Phase-dependent intake and 90-day mortality by nutrition status in invasive mechanical ventilation critically ill adults: A retrospective cohort study

doi: 10.6133/apjcn.202602/PP.0006
Published online: February 2026

Running title: Phase-dependent nutrition and ICU mortality

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ABSTRACT

Background and Objectives: There has been a debate regarding appropriate nutrition support during the early stages of intensive care unit (ICU) admission. This study investigated nutrition support implementation and its relationship with clinical outcomes based on nutrition status. **Methods and Study Design:** We performed a retrospective cohort study of 595 critically ill adults receiving invasive mechanical ventilation. Patients were assessed by Global Leadership Initiative on Malnutrition criteria. Stages following ICU admission were categorized as early acute phase (days 1–3), late acute phase (days 4–6), and recovery phase (days 7–10). Patients were divided into energy intake categories (<10, 10–20, and >20 kcal/kg/day) and protein intake categories (<0.8, 0.8–1.2, and >1.2 g/kg/day). We examined differences in 90-day mortality at each stage using Cox proportional hazards analyses for total cohort, well-nourished, and malnourished groups. **Results:** Mortality was not associated with nutrition intakes during the early and late acute phases. However, higher energy intake during the recovery phase was associated with lower mortality in total cohort ($p = 0.002$). Significant associations between energy intake and mortality during the recovery phase were observed in both well-nourished and malnourished patients ($p = 0.007$ and $p = 0.05$, respectively). Additionally, protein intake during the recovery phase was associated with mortality, specifically in malnourished patients ($p = 0.007$), but not in well-nourished patients. **Conclusions:** Energy intake after 7 days in ICU was associated with mortality in both nutrition status groups, while protein intake showed benefit only in malnourished patients. Therefore, phase-dependent nutrition intake depending on nutrition status may be applicable for optimizing ICU nutrition support strategies.

Key Words: critical care, nutrition support, nutrition status, energy intake, protein intake

INTRODUCTION

It has been recognized that nutrition support plays a critical role in the management of patients in Intensive Care Units (ICU). However, significant debate exists regarding the specifics of nutrition support during the early stages of ICU admission. A previous observational study demonstrated that an increase in nutrition intake is associated with a decrease in mortality.[1] Nevertheless, in another study,[2] early full enteral nutrition support for 14 days in the ICU was not beneficial. Recent studies reported that low energy and protein intake during the first week in the ICU was associated with a shorter time to discharge

readiness and fewer complications.[3] Integrating these results, the latest American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines suggest that there are no significant differences between patients with higher vs lower levels of energy intake and clinical outcomes within 7 to 10 days of ICU admission.[4] Therefore, it remains unclear regarding the timepoint when a significant association between the amount of nutrition intake and improved clinical outcomes becomes evident. We aimed to categorize early stage of ICU into phases and examine whether there are phase-dependent differences in the association between the amount of nutrition support and the 90-day mortality.

Malnutrition is common among critically ill patients, accounting for 40–80% of individuals admitted to the ICU.[5] Patients diagnosed with malnutrition upon ICU admission reportedly experience longer ICU stays and higher mortality.[5,6] For patients with malnutrition who have low nutrient reserves in the body, the immediate initiation of nutrition support was recommended in the 2016 ASPEN guidelines.[7] However, recent ASPEN guidelines,[4] owing to insufficient randomized controlled trials (RCTs), do not differentiate nutrition guidelines based on nutrition status. Although several studies have examined nutrition intake and clinical outcomes,[2,3,8] few have analyzed these aspects according to nutrition status.

To evaluate whether differences in nutritional status influence the association between nutrition intake and clinical outcomes, we investigated the timing of nutrition intake and its association with 90-day mortality in the overall cohort and according to nutritional status defined by the Global Leadership Initiative on Malnutrition (GLIM) criteria. Specifically, we hypothesized that higher energy and protein intake would be associated with lower 90-day mortality in critically ill adults receiving invasive mechanical ventilation, and that these associations would differ according to both the phase of ICU admission and baseline nutrition status. To test these hypotheses, we examined phase-specific energy and protein intake during three predefined periods within the first 10 days of ICU stay (days 1–3, 4–6, and 7–10) and compared their associations with 90-day mortality between GLIM-defined well-nourished and malnourished patients.

MATERIALS AND METHODS

Study design and population

A single-center cohort study of patients admitted to medical and surgical ICUs was conducted at a tertiary care hospital. Data from January 2020 to December 2022 were retrospectively collected. This study was approved by the institutional review board (IRB No. 2023-03-042).

The requirement for informed consent was waived due to the retrospective nature of the study and the use of de-identified data.

We collected data from patients fulfilling inclusion criteria, which were as follows: critically ill adult patients (aged ≥18 years) requiring invasive mechanical ventilation for >24 h within 14 days who stayed in the ICU for ≥7 days. Patients who were receiving palliative care, brain death or in a coma, receiving exclusive oral treatment without nutrition support, transferred after stabilization from another ICU, or undergoing routine transplantation care, and those who did not consent to providing information were excluded.

Exposure of interest was phase-dependent intake defined as the actual amount of supplied nutrition during the early acute phase (days 1–3), late acute phase (days 4–6), and recovery phase (days 7–10).[9,10] To make it applicable in clinical practice, comparator was the standard of care, defined as isocaloric nutrition which is at least 80% of the target amount,[4,8] and nutrition intake was classified into three energy intake categories and three protein intake categories.

Data collection

Data were retrospectively collected from the electronic database and included baseline characteristics, daily nutrition therapy, laboratory results, and clinical outcomes. Baseline was defined as demographic and laboratory data collected within the first 24 hours of ICU admission. Baseline characteristics comprised age, sex, ICU type, comorbidities, baseline Sequential Organ Failure Assessment (SOFA),[11] and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores,[12] vital signs, reasons for ICU admission, and requirements for mechanical ventilation and hemodialysis. Laboratory results included hemoglobin, hematocrit, total bilirubin, aspartate aminotransferase, alanine aminotransferase, blood urea nitrogen, creatinine, electrolytes (potassium, sodium, phosphate, magnesium), C-reactive protein (CRP), and lactic acid levels.

For nutrition assessment, we collected anthropometric data including usual body weight, current body weight, ideal body weight (body mass index [BMI]: women, 21; men, 22)[13] and height. When BMI exceeded 30, adjusted body weight was used per established guidelines.[14] Evaluation of nutritional status included gastrointestinal symptoms, dietary intake history (as percentage of usual intake), baseline frailty scale,[15] and Nutrition Risk Screening 2002 (NRS 2002) score.[16] For descriptive analyses, NRS 2002 was analyzed as both a continuous variable and as a categorical variable (<3 vs ≥3), consistent with established cut-offs for nutritional risk. For all new ICU admissions, excluding routine postoperative patients, these nutrition

screening and assessment procedures were performed prospectively by trained dietitians within 48 hours of ICU admission as part of the standard hospital protocol. Because all patients were receiving invasive mechanical ventilation and were unable to communicate, dietary intake for the 5 days preceding ICU admission and recent weight loss history were obtained from caregivers and previous medical records and documented. As these items were mandatory in the protocol, GLIM-related variables had no relevant missing data and were considered reliable.

Global Leadership Initiative on Malnutrition (GLIM) criteria

GLIM criteria were applied at ICU admission based on five proposed criteria: three phenotypic and two etiologic[17,18] Phenotypic criteria included: (1) unintentional weight loss (>5% within 6 months or >10% beyond 6 months), (2) low BMI (for the Asian population, <18.5 kg/m^2 for patients <70 years or <20 kg/m^2 for patients ≥70 years),[18] and (3) reduced muscle mass (assessed using the frailty scalescale[15,19] recorded in the electronic medical records). For the phenotypic component, the criterion was considered present when at least one of the three phenotypic criteria (weight loss, low BMI, or reduced muscle mass) was fulfilled. Etiologic criteria included: (1) reduced food intake or assimilation (documented by dietitians in electronic medical records, including usual intake patterns and recent reductions before ICU admission), and (2) inflammation (CRP >5 mg/dL).[20,21] Patients were classified as malnourished if they fulfilled at least one phenotypic criterion and at least one etiologic criterion. Patients not meeting this combination were categorized as well-nourished. The degree of malnutrition was assessed based on phenotypic criteria.

Nutrition parameters and goals

Data on nutrition intake during the first 10 days of ICU admission including actual administered amount of energy (kcal) and protein (g) from enteral (EN) and parenteral (PN) nutrition were collected. Additionally, calories from dextrose, propofol, glycerin, and mannitol were calculated and subsequently incorporated into the total energy intake calculation.[22] Nutrition goal was 25 kcal/kg body weight/day, and target for protein intake was 1.2 g/kg body weight/day.[4,7]

Energy and protein intake categories

Patients were divided into three energy intake categories (<10, 10–20, and >20 kcal/kg body weight/day) and three protein intake categories (<0.8, 0.8–1.2, and >1.2 g/kg body

weight/day).[23] Average amount of nutrients actually supplied during each phase was determined and used as a reference for establishing nutrition intake categories.

Outcomes

The primary outcome was 90-day mortality, analyzed according to nutrition status and categorized by energy and protein intake levels. Secondary outcomes included ICU death, hospital death, ICU length of stay (LOS), hospital LOS, mechanical ventilation duration, and ICU readmission rate. Time to discharge alive (TDA) was calculated as an unbiased LOS measurement that excludes the shorter stays of in-hospital deceased patients. All clinical outcomes were obtained from hospital records, with out-of-hospital deaths confirmed through linkage with the Korea Disease Control and Prevention Agency (KDCA) to ensure complete mortality tracking.

Statistical analysis

For descriptive statistics, categorical variables are presented as absolute (n) and relative (%) frequencies, while continuous variables are expressed as either the mean and standard deviation or median and interquartile range. All variables required for nutritional assessment, phase-specific nutritional intake calculations, and assessment of 90-day mortality were complete, with no missing data. Age, sex, and baseline SOFA score, which were included as covariates in the multivariable models, were also fully available. Occasional missing values in other baseline characteristics were used solely for descriptive purposes and did not affect the primary analyses.

A comparative analysis between patients with and without malnutrition was conducted using the Student's t-test and chi-square test for parametric and categorical variables, respectively. Kaplan–Meier survival curves were used to assess 90-day survival according to nutrition status and the severity of malnutrition determined by the GLIM criteria. Cox proportional hazards models were applied to assess differences in mortality among different intake groups at each stage. For phase-specific intake analysis, energy and protein intake were averaged within three predefined time periods after ICU admission, and each summarized intake measure was treated as a prespecified exposure variable. Because these exposures were defined as a priori rather than derived through repeated post-hoc testing, no formal multiple-comparison correction was applied. The Cox models were adjusted for potential confounders including age, sex, baseline SOFA score, and nutrition status. Furthermore, Cox analysis was performed separately for each nutrition status group. Effect sizes were expressed as Hazard

Ratios (HR) with 95% Confidence Intervals (CI). The proportional hazards assumption for Cox models was tested and confirmed. Statistical significance was set at p <0.05. SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA) was used for all analyses.

RESULTS

Characteristics of study population

Data were collected from 653 patients who met the inclusion criteria. We excluded 24 patients who were receiving palliative care, seven who had been declared brain dead, and 36 who were undergoing routine transplantation care. Additionally, 12 patients who had been stabilized in other ICUs and transferred were excluded. We also excluded 12 patients who were on oral intake without nutrition support and five who did not consent to the use of their information. Therefore, a total of 595 patients were analyzed in this study.

Table 1 presents the characteristics of patients. Of the 595 patients, 248 (41.7%) were classified as well-nourished and 347 (58.3%) as malnourished according to GLIM criteria. Eighty-five percent of the patients were admitted to a medical ICU, and 22.2% underwent surgery during their hospital stay. Forty-one percent of the patients were diagnosed with sepsis while in the ICU and 54.0% of the patients were diagnosed with malignancy. Five percent of the patients were diagnosed with coronavirus disease 2019 (COVID-19), and 30.8% received continuous renal replacement therapy (CRRT). Regarding clinical outcomes, the ICU and hospital mortality rates were 34.3% and 51.9%, respectively. The median lengths of ICU stay and total hospital stay were 15 and 29 days, respectively. The duration of being on ventilator was 11 days, and the ICU readmission rate was 20.6%.

Prevalence and characteristics of malnutrition

The prevalence of malnutrition according to the GLIM criteria was 58.3% (n = 347). Patients diagnosed with malnutrition according to the GLIM criteria had significantly higher frailty scores, C-reactive protein levels and NRS 2002 scores compared to well-nourished patients. Given the limited discrimination of the NRS 2002 ≥3 cut-off in this cohort, NRS 2002 is presented as a continuous variable in Table 1. They also exhibited significantly lower serum albumin levels, serum creatinine levels, body weight and BMI compared to well-nourished patients. Additionally, malnourished patients showed a higher prevalence of malignancy diagnosis. However, no differences were noted in age, sex, ICU type, surgical status, sepsis diagnosis, COVID-19 diagnosis, APACHE II score, SOFA score, vasopressor use, or renal function and dialysis status between well-nourished and malnourished groups. Moreover, no

differences were observed in total bilirubin or serum phosphate concentrations. Regarding nutritional support, malnourished patients were more likely to receive combined enteral and parenteral nutrition support and less likely to be on only enteral nutrition support compared to well-nourished patients. Malnourished patients also experienced significantly higher rates of enteral nutrition intolerance, particularly high gastric residual volume or vomiting (Table 1).

Furthermore, patients with malnutrition received significantly more energy and protein in all phases (Figure 2). In the early acute phase, well-nourished patients received 12.9 ± 6.9 kcal/kg body weight/day of energy and 0.37 ± 0.34 g/kg body weight/day of protein, while malnourished patients received 16.5 ± 7.9 kcal/kg body weight/day of energy and 0.54 ± 0.40 g/kg body weight/day of protein. During the late acute phase, well-nourished patients were provided with 18.6 ± 6.8 kcal/kg body weight/day of energy and 0.70 ± 0.36 g/kg body weight/day of protein, whereas malnourished patients received 21.5 ± 7.4 kcal/kg body weight/day of energy and 0.81 ± 0.39 g/kg body weight/day of protein. In the recovery phase, well-nourished patients were administered 20.3 ± 6.6 kcal/kg body weight/day of energy and 0.79 ± 0.38 g/kg body weight/day of protein, whereas malnourished patients were given 23.6 ± 7.0 kcal/kg body weight/day of energy and 0.91 ± 0.39 g/kg body weight/day of protein.

Clinical outcomes

The 90-day mortality of well-nourished and malnourished patients were 41% and 55%, respectively, and this difference was statistically significant (p <0.05; Figure 1). ICU mortality rates were significantly higher among malnourished patients than among well-nourished patients, as were mortality rates during the hospital stay. However, no difference was noted in ICU LOS between malnourished and well-nourished patients. When calculated as the TDA, the results were consistent. Additionally, no differences were observed in the total duration of hospital stay and duration of ventilation between malnourished and well-nourished patients. However, ICU readmission rates were significantly lower among malnourished patients compared to well-nourished patients (Table 1).

Phase-dependent nutrition intake and mortality

According to the Cox regression analysis results, no difference in mortality was noted among the different energy intake groups in the early and late acute phases. However, the lowest-energy-intake group during the recovery phase showed higher mortality in total cohort (Table 2). Separate analysis according to nutrition status revealed that the association between lower

mortality and high energy intake was observed in both well-nourished and malnourished patients during the recovery phase (Table 3).

For protein intake, no association was observed between the amount of protein provided and mortality in the total patients in the early and late acute phases (Table 2). When well-nourished and malnourished patients were analyzed separately, no relationship was observed between protein intake and mortality rates at any phase among well-nourished patients. Nevertheless, among malnourished patients, higher protein intake was significantly associated with a reduced risk of 90-day mortality during the recovery phase. When level of protein intake was categorized to three groups, a significant association with lower mortality was observed in the highest-protein intake group compared to the lowest-protein intake group during the recovery phase among patients with malnutrition (Table 3).

In sensitivity analyses restricted to the recovery phase (ICU days 7–10), we repeated the Cox model with additional adjustment for AKI and then after excluding patients who received CRRT. In both models, the overall association between recovery-phase protein intake categories and 90-day mortality was attenuated and no longer statistically significant ($p = 0.13$ and $p = 0.12$, respectively).

DISCUSSION

This study investigated the association between the actual amount of nutrition support provided during the early stage of ICU admission and clinical outcomes depending on the nutrition status using GLIM, the latest nutrition assessment tool. The early stage of ICU admission was subdivided to three phases based on the days of ICU stay for the determination of optimal timing for nutrition support. Nutrition support provided within the first 6 days of ICU admission did not associate with clinical outcomes, regardless of nutrition status. However, the amount of energy supplied on recovery phase (days 7-10 of admission) significantly associated with the 90-day mortality. Additionally, the association between protein intake in the recovery phase and 90-day mortality differed according to nutritional status. In malnourished patients, higher protein intake in the recovery phase was significantly associated with lower 90-day mortality, whereas no significant association was observed in well-nourished patients. This study aimed to provide insights into that may help the best practices for nutritional management during the early stages of ICU admission.

Results from several large-scale RCTs[2,3,24,25] have indicated that the amount of energy supplied is not associated with clinical outcomes in adult critically ill patients. This time-dependent pattern may be explained by the physiological course of critical illness. During the

early phase, pronounced catabolic and inflammatory responses limit the body's ability to effectively utilize exogenous nutrition, whereas patients begin to stabilize metabolically in the later stage (days 7–10) may allow nutritional intake to exert a greater influence on outcomes. Nonetheless, in these previous studies, their definitions of the early ICU phase varied. In NUTRIREA-3 trial,[3] investigating whether early energy and protein restriction improves outcomes compared to standard feeding in critically ill patients during the first 7 days of ICU admission, 90-day mortality was similar between the low-energy group and the standard feeding group. Arabi et al[24] evaluated the effects of permissive underfeeding focused on the first 14 days of ICU admission, and found that the administration of nonprotein calories to critically ill adults was not associated with mortality. Furthermore, other studies[26,27] showed that outcomes of nutrition support vary depending on the timing of the support during the early stage of ICU admission. Koekkoek et al.[26] suggested that a gradual increase in protein intake during ICU stays from low protein intake during the first 2 days and high protein intake from day 6 of ICU is associated with lower mortality. However, the specific time duration when differences in the amount of nutrition support begins to affect outcomes varies across studies. Even though nutrition support during the first six days of ICU admission had no significant impact on clinical outcomes, the energy provided between days 7 and 10 significantly influenced 90-day mortality in the present study.

Limited number of studies[23,28] have examined nutrition intake and clinical outcomes according to the nutrition status. Compher et al.[28] showed that increased nutrition intake correlated with reduced mortality among patients at high nutrition risk using the NUTRIC score. Similarly, Jeong et al.[23] reported that amount of nutrition support was associated with 28-day mortality in malnourished patients but not in those with normal nutrition status based on NUTRIC scoring. These findings are consistent with our results suggesting differential associations of nutrition intake on clinical outcomes depending on nutrition status. The present study utilized GLIM criteria,[17,20,21] the most recent nutrition assessment tool endorsed by major global clinical nutrition societies, rather than the NUTRIC score used in previous studies. While recent studies have used GLIM to assess nutrition status and examine the relationship between nutrition intake and clinical outcomes, only protein intake was exclusively investigated.[29] It was reported that high protein treatment was not associated with better outcomes than usual protein treatment regardless of malnutrition diagnosis. Our study provides a more comprehensive analysis by examining both energy and protein intake across different phases of ICU stay according to GLIM-defined nutrition status.

Conducting RCTs that involve underfeeding of malnourished patients, who typically have low nutrient storage, presents ethical challenges. Consequently, while numerous studies have examined the association between nutrition intake and clinical outcomes, few have specifically analyzed differences in nutrition intake and outcomes according to nutrition status, as careful study design is required to minimize the harm to the patients. Furthermore, even the recent 2022 ASPEN guidelines4 acknowledge the lack of sufficient evidence to establish differing guidelines according to nutrition status. Therefore, more diverse research is needed to evaluate the relationship between nutrition intake and clinical outcomes by nutritional status.

This study has several limitations. First, it is a single-center, retrospective study exclusively involving an Asian cohort. Second, the observational study design limits our ability to establish causality. Nutritional intake may have been influenced by clinicians' assessment of illness severity and patients' ability to tolerate feeding, implying that feeding decisions and actual intake may reflect the underlying disease trajectory rather than a direct treatment effect. Despite adjustment for major confounders, residual confounding by indication and reverse causality remain possible. Third, we calculated nutrition requirements using weight-based equations not indirect calorimetry. However, indirect calorimetry has not been widely used in practice; hence, this study potentially reflects real-world conditions and could offer recommendations in practical setting. Fourth, no difference was observed between the amount of protein supplied and clinical outcomes, suggesting that the actual amount supplied might have been lower than that provided in prior research. The commercial EN formulations used in our study were those commonly used in ICUs were relatively low in protein concentration (40–50 g/L), reflecting actual clinical practice. Therefore, the actual amount of protein supplied was less than that recommended by the guidelines.30 In a future study, we intend to determine whether increasing protein supply improves outcomes. Furthermore, although we performed sensitivity analyses with additional adjustment for AKI and after excluding patients receiving CRRT, these analyses were exploratory and constrained by small numbers in several protein-intake strata. Therefore, our findings regarding protein intake during the recovery phase should be regarded as hypothesis-generating and interpreted with caution.

Conclusion

The results from the present study showed that energy intake after 7 ICU days is associated with mortality in both well-nourished and malnourished patients, while higher protein intake

in this phase was associated with lower mortality in only malnourished patients. Therefore, phase-dependent nutrition intake according to nutrition status may help optimize ICU nutrition support strategies.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflict of interest.

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Table 1. Characteristics of critically ill patients grouped according to the presence of malnutrition diagnosed by GLIM criteria[†‡]

Variables	Total	Well-nourished (n = 248)	Malnourished (n = 347)	*p* value
Clinical characteristics				
Age (years)	63.2 (14.3)	61.9 (15.6)	64.1 (13.2)	0.07
Sex				0.18
Men, n (%)	383 (64.4)	152 (61.3)	231 (66.6)	
Women, n (%)	212 (35.6)	96 (38.7)	116 (33.4)	
Type of ICU, n (%)				0.56
Medical, n (%)	505 (84.9)	208 (83.9)	297 (85.6)	
Surgical, n (%)	90 (15.1)	40 (16.1)	50 (14.4)	
Surgical procedures, n (%)	132 (22.2)	53 (21.4)	79 (22.8)	0.51
Elective OP	101 (17.0)	39 (15.7)	62 (17.9)	
Emergency OP	31 (5.2)	14 (5.6)	17 (4.9)	
Sepsis diagnosis, n (%)	243 (40.8)	95 (38.3)	148 (42.7)	0.29
Malignancy diagnosis, n (%)	321 (54.0)	115 (46.4)	206 (59.4)	<.01**
COVID 19 diagnosis, n (%)	30 (5.0)	9 (3.6)	21 (6.1)	0.18
APACHEII score	24.2 (7.2)	24.0 (7.0)	24.3 (7.4)	0.53
Baseline SOFA score	9.2 (4.0)	9.2 (4.1)	9.2 (3.9)	0.94
Frailty score	4.6 (1.7)	3.5 (1.3)	5.3 (1.5)	<.01**
Vasopressor Use, n (%)	290 (48.7)	125 (50.4)	165 (47.6)	0.49
Vasopressor days, median [IQR]	3 [2,7]	3 [2, 7]	3 [2, 8]	0.78
CRRT, n (%)	183 (30.8)	79 (31.9)	104 (30.0)	0.62
AKI, n (%)	330 (55.5)	137 (55.2)	193 (55.6)	0.93
CKD, n (%)	101 (17.0)	40 (16.1)	61 (17.8)	0.64
Serum creatinine (µmol/L)	1.4 (1.6)	1.6 (1.3)	1.3 (1.5)	0.04*
C reactive protein (mg/dL)	11.9 (10.2)	10.4 (9.0)	13.0 (9.8)	<.01**
Serum albumin (g/L)	2.8 (0.5)	3.0 (0.6)	2.8 (0.5)	<.01**
Total bilirubin (mg/dL)	2.7 (5.6)	3.0 (6.3)	2.6 (5.0)	0.39
Serum phosphate (mg/dL)	3.6 (1.6)	3.6 (1.6)	3.6 (1.7)	0.81
Nutrition characteristics				
Current weight (kg)	61.8 (13.3)	67.1 (13.7)	58.0 (11.7)	<.01**
BMI (kg/m2)	22.8 (4.3)	24.9 (4.2)	21.4 (3.8)	<.01**
NRS2002 score	4.4 (1.2)	3.9 (1.0)	4.8 (1.1)	<.01**
EN only, n (%)	239 (40.2)	112 (45.2)	127 (36.6)	0.04*
PN only, n (%)	99 (16.6)	41 (16.5)	58 (16.7)	0.95
EN+PN, n (%)	251 (42.2)	89 (35.9)	162 (46.7)	0.01*
EN intolerance				
High GRV / vomiting	90 (15.1)	28 (11.3)	62 (18.9)	0.03*
Diarrhea	110 (18.5)	44 (17.7)	66 (19.0)	0.69
Abdominal pain/discomfort	9 (1.5)	5 (2.0)	4 (1.2)	0.39
Clinical outcomes				
ICU death, n (%)	204 (34.3)	69 (27.8)	135 (38.9)	<.01**
ICU LOS days	15 [9, 24]	14.0 [9, 23]	15.0 [9, 25]	0.36
ICU TDA LOS, days	15 [9, 25]	14.0 [9, 23]	15.0 [9, 25]	0.41
Hospital death, n (%)	309 (51.9)	102 (41.1)	207 (59.7)	<.01**
Hospital LOS days, median [IQR]	29 [16, 58]	30.0 [18, 57]	28.0 [15, 60]	0.70
Hospital TDA LOS days, median [IQR]	46 [26, 73]	41.5 [23, 69]	49.5 [28, 78]	0.10
Ventilation duration days, median [IQR]	11 [6, 21]	11.0 [6, 21]	11.0 [6, 22]	0.80
Ventilation duration days (extubated alive) median [IQR]	8 [5, 17]	9.0 [6, 17]	8.0 [5, 17]	0.16
ICU readmission, n (%)	79 (20.6)	35 (14.1)	44 (12.7)	<.01**

ICU, intensive care unit; OP, operation; COVID 19, corona virus disease; SOFA, sequential organ failure assessment; APACHEII, acute physiology and chronic health evaluation II; CRRT, continuous renal replacement therapy; AKI, acute kidney injury; CKD, chronic kidney disease; BMI, body mass index; NRS 2002, nutrition risk screening 2002; EN, enteral nutrition; PN, parenteral nutrition; GRV, gastric residual volume; LOS, length of stay; TDA, time to discharge alive.

[†]Data are mean (SD), n (%), interquartile range [1st quartile, 3rd quartile].

[‡]Percentages may not sum to 100% because a small number of patients did not receive EN or PN during the early ICU phase (n = 6).

*p <0.05; **p< 0.01

Table 2. Adjusted Cox regression analysis for 90-days mortality in total study population[†]

	Early acute phase			Late acute phase			Recovery phase		
	n	HR (95% CI)	*p* value	n	HR (95% CI)	*p* value	n	HR (95% CI)	*p* value
Energy intake (kcal/ kg body weight/ day)									
<10	189	0.94 (0.70-1.27)	0.70	55	0.99 (0.66-1.48)	0.96	27	2.28 (1.43-3.65)	0.001**
10 to <20	249	1.08 (0.82-1.43)	0.58	221	1.06 (0.84-1.35)	0.63	160	0.98 (0.76-1.27)	0.88
≥20	153	Reference	0.58	310	Reference	0.87	353	Reference	0.002**
Protein intake (g/ kg body weight/ day)									
<0.8	482	0.93 (0.55-1.56)	0.78	306	1.20 (0.84-1.70)	0.32	271	1.31 (0.94-1.82)	0.11
0.8 to <1.2	86	0.85 (0.47-1.53)	0.59	212	1.12 (0.77-1.61)	0.55	225	1.01 (0.72-1.42)	0.94
≥1.2	27	Reference	0.82	77	Reference	0.59	99	Reference	0.10

HR, hazard ratio; CI confidence interval.
[†]Adjusted by age, sex, baseline SOFA score, nutrition status.
*p <0.05; **p< 0.01

Table 3. Adjusted Cox regression analysis for 90-day mortality according to the presence of malnutrition diagnosed by GLIM criteria[†]

	Early acute phase			Late acute phase			Recovery phase		
	n	HR (95% CI)	*p* value	n	HR (95% CI)	*p* value	n	HR (95% CI)	*p* value
Well-nourished									
Energy intake (kcal/ kg body weight/ day)									
<10	105	0.93 (0.54-1.61)	0.80	31	1.16 (0.63-2.13)	0,64	15	2.74 (1.40-5.33)	0.003
10 to <20	102	0.94 (0.55-1.61)	0.83	103	0.97 (0.64-1.46)	0.87	83	0.96 (0.62-1.47)	0.83
≥20	41	Reference	0.97	110	Reference	0.84	119	Reference	0.007
Protein intake (g/ kg body weight/ day)									
<0.8	223	1.13 (0.36-3.56)	0.84	145	0.85 (0.40-1.79)	0.67	135	1.13 (0.60-2.15)	0.70
0.8 to <1.2	18	1.10 (0.29-4.19)	0.88	88	0.80 (0.37-1.72)	0.56	84	1.06 (0.55-2.04)	0.86
≥1.2	7	Reference	0.98	15	Reference	0.83	29	Reference	0.91
Malnourished									
Energy intake (kcal/ kg body weight/ day)									
<10	84	1.12 (0.77-1.64)	0.55	24	0.97 (0.56-1.70)	0.92	12	2.28 (1.14-4.54)	0.02
10 to <20	147	1.24 (0.90-1.72)	0.19	118	1.24 (0.92-1.66)	0.15	77	1.17 (0.84-1.64)	0.35
≥20	112	Reference	0.43	200	Reference	0.33	234	Reference	0.05
Protein intake (g/ kg body weight/ day)									
<0.8	259	1.56 (1.03-2.36)	0.03	161	1.56 (1.03-2.36)	0.03	136	1.64 (1.10-2.43)	0.01
0.8 to <1.2	68	0.76 (0.39-1.48)	0.42	124	1.37 (0.90-2.10)	0.15	141	1.04 (0.70-1.55)	0.84
≥1.2	20	Reference	0.42	62	Reference	0.11	70	Reference	0.007

HR, hazard ratio; CI confidence interval.
[†]Adjusted by age, sex, baseline SOFA score.
*p <0.05; **p< 0.01

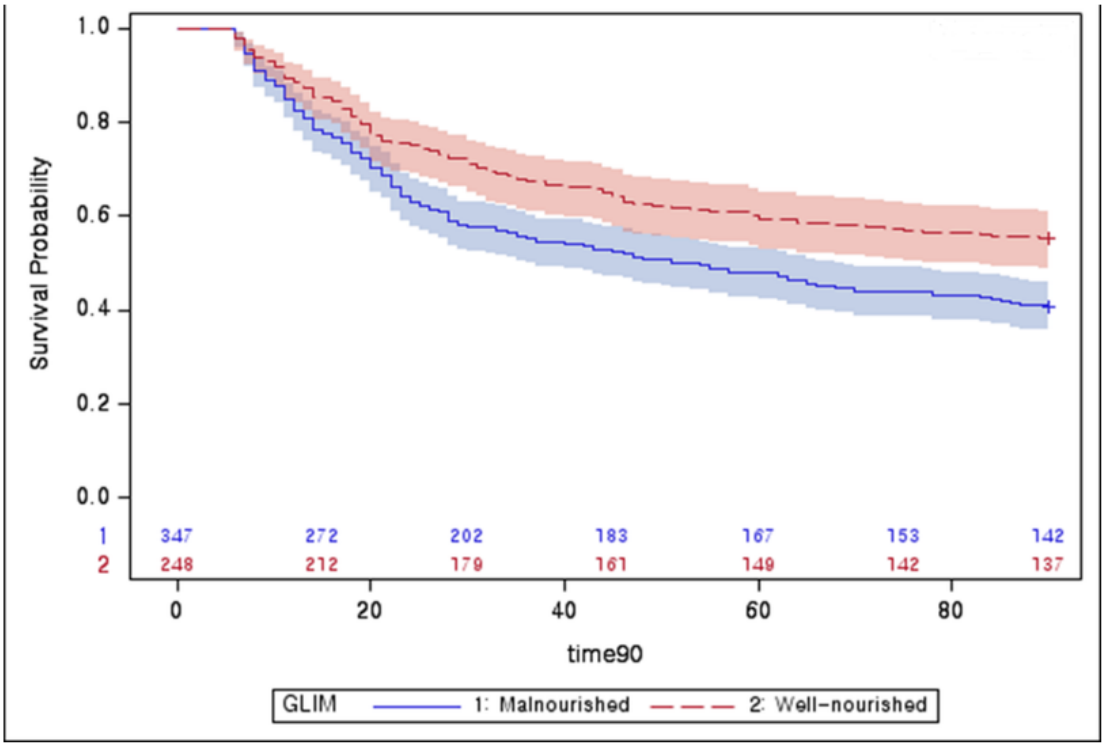

Figure 1. Kaplan-Meier survival curve of 90-day mortality according to the presence of malnutrition diagnosed by GLIM criteria. 1 = malnourished patients, 2 = well-nourished patients

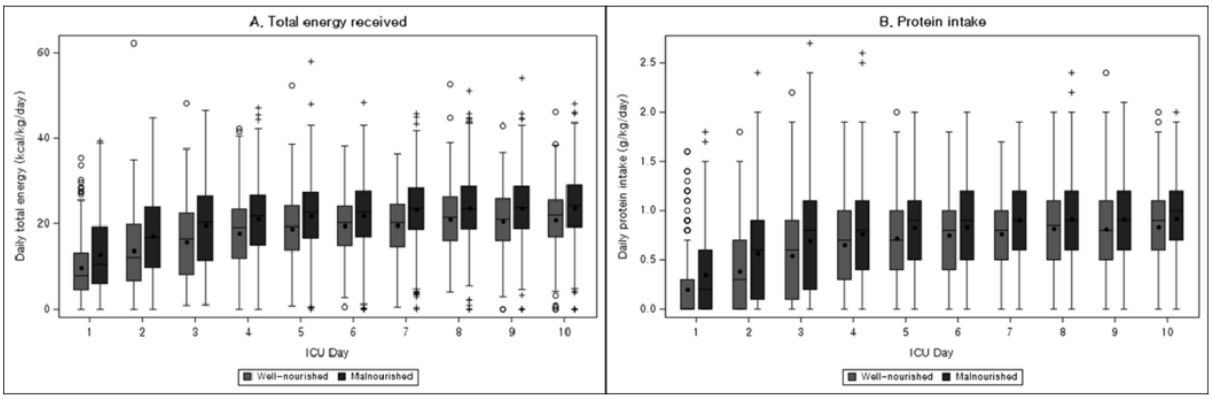

Figure 2. Daily amount of nutrients actually supplied per day according to the presence of malnutrition diagnosed by GLIM criteria. (A) Daily total energy intake (kcal/kg body weight/day) received. (B) Daily protein intake (g/kg body weight/day) received