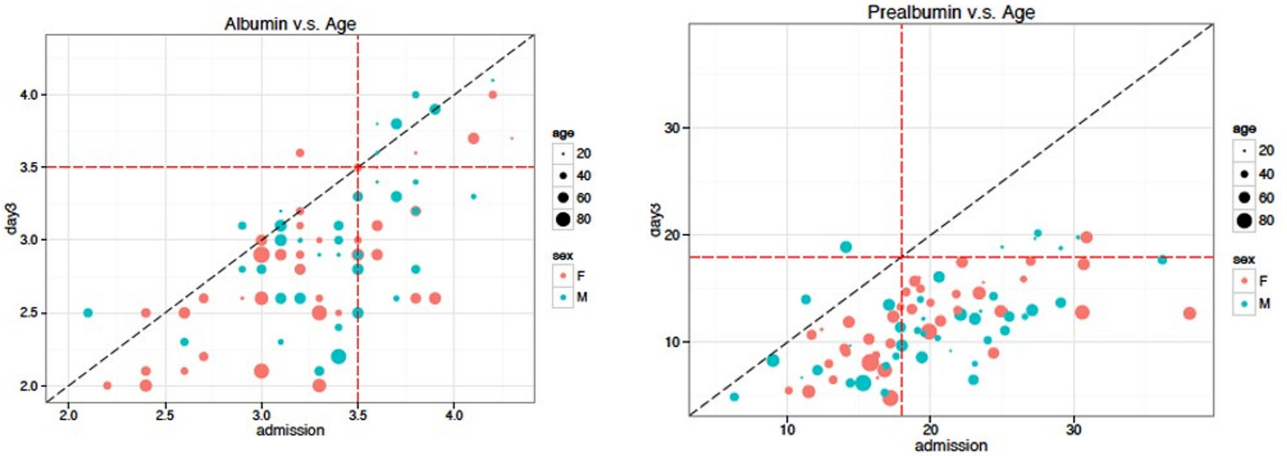


**Figure 1. Three nutritional value plots (albumin, prealbumin, RMNI) and inflammatory value plot (CRP). The dashed black diagonal line is the identity line in each plot. The dashed horizontal and vertical red lines delineate the suboptimal nutrition thresholds. Points in the lower right quadrant represent patients who dropped from adequate to suboptimal nutrition levels while those in the lower left quadrant represent patients who had suboptimal nutrition levels at admission and at 3 days. Points in the upper left hand quadrant of the CRP plot represents patients who had elevated CRP at day but not on admission. The right upper quadrant represents patients who had elevated CRP on admission and at 3 days. Males are marked with blue circles, and females are marked with red circles. Circle size represents age, with an older age represented by larger circles.**

significance of the changes in marker levels from admission to day 3 [Figure 1].The dashed black diagonal line is the identity line and the fact that almost all the points are below the line for ALB, PALB, and RMNI shows that almost everyone demonstrated a drop in these nutritional markers. Correspondingly, most patients showed an increase in CRP levels. The dashed horizontal and vertical red lines delineate the suboptimal nutrition thresholds. Points in the lower right quadrant represent patients who dropped from adequate to suboptimal nutrition levels while those in the lower left quadrant represent patients who had suboptimal nutrition levels at admission and at 3 days. There is no significant difference between the males and females, marked in different colors, but there is a significant difference in the size of the plotting symbols with the larger circles, representing older patients, tending to be lower in the panels for ALB, PALB, and RMNI, indicating greater drops in nutrition. Age was not significantly related to day 3 levels of CRP.

Nine patients experienced complications, with 3 cases of deep infection requiring operative debridement and 7 cases of superficial infection requiring oral antibiotics (one patient had multiple complications). Patients experiencing complications had significantly longer hospital stays (11 d vs. 6 d), a higher mean number of co-morbidities (1.22 vs. 0.87), and more surgeries (2.22 vs. 0.93). In addition, patients having complications had lower laboratory nutritional markers and higher rates of malnutrition at nearly all time points for nearly all lab values [Table 5]. The most notable finding was that patients who had complications had significantly lower prealbumin levels on admission compared to patients that did not have complications.

**Table 5. Laboratory nutritional marker values comparison between patients with and without complications**

| | No complications | Complications | |
|---|---|---|---|
| **Nutritional variable** | **n=89** | **n=9** | ***P-value*** |
| | **Median** | **Median** | |
| **BMI** | 27.05 | 32.70 | 0.151 |
| **CRP (mg/L)** | | | |
| Admit | 37.60 | 78.70 | **0.484** |
| HD3 | 99.30 | 193.05 | 0.710 |
| HD7 | 70.35 | 210.00 | 0.946 |
| 6WK | 3.30 | 24.95 | 0.194 |

**Table 5. Continued**

| | | | |
|---|---|---|---|
| **Albumin (g/dL)** | | | |
| Admit | 3.40 | 3.00 | 0.056 |
| HD3 | 3.00 | 2.60 | 0.085 |
| HD7 | 2.90 | 2.30 | 0.052 |
| 6WK | 4.00 | 3.60 | 0.087 |
| **Prealbumin (mg/dL)** | | | |
| Admit | 19.70 | 17.20 | **0.039** |
| HD3 | 12.40 | 9.20 | 0.736 |
| HD7 | 11.05 | 6.40 | 0.243 |
| 6WK | 26.75 | 23.65 | 0.665 |
| **Transferrin (mg/dL)** | | | |
| Admit | 205.50 | 195.00 | 0.974 |
| HD3 | 169.00 | 160.50 | 0.736 |
| HD7 | 171.00 | 133.00 | 0.332 |
| 6WK | 244.50 | 249.50 | 0.664 |
| **RMNI** | | | |
| Admit | 0.32 | -0.26 | 0.171 |
| HD3 | -0.58 | -1.16 | 0.063 |
| HD7 | -0.65 | -1.71 | 0.114 |
| 6WK | 1.72 | 1.21 | 0.664 |

## Discussion

Malnutrition is a primary concern in hospitalized patients, and patients with poor nutritional status may have prolonged hospital stays with more complications and worse outcomes. People with trauma often are under extreme metabolic stress owing to a severe inflammatory response and in the acute orthopaedic patient, fractures are associated with increased rates of catabolism (8,9,18-21,24). Due to this profound response to injury, even those patients that do not present with concerns for malnutrition may rapidly become undernourished.

This study examined nutritional status changes in orthopaedic trauma patients using nutritional markers throughout the acute hospital stay and at the 6-week follow-up visit. The primary aim of the study was to evaluate the prevalence of malnourished patients on presentation and track nutritional status changes during the acute hospital stay. The secondary aim was to determine if the senior patients are at increased risk of becoming malnourished compared to a younger cohort and to determine if being malnourished increases the risk of postoperative complications. While there is no current consensus on a gold standard for diagnosing protein-energy malnutrition, we believe that early identification and intervention in malnourished orthopaedic trauma patients may help avoid those complications shown to be associated with malnutrition. This study suggests that serum lab markers frequently used to assess nutritional status rapidly decline in the acute orthopaedic trauma patient. Additionally, increasing age is associated with an increased risk of being malnourished during the acute hospital stay and patients who have lower pre-albumin levels on admission have a higher complication rate. While the number of complications was relatively low, we did note a statistically significant difference between admission prealbumin levels in patients with and without complications.

Many methodologies in addition to biochemical markers have been examined for the identification of malnutrition in the hospitalized patient, including anthropometric approaches such as BMI, fat folds, middle upper arm circumference, and handgrip strength. Subjective tests include: the detailed nutritional assessment (DNA), subjective global assessment (SGA), and the Mini Nutritional Assessment (MNA). However, anthropometric criteria reflect more chronic malnutrition and would potentially fail to detect an acute nutritional status decline in its earliest stages. The complexities and costs associated with malnutrition screening tests, such as the MNA and SGA, are prohibitive to their widespread adoption in clinical practice. Studies have also demonstrated that both anthropometric criteria and screening tests, when applied as nutritional assessment measures in hip fracture patients, will lead to under-diagnosis of malnourished individuals (25,26).

Reproducibility and ease of introduction into clinical practice make biochemical markers an appealing means for detecting patients at risk of malnutrition. Albumin has been an especially attractive option due to its wide availability and low cost, however, its long half-life and variable response in patients with longer-term nutritional impairment, and sensitivity to inflammation have brought into question its use as a nutritional marker. Despite this, several studies report an association between albumin levels measured at hospital admission and patient outcomes in hip fracture patients (18-21). Reported prevalence of malnutrition based on albumin measurements in hip fracture patients over age 65 has varied, ranging from 22% reported by Symeonidis et al. to 52% reported by O'Daly et al. This is compared to a prevalence of 57% on admission in patients aged over 60 years in this study. Prealbumin is another popular marker for malnutrition owing to its short half-life and sensitivity to changes in nutritional status. It has been described as a useful alternative to SGA and DNA as a screening tool for malnutrition (23). It was demonstrated to be an effective marker for both predicting complications after gastric surgery and predicting microvascular free flap failure (27,28).

While this is a prospective study it does have some limitations. The number of patients with available laboratory markers after day 3 is different. For example, the loss of patients that were discharged prior to hospital day 7 could result in simple descriptive statistics being misleading. It is likely that patients who recovered the fastest or suffered less trauma left the hospital before day 7. This is the reason why we only performed the statistical analysis that is displayed in for admission and day 3 laboratory values [Figure 1]. Definitive conclusions should not be made in regards to the nutritional markers and complication rates due to the small number of patients in each group.

Another limitation of this study and any study utilizing biochemical markers for malnutrition is the expected negative effects on these markers that occur during the acute phase response. For example, prealbumin concentrations are well known to be inversely correlated to CRP(29,30). We tried to control for this effect by also obtaining CRP values and assessing trends between CRP levels and nutritional marker levels. Gariballa et al. confirm the correlation between poor nutritional status and acute-phase response and recommend the incorporation of measurements of the acute-phase response as part of the criteria for nutritional screening (29). Shenkin suggests that a clearer interpretation of nutritional status could be achieved through two measurements of prealbumin and CRP, performed three to five days apart, in order to assess trends (30). An etiology-based approach to malnutrition with a redefinition of the disease to include several subsets, including injury-related malnutrition has been suggested to be a more accurate means of assessing for malnutrition (8,9). To our knowledge, no studies have examined the evolution and interaction of malnutrition and acute phase response during the acute hospital stay in the trauma patient. Results of this study indicate increased acute-phase response (CRP) from admission to the hospital on day 3, followed by a decrease in CRP values by day 7. Interestingly, while the CRP levels trend down during this time period indicating decreasing acute phase response, nutritional markers continue to further decline to poorer values. Thus, the continued diminishment of nutritional markers despite decreasing CRP levels in our subjects is indicative of rapidly decreasing nutritional status superimposed on a waning acute-phase response.

In conclusion, malnutrition in the acute orthopaedic trauma patient, as defined by frequently used biochemical markers, is a common disease that increases in prevalence throughout the hospital stay. We advocate routine assessment of nutritional status in this population, specifically obtaining nutritional markers (prealbumin or albumin) on hospital day 3 to identify patients that will be at risk for being malnourished in the postoperative course. The authors advocate nutritional counseling and protein supplementation if malnutrition is identified.

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