

Early enteral nutrition administration and time to achieve resting energy expenditure in critically ill children

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Abstract

Background Malnutrition in critically ill children remains a significant concern, as a standardized nutritional support protocol has yet to be developed. Resting energy expenditure (REE) is recommended as a parameter for determining the fulfillment of energy needs in critically ill children, which should ideally be achieved within 72 hours. To achieve these energy needs, enteral nutrition (EN) is believed to have a lower mortality rate and a shorter length of stay compared to parenteral nutrition (PN).

Objective To evaluate the factors associated with delayed EN initiation and late achievement of REE.

Methods Data consisting of age, sex, nutritional status, timing of EN initiation, time required to achieve REE targets, PELOD-2 score, use of ventilators, duration of ventilation, hemodynamic status, use of inotropes and inotropic score, use of sedation, gastrointestinal symptoms, procedures performed during treatment, and technical issues were collected retrospectively from medical records from 2017-2018 in the Pediatric Intensive Care Unit (PICU) at Dr. Cipto Mangunkusumo Hospital. The REE was calculated using Schofield formula based on age and sex. These data were used to compare the proportion of the subjects receiving early EN (<48 hours) and delayed EN (>48 hours) and those who achieved REE <72 hours and delayed REE (>72 hours). Multivariate analysis was performed to determine which factors affecting late EN initiation and delayed REE achievement using logistic regression analysis.

Results Of 203 subjects, 63.1% received early EN and 67.5% achieved REE at ≤72 hours. Delayed EN was associated with post-abdominal surgery (OR 10.89; 95%CI 4.31 to 27.50; P<0.001), ventilator use (OR 4.60; 95%CI 1.78 to 11.90; P=0.004), inotrope use (OR 4.18; 95%CI 1.56 to 11.17; P=0.002), gastrointestinal symptoms (OR 3.41; 95%CI 1.59 to 7.29; P=0.002), and abnormal nutritional status (OR 2.49; 95%CI 1.09 to 5.72; P=0.031). The REE >72 hours was associated with late EN (OR 20.62; 95%CI 6.48 to 65.65; P<0.001), enteral intolerance after receiving EN (OR 14.77; 95%CI 4.40 to 49.6; P<0.001), and PELOD-2 score ≥7 (OR 3.98; 95%CI 1.01 to 15.66; P=0.048).

Conclusion The prevalence of EN and REE within 72 hours in the PICU is quite encouraging. Factors contributing to delayed EN administration include post-abdominal surgery, ventilator use,

inotrope use, gastrointestinal symptoms, and abnormal nutritional status. Delayed EN >48 hours, enteral intolerance after receiving EN, and PELOD-2 score >7 were the factors contributing to delayed REE achievement. However, these delays can be reduced by developing a comprehensive enteral feeding protocol. The factors influencing delayed EN and late REE achievement are an important basis for designing enteral feeding protocols to improve the clinical outcomes of critically ill children in the PICU. [Paediatr Indones. 2025;65:390-8; DOI: <https://doi.org/10.14238/pi65.5.2025.390-8>].

Keywords: critically ill; children; enteral nutrition; resting energy expenditure

Malnutrition in critically ill children in intensive care units is closely associated with morbidity and mortality. The increased metabolic demands of critically ill children and the failure to provide optimal nutritional support during treatment are suspected factors contributing to the deterioration of nutritional status during care.^{1,2} Failure to meet nutritional needs

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during this phase due to sub-optimal calorie provision can exacerbate clinical outcomes, particularly in children with low energy reserves.^{1,3} The delivery route, timing of administration, and energy target goals in providing nutrition for critically ill children remain controversial. Early enteral nutrition (EN) is defined as the initiation of enteral feeding <48 hours of hospital admission.⁴ Several studies reported that EN is believed to have a lower mortality rate, a better fulfillment of energy and protein needs, and a shorter length of stay compared to parenteral nutrition (PN).^{2,5-7} Additionally, PN is closely associated with a relatively high incidence of infectious complications.⁸

The American Society for Parenteral and Enteral Nutrition (ASPEN) and the Society for Critical Care Medicine (SCCM) recommend using indirect calorimetry to determine energy needs for critically ill children and, if not available, estimating resting energy expenditure (REE) with Schofield formula.⁹ Achieving two-thirds of daily nutritional needs should ideally occur within the first week of PICU care. Wong et al. found that adequate calorie provision ($\geq 80\%$ of REE according to Schofield's formula by day 3) in patients with acute respiratory distress syndrome (ARDS) was associated with lower PICU mortality.¹⁰

Nutritional support for critically ill children in the PICU at Dr. Cipto Mangunkusumo Hospital, Jakarta, a national referral hospital currently lacks standardized guidelines. The optimal route, delivery method, and protocols for meeting energy requirements, as well as the impact of nutritional support, remain unclear. Previous studies have not assessed the proportion of patients receiving early EN, the time required to meet REE targets, and the factors hindering the achievement of these targets.

We aimed to examine the timing of EN initiation and the time required to achieve REE targets. We also retrospectively evaluate the factors influencing early EN provision and REE attainment in critically ill children in the PICU using medical record data. The findings are expected to provide valuable insights into optimizing nutritional support for critically ill children to prevent malnutrition and adverse outcomes in the PICU and provide a basis for developing new protocols for early EN administration for critically ill children.

Methods

This analytical cross-sectional study was done to evaluate the timing of EN initiation, the time required to achieve REE, and the factors influencing both in critically ill children in the PICU at Dr. Cipto Mangunkusumo Hospital (CMH). The research was conducted from April to July 2019 by reviewing medical records of critically ill children treated in the PICU in 2017 and 2018. The sample consisted of critically ill children in the PICU who met the inclusion criteria. Inclusion criteria were children aged 1 month to ≤ 18 years admitted to the PICU. Exclusion criteria were incomplete medical records, PICU patients who were not classified as critically ill, and those with a length of stay of less than one day.

The variables studied included age, sex, nutritional status, timing of EN initiation, the time required to achieve REE targets, PELOD-2 score for disease severity (PELOD-2 score >7 indicating multiorgan dysfunction syndrome), use of ventilators (both invasive and non-invasive), duration of ventilation, hemodynamic status, use of inotropes and inotropic score, use of sedation, gastrointestinal symptoms, procedures performed during treatment, and technical issues. Laboratory parameters which were not available to assess PELOD-2 score were assumed to be normal and assigned a score of zero. We determine abnormal nutritional status as overweight, obesity, wasted, and severely wasted. We classify EN into early EN if administered in less than 48 hours and late EN if administered >48 hours. As for time to REE achievement is classified into within 72 hours and >72 hours. Sample size was calculated using a formula for multivariate predictive categorical sampling with a single measurement, resulting in a minimum required sample size of 200, with a 10% dropout possibility.

Subjects were included based on their medical records. The PICU utilizes a specialized daily monitoring sheet that provides detailed and accurate information on enteral and parenteral nutrition, including the amount of calories administered, the type of nutrition supplied, issues encountered, and the patient's clinical condition every hour over 24 hours. These sheets can also identify factors affecting enteral nutrition and the accomplishment of REE.

Enteral nutrition in critically ill children in the PICU is administered gradually until the target

REE is reached. REE calories are calculated using the Schofield formula and typically represent approximately 50-70% of daily caloric needs.⁹ All data obtained were entered into a computer database and analyzed using Statistical Product and Service Solutions (SPSS) version 20 software. Bivariate analysis was conducted using Chi-square test. Factors with P values <0.25 were further analyzed using a logistic regression method. Factors were considered statistically significant if multivariate analysis using logistic regression results had P values <0.050. This study received ethical approval from the Faculty of Medicine Universitas Indonesia/Dr. Cipto Mangunkusumo Hospital Research Ethics Committee.

Results

A total of 457 patients were treated in the PICU during 2017 and 2018. Of these, 203 patients met the inclusion criteria (**Figure 1**). The study utilized retrospective data by reviewing existing medical records. The REE, degrees of gastrointestinal symptoms, and PELOD-2 scores were not explicitly stated in all available medical records, necessitating a re-evaluation of the existing data according to the operational definitions of the study.

Most PICU patients were male (120; 59.1%), and subjects' median age was 35 (range 1-209) months.

Post-surgical cases were more prevalent (125; 61.6%). Normal nutritional status at admission was found in 87 (42.9%) subjects. The clinical characteristics of subjects are detailed in **Table 1**. Early EN was administered in less than 48 hours to 128 (63.1%) subjects, 103 (80.5%) of these subjects received EN in less than 24 hours. Analysis of potential factors influencing delayed EN are shown in **Table 2**. In multivariate analysis, factors associated with delayed EN initiation included abdominal surgery, use of ventilators and inotropes, GI symptoms occurring before EN, and abnormal nutritional status (**Table 2**). A significant p-value was also found for technical issues arising during EN administration, although with an odds ratio (OR) <1, indicating that these technical issues reduced the risk of delayed EN.

Early EN was administered to 128 subjects (63.1%), while delayed EN was observed in 75 subjects (36.9%). Eighteen patients faced critical conditions, primarily sepsis, and unfortunately did not receive EN before passing away. Additionally, 14 post-abdominal surgery patients received delayed EN according to their feeding protocol, which the Surgery Department still managed. This resulted in fasting during the PICU stay, and EN was administered in the general ward. Early EN was still offered to other post-abdominal surgery patients, although only 19 (14.8%) subjects received it, including 5.6% post-intestinal anastomosis patients. In our study, of the 19 post-

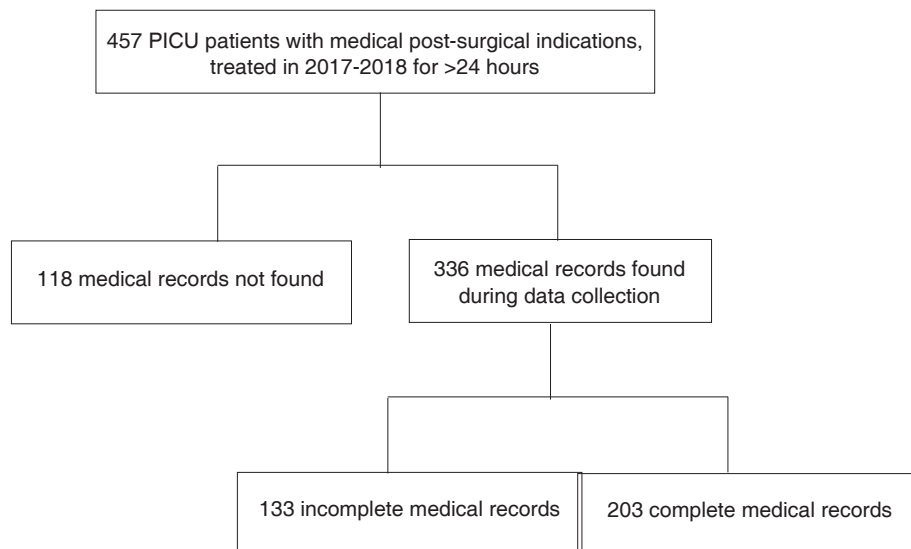


Figure 1. Subject selection process

Table 1. Clinical characteristics of subjects

Characteristics	(N=203)
Gender, n(%)	
Male	120 (59.1)
Female	83 (40.9)
Median age (IQR), months	35 (8-99)
Nutritional status, n(%)	
Obesity	9 (4.4)
Overweight	11 (5.4)
Normal	87 (42.9)
Wasted	48 (23.6)
Severely wasted	48 (23.6)
Use of invasive and non-invasive mechanical ventilation, n(%)	124 (61.1)
Median duration of ventilator use (IQR), hours	28 (8.75-93.50)
Administration of inotropic drugs, n(%)	46 (22.7)
Mean inotropic score (SD)	21.92 (15.4)
Median PELOD-2 score (IQR)	3 (0-4)
Administration of sedation, n(%)	111 (54.7)
Gastrointestinal (GI) symptoms before enteral initiation, n(%)	92 (45.3)
Degree of GI symptoms before enteral initiation (GI symptoms, n(%)	
1 st degree: risk of GI dysfunction	20 (9.8)
2 nd degree: GI dysfunction	17 (8.4)
3 rd degree: GI failure	13 (6.4)
4 th degree: GI failure with other severe organ dysfunction	42 (20.7)
Diagnosis in PICU, n(%)	
Post-surgical	125 (61.6)
Abdominal surgical	58 (28.6)
Non-surgical	78 (38.4)
Underwent procedures affecting EN administration, n(%)	114 (56.2)
Technical problems affecting enteral nutrition administration, n(%)	31 (15.3)
EN initiation, n(%)	
Early EN (<48 hours)	128 (63.1)
Delayed EN (≥ 48 hours)	75 (36.9)
Median time to achieve REE target through enteral nutrition (IQR), hours	48 (24-72)
REE achievement within ≤72 hours, n(%)	137 (67.5)
Median length of stay in PICU (IQR), days	3 (2-6)
Died during treatment, n(%)	31 (15.3)

abdominal surgery patients who received early EN, 15 (79%) achieved REE at ≤72 hours. In contrast, of the 39 post-abdominal surgery patients who experienced delayed EN, 20 (52%) achieved REE at >72 hours.

Following the initiation of enteral feeding, caloric intake through EN gradually increased to meet the REE target. **Table 3** details analysis of potential factors influencing the achievement of REE at >72 hours. Multivariate analysis showed that a PELOD-2 score ≥7, delayed EN, and EN intolerance manifested as varying degrees of GI symptoms were significant risk factors for achieving REE at >72 hours (**Table 3**).

Discussion

The prevalence of early EN in this study aligns with previous local findings.^{11,12} It was also comparable to international studies.^{13,14} Over the past 2-3 years, the approach to early enteral feeding has become more aggressive, targeting initiation within <24 hours. In our study, early EN was administered in less than 48 hours to 128 (63.1%) subjects, 103 (80.5%) of these subjects received EN in less than 24 hours. Other studies reporting early EN administration rates of 40-60%.^{11,13-15}

Table 2. Bivariate and multivariate analysis of factors influencing EN administration time in critically ill children in PICU

Variables	Bivariate analysis ^a		Multivariate analysis ^b	
	Early EN (<48 hours) (n=128)	Delayed EN (≥48 hours) (n=75)	OR (95%CI)	P value
Median age (range), months	41.5 (1–209)	27 (2–209)		0.811
Gender (male), n(%)	73 (57.0)	47 (62.7)		0.431
Abnormal nutritional status, n(%)	69 (53.9)	47 (62.7)	2.49 (1.09 to 5.72)	0.031*
Use of mechanical ventilation, n(%)	62 (48.4)	60 (80)	4.18 (1.56 to 11.17)	0.004*
Administration of inotropes, n(%)	16 (12.5)	30 (40)	4.60 (1.78 to 11.90)	0.002*
PELOD-2 score ≥ 7, n(%)	9 (7.0)	16 (21.3)	1.48 (0.47 to 4.66)	0.503
Administration of sedation, n(%)	60 (46.9)	51 (68)	1.28 (0.54 to 3.08)	0.676
GI symptoms before EN initiation, n(%)	40 (14.8)	52 (69.3)	3.41 (1.59 to 7.29)	0.002*
Post-abdominal surgery, n(%)	19 (14.8)	39 (52)	10.89 (4.31 to 27.50)	<0.001*
Undergoing procedures affecting EN administration, n(%)	69 (53.9)	45 (60)		0.398
Technical problems affecting EN administration, n(%)	27 (21.1)	4 (5.3)	0.18 (0.05 to 0.65)	0.009*

Table 3. Bivariate and multivariate analysis of factors influencing prolonged achievement of REE in critically ill children in PICU

Variables	Bivariate analysis ^a		Multivariate analysis ^b	
	REE achievement <72 hours (n=137)	REE achievement >72 hours (n=66)	OR (95%CI)	P value
Abnormal nutritional status, n(%)	76 (55.5)	40 (60.6)		0.489
Use of mechanical ventilation, n(%)	67 (48.9)	55 (83.3)	1.74 (0.55 to 5.47)	0.345
Administration of inotropes, n(%)	12 (8.8)	34 (51.5)	2.65 (0.93 to 7.57)	0.068
PELOD-2 score ≥ 7, n(%)	7 (5.1)	18 (27.3)	3.98 (1.01 to 15.66)	0.048*
Administration of sedation, n(%)	65 (47.4)	46 (69.7)	0.93 (0.33 to 2.64)	0.890
GI symptoms before EN, n(%)	55 (40.1)	37 (56.1)	0.53 (0.22 to 1.32)	0.173
GI symptoms after EN, n(%)	12 (8.8)	23 (34.8)	14.77 (4.40 to 49.60)	<0.001*
Post-abdominal surgery, n(%)	34 (24.8)	24 (36.4)	0.88 (0.33 to 2.32)	0.795
Undergoing procedures affecting EN administration, n(%)	76 (55.5)	38 (57.6)		0.777
Technical problems affecting EN administration, n(%)	27 (19.7)	4 (6.1)	0.28 (0.06 to 1.35)	0.112
Delayed EN, n(%)	27 (19.7)	48 (72.7)	20.62 (6.48 to 65.65)	<0.001*

Evaluating the achievement of caloric targets through EN in the PICU is crucial, as previous research has shown that reduced mortality rates are associated with critically ill children who reach their caloric target within less than three days of initiation.^{10,14} According to previous studies, most REE values reach only 50-70% by day 7.¹⁶⁻¹⁸ The median time to achieve REE in our study was 48 hours post-initiation. According to the 2017 ASPEN Guidelines, at least two-thirds of the REE should be achieved within the first week of treatment.² Two previous studies recommended achieving the caloric intake necessary within 3 to 4 days following the initiation of enteral feeding.^{19,20} In our study, the achievement of REE was reasonably good. A total of 137 subjects (67.5%) achieved REE within ≤ 72 hours of EN initiation.

The earlier the initiation of EN, the quicker the achievement of caloric targets and the prevention of undesirable outcomes. Delayed EN was a risk factor for slower REE achievement (OR 20.62; 95%CI 6.48 to 65.65; $P < 0.001$). Canarie et al. noted a lower finding than in our study (OR 4.09; 95%CI 1.97 to 8.53).²¹ Bagci et al. also found that patients who received early EN (< 24 hours) were significantly more likely to reach their caloric target ($> 25\%$ within 48 hours) ($P = 0.001$). The rapid achievement of caloric targets in their study was associated with lower mortality rates ($P < 0.001$).¹⁴

Early EN is particularly critical in post-abdominal surgery patients compared to other types of surgery, especially in patients following bowel anastomosis. Fasting is typically required for 2-5 days in patients undergoing bowel anastomosis. Post-abdominal surgery was the admission diagnosis in 58 subjects, with 39 (67.2%) subjects receiving delayed EN. In our study, post-abdominal surgery was the most significant risk factor for delayed EN (OR 10.89; 95%CI 4.31 to 27.50; $P < 0.001$). Patients who underwent stoma closure with bowel anastomosis had good gastrointestinal tolerance with faster recovery and fewer complications when EN was administered within 24 hours after the procedure, as demonstrated in previous studies.^{22,23} Both studies concluded that traditional methods of determining the timing of enteral feeding for postoperative bowel surgery patients, such as the presence of flatus and bowel movements, should no longer be used. Similar results

were found in a 2018 which showed that early EN (within 24 hours) in postoperative gastrointestinal anastomosis patients led to faster recovery of gastrointestinal function (3.1 vs. 3.8 days, respectively; $P = 0.042$), lower infection complications (117 vs. 137, respectively; $P = 0.046$), and shorter postoperative hospital stays (7.4 vs. 9.2 days, respectively; $P = 0.007$) compared to patients receiving late EN.²⁴ In our study, of the 19 post-abdominal surgery patients who received early EN, 15 (79%) achieved REE at ≤ 72 hours. In contrast, of the 39 post-abdominal surgery patients who experienced delayed EN, 20 (52%) achieved REE at > 72 hours. Therefore, early EN in post-abdominal surgery patients significantly increased the likelihood of achieving REE at ≤ 72 hours ($P = 0.028$).

Patients receiving high doses of inotropes or multiple inotropic agents, and those requiring prolonged administration (> 24 hours) have a relative contraindication for EN. In our study, 46 (22.6%) subjects received inotropes, with an average inotrope score of 21.92, and most received more than one inotropic agent, leading to a significantly increased risk of delayed EN (OR 4.60; 95%CI 1.78 to 11.90; $P = 0.002$). A study reported similar risks, indicating that the use of alpha-adrenergic vasoactive drugs (dopamine, norepinephrine, epinephrine) could result in suboptimal EN support (OR 4.27; $P = 0.043$).¹⁸ Inotropic use is generally maintained until hemodynamic parameters normalize and are then tapered within a short period (< 24 hours), so inotropic use does not significantly delay REE achievement (OR 2.66; 95%CI 0.93 to 7.56; $P = 0.068$).

Ventilation was used in 124 (61.1%) subjects. The median duration was 28 (IQR 8.75 to 93.5) hours, starting from PICU admission or during treatment. Ventilator use in this study significantly increased the risk of delayed EN (OR 4.18; 95%CI 1.56 to 11.17; $P = 0.004$). A study found that ARDS patients using a ventilator and receiving early EN (< 72 hours) had shorter PICU and hospital stays ($P < 0.05$) and better achievement of caloric and protein targets ($P < 0.002$).²⁵ Other studies have also shown that adequate calorie fulfillment (REE calories according to the Schofield formula $\geq 80\%$ by day 3) in ARDS patients was associated with lower PICU mortality ($P = 0.003$), and adequate protein intake (≥ 1.5 g/kg/day) was linked to lower mortality

rates ($P=0.002$) and longer ventilator-free days ($P=0.005$).¹⁰ Thus, early EN and adequate caloric intake are not contraindicated in critically ill children with respiratory distress and ventilator use.

The gastrointestinal symptom was classified based on adult subjects, while pediatric cases do not have a specific classification. We attempted to follow this classification to assess ongoing gastrointestinal symptoms.²⁴ A total of 92 (45.3%) children had mild or severe gastrointestinal symptoms, such as bowel ischemia, obstruction, or gastrointestinal bleeding before EN administration. Gastrointestinal symptoms occurring before initiation of EN was a significant risk for delayed EN (OR 3.41; 95%CI 1.60 to 7.29; $P=0.002$). Shock, the use of catecholamine drugs, sedation, and muscle relaxants are risk factors for the development of gastrointestinal symptoms in critically ill children, though these occurrences are less frequent (10-20%) compared to adults.²⁶ In our study, although gastrointestinal symptoms post-EN administration were a risk factor for delayed REE achievement, the use of catecholamine and inotrope medications did not have a significant effect on REE achievement.

Post-initiation of EN, gastrointestinal symptoms may occur as a form of intolerance. In our study, 35 children experienced EN intolerance manifesting as gastrointestinal symptoms, with the majority (57.1%) experiencing gastrointestinal dysfunction, including increased postprandial residuals, vomiting, and diarrhea. In multivariate analysis, gastrointestinal symptoms which occurred after EN administration was one of the risk factors of delayed REE achievement >72 hours (OR 14.77; 95%CI 4.40 to 49.60; $P<0.001$). A similar study by Oliveira et al. reported an OR of 2.85, but this finding was not statistically significant in multivariate analysis ($P=0.124$).¹⁸

Suboptimal nutritional support can also increase the incidence of malnutrition in critically ill children, which may hinder adequate nutritional delivery in the PICU.^{27,28} Multivariate analysis showed that abnormal nutrition status including overweight, obesity, wasted, and severely wasted increased the risk of delayed EN (OR 2.4; 95%CI 1.09 to 5.72; $P=0.031$). However, abnormal nutritional status was not a risk factor that hindered achieving REE caloric targets in this study. A multicenter study by Mehta et al. found that EN support in the PICU was very

low in caloric (38%) and protein (43%) achievement and was associated with longer hospital stays and higher mortality. However, nutritional status did not influence the risks of suboptimal enteral nutrition practices or not achieving prescribed caloric goals.²⁹

Use of PELOD-2 score has been conducted in the PICU in recent years to predict severe multiple organ dysfunction syndrome (MODS) in critically ill children. Patients with severe MODS generally experienced slower and more cautious decisions regarding EN administration, as many in this group used ventilators and required inotropes for more severe diagnoses. However, in our study, severe MODS (PELOD2 score >7) did not significantly increase the risk of delayed EN (OR 1.4; $P>0.050$), but it did increase the risk of achieving REE >72 hours (OR 3.98; 95%CI 1.01 to 15.66; $P=0.048$).

Technical issues in EN administration did not increase the risk of late EN initiation (OR 0.18; 95% CI 0.05 to 0.65) and delayed REE achievement (OR 0.28; 95% CI 0.06 to 1.35). The technical issues that occurred were immediately resolved in less than 24 hours. The common technical issues found in this study were patients being moved to different rooms during enteral feeding hours, and the specific specialized EN formula not being immediately available. One of the efforts to address these issues was to schedule attending physician rounds on weekends/holidays and to have dietitians on weekend/holiday standby, so that enteral instructions were not delayed and the desired EN formula could be provided promptly.

Our study results are expected to serve as a basis for considering early EN and positively impacting outcomes. These findings can also be used to develop guidelines for nutritional support in critically ill children. Consensus on assessing nutritional support for critically ill children in the PICU among pediatric intensivists, nutritionists, gastrohepatologists, and pediatric surgeons is necessary to avoid increases in morbidity, mortality, and length of stay. This has been done in various countries, such as the United States, the United Kingdom, Spain, and Canada, which have conducted post-implementation evaluations to achieve better outcomes.^{2,17,30,31}

Limitations of this study include its reliance on retrospective data based on medical records. Many patient records were missing during the data collection period, either due to unavailability or loss, resulting

in less than 50% of the total PICU patients in 2017 and 2018 meeting the inclusion criteria. Another limitation was the high number of subjects for whom laboratory parameters were not available to assess PELOD-2 score. These unexamined parameters were assumed to be normal and assigned a score of zero, thereby reducing the overall PELOD-2 score, so the bias in the PELOD-2 score should be considered.

In conclusion, risk factors that impede early EN administration include abdominal surgery, use of inotropes and ventilators, gastrointestinal symptoms before EN initiation, and abnormal nutritional status. Factors hindering REE at ≤ 72 hours include delayed EN initiation, enteral intolerance, and a PELOD-2 score ≥ 7 . These factors influencing delayed EN administration and the achievement of REE can be minimized by developing guidelines and protocols covering indications and contraindications for enteral feeding, timing of initiation, route of enteral administration, caloric needs, methods or targets for caloric achievement, and monitoring. Further prospective research applying these guidelines and monitoring obstacles are needed to evaluate effectiveness.

Conflict of interest

None declared.

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