Original Article

The influence of protein provision in the early phase of intensive care on clinical outcomes for critically ill patients on mechanical ventilation

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Background and Objectives: Mechanically ventilated patients often face progressive and rapid losses of body mass and muscle because of hypermetabolism and increased protein catabolism. To investigate the impact of adequate nutritional provision during the early phase of intensive care unit (ICU) admission on the clinical outcomes in patients with medical illnesses receiving mechanical ventilation support. **Methods and Study Design:** Two hundred and eleven mechanically ventilated patients admitted to a 30-bed medical ICU were included. Three groups, based on nutrition intake, were examined: adequate protein intake (aPI), n=34; insufficient protein intake/adequate energy intake (iPI/aEI), n=25; insufficient protein and energy intake (iPI/iEI), n=152. **Results:** Patients' mean age was 65±14 years; body mass index, 22±4; Acute Physiology and Chronic Health Evaluation II score, 24±7. The aPI group had significantly lower rates of in-ICU (14.7%) and in-hospital (23.5%) mortality than patients with insufficient protein intake: in-ICU mortality, iPI/aEI, 36%; iPI/iEI, 44.1% (*p*=0.006); in-hospital mortality, iPI/aEI, 56.0%; iPI/iEI, 52.0% (*p*=0.008). In the multivariate analysis, the hazard ratios (95% confidence intervals) for 60-day survival were 2.59 (1.02-6.59; *p*=0.046) and 2.88 (1.33-6.26; *p*=0.008) for the iPI/aEI and iPI/iEI groups, respectively. **Conclusions:** Despite possible selection bias owing to the retrospective nature of the study, achievement of >90% of target protein intake was associated with improved ICU outcomes in mechanically ventilated critically ill patients, based on real-world clinical circumstances.

Key Words: protein provision, nutrition, intensive care, mechanical ventilation, respiratory failure

INTRODUCTION

Unlike healthy individuals, critically ill patients have a compromised ability to adequately adapt to endocrine and metabolic processes such as ketogenesis stimulation and ketone body oxidation, while suppressing protein breakdown to tolerate prolonged starvation.[1] The resulting acceleration of protein–calorie malnutrition leads to impaired immune function, an increased risk of infections, and delayed recovery with a subsequently prolonged length of hospital stay, unless nutritional support is provided.[1-4] Mechanically ventilated patients, especially those with a longer duration of mechanical ventilation or admitted with limited nutritional reserves, often face progressive and rapid losses of body mass and muscle because of hypermetabolism and increased protein catabolism.[5] Therefore, optimal nutrition therapy meant to conserve or restore the body protein mass and provide adequate energy is vital for these critically ill patients.

According to previous studies, more than half of all patients in intensive care units (ICU) world-wide are significantly underfed, based on the energy they are prescribed to receive within 2 weeks of ICU admission.[6-9] These unmet nutritional requirements become more problematic when the sole source of nutritional intake is enteral nutrition (EN),[10,11] which has long been the recommended method of artificial feeding in the ICU.[12] According to the results of the Early Parenteral Nutrition Completing Enteral Nutrition in Adult Critically ill Patients (EPaNIC) trial, early provision of parenteral nutrition (PN) was associated with a higher infectious complication rate and longer mechanical ventilation time, although no significant impact on mortality was shown.[13] In contrast, recent randomized controlled trials demonstrated lower

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rates of nosocomial infections in patients receiving PN than in those receiving EN only[14] and a shorter duration of mechanical ventilation in an early PN group when compared with a standard care group.[15]

Disagreement remains, however, among consensus nutrition guidelines with respect to the recommended timing and route of nutrition delivery for ICU patients,[8,16-18] and studies to determine the optimal goals for protein and energy provision in critically ill patients have yielded conflicting results.[19,20] This controversy can be explained by the heterogeneity in study designs, illness severity in the patient population, and mode of nutrition. Different methodologies used to estimate energy expenditure, muscle mass, or fat-free mass in critically ill patients can be biased, to some extent.[21,22] Nevertheless, our understanding of the importance of protein in the nutritional support provided to critically ill patients is increasing, and a growing body of evidence supporting the favorable effects of adequate protein provision on various clinical outcomes in ICU patients, especially those under prolonged mechanical ventilation, has accumulated in recent years.[1,23-26] Herein, we aimed to evaluate the relationship between the average nutritional intake provided during the early periods of ICU admission and clinical outcomes in mechanically ventilated, critically ill patients.

PATIENTS AND METHODS

Patients

This was a cross-sectional observational study of a group of medically ill patients admitted to the 30-bed medical ICU at Yonsei University Severance Hospital, a tertiary referral hospital in South Korea, between January 2012 and July 2013. From all patients admitted to the ICU during this period (n=577), we selected adult patients who were treated with mechanical ventilation within the first 48 hours of ICU admission and survived for at least 72 hours in the ICU. Patients were excluded for any of the following reasons: age <18 years, elective admission, pregnancy, and missing data regarding energy and protein provision. Because this study focused on the relationship between nutritional provision and clinical outcomes, we also excluded patients who recovered and were discharged from the ICU before day 7. We assessed baseline patient characteristics including age, sex, body mass index (BMI), ICU admission diagnosis, co-morbid conditions, and the acute physiology and chronic health evaluation (APACHE II) score within 24 hours of ICU admission. All patients were followed until death or discharge. This study was approved by the Institutional Review Board of our Institute. (2013-0500).

Nutrition support and assessment

Data on the daily energy and protein intakes from EN and/or PN and other nutritional support-related assessments during ICU admission were prospectively recorded by a specialized clinical team of dietitians and were available for all patients. Data regarding patients' clinical outcomes were retrospectively reviewed from electronic medical records. No patients were switched to oral feeding during the first 7 days of their ICU stay.

Nutritional support was provided according to the institutional policy, which was based on the guideline of the Korean Society of Critical Care Medicine. Briefly, at our institution, we initiate early enteral feeding in hemodynamically stable patients within the first 24 hours of ICU admission, preferably via the gastrointestinal route. We allow gastric residuals up to 300 mL per 6 hours; if the residuals exceed this volume, we hold feeding for 2 hours and recheck the residual volume. If the residuals again exceed this volume, we suspend feeding and plan to restart enteral feeding at the previous rate on the next day. PN is generally initiated after 3 days of an ICU stay and is provided when effective EN is not feasible because of gastrointestinal intolerance. In this study, EN was supplemented with PN when required and early PN initiation was allowed when necessary.

We used the American College of Chest Physicians equation (based on BMI) to predict the resting energy expenditure. The target energy requirement based on this calculation was 25 kcal/kg/day, and adjustments were made to use ideal body weight for patients with a BMI >25 kg/m^2 and 120% of the measured energy requirement for medical stress. The initial protein target was 1.2-1.5 g/kg per day until 24-h urea excretion data were available. Measurements were performed as soon as possible within 72 hours after ICU admission and repeated weekly. Urine was collected on the day of measurement and analyzed for 24-h urinary nitrogen excretion. The total nitrogen loss was determined by adding 4 g of nitrogen (2 g for urinary non-urea nitrogen and 2 g for nitrogen in feces, skin, and miscellaneous). The nitrogen balance was calculated as the difference between nitrogen intake (total protein provision via EN and/or PN divided by 6.25) and total nitrogen losses (total urinary nitrogen plus 4 g nitrogen per day as described in the previous sentence).

Then, we divided the patients into three groups according to calorie or protein intake: adequate protein intake (aPI) group, protein intake >90% of the minimal protein target (1.2 g/kg/day) irrespective of energy intake; insufficient protein intake (iPI)/adequate energy intake (aEI) group, protein intake ≤90% of the minimal protein target and energy intake >90% of the energy target (25 kcal/kg/day); and iPI/inadequate energy intake (iEI) group, neither protein nor energy intake reached the target.

Statistical analysis

Categorical variables are reported as counts and percentages. Continuous variables are reported as means and standard deviations. Survival was subjected to categorical analysis using Kaplan-Meier plots; mortality and discharge were coded as events and censoring, respectively. Survival curves were compared using both the log-rank test and Breslow test, which is more sensitive to early survival differences. Cox regression analyses were performed using the length of hospital stay as the time variable; ICU, 28-day, and hospital mortality as outcome variables; and target protein levels reached, target calorie levels reached, or failure to reach target protein and calorie levels as the independent variable. Hazard ratios (HRs; 95% confidence interval) were adjusted for age, sex, BMI, APACHE II score, and diagnostic category. A 2-tailed *p*-value <0.05 was considered significant. All statistical analyses were performed using SPSS version 18.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Demographic data of study patients

Two hundred and eleven patients (mean age, 65±14 years) treated with mechanical ventilation were included. The mean BMI was 22.2±4.0 kg/m^2, and 65% of the participants (n=137) were men. The mean daily protein and energy intakes via EN and/or PN during the first 10 days of ICU admission are illustrated in Figure 1. During the first 7 days in the ICU, the mean daily energy and protein intakes were 18.2±6.8 kcal and 0.7±0.3 g/kg, respectively. Fifty (24%) and 34 (16%) patients received adequate energy and protein intake (>90% of each target goal), respectively. There were 34 patients in the aPI group, 25 patients in theiPI/aEI group, and 152 patients in the iPI/iEI group. Of the 34 patients in the aPI group, 25 (74%) also achieved >90% of the target energy intake.

Table 1 shows the baseline characteristics and nutrition intake of the total sample and for each of the three groups. The main ICU admission diagnosis was respiratory failure (n=185), and the mean APACHE II score was 24±7 in all patients. The three groups had similar distributions of admission diagnoses and APACHE II scores. However, patients in the iPI/aEI group were significantly older, and patients in the aPI group had significantly lower mean

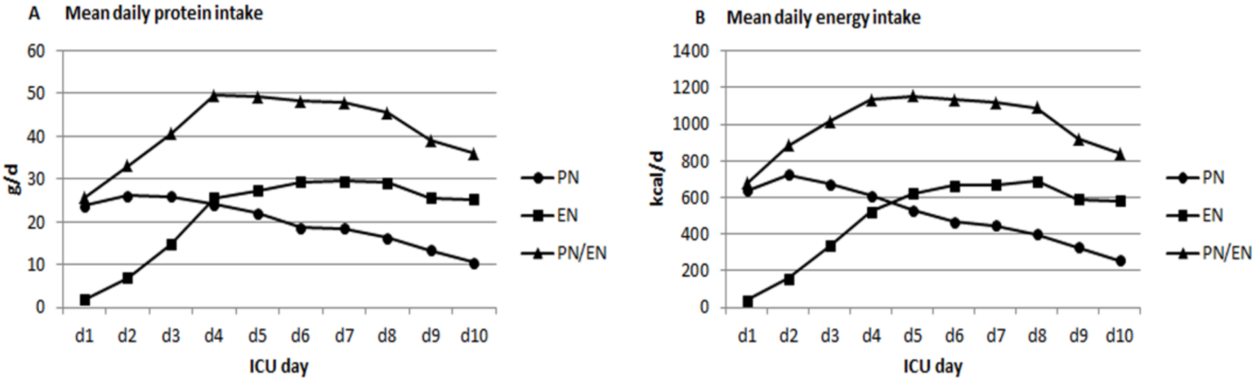

Figure 1. Mean daily amount of protein (A) and energy (B) intake during the first 10 days of ICU admission. PN: parenteral nutrition; EN: enteral nutrition

Table 1. Differences in patient profiles according to achievement of energy or protein delivery

Variables	Total (n=211)	aPI (n=34)	iPI/aEI (n=25)	iPI/iEI (n=152)	*p* value
Age, years	65±14	65±16	72±12	64±13	0.006
Sex, n (%)					
Men	137 (65)	16 (47)	14 (56)	107 (70)	
Women	74 (35)	18 (53)	11 (44)	45 (30)	0.022
Admission diagnosis, n (%)					
Respiratory	185 (88)	30 (88)	21 (84)	134 (88)	
Cardiovascular	4 (2)	0	0	4 (3)	
Gastrointestinal	3 (1)	0	1 (4)	2(1)	
Sepsis	12 (6)	3 (9)	3(12)	6(4)	
Others	7 (3)	1 (3)	0	6 (4)	0.689
APACHE II score, mean±SD	24.2±7.1	23.2±6.6	24.8±7.2	24.4±7.2	0.604
Procalcitonin, ng/mL	11.4±26.7	14.4±36.8	16.4±27.7	9.9±24.6	0.368
C-reactive protein, mg/L	129±101	99±78	178±128	127±97	0.029
Height, meters	163±8.6	160±10	160±7	164±8	0.006
Weight, kg	58.8±11.5	47.1±8.4	56.8±7.0	61.7±11.0	<0.0001
BMI, kg/m^2	22.2±4.0	18.5±3.3	22.2±2.6	22.9±3.9	<0.0001
24 h urine nitrogen excretion, mg/day[†]	8742±5011	7646±3673	9017±4357	8944±5360	0.491
Nitrogen balance[†]	-6.6±5.8	-2.4±4.3	-3.6±5.8	-8.0±5.4	<0.0001
Positive nitrogen balance, n (%)	27 (13)	12 (35)	7 (28)	8 (5)	
Negative nitrogen balance, n (%)	184 (87)	22 (65)	18 (72)	144 (95)	<0.0001
Energy intake, kcals	1024±312	1283±182	1340±163	914±284	<0.0001
Protein intake, g	41.5±16.3	58.3±8.8	53.8±6.9	35.7±14.9	<0.0001
Energy intake by weight, kcal/kg	18.2±6.8	27.7±4.2	23.6±2.0	15.2±5.0	<0.0001
Protein intake by weight, g/kg	0.7±0.3	1.3±0.1	0.9±0.1	0.6±0.2	<0.0001

aPI: adequate protein intake; iPI/aEI: insufficient protein intake/adequate energy intake; iPI/iEI: insufficient protein and energy intake; APACHE II: acute physiology and chronic health evaluation; BMI: body mass index [weight (kg)/height (m^2)].

Data are presented as mean±standard deviation unless otherwise indicated.

[†] 24 h urine nitrogen excretion and nitrogen balance were measured and calculated within 72 hours of ICU admission in all patients (n=211).

Table 2. Clinical outcomes according to nutrition provision status

Outcomes	aPI	iPI/aEI	iPI/iEI	*p* value
All patients (n=211), n	34	25	152	
Weaning rate, n (%)	29 (85.3)	15 (60.0)	85 (55.9)	0.006
Ventilator free days, median (IQR)	45 (23-53)	33 (0-55)	31 (0-51)	0.047
In-ICU mortality, n (%)	5 (14.7)	9 (36.0)	67 (44.1)	0.006
In-hospital mortality, n (%)	8 (23.5)	14 (56.0)	79 (52.0)	0.008
60-day ICU survival, % (SE)	79.4 (6.9)	52.0 (10.0)	52.0 (4.1)	0.016
In-hospital survival, % (SE)	55.0 (14.5)	17.8 (13.9)	18.3 (6.4)	0.014
Survivors (n=110), n	26	11	73	
Ventilator free time, median (IQR)	49 (41-53)	50 (46-52)	51 (45-53)	0.543
Length of mechanical ventilation, median (IQR)	11 (7-19)	10 (8-14)	9 (7-16)	0.543
Length of ICU stay, median (IQR)	14 (10-23)	12 (9-20)	12 (9-17)	0.321
Length of in-hospital stay, median (IQR)	32 (18-54)	45 (21-72)	26 (19-50)	0.549

aPI: adequate protein intake; iPI/aEI: insufficient protein intake/adequate energy intake; iPI/iEI: insufficient protein and energy intake; IQR: interquartile range; ICU: intensive care unit; SE: standard error.

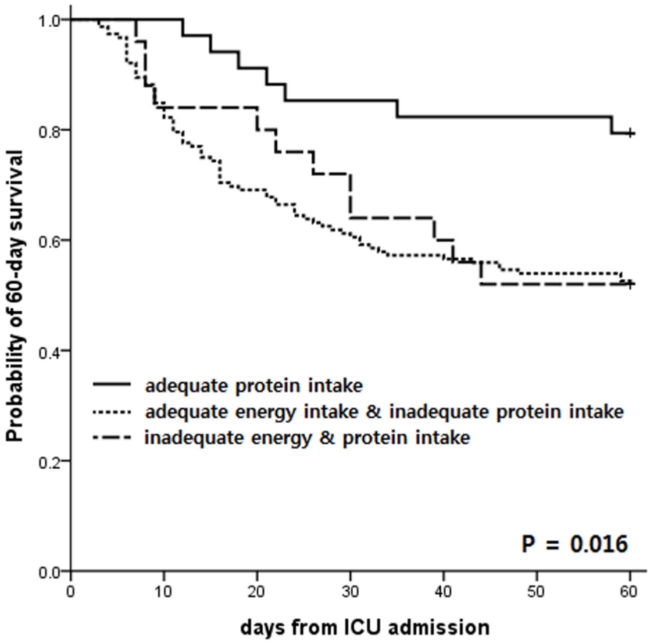

Figure 2. Kaplan-Meier 60-day survival curves according to nutrition provision status

body weight and BMI at admission. Specifically, the mean BMI values were 18.5 kg/m^2 in the aPI group, 22.2 kg/m^2 in the iPI/aEI group, and 22.9 kg/m^2 in the iPI/iEI group. Most patients (n=184, 87%) had a negative nitrogen balance (<0), with a mean nitrogen balance value of -6.6±5.8/day. Among the 27 patients with a positive nitrogen balance on day 1, the mean nitrogen balance value was 1.8±1.4/day. Significantly more patients in the iPI/iEI group had a negative nitrogen balance on day 1. The average energy intakes were 1283±182 kcal/day, 1340±163 kcal/day, and 914±284 kcal/day for the aPI, iPI/aEI, and iPI/iEI groups, respectively ($p<0.0001$); the corresponding protein intakes were 58.3±8.8 g/day (1.3±0.1 g/kg/day), 53.8±6.9 g/day (0.9±0.1 g/kg/day), and 35.7±14.9 g/day (0.6±0.2 g/kg/day), respectively ($p<0.0001$; Table 1).

Clinical outcomes according to nutritional provision

The overall ICU mortality rate in our study cohort was 38.4% (n=81), and the median time from ICU admission to death in the ICU was 14 days (range, 3-118 days). The remaining 130 (61.6%) patients recovered and were discharged from the ICU after a median of 13 days (range, 7-108 days). The overall in-hospital mortality rate was 47.9% (n=101). Among survivors (n=110), the median number of days on mechanical ventilation was 10 (interquartile range [IQR], 7-16) and the median lengths of ICU and hospital stays were 13 (IQR, 9-19) and 31 (IQR, 19-52) days, respectively.

Clinical outcomes were significantly better in the aPI group (Table 2). The aPI group had significantly lower rates of ICU (14.7%) and in-hospital (23.5%) mortality compared with patients with insufficient protein intake (ICU mortality, iPI/aEI, 36.0%; iPI/iEI, 44.1%; $p=0.006$ and in-hospital mortality, iPI/aEI, 56.0%; iPI/iEI, 52.0%; $p=0.008$). The Kaplan–Meier survival analysis showed that survival at 60 days after ICU admission differed significantly among these groups, with rates of 79.4%±6.9% in the aPI group, 52.0%±10.0% in the iPI/aEI group, and 52.0%±4.1% in the iPI/iEI group ($p=0.016$; Figure 2). In-

Table 3. Cox regression analysis for clinical outcome (n=211)

Variable	Univariate		Multivariate[‡]	
	HR (95% CI)	p value	HR (95% CI)	p value
Weaning rate[†]				
Nutrition provision status				
aPI	1		1	
iPI/aEI	3.87 (1.12-13.4)	0.033	3.59 (1.03-12.5)	0.045
iPI/iEI	4.57 (1.68-12.4)	0.003	3.91 (1.37-11.2)	0.011
APACHE2[‡]	1.03 (0.99-1.08)	0.091	1.03 (0.99-1.08)	0.119
Nitrogen balance[§]	0.96 (0.91-1.01)	0.090	0.98 (0.93-1.03)	0.399
In-ICU mortality				
Nutrition provision status				
aPI	1		1	
iPI/aEI	3.26 (0.93-11.4)	0.064	2.98 (0.84-10.5)	0.090
iPI/iEI	4.57 (1.68-12.5)	0.003	3.65 (1.28-10.4)	0.016
APACHE2[†]	1.03 (0.99-1.07)	0.121	1.03 (0.99-1.08)	0.125
Nitrogen balance[†]	0.95 (0.90-0.99)	0.031	0.97 (0.91-1.02)	0.200
In-hospital mortality				
Nutrition provision status				
aPI	1		1	
iPI/aEI	4.14 (1.35-12.7)	0.013	3.82 (1.24-11.8)	0.020
iPI/iEI	3.52 (1.50-8.26)	0.004	2.92 (1.18-7.25)	0.021
APACHE2[†]	1.04 (1.00-1.08)	0.060	1.04 (1.00-1.08)	0.070
Nitrogen balance[†]	0.96 (0.92-1.00)	0.103	0.97 (0.92-1.03)	0.305
60-day ICU survival				
Nutrition provision status				
aPI	1		1	
iPI/aEI	2.73 (1.07-6.93)	0.035	2.59 (1.02-6.59)	0.046
iPI/iEI	2.93 (1.35-6.37)	0.007	2.88 (1.33-6.26)	0.008
APACHE2[†]	1.03 (1.00-1.06)	0.038	1.03 (1.00-1.06)	0.049

HR: hazard ratio; CI: confidence interval; aPI: adequate protein intake; iPI/aEI: insufficient protein intake/adequate energy intake; iPI/iEI: insufficient protein and energy intake; APACHE II: acute physiology and chronic health evaluation; ICU: intensive care unit.

[†] Successfully off the mechanical ventilator for >48 hours.

[‡] Covariates treated as continuous variables.

[§] Outcomes were analyzed with the adjustment with APACHE II score regardless of the p value in univariate analysis.

hospital survival was also significantly higher in the aPI group (55%±14.5%) relative to the iPI/aEI (17.8%± 13.9%) and iPI/iEI groups (18.3%±6.4%, $p=0.014$). Regarding the outcomes of mechanical ventilation therapy, the weaning from ventillation rate and ventilation-free days (VFDs) also differed significantly among the groups. The successful weaning rate was significantly higher in the aPI group (85.3%) relative to the iPI/aEI (60.0%) and iPI/iEI groups (55.9%). Similar outcomes of VFDs were observed for all groups within 60 days of ICU admission, although the data favored the aPI group ($p=0.047$).

Cox regression analysis

Among the covariates (nutrition intake, age, sex, BMI, APACHE II score, diagnosis at ICU admission, and nitrogen balance), we included those with $p<0.1$ in the final multivariate analysis model. The multivariate analysis results are shown in Table 3. The HRs for iPI/iEI indicated that insufficient energy and protein intakes were associated with significantly higher ICU (HR 3.65, $p=0.016$) and in-hospital (HR 2.92, $p=0.021$) mortality rates and significantly lower weaning from ventillation (HR 3.91, $p=0.011$) and 60-day ICU survival (HR 2.88, $p=0.008$) rates when compared with patients receiving adequate protein intake. Adequate energy intake alone (iPI/aEI) was also associated with higher mortality rates (ICU mortality, HR 2.98, $p=0.09$; in-hospital mortality, HR 3.82, $p=0.020$), lower weaning rates (HR 3.59, $p=0.045$), and lower 60-day ICU survival rates (HR 2.59, $p=0.046$) relative to the aPI group. Although the iPI/iEI group had a greater risk for all factors except in-hospital mortality, we observed no significant differences in the clinical outcomes between the iPI/aEI and iPI/iEI groups.

DISCUSSION

This cross-sectional retrospective study investigated the influence of nutrition intake on clinical outcomes in a group of medically ill patients indicated to receive mechanical ventilation support during a prolonged ICU stay. A previous study of critically ill patients on mechanical ventilation reported that the achievement of individualized energy and protein targets resulted in a 50% reduction in 28-day hospital mortality relative to patients who failed to reach either target.[26] In agreement with that report and others,[23,26] our multivariable regression analysis found that patients who failed to receive adequate protein provision during the first week of ICU admission had increased risks of ICU and hospital mortality and failed weaning from ventilation. The overall outcomes of patients with adequate energy intake but inadequate protein intake were improved relative to the group with inadequate intakes of both energy and protein, consistent with studies that have reported correlations between reduced energy provision and worse clinical outcome measures.[3,27,28] However, among only survivors in the present study, we found no differences between the groups in terms of the VFDs and hospital length of stay.

Although the definitions of optimal protein provision in terms of the amount, mode and timing are still limited and controversial, recent guidelines recommend a protein target of at least 1.3 g/kg ideal body weight[18] or 1.2 g/kg actual body weight/day.[17] Similar to the results of previous studies,[25,29] our data also showed that the overall protein provision within the first week of ICU admission was considerably less than the recommended levels; the mean protein provision within the first 7 days of ICU care was 0.7±0.3 g/kg/day for all study patients and only 15% of the patients achieved >90% of the target goal (aPI). The median nitrogen balance value measured within 72 hours of ICU admission, which is commonly used as the basis for estimating protein requirements, suggested that our study population was in a state of hypercatabolism reflective of illness severity. However, significantly more patients in the group with inadequate energy and protein intakes had larger negative nitrogen balance values at ICU admission indicating that protein intake was not sufficiently provided as prescribed based on the individual nitrogen balance measurements.

Numerous previous studies have clarified that there are large variations in both protein loss and energy expenditure across various critically ill patient populations; however, it remains unclear whether the provision of nutrition to patients at levels that meet their protein and energy expenditures is associated with improved outcomes.[30] An observational study of ICU patients by Allinstrup et al demonstrated that the positive effect of adequate protein provision on ICU mortality was not related to the achievements of energy and nitrogen balance.[23] Moreover, studies of the relationship between nutrition intake and nitrogen balance showed that even in the context of adequate energy and protein provision, a negative nitrogen balance is not always reversed.[30,31] Future large studies based on nutritional assessments with high quality tools are needed to determine the impacts of a negative nitrogen balance (greater protein loss) and higher energy expenditure on clinical outcomes and the benefit–harm trade-offs of matching protein and energy intakes to these expenditures.

There are a number of limitations to consider when interpreting our study results. The main inevitable weakness is related to the observational design of this study, as the data were not collected with the intent to prove causality. Therefore, we could not analyze the causes of underfeeding by providing less than the doses intended (or recommended) by the ICU dietitian. We further acknowledge that PN was initiated on the day of ICU admission in some patients, although the initial amount was small and then gradually increased. This suggests that our feeding protocol was not strictly respected and highlights the gap between protocols and real clinical practice. Interestingly, patients in the aPI group, who were provided with >90% of their target protein provision, had significantly lower body weights and BMIs at ICU admission that patients in the other groups (inadequate protein and/or adequate calorie provisions), although this finding might suggest the early initiation of PN at the physician's discretion. This observation is consistent with a study by Alberda et al in which the beneficial effect of an increase in the nutritional provision on clinical outcomes appeared to be greatest in patients with a lower BMI (<25 kg/m^2).[29] The significant association between adequate protein provision and clinical outcomes in the multivariate analysis was not affected after adjusting for body weight or BMI in our study. Finally, the inclusion of severely critically ill patients with indications for artificial nutrition might have introduced selection bias by precluding the inclusion of patients who switched to oral feeding or were discharged from ICU before our arbitrary cut-off time point of day 7. In the EPaNIC trial, early PN initiation, which supplied greater amounts of protein and calories during the early treatment period, was associated with a higher ICU infection rate and longer ICU stay when compared with late PN initiation.[13] In contrast, the Tight Calorie Control Study trial, another supplemental PN trial, reported a lower mortality rate in the intervention group that received targeted nutrition intake, compared with a group receiving standard care.[32] The relatively lower ICU mortality rate reported in the EPaNIC trial (approximately 6%), which included mainly patients undergoing cardiac surgery, should be taken into account when interpreting the results of these trials.

Despite the possibility of selection bias among our patients because of the retrospective observational nature of the study, we studied mechanically ventilated patients in a likely hypercatabolic state who stayed in the ICU for at least 7 days and were clearly indicated to receive optimal nutritional support. The results showed that, while a substantial number of patients received inadequate protein intake, achievement of >90% of target protein provision was associated with improved ICU outcomes.

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AUTHOR DISCLOSURES

All the authors declare that there are no relevant conflicts of interest to disclose.

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