An Assessment of Nutritional Support to Critically Ill Patients and Its Correlation With Outcomes in a Respiratory Intensive Care Unit

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BACKGROUND: Nutritional support is frequently neglected in a busy intensive care unit (ICU) with overworked staff. There is a paucity of investigations on ICU nutrition from India. OBJECTIVES: To assess the adequacy of nutritional support administered to patients requiring mechanical ventilation in the respiratory ICU of a tertiary-care institute, and its correlation with outcomes. METHODS: This was a prospective cohort study of patients ≥ 15 years old who underwent mechanical ventilation for at least 24 hours and had a respiratory ICU stay of at least 48 hours. Enteral nutritional support was initiated as early as possible after respiratory ICU admission. The daily calorie and protein prescription was 30 kcal/kg and 1.2 g/kg ideal body weight, respectively, with appropriate adjustments for critical illness(es) and comorbidities. Anthropometric and laboratory parameters were assessed serially. Risk factors for hospital mortality were evaluated using multivariable logistic regression analysis. RESULTS: During the study period, 258 patients were admitted to the respiratory ICU, of whom 93, who fulfilled all the inclusion criteria, composed the study population. Calorie prescription increased from a median and interquartile range (IQR) of 88.9% (80.4–99.0%) of the recommended value on day 1 to 114.4% (99.9–122.5%) on day 21. Protein prescription improved from 80.1% (67.1–90.6%) of the recommended value on day 1 to 98.4% (76.1–120.8%) on day 28. Calorie delivery increased from 55.1% (35.4–81.3%) of the recommended value on day 1 to 92.0% (35.7–124.6%) on day 28. Protein delivery improved from 46.7% (31.6–72.1%) of the recommended value on day 1 to 75.3% (54.3–85.5%) on day 28. Risk factors for hospital mortality identified were admission Sequential Organ-Failure Assessment score (odds ratio 1.30, 95% confidence interval 1.03–1.63) and mean daily calorie delivery of ≤ 50% of the recommended value (odds ratio 12.08, 95% confidence interval 1.40–104.11). CONCLUSIONS: Calorie and protein delivery to critically ill patients remains less than the recommended values. Inadequate calorie delivery is associated with higher odds of mortality. *Key words: calorie, delivery, intensive care unit, enteral nutrition, prescription, protein*. [Respir Care 2009;54(12):1688–1696.

Introduction

Critical illness, like any other form of stress, can affect all components of nutritional homeostasis, namely require-ment, intake, and losses. The importance of providing appropriately timed and quantified nutritional support during this period cannot, therefore, be overemphasized.[1,2] Nutritional support of critically ill patients is often suboptimal, due to problems with both nutrient prescription and delivery.[3,4] This scenario is more common in the developing countries, where health-care resources are constrained and the busy intensive care units (ICUs) are generally understaffed. Although critical care is fast evolving in India, there are limited data on nutritional support of critically ill patients, while several aspects of critical illness nutrition are apparently different from those practiced in the Western countries.

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The current study was carried out with the primary objectives of assessing the adequacy of nutritional support administered to patients admitted to the respiratory ICU at the Postgraduate Institute of Medical Education and Research, Chandigarh, India, and its correlation with outcomes.

Methods

All adult patients (age 15 years and above) who were admitted over a 15-month period (July 2004 to September 2005) to the respiratory ICU and required mechanical ventilation were included in this study. Informed consent was obtained for all subjects. The study was cleared by the institute's ethics committee. Patients with ≤ 24 hours duration of mechanical ventilation or respiratory ICU stay of ≤ 48 hours were excluded.

Assessment of nutritional support for each patient was done from the time of initiation of mechanical ventilation till he/she started unassisted oral feeding or was discharged from respiratory ICU, whichever happened earlier. Demographic particulars of all admitted patients were recorded, and serial assessments of severity of critical illness scores were done. History of recent weight loss prior to hospitalization was specifically asked for and recorded.

Severity of Critical Illness Scores

Calculation of the Acute Physiology and Chronic Health Evaluation Score (APACHE II) score and Sequential Organ-Failure Assessment (SOFA) score was done at the time of initiation of nutritional support.[5-7] The SOFA score was also calculated daily, and the maximum SOFA score was determined and used to calculate the difference between the maximum and the initial SOFA score.[8]

Anthropometry and Laboratory Measurements

At admission, height was measured with the patient in the supine position, and the ideal body weight was calculated from the height. Assessment of mid-upper-arm circumference and triceps-skin-fold thickness was done on day 1 of initiation of nutritional support, and subsequently on days 4, 7, 14, 21, and 28. The mid-arm-muscle circumference and mid-arm-muscle area were calculated as:

$$\text{Mid-arm-muscle circumference} = \text{mid-upper-arm circumference} - (\pi \times \text{triceps-skin-fold thickness})$$

$$\text{Mid-arm-muscle area} = \frac{[\text{mid-upper-arm circumference} - (\pi \times \text{triceps-skin-fold thickness})]^2}{4\pi}$$

All the measurements were done with the patient in the supine position, on the non-dominant arm, and in triplicate. The mean values of these measurements, expressed to the nearest 0.1 cm, were used in the analyses. Serial assays of serum albumin and absolute lymphocyte count were done along with the anthropometric measurements.

Dietetic Routine and Recording

All patients, in the absence of a contraindication, were initiated on enteral feeding, as early as possible after admission. Trained nursing staff of the respiratory ICU, under the supervision of pulmonary medicine and critical care fellows posted in the respiratory ICU, administered enteral nutrition feeds prepared by the department of dietetics, through a nasogastric tube (or nasojejunal tube, if in place). The composition (per 1,000 mL) of the different types of feeds was:

- Normal: 1,000 kcal, 36.0 g protein, 50.5 g fat, 93.0 g carbohydrate
- High Protein 1: 1,554 kcal, 80.3 g protein, 31.5 g fat, 186.0 g carbohydrate
- High Protein 2: 1,228 kcal, 46.6 g protein, 59.0 g fat, 128.2 g carbohydrate
- Jejunostomy: 1,115 kcal, 57.0 g protein, 20.1 g fat, 146.2 g carbohydrate
- Renal: 1,437 kcal, 30.7 g protein
- Hepatic: 1,350 kcal, 22.6 g protein

In accordance with the hospital policy, all feeds prepared by the department of dietetics were vegetarian in origin. The treating team took all the decisions regarding the feeding. The daily calorie and protein prescriptions were calculated from standard recommendations (calories 30 kcal/kg/d, proteins 1.2 g/kg/d) after making appropriate adjustments for the severity of critical illness and comorbid conditions.[9] A meticulous record of the prescription and delivery of the volume, calories, and protein content of enteral (and/or parenteral) nutritional supplements was maintained.

The enteral feeds were administered as boluses. A total of 8 aliquots were administered at 3-hourly intervals (30 min infusion period, followed by a 2-hour 30 min standby period) in a daily feeding period of 24 hours, with the patient positioned 30° head-up. Feeding was withheld in the presence of hypotension, abdominal distention, active gastrointestinal bleeding, or other contraindications to enteral feeding, as well as 3 hours prior to an elective procedure. In the event of a gastric residual volume greater than 150 mL immediately prior to administration of an enteral feed, the scheduled feed was withheld and a recheck of gastric residual volume was done after 90 min. If at the 90-min recheck, gastric residual volume was still greater than 150 mL, the scheduled feed was skipped and the volume of the subsequent feed was reduced by 50 mL. On the other hand, if gastric residual volume at the 90-min recheck was ≤ 150 mL, the scheduled feed was administered without any reduction in its volume, and the subsequent feed was given after 3 hours. Intravenous metoclopromide (10 mg every 8 hours) was also added as a prokinetic for patients with high gastric residual volume. Nasojejunal feeding was attempted in patients who could not tolerate nasogastric feeding despite the use of metoclopromide. A no-feed-day was defined as a 24-hour period in which the patient did not receive any kind of nutritional support, either enterally or parenterally.

The outcome variables that were assessed included status on discharge from the respiratory ICU and hospital, duration of mechanical ventilation, respiratory ICU stay, hospital stay, and occurrence of ventilator-associated pneumonia (VAP).[10]

Statistical Analysis

Statistical analyses were performed (SPSS version 10.0, SPSS, Chicago, Illinois). Descriptive frequencies were expressed using the mean ± standard deviation, and the median and interquartile range. Differences between the median values of continuous variables within a group and between 2 groups were compared using the Wilcoxon signed-rank test and the Mann-Whitney U test, respectively. For categorical variables, the chi-square test was used to compare differences. Risk factors for hospital mortality were evaluated using multivariable logistic regression analysis. Initially, the variables were analyzed using univariable analysis to derive crude odds ratios, and if found significant ($P < .10$), these variables were then entered in a multivariable model to derive adjusted odds ratio and confidence limits. Variables that were considered clinically relevant, even if they were not found to be significant on univariable analysis, were included in the multivariable model. No multiplicative interaction terms were included in the model. Level of significance was expressed as probability values (*P* value) and odds ratio (95% confidence intervals). Survival curves were constructed to study the effect of nutritional support on respiratory-ICU stay, using Kaplan-Meier analysis. Differences between the survival curves were analyzed using the log-rank test.

Table 1. Demographic Characteristics of Patients ($n = 93$)

Age (mean ± SD y)	38.8 ± 15.8
Male (*n*)	55
Female (*n*)	38
Height (mean ± SD cm)	164.7 ± 8.9
Ideal body weight (mean ± SD kg)	61.5 ± 10.8
Mid-upper-arm circumference (mean ± SD cm)	2.4 ± 0.3
Triceps-skin-fold thickness (mean ± SD cm)	1.1 ± 0.5
APACHE II score (mean ± SD)	14.3 ± 8.7
Admission SOFA score (mean ± SD)	6.1 ± 3.6
Maximum SOFA score (mean ± SD)	7.9 ± 3.9
Difference between admission and maximum SOFA score (mean ± SD)	1.8 ± 2.4
Hospital stay before respiratory ICU admission (mean ± SD d)	3.8 ± 7.4
Respiratory ICU stay (mean ± SD d)	9.6 ± 7.6
Hospital stay (mean ± SD d)	16.5 ± 12.9
Duration of mechanical ventilation (mean ± SD d)	7.7 ± 7.0
Time to initiation of mechanical ventilation after admission (mean ± SD h)	7.9 ± 45.2
Time to initiation of nutritional support after initiation of mechanical ventilation (mean ± SD h)	9.9 ± 13.7
Time of initiation of nutritional support after admission (mean ± SD h)	17.7 ± 46.4
Diagnostic categories mandating respiratory ICU admission (*n*, %)	
Acute respiratory failure related to neuroparalytic snake bite	27 (29.0)
Acute lung injury/acute respiratory distress syndrome	24 (25.8)
Severe community-acquired pneumonia	11 (11.8)
Exacerbation of COPD or bronchial asthma	09 (09.7)
Acute respiratory failure related to neuromuscular disease	07 (07.5)
Febrile encephalopathy	03 (03.2)
Fulminant hepatic failure	03 (03.2)
Miscellaneous	09 (09.8)

APACHE = Acute Physiology and Chronic Health Evaluation
SOFA = Sequential Organ Failure Assessment
ICU = intensive care unit
COPD = chronic obstructive pulmonary disease

Results

During the study period, 258 patients were admitted to the respiratory ICU, of whom 93, who fulfilled all the inclusion criteria, composed the study population. The demographic profile and baseline characteristics of the study population are depicted in Table 1.

Prescription and Delivery of Enteral Nutrition

Ninety-one (97.8%) patients received enteral nutrition, either alone ($n = 88$) or in combination with parenteral nutrition ($n = 3$). Fourteen patients required administration of metoclopromide. One patient continued to be intolerant of enteral nutrition feeds administered via nasogastric tube, despite use of metoclopromide. He subsequently underwent nasojejunal tube insertion, and enteral nutrition feeds were successfully administered thereafter. During the study period, 86 patients (92.5%) did not experience a no-feed day. Three patients had 3 no-feed days each, while 4 others experienced a single no-feed day.

Calorie prescription increased from a median (and interquartile range) of 88.9% (80.4–99.0%) of the recommended value on day 1 to 114.4% (99.9–122.5%) on day 21. Protein prescription improved from 80.1% (67.1–90.6%) of the recommended value on day 1 to 98.4% (76.1–120.8%) on day 28. Calorie delivery increased from 55.1% (35.4–81.3%) of the recommended value on day 1 to 92.0% (35.7–124.6%) on day 28. Protein delivery improved from 46.7% (31.6–72.1%) of the recommended value on day 1 to 75.3% (54.3–85.5%) on day 28. The number of patients for whom assessment of prescription-cum-delivery of calories and proteins was done at different time points of their respiratory ICU stay is as follows: day 1, $n = 93$; day 4, $n = 69$; day 7, $n = 41$; day 14, $n = 21$; day 21, $n = 10$, and day 28, $n = 3$. The trend of prescriptions-cum-delivery of both calories and protein in relation to the recommended values, as well as of anthropometric and laboratory measurements, varied with time (Figs. 1 and 2). The values of mid-upper-arm circumference on days 14 and 21, of mid-arm-muscle circumference on days 14 and 21, and of mid-arm-muscle area on day 14 differed significantly, in comparison to baseline values (day 1).

Clinical Outcomes and Relationship With Caloric Intake

Sixty (64.5%) of the patients were transferred out alive from the respiratory ICU. However, 3 patients who were shifted out to other wards subsequently died while in the hospital, the overall hospital mortality being 38.7%. VAP occurred in 32 patients (34.4% of the study population). A previous study conducted in our respiratory ICU had shown similar rates of respiratory ICU survival and VAP incidence.[10] The distribution of VAP among 4 groups stratified according to mean daily calorie delivery was as follows: 44.4% in the group ($n = 18$) with mean daily calorie delivery of > 90% of the recommended value, 39.3% in the group ($n = 28$) with mean daily calorie delivery of > 70–90% of the recommended value, 23.3% in the group ($n = 30$) with mean daily calorie delivery of > 50–70% of the recommended value, and 35.3% in the group ($n = 17$) with mean daily calorie delivery of ≤ 50% of the recommended value. The observed differences in the rate of VAP among the 4 groups were not statistically significant.

Analysis of nutrition assessment parameters and variables among survivors and non-survivors (Table 2) revealed that, at admission, survivors had higher serum protein and albumin and lower serum creatinine, in comparison to nonsurvivors. No significant differences were observed in the other baseline anthropometric or laboratory parameters (see Table 2).

Using logistic regression analysis of variables affecting hospital outcome (Table 3), the risk factors for hospital mortality identified in the multivariable model were admission SOFA score and mean daily calorie delivery of ≤ 50% of the recommended value.

Survival curves were plotted for patients according to the mean calorie delivery achieved (Fig. 3). Analysis using the log-rank test showed statistically significant differences between the curves for those with mean daily calorie delivery of ≤ 50% of the recommended value, in comparison to those with mean calorie delivery of > 70–90%, as well as for those with > 90% of the recommended value ($P < .001$).

Subgroup analysis of all patients who experienced early mortality was carried out. The time point for this analysis was taken as 3 days of admission, based on data published by the authors from a similar patient population in their respiratory ICU.[11] Early and delayed mortality were thus defined as that occurring in ≤ 3 days and > 3 days after admission, respectively. However, neither calorie delivery nor any of the other nutrition-related parameters were observed to have any association with early mortality.

Discussion

Benefits of early enteral nutrition in critically ill patients have been demonstrated previously, in the form of an association with a decreased risk of death in the ICU and the hospital.[2] Higher adequacy of enteral nutrition has been observed with the use of a feeding protocol as well as the initiation of enteral nutrition within the first 48 hours of admission.[12-14] In the current study, despite efforts to initiate all patients on enteral nutrition feeds as early as possible after admission, calorie and protein delivery both remained suboptimal. Although no a priori definition of adequacy of feeding was made in the current study, the results indicated that, as in other ICUs, patients in this respiratory ICU were also underfed.[4,15] However, the daily prescription and delivery of both calories and protein (as a percentage of the recommended values) increased with time—a trend that has been documented in previous studies also.[16] Daily prescription and delivery was lesser for protein, in comparison to that for calories. Other studies that have compared actual with recommended energy and protein intake have also revealed protein delivery to be the area of largest overall deficit.[16,17]

In the current study, enteral nutrition feeds were administered as boluses rather than as an infusion. The latter can be accomplished by the use of an infusion pump and remains the preferred modality, since it is associated with a

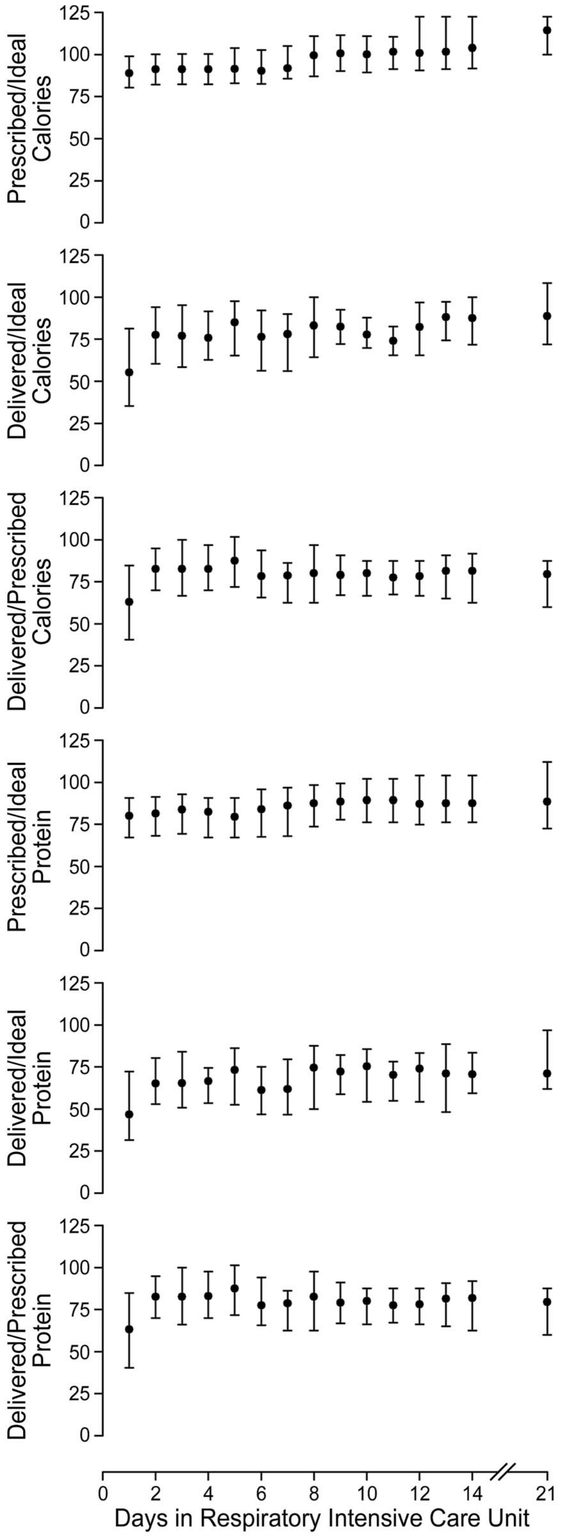

Fig. 1. Trend in prescription and delivery of calories and protein in relation to duration of stay in the respiratory intensive care unit. The circles represent the medians, and the error bars indicate the interquartile ranges. The ideal calories value is 30 kcal/kg/d. The ideal protein value is 1.2 g/kg/d. Ninety-three patients were assessed on day 1, 69 on day 4, 41 on day 7, 21 on day 14, 10 on day 21, and 3 on day 28.

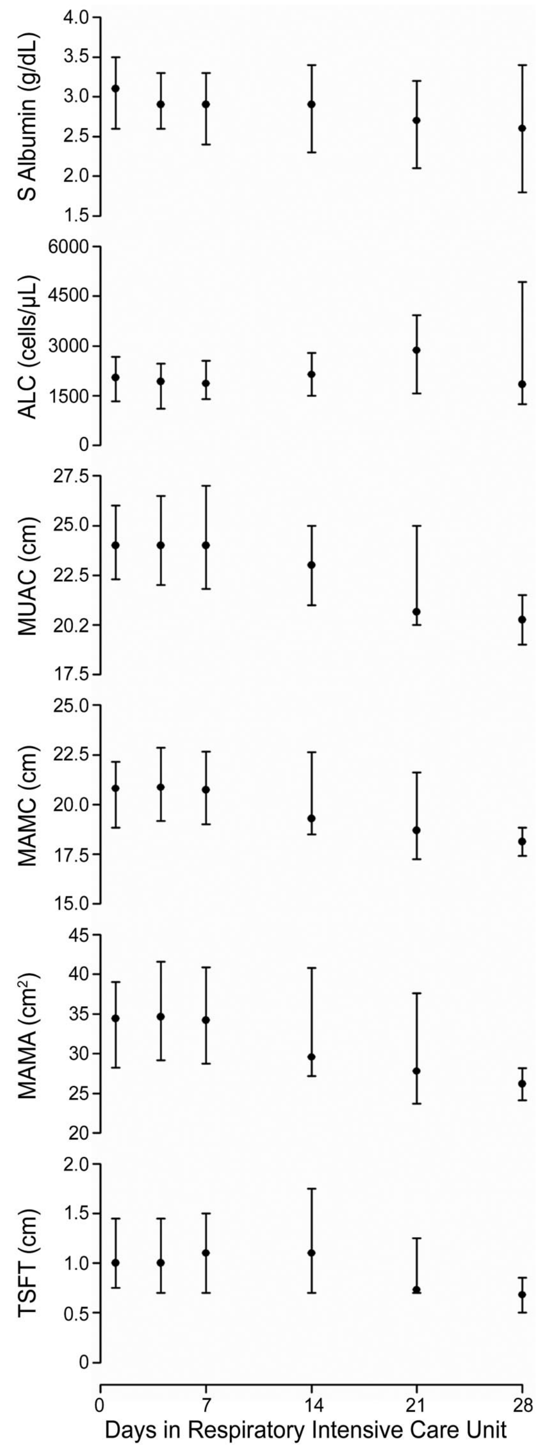

Fig. 2. Trend in anthropometric and laboratory measurements in relation to duration of stay in the respiratory intensive care unit. The circles represent the medians, and the error bars indicate the interquartile ranges. ALC = absolute lymphocyte count. MUAC = mid-upper-arm circumference. MAMC = mid-arm-muscle circumference. MAMA = mid-arm-muscle area. TSFT = triceps-skin-fold thickness. The values of MUAC on days 14 and 21, of MAMC on days 14 and 21, and of MAMA on day 14 differed significantly from the day-1 baseline values.

Table 2. Comparison of Anthropometric, Laboratory, and Other Variables Between Survivors and Non-survivors

	Survivors (n = 57)	Non-survivors (n = 36)	P
Age (median, IQR y)	34.0 (26.0–46.0)	44.0 (24.0–59.0)	.26
Male (n, %)	36 (63.2)	19 (52.8)	.39
Day-1 Measurements			
Mid-upper-arm circumference (median, IQR cm)	23.5 (22.5–26.0)	24.0 (22.0–26.0)	.96
Triceps-skin-fold thickness (median, IQR cm)	1.0 (0.7–1.4)	1.2 (0.8–1.6)	.20
Serum protein (median, IQR g/dL)	6.4 (5.8–7.0)	6.0 (4.8–6.5)	.02
Serum albumin (median, IQR g/dL)	3.2 (2.9–3.6)	2.8 (2.2–3.2)	.001
Absolute lymphocyte count (median, IQR cells/μL)	1,824 (1,232–2,660)	2,137 (1,659–2,844)	.25
Urea (median, IQR mg/dL)	44.0 (33.0–60.0)	54.0 (35.0–99.0)	.07
Creatinine (median, IQR mg/dL)	0.9 (0.7–1.1)	1.1 (0.9–2.5)	.02
Bilirubin (median, IQR mg/dL)	0.7 (0.7–1.0)	0.7 (0.7–0.7)	.24
Aspartate transaminase (median, IQR IU/L)	22.0 (14.0–27.0)	23.0 (13.0–41.0)	.41
Alanine transaminase (median, IQR IU/L)	16.0 (11.0–21.0)	15.0 (10.0–37.0)	.72
Alkaline phosphatase (median, IQR kAU/L)	8.0 (7.0–12.0)	9.0 (7.0–13.0)	.41
APACHE II score (median, IQR)	10.0 (6.0–17.0)	18.5 (12.0–24.0)	< .001
SOFA Score (median, IQR)			
Admission	4.0 (3.0–7.0)	9.0 (5.5–11.0)	< .001
Maximum	6.0 (4.0–8.0)	11.0 (8.0–13.5)	< .001
Difference between admission and maximum	0.0 (0.0–2.0)	2.0 (0.0–3.0)	.04
Hospital stay before respiratory ICU admission (median, IQR d)	0.0 (0.0–2.0)	2.0 (1.0–11.0)	< .001
Respiratory ICU stay (median, IQR d)	7.0 (4.0–12.0)	8.0 (4.0–17.0)	.89
Hospital stay (median, IQR d)	12.0 (5.0–21.0)	15.0 (8.0–27.0)	.34
Duration of mechanical ventilation (median, IQR d)	4.0 (3.0–8.0)	5.0 (3.0–17.0)	.13
Ventilator-associated pneumonia (n, %)	16 (28.1)	16 (44.4)	.08
Time to initiation of mechanical ventilation after respiratory ICU admission (median, IQR h)	0.3 (0.3–0.3)	0.3 (0.3–0.4)	.21
Time to initiation of nutritional support after initiation of mechanical ventilation (median, IQR h)	4.3 (2.5–9.3)	7.3 (3.1–18.9)	.04
Time to initiation of nutritional support after respiratory ICU admission (median, IQR h)	4.5 (2.8–9.8)	12.3 (3.8–25.6)	.005
Daily calories delivered (mean, IQR kcal/d)	1,378.6 (1,279.3–1,562.6)	1,109.2 (764.6–1,325.2)	< .001

IQR = interquartile range
APACHE = Acute Physiology and Chronic Health Evaluation
SOFA = Sequential Organ-Failure Assessment
ICU = intensive care unit

lower risk of gastroesophageal reflux and aspiration pneumonia. In countries where economic and health-care resources are constrained and the nurse/patient ratio is suboptimal, the nutritional protocol of administering enteral nutrition as intermittent boluses may be an acceptable alternative to continuous feeds.[18,19]

On analyzing the differences between patients who were discharged from the respiratory ICU alive with those who died, we found that survivors had higher baseline serum protein and albumin than nonsurvivors. A low serum albumin level has been proven to be an independent predictor of morbidity and mortality in previous studies.[20-23] Its serial assessment remains one of the most commonly used parameters for nutrition assessment, despite its limitations in critically ill patients. Nonsurvivors, as expected, had higher values of APACHE II, admission SOFA, maximum SOFA, and change in SOFA score. These scoring systems, which reflect the severity of critical illness, have previously been proven to be good predictors of outcome, and similar results in the current study only strengthen the validity of our data collection and interpretation.[6-8,24] In addition, we found that nonsurvivors had required longer time to initiation of nutritional support after respiratory ICU admission and after mechanical ventilation initiation. This was likely to be related to the greater severity of critical illness in this group, since none of these variables was associated with increased odds of hospital mortality on multivariable analysis. Although an attempt was made to administer parenteral nutrition in case of prolonged intolerance to enteral feeds, the significant cost differences between the two precluded the use of the former in patients with poor socioeconomic backgrounds who developed this problem. These, as well as the successful administration of

Table 3. Risk Factors for Hospital Mortality

	Logistic Regression Model			
	Univariable (odds ratio, 95% CI)	*P*	Multivariable (odds ratio, 95% CI)	*P*
Male	1.00 (NA)		NA	
Female	1.53 (0.66–3.58)	.33	NA	
Age	1.02 (0.99–1.05)	.16	1.01 (0.97–1.05)	.59
APACHE II score	1.14 (1.07–1.21)	< .001	NA	
Admission SOFA score	1.36 (1.17–1.57)	< .001	1.30 (1.03–1.63)	.03
Difference between admission and maximum SOFA score	1.17 (0.98–1.40)	.08	1.30 (0.96–1.78)	.09
Weight loss prior to respiratory ICU admission				
No	1.00 (NA)		NA	
Yes	6.80 (2.33–19.85)	< .001	2.51 (0.51–12.23)	.26
Diet				
Non-vegetarian	1.00 (NA)		NA	
Vegetarian	1.59 (0.68–3.75)	.29	NA	
Day-1 Measurements				
Triceps-skin-fold thickness	1.39 (0.61–3.13)	.43	NA	
Mid-arm-muscle circumference	0.97 (0.84–1.13)	.74	NA	
Serum albumin	0.26 (0.12–0.60)	.001	0.80 (0.27–2.40)	.69
Absolute lymphocyte count	1.00 (1.00–1.00)	.27	NA	
Hospital stay before respiratory ICU admission	1.12 (1.03–1.22)	.005	1.05 (0.95–1.16)	.33
Time to initiation of nutritional support after initiation of mechanical ventilation	1.06 (1.01–1.11)	.02	0.98 (0.91–1.06)	.67
Time to initiation of nutritional support after respiratory ICU admission	1.04 (1.01–1.07)	.01	1.03 (0.99–1.07)	.13
Occurrence of no-feed day	3.2×10^9 (< 0.0001–∞)	.99	NA	
Mean calorie delivery (percent of the recommended value)				
Overall	0.96 (0.94–0.99)	.001	NA	
> 90%	1.00 (NA)		NA	
> 70–90%	0.54 (0.14–2.07)	.37	0.60 (0.11–3.31)	.56
> 50–70%	0.86 (0.24–3.00)	.81	0.63 (0.12–3.25)	.58
≤ 50%	15.00 (2.55–88.17)	.003	12.08 (1.40–104.11)	.02

CI = confidence interval
NA = not applicable
APACHE = Acute Physiology and Chronic Health Evaluation
SOFA = Sequential Organ-Failure Assessment
ICU = intensive care unit

enteral feeds in the majority of patients, are responsible for the small number of patients who received parenteral nutrition. It is worthwhile to note that all the survivors received enteral nutrition alone.

Patients with mean daily calorie delivery of ≤ 50% of the recommended value had higher odds of death, both on univariable and multivariable analyses. There were no statistically significant differences among the patient groups with mean calorie delivery of > 50–70%, > 70–90%, and > 90% of the recommended value. These results were somewhat different from those of a prospective cohort study wherein the authors had assessed the relationship of caloric intake with clinical outcomes and had reported that patients who had received 33–65% (tertile II) of the recommended value had a significantly greater likelihood of achieving spontaneous ventilation prior to ICU discharge than those who had received ≤ 32% of the recommended value (tertile I).[25] Patients with caloric intake greater than 66% of the recommended value (tertile III) had a significantly lower likelihood of both hospital discharge alive and spontaneous ventilation prior to ICU discharge, in comparison to tertile I. The authors had suggested the presence of a "therapeutic window" of calorie intake, above which there exists no additional benefit and, in fact, could be potentially associated with worse outcomes.[25] In our study we could not demonstrate any such type of "therapeutic window" for calorie intake, although the current study was under-powered to pick up a similar level for optimal feeding, even if it existed.

In the current study, subgroup analysis failed to demonstrate an association between early mortality and calorie delivery. Concerns about the potential risks associated

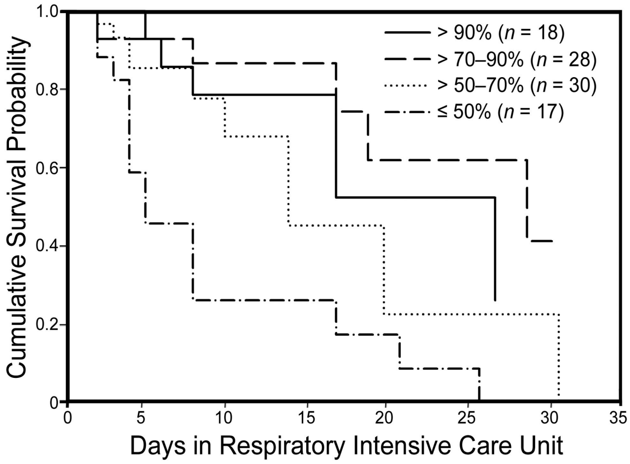

Fig. 3. Kaplan-Meier analysis of the probability of survival, stratified according to mean calorie delivery (as a percentage of the recommended value). Mean calorie delivery of 50% or less of recommended significantly reduced the probability of survival, via log-rank test.

with a higher calorie intake have been raised previously by the authors of a randomized trial that was specifically designed to assess the effect of timing of enteral feeding on outcomes in critically ill medical patients.[26] In this trial, the recommended level of calorie delivery was initiated on day 1 and day 5 of mechanical ventilation of patients in the early-feeding and late-feeding groups, respectively. The early-feeding group received higher total calories and protein in the first 5 days but also had statistically higher incidences of VAP and *Clostridium-difficile*-related diarrhea, as well as longer ICU and hospital stay. However, it is important to note that patients in both groups failed to reach their targeted nutritional goals and had similar rates of hospital mortality.[26] The concept of existence of a therapeutic window, as well as the optimal timing for initiation of nutritional support, need to be addressed in future randomized trials.

The major limitations of the current study include the relatively small number of patients, as well as the lack of availability of facilities for determining actual body weight, and, therefore body mass index. Moreover, no multi-parameter nutritional indices or biochemical tests other than serum albumin were used for assessment of nutritional status. The latter was carried out by supplementation of clinical features (relevant details of medical history and clinical examination) with serum albumin levels and anthropometric measurements. Anthropometry has limited value in critically ill patients, since it may be influenced by changes in water distribution related to critical illness. Serum albumin is also affected by changes in the hydration status and metabolic changes associated with critical illness that can modify its synthesis and degradation. However, all tools used in the process of nutritional assessment have their individual limitations and there is no accepted standard for accurately determining the nutritional status of such patients. There is no universally accepted clinical definition of malnutrition, and insufficient data are available to compare different commonly used nutritional assessment parameters.[27] Another limitation was that events that led to discrepancies between calorie prescription and delivery were not specifically recorded in the current study. The most common reasons were similar to those seen in other studies: namely, intolerance to enteral feeds, airway management, and diagnostic procedures.[3,28]

In addition to the presence of limitations in assessing nutritional status, there are no clearly defined measures of outcome in critically ill patients that can be correlated to nutrition directly, and this makes the process of conducting clinical trials in the field of nutrition difficult.[29] Association of low caloric intake with nosocomial bloodstream infections in medical ICU patients has been observed previously and may serve as another outcome measure, although in this case also it was unclear whether the relationship was causal or not.[30] In the current study, although patients with inadequate calorie delivery had higher odds of hospital mortality, we cannot say with certainty that the association was causal in nature. This is in part related to the observational nature and the small sample size of this study. Confounding by indication/severity, the instability in the regression coefficient for $\leq$ 50% of the recommended value in the multivariable logistic regression model (as illustrated by its wide confidence interval coefficient), as well as the potential for biased coefficients and biased confidence intervals resulting from a small number of outcomes relative to the number of variables in this model, also pose limitations to the validity of the observed association between calorie delivery and mortality.[31,32]

Conclusions

In summary, the current study reinforces the fact that calorie and protein delivery to critically ill patients remains less than the recommended values. Inadequate calorie delivery was associated with higher odds of mortality in the current study. The findings of the current study, despite its observational nature and presence of certain limitations, could be applicable to other ICUs, which have a similar patient profile and are located in health-care-resource-constrained regions of the world, especially India and neighboring countries in South Asia. Future studies involving a larger number of patients and those that are designed specifically to determine the optimal timing and level of nutritional support to critically ill patients could help answer some of the unanswered questions that exist today in relation to critical care nutrition.

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