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Original Article

Impact of an enteral nutrition protocol in critically ill patients with burn injuries

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Abstract: Objectives: The objective of this study is to characterize the University of Florida (UF) Health Shands Burn Centers enteral nutrition protocol as it relates to total protein intake and clinical outcomes. Methods: This retrospective chart review study included 99 adult patients admitted to the UF Health Shands Burn Center from January 2012 through August 2016 with burns of twenty percent or greater TBSA and required enteral nutrition supplementation. Results: Patients received an average of 137.8 g or 2.03 g/kg protein daily. Fifteen percent of patients experienced graft loss. The median length of stay was 35 days. Seventy-six percent survived to hospital discharge. There was no significant association between total protein intake and incidence of severe diarrhea (P=0.132). Conclusion: The institutions protocol achieved high protein administration while still being consistent with recommendations from the American Society of Enteral and Parenteral Nutrition (ASPEN).

Keywords: Protein, enteral nutrition, critically ill, diarrhea, burn, thermal injury

Introduction

Nutrition support is crucial to the management of critically injured patients with thermal injury. Shortly after the burn injury, patients enter a hypermetabolic phase characterized by accelerated metabolic rate that can be as high as twice the normal rate of critically ill patients without burn injury. Such a hypermetabolic state may continue to linger for more than a year. Severe burns cause a profound pathophysiological stress response and a radially increased metabolic rate that can persist for years after injury [1, 2].

Early feeding has been shown to mitigate the hypermetabolic and hypercatabolic response following burn injury [3]. Enteral nutrition in particular helps preserve gut-associated lymphoid function and reverse shock-induced mucosal hypoperfusion [4]. All burn patients should receive enteral nutrition unless there is a contraindication. Contraindications include, but are not limited to, massive small bowel resection, high output fistula, and non-occlusive bowel necrosis. It has been noted in the literature that burn patients have increased protein requirements due to increased metabolism. Most burn patients will experience some degree of muscle protein loss due to the hormonal and proinflammatory response to burn injury. Adequate protein provision is essential for post burn as the depletion of protein stores for the purposes of energy production is associated with decreased immune function, delayed wound healing, which ultimately can lead to mortality [5].

The American Society of Enteral and Parenteral Nutrition (ASPEN) Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient recommend 1.5 to 2 grams (g) per kilograms per day (g/kg/d) for burn patients; however, the optimal protein intake remains controversial [6, 7]. In 2012, the UF Health Shands Burn Center implemented an

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enteral nutrition protocol that provides guidelines on protein requirements based on total body surface area (TBSA) burned. The purpose of this study is to characterize the institution's current practice as it relates to total protein intake and clinical outcomes.

Materials and methods

Study design

This retrospective chart review study included adult patients 18 years or older admitted to the UF Health Shands Burn Center from January 2012 through August 2016 with burns of twenty percent or greater TBSA and required enteral nutrition. Patients less than 18 years old, had less than twenty percent TBSA burns, isolated inhalational injuries, and no documented enteral nutrition were excluded. No documented enteral nutrition was defined as no orders for enteral nutrition in the electronic medical record or if the patient expired prior to initiating enteral nutrition. Data was collected from the institution's electronic medical record and for the first 30 days of admission. Additional baseline characteristics collected specific to the burn population include the mechanism of burn injury and the Burn Frailty Index. The Burn Frailty Index is a scoring model to predict morbidity and mortality in elderly frail patients suffering burn injuries. Frailty is defined as the correlation between accumulation of comorbidities with advancing age and increasingly poor outcomes in an elderly patient. The score is calculated by adding each questionnaire item's point value and dividing by 15. The maximum score is 1.13 with scores greater than or equal to 0.30 indicating frailty [8]. The study was approved by the UF Institutional Review Board. As this was a retrospective chart review, approval from the ethics committee was not required.

UF Health Shands Hospital is a 1,040-bed, tertiary academic and level I trauma center with a total of 231 intensive care unit (ICU) beds. The UF Health Shands Burn Center at the time of the study was an 8-bed unit in addition to an average of 7 burn patients on a general medicine floor daily. In 2019, the center expanded to a 27-bed unit with approximately 600 admissions per year.

Enteral nutrition protocol protein requirements

The enteral nutrition protocol at the UF Health Shands Burn Center based protein requirements on the percent TBSA burned. Protein was dosed in g/kg/d using the patient's actual body weight. Per protocol, patients with less than 20% TBSA burned should receive 1-1.5 g/kg/d, 20-40% TBSA burned should receive 2-3 g/kg/d, >40% TBSA burned should receive 2.5-4 g/kg/d. Sources of protein included tube feeding formulas, therapeutic nutrition powders (Juven®), and liquid protein packets (ProSource No Carb®). The protein content from tube feedings ranged from 50 to 81 g per liter depending on which formula was used. Each packet of Juven® contained 14 g of protein and each packet of ProSource No Carb® contained 15 g of protein.

Outcomes

The primary outcome was the average daily amount of protein administered. Secondary outcomes included skin graft loss, diarrhea, length of stay, and survival to hospital discharge. Skin graft loss was defined as the incidence of surgical intervention for regrafting and determined based on chart documentation of an operation note from the burn surgery team. Diarrhea was further characterized by severity. Mild diarrhea was defined as 1 to 2 bowel movements or 200-400 mL stool output from a Flexi-Seal® fecal management system daily. Moderate diarrhea was defined as 3 to 4 bowel movements or 401-600 mL stool output daily. Severe diarrhea was defined as greater than 4 bowel movements or over 600 mL of stool output daily.

Statistical analysis

Statistical analysis was performed using SAS JMP software (version 15.0) and the R Foundation for Statistical Computing software package (version 4.1.1). Continuous variables were summarized as mean and standard deviation for parametric data and median and interquartile range for non-parametric data. Categorical variables were summarized as counts and frequencies. Dichotomized data were compared using the Student's t-test. Linear regression analyses and the Mann-Whitney U test were used to assess the rela-

Table 1. Baseline characteristics

	N=99
Age (years), mean (SD)	47 (17.1)
Male, n (%)	62 (62.6)
Ethnicity, n (%)	
Caucasian	62 (65.3)
African American	26 (27.4)
American Indian	5 (5.3)
Hispanic	2 (2)
Unknown	4 (4)
Weight (kg), mean (SD)	69.4 (14.7)
Body Mass Index Classification, n (%)	
Underweight	8 (7.9)
Normal	42 (42.4)
Overweight	24 (23.8)
Class I Obese	12 (11.9)
Class II Obese	7 (6.9)
Class III Obese	6 (5.9)
%TBSA, n (%)	
20-29	35 (35.4)
30-39	27 (27.3)
40-49	21 (21.2)
50-59	11 (11.1)
60-69	3 (3)
70-79	1 (1)
≥80	1 (1)
Mechanism of Burn Injury, n (%)	
Thermal	78 (83.9)
Chemical	1 (1.1)
Flash	6 (6.5)
Electrical	2 (2.1)
Scald	6 (6.5)
History of Gastric Surgery, n (%)	6 (6.3)
Modified Baux Score, mean (SD) (n=18)	84.7 (19)
Burn Frailty Score, median (IQR) (n=18)	0.13 (0.07-0.20)

Table 2. Daily protein intake

	N=99
Total protein (g), mean (SD)	137.8 (40)
Weight-based total protein (g/kg/d), mean (SD)	2 (0.61)
Weight-based total protein by TBSA burned (g/kg/d), mean (SD)	
20-29%	1.87 (0.60)
30-39%	2.11 (0.58)
40-49%	2.11 (0.54)
50-59%	2.19 (0.78)
60-69%	2.7

tionship between total daily protein and diarrhea, graft failure, and mortality.

Results

Baseline characteristics

A total of 183 patients were screened for inclusion. Eighty-four patients were excluded for missing enteral nutrition prescription documentation. Ninety-nine patients were included for analysis. **Table 1** lists the baseline characteristics. The mean age was 47 years. Sixty-two percent were male. Sixty-two patients had 20-40% TBSA burned and 36 patients had greater than 40% TBSA burned. The predominant mechanism of burn injury was thermal (83.9%). Eighteen patients had a Burn Frailty Index calculated with a median score of 0.13.

Protein intake

Table 2 characterizes the patients' daily protein intake. Patients received a mean of 137.8 g or 2.03 g/kg protein daily. The mean (SD) weight-based total protein was 2.01 (0.62) g/kg/d for patients with 20-40% TBSA burned and 2.02 (0.61) for patients with greater than 40% TBSA burned. Overall, total daily protein increased by 0.12 g/kg/d with each 10% TBSA burned (**Figure 1**).

Secondary outcomes

79% patients required mechanical ventilation within the first 30 days of admission. 11% required renal replacement therapy within the first 30 days. The median length of stay was 35 days. 77% survived to hospital discharge (**Table 3**). There was no significant association

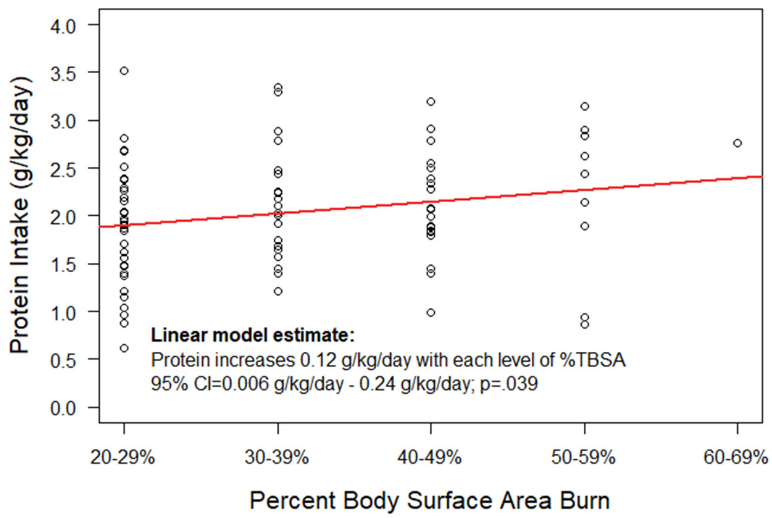

Figure 1. Protein intake/day by percent TBSA with best-fit line.

Table 3. Secondary outcomes

	N=99
Graft Loss, n (%)	14 (14.1)
Mechanical ventilation in first 30 days, n (%)	78 (78.8)
Renal replacement therapy in first 30 days, n (%)	11 (11.1)
Days with Diarrhea (days), median (IQR)	
Mild	3 (1-5)
Moderate	1 (0-3)
Severe	1 (0-6)
Length of Stay (days), median (IQR)	35 (21-73)
Survival at Hospital Discharge, n (%)	76 (76.8)
Disposition at Discharge, n (%) (n=76)	
Home	26 (34.2)
Rehabilitation Center	40 (52.6)
Skilled Nursing Facility	6 (7.9)
Long-term Acute Care	4 (5.3)

between total daily protein and length of stay or survival to hospital discharge.

The median days with mild and moderate diarrhea was 3 days and 1 day respectively. The median days with severe diarrhea was 1 day. A regression analysis was done to assess the relationship between the number of days with severe diarrhea and total grams of daily protein intake, and found no correlation (P=0.132) (**Figure 2**).

15% patients experienced graft loss. Patients who had graft loss received a median of 126 g of protein or 1.9 g/kg daily. Patients who did not experience graft loss received higher amounts of protein, however, it was not statistically significant (**Table 4**).

Discussion

Patients in this cohort received an average of 2.03 g/kg of protein daily through our enteral nutrition protocol, which is within the upper limit of the recommended protein intake for critically ill patients per the ASPEN guidelines [4, 5]. Tube feed formulas without added modular protein did not provide adequate protein at the target goal rate to provide required calorie estimates. Increasing the rate was limited by the osmolality of the tube feeding formula, which therefore limited the patient's tolerability. Furthermore, overfeeding macronutrients in critically ill patients can negatively impact organ function [9]. Van Zanten and colleagues optimized protein intake in their randomized, controlled, double-blind, multicenter trial by utilizing a very high intact-protein formula (8 g protein/100 kcal). Patients in the very high intact-protein formula group received 1.49 g/kg of protein at day 5 compared to the standard high protein formula (5 g protein/100 kcal) group who received 0.76 g/kg of protein (95% CI 0.49-1.03, P<0.001). There were no differences between the groups in terms of gastrointestinal parameters including diarrhea, constipation, and vomiting [10]. Fetterplace and colleagues implemented a protocol that calculated a target volume of tube feedings based on 25 kcal/kg of caloric intake and 1.5 g/kg protein daily. Beneprotein® packets were incorporated as 6 g boluses throughout the day to meet target protein requirements [11].

Previously at UF Health Shands, modular protein supplements were administered in a 60-mL

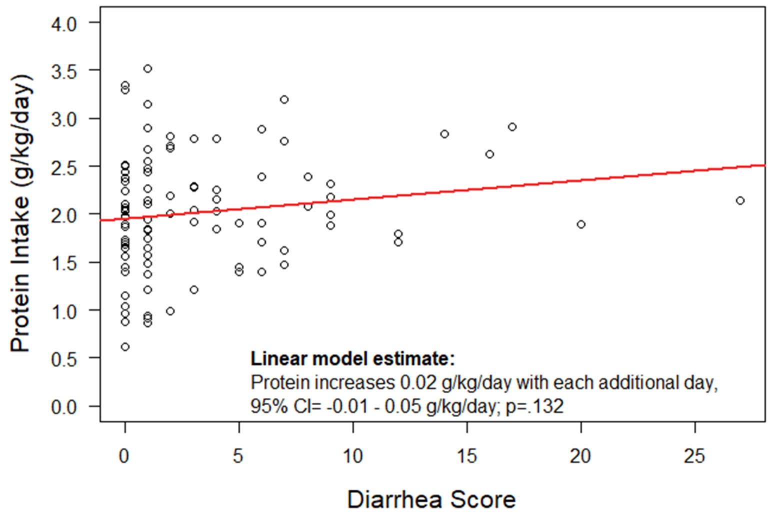

Figure 2. Daily protein intake by number of severe diarrhea days with best-fit line.

syringe as intermittent boluses 2 to 3 times daily to allow for more efficient administration for nursing staff. This method often produced intolerance such as immediate diarrhea or complaints of abdominal cramping, likely due to the high osmolarity. Subsequently, protein supplements were either skipped or missed, contributing to inadequate nutrition and worsening catabolism. Enteral protocol changes allowed for modular protein supplements to be combined in a tube feeding water flush bag and administered as a continuous system at an hourly rate over 24 hours to augment tube feed protein intake, improve compliance and patient tolerability. This method increased the total protein burn patients received to according to the %TBSA burn without increasing the incidence of severe diarrhea.

Of note, the weight-based total protein intake reported in **Table 2** is an average of the daily protein intake based on the first 30 days of admission. Although it appears as though there were protocol deviations and not all groups met their target protein requirements, the initial protein recommendations could be modified later in the hospital course at the discretion of the registered dietitian. Additionally, twenty-five percent of the cohort was obese. While our protocol calculated protein requirements based on actual body weight, the ASPEN guidelines recommend using the ideal body weight if the body mass index is 40 or greater [6]. A randomized, double-blind prospective study by Choban and colleagues found that a parenteral nutrition regimen providing 2 g/kg protein based on ideal body weight preserved nitrogen balance and allowed for adequate wound healing in hospitalized obese patients [12].

The recommended amount of protein in critically ill burn patients continues to be a topic of debate due to the paucity of literature and randomized controlled trials. An observational study by Allingstrup and colleagues showed higher ICU mortality in patients receiving low protein (roughly 1 g/kg daily) compared to patients receiving high protein (roughly 1.7 g/kg daily). The study comprised of a mixed medical-surgical critically ill population, including patients with >15% TBSA burns, but subgroup analyses of the burn population were not performed [13]. A recent large multicenter database analysis by Hartl and colleagues suggested that high protein intake (greater than 1.2 g/kg daily) compared to standard protein intake (0.8 to 1.2 g/kg daily) after ICU admission was not associated with an improvement in outcomes (e.g. in-hospital mortality and live hospital discharge) and may even prolong time to hospital discharge [14]. This analysis, however, generalized all critically ill patients whereas higher protein may benefit burn patients due their hypermetabolic physiology. Our protocol challenges the definition of high protein documented in the literature by pushing the protein intake as high 2.7 g/kg daily. Notably, a limitation of the ASPEN guidelines is the lack of inclusion of clinical trials specifically in the burn or multi-trauma population. The Effect of Higher Protein Dosing in Critically Ill Patients (The EFFORT Protein Trial) trial was an international, single-blinded randomized trial that compared prescribing of high-dose protein (greater than or equal to 2.2 g/kg/day) with usual dose protein (less than or equal to 1.2 g/kg/day) in nutritionally high-risk adults undergoing mechanical ventilation. The patient's dry weight prior to ICU admission was used or their IBW if their BMI was above 30 kg/m^2. No differences

Table 4. Protein intake and graft loss

	Graft Loss (n=14)	No Graft Loss (n=85)	*P*-value
Total protein (g), median (IQR)	129 (106-149)	143 (121-163)	0.217
Weight-based total protein (g/kg/d), median (IQR)	1.9 (1.6-2.1)	2.1 (1.7-2.5)	0.206

were observed in 60-day mortality, hospital and ICU length of stay, and duration of mechanical ventilation. The authors do caution clinicians about high protein doses in acute kidney injury (AKI) and high sepsis-related organ failure assessment scores. Patients with AKI experience increased ureagenesis, which coupled with impaired muscle protein synthesis, can have metabolic burden due to excessive protein-amino acid breakdown [15].

Apart from total protein intake, the ASPEN guidelines also recommend initiating enteral nutrition within 24 to 48 hours of admission for critically ill patients [4]. Our protocol prompts the placement of a Dobhoff tube within 24 hours of admission to guarantee early enteral nutrition administration. Tube feedings are initiated at a trickle rate of 20 mL/hr. If no moderate or severe intolerances exist, tube feedings are advanced by 10 mL/hr every 4 hours as tolerated until the targeted goal rate is reached. Enteral nutrition protocols in critically ill patients with burn injury can have significant patient outcomes including increased caloric and protein intake, reduced ICU and hospital length of stay, and reduced incidence of infectious complications [16]. Protocols also allow for tailoring nutrition prescriptions to patient specific clinical scenarios to ensure the provision of optimal nutrition support throughout the course of treatment.

Notably, 15.2% of patients experienced graft loss, which is expected as burn patients lose their protective barriers following injury. Grafts are prone to failure if they are unsuccessful in adhering to the wound site and if any factors impede the revascularization process. Well-known risk factors include hematoma formation, hyperglycemia, peripheral vascular disease, congestive heart failure, and the presence of certain bacterial organisms [17]. The effect of protein on graft loss has not been well elucidated. Gore and colleagues conducted an isotopic trial showing that there is a net catabolism of muscle and a net anabolism of burned skin in patients following burn injury [18]. The muscle protein breakdown supplies the precursors needed for protein synthesis within the healing wound, however, whether the amount of protein synthesized from this process alone is enough to support adequate healing is not yet known. In addition, glutamine and arginine are crucial amino acids that improve the function of the gut mucosa and immune system, which may reduce infectious complications and reduce the likelihood of graft loss in burn patients. There appeared to be a trend towards a lower incidence of graft loss in patients receiving higher total protein, but a larger cohort is needed to explore this clinical outcome. A major limitation of this study is the descriptive nature with no comparator group. Furthermore, this study was reliant on documentation in the electronic health record, which was either inconsistent or incomplete.

Conclusion

This study characterizes the implementation of an enteral nutrition protocol with protein requirements based on percentage of TBSA burned. Our institution's protocol achieved high protein administration while still being consistent with recommendations from the ASPEN guidelines. There was no significant association between total protein intake and incidence of severe diarrhea. Further studies are needed to assess whether a higher protein target will lead to improved clinical outcomes for critically ill burn patients.

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Disclosure of conflict of interest

Dr. Amalia Cochran receives a salary as editor for JAMA Surgery and royalties as editor for UpToDate®.

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