ORIGINAL

Serum albumin levels correlate with inflammation rather than nutrition supply in burns patients : a retrospective study

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Abstract : The aim of this retrospective study was to examine whether serum albumin levels offer a good marker of nutritional status in patients with burns. Serum albumin levels have been used to evaluate nutritional status in burns patients, even though these levels are affected by various factors and are not specific to malnutrition. To clarify whether provision of nutrition or presence of inflammation affects serum albumin levels, we studied serum albumin levels, C-reactive protein (CRP) levels and caloric intake over time in 30 patients with burns. Serum albumin levels did not respond to provision of nutrition, but correlated negatively with CRP levels, suggesting that serum albumin levels are more closely associated with inflammation than nutrition. This study also suggests that hypoalbuminemia is a good indicator of the severity of burns or associated complications. We conclude that serum albumin levels do not offer a good nutritional marker in burns patients. J. Med. Invest. 61 : 361-368, August, 2014

Keywords **:** *serum albumin, nutritional status, burn injury, C-reactive protein, inflammation*

INTRODUCTION

Albumin is the main protein synthesized by the liver and has several important functions : it is essential for the maintenance of normal plasma colloid oncotic pressure and is the primary binding protein in serum, responsible for the transport of various substances in the circulation including fatty acids, hormones, and drugs.

Serum albumin level has been considered one of the best indicators of nutritional status and hypoalbuminemia has been thought to mean protein malnutrition (1, 2). In some recent reports, however, serum albumin has been more significantly influenced by factors other than nutritional intake (3-5). Inflammation may reduce serum albumin concentrations independently of malnutrition, and severe hypoalbuminemia is common in critically ill patients, including burns patients. Ramos *et al.* (6) recently found that hypoalbuminemia was strongly associated with an increase in the affected body surface area (BSA), greater burn severity, and higher mortality rate. They concluded that serum albumin level can be used as a marker for trauma severity, rather than nutritional status. Hypoalbuminemia in burns patients results from fluid resuscitation and higher

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vascular permeability in burn wounds that allows exudation with substantial protein loss through the burn wound. Many physicians are still using serum albumin levels to evaluate nutritional status, and specifically the response of burns patients to the nutrition. However, the association between serum albumin level and nutritional state has not been well established (7). Over-nutrition has recently been associated with increased risk of complications such as hyperglycemia, carbon dioxide retention, and azotemia, which delay wound healing in burns patients. The primary goal of nutritional support is to meet the metabolic needs of burned patients adequately, and to promote wound healing, and not simply to increase caloric or protein intake according to serum albumin levels. The aim of this retrospective study was therefore to examine the relationships of serum albumin levels after burn injuries with C-reactive protein (CRP) levels, as a marker of inflammation, and caloric intake to clarify whether albumin offers a good marker of nutritional status.

Table 1. Patient characteristics (n=30)

Variable		Value
Sex		
	Male	24 (80%)
	Female	6 (20%)
Age		52.6±23.6 years
Number of in-hospital deaths		1 (3.3%)
Average length of hospital stay		72.7±51.4 days
Body weight		54.6±17.8 kg
	Male	55.0±19.4 kg
	Female	52.7±8.5 kg
Body mass index		22.3±3.3
*Total body surface area burned		23.9±18.4 (%)
Cause of burn		
	Scald	7 (23.3%)
	Flame	22 (73.3%)
	Unknown	1 (3.3%)

Number and percentage of patients are shown unless otherwise indicated.
* Total body surface area burned was determined by the rule of nines.

METHODS

Patients

The study included 30 patients with burn injuries who were treated at Tokushima University Hospital between March 2005 and February 2012. Only patients who underwent blood tests between the time of admission and the time of discharge or in-hospital death were included in this study. Patients who underwent blood transfusion or albumin supplementation were also included. All patients underwent operations such as relaxation incision, burn wound excision and skin grafting on one or more occasions. Characteristics of the participating patients, including the cause of burn injuries, total BSA (TBSA) burned, and Burn Index, are shown in Table 1.

Data collection

Patient data including demographic characteristics, blood test results, and caloric intake were collected from medical records. Blood test results included serum levels of albumin and C-reactive protein (CRP). The caloric intake of each patient was calculated according to the amount of enteral or parenteral nutrition, contents of the parenteral or enteral solution, and feeding rate, from the patient's medical records. Caloric intake from the day of a blood test until the day of the next blood test was totaled and then averaged per number of days between tests to yield a daily value. In addition, basal energy expenditure (BEE, as determined by the Harris-Benedict equation), caloric intake/BEE, and caloric intake/body weight were calculated.

Analyses

Serum albumin levels and caloric intake

To analyze correlations with caloric intake or CRP levels, serum albumin levels were obtained at two time points : the first time point at which serum albumin level became minimal from 3 days postburn or after influence of supplemental human albumin (HA) was thought to have disappeared in cases where supplemental HA was provided on consecutive days, and the second time point at which a latest serum albumin level could be acquired by discharge from the hospital or transfer to another hospital. To analyze serum albumin levels in relation to caloric intake, patients were divided into two groups : a greater caloric intake group (mean caloric intake > 30 kcal/kg/day between the two time points) ; and a lesser caloric intake group (mean caloric intake < 30 kcal/kg/day between the two time points). Serum albumin values obtained at the two time points were compared between caloric intake groups using the Wilcoxon signed-rank test. To analyze serum albumin levels in relation to caloric intake, patients were divided into two groups : those in whom serum albumin increased by more than +0.3 g/dl ; and those in whom serum albumin changed by between +0.3 and -0.3 g/dl. There was no patient with a change of more than -0.3 g/dl. Changes were based on the difference in serum albumin levels between the two time points in each group. Mean caloric intake between the two groups was compared using the Mann-Whitney U test.

Changes in CRP level were also analyzed in relation to caloric intake. Patients were again divided into two groups : a group with lower CRP change (CRP level decreased by > 7.0 mg/dl) and the CRP higher change group (CRP level decreased by < 7.0 mg/dl). Mean caloric intake was compared between groups using the Mann-Whitney U test.

Changes in serum albumin level in relation to CRP level

To analyze serum albumin levels in relation to CRP levels, changes in CRP level in the serum albumin minimal change group and serum albumin increasing group were analyzed using the Wilcoxon signed-rank test.

To analyze the rate of CRP change in relation to serum albumin change between the first and second time points, the correlation coefficient for the two values was calculated. The significance of the correlation coefficient was determined using Student's t-distribution.

Statistical analyses

Data are expressed as mean (± standard deviation). All analyses were performed using Excel 2010 software (Microsoft, Redmond, WA, USA).

RESULTS

The study included 30 patients. Table 1 shows background characteristics of the patients.

Caloric intake, serum albumin levels and CRP levels

In the lesser caloric intake group, serum albumin levels at the first and second time points were 2.2 ± 0.4 g/dl and 2.9 ± 0.6 g/dl, respectively ($p < 0.01$). In the greater caloric intake group, serum albumin levels at the first and second time points were 1.5 ± 0.5 g/dl and 2.7 ± 0.7 g/dl, respectively ($p < 0.01$) (Fig. 1). A significant difference in serum albumin levels was seen between the first and second time points in the lesser and greater caloric intake groups ($p < 0.01$). Caloric intake was 28.2 ± 10.0 kcal/kg in the group of patients in whom serum albumin increased, and 26.2 ± 9.6 kcal/kg in the albumin minimal change group, showing no significant difference (Fig. 2). In addition, no significant difference in caloric intake was apparent between the CRP greater change group (26.9 ± 9.7 kcal/kg) and the CRP lower change group (28.7 ± 10.2 kcal/kg) (Fig. 3).

Changes in serum albumin levels in relation to CRP levels

In the group of patients in whom serum albumin increased, CRP level was 11.6 ± 6.8 mg/dl at the first time point and 2.1 ± 5.1 mg/dl at the second

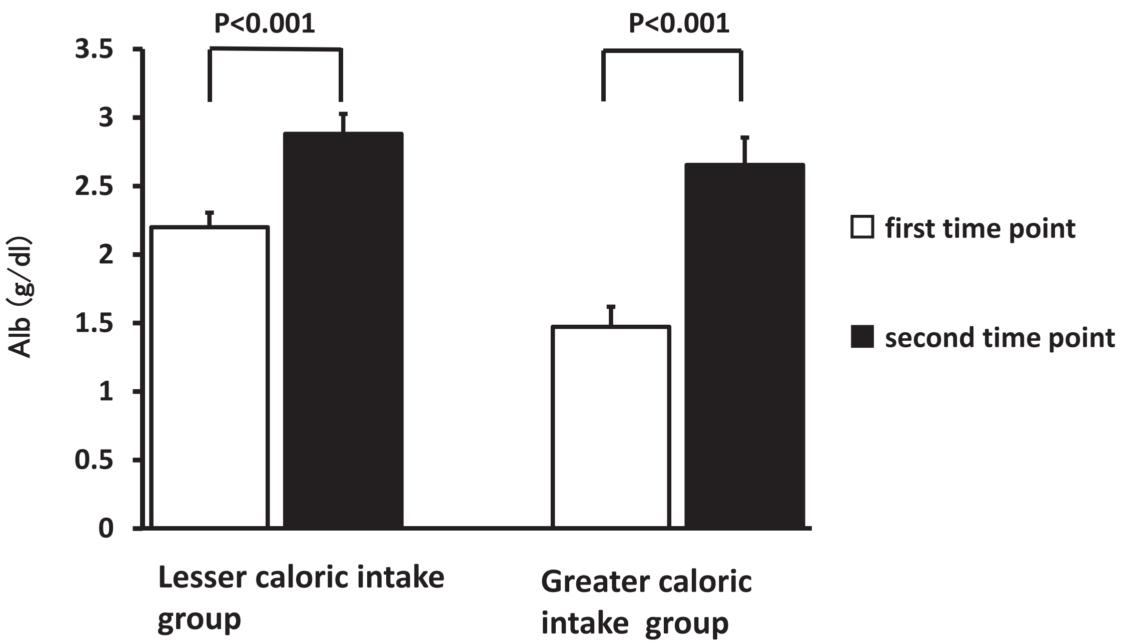

Figure 1. Serum albumin level in lesser and greater caloric intake groups (n = 27 ; three infants were excluded)
Lesser caloric intake group (n = 16), < 30 kcal/kg/day ; Greater caloric intake group (n = 11), > 30 kcal/kg/day. Significant within-group differences were found.

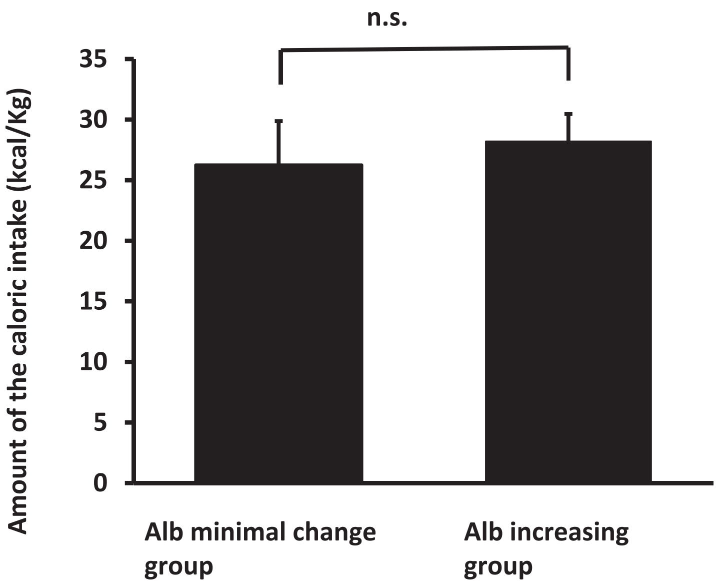

Figure 2. Caloric intake in the two groups with albumin changes (n=27 ; three infants were excluded)
Alb minimal change group (n=7), serum albumin changed only minimally (between +0.3 and -0.3 g/dl) ; Alb increased group (n=20), serum albumin increased by more than +0.3 g/dl. No significant difference between the two groups was found.

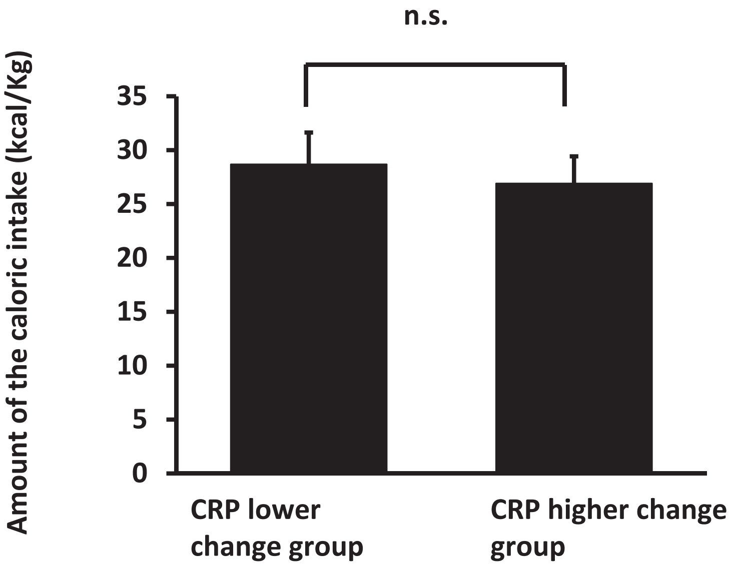

Figure 3. Caloric intake in the two groups with CRP changes (n=27 ; three infants were excluded)
CRP lower changing group (n=12), CRP decreased by <7.0 g/dl ; CRP higher changing group (n=15), CRP decreased by >7.0 g/dl. No significant difference between the two groups was found.

time point. CRP levels were significantly different between the first and second time points in the albumin increasing group ($p<0.01$). In the albumin minimal change group, the change in CRP levels was not significantly different. CRP levels at the first and second time points were 8.6 ± 5.7 mg/dl and 4.1 ± 3.5 mg/dl, respectively (Fig. 4). Changes in serum albumin levels correlated negatively with changes in CRP. The correlation coefficient of changes in serum albumin levels and CRP was -0.497 ($P<0.01$) (Fig. 5).

Case presentation

Case 1

A 25-year-old man suffered from a 39% TBSA burn after setting fire to his clothes in a suicide attempt. He had sustained burns to the neck, chest, abdomen, two-thirds of the back, and both upper arms. No inhalation injuries were present. On arrival, the patient was intubated and underwent relaxation incision on the chest and both upper arm because of difficulty with ventilating the patient. He was resuscitated according to the Parkland formula

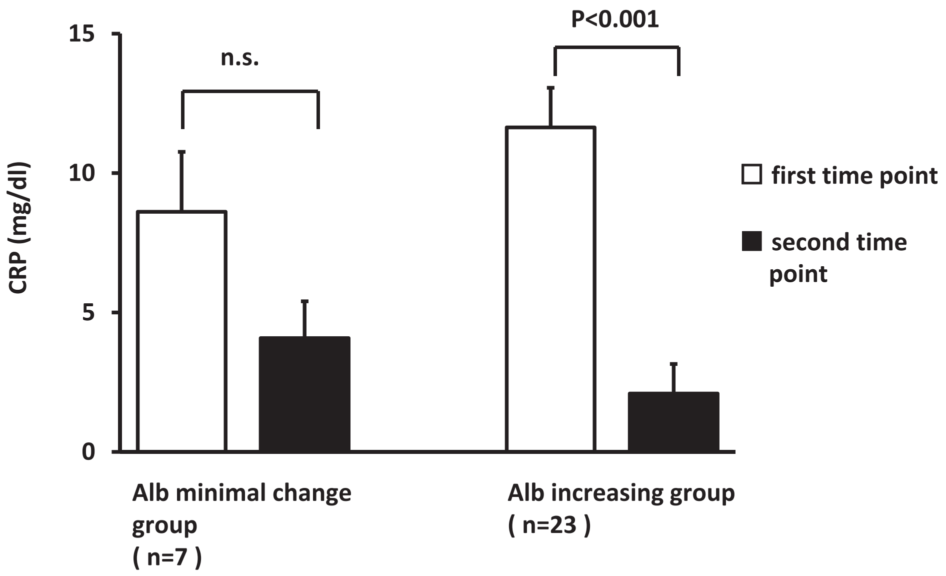

Figure 4. Values of CRP in the two groups with albumin changes
Alb minimal change group (n=7), serum albumin changed only minimally (between +0.3 and -0.3 g/dl) ; Alb increased group (n=20), serum albumin increased by more than +0.3 g/dl. No significant difference within the alb minimal change group was found. A significant difference within the alb increasing group was found.

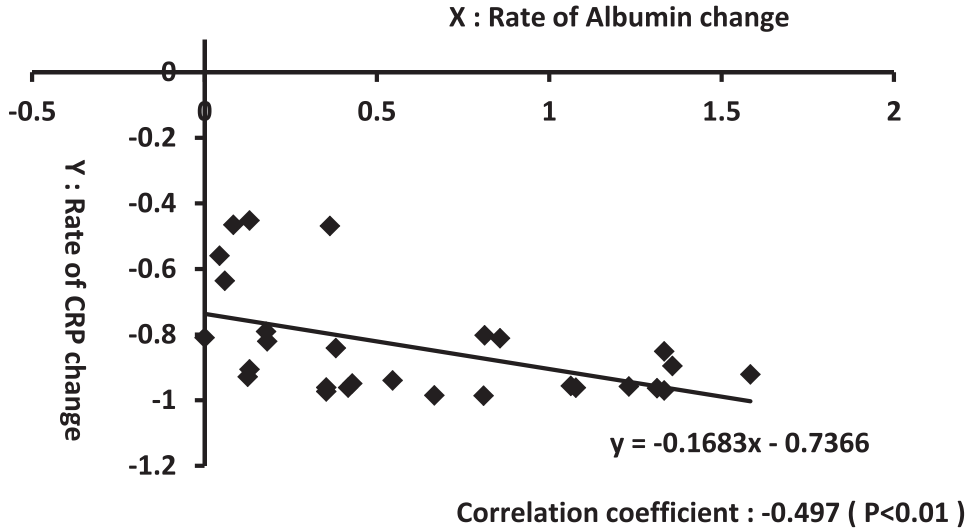

Figure 5. Relationship between rate of CRP change and rate of albumin change (n=28 ; two outliers were rejected)
Changes in serum albumin levels correlated negatively with changes in CRP.

and supplemental HA (5% or 25% HA) was administered from postburn (PB) day 1 to 9. He underwent burn wound excision and skin grafting on PB days 19, 34, 47, 61, and 93. Operations were performed under general anesthesia. Serum albumin levels correlated negatively with CRP levels after completion of supplemental HA administration on subsequent days. Serum albumin levels gradually increased as TBSA burned decreased to < 5% (Fig. 6).

Case 2

A 77-year-old man suffered from a 15% TBSA burn after his clothes caught fire while he was making a bonfire. He had a medical history of diabetes mellitus, high blood pressure and prostate hyperplasia. He sustained burns to the lumbar and gluteal regions, both thighs, and both hands. No inhalation injury was present. The patient was resuscitated according to the Parkland formula and supplemental HA was administered from PB day 3 to 10. Burn wound excision and skin grafting were performed on PB days 26 and 69 under general anesthesia. Serum albumin levels seemed to correlate negatively with CRP levels from PB day 1, but serum albumin levels did not increase even though CRP levels were decreased on PB day 28 (Fig. 7).

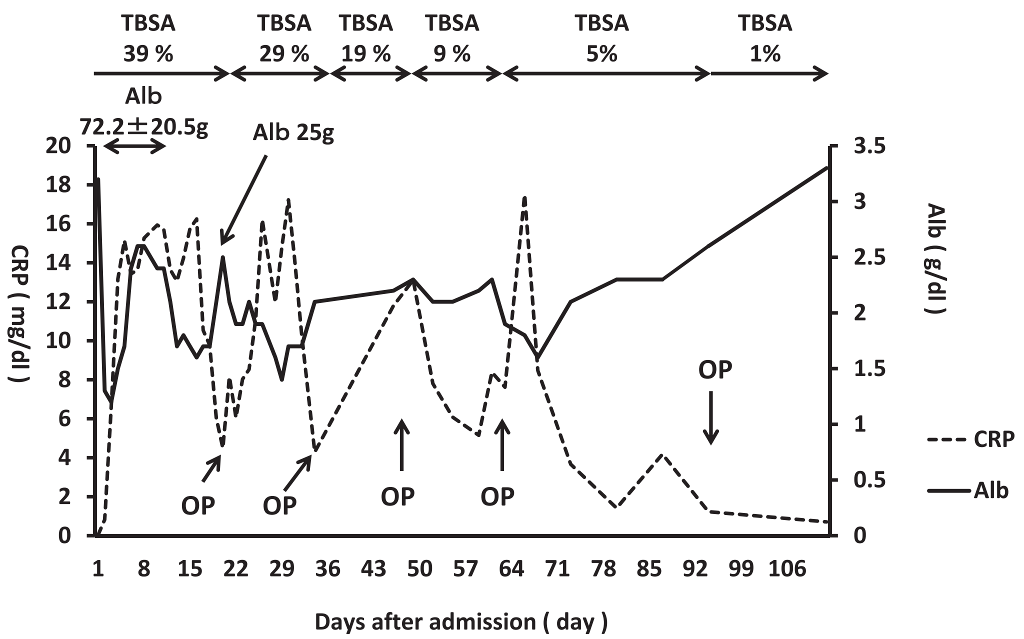

Figure 6. Time course of serum albumin, CRP levels, and TBSA in Case 1

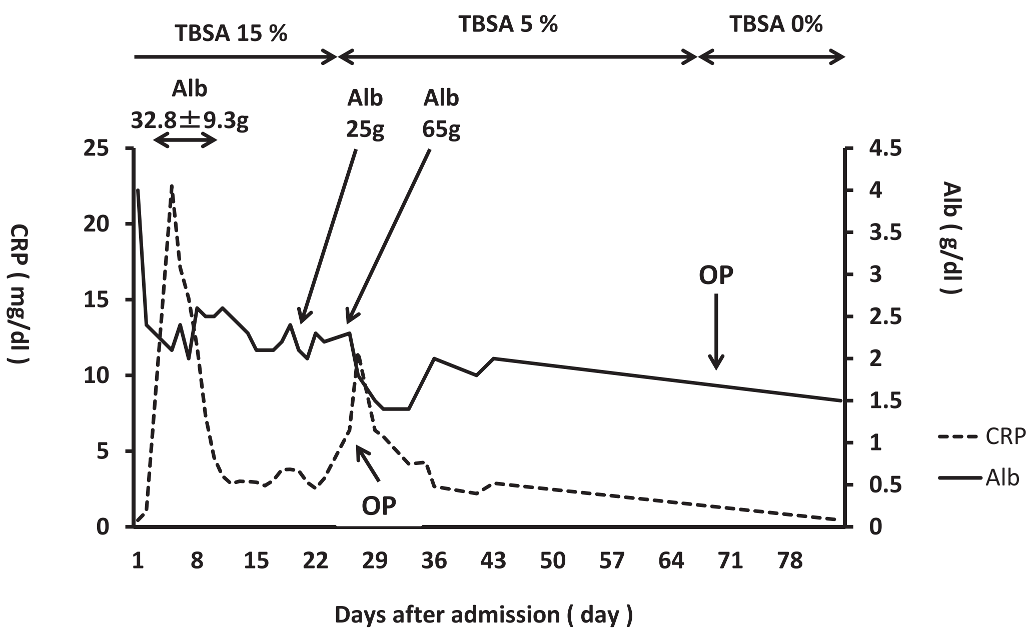

Figure 7. Time course of serum albumin, CRP levels, and TBSA in Case 2

DISCUSSION

We have studied the clinical significance of serum albumin levels as a marker of nutritional status in patients with burns. Our results showed that serum albumin levels did not correlate with caloric intake, but did correlate with CRP and wound healing. Burn wounds produce local and systemic inflammation, increased vascular permeability and hypermetabolism, all of which act to decrease serum albumin levels. In the present study, serum albumin levels increased with improvement of burn wounds, indicating that serum albumin level is a poor marker of nutritional status in patients with burns, but offers a good marker of wound healing.

After admission, hypoalbuminemia is seen in most patients and worsening of existing hypoalbuminemia occurs after hospitalization. Serum albumin levels have historically been linked in clinical practice to nutritional status (1, 2). Particularly with burn injuries, many physicians are still using serum albumin level as a marker of nutritional status, especially for determining response to nutrient provision in burns patients.

During the acute phase of burns, hypoalbuminemia is related to the acute inflammatory response (8). Albumin is considered to be a negative acute-phase protein, which decreases during inflammation (9). Acute-phase reactants including inflammatory cytokines increase acute-phase protein synthesis in the liver and decrease the synthesis of albumin as a negative acute-phase protein (3). Furthermore, reductions in albumin in burns patients might be due to many other factors, including fluid resuscitation and higher vascular permeability in the burn wound that produces exudation with protein loss through the wound (10). In agreement with this theory, we found a good inverse correlation between a marker of inflammation (CRP) and serum albumin level, even if the difference in half-lives results in a time lag between the two biomarkers. The half-life of CRP is about 4-6 h, and that of serum albumin is about 20 days.

In this concept, serum albumin is regarded as an inflammatory marker, rather than a marker representing body composition or adequacy of the nutrition provided (11). In addition, inflammation in our patients was caused not only by the burn injury itself, but also by the underlying disease states, surgeries and infections in the individual patients. In fact, we also found decreased albumin levels together with increased CRP levels after surgical operations and during infections.

Nutritional support for malnourished patients reportedly has no direct effect on serum albumin levels (8, 9, 12). In burns patients, Pérez-Guisado *et al.* (7) found no association between initiation of oral/enteral nutrition and serum albumin level, and concluded that serum albumin level offers a poor nutritional marker in hospitalized patients. Likewise, the present study identified no correlation between serum albumin level and caloric intake. Furthermore, no difference in serum albumin levels was seen between individuals with greater and lesser caloric intake in this study. Such findings suggest that serum albumin levels are unsuitable for assessing nutritional support, which should instead be based on the individual requirement for nutrients.

In the present study, albumin was sometimes infused during fluid resuscitation in the most severely burned patients, altering the significance of hypoalbuminemia, particularly in the first few days after initial fluid resuscitation (8). Due to these factors, our study also showed that serum albumin and CRP levels fluctuated independently, especially for severe burns patients who received infusion of a large amount of albumin in the first few days post-burn, like Case 1. Therefore, in this study, statistical analysis was performed from the end of the two factor's fluctuating independently.

Hypoalbuminemia has been reported as a useful indicator of disease prognosis, development of complications, and mortality (13). In the present study, CRP level decreased significantly in the albumin increasing group, but not in the albumin minimal change group. Some of our cases, however, showed that a state of decreased serum albumin levels continued even though CRP levels had normalized, as in Case 2. In such cases, serum albumin levels decreased due to various factors other than inflammatory mediators, such as severe liver and renal disease, malabsorption, intravascular volume overload, and zinc deficiency (5). Although, serum albumin level may be a good indicator of inflammation in most burns patients, we should always consider other factors that may act to reduce serum albumin levels.

In burns patients, serum albumin levels are reportedly a risk factor for mortality and TBSA burned (8, 14, 15). In our study, mortality could not be investigated because only one patient died. In addition, investigating the association between albumin level in the acute phase and TBSA burned or length of hospital stay was difficult, because serum albumin levels were influenced by fluid resuscitation.

In conclusion, serum albumin levels do not represent a good nutritional marker and should not be depended on excessively when assessing nutritional status in burns patients. Serum albumin levels are not always high in patients with good caloric intake, and low albumin levels do not always indicate malnutrition or insufficient provision of nutrients. Further research is required to establish efficient methods of nutritional assessment in the management of burn injuries.

CONFLICT OF INTEREST

None of the authors have any conflicts of interest to declare.

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