

## ORIGINAL RESEARCH

# Isocaloric nutritional support reduces ventilator duration time in major trauma patients

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## Abstract

**Aims:** Major trauma patients need adequate nutrition for recovery. This study aimed to evaluate the adequacy of nutritional supply and the correlation between nutritional supply and clinical outcome.

**Methods:** A single-centre retrospective observational study was undertaken, describing the amounts of energy and proteins provided to 320 critically ill trauma patients during the first 10 days after admission. The data were collected from the electronic medical records of patients admitted to the trauma intensive care unit during the study period and descriptive statistical analyses were performed with the SPSS software.

**Results:** The mean proportion of supplied energy to recommended energy during the first 10 days after admission was 57.5%, and the mean percentage of supplied protein to recommended protein intake was 51.3%. The patients were divided into those who received  $\geq 70\%$  (isocaloric nutrition group) and those who received  $< 70\%$  (hypocaloric nutrition group) of their estimated requirements. Both the duration of ventilator use ( $12.7 \pm 10.5$  vs.  $16.0 \pm 15.8$  days, respectively,  $p = 0.009$ ) and duration of parenteral nutrition ( $1.1 \pm 1.4$  vs.  $2.0 \pm 2.0$  days, respectively,  $p = 0.001$ ) were shorter in the isocaloric nutrition group ( $n = 83$ ) than in the hypocaloric nutrition group ( $n = 237$ ).

**Conclusion:** Total energy and the amount of protein supplied were insufficient compared to the recommended amount. The duration of ventilator use was shorter in the isocaloric nutrition group than in the hypocaloric nutrition group. The association between shortened ventilator use and isocaloric nutrition requires further investigation as a potential intervention to reduce the risk of complications such as ventilator-related pneumonia.

## KEYWORDS

critical care, mechanical ventilation, nutritional support, trauma, ventilators

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## 1 | INTRODUCTION

Major trauma patients account for a large proportion of patients in the surgical intensive care unit (ICU). Most trauma patients are admitted with no noticeable nutritional concerns, but the risk of malnutrition increases due to changes in the neural and hormonal systems associated with trauma and pathological physiological changes caused by cytokine storms.<sup>1</sup> Metabolism increases in response to the stress caused by trauma. If their condition persists without correction, the risk of malnutrition and associated infectious complications can be high.<sup>2,3</sup>

An insufficient nutrient supply is more often seen in severe trauma patients and is due to multiple surgical treatments.<sup>4</sup> Although malnutrition is a major problem for patient recovery, surgical treatments make it difficult to provide severe trauma patients with sufficient nutrition. In addition, patients who have undergone surgery are nutritionally affected due to long-term admission to the ICU, a prolonged period until recovery, and frequent comorbid conditions, such as alcoholism, lung disease and cancer.

Appropriate and timely nutritional support prevents hypermetabolism and malnutrition, maintains immune function, minimises reduction in lean body mass and reduces cell damage by free radicals. In particular, early commencement of enteral nutrition (EN) reduces infectious complications by maintaining the protective function of the intestinal mucosa and immune system.<sup>5</sup> Appropriate nutrient supply during the early stages of treatment can positively affect clinical outcomes, such as the length of hospital and ICU stays, ventilator use, and mortality. A recent meta-analysis showed that initial nutritional supply reduced mortality in three randomised controlled trials involving 126 patients.<sup>6</sup> The 2008 nutrition guidelines from the Society of Critical Care Medicine and the American Society for Parenteral and Enteral Nutrition recommend that enteral feeding be initiated in trauma patients within the first 24–48 h after admission to the ICU.<sup>5</sup> Factors impeding delivery of adequate EN to trauma patients include delayed EN initiation, frequent surgeries and procedures, and postoperative ileus. Lee et al. reported that implementation of multi-targeted feeding strategies such as early EN initiation, preoperative 'nil by mouth' feeding protocol, and a catch-up feeding protocol increased nutritional adequacy and was associated with reduced pneumonia in ill trauma patients.<sup>7</sup>

In a study of 83 surgically ill patients, Charles et al. found that insufficient nutrition increased the rate of infection.<sup>8</sup> Despite the importance of adequate nutritional support, a study by Heyland et al. involving 201 ICUs in 26 countries showed that the goal of

providing more than 80% of the recommended energy intake was not achieved in 74.0% of patients.<sup>9</sup> The 2018 European Society for Clinical Nutrition and Metabolism critical care nutrition guideline defines isocaloric and hypocaloric nutrition as the provision of  $\geq 70\%$  and  $< 70\%$  of the estimated needs, respectively.<sup>10</sup> In an observational study of ICU patients, Villet et al. frequently encountered a negative cumulative energy balance, which they reported was associated with complications (mainly infections).<sup>11</sup> These observations led to the widespread assumption that energy deficit should be prevented, which is referred to as the cumulative energy deficit. Due to the severity of their condition and the requirements for critical care therapy, providing normal oral nutritional intake is impractical or impossible in most critically ill patients, necessitating enteral or parenteral provision of energy, proteins, electrolytes, vitamins, minerals, trace elements and fluids.

Trauma patients are expected to have reduced energy and protein intake compared with the recommended intake in non-trauma patients because of prolonged fasting periods due to frequent surgery and various tests. This seems to be associated with undesirable effects on clinical outcomes.<sup>12</sup> However, little information is available on the nutritional support, nutritional assessment, and clinical outcomes of trauma patients. This study aimed to evaluate the relationship between the adequacy of nutrient supply and clinical outcomes in trauma patients in the ICU.<sup>13</sup>

## 2 | METHODS

This study was conducted retrospectively on patients admitted to a single trauma ICU affiliated to an acute care hospital. Data were obtained from the electronic medical records. Among 2146 patients aged  $\geq 18$  years admitted to the trauma ICU between January 2016 and March 2018, 1026 patients (47.8%) were enrolled in the study. Inclusion criteria was critically ill adults admitted to the ICU with major traumatic event and stayed at least 3 days. Patients were included when EN or PN, or a combination of both, were provided. Patients who died and/or were discharged within 3 days or who were able to eat normal food or who stayed in ICU for more than 30 days were excluded. Nutritional status was determined by dietitian within 24 hours after the patient was admitted to the hospital, using the hospital's nutrition screening tool to find patients at risk of malnutrition. In addition, after meeting patients in the medium-risk group and high-risk group within 48 h of hospitalisation, nutritional status was further diagnosed based on ICD-9-CM. This study received ethical approval in June 2018 from the

Institutional Review Board of Ajou University (AJIRB-MED-MDB-18-152).

The data collected on patient characteristics included sex, age, weight, body mass index (BMI), ideal body weight (calculated as male:  $IBW [kg] = Ht [m]^2 \times 22$  female:  $IBW [kg] = Ht [m]^2 \times 21$ ), blood sample results, injury severity (the injury severity score or the Acute Physiology Assessment and Chronic Health Evaluation II [APACHE II] score), the mechanism of the injury, the number of operations, daily calculated energy and protein requirements and daily supplied energy and protein on days 1–10 in the ICU. Daily energy and protein intake were based on those from all sources, including total PN, EN and all types of glucose, lipids and amino acid solutions. Patients were divided into those who received  $\geq 70\%$  of their estimated needs (isocaloric nutrition group) and those who received  $< 70\%$  of their estimated needs (hypocaloric nutrition group).<sup>10</sup>

Serum albumin, total lymphocyte count, blood urea nitrogen, creatinine, haemoglobin, haematocrit and C-reactive protein levels were analysed in blood samples taken from the brachial vein during the ICU stay. Energy requirements were calculated by clinical dietitians using a simplistic weight-based equation (105–125 kJ/kg/day). If the patient was receiving continuous renal replacement therapy, the energy requirement was calculated as 125 kJ/kg/day. In patients with obesity (BMI  $> 25$  kg/m<sup>2</sup>, according to Asia-Pacific guideline), we used the weight-based equation of 46–58 kJ/kg actual body weight/day.<sup>5</sup> Protein requirements were calculated according to the American Society for Parenteral and Enteral Nutrition guidelines<sup>5</sup> for ICU patients as 1.2–1.5 g protein/kg ideal body weight/day or 1.5 g–2.0 g/kg if the patient was receiving continuous renal replacement therapy. The percentages of energy and protein in the EN, PN and PN + EN groups from days 1 to 10 in the ICU were examined by date, and the mean values were calculated.

The sample size was not calculated statistically since the number of subjects of interest was fixed during the study period. The statistical analyses were performed using SPSS 25.0 (IBM Corp., Armonk, NY). The mean  $\pm$  standard deviation values for age, BMI, length of ICU stay, length of hospital stay, the total number of operations, period of continuous renal replacement therapy use, period of ventilator use, severity scores (APACHE II and injury severity score), the proportions of nutritional supply from EN and PN supplementation, the total lymphocyte count and the blood urea nitrogen, creatinine, haemoglobin, haematocrit and C-reactive protein levels and the clinical outcomes were calculated by frequency analyses. One-way ANOVA and the  $\chi^2$  test were used to analyse the significance of differences in the clinical outcomes according to the nutritional support route.

### 3 | RESULTS

A total of 320 critically ill trauma patients, consisting of 248 men (77.5%) and 72 women (22.5%) admitted to the trauma ICU during the study period, were included in the analysis (Figure 1). The study population had a mean age of  $56.2 \pm 16.8$  years, a mean BMI of  $23.4 \pm 3.7$  kg/m<sup>2</sup>, a mean hospital stay of  $39.2 \pm 34.2$  days and a mean ICU stay of  $13.7 \pm 7.5$  days. Forty-seven patients (14.7%) received continuous renal replacement therapy for a mean period of  $12.2 \pm 20.2$  days, and 123 (38.4%) patients received ventilator treatment for a mean period of  $15.1 \pm 14.8$  days.

Out of 320 patients, 219 patients were classified as well-nourished (68.4%), while 101 (31.6%) patients were at medium and high risk for malnutrition, and were classified as malnourished. The mean total number of operations was  $1.6 \pm 1.6$ , the average number of laparotomies was  $0.2 \pm 0.7$  and the average number of gastrointestinal operations was  $0.1 \pm 0.4$  (Table 1). The ICU outcomes were death in 74 (34.7%) cases, discharge to home in 93 (29.0%) cases, and transportation to other hospitals in 153 (47.8%) cases.

With regard to the nutritional support route, 108 patients (33.8%) were fed by EN alone (EN group), 67 patients (20.9%) by PN alone (PN group), and 145 patients (45.3%) by both PN and EN (PN + EN group). The mean start dates of PN and EN were  $1.7 \pm 1.9$  days and  $6.3 \pm 8.1$  days, respectively, from ICU admission. The mean recommended amounts of energy and protein needs for the total population were  $102.9 \pm 14.6$  kJ/kg/day and  $1.2 \pm 0.2$  g/kg/day, respectively, and the mean amounts of energy and protein supplied per actual body weight were  $59.4 \pm 25.5$  kJ/kg/day and  $0.6 \pm 0.4$  g/kg/day, respectively. During the initial 10 days after ICU admission, the mean percentages of energy and protein supplied relative to the recommendations were  $57.5\% \pm 22.4\%$  and  $51.3\% \pm 26.6\%$ , respectively (Table 1). The mean amount of protein supplied during the initial 10 days after ICU admission was highest on day 7 ( $56.4\% \pm 41.4\%$ ), and it decreased to  $56.0\% \pm 41.6\%$  on day 8,  $52.7\% \pm 40.7\%$  on day 9 and  $50.7\% \pm 42.6\%$  on day 10 (Table 2).

The clinical outcomes according to the nutritional support route indicated a shorter mean hospital stay ( $27.3 \pm 26.0$  vs.  $45.4 \pm 40.2$  and  $45.3 \pm 34.5$  days, respectively,  $p < 0.001$ ). The PN group had lower survival rate (44.4%) compared to the EN group (94.0%) and EN + PN group (93.1%), respectively ( $p < 0.001$ ). In comparison with the PN and EN groups, the PN + EN group showed a significantly greater mean energy intake ( $p < 0.001$ ), but there were no significant differences in the length of ICU stay ( $p = 0.776$ ) or amount of protein intake ( $p = 0.256$ ) among the three groups (Table 3).

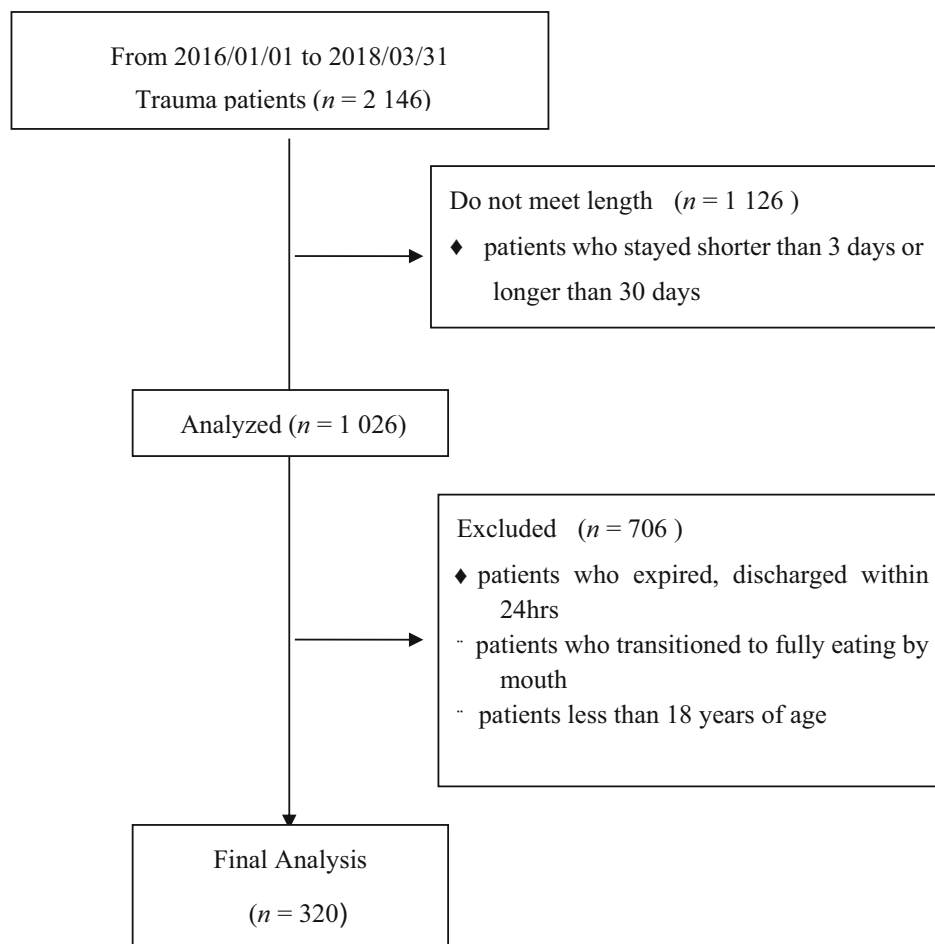


FIGURE 1 Diagram of the flow of subjects in the study.

In accordance with the 2018 European Society for Clinical Nutrition and Metabolism critical care nutrition guideline,<sup>10</sup> the study population was divided into a hypocaloric nutrition group (<70% of estimated needs) and an isocaloric nutrition group ( $\geq 70\%$  of estimated needs). The patients in the hypocaloric nutrition group were, on average, younger than those in the isocaloric nutrition group ( $54.6 \pm 17.0$  vs.  $60.9 \pm 15.6$  years, respectively,  $p = 0.002$ ). No significant difference was found in the in-hospital mortality rate between the hypocaloric and isocaloric nutrition groups (24.1% vs. 20.5%, respectively;  $p = 0.507$ ). In comparison with the hypocaloric nutrition group, the isocaloric nutrition group had a shorter mean duration of ventilation use ( $16.0 \pm 15.8$  vs.  $12.7 \pm 10.5$  days, respectively,  $p = 0.009$ ) and a shorter time until PN initiation ( $2.0 \pm 2.0$  vs.  $1.1 \pm 1.4$  days, respectively,  $p = 0.001$ ). The hypocaloric nutrition group had a significantly lower mean total lymphocyte count ( $11.9 \pm 5.5$  vs.  $13.8 \pm 5.5$  cells/mm<sup>3</sup>, respectively,  $p = 0.009$ ), a significantly higher mean creatinine level ( $1.1 \pm 1.1\%$  vs.  $0.9 \pm 0.3\%$ , respectively,  $p = 0.048$ ) and a significantly greater mean number of total operations ( $1.7 \pm 1.7$  vs.  $1.1 \pm 1.3$ , respectively,

$p = 0.002$ ) compared with the isocaloric nutrition group (Table 4).

The correlations between clinical outcome and the total number of operations are shown in Table 5. The total number of operations was significantly positively correlated with the length of hospital stay ( $r = 0.146$ ,  $p = 0.009$ ) and injury severity score ( $r = 0.196$ ,  $p = 0.017$ ) and significantly negatively correlated with age ( $r = -0.198$ ,  $p = 0.016$ ) and energy ratio (ratio of supplied energy to recommended energy;  $r = -0.060$ ,  $p = 0.468$ ; Table 5).

## 4 | DISCUSSION

Appropriate treatment is vital to minimise the substantial national, social, economic and health consequences of trauma.<sup>10</sup> We found that the amount of nutrition (both kJ and protein) support for the critically injured trauma patients were not sufficient compared to the guidelines. However, patients who received at least 70% of their required needs, showed a positive effect on the duration of ventilator use.

**TABLE 1** Patient characteristics and nutritional outcomes. (*n* = 320).

Characteristic	Mean, SD/ <i>n</i> (%)
On admission	
Age, years	56.2 ± 16.8
Sex	
Male	248 (77.5)
Female	72 (22.5)
Height, cm	167.1 ± 8.5
Weight, kg	65.9 ± 13.5
BMI, kg/m <sup>2</sup>	23.4 ± 3.7
APACHE II score ( <i>n</i> = 123)	14.1 ± 6.8
ISS ( <i>n</i> = 148)	25.5 ± 10.9
Blood test results	
Albumin, g/dL (3.5–5.2) <sup>a</sup>	3.5 ± 0.8
TLC, cells/mm <sup>3</sup> (>2.0)	12.4 ± 5.6
CRP, mg/dL (0.0–0.5)	8.5 ± 9.7
Hb, mg/dL (12.5–17.5)	11.8 ± 2.5
Hct, % (37.0–51.6)	35.9 ± 7.1
BUN, mg/dL (6.0–20.0)	17.1 ± 9.5
Cr, mg/dL (0.70–1.20)	1.05 ± 1.0
Cause of injury	
Transportation accident	152 (47.5)
Fall/slip	91 (28.4)
Industrial accident	23 (7.2)
Laceration, stab, cut or penetration injury	4 (1.3)
Burn and others	50 (15.6)
Admission department	
Trauma surgery	143 (44.7)
Neurosurgery	113 (35.3)
Rehabilitation	36 (11.3)
Emergency and others	28 (8.7)
Nutritional status	
Well-nourished	219 (68.4)
Malnutrition	101 (31.6)
At discharge	
Length of hospital stay, days	39.2 ± 34.2
Length of ICU stay, days	13.7 ± 7.5
Length of CRRT use, days ( <i>n</i> = 47)	12.2 ± 20.2
Length of ventilator use, days ( <i>n</i> = 123)	15.1 ± 14.8
Discharge status	
Died	74 (23.1)
Home	93 (29.0)
Transfer	153 (47.8)

(Continues)

**TABLE 1** (Continued)

Characteristic	Mean, SD/ <i>n</i> (%)
Surgical procedures	
Number of laparotomies	0.2 ± 0.7
Number of gastrointestinal operations	0.1 ± 0.4
Total number of operations	1.6 ± 1.6
Route of nutritional support	
PN	108 (33.8)
EN	67 (20.9)
PN + EN	145 (45.3)
Timing of nutritional support	
Initiation of EN, days	6.3 ± 8.1
Initiation of PN, days	1.7 ± 1.9
Prescribed nutrition	
Prescribed energy, total kJ	6660.5 ± 958.1
Prescribed energy, kJ/kg/day	102.9 ± 14.6
Prescribed protein, g	78.4 ± 14.3
Prescribed protein, g/kg/day	1.2 ± 0.2
Received nutrition	
Average energy provided over 10 days, kJ	3775.6 ± 1412.5
Average energy provided over 10 days, kJ/kg/day	59.4 ± 25.5
Average protein provided over 10 days, g	39.8 ± 24.9
Average protein provided over 10 days, g/kg/day	0.6 ± 0.4
Adequacy of nutrition	
Total provided/required energy, %	57.5 ± 22.4
Total provided/required protein, %	51.3 ± 26.6

Abbreviations: APACHE II, Acute Physiology Assessment and Chronic Health Evaluation II; BMI, body mass index; BUN, blood urea nitrogen; Cr, creatinine; CRP, C-reactive protein; CRRT, continuous renal replacement therapy; EN, enteral nutrition exclusively; Hb, haemoglobin; Hct, haematocrit; ICU, intensive care unit; ISS, injury severity score; PN, parenteral nutrition exclusively; PN + EN, combined parenteral and enteral nutrition; TLC, total lymphocyte count.

<sup>a</sup>Values in parenthesis are reference values.

The American Society for Parenteral and Enteral Nutrition guidelines recommend immediate EN with high-protein composition in trauma patients (i.e. within 24–48 hours of haemodynamic stabilisation), similar to other critically ill patients.<sup>5</sup> In the present study, PN was started 1.7 days after admission on average, while EN was delayed by 6.3 days in trauma patients on average. Bakker et al. reported that early EN had no significant effect on the use of mechanical ventilation and the rates of infectious complications in acute pancreatitis patients.<sup>14</sup> Conversely, the 2018 systematic review for the Canadian

TABLE 2 Total supplied/recommended energy and protein ratio (%) during the initial 10 days in the intensive care unit.

	Provided/recommended energy (%)				Provided/recommended protein (%)			
	PN	EN	PN + EN	Total	PN	EN	PN + EN	Total
	(n = 108)	(n = 67)	(n = 145)	(n = 320)	(n = 108)	(n = 67)	(n = 145)	(n = 320)
Day 1	19.8 ± 21.3 <sup>a</sup>	15.3 ± 21.4	19.0 ± 21.7	18.5 ± 21.5	14.4 ± 33.2	21.6 ± 37.5	17.1 ± 26.5	17.1 ± 31.4
Day 2	42.9 ± 27.9	26.2 ± 24.6	45.5 ± 34.6	40.6 ± 31.3	30.7 ± 35.4	38.8 ± 50.5	37.4 ± 41.6	35.5 ± 41.7
Day 3	51.9 ± 31.8	41.7 ± 32.2	59.5 ± 38.7	53.2 ± 35.7	42.6 ± 41.8	46.5 ± 46.1	45.5 ± 38.7	44.7 ± 41.3
Day 4	53.0 ± 25.7	48.7 ± 30.3	63.5 ± 36.1	56.9 ± 32.3	43.3 ± 36.3	51.2 ± 41.4	51.4 ± 37.5	48.6 ± 38.0
Day 5	47.4 ± 32.0	56.1 ± 34.2	73.9 ± 39.0	61.2 ± 37.6	48.3 ± 38.4	54.8 ± 42.4	58.4 ± 38.9	54.3 ± 39.6
Day 6	48.3 ± 35.2	56.2 ± 39.0	77.2 ± 35.4	63.1 ± 38.3	52.9 ± 40.2	53.8 ± 39.3	60.0 ± 38.4	56.3 ± 39.2
Day 7	45.4 ± 37.2	57.5 ± 41.0	78.4 ± 40.2	62.9 ± 42.0	51.4 ± 42.6	53.9 ± 42.0	61.3 ± 39.9	56.4 ± 41.4
Day 8	43.1 ± 38.2	55.5 ± 43.3	77.9 ± 39.7	61.5 ± 42.8	51.1 ± 41.5	54.0 ± 40.8	60.5 ± 41.9	56.0 ± 41.6
Day 9	40.8 ± 39.7	52.3 ± 44.2	73.3 ± 39.6	57.9 ± 43.1	49.8 ± 41.8	49.0 ± 40.3	56.5 ± 40.1	52.7 ± 40.7
Day 10	37.3 ± 40.2	51.4 ± 47.8	71.6 ± 42.2	55.8 ± 45.3	48.7 ± 43.3	50.2 ± 44.3	52.4 ± 41.6	50.7 ± 42.6
Average over 10 days	49.3 ± 20.5	49.2 ± 21.7	67.3 ± 20.1	57.5 ± 22.4	48.8 ± 25.4	50.9 ± 31.3	53.4 ± 25.2	51.3 ± 26.6

Abbreviations: EN, enteral nutrition; PN, parenteral nutrition.

<sup>a</sup>Mean ± standard deviation.

TABLE 3 Clinical results according to the nutritional support route.

Variable	Total (n = 320)	Group			p-value
		PN <sup>a</sup> (n = 108)	EN <sup>b</sup> (n = 67)	PN + EN <sup>c</sup> (n = 145)	
Length of hospital stay of all patients, days	39.2 ± 34.2 <sup>d</sup>	27.3 ± 26.0 <sup>***c</sup>	45.4 ± 40.2 <sup>*</sup>	45.3 ± 34.5 <sup>**</sup>	<0.001 <sup>***f</sup>
Length of ICU stay of all patients, days	13.7 ± 7.5	13.5 ± 8.4	13.2 ± 7.1	14.0 ± 7.0	0.776
Overall survival	246 (76.9)	48 (44.4) <sup>***</sup>	63(94.0) <sup>*</sup>	135 (93.1) <sup>**</sup>	<0.001 <sup>***</sup>
Total provided/recommended energy, %	57.5 ± 22.4	49.3 ± 20.5 <sup>*</sup>	49.2 ± 21.7 <sup>**</sup>	67.3 ± 20.1 <sup>***</sup>	<0.001 <sup>***</sup>
Total provided/recommended protein, %	51.3 ± 26.6	48.8 ± 25.4	50.9 ± 31.3	53.4 ± 25.2	0.256

Abbreviation: ICU, intensive care unit.

<sup>a</sup>PN, parenteral nutrition exclusively.<sup>b</sup>EN, enteral nutrition exclusively.<sup>c</sup>PN + EN, combined parenteral and enteral nutrition.<sup>d</sup>Mean ± standard deviation or n (%).<sup>e</sup>Significant difference between groups according to one-way ANOVA and post hoc Scheffé's test.<sup>f</sup>One-way ANOVA.<sup>\*</sup>p < 0.05; <sup>\*\*</sup>p < 0.01; <sup>\*\*\*</sup>p < 0.001.

clinical practice guidelines<sup>15</sup> suggests that early EN reduces mortality rates and infectious complications, supporting the early commencement of EN. Unfortunately, EN supply in our trauma patients was delayed compared with the recommendations in other guidelines due to the requirement for multiple surgeries, various clinical examinations and haemodynamic instability, making it difficult to provide sufficient nutritional support to trauma patients. According to the Canadian Critical Care Practice Guideline group,<sup>10</sup> when a patient is severely malnourished, and EN is not feasible, the initiation of low-dose PN should be carefully considered which may outweigh the

expected benefits of early EN. We think that since the patients in our study were admitted with severe trauma, it may be possible that early EN was not feasible.

The patients in our study received only 57.4% and 51.3% of the recommended energy and protein intakes, respectively. Heyland et al. reported that 201 ICUs in 26 countries provided 61.2% and 57.6% of the recommended energy and protein, respectively. Differences in the proportion of adequate nutrition for trauma patients in the ICU according to geographic area were reported, with 53.5% and 51.9% of patients in Asia receiving the recommended energy and protein, respectively,

**TABLE 4** Clinical results of the hypocaloric (<70%) and isocaloric (≥70%) nutrition groups, based on the total supplied/recommended energy (%) during the initial 10 days in the intensive care unit.

Variable	Hypocaloric nutrition group (<70%) ( <i>n</i> = 237, 74.1%) <sup>a</sup>	Isocaloric nutrition group (≥70%) ( <i>n</i> = 83, 25.9%)	<i>p</i> -value
Age, years	54.6 ± 17.0	60.9 ± 15.6	0.002 <sup>**b</sup>
Male	191 (80.6%)	57 (68.7%)	0.025 <sup>*</sup>
Overall survival	180 (75.9%)	66 (79.5%)	0.507
Height, cm	168.1 ± 8.2	164.3 ± 8.6	0.001 <sup>**</sup>
Weight, kg	67.4 ± 12.9	61.5 ± 14.3	0.001 <sup>**</sup>
Body mass index, kg/m <sup>2</sup>	23.7 ± 3.4	22.7 ± 4.4	0.058
APACHE II ( <i>n</i> = 123)	14.4 ± 7.1 ( <i>n</i> = 91)	13.1 ± 5.9 ( <i>n</i> = 32)	0.310
Injury severity score ( <i>n</i> = 148)	25.3 ± 11.3 ( <i>n</i> = 115)	26.2 ± 9.6 ( <i>n</i> = 33)	0.753
Total number of operations	1.7 ± 1.7	1.1 ± 1.3	0.002 <sup>**</sup>
Length of hospital stay, days	39.5 ± 36.7	38.6 ± 26.0	0.809
Length of ICU stay, days	13.4 ± 7.6	14.5 ± 7.2	0.201
Length of CRRT use, days ( <i>n</i> = 47)	13.6 ± 22.2 ( <i>n</i> = 38)	6.4 ± 4.6 ( <i>n</i> = 9)	0.070
Length of ventilator use, days ( <i>n</i> = 123)	16.0 ± 15.8 ( <i>n</i> = 95)	12.7 ± 10.5 ( <i>n</i> = 28)	0.009 <sup>**</sup>
Results of blood tests			
Albumin, g/dL (3.5–5.2) <sup>c</sup>	3.5 ± 0.8	3.6 ± 0.8	0.228
TLC, cells/mm <sup>3</sup> (>2.0)	11.9 ± 5.5	13.8 ± 5.5	0.009 <sup>**</sup>
CRP (mg/dL) (0.0–0.5)	8.8 ± 9.8	7.9 ± 9.4	0.450
Hb, mg/dL (12.5–17.5)	11.9 ± 2.5	11.7 ± 2.3	0.622
Hct, % (37.0–51.6)	36.0 ± 7.3	35.5 ± 6.7	0.574
BUN, mg/dL (6.0–20.0)	16.7 ± 8.5	18.4 ± 12.0	0.239
Cr, mg/dL (0.70–1.20)	1.1 ± 1.1	0.9 ± 0.3	0.048 <sup>**</sup>
Timing of nutrition			
Initiation of EN, day	8.7 ± 28.2 ( <i>n</i> = 182)	4.9 ± 4.2 ( <i>n</i> = 72)	0.071
Initiation of PN, day	2.0 ± 2.0 ( <i>n</i> = 181)	1.1 ± 1.4 ( <i>n</i> = 73)	0.001 <sup>**</sup>
Recommended nutrition			
Energy, kJ	6819.1 ± 939.7	6207.4 ± 865.3	<0.001 <sup>***</sup>
Protein, g	80.3 ± 13.3	72.8 ± 15.4	<0.001 <sup>***</sup>
Supplied nutrition			
Average amount of energy over 10 days, kJ	3243.4 ± 1130.5	5288.2 ± 972.4	<0.001 <sup>***</sup>
Average amount of protein over 10 days, g	39.3 ± 16.8	41.2 ± 40.0	0.553
Adequacy of nutrition			
Total provided/recommended energy, %	47.7 ± 15.7	85.3 ± 13.3	<0.001 <sup>***</sup>
Total provided/recommended protein, %	51.7 ± 24.3	50.2 ± 32.6	0.657

<sup>a</sup>Mean ± standard deviation or *n* (%).<sup>b</sup>χ<sup>2</sup> test.<sup>c</sup>Normal reference range.

Abbreviations: APACHE II, Acute Physiology Assessment and Chronic Health Evaluation II; BUN, blood urea nitrogen; Cr, creatinine; CRP, C-reactive protein; CRRT, continuous renal replacement therapy; EN, enteral nutrition; Hb, haemoglobin; Hct, haematocrit; ICU, intensive care unit; PN, parenteral nutrition; TLC, total lymphocyte count.

<sup>\*</sup>*p* < 0.05; <sup>\*\*</sup>*p* < 0.01; <sup>\*\*\*</sup>*p* < 0.001.

TABLE 5 Correlations between clinical outcomes and total number of operations.

	Age	Length of hospital stay	Length of ICU stay	Weight change	Length of ventilator use	Length of CRRT use	Total supplied/recommended energy	Total supplied/recommended protein	ISS
Total number of operations	-0.122 (0.030)*	0.146 (0.009)**	0.108 (0.053)	0.027 (0.632)	0.146 (0.106)	0.248 (0.092)	-0.175 (0.002)**	0.061 (0.275)	0.196 (0.017)*

Note: Values are Spearman's correlation coefficients (*p*-value).

Abbreviations: CRRT, continuous renal replacement therapy; ICU, intensive care unit; ISS, injury severity score.

\**p* < 0.05; \*\**p* < 0.01.

compared with 75.5% and 69.8%, respectively, in Europe and South Africa.<sup>9</sup> In contrast, Jiang et al. reported that hypocaloric PN (63–84 kcal/kg/day) was most beneficial for trauma and pancreatic surgery patients.<sup>16</sup> In the present study, the amount of energy supplied during the initial 10 days after ICU admission was highest on day 6 ( $63.1 \pm 38.3\%$ ), and the amount of protein was highest on day 7 ( $56.4 \pm 41.4\%$ ); both decreased slightly thereafter.

No increase in nutrient intake was found in the trauma patients in this study for the following reasons: transfer to other hospitals, fasting because of various tests and surgeries and insufficient intake due to changing the feeding type from EN to oral or from PN + EN to EN only. Likewise, Lee et al. reported that approximately 72% of the total duration of EN feeding interruptions was due to potentially avoidable procedural causes, primarily human factors, while only approximately 20% was due to feeding intolerances. Therefore, it may be possible to minimise EN feeding interruption by adhering to evidence-based feeding protocols, as determined by a nutrition support team.<sup>17</sup>

Most critical trauma patients did not receive enough energy in the present study, as 74.1% were in the hypocaloric nutrition group ( $n = 237$ ) and only 25.9% ( $n = 83$ ) were in the isocaloric nutrition group. A study that used predictive equations for estimated nutritional requirements suggested that the mortality rate was reduced by hypocaloric nutrition with EN feeding.<sup>18</sup>

Comparison of the hypocaloric and isocaloric nutrition groups showed no significant difference in injury severity or survival rates in the present study. Only the duration of ventilator use was shorter in the isocaloric nutrition group than in the hypocaloric nutrition group. This is consistent with previous studies that showed that an accumulated energy deficit increased the duration of ventilator use.<sup>19,20</sup> On the contrary, Wischmeyer et al. found that isocaloric nutrition is associated with unfavourable effects on infection rates in critically ill patients in the ICU.<sup>21</sup> It is recommended to provide

hypocaloric nutrition for 1 week when demand is calculated using the predictive equation in the 2018 European Society for Clinical Nutrition and Metabolism critical care nutrition guidelines.<sup>10</sup> Controversy remains regarding the amount of energy that should be given to trauma patients in the ICU. However, it has been recommended that the target dose should not be met, regardless of the calculation method during the acute phase.<sup>15</sup>

The amount of protein supplied to trauma patients in the present study was insufficient, with an average of only  $0.6 \pm 0.4$  g/kg/day for 10 days and a total supplied/recommended proportion of protein was 52.7%. This may have been due to the insufficient availability of high-protein EN products and single-protein products in Korea and the inconvenience of providing ready-to-hang products for use in the ICU. The 2015 European Society for Clinical Nutrition and Metabolism clinical practice guidelines recommend hypocaloric nutrition corresponding to as low as 40%–70% of the estimated requirement but recommend a protein amount of 1.1–1.5 g/kg/day for patients in the ICU.<sup>22</sup> Arabi et al. reported that the provision of similar protein, even with reduced energy supply, was similar to both the mortality rate and the duration of mechanical ventilation use in patients in the ICU.<sup>23</sup> Deutz et al. also notes that adequate protein should be supplied independent of the energy demands of malnourished patients.<sup>24</sup> The current study's results indicate the necessity of the development of commercial products for adequate protein supply, convenient methods for supply when providing ready-to-hang products Heyland et al. developed and validated a feeding protocol, the Enhanced Protein Energy Provision via the Enteral Route Feeding Protocol, which was shown to increase protein supply by 14% and energy supply by 12% in a multi-centre trial.<sup>25</sup>

As shown in various guidelines,<sup>25</sup> sufficient energy and protein supply are needed for patients with severe trauma, but we still do not know how much nutrition is actually supplied to patients with severe trauma in Korea.



Therefore, this study evaluated the adequacy of nutritional supply in a relatively large number of patients with severe trauma, and the results will be helpful in determining the degree of nutritional intervention for patients in the future.

As this study was a retrospective review of medical records, inherent limitations should be taken into consideration. Because of the nature of the study design, we could not set an appropriate control group, but, rather classified the patients according to the intake level, and thus prone to selection bias. Also, some of the confounding variables, such as trauma site, the severity of trauma, length of stay at the ICU were not taken into account. Penetrating injury and laparotomy were associated with a higher energy intake, while higher BMI, traumatic brain injury and gastrointestinal tract injuries were associated with smaller increase of the energy intake.<sup>4</sup> These variables need to be considered in the future study.

Although the retrospective design enabled delineation of the nutritional treatment without interfering with the treatment process, it was inevitable to have some missing data. Also, the timing of the commencement of nutritional support was not identified accurately, and the contributions of EN and PN to the total energy intake could not be confirmed in this study.

Despite the above-mentioned limitations, the significance of this study should not be overlooked. Although numerous studies reported the importance of nutritional support in ICUs, not many reported the clinical results of over 300 trauma patients alone. Therefore, the results of this study can be surely generalised and suggest that adequate nutrition supply cannot be overemphasised in the patient's prognosis even for severe trauma.

#### AUTHOR CONTRIBUTIONS

JHL and JK contributed equally to the conception and design of the research; JK and YKP contributed to the design of the research; JHL, MK and DC contributed to the acquisition and analysis of the data; and JK and YKP contributed to the critical interpretation of the data. All authors drafted the manuscript, revised the manuscript, agreed to be fully accountable for ensuring the integrity and accuracy of the work and read and approved the final manuscript.

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#### CONFLICT OF INTEREST STATEMENT

The authors declare no potential conflicts of interest with respect to the research, authorship and publication of this article.

#### DATA AVAILABILITY STATEMENT


The data that support the findings of this study are available from the corresponding author upon reasonable request.

#### ETHICS STATEMENT

This study received ethical approval on 2018, June from the Institutional Review Board of Ajou University (AJIRB-MED-MDB-18-152).

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