First-week caloric intake and 1-year mortality in critically ill medical patients with mechanical ventilation: A retrospective study

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Running title: Caloric intake and 1-year mortality in ICU

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ABSTRACT

Background and Objectives: Higher caloric intake may reduce hospital mortality in critically ill patients at high nutritional risk, but the optimal dose for short-term outcomes remains uncertain and evidence on long-term effects is limited. This study evaluated the association between caloric intake and one-year mortality and identified subgroups that may benefit from higher intake. **Methods and Study Design:** We conducted a retrospective cohort study in a tertiary medical ICU (2015–2019) including adults receiving mechanical ventilation; ICU stays <48 h were excluded. The exposure was mean caloric intake during ICU days 1–7, defined as total energy from enteral and parenteral routes normalized to body weight. Outcomes included ICU length of stay, ventilator days, and one-year mortality from the Taiwan National Health Insurance Database. Multivariable Cox models adjusted for age, sex, albumin, hemoglobin, blood glucose, ICU admission etiology, APACHE II score, shock category, mNUTRIC score, renal replacement therapy, and cumulative day-1–7 fluid balance. **Results:** Among 3,764 patients (mean age 67.1 years; mean Acute Physiology and Chronic Health Evaluation II score 26.5), older age, male sex, lower albumin and hemoglobin, shock requiring multiple vasopressors, greater positive fluid balance, and lower caloric intake were associated with higher one-year mortality. Subgroup analyses showed that patients younger than 65 years, those with an APACHE II score ≥26, and those with refractory shock derived greater benefit from higher caloric intake. **Conclusions:** Higher first-week caloric intake was associated with lower one-year mortality, particularly in younger patients, in those with greater illness severity, and in those requiring multiple vasopressors.

Key Words: caloric intake, critical illness, intensive care unit, long-term mortality, nutrition support

INTRODUCTION

The optimal energy intake for critically ill patients remains a subject of debate, and several randomized controlled trials (RCTs) have attempted to address this question.[1-3] A randomized controlled trial conducted by Rice et al enrolled 1000 acute lung injury patients, found no difference in 90-day mortality when comparing trophic feeding to full caloric feeding.[1] The Permissive Underfeeding or Standard Enteral Feeding in Critically Ill Adults (PermiT) study was conducted by Arabi et al also failed to show differences in 90-day mortality when comparing permissive underfeeding to full caloric feeding.[2] Similarly, the Augmented Versus Routine Approach to Giving Energy Trial study in 2018 has shown no difference in 90-day

mortality between an energy-dense group and a routine enteral nutrition (EN) group.[3] These studies have led to varying recommendations for energy intake in guidelines, with the European Society for Clinical Nutrition and Metabolism (ESPEN) guideline suggesting that intake should be below 70% of estimated energy intake in the acute stage and the American Society for Parenteral and Enteral Nutrition (ASPEN) guideline providing a wider range of energy intake suggestions from 12 kcal/kg/day to 25 kcal/kg/day in the first 7-10 days of ICU admission.[4,5]

Due to the high heterogeneity in critically ill studies, short-term outcomes have often failed to demonstrate statistical differences regarding the effect of different nutritional support strategies. As a result, researchers have recommended the use of long-term mortality or lean body mass as outcomes in clinical studies.[6-8] For instance, Wei et al. have explored the association between nutritional support and 3- and 6-month outcomes in patients requiring prolonged mechanical ventilation.[9] Needham et al. have measured one-year mortality in patients with acute lung injury.[10] Deane et al. have also calculated 6-month mortality after delivering 100% and 70% caloric intake in the TARGET study.[11] In a review article by Looijaard et al., lean body mass is considered a useful guide to reflect the effectiveness of nutritional support. Methods such as computed tomography scan, musculoskeletal ultrasonography, and bioelectrical impedance analysis have been identified as measurable tools for assessing lean body mass.[7,12]

To investigate the potential role of caloric intake in long-term outcomes for critically ill patients, we conducted a study to determine whether one-year mortality differs based on varying levels of caloric intake.

MATERIALS AND METHODS

Study design and patient enrollment

This retrospective cohort study was conducted in the medical intensive care unit of a tertiary medical center from January 2015 to December 2019. The study was approved by the Institutional Review Board of the hospital (IRB number: CE22489A). Informed consent was waived due to retrospective study design. The enrolled criteria were medical ICU admission, respiratory failure requiring mechanical ventilator support, no contraindication to receive feeding protocol and age older than 20 years old. The exclusion criteria were patients stay at ICU less than 48 hours and patients who admitted to cardiac ICU. To estimate the required sample size, we assume a correlation coefficient (r) of 0.15, with a two-sided alpha of 0.05 and a power of 90%, the estimated required sample size was 934 patients. The assumed effect

size was referenced from prior studies evaluating the association between nutritional intake and clinical outcomes in critically ill patients, notably the international multicenter observational study by Alberda et al.[13]

The feeding protocol for all participants followed a standardized regimen with a daily target of 25 kcal/kg. EN started on day 1 and increased to the target rate by day 2, if there were no contraindications. A semi-elemental formula was used initially, with intravenous metoclopramide (10 mg every 8 h) unless contraindicated. If gastric residual volumes (GRVs) exceeded 250 mL twice, erythromycin (250 mg every 12 h) was added. The GRV threshold was set at 250 mL. The nurse in-charge determined whether there were any signs of feeding intolerance (FI) or contraindications to EN, which would necessitate stopping the feeding. Clinical physicians decided when to initiate parenteral nutrition, trophic feeding, or to stop feeding altogether.

Data collection

Patient characteristics, including age, gender, Charlson comorbidity index, body weight, and body mass index were recorded. The Modified Nutrition Risk in the Critically Ill (mNUTRIC) score was used to calculate nutritional risk. This score includes factors such as age, APACHE II score, SOFA score, number of comorbidities, and days of hospitalization before ICU admission. A score of ≥5 indicates high nutritional risk, while a score ≤4 indicates low nutritional risk. The first 7-day average caloric intake included both EN and parenteral nutrition (PN), and the first 7-day average fluid balance were recorded. For patients who stayed for less than 7 days, their data was calculated based on the actual length of their stay. Shock was defined as a condition requiring any type of vasoactive medication administered through a central venous catheter to maintain blood pressure and tissue perfusion. The vasoactive medications included adrenaline, dobutamine, dopamine, or noradrenaline.

Outcome measurement

We also collected length of intensive care unit stay and duration of ventilator dependence. Long term outcome as 1-year mortality was also recorded. The data of 1-year mortality was obtained from the National Health Insurance Database (NHID) in Taiwan. The medical claims of NHID have covered nearly 99.6% coverage of the 23.3 million Taiwanese residents.[14]

Statistical analysis

Data analysis was conducted using the SPSS statistical software package (version 22.0; International Business Machines Corp, Armonk, NY, USA). We used Student's t-test or the Mann-Whitney Rank Sum test for continuous variables, depending on the data distribution, to assess differences between groups. For categorical variables, we employed the Chi-square test or Fisher's exact test to analyze associations between variables and outcomes.

To identify factors linked to one-year mortality, we utilized Cox regression analysis. The hazard ratio along with its 95% confidence interval (CI) was employed to quantify the strength of association between variables and the outcome.

All statistical tests were conducted with a two-sided approach, and statistical significance was set at a *p* value of less than 0.05.

RESULTS

There were 3764 patients enrolled in the study (Figure 1). 2018 patients were dead during follow up for 1 year. The overall one-year mortality was 53.6%. The average age was 67.1 years old. The average APACHE II score was 26.5. 90% of participants were a high nutrition risk group. 43.8% of patients experienced shock (Table 1).

The non-survival groups were associated with elder age, male gender, higher Charlson comorbidity index, lower body weight, higher mNUTRIC score, lower albumin levels, lower hemoglobin levels, higher APACHE II score, more than one vasopressor usage, received renal replacement therapy (RRT) during acute illness, and more positive fluid balance. (Table1) Higher average total caloric intake, EN intake, and lower PN intake in the first 7 days were associated with lower one-year mortality. The advantages of total caloric and EN intake were more significant after the 3rd day (Table 2).

One-year mortality was lower in patients with an average caloric intake ≥15 kcal/kg/day compared with <15 kcal/kg/day, as illustrated by the Kaplan-Meier survival curves (Figure 2). The benefit of higher caloric intake to one-year mortality was significant among several subgroups. The effect was more obvious in age younger than 65-years old (adjusted HR:0.64 95% CI:0.556-0.737), APACHE II higher than 26 (adjusted HR:0.587 95% CI:0.520-0.662), and shock status need more than two kinds of vasopressors (adjusted HR:0.342 95% CI:0.264-0.443) (Table 4).

DISCUSSION

Our findings reveal that increased caloric intake is linked to reduced one-year mortality in medically critically ill patients (HR: 0.86, 95% CI: 0.796-0.933). In sensitivity analysis, an intake exceeding 15 kcal/kg/day during the first 7 days of ICU admission is associated with lower one-year mortality, particularly in patients aged less than 65, those with an APACHE II score higher than 26, and those experiencing shock requiring more than one vasopressor.

Determining the most optimal caloric intake to improve clinical outcomes in critically ill patients remains a challenge.15 Recent RCT trials have shown that higher caloric intake does not necessarily lead to improved 90-day mortality compared to lower caloric intake.[2,3,16] Most RCTs included both medical and surgical patients, and due to the heterogeneity of critically ill patients, intervention studies in the ICU can often struggle to demonstrate statistical differences in short-term outcomes. Consequently, researchers have turned to alternative measures, such as long-term mortality,[9,10,17,18] post-ICU cognitive function,[11,19] or body composition.[20,21]

Despite being a single-center, retrospective study, our research focused exclusively on medical ICU patients to reduce heterogeneity. We also extended our follow-up to one year. Moreover, our study enrolled 3764 patients, which is close to the 3957 patients in the TARGET study. This larger sample size might mitigate the risk associated with small sample sizes and inadequate statistical power.

Feeding barriers are a common challenge in the clinical practice of ICU care.[22-24] The actual caloric intake often differs from the estimated energy intake, and achieving precise energy delivery can be challenging. In studies like the TARGET study, a rigorous RCT achieved approximately 80% of estimated energy delivery, the overall caloric intake in the 1.0-kcal Group was 17.4 kcal/kg/day. In the PERMIT study, the actual caloric intake in the permissive underfeeding group was 46% of the calculated caloric requirements, while the standard enteral feeding group received 71% of the calculated caloric requirements. The real caloric achievement rate ranged from 70-80%. The ASPEN guideline suggests that optimal energy intake should fall between 12 and 25 kcal/kg in the first 7–10 days of ICU stay.[5] In our study, the average caloric intake in the first several days was approximately 16 kcal/kg, well within the guideline recommendation.

One explanation for the disparity in caloric intake might be FI in critically ill patients. FI, defined by Blaser et al. as a reduction in the delivery of enteral feeding for any reason, often accompanied by gastrointestinal symptom and poses a challenge to achieving estimated caloric intake.[25]

Heyland et al. have conducted a prospective study to survey the incidence of FI in critically ill patients.[26] The presence of FI was associated with higher disease severity. In our study, the average APACHE II score was 26.5, which is significantly higher than the APACHE II score of 21 in the PermiT study and 22 in the TARGET study. Given this higher severity, it is not surprising that the achieved rate of estimated caloric intake was lower, even with the use of a feeding protocol to facilitate caloric intake.

While these results align with our findings, they primarily explain the relationship between caloric delivery and short-term outcomes in different nutrition risk patients rather than long-term outcomes. There have been some studies exploring the relationship between energy intake and long-term outcomes, but the results have been inconsistent. For instance, Wei et al conducted a retrospective study that examined the relationship between nutrition intake and 6-month survival, finding that a caloric intake of more than 80% was associated with lower 6-month mortality compared to lower caloric intake in prolong mechanical ventilation patients.[9] On the other hand, Deane et al analyzed the 6-month mortality data from the TARGET study and found no difference between the standard group and the energy-dense group.[11]

Notably, our study extended its follow-up duration to one year, revealing the advantages of higher energy intake. However, it remains unknown whether a longer follow-up period would yield different results. Therefore, conducting another well-designed prospective study to address this question would be valuable.

The correlation between the use of more than two kinds of vasopressors and a lower hazard ratio for one-year mortality compared to non-shock or norepinephrine alone is intriguing. Our findings underscore the benefit of caloric intake regardless of the presence of shock (Table 4). However, the relationship between early EN and shock status remains variable. Some studies have reported associations between early EN and improved outcomes in specific patient populations. For instance, Renaudier et al. found that early EN was linked to a lower risk of mesenteric ischemia in patients receiving venoarterial extracorporeal membrane oxygenation.[27] Ohbe et al. conducted a large observational study, revealing that early EN, particularly with low- or medium-dose noradrenaline but not in those requiring high-dose noradrenaline, was associated with lower mortality in circulatory shock patients.[28]

In contrast, two large RCTs, suggested that the route or amount of nutrition may not be the key determinant for clinical outcomes.[16,29] Nonetheless, our findings align with the importance of energy intake during the acute stage. There are limited large sample studies discussing the dosage and long-term outcomes. Our results indicate that EN might be beneficial in shock patients, even in those receiving higher doses of vasopressin. Since our

study is retrospective and observational, these findings warrant careful examination through well-designed prospective RCTs.

Our study revealed a significant association between higher hemoglobin levels and reduced one-year mortality. This finding aligns with a meta-analysis conducted by Song et al., which indicated that anemia increase ICU or 90-day mortality in critically ill patients.[30] Furthermore, lower discharge hemoglobin levels have been demonstrated to increase one and two-year mortality in patients undergoing primary percutaneous coronary intervention after acute myocardial infarction.[31] This consistency extends to the Impact of Early Enteral vs. Parenteral Nutrition on Mortality in Patients Requiring Mechanical Ventilation and Catecholamine (NUTRIREA -2) study, where low hemoglobin levels were associated with acute mesenteric ischemia in shock patients.[32] However, while improved oxygen delivery in shock patients may explain this association, the long-term implications remain complex.

Our study enrolled 1646 patients (43.7%) with circulatory shock. The results reaffirm the connection between low hemoglobin levels and adverse outcomes. Nevertheless, further research is necessary to pinpoint the optimal hemoglobin levels for these patients and fully comprehend the implications, particularly within the context of long-term outcomes.

Several limitations in our study should be acknowledged. Firstly, being a single-center study, the generalizability of our findings to other institutes may be limited. Secondly, the retrospective design of the study might not fully elucidate causal relationships among risk factors and outcomes. Thirdly, due to data limitations, we were unable to collect daily protein intake. Fourthly, comprehensive control of factors influencing outcomes after patient discharge from the hospital might not have been feasible.

Despite these limitations, our study possesses several notable strengths. Most prominently, the inclusion of over 3,000 critically ill patients substantially mitigates the risk of selection bias through the advantage of a large sample size. Furthermore, the number of enrolled patients markedly exceeded the 934 participants estimated to achieve 90% statistical power, thereby reinforcing the robustness and credibility of our findings. Secondly, the one-year mortality data was derived from withdrawal from the NHID, a reliable and validated source. Further research, preferably in the form of prospective multicenter studies, is warranted to validate our findings and to address the limitations identified in this study.

Conclusion

Our study indicates that higher caloric intake might be linked to reduced one-year mortality in critically ill medical patients. This association is notably strong in patients younger than 65

years old, those with an APACHE II score exceeding 26, or individuals experiencing shock requiring more than one vasopressors. These findings emphasize the potential role of caloric intake in improving long-term outcomes in this patient population.

SUPPLEMENTARY MATERIALS

All supplementary tables and figures are available upon request from the editorial office, and are also accessible on the journal's webpage (apjcn.qdu.edu.cn).

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CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflicts of interest.

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Table 1. Patient characteristics categorized by one-year mortality

	All n=3,764	Survivor n=1,746	Non-survivor n=2,018	*p* value
Basic characteristics				
Age, years	67.1±16.3	64.7±16.9	69.1±15.6	<0.001
Male (n, %)	2413 (64.1)	1063 (60.9)	1350 (66.9)	<0.001
Charlson Comorbidity Index	2.3±1.7	2.1±1.7	2.5±1.6	<0.001
Nutrition relevant variables				
Body mass index	23.5±4.8	23.7±4.9	23.3±4.8	0.005
Body weight, kg	61.4±14.1	62.1±14.4	60.7±13.9	0.004
mNUTRIC score	6.4±1.5	6.0±1.6	6.8±1.2	<0.001
High nutrition risk (mNUTRIC ≥ 5) (n, %)	3389 (90.0)	1451 (83.1)	1938 (96.0)	<0.001
Albumin (g/dL)	3.0±0.7	3.1±0.7	2.8±0.7	<0.001
Hemoglobin (g/dL)	10.0±2.0	10.6±2.0	9.5±1.7	<0.001
Blood glucose (mg/dL)	181±106	183±108	180±105	0.472
Etiologies for admitting to ICU (n, %)				<0.001
Acute respiratory failure	1176 (31.2)	509 (29.2)	667 (33.1)	
Acute neurological dysfunction	365 (9.7)	231 (13.2)	134 (6.6)	
Acute cardiac dysfunction	126 (3.3)	82 (4.7)	44 (2.2)	
Acute kidney failure	502 (13.3)	259 (14.8)	243 (12.0)	
Acute hematological condition	289 (7.7)	62 (3.6)	227 (11.2)	
Others	1306 (34.7)	603 (34.5)	703 (34.8)	
Severity and management				
APACHE II score	26.5±6.8	24.3±6.3	28.5±6.7	<0.001
Presence of shock				
Norepinephrine-alone (n, %)	1132 (30.1)	511 (29.3)	621 (30.8)	0.332
Norepinephrine and other vasopressors (n, %)	514 (13.7)	87 (5.0)	427 (21.2)	<0.001
Renal replacement therapy (RRT) (n, %)				
RRT for acute illness	97 (2.6)	24 (1.4)	73 (3.6)	<0.001
RRT for end-stage renal disease	280 (7.4)	137 (7.8)	143 (7.1)	0.410
Fluid balance, day 1-7	1300±5340	-352±4330	2740±5710	<0.001
Outcomes				
ICU-stay, days	12.4±10.6	11.6±9.2	13.1±11.6	<0.001
Ventilator-day, days	11.0±12.7	9.0±10.0	12.7±14.5	<0.001

BMI, Body Mass Index; APACHE II, Acute Physiology and Chronic Health Evaluation; RRT, Renal Replacement Therapy; ICU, Intensive Care Unit; mNUTRIC, Modified Nutrition Risk in the Critically Ill.
Values are mean ± standard deviation

Table 2. Daily feeding calories in critically ill ventilated patients categorized by one-year mortality

	Survivors n=1,746	Non-survivors n=2,018	*p* value
Total calories (kcal)			
Day 1	797±596	761±648	0.086
Day 2	953±726	900±740	0.033
Day 3	1060±823	990±803	0.017
Day 4	1140±830	1060±845	0.012
Day 5	1120±863	1100±856	0.003
Day 6	1250±968	1140±881	0.002
Day 7	1260±942	1180±943	0.040
Day 1-7 average	1020±657	941±652	<0.001
Enteral nutrition (kcal)			
Day 1	787±613	748±709	0.129
Day 2	946±736	896±787	0.081
Day 3	1050±836	972±841	0.018
Day 4	1130±833	1050±882	0.017
Day 5	1180±869	1090±887	0.008
Day 6	1230±973	1120±913	0.002
Day 7	1250±943	1170±977	0.030
Day 1-7 average	1010±688	918±705	<0.001
Parenteral nutrition (kcal)			
Day 1	143±198	217±289	<0.001
Day 2	115±201	169±256	<0.001
Day 3	94.4±182	144±252	<0.001
Day 4	77.0±183	128±247	<0.001
Day 5	62.9±170	115±247	<0.001
Day 6	56.0±160	106±242	<0.001
Day 7	48.1±148	97.3±239	<0.001
Day 1-7 average	129±165	209±257	<0.001

Values are mean ± standard deviation.

Table 3. Cox proportional hazard regression analysis for long-term mortality

Characteristics	Univariable		Multivariable	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Age, per year increment	1.01 (1.01-1.01)	<0.001	1.00 (1.00-1.01)	0.009
Sex (male)	1.18 (1.08-1.30)	<0.001	1.20 (1.09-1.32)	<0.001
CCI, per 1 score increment	1.07 (1.04-1.09)	<0.001	1.04 (1.01-1.07)	0.005
BMI, per 1 kg/m2 increment	0.997 (0.988-1.01)	0.515	1.01 (0.995-1.02)	0.316
High nutrition risk (mNUTRIC ≥5)	3.52 (2.81-4.40)	<0.001	1.61 (1.25-2.07)	<0.001
Albumin, per 1 g/dL increment	0.562 (0.523-0.602)	<0.001	0.835 (0.773-0.902)	<0.001
Hemoglobin, per 1 g/dL increment	0.786 (0.764-0.808)	<0.001	0.885 (0.858-0.913)	<0.001
Blood glucose (mmol/L)	0.998 (0.990-1.01)	0.580	0.990 (0.983-0.998)	0.017
APACHE II score, per 1 increment	1.08 (1.07-1.09)	<0.001	1.04 (1.03-1.04)	<0.001
Presence of shock				
Norepinephrine-alone	1.30 (1.17-1.43)	<0.001	1.04 (0.937-1.16)	0.461
Norepinephrine and other vasopressors	4.34 (3.87-4.87)	<0.001	2.26 (1.98-2.59)	<0.001
RRT during ICU admission	1.67 (1.33-2.11)	<0.001	1.03 (0.812-1.32)	0.785
Fluid balance, day 1-7, per liter	1.10 (1.09-1.11)	<0.001	1.08 (1.07-1.09)	<0.001
Etiology of ICU admission				
Acute respiratory failure	Reference		Reference	
Acute neurological dysfunction	0.554 (0.461-0.667)	<0.001	0.668 (0.550-0.810)	<0.001
Acute kidney failure	0.541 (0.399-0.735)	<0.001	0.538 (0.394-0.734)	<0.001
Acute cardiac dysfunction	0.851 (0.735-0.986)	0.032	0.631 (0.542-0.734)	<0.001
Acute hematological condition	2.03 (1.75-2.36)	<0.001	1.20 (1.02-1.41)	0.025
Calories intake				
Calories intake, day 1–7, per kcal/10^3/day	0.729 (0.673-0.790)	<0.001	0.862 (0.796-0.933)	<0.001

HR, Hazard Ratio; CI, Confidence Interval; CCI, Charlson Comorbidity Index; BMI, Body Mass Index; mNUTRIC, Modified Nutrition Risk in the Critically Ill; APACHE II, Acute Physiology and Chronic Health Evaluation II; RRT, Renal Replacement Therapy; ICU, Intensive Care Unit.

Table 4. Effect modification of variables on the association between day 1-7 calories intake and risk of mortality

Variables	Crude HR (95%CI)	*p* for interaction	Adjusted HR (95% CI)	*p* for interaction
Age group		0.032		0.009
< 65 years	0.650 (0.568-0.743)		0.640 (0.556-0.737)	
≥ 65 years	0.771 (0.697-0.852)		0.792 (0.714-0.879)	
Gender		0.342		0.480
Female	0.769 (0.672-0.880)		0.760 (0.660-0.875)	
Male	0.708 (0.641-0.782)		0.714 (0.644-0.792)	
BMI		0.202		0.319
<18	0.818 (0.670-0.998)		0.776 (0.626-0.963)	
≥18	0.714 (0.655-0.779)		0.720 (0.658-0.788)	
Charlson Comorbidity Index		0.863		0.326
< 3	0.719 (0.644-0.803)		0.703 (0.626-0.789)	
≥ 3	0.726 (0.646-0.816)		0.766 (0.679-0.863)	
APACHE II		<0.001		<0.001
< 26.0	0.939 (0.847-1.04)		0.867 (0.779-0.966)	
≥ 26.0	0.577 (0.511-0.651)		0.587 (0.520-0.662)	
Shock		<0.001		<0.001
Absence of shock	0.908 (0.824-1.00)		0.903 (0.817-0.997)	
Norepinephrine-alone	0.778 (0.673-0.899)		0.780 (0.673-0.904)	
Norepinephrine and other vasopressors	0.326 (0.252-0.421)		0.342 (0.264-0.443)	
Nutrition risk		0.172		0.345
Low risk (mNUTRIC ≤ 4)	0.918 (0.627-1.35)		0.870 (0.577-1.31)	
High risk (mNUTRIC≥5)	0.700 (0.644-0.760)		0.725 (0.666-0.790)	
Acute respiratory failure		0.003		<0.001
No	0.673 (0.609-0.744)		0.668 (0.601-0.741)	
Yes	0.859 (0.754-0.979)		0.881 (0.772-1.01)	
Acute neurological dysfunction		0.006		0.033
No	0.715 (0.657-0.777)		0.724 (0.662-0.791)	
Yes	1.05 (0.819-1.35)		0.983 (0.753-1.28)	
Acute cardiac dysfunction		0.242		0.719
No	0.718 (0.661-0.780)		0.739 (0.678-0.806)	
Yes	0.862 (0.636-1.17)		0.772 (0.529-1.13)	
Acute kidney failure		0.010		0.001
No	0.762 (0.700-0.829)		0.787 (0.720-0.859)	
Yes	0.553 (0.434-0.704)		0.522 (0.401-0.679)	
Acute hematological condition		0.296		0.406
No	0.745 (0.686-0.810)		0.751 (0.688-0.820)	
Yes	0.634 (0.471-0.852)		0.669 (0.495-0.904)	

HR, Hazard Ratio; CI, Confidence Interval; BMI, Body Mass Index; APACHE II, Acute Physiology and Chronic Health Evaluation; mNUTRIC, Modified Nutrition Risk in the Critically ill.

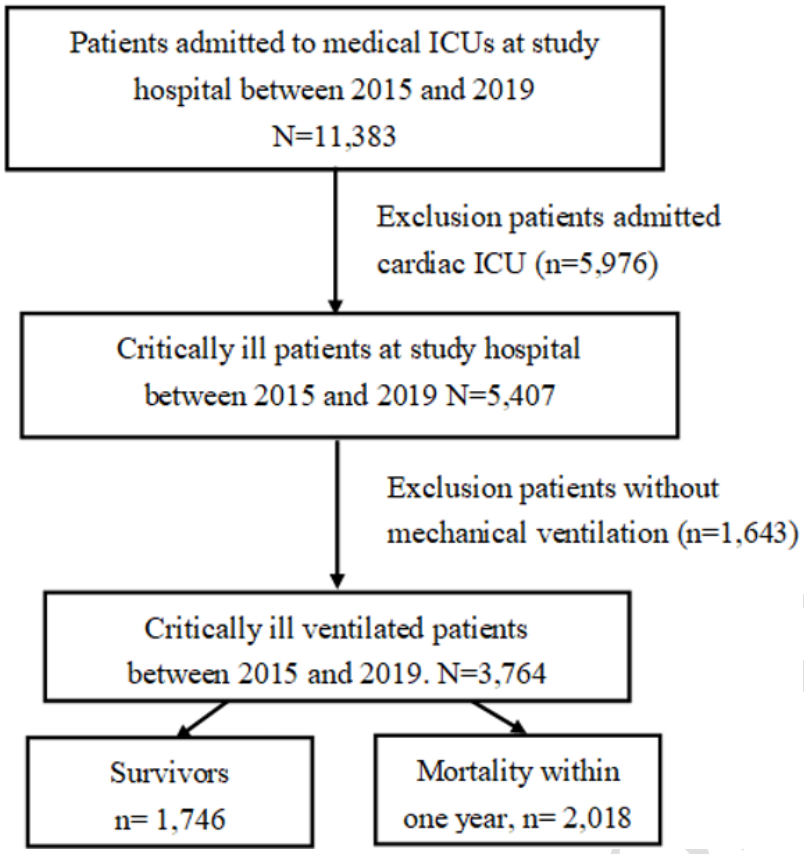

Figure 1. Flow diagram of patient screening, exclusions, and final enrollment in the medical intensive care unit cohort. Abbreviations: ICU, intensive care unit.

Figure 2. Kaplan–Meier survival curves stratified by average caloric intake during days 1–7 of intensive care unit admission (≥15 vs <15 kcal/kg/day). Patients with higher intake showed significantly better one-year survival.

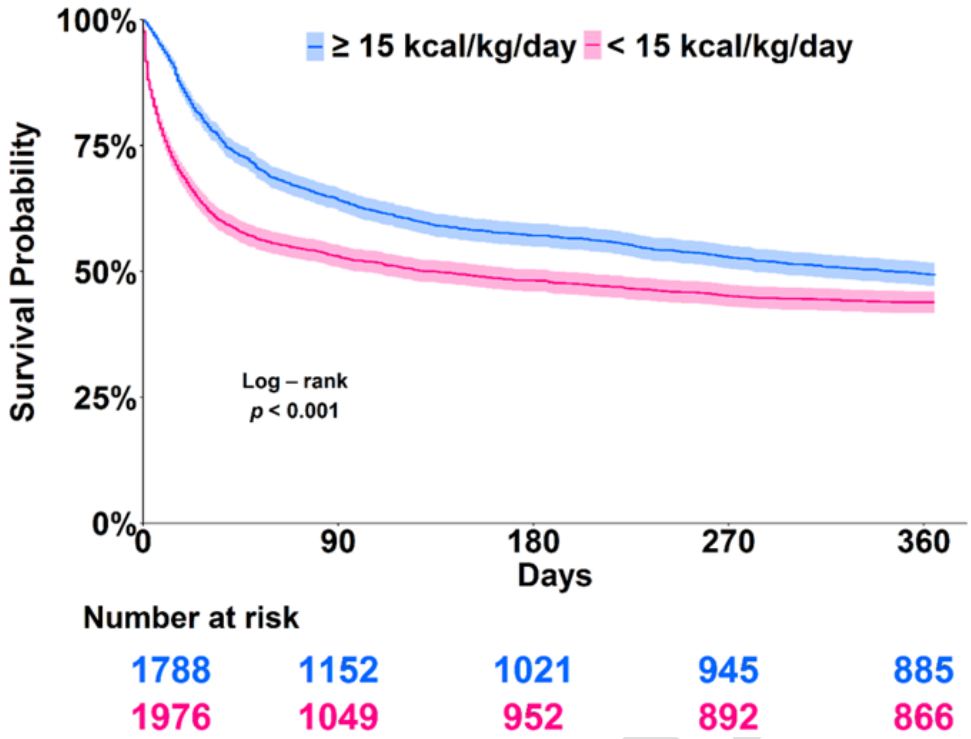

Figure 2. Kaplan–Meier survival curves stratified by average caloric intake during days 1–7 of intensive care unit admission (≥15 vs <15 kcal/kg/day). Patients with higher intake showed significantly better one-year survival.