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Nutritional practices and their relationship to clinical outcomes in critically ill children—An international multicenter cohort study*

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Abstract

Objectives—To examine factors influencing the adequacy of energy and protein intake in the pediatric intensive care unit and to describe their relationship to clinical outcomes in mechanically ventilated children.

Design, Setting, Patients—We conducted an international prospective cohort study of consecutive children (ages 1 month to 18 yrs) requiring mechanical ventilation longer than 48 hrs in the pediatric intensive care unit. Nutritional practices were recorded during the pediatric intensive care unit stay for a maximum of 10 days, and patients were followed up for 60 days or until hospital discharge. Multivariate analysis, accounting for pediatric intensive care unit clustering and important confounding variables, was used to examine the impact of nutritional variables and pediatric intensive care unit characteristics on 60-day mortality and the prevalence of acquired infections.

Main Results—31 pediatric intensive care units in academic hospitals in eight countries participated in this study. Five hundred patients with mean (*SD*) age 4.5 (5.1) yrs were enrolled and included in the analysis. Mortality at 60 days was 8.4%, and 107 of 500 (22%) patients acquired at least one infection during their pediatric intensive care unit stay. Over 30% of patients had severe malnutrition on admission, with body mass index z-score >2 (13.2%) or <−2 (17.1%) on admission. Mean prescribed goals for daily energy and protein intake were 64 kcal/kg and 1.7 g/kg respectively. Enteral nutrition was used in 67% of the patients and was initiated within 48 hrs of admission in the majority of patients. Enteral nutrition was subsequently interrupted on average for at least 2 days in 357 of 500 (71%) patients. Mean (*SD*) percentage daily nutritional intake (enteral nutrition) compared to prescribed goals was 38% (34) for energy and 43% (44) for protein. A higher percentage of goal energy intake via enteral nutrition route was significantly associated with lower 60-day mortality (Odds ratio for increasing energy intake from 33.3% to 66.6% is 0.27 [0.11, 0.67], *p* = .002). Mortality was higher in patients who received parenteral nutrition (odds ratio 2.61 [1.3, 5.3], *p* = .008). Patients admitted to units that utilized a feeding

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protocol had a lower prevalence of acquired infections (odds ratio 0.18 [0.05, 0.64], $p = .008$), and this association was independent of the amount of energy or protein intake.

Conclusions—Nutrition delivery is generally inadequate in mechanically ventilated children across the world. Intake of a higher percentage of prescribed dietary energy goal via enteral route was associated with improved 60-day survival; conversely, parenteral nutrition use was associated with higher mortality. Pediatric intensive care units that utilized protocols for the initiation and advancement of enteral nutrient intake had a lower prevalence of acquired infections. Optimizing nutrition therapy is a potential avenue for improving clinical outcomes in critically ill children.

Keywords

adequacy; critical care; enteral; infections; mortality; nutrition; parenteral; pediatric; pediatric intensive care unit

The provision of optimal nutrition therapy is a fundamental goal of critical care. Careful assessment of energy needs and provision of nutrients through the appropriate route are key steps toward achieving this goal. However, a significant proportion of eligible adult patients in the intensive care unit fail to achieve nutrition intake goals (1, 2). Suboptimal nutrient provision during critical illness results in deterioration of nutritional status, and has been associated with higher rates of multiple organ dysfunction, complications, length of stay, and mortality (2, 3).

Infants and children may also be at a risk of morbidity and mortality from cumulative nutritional deficiencies during their course in the pediatric intensive care unit (PICU). A variety of barriers impede the delivery of enteral nutrition (EN) in the PICU, resulting in failure or delay in reaching nutrition goals (4, 5). Suboptimal nutritional intake has been shown to result in cumulative deficits in energy and protein, with anthropometric deterioration in single center reports (6–8). We conducted the first multicenter collaborative prospective cohort study of nutritional practices for mechanically ventilated children in the PICU. We aimed to examine the variables associated with achieving optimal enteral nutrient intake, and explore the relationship between adequacy of energy intake (in relation to prescribed goal) and clinical outcomes in this cohort. We hypothesized that the successful delivery of a higher percentage of prescribed energy goal is associated with lower mortality and decreased number of infectious complications.

MATERIALS AND METHODS

Ethics approval for the study was obtained from the Institutional Review Board of Children's Hospital, Boston, and each participating site. Academic institutions were recruited through the Pediatric Acute Lung Injury and Sepsis Investigators research network and the World Federation of Pediatric Intensive and Critical Care Society, by e-mailing individual healthcare providers, and by disseminating study information through membership registries of national and international societies, including the American Society of Parenteral and Enteral Nutrition and the Society of Critical Care Medicine. To be eligible, sites were expected to have a PICU with eight or more beds, and identify a dietitian or an individual with knowledge of clinical nutrition to complete data collection.

All consecutive children (aged 1 month to 18 yrs) admitted to the PICU, who required mechanical ventilatory support longer than 48 hrs were eligible for enrollment. Patients who were not ventilated within the first 48 hrs of admission to PICU, on compassionate care toward end-of-life, those achieving full oral diet prior to 3 days in the PICU, and those enrolled in any other nutritional interventional trial were excluded. The participating sites simultaneously began screening for eligible patients, followed by enrollment and data

collection. Dietitians (or designated healthcare practitioners) at each site used a remote Web based data capture tool to record site characteristics, patient demographics, illness severity score, length of PICU stay, length of hospital stay, and duration of mechanical ventilation. Nutritional variables including macronutrient prescription, actual daily macronutrient delivery, route of delivery, frequency and duration of feeding interruptions, and use of adjunctive drugs, were recorded. The energy and protein intake adequacy was described as the percentage of the prescribed goal that was actually delivered. The primary outcome for this study was 60-day mortality. Acquired nosocomial infections, including ventilator acquired pneumonia, urinary tract infection, and blood stream infections, were secondary outcomes (9). The end point for nutritional data collection was 10 days or discharge from the PICU, whichever was sooner. Outcome data were collected until 60 days after PICU admission. Ranges for individual variables, data completeness, and logic checks were incorporated into the Web based data collection tool and database. The entered data were checked to identify errors, inconsistencies, and omissions.

Energy adequacy (actual energy intake described as a percentage of the calories prescribed at baseline assessment) was calculated using the average of daily amount of calories received by EN (or EN plus parenteral nutrition [PN]), over 10 days in the PICU. Evaluable nutrition days where no EN (or EN + PN) was received were counted as 0%. We did not include the days that followed permanent progression to exclusive oral intake. Since Pediatric Risk of Mortality II, Pediatric Risk of Mortality III, and Pediatric Index of Mortality scores were used at different sites to indicate severity of illness, we defined each severity of illness score where mild, moderate, and severe corresponded to tertiles of the given score. Thus, a patient was considered severe if their score was in the highest third tertile of the group of patients who used the same scoring system. In the rare case where more than one scoring system was recorded for a patient, we used the lowest score. Patients without a recorded severity of illness score were categorized as “unknown severity of illness”.

Descriptive statistics were used for sample distributions of the PICU and patient characteristics, as well as the nutrition and clinical outcomes. Categorical variables are reported as counts and percentages and continuous variables are summarized by their means and s_{ds} . Due to their positive skew, length-of-stay variables are described by their quartiles. Linear mixed effects regression models estimated by residual maximum likelihood were used to model the effect of PICU and patient characteristics on the percent of energy prescription received by the EN route. Logistic mixed effects models estimated by residual pseudo likelihood were then used to model the effects of PICU characteristics, patient characteristics, and energy adequacy on 60-day hospital mortality and acquired infections. Patients discharged from the hospital prior to 60 days were considered survivors. All models included the PICU site as a random effect to account for within PICU dependence. The number of evaluable nutrition days was controlled in all models involving the energy adequacy. A separate model was estimated for each predictor and then backward selection was used to select multivariable models, which included all predictors independently associated with outcome at $p < .15$ and certain key variables such as body mass index-Z (BMI-Z) scores and severity of illness scores that were selected *a priori*. All tests were two-sided without adjustment for multiplicity. The statistical analysis was conducted using SAS 9.2 (SAS, Cary, NC).

RESULTS

Site and Patient Characteristics

Thirty-one PICUs with mean 17 ± 8 beds from teaching (academic) institutions in eight countries participated in this study. Table 1 describes characteristics of the participating

sites. A majority (93%) of sites reported the presence of a dedicated intensive care unit dietitian (an average of 0.4 full-time equivalent position per ten beds), and ten (32%) units reported using specific guidelines or protocols for initiating and advancing EN intake. Of 524 patients that were enrolled, 24 were excluded as they achieved full oral diet prior to 3 days in the unit. Completed data from 500 patients with mean (*SD*) age 4.5 (5.1) yrs, 239 (48%) female, were analyzed. Patient characteristics, including nutritional status, clinical diagnosis, and severity score on admission are shown in Table 2. The cohort included a variety of medical, surgical elective, and surgical emergency patients.

Nutritional Variables

For the entire cohort, mean (*SD*) weight was 20.3 (21.7) kg and height was 93.9 (37.2) cm on admission. A large proportion of the patients had abnormal nutritional status at the time of admission, with BMI z-scores (BMI-Z) $> +2$ (13.2%) or < -2 (17.1%). More than 60% had BMI-Z < -1 or > 1 . Table 3 shows nutritional intake variables. Mean (*SD*) prescribed goals for daily energy and protein intake were 64 (29) kcals/kg and 1.7 (0.7) g/kg respectively. Actual mean daily intake was 28 kcals/kg and 0.8 g protein/kg. Nutrition was provided in the form of EN in 67%, PN in 8.8%, and mixed support (EN + PN) in 21% of patients. Overall, the actual macronutrient intake compared to prescribed goals was highly inadequate during the PICU course, with mean (*SD*) daily enteral adequacy of 38% (34) for energy and 43% (44) for protein (Table 3). EN was initiated within 48 hrs of admission in 60% of the patients. Figure 1 shows mean cumulative energy intake (as a percentage of prescribed goal) by PICU days. On average, cumulative enteral energy intake reached just over 50% of the prescribed goal by day 6 in the PICU.

Relationship between Clinical or Nutritional Variables and Energy Adequacy

Table 5 describes the results of univariate and multivariate analyses examining variables associated with percentage energy intake (in relation to prescribed goal) via EN. Using a multiple predictor model, and after accounting for nutrition days and random PICU effects, we observed that younger age, longer duration of PICU stay, shorter duration of mechanical ventilation, medical vs. surgical diagnosis, non use of PN, and shorter interruptions to EN were associated with higher percentage energy intake from EN.

Relationship between Energy Adequacy and Clinical Outcomes

Overall mortality at 60 days was 8.4%, and 107 of 500 (22%) patients acquired at least one infection during their PICU stay (Table 4). Infectious outcomes included, ventilator associated pneumonia in 12.6%, culture-proven blood stream infections in 9.1%, and urinary tract infection in 6.8% of the patients. Median (interquartile range) duration for mechanical ventilation was 7 (4, 13) days, median PICU length of stay was 10 (6, 20) days, and median hospital stay was 23 (12, 45) days. Table 6 describes the results of single and multivariable modeling for factors that influence the association between energy intake (from both EN alone and EN plus PN) and 60-day mortality. When compared with patients with energy intake from EN $< 33.3\%$ of prescribed, mortality was significantly lower in the group with energy intake 33.3%–66.6% prescribed (OR 0.27 [0.11, 0.67]) and in those with energy intake $> 66.7\%$ prescribed (OR 0.14 [0.03, 0.61]) ($p = .002$). Mortality was higher in patients who received PN (OR 2.6 [1.3, 5.3]), $p = .008$. Table 7 describes the results of single and multivariable modeling for factors that influence the association between energy intake (from both EN alone and EN plus PN) and the risk of acquiring at least one infection during the PICU course. Increased PICU length of stay was associated with increased risk of acquiring infections (OR 1.06 [1.04, 1.08], $p < .001$). Patients admitted to units that utilized a feeding protocol had a lower prevalence of acquired infections (OR 0.18 [0.05, 0.64]), $p = .008$, and this association was independent of the severity of illness and the amount of energy or protein intake.

DISCUSSION

We have reported the results of an international, multicenter effort to examine nutrition practices in mechanically ventilated children in the PICU. The findings of this study are notable for the high prevalence of malnutrition on admission, and a striking inability to deliver the prescribed energy and protein in critically ill children during their course in the PICU. Failure to deliver the prescribed energy goal was associated with higher likelihood of mortality in this vulnerable population. The use of a protocol for initiating and advancing nutrition delivery was associated with decreased infectious complications during the PICU course. To our knowledge, this is the first study describing the association of actual nutrition bedside practices over time in a wide distribution of PICUs, with relevant clinical outcomes such as mortality and nosocomial infections.

The prevalence of severe malnutrition on admission to the PICU was over 30%, and reflects similar numbers reported in critically ill children for the past 3 decades (10). We recorded a widespread inadequacy of both energy (34% prescribed) and protein (35% prescribed) delivered via enteral route over the course of this vulnerable population. Fluid restriction, feeding intolerance, and interruption of EN for procedures are some of the reasons responsible for energy and protein deprivation in the acute phase of pediatric critical illness previously reported in single centers (5, 11–13). On average, nearly half the patients in most reports fail to reach nutrition goals, with 37%–70% of prescribed energy delivered prior to discharge from the PICU (5, 13, 14). Patients with cardiac diagnoses and those on mechanical ventilator support have previously been identified as groups that are most at risk of suboptimal nutrition in the PICU (4, 5). Mechanically ventilated children with a surgical diagnosis were more likely to have suboptimal macronutrient intake in our current study. This relationship has been previously shown in adult critical care population, and is likely multifactorial (15). Future studies must explore challenges to optimal nutrient intake in this subpopulation. The failure of nutrient delivery may result in a significant decline in weight-for-age z-score at the time of discharge from the PICU (5). Our international cohort study confirms these findings and in addition, demonstrates an association between suboptimal macronutrient intake and outcomes such as mortality and acquired infections in the PICU population.

We divided patients into tertiles based on the percentage of energy intake (in relation to prescribed goal). Patients receiving less than a third of the prescribed energy on average during the first 10 days after admission to the PICU had significantly higher odds of mortality compared to the rest. An increase in the energy intake by one tertile (33%–66% prescribed goal) significantly decreased the odds of mortality. This relationship with survival was only observed for increased energy intake via the enteral route, and was significant even after adjusting for severity of illness scores, nutrition days, and PICU site. Energy deficit from suboptimal energy intake has been associated with poor outcomes in critically ill adults (16, 17). Negative energy balance is associated with complications such as adult respiratory distress syndrome, sepsis, renal failure, pressure sores, and need for surgical intervention (18). Increasing intakes of energy by 1000 kcal/day in critically ill adults is associated with significant reduction in the odds of mortality (OR 0.76; [0.61–0.95], $p = .014$), especially in those with preexisting malnutrition (19). Based on our results, increasing the energy adequacy from 33% to 66% could result in significant improvement in mortality.

The acute stress response to critical illness is characterized by extreme protein catabolism, which in the absence of adequate protein intake results in ongoing negative nitrogen balance and loss of lean body mass. Protein underfeeding during critical illness exaggerates the cumulative protein deficit, which is most notable in the preterm infants with low reserves of

lean body mass (7, 11). Significantly higher protein intake (up to 3g/kg/day) via an aggressive feeding strategy and protein supplements may be essential to offset the catabolic losses and achieve positive nitrogen balance in children with acute illness (20–23). Although, daily protein prescribed in our cohort was on average 1.7 g/kg, actual intake delivered was much lower. Optimizing protein intake to prevent lean body mass depletion is one of the most important goals of nutrition therapy in the PICU.

Healthcare associated infections significantly impact patient outcomes, including morbidity and mortality rates, length of hospital stay, and costs of intensive care unit care. Prevention of ventilator-associated pneumonia, blood stream infections, and urinary tract infections is a national patient safety goal and an area of intense research. Optimizing energy and protein delivery significantly reduces infections in critically ill adults (24, 25). The use of protocols for feeding was associated with reduced prevalence of acquired infections in our study, and this effect was independent of PICU site, severity of illness scores, energy intake, and nutrition days. The use of a protocolized or standardized approach allows early initiation of nutrition and achievement of energy goals in critically ill children and adults (26–29). However, existing PICU protocols are varied in their approach and include strategies that are based on insufficient evidence (30). The common features in all protocols adopted by sites in our study included, guidelines for nutrition assessment, early initiation of EN, explicit rates for advancement of feeds, and determination of energy delivery goal. Furthermore, a majority of these protocols outlined guidelines for monitoring and managing intolerance to enteral feeding such as high gastric residual volumes, had clear indications for the use of prokinetic drugs and recommended post-pyloric feeding in eligible patients, as adjuncts to nutrition support. Increased duration of interruptions to EN was associated with decreased energy adequacy achieved via EN route in our study. EN is preferred in the PICU due to decreased risk of infectious complications and lower costs compared to PN (4, 31, 32). Consequently, a variety of measures have been used to optimize EN, and PN use in the intensive care unit has been declining (13, 33). Less than 9% of patients received PN as the source of nutrition in our study, and a majority of the patients were fed exclusively via the enteral route. We observed a trend towards higher energy adequacy achieved via EN and the use of promotility agents. This effect was not statistically significant, especially in multiple predictor modelling. Although promotility agents have been increasingly applied in adult intensive care units, the evidence for their use in the pediatric population has been lacking (30, 34, 35). The use of post-pyloric (small bowel) feeding did not influence adequacy of energy intake in our study. Small bowel feeding has been associated with delivery of a higher proportion of daily energy goal compared to the gastric fed group in the PICU, but it did not impact the prevalence of micro-aspiration or feed intolerance (36). The benefits of post-pyloric enteral feeding in the PICU have not yet been demonstrated, although the use of post-pyloric enteral feeding may be prudent in patients who have failed gastric feeding or are at risk of aspiration.

We would like to acknowledge some of the weaknesses of our study. Due to inaccuracies associated with the use of equations to estimate energy expenditure, indirect calorimetry has been recommended as the gold standard method for assessing energy needs during critical illness (30, 37). However, similar to previous reports, indirect calorimetry was used in a minority of centers in our study (6, 38–40). The likelihood of both underestimation and overestimation of energy needs by standard equations cannot be ruled out (39–41). Severity of illness is an important confounder that might influence the ability to achieve adequate enteral nutrient intake and consequentially the reliance on PN. We adjusted for severity of illness using admission scores; however, data were missing for this variable in 31% of patients in our study. Hence despite accounting for this variable, the impact of severity on nutrient intake cannot be eliminated. We restricted the study to centers with eight or more PICU beds, in an effort to homogenize the group in terms of size, and available resources.

However, the variability in medical staff skills, availability and adherence to nutrition protocols, availability of resources, and the case mix in individual units might have influenced our results. Given the observational nature of this study, we cannot make definitive causal inferences from our findings.

CONCLUSIONS

Nutrition delivery is generally inadequate in mechanically ventilated children across the world. Improved adequacy of energy intake (to a minimum of 66.7% prescribed) is associated with significant decrease in 60-day mortality. Protocols that incorporate guidelines for nutrition assessment, early initiation of enteral feeds with protocolized regular advancement, monitoring for energy balance, defining intolerance, and minimizing interruptions to EN are desirable, and may decrease infectious complications. Improving nutrition therapy may impact important clinical outcomes in critically ill children and must be prioritized in the PICU.

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Figure 1.

Daily mean cumulative energy intake (as percentage of prescribed goal) for the cohort. *EN*, enteral nutrition; *PN*, parenteral nutrition; *PICU*, pediatric intensive care unit.

Table 1

Characteristics of participating pediatric intensive care units (n = 31)

Characteristics	Mean (sd) or N (%)
PICU size (beds)	17 (8.5)
11–20 beds	14 (45.2%)
20+ beds	8 (25.8%)
Hospital size (beds)	442.3 (418.3)
Multiple PICUs in hospital	9 (29%)
PICU type	Open unit
Closed unit	8 (25.8%)
PICU type (cases admitted)	23 (74.2%)
Medical	27 (87.1%)
Surgical	27 (87.1%)
Trauma	25 (80.6%)
Multidisciplinary	26 (83.9%)
Neurological	25 (80.6%)
Neurosurgical	25 (80.6%)
Cardiac Surgery	20 (64.5%)
Burns	15 (48.4%)
Feeding protocol used	10 (32.3%)
Presence of a dedicated dietician(s)	29 (93.5%)
Full time equivalent dietician (per 10 beds)	0.4 (0.2)

PICU, pediatric intensive care unit.

Table 2

Demographic, anthropometric, and clinical characteristics of subjects enrolled (n = 500, unless specified)

Variable	Mean (sd) or N (%)
Age (yrs)	4.5 (5.1)
Female (sex)	239 (47.8%)
Weight (kg)	20.3 (21.7)
Height (cm)	93.9 (37.2)
Z-score for body mass index (N = 483)	
<-2	83 (17.1%)
-2 to <-1	70 (14.4%)
-1 to <+1	189 (39.0%)
+1 to +2	79 (16.3%)
>+2	64 (13.2%)
Admission category	
Medical	321 (64.2%)
Surgical: elective	123 (24.6%)
Surgical: emergency	56 (11.2%)
Admission diagnosis	
Respiratory	218 (43.6%)
Cardiac	100 (20%)
Infectious disease	26 (5.2%)
Neurology	54 (10.8%)
Trauma/orthopedic	36 (7.2%)
Renal/endocrine	3 (0.6%)
Hematology/oncology	12 (2.4%)
Others	51 (10.2%)
Acute respiratory distress syndrome	72 (14.4%)
Pediatric risk of mortality II score (n = 43)	7.1 (8.9)
Pediatric risk of mortality III score (n = 185)	9.6 (8.0)
Pediatric index of mortality score (n = 197)	6.4 (14.5)
Severity of illness (grade)	
Mild	92 (18.4%)
Moderate	112 (22.4%)
Severe	141 (28.2%)
Unknown	155 (31.0%)

Table 3

Nutritional variables for the study cohort (n = 500)

Variable	Mean (SD) or N (%)
Prescribed energy intake (kcal)	916 (575.5)
Prescribed protein intake (g)	29.2 (26.7)
Prescribed energy intake by weight (kcal/kg)	64.2 (28.5)
Prescribed protein intake by weight (g/kg)	1.7 (0.7)
Actual energy intake (EN+parenteral nutrition) as % of prescribed	51.2 (33.3)
Actual protein intake (EN+parenteral nutrition) as % of prescribed	61.2 (93.6)
Actual energy intake (EN only ^a) as % of prescribed	37.7 (34.5)
Actual protein intake (EN only ^a) as % of prescribed	42.9 (44.3)
Motility agent used	84 (16.8%)
Initiation of EN ^a	
Prior to ICU admission	39 (8.8%)
On the first ICU day	83 (18.8%)
On the second ICU day	146 (33.1%)
On the third ICU day	86 (19.5%)
On the fourth ICU day or later	87 (19.7%)
Frequency of EN interruptions (days) ^a	1.9 (1.9)
Duration of EN interruptions (hrs/day) ^a	1.8 (2.1)

EN, enteral nutrition; ICU, intensive care unit.

^aData from patients receiving EN (N = 440)

Table 4

Clinical Outcomes (N = 500 unless specified)

Outcome	N (%) or Median (Q1, Q3)
60-day mortality	42 (8.4%)
Infectious outcomes (N = 484)	
At least one infection	107 (22%)
Ventilator associated pneumonia	61 (12.6%)
Blood stream infection	44 (9.1%)
Urinary tract infection	33 (6.8%)
Length on mechanical ventilation (days)	7(4, 13)
Length of stay in pediatric intensive care unit (days)	10(6, 20)
Length of stay in hospital (days)	23(12, 45)

Q1, first quarter; Q3, third quarter.

Table 5

Predictors of the percentage of energy prescription received by enteral nutrition

Effect	n/N ^a	Single Predictor Models ^b			Multivariable Model ^c		
	498	Estimate	Standard Error	p	Estimate	Standard Error	p
PICU Level							
PICU size (beds)	498	−0.65	0.31	.03			
Protocols present	215/498	4.07	5.83	.49			
Full time equivalent dietician (per 10 beds)	498	15.2	15.42	.32			
PICU type (close vs. open)	345/498	1.71	6.25	.78			
Patient Level							
Evaluable nutrition days	498	2.3	0.52	<.0001	2.65	0.62	<.0001
Age (yrs)	498	−1.16	0.29	<.0001	−0.78	0.26	.003
Gender (female vs. male)	238/498	−1.42	2.89	.62			
Z-score for body mass index	.87						
Z-score <−1	152/483	1.9	3.58				
Z-score (−1, 1)	188/483	Referent					
Z-score ≥ 1	143/483	0.74	3.61				
Admission diagnosis (surgical vs. medical)	177/498	−6.81	3.19	.03	−6.98	2.77	.01
Severity	.008						
Mild	92/498	Referent					
Moderate	112/498	−14.38	4.64				
Severe	140/498	−15.3	4.86				
Unknown	154/498	−10.76	5.1				
Initiation to EN (days)	400	−7.76	0.82	<.0001			
Frequency of EN interruptions (days)	498	3.14	0.88	.0004	3.07	1.11	.006
Duration of EN interruptions (hrs/day)	498	−0.41	0.73	.58	−3.60	0.91	<.0001
Route of EN (ever postpyloric vs. gastric only)	119/438	3.99	3.98	.32			
Motility agent	83/498	9.21	4.36	.04			
PN used	149/498	−37.49	2.94	<.0001	−36.82	3.48	<.0001
Length of PICU stay (days)	498	0.17	0.12	.14	0.55	0.15	.0003
Duration of ventilation (days)	478	−0.06	0.11	.58	−0.43	0.15	.004

EN, enteral nutrition; PICU, pediatric intensive care unit.

^aThe sample includes 500 patients who had at least 3 days of EN prior to permanent oral intake. Two patients are excluded due to no prescription of EN. Four hundred and ninety-eight patients remain in the analysis. For categorical variables, n is the number of patients in the given group and N is the total number of non-missing values. For binary variables n is the number in the non-referent group. For continuous variables, the total number of non-missing observations is provided. Denominators of some variables are slightly less than 498 due to sporadic missing values. The multivariable model is based on 478 patients due to 20 patients missing duration of ventilation;

^beach “single” predictor model actually includes PICU as a random effect and evaluable nutrition days as a continuous fixed effect;

^cthe multivariable model includes all predictors select by backwards selection with retention criteria of $p < .15$.

Table 6

Relationship between energy adequacy and 60-day hospital mortality

	N ^a	Unadjusted			<i>p</i> ^b	Adjusted			<i>p</i>
		Odds Ratio	95% Confidence Limits			Odds Ratio	95% Confidence Limits		
Energy delivered (as a percentage of energy prescribed) from enteral nutrition + parenteral nutrition	498				.84				.84 ^c
<33.3%	141	referent				referent			
33.3%–66.7%	220	0.79	0.35	1.75		0.79	0.34	1.83	
>66.7%	137	0.88	0.35	2.19		0.78	0.3	2.05	
Energy delivered (as a percentage of energy prescribed) from enteral nutrition only	498				.005				.002 ^d
<33.3%	247	referent				referent			
33.3%–66.7%	167	0.38	0.18	0.83		0.27	0.11	0.67	
>66.7%	84	0.16	0.04	0.67		0.14	0.03	0.61	

^aThe sample includes 500 patients who had at least 3 days prior to permanent oral intake. For energy intake as % of prescribed from enteral nutrition + parenteral nutrition, the adjusted odds ratios (95% confidence interval) and *p* values are based on 483 patients due to 15 patients with missing values in Z-scores and two patients with missing prescribed calories. For energy intake as percent of prescribed from enteral nutrition only, the adjusted odds ratios (95% confidence interval) and *p* values are based on 478 patients due to 20 patients with missing duration of ventilation and two patients with missing prescribed calories;

^b adjusting evaluable nutrition days;

^c adjusting evaluable nutrition days, Z-score for body mass index, and severity and use of parenteral nutrition by backward selection at *p* < .15;

^d adjusting evaluable nutrition days, age, severity, use of motility agent, and duration of ventilation by backward selection at *p* < .15.

Table 7

Relationship of energy adequacy (tertile) and infection (urinary track, ventilator associated, or blood)

Effect	n/N ^a	Single Predictor Model				Multiple Predictors Model ^c							
		OR	95% CI	p	OR	EN+PN			OR	EN only			p
						95%	CI	p		95%	CI	p	
Patient level													
Nutrition days	486				1.18	1.02	1.34	.03	1.18	1.03	1.34	.02	
Severity				.10				.26				.31	
Mild	92/486	Referent			Referent				referent				
Moderate	109/486	1.02	0.46	2.27	0.98	0.40	2.42			0.95	0.38	2.35	
Severe	133/486		2.03	0.90	2.10	0.84	5.25			1.99	0.79	5.02	
Unknown	152/486	2.25	0.94	5.37	1.62	0.61	4.35			1.56	0.58	4.18	
Length of PICU stay (days)	486	1.07	1.06	<.0001	1.06	1.04	1.08	<.0001	1.06	1.04	1.08	<.0001	
Duration of ventilation (days)	468	1.06	1.04	<.0001									
Severity				.10				.26	0.31				
Mild	92/486	Referent			Referent				Referent				
Moderate	109/486	1.02	0.46	2.27	0.98	0.40	2.42		0.95				
Severe	133/486	2.03	0.90	4.59	2.10	0.84	5.25		1.99				
Unknown	152/486	2.25	0.94	5.37	1.62	0.61	4.35		1.56				
Energy adequacy from EN+PN ^b				.61				.97	N/A				
<33.3%	139/484	Referent			Referent								
33.3%–66.7%	211/484	0.94	0.47	1.87	0.93	0.44	1.94						
>66.7%	134/484	1.27	0.58	2.77	0.90	0.38	2.13						
Energy adequacy from EN ^b				.44	N/A							.74	
<33.3%	243/484	Referent			Referent				Referent				
33.3%–66.7%	159/484	0.68	0.37	1.25					0.78	0.40	1.52		
>66.7%	82/484	0.93	0.45	1.93					0.81	0.36	1.83		
PICU level													
PICU size (beds)	486	0.98	0.92	1.04	0.95	0.88	1.02	.14	0.95	0.88	1.02	.14	
Protocols present	206/486	0.26	0.1	0.68	0.18	0.05	0.64	.008	0.18	0.05	0.64	.008	

OR, odds ratio; CI, confidence interval; EN, enteral nutrition; PN, parenteral nutrition; PICU, pediatric intensive care unit; N/A, not applicable.

^aThe sample includes 500 patients who had at least 3 days prior to permanent oral intake. Fourteen patients are excluded due to missing values on having an infection. 486 patients remain in the analysis. For categorical variables, *n* is the number of patients in the given group and *N* is the total number of non-missing values. For binary variables, *n* is the number in the non-referent group. For continuous variables, the total number of non-missing observations is provided. Denominators of some variables are slightly less than 486 due to sporadic missing values. The multivariable modeling (both EN+PN and EN only) are based on 484 patients due to two patients with missing prescribed calories;

^b adjusted for nutrition days;

^c backward selection with $p < .15$.