

## Original Article

# Impact of clinical factors on calorie and protein intakes during Icu stay in adults trauma patients: results from a prospective observational study

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**Abstract:** Propose: Nutritional requirements are often escalated following major trauma. Underfeeding and adverse outcomes were seen in critically ill trauma patients. The aim of the study was to quantify actual amount of calories and protein intakes, and extent to which those clinical factors may affect adequate intake. Material and methods: An observational study carried out in a medical intensive care unit (ICU) of Tabriz University of medical science during April 2017 and December 2018. A total of 85 adult trauma patients with a 7 days ICU length of stay and who received Enteral nutrition (EN) were included in this study. The data on estimated and actual intake of energy and protein, severity of illness (i.e., Acute Physiology and Chronic Health Evaluation II (APACHE II), The Glasgow Coma Scale (GCS) and markers of nutritional status (i.e., serum albumin level and body mass index) were recorded. Results: In this study, sixty-six patients (77%) were underfed in terms of energy and 19 patients (23%) had adequate energy intake. Logistic regression showed that only GCS possibly predict energy status. For every one-unit additional decrease in GCS scores, the odds of being underfed in terms of energy were increased by 1.32 times, after controlling for other factors (95% CI, 1.07 to 1.75,  $P$ -value = 0.044). No association was observed between nutritional status and clinical outcomes. Conclusions: The definite nutritional intake did not coverage the calculated requirements during ICU stay. The current study proposed that there was an inverse association between some clinically important factors (APACHE II score, intubation time) and mean energy intake. Nutritional support was not associated with any complications.

**Keywords:** Multiple trauma, critical illness, nutritional support, caloric requirement, protein requirement, observational study

## Introduction

Severely injured trauma patients are accompanied with metabolic changes and major trauma patients are at risk of underfeeding and adverse outcomes [1]. Optimal nutritional support provides energy, protein and other nutrients for critically ill patients in the intensive care unit (ICU) [2]. However, the type and amount of nutritional support requirements to the critically ill patients are not clearly understood. Enteral nutrition (EN) is the favored route

of management for patients who cannot be fed orally. This method is associated with significant nutrition deficits due to insufficient caloric and protein intakes [3, 4]. For instance, only 50% of patients 'nutritional requirements are met by enteral nutrition [5]. Insufficient calorie and protein intakes have been shown to be associated with poor outcomes among hospitalized patients, including extended hospital and ICU stay, infectious complications, continued mechanical ventilation, and higher mortality rates [6, 7]. In addition to insufficient energy

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intake and increased need for the calorie in conditions of critically ill individuals, the protein depletion are reported to be as high in the first days after major trauma [8].

Based on the severity of injury and the time of EN administration, between 33% and 66% of estimated energy needs must also be administered [9]. Although equations based on specific anthropometric individuals have long been accessible to clinicians for the determination of the energy intake necessary in critically ill patients, many clinical conditions cause discrepancies between estimated and measured values [10]. Previous studies recommended that monitoring and evaluating nutritional requirements are key factors in defining adequate nutritional support and provision which may improve clinical outcomes [11, 12].

While increased caloric and protein needs are well-defined in critically ill patients, underfeeding and overfeeding have been exposed to be associated with adverse outcomes in patients requiring EN or parenteral nutrition. On the other hand, there is a paucity of data on the actual protein and caloric intakes over time as well as the clinical factors affecting the caloric and protein intakes in this patient. The aim of this prospective observational study was so, to evaluate the caloric and protein intakes and the clinical factors that affect the intake during ICU stay and to assess their impacts on the outcomes in critically ill trauma patients.

### Methods

#### *Study design*

An observational study was conducted in all multi-trauma patients at Tabriz Hospital in Iran, from April 2017 to December 2018 who received enteral tube feeding during ICU admission. Patients would be eligible for the study if they were 18 years or older, hospitalized in the ICU, and were expected to require EN for at least seven days. Patients would be excluded if they were receiving parenteral or oral feeding and had been discharged from ICU before 7 days. The study protocol was approved by governmental Regional Committee for Medical and Health Research Ethics (Tabriz University of Medical Science, Tabriz, Iran, No: TBZMED.REC.167.259). Informed consent was obtained

by the use of a written form, which was to be signed by the participants and parents and/or legal guardians. A total of 120 subjects met our inclusion criteria, agreed to contribute and were joined in the study. Thirty-five patients (29%) were quiet from the analyses for the next details: altered to parental nutrition (n = 8), changed to oral feeding (n = 10), moved from the ICU (n = 12) or died (n = 5) during the seven-day study period.

#### *Data collection*

Included patients were observed for 7 days or until oral nutrition was resumed. Data collection included patient features (age, sex, weight, body mass index [BMI], ideal body weight [IBW], serum albumins, C-reactive protein (CRP), injury severity (via the Acute Physiology Chronic Health Evaluation II [APACHE II] score), daily planned caloric and protein requirements, daily administered calories and protein, and daily recorded vital signs. The Glasgow Coma Scale (GCS) is used to describe the general level of consciousness. Daily caloric and protein intake were recorded from all sources including total par enteral nutrition (TPN), EN, Ringer's lactate, and 5% or 10% glucose solutions, Propofol solutions, albumin infusions, and EN protein supplements. Apart from that, the clinical factors that had impacts on the sufficiency of energy intake were also collected.

In order to identify critically ill patients with high nutritional risk, we used the modified 9 points scale of the modified Nutrition Risk in the Critically ill (mNutric) score.

#### *Calculated caloric and protein requirements*

Caloric requirements were planned daily by the Harris Benedict Equation (HBE) for all patients and the Penn State Equation (PSE) for mechanically ventilated subjects. For the HBE, an activity factor of 1.2 (confined to bed) and 1.6 (if a systemic inflammatory response existed) as an injury factor were considered [13]. Protein requirements were considered daily based on the European Society for Clinical Nutrition and Metabolism guidelines for ICU patients. Both the minor (1.2 g protein per kg of IBW per day) and the upper estimates (1.5 g protein per 27 kg of IBW per day) were calculated [14].

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**Table 1.** Participants' Characteristics based on energy requirement received

Variables	Underfed (n=66)	Adequately fed (n=19)	P value
Gender (male/female) <sup>a</sup>	44/23	12/6	0.586
Age (years) <sup>a</sup>	46.04±19.2	15.3± 43.7	0.650
BMI (kgm <sup>-2</sup> ) <sup>a</sup>	24.98±4.50	3.21±25.08	0.928
Weight <sup>b</sup>	71.80±13.10	74.42±10.04	0.424
Estimated required energy (kcal/day) <sup>a</sup>	1428.67±430.49	1389±243.41	0.866
Mean of required energy received (kcal/day) <sup>a</sup>	795.60±221.38	1260.97±296.23	0.001
% of required energy received <sup>b</sup>	63	90	0.001
Estimated required protein (g/day) <sup>a</sup>	59.51±10.31	60.92±11.16	0.608
Mean of required protein <sup>a</sup> received (g/day) <sup>a</sup>	32.76±10.95	53±28.3	0.001
% of required protein received <sup>b</sup>	66	95	0.001
Albumin, mean (g/d) <sup>a</sup>	2.77±0.87	3.29±0.81	0.023
C-reactive protein (mg/d) <sup>a</sup>	27.25±11.17	29.42±9.58	0.444
GCS <sup>a</sup>	8.75±3.76	10.84±3.91	0.037
APACHE II score <sup>a</sup>	14.73±6.23	13.15±5.59	0.332
SOFA score <sup>a</sup>	7.74±1.98	7.78±1.83	0.933
mNutric <sup>a</sup>	3.40±1.75	2.89±1.72	0.268

APACHE II: acute physiology chronic health evaluation II, <sup>a</sup>Data are expressed as mean±sd. <sup>b</sup>Data are expressed as number.

**Table 2.** Summary of linear regression analysis based on mean energy received as outcome

Variables	B	SE	95% CI	P-value
GCS	-13.46	12.5	-29.4, 20.05	0.723
APACHE II score	14.73	5.9	2.9, 28.4	0.015
SOFA score	31.2	26.5	-21.13, 83.1	0.237
Intubation time	19.7	7.1	3.5, 32.1	0.015
mNutric	-89.2	41.1	-172.1, -6.3	0.035
Adjusted R <sup>2</sup>	0.21			

For abbreviations see **Table 1**. Adjusted for age, sex, and BMI.

### Statistical analysis

Data were analyzed with SPSS v 19.0 (SPSS Inc., Chicago, IL, USA). Normality of distribution was assessed via skewness, and kurtosis test. The level of statistical significance was considered at  $P < 0.05$ . Categorical variables are presented as counts and percent and continuous variables are reported as means and standard deviations. The features of the subjects who were underfed/not underfed were analyzed using independent t-test and chi-square tests. Subjects were classified into two groups, adequately fed or underfed, based on the 90 percentage of energy and/or protein requirement received. Logistic regression was performed to assess the impact of some clinical important

factors on feeding status. Linear regression was performed to assess the ability of the impact of some clinically important factors to predict mean of protein/energy received as outcomes.

### Results

In this study, 85 adult trauma patients (56 males and 29 females) were participated. The baseline characteristics of the participants are presented in **Table 1**. Sixty-six patients (77%) were underfed in terms of energy and 19 patients (23%) had adequate energy intakes. In addition, the protein intake subjects were divided into two groups, 67 patients (79%) that were underfed for protein, and 18 patients (21%) that had adequate protein intakes. There was no significant difference between underfed patients and adequately fed in terms of energy in gender, age, BMI, weight, CRP, Albumin, and APACHE II scores. Other data are presented in **Table 1**.

Both the caloric and protein intakes significantly increased over time from the first to the seventh day (466±244, 516±310, 696±386, 918±475, 985±479, 1205±486, 1446±502, respectively). The average caloric and protein intakes never met the median calculated requirements over the study period (data not shown).

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**Table 3.** Summary of linear regression analysis based on mean protein received as outcome

Variables	B	SE	95% CI	P-value
GCS	0.16	0.39	-16.6, 31.2	0.544
APACHE II score	-0.36	0.18	-0.74, -0.06	0.046
SOFA score	1.23	0.58	0.54, 2.63	0.043
Intubation time	-2.10	2.24	-2.20, 2.98	0.338
mNutric	1.91	2.50	-3.97, -6.66	0.457
Albumin	0.69	1.53	-2.36, 3.75	0.653
Adjusted R <sup>2</sup>	0.51			

For abbreviations see **Table 1**. Adjusted for age, sex, and BMI.

**Table 4.** Summary of logistic regression analysis with energy feeding status as outcome

Variables	Odds Ratio	95% CI	P-value
GCS	1.32	1.07 to 1.75	0.044
APACHE II score	1.12	0.90 to 1.40	0.297
SOFA score	1.48	0.85 to 2.52	0.163
Intubation time	2.56	0.60 to 10.20	0.201
mNutric	9.84	0.76 to 121.2	0.080
Albumin	2.12	0.81 to 5.61	0.121

For abbreviations see **Table 1**. Adjusted for age, sex, and BMI. Hosmer and Lemeshow Test showed an acceptable of model fit (Chi-square (8) = 3.57, P = 0.879).

**Table 5.** Summary of logistic regression analysis with protein feeding status as outcome

Variables	Odds Ratio	95% CI	P-value
Calorie intake	16.54	2.9 to 92.1	0.001
APACHE II score	0.90	0.72 to 1.10	0.336
SOFA score	1.07	0.74 to 1.79	0.791
Intubation time	2.56	0.60 to 10.20	0.201
mNutric	1.63	0.72 to 3.62	0.237
GCS	0.80	0.61 to 1.04	0.101

For abbreviations see **Table 1**. Adjusted for age, sex, and BMI. Hosmer and Lemeshow Test showed an acceptable of model fit (Chi-square (8) = 13.88, P = 0.085).

Hierarchical multiple regression was used to assess the ability of the impact of some clinically important factors (GCS, APACHE II score, SOFA score, intubation time mNutric) to predict mean of energy received, after controlling for age, sex, and BMI. Preliminary analyses were conducted to ensure no violation of the assumptions of normality, linearity, and multicollinearity. A set of variables were entered at Step 1, explaining 21% of the variance in energy

received. In total, only the two control measures were statistically significant, with the mNutric a higher beta value (beta = -89.2, P = 0.035) than the APACHE II score (beta = -14.7, P = 0.015) (**Table 2**).

Linear regression mode including mean protein received as outcome was used to assess the ability of the impact of some clinically important factors (GCS, APACHE II score, SOFA score, Intubation time, mNutric, and Albumin) to predict mean of protein received. APACHE II score, was inversely associated with protein intake ( $\beta = -0.36$ , 95% CI: -0.74, -0.06; P = 0.046). No significant association was found between the protein intake and GCS, Intubation time, mNutric, and Albumin. Finally, adding the set of variables significantly predicted of protein intake by 51% [F Change (30, 578) = 166, P = 0.001] (**Table 3**).

Logistic regression was done to quantify the impact of some clinical important factors (GCS, APACHE II score, SOFA score Intubation time, mNutric, Albumin) on feeding status. The model clarified 85% of the variance in underfeeding of energy. As seen in **Table 4**, only GCS possibly predict energy status. For every one-unit additional decrease in GCS score, the odds of being underfed for energy increased by 1.32 time, after controlling for other factors (95% CI, 1.07 to 1.75, P-value = 0.044).

As wells, logistic regression was performed to assess the impact of a number of factors that impact on protein status. The model contained six independent variables (calorie intake, APACHE II score, SOFA score, intubation time, mNutric, and GCS). The full model containing all predictors was statistically significant, and correctly classified 73% of cases. As shown in **Table 5**, only one of the independent variables made a unique statistically significant contribution to the model (calorie intake). Odds ratio of 16.54 indicating that subjects who had adequate calorie intake, were over 16.54 times more likely to receive adequate a protein intake than those who had underfed energy, controlling for all other factors in the model.

### Discussion

Our findings revealed that about 70% of subjects failed to meet 90% of their energy requirements during the first seven days after the

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beginning of EN. The current study revealed that there was an inverse association between some clinically important factors (APACHE II scores and intubation time) and mean energy intake. To the best of our knowledge, this study was the first observational study that reports the inverse association of APACHE II and SOFA scores with protein intakes. Our results indicated that lower GCS was correlated with lower energy intakes. We did not observe any associations between several individual nutritional parameters and adverse outcomes.

Among studied participants, only 25% and 23% met their energy and protein requirements during ICU stay, respectively. A study carried out by O'Leary-Kelley et al. reported that the 68% of patients who undergone mechanical ventilation were underfed [15]. Likewise, Engel et al. stated that 65% of patients hospitalized in the surgical ICU failed to meet 80% of their required energy [16]. Although our result showed that estimated energy requirements supported the calorie need of participant, incomplete delivery of EN led to increased proportions of underfeeding of subjects in this observational study. Previous studies have perceived the multiple factors which were likely to contribute to failure in energy requirements like repeated surgeries and obligatory nil per os (NPO).

To the best of our knowledge, this is the first study to examine these types of clinically important factors with energy intake. In the present study, higher PACHE II scores and mNutric were associated with lower level of energy intake suggesting that higher severity of injury increased the risk of underfed status. Krishnan et al. [17] indicated that clinical factors did not significantly predict underfeeding of energy. Under these circumstances, any improvement in clinical conditions would be of benefit in nutritional status.

There are inadequate studies with controversial results on the relationship between protein intakes and clinical outcomes [1, 12]. On the other hands, previous studies proposed some complications that were mostly affected by the protein balance. Others have revealed that increased protein intakes lead to renal insufficiency [18]. Therefore, this phenomenon might be prevented through direct observation and measurement in the patients receiving protein. Moreover, our study highlighted that APACHE II and SOFA scores can predict the

amount of protein that received. It appears that the physicians prescribe the protein requirements based on clinical conditions of the patients rather than nutritional needs.

Our results also clearly showed an association between some clinical factors with the amount of received calorie and protein and suggesting that the severity of illness might lead to a decrease in calorie intake. Although the initially prescribed the volume and type of formulas, the size of feeding tubes and the type of nutritional supports vary and they contribute to considerable levels of underfeeding. However, our study indicated that clinical status is a more important factor which determines the calorie and protein intakes. Therefore, it could be deduced that improvement of clinical state may prevent the progress of malnutrition or the overload of protein in patients during their stay in ICU.

Most of the previous studies have observed the benefits of nutritional support in critical illness, and have concluded that early enteral feeding leads to better clinical outcomes [19, 20]. However, we failed to observe any additional benefits in terms of the time of nutritional support based on the outcomes including sepsis, ICU stay, death, and rates of hospital discharge (data not shown). In other words, underfeeding has been shown to be related to increased infectious complications, increased mortality and longer hospital and ICU stay. Although the results of some studies have suggested that calorie intake may be a predictive factor in clinical outcomes in ill patients [19], interestingly, in our study, no differences were observed between the level of caloric consumption and clinical outcomes in critically ill patients. In line with our results, Arabi et al. [21] showed that admissible underfeeding was not connected with worse outcomes, including the mortality rate. A strong correlation was establish between energy intake during the ICU stay and some complications including acute respiratory distress syndrome (ARDS), renal failure, pneumonia and sores [12]. Additional study is necessary to validate these results in critically ill subjects. In addition, future studies are needed to explore the effects of higher energy intakes on outcomes in ICU patients that were fed entirely. Although both the protein and caloric intake significantly increased over time, the caloric and protein intakes were unable to meet the intended requirements during the ICU stay.

Seventy-seven percent of EN patients did not receive adequate energy intake (**Table 1**). In the other words, two groups were statistically significant different in terms of albumin and GCS. The statistical significance in the simple comparisons of adequate feeding in the two mentation groups may in part be due to the relatively low levels of consciousness that might lead to lower energy intakes. Surgical patients and the patients with lower GCS scores were less likely to receive enteral nutrition. For each 1-point increase in a patient's GCS score, the likelihood of being underfed for energy increased by 1.32 time, after controlling for other factors.

Even though, patients in the present study did not receive adequate nutrition which normally contributes to underfeeding, numerous factors for the failure to meet energy requirements have been proposed in former studies [22, 23]. The current study adds more evidence identifying some clinical factors that contribute to underfeeding of energy and protein in Iranian medical ICU patients.

It is already accepted that malnourished patients are at higher risks for developing complications compared to well-fed subjects and, hence, require longer stays in ICU. Although ICU stay and complications were not affected by nutritional status in our patients, malnutrition was increased in patients whose feeding was postponed or received inadequate energy intakes. As a result, to maintain the nutritional status of patients, sufficient amounts of protein and calories have to be given.

### Limitations and strengths

The present study had some limitations. First, this study was a cross-sectional one; therefore, the cause or effects of events on clinical condition and calorie or protein intakes were not predictable. Second, we cannot measure the other indices of nutritional status, such as body composition and inflammatory markers. Such information, either alone or in combination, might have been useful in identifying patients as increased risk with adverse outcomes. Another limitation is that there is no method to assess the proposed caloric requirements that are sufficient in terms of nutritional support and there is no standardization of the nutrition evaluation used for prescription. We defined trauma based on the APACHE II diag-

nostic classification which imposes a limitation because it does not permit the severity of the traumatic injury to be identified, which is assumed to have an effect on energy requirements. However, the study also had some strength, including the relatively large sample size, and participation of trauma subjects.

In summary, while individual indices of nutritional status were not related with various adverse outcomes, one or a combination of clinical factors was of reliable predictive value in forecasting calorie and protein intakes. These results propose that either calorie intake-sin ICU are primarily determined by other factors such as nutritional status or clinical factors can neutralize the adverse effects of malnutrition on patient outcomes.

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Written informed consent was obtained from each study participant and/or legal guardians after explaining the purpose of the study. The right of a participant to withdraw from the study at any time and patient information is reserved and will not be published.

### Disclosure of conflict of interest

None.

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