

Enteral nutrition in intensive care unit patients: does initiating it within 24 hours improve clinical and nutritional outcomes?

Nutrição enteral em pacientes internados em unidade de terapia intensiva: iniciá-la antes de 24 horas melhora os desfechos clínicos e nutricionais?

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ABSTRACT

Introduction: Patients admitted to intensive care units are frequently at nutritional risk, requiring early interventions to prevent complications. Enteral nutrition initiated within 24 hours of ICU admission has been associated with better clinical and nutritional outcomes. Therefore, the objective of this article was to describe the clinical and nutritional outcomes of enteral nutritional therapy (ENT). **Methods:** The study was conducted as a prospective cohort, dividing patients into two groups based on the timing of ENT initiation: before (ENT<24) and after 24 hours (ENT>24) of ICU admission. Patients exclusively receiving enteral nutrition for at least 7 days were included. Data on admission and outcomes such as death, length of stay, need for hemodialysis, and duration of invasive mechanical ventilation were collected. Caloric and protein targets were recorded daily. **Results:** A total of 131 patients were studied, with a mean age of 59.5 years, and 60.3% were male. The mean body mass index was 26.74 kg/m². The ENT<24 group comprised 72 patients, while the ENT>24 group included 56. Death occurred in 61.8% of the patients; among these, 56.9% were from the ENT<24 group and 67.8% from the ENT>24 group. The length of stay was longer in the ENT>24 group. Only 47.3% of the patients met their caloric target after 7 days in the ICU, with 52.1% in the ENT<24 group and 42.4% in the ENT>24 group. Regarding protein intake, 42.6% of patients reached the target (42.9% ENT<24; 42.4% ENT>24). **Conclusion:** Both groups presented similar outcomes regarding mechanical ventilation time, hemodialysis, and mortality. Caloric and protein targets were achieved by a small portion of the sample in both groups, and the ENT<24 group appeared to have a shorter length of stay.

RESUMO

Introdução: Pacientes internados em unidades de terapia intensiva frequentemente apresentam risco nutricional, exigindo intervenções precoces para evitar complicações. A nutrição enteral iniciada em até 24 horas da admissão em UTI tem sido associada a melhores desfechos clínicos e nutricionais. Diante disto, o objetivo deste artigo foi descrever desfechos clínicos e nutricionais da terapia nutricional enteral (TNE). **Método:** O estudo foi realizado por coorte prospectiva, separado a TNE em dois grupos: iniciada antes (TNE<24) e após 24 h (TNE>24) da admissão em UTI. Foram incluídos pacientes sob nutrição enteral exclusiva por pelo menos 7 dias. Foram coletados dados de admissão e desfechos de óbito, tempo de internação, necessidade de hemodialis e tempo de ventilação mecânica invasiva. As metas calóricas e proteicas foram anotadas diariamente. **Resultados:** Foram estudados 131 pacientes com média de 59,5 anos, 60,3% do sexo masculino. O índice de massa corporal médio da amostra foi 26,74 kg/m². O grupo TNE<24 possuiu 72 pacientes, enquanto o grupo TNE>24, 59. O óbito ocorreu em 61,8% dos pacientes. Destes, 56,9% do grupo TNE<24 e 67,8% do grupo TNE>24. O tempo de internação foi mais prolongado no grupo TNE>24. Apenas 47,3% atingiram meta calórica após 7 dias de UTI, sendo 52,1% foram do grupo TNE<24 e 42,4% TNE>24. Em relação ao aporte proteico, 42,6% dos pacientes atingiram meta (42,9% TNE<24; 42,4% TNE>24). **Conclusão:** Ambos os grupos apresentaram desfechos semelhantes em relação ao tempo de ventilação mecânica, hemodialis e mortalidade. As metas calórica e proteica foram atingidas por uma pequena parcela da amostra de ambos os grupos e o grupo TNE<24 parece apresentar menor tempo de internação.

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INTRODUCTION

In intensive care unit (ICU) patients, increased catabolism, prolonged immobilization, and inadequate nutritional intake can lead to a negative energy balance, where energy expenditure exceeds intake^{1,2}. Providing adequate energy to critically ill patients present significant challenges, as enteral nutritional therapy (ENT), the first option when oral feeding is not possible or sufficient, often results in inadequate energy supply. Numerous factors can lead to interruption in the supply of enteral formula, such as gastrointestinal intolerance (abdominal distension, vomiting, diarrhea) and fasting for procedures, especially in critically ill patients.

Enteral nutrition (EN) maintains intestinal trophism, reduces the inflammatory response, modulates the metabolic response, and preserves immunity. It is indicated for patients with a functioning gastrointestinal tract but impaired oral intake^{1,2}. Several organizations, including the Brazilian Society of Parenteral and Enteral Nutrition (BRASPEN)², the European Society of Enteral and Parenteral Nutrition (ESPEN)³, and the American Society of Enteral and Parenteral Nutrition (ASPEN)⁴, have developed guidelines to standardize nutritional support for critically ill patients.

Early ENT is traditionally defined as initiation within 48 hours of ICU admission for hemodynamically stable patients^{5,6}. According to the literature, early initiation may bring benefits to patients, such as attenuation or prevention of body mass loss, reduction in mortality, and risk of infectious complications⁷⁻⁹. However, other studies have not found a significant association between the reduction in mortality associated with early ENT among patients with sepsis¹⁰ or critical patients in general¹¹. Controversies have also been found in the literature regarding the ability of early ENT to adequately provide protein and caloric intake^{5,12}.

In a hospital setting, it is recommended that the ENT be initiated as soon as the patient is clinically fit and has a preserved gastrointestinal tract. At our institution, most patients receive ENT before 48 hours, which creates a contradiction between the recommendations of the societies and clinical practice. In fact, some studies already address the ENT administration within the first 24 h, specially in acute pancreatitis^{13,14}.

In addition to the conflict between the guidelines and the quality of the available scientific information, there is a lack of prospective studies on the subject in Brazil. Therefore, the objective of the present study was to monitor patients admitted to the ICU and undergoing "ultra early" ENT (started before 24 hours of ICU admission) or early/late ENT (started after 24 hours of ICU admission) for 7 days and to compare the main clinical outcomes and caloric and protein adequacy.

METHODS

This exploratory prospective cohort, with parallel non-randomized groups, was conducted in the adult ICU of the Hospital de Clínicas de Itajubá, a level III unit that has 25 beds and is a reference in the Microregion of Alto Sapucaí, southern Minas Gerais, Brazil. Data were collected from January 2022 to November 2023.

The study was approved by the ethics committee of the Itajubá School of Medicine (CAAE 52522421.0.0000.5559) and was conducted in accordance with the CNS Resolution 466/2012. All measures to preserve the participants' data and confidentiality were taken. Patients were only included in the study if they signed an informed consent form by themselves or by their legal representatives.

Patient selection

All patients ≥ 18 years admitted to the ICU for at least seven days and receiving exclusive ENT via nasogastric or orogastric tubes were sequentially included. Exclusion criteria were palliative care, pregnancy, brain death protocols, mixed nutrition therapy (enteral plus oral or parenteral), and refusal to consent.

Study groups

Considering that most patients in the sample started ENT before 48 h of ICU admission, the present study aimed to verify whether the clinical outcomes of nutritional therapy administered "ultra early" (between 12 h and 24 h of ICU admission) and early/late (after 24 h of ICU admission) were different. Therefore, the cohort was divided into two groups:

- ENT < 24 (who received enteral nutritional support before the first 24 h of ICU admission) and;
- ENT > 24 (who received enteral nutritional support after the first 24 h of ICU admission).

Enteral nutrition was delivered intermittently via an infusion pump in a closed system. According to the institutional protocol, infusion occurs over 20 h, with a pause at 10 A.M. and restarted at 2 P.M. To start ENT, a normocaloric, normo-protein, and fiber-free formula was prescribed, and progression to a hypercaloric, hyperprotein formula could occur after the third day, depending on the patient's tolerance. The insertion of the nasoenteric or oroenteric tube was performed by an ICU nurse, confirmed radiographically.

Data collection

Demographic data, comorbidities, and anthropometric measurements were collected at ICU admission by the nutrition team, using an anthropometric tape, which measured arm circumference (AC), calf circumference (CC), and knee height (AH) so as to cause the least possible movement of the

patient. The weights and heights of the patients were estimated using the Chumlea formulas¹⁵.

The Body Mass Index (BMI) or Quételet Index, used to assess nutritional status, was obtained by dividing weight in kilograms by height in meters squared (kg/m²). The following BMI categories were considered for analysis purposes for adults and the elderly: <18.5 kg/m²: underweight; 18.5–24.99 kg/m²: eutrophic; 25 kg/m² to 29.99 kg/m²: overweight; and ≥30 kg/m²: obesity. For the elderly, the parameters proposed by Lipschitz (1994) were used, in which BMI between 22 kg/m² and 27 kg/m² are classified as eutrophic, BMI less than 22 kg/m² as thinness, and BMI above 27 kg/m² as overweight¹⁵.

Based on the ASPEN recommendations, the energy and protein goals were set at 25 kcal/kg/day and 1.2–2 g/kg/day, respectively⁴. Dietary prescriptions were calculated by nutritionists from the hospital’s Nutrition and Dietetics Department, according to the current institutional protocol. The progress of nutritional therapy was recorded daily by the researchers in electronic medical records.

The following clinical outcomes were recorded: death, length of hospital and ICU stay, progression to renal replacement therapy (RRT), and number of days of invasive mechanical ventilation (IMV). RRT was defined as the onset of the need for hemodialysis in the ICU in a patient previously not on dialysis, either due to decompensation of previous chronic kidney disease or acute kidney injury in a previously healthy patient. The need for IMV was referred to the installation of invasive ventilator support at any time after ICU admission.

Statistical analysis

The database was compiled in a spreadsheet shared among researchers via Google Sheets. Quantitative variables were reported as mean and standard deviation or median and interquartile ranges. Qualitative variables were described by absolute and relative frequencies. Normality was assessed using the histogram distribution of numerical variables and the Kolmogorov-Smirnov test. Group comparison was performed using Student’s t-test (parametric data) or Chi-square or Fisher’s exact test for (categorical variables). Survival analysis was performed using Kaplan–Meier distributions with log-rank tests. Data were analyzed using GraphPad Prism, version 8.0 (San Diego, CA, USA).

RESULTS

Of 185 eligible patients initially included in the study, 54 were excluded due to missing data or changes in diet or outcome before the initial 7 days, leaving 131 patients for analysis. The ENT<24 group included 72 patients (55%), while the ENT>24 group had 59 patients (45%). The median age was 59.5 years (range: 20-93). Malnutrition was present in 24 participants (19.8%) upon ICU admission. The main clinical characteristics, comorbidities, and associated diseases are presented in Table 1.

Table 2 presents the main clinical outcomes studied (length of hospital stay, hemodialysis, days of IMV and death).

Table 1 – Comorbidities or associated diseases in patients admitted to the ICU and subjected to exclusive enteral nutrition (ENT<24 and ENT>24).

Features	Totais	TNE<24	TNE>24	p-value
Age; mean (SD)	59.5 (17.1)	60.5 (18.0)	58.4 (16.1)	0.487
Sex; n (%)				
Masculine	79 (60.3)	43 (59.7)	36 (61.0)	0.880
Feminine	52 (39.7)	29 (40.3)	23 (39.0)	
BMI; mean (SD)	26.7 (4.7)	27.5 (5.1)	25.9 (4.1)	0.053
Comorbidities and associated diseases; n (%)				
Systemic arterial hypertension	68 (51.9)	39 (54.2)	29 (49.2)	0.567
Type 2 diabetes	46 (35.1)	30 (41.7)	16 (27.1)	0.082
Respiratory disease	61 (49.6)	33 (45.8)	32 (54.2)	0.338
Neoplasia	13 (9.9)	5 (6.9)	8 (13.6)	0.248
Neurological disease	71 (54.2)	40 (55.6)	31 (52.5)	0.270
Gastrointestinal symptoms	63 (48.1)	30 (41.7)	33 (55.9)	0.104
Sepsis	58 (44.3)	27 (37.5)	31 (52.5)	0.084
Surgery	74 (56.9)	36 (50.0)	38 (65.5)	0.075
Digestive system surgery	6 (4.6)	1 (1.4)	5 (8.5)	0.899

SD = standard deviation; BMI = body mass index; ENT = enteral nutritional therapy.

Table 2 – Clinical outcomes in patients undergoing exclusive enteral nutrition before and after 24 hours of ICU admission (ENT<24 and ENT>24).

Outcome	Total	ENT<24	ENT>24	p-value
Length of hospital stay (days)				
Mean (SD)	21.5 (12.2)	18.67 (10.58)	24.98 (13.19)	0.0034
Minimum-Maximum	3-69	3-59	8-69	
Hemodialysis; n (%)	58 (44.3)	33 (46)	25 (42)	0.691
IMV Days				
Mean (SD)	15.43 (11.39)	14.26 (9.84)	16.83 (12.94)	0.207
Minimum-Maximum	0-69	1-59	0-69	
Death; n (%)	81 (61.8)	41 (56.9)	40 (67.8)	0.203

SD = standard deviation; IMV = invasive mechanical ventilation; ENT = enteral nutritional therapy; n = sample size.

Only 47.3% (62/131) of the patients reached the caloric goals after 7 days. Of these, 52.1% (37/72) were in the ENT<24 group and 42.4% (25/59) in the ENT>24 group ($p=0.268$). Regarding protein intake, 42.6% (55/131) of patients reached the goal, of which 42.9% (30/72) were in the ENT<24 group and 42.4% (25/59) in the ENT>24 group ($p=0.99$). Among the reasons for discontinuing EN, the following stand out: fasting for the procedure, clinical instability, fasting for extubation, delay in connecting the diet, and vomiting, and consequently nasogastric tube in drainage. Figure 1 shows the relationship between calories and proteins prescribed and administered within the first 7

days of hospitalization. The results demonstrated that during the first 7 days, both caloric and protein intake were administered in amounts lower than those prescribed in both groups (ENT<24 and ENT>24), particularly during the first three days. Even the group that received nutrition within 24 hours showed discrepancies between the prescribed and administered amounts. The quantities of calories and proteins administered approached the prescribed targets from the 4th and 5th days onward, suggesting a progressive adaptation and/or clinical improvement of the patients, allowing for better nutritional delivery. The error bars indicate high variability within the sample.

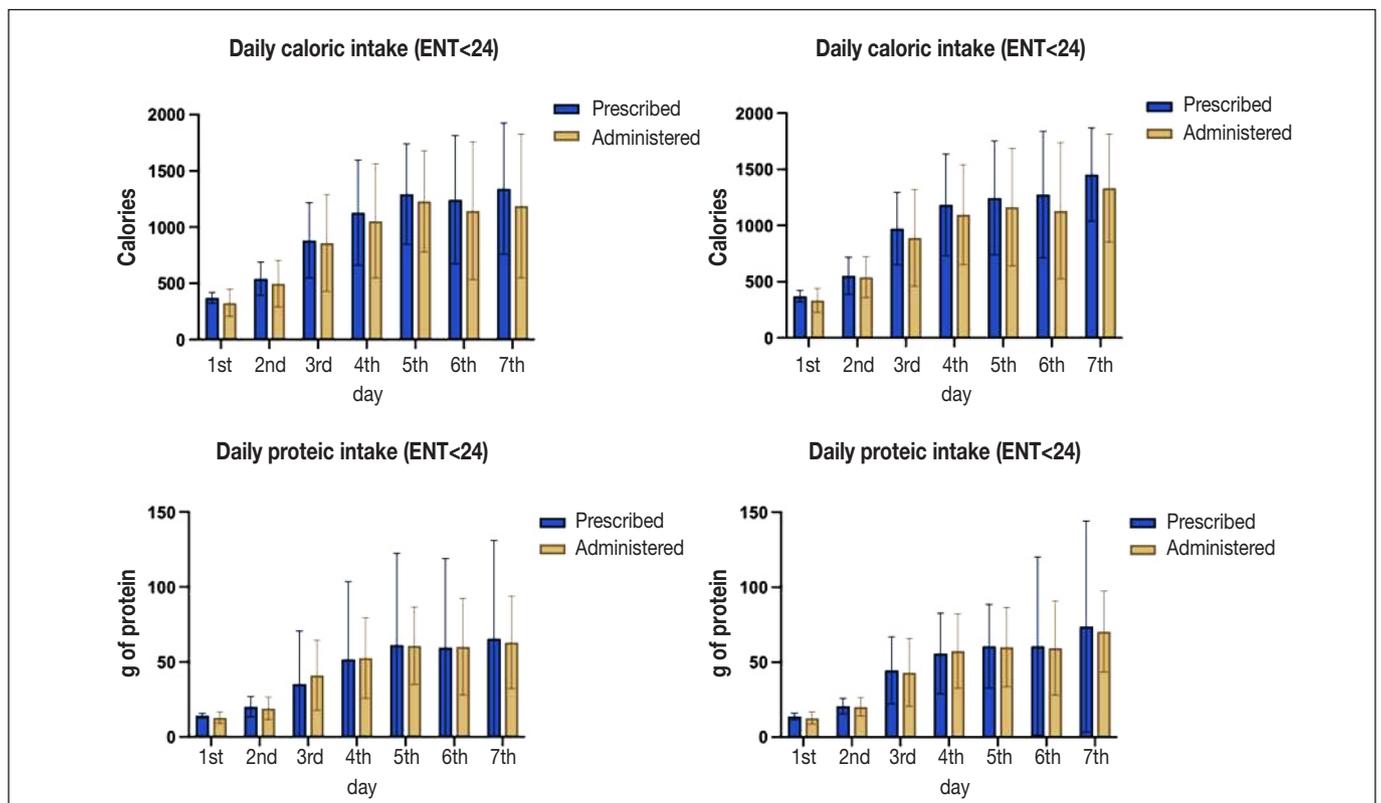


Figure 1 - Distribution of calories and proteins prescribed and administered within the first 7 days of intensive care unit admission according to the groups studied. The error bars represent the standard deviation.

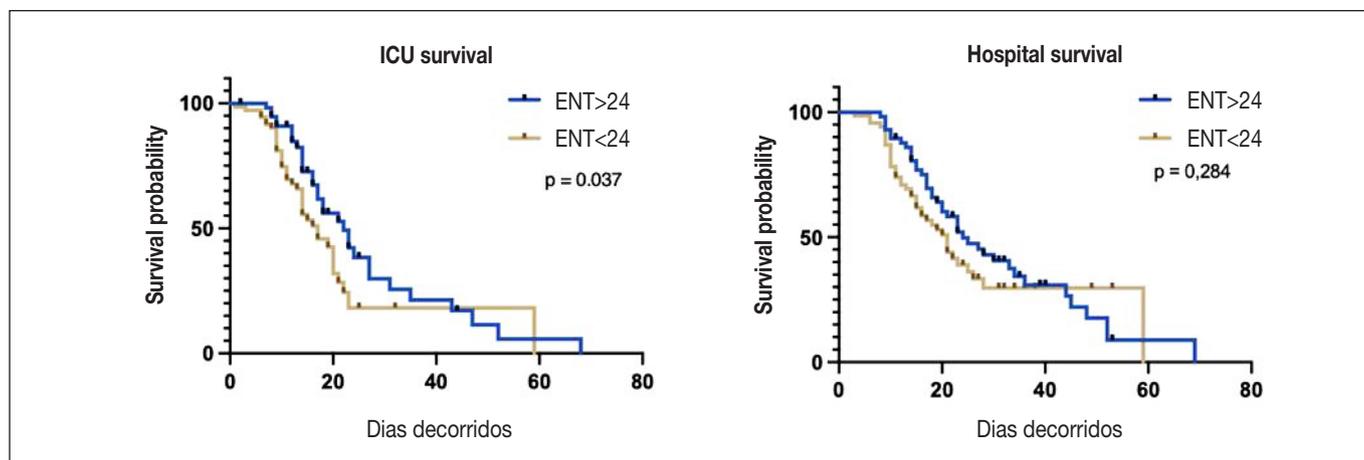


Figure 2 - Kaplan-Meier distributions demonstrating the probability of ICU survival and overall hospital survival of patients undergoing ENT starting before (ENT<24) and after (ENT>24) 24 h of ICU admission.

The ENT>24 group had a higher median number of days of survival in the ICU, with a statistically significant difference (ENT<24: 17 days vs. ENT>24: 22 days; $p=0.037$). The ENT>24 group had a higher median number of days of overall survival, but without a statistical difference (ENT<24: 21 days vs. ENT>24: 24 days; $p=0.284$).

DISCUSSION

This cohort compared the clinical outcomes of ICU patients undergoing ENT <24 h or >24 h after ICU admission. Patients in both groups presented with similar outcomes regarding the time of mechanical ventilation, need for hemodialysis, achievement of protein and energy goals, and mortality. However, the length of hospital stay for patients who received ENT <24 h of admission was shorter. The study by Maia et al.¹⁶, on the other hand, showed a lower proportion of hospital stay among patients undergoing “standard” early enteral nutrition (<48 h of admission) (67.2%), and of these, only 14.3% died.

The mean age was higher in the present study than in a similar retrospective study¹⁷ of ICU patients in João Pessoa, PB, Brazil, in which the median age was 46 years. In the same study, there was a predominance of females (53.4%), which is a discrepant result from this study. The estimated BMI in this study (26.74 kg/m²) was higher than that observed in other studies. In Jesus et al.¹², the BMI was not determined, but nutritional adequacy was determined using the index. In this case, 57.6% of the samples were within the appropriate weight range. In the cohort study by Cirilo et al.¹⁸, an average BMI of 23.6 kg/m² was observed in the sample, representing mostly eutrophic patients.

Regarding ICU stay, Jesus et al.¹² observed longer stays in patients who received EN after the first 48 h (median 13 vs. 21 days). This trend may reflect not the time of nutrition initiation but distinct clinical characteristics, given that the aforementioned study did not show clinical or demographic

differences between the groups. In retrospective studies without randomization, causality is impractical.

Regarding the achievement of the caloric and protein goals on the 7th day of ENT, only 47.3% of patients reached the caloric goal and 42.6% the protein goal. These data corroborate the need to implement institutional protocols to avoid long periods of fasting due to delays in prescriptions and installation of the feeding instrument (nasogastric/enteric tube). In the study by Jesus et al.¹², the majority (67.4%) of patients reached >80% of their caloric needs at the end of the first week. Of those who did not achieve the goal, complications were instability and/or intolerance to the diet. In terms of protein adequacy, 57.4% of the samples did not reach the target values. In a study conducted in an ICU in the state of Rio Grande do Sul, Brazil⁵, that aimed to evaluate the adequacy of ENT between what was prescribed and administered, 76% of patients obtained caloric adequacy greater than 80%, 12% between 60% and 80%, and 12% less than 60%. Regarding protein intake, 68% had adequacy above 80%, 16% between 60% and 80%, and 16% below 60%. The provision of calories and proteins in amounts lower than prescribed, both in the group that received ENT within 24 hours and in the group that received ENT after 24 hours, may compromise the prognosis of critically ill patients, considering the importance of early nutrition¹⁹. Delays in achieving nutritional targets may contribute to loss of lean body mass, immunosuppression, and increased risk of mortality²⁰.

Although not yet fully established in current clinical guidelines, the ultra early initiation of ENT appears to be driven by the imperative to provide caloric and protein support at the earliest possible stage in critically ill patients. This approach has been particularly highlighted in the literature concerning acute pancreatitis^{13,14,21}. Evidence suggests that enteral nutrition should ideally be initiated within the first 24 hours of admission to an ICU, provided the patient is hemodynamically stable and capable of tolerating enteral feeding.

Among the limitations of this study, there is its observational nature, which limits the conclusions of causality between the nutrition provided and the observed outcomes. The clinical and laboratory data provided in the protocol was also difficult to obtain because the medical records were not always complete. This resulted in the exclusion of many patients, which further limited the sample.

Although the outcomes analyzed are significant for clinical practice (length of hospital stay, IMV and death), it is still necessary to improve the data in medical records to obtain severity indexes, quality of the ventilatory pattern, and correlate them with the nutritional support offered.

We believe this study provides relevant information for the clinical practice of early implementation of ENT, which may reduce hospital length of stay and improve clinical outcomes, including the reduction of hospital costs. In addition to early intervention, a structured approach is necessary to ensure effective and safe caloric and protein delivery. However, the limited sample size may have hindered the detection of true differences between the groups. Pragmatic, multicenter studies with larger samples may be useful to better determine whether there is a clinically meaningful difference between patients receiving ENT initiated at different time points.

CONCLUSION

No significant differences were found regarding invasive mechanical ventilation duration, dialysis needs, achievement of nutritional goals and mortality between patients who received ENT before or after 24 h of ICU admission. Patients who received ENT within 24 hours of ICU admission had a shorter hospital stay.

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