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# Enteral nutritional therapy in septic patients in the intensive care unit: compliance with nutritional guidelines for critically ill patients

*Terapia nutricional enteral em pacientes sépticos na unidade de terapia intensiva: adequação às diretrizes nutricionais para pacientes críticos*

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## ABSTRACT

**Objective:** Evaluate the compliance of septic patients' nutritional management with enteral nutrition guidelines for critically ill patients.

**Methods:** Prospective cohort study with 92 septic patients, age  $\geq 18$  years, hospitalized in an intensive care unit, under enteral nutrition, evaluated according to enteral nutrition guidelines for critically ill patients, compliance with caloric and protein goals, and reasons for not starting enteral nutrition early or for discontinuing it. Prognostic scores, length of intensive care unit stay, clinical progression, and nutritional status were also analyzed.

**Results:** The patients had a mean age of  $63.4 \pm 15.1$  years, were predominantly male, were diagnosed predominantly with septic shock (56.5%), had a mean intensive care unit stay of 11 (7.2 to 18.0) days, had  $8.2 \pm 4.2$  SOFA and  $24.1 \pm 9.6$  APACHE II scores, and had 39.1% mortality. Enteral nutrition

was initiated early in 63% of patients. Approximately 50% met the caloric and protein goals on the third day of intensive care unit stay, a percentage that decreased to 30% at day 7. Reasons for the late start of enteral nutrition included gastrointestinal tract complications (35.3%) and hemodynamic instability (32.3%). Clinical procedures were the most frequent reason to discontinue enteral nutrition (44.1%). There was no association between compliance with the guidelines and nutritional status, length of intensive care unit stay, severity, or progression.

**Conclusion:** Although the number of septic patients under early enteral nutrition was significant, caloric and protein goals at day 3 of intensive care unit stay were met by only half of them, a percentage that decreased at day 7.

**Keywords:** Sepsis; Intensive care units; Intensive care; Nutrition therapy; Guidelines as topic; Enteral nutrition

This study was conducted at the Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul - UFRGS - Porto Alegre (RS), Brazil.

**Conflicts of interest:** None.

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## INTRODUCTION

Sepsis is defined as an infection associated with systemic inflammation.<sup>(1)</sup> Sepsis is the leading cause of in-hospital mortality in adult patients in the United States.<sup>(2)</sup> In Brazil, approximately 25% of patients admitted to intensive care units (ICUs) meet the diagnostic criteria for severe sepsis or septic shock, with mortality rates progressively increasing as the disease worsens: sepsis (34.7%), severe sepsis (47.3%), and septic shock (52.2%).<sup>(3)</sup>

The systemic inflammatory response is accompanied by metabolic changes that can lead to an accelerated loss of lean body mass, making the patient refractory to the anabolic effect of nutritional intake. Malnutrition contributes to reduced immunity, which increases the risk of infections,

hypoproteinemia, and edema, and to a reduction in wound healing, increased hospitalization time, and consequently increased expenditure.<sup>(4)</sup> Observational studies indicate the existence of an association between negative energy balance and the occurrence of a higher number of complications, especially of infectious origin, and increased length of ICU stay.<sup>(5)</sup>

In recent decades, professional organizations and societies have developed guidelines for the nutritional care of critically ill patients, including septic patients, with the goal of gathering evidence to support decisions on these patients' treatment.<sup>(6,7)</sup> These guidelines include the Brazilian Guidelines for Nutritional Therapy (Diretrizes Brasileiras em Terapia Nutricional - DITEN),<sup>(8)</sup> the European Society of Parenteral and Enteral Nutrition (ESPEN),<sup>(9)</sup> and the American Society for Parenteral and Enteral Nutrition (ASPEN).<sup>(10)</sup>

The recommendations of these guidelines regarding the early start of enteral nutrition (EN) recommend that EN be started within 24<sup>(9,10)</sup> to 48 hours<sup>(8,10)</sup> if the digestive tract is viable and the patient is hemodynamically stable. The recommendation is to avoid EN or parenteral nutrition until perfusion is restored in the case of hemodynamically unstable septic patients.<sup>(8-10)</sup> The guidelines stipulate that patients should receive approximately 25-27 kcal/kg body weight and 1.5 g protein/kg.<sup>(8)</sup> This recommendation changes to 20-25 kcal/kg and 1.5-2 g protein/kg for acute-phase patients<sup>(9)</sup> and increases to 25-30 kcal/kg and 1.5-2.5 g protein/kg in anabolic-phase or severely malnourished patients.<sup>(9)</sup> The recommendations are specific for critically ill obese patients: a calorie intake of 11-14 kcal actual weight or 22 to 25 kcal/kg ideal weight when body mass index (BMI) >30 kg/m<sup>2</sup>. Regarding the protein value, the recommendation is 1.2-2 g/kg actual weight when BMI <30 kg/m<sup>2</sup>, ≥2 g/kg ideal weight when BMI ranges from 30 to 40 kg/m<sup>2</sup>, and ≥2.5 g/kg ideal weight when BMI >40 kg/m<sup>2</sup>.<sup>(10)</sup>

ASPEN recommends continuing the nutrition until the patient meets 50 to 65% of their caloric needs within 48 to 72 hours of hospitalization.<sup>(10)</sup> Supplemental parenteral nutrition should be considered when the patient is unable to meet the calorie demands (100% kcal) after 7 to 10 days of EN only.<sup>(9,10)</sup>

Strategies currently available for managing patients with sepsis include early patient diagnosis and identification of the causative organisms, adequate and early antimicrobial therapy, early hemodynamic support, glycemic control, proper nutrition, effective supportive therapies, and patient management by

highly qualified staff.<sup>(11)</sup> This multifaceted approach, the use of evidence-based methods, and the adoption of strategies focused on clear clinical objectives are vital to combat this complex, aggressive, and increasingly prevalent syndrome.<sup>(11)</sup>

Supplying the patient with adequate nutrition is a proactive therapeutic strategy that can reduce disease severity, complications, and length of ICU stay; improve the patient's treatment outcome; and minimize costs.<sup>(10)</sup> The use of EN protocols increases the percentage of goals met regarding caloric quotas and should be implemented.<sup>(10)</sup>

Identifying gaps in patient care is being attentive in order to provide service improvements. In that context, assessing the compliance with evidence-based nutritional recommendations and identifying possible obstacles to the application of these guidelines may provide support for the creation and implementation of a clinical protocol based on the data analyzed, which, in turn, can generate improvements in service quality. Thus, this study aimed to assess the compliance of ICU-admitted septic patients' nutritional management with EN guidelines for critically ill patients.

## METHODS

A prospective cohort study was conducted with patients aged ≥18 years old who were admitted to the ICU of the Hospital de Clínicas de Porto Alegre (HCPA), a public, university, and tertiary hospital, between March and August 2012; who were diagnosed with sepsis upon admission to the ICU; who had an expected minimum length of hospital stay of 48 hours; and who were under EN or indicated for EN, excluding patients that were being fed orally or parenterally. The study included only patients whose Informed Consent Form was freely signed by their legal guardians. Furthermore, all researchers signed the Data-Use Agreement Form. The project was approved by the HCPA Research Ethics Committee under protocol 11-0664.

The patients' identification data (age and gender), Acute Physiology and Chronic Health Evaluation II (APACHE II)<sup>(12)</sup> and Sequential Organ Failure Assessment (SOFA)<sup>(13)</sup> scores, length of stay (LOS), and dependence on mechanical ventilation (MV) were collected from their medical records. Those patients' progress into severe sepsis, septic shock, and death was monitored.

The patients were considered septic when at least

two of the following criteria were met: (i) temperature  $>38^{\circ}\text{C}$  or  $<36^{\circ}\text{C}$ ; (ii) heart rate (HR)  $>90$  beats per minute (bpm); (iii) respiratory rate (RR)  $>24$  breaths per minute or  $\text{PCO}_2 <32$  mmHg or need for MV; (iv) leukocytes  $>12,000$  or  $<4,000$  or band neutrophils  $>10\%$ , in the presence of a documented or strongly suspected infectious focus. Patients with hypotension (systolic blood pressure (SBP)  $<90$  mmHg or mean arterial pressure (MAP)  $<60$  mmHg) or evidence of at least one organ dysfunction, namely, altered level of consciousness, lactate  $>2$  mmol/L, diuresis  $<0.5$  mL/kg in 6 hours,  $\text{PO}_2/\text{FiO}_2$  ratio  $<300$ , or thrombocytopenia, were diagnosed with severe sepsis. Patients requiring the use of vasopressors despite adequate fluid resuscitation, that is, at least 20 mL crystalloids per kg of weight,<sup>(1)</sup> were diagnosed with septic shock.

Weight and nutritional status classification according to BMI were assessed to estimate the calorie and protein requirements according to the ESPEN,<sup>(9)</sup> ASPEN,<sup>(10)</sup> and DITEN<sup>(8)</sup> guidelines. For this purpose, body weight was assessed using a bed scale (Hill Rom<sup>®</sup>) or also it was used an weighing equipment by lifting patients (Eleve Dymat E3- Phoenix Mecano Company<sup>®</sup>), and height was assessed using a Luft ruler.<sup>(14)</sup> BMI was calculated by dividing the weight (in kilograms) by the height (in meters) squared. BMI values were classified according to the World Health Organization.<sup>(15)</sup>

The start date of enteral feeding and the progress of calories and proteins were recorded and compared with the guidelines at day 3 (D3) of ICU stay, comprising 50% of the requirements, and D7, comprising 100% of the requirements.<sup>(8-10)</sup> The start of EN within 48 hours of ICU admission was considered an early start.

Factors affecting the nutritional therapy progress, including breaks for procedures, terminality, hemodynamic instability, and gastrointestinal tract (GT) complications, among other reasons, were also assessed and were collected from the diet start day and followed until EN therapy discontinuation.

The Statistical Package for the Social Sciences (SPSS) version 18.0 (SPSS Inc., Chicago, IL) was used to analyze the data. The Kolmogorov-Smirnov test was used to assess the normality of the distribution of variables. Categorical variables are expressed as frequencies and percentages and continuous variables as means  $\pm$  standard deviations or as medians with interquartile ranges. The chi-squared test was used to test the associations between categorical variables, and Student's *t*-test was used for comparisons between independent samples. For comparison between medians

the nonparametric Mann-Whitney and Kruskal-Wallis tests were used. Cox regression was performed to evaluate the effect of early EN on LOS and mortality, adjusting the MV, severity of sepsis, APACHE score, and SOFA score. Differences were considered statistically significant at  $p < 0.05$ .

A 4% margin of error, 95% confidence interval (CI), and 95% prevalence of compliance with the guidelines were considered to calculate the necessary sample size,<sup>(16)</sup> which was 115 patients.

## RESULTS

Seventeen of the 115 patients hospitalized in the HCPA ICU for sepsis during the study period refused to participate in the study, and 6 were excluded because they were being fed orally. Therefore, the present sample included 92 patients (80% of potential study subjects) and was predominantly composed of male subjects, in septic shock, with LOS of 8-14 days, and high prognostic scores (SOFA and APACHE II). These 92 patients had a mean age of  $63.4 \pm 15.1$  years. Approximately 20% of patients were malnourished upon admission, according to the BMI. The mortality rate was 39.1% (Table 1).

EN started early in 63% of patients, although only approximately 50% met the calorie and protein goals at D3 of ICU stay, while that percentage decreased at D7. The main reasons described in the medical records for starting EN after 48 hours were GT complications and hemodynamic instability. Conversely, procedures were the most frequent reason for discontinuing EN (Table 2).

The early start of EN was not associated with LOS, use of MV, mortality, severity, or nutritional status (Table 3). LOS and mortality were not associated with early EN, even when adjusted for the independent variables (MV, severity of sepsis, SOFA, and APACHE) (Cox regression,  $p=0.640$ ). Meeting the calorie and protein goals, both at D3 and D7 of ICU stay, was not associated with nutritional status, LOS, use of MV, severity, or mortality (Tables 4 and 5).

The mean prognostic APACHE II and SOFA scores were similar between patients who did and did not meet the calorie and protein goals at D3 and D7 (Tables 4 and 5).

The median compliance with kilocalorie goals of patients under EN at D3 ( $n=64$ ) and D7 ( $n=63$ ), excluding all patients who discontinued EN, was 130.75% (80.0 to 167.1) and 75.9% (48.2 to 107.4), respectively ( $p=0.20$ ). The compliance with protein goals was 121.05% (78.6 to 153.7) at D3 and was 76.0%

**Table 1** - Characterization of septic patients admitted to the intensive care unit

Characterization	Results N=92
Gender	
Male	54 (58.7)
Age (years)	63.4±15.1
Severity of sepsis	
Sepsis	23 (25.0)
Severe sepsis	17 (18.5)
Septic shock	52 (56.5)
Infectious focus	
Respiratory	37 (40.2)
Abdominal	18 (19.6)
Other	14 (15.2)
No defined focus	23 (25.0)
SOFA	8.2±4.2
APACHE II	24.1±9.6
Hemodialysis	49 (53.3)
Use of MV	88 (95.7)
Length of MV (days)	7.5 (4.0-12.7)
Length of ICU stay (days)	11 (7.2-18.0)
Length of ICU stay categorized in days	
≤7	13 (15.9)
8-14	35 (42.7)
15-21	16 (19.5)
22-28	13 (15.9)
>28	5 (6.1)
Mortality	36 (39.1)
Mean BMI (kg/m <sup>2</sup> )	24.3 (21.8-28.4)
Nutritional status classification*	
Malnutrition	18 (20.2)
Normal	35 (39.3)
Overweight	36 (40.4)

SOFA - Sequential Organ Failure Assessment; APACHE II - Acute Physiology and Chronic Health Evaluation II; MV - mechanical ventilation; ICU - intensive care unit; BMI - body mass index. n=89. Data are expressed as numbers (%), means±standard deviation, or medians and interquartile ranges (25th-75th percentile). \*Classification of nutritional status according to body mass index.<sup>(15)</sup>

(44.2 to 91.2) at D7 (p=0.75, Mann-Whitney test). When the same parameters were analyzed considering the patients' severity, both the protein and kilocalorie goals at both D3 and D7 were higher in septic patients (at D3, n=15; at D7, n=17) than in patients with severe sepsis (at D3, n=13; at D7, n=12) or septic shock (at D3, n=35; at D7, n=34), although with no significant difference between them. The median compliance with protein goals at D3 was 139% (82.5 to 166.4%), 122.8% (89.4 to 167.5%), and 112.1% (75.2 to 145.3%) in patients with sepsis, severe sepsis, and septic shock, respectively (p=0.43). At D7, compliance was 83.0% (46.3 to 102.0%); 69.9% (44.2 to 93.6%), and 74.5% (41.7 to 88.2%) for patients with sepsis, severe sepsis, and septic shock, respectively (p=0.62). In turn, the compliance with kilocalorie goals at D3

**Table 2** - Characteristics of supply of enteral nutrition to septic patients: early start, reasons for a late start and discontinuation, compliance with calorie and protein goals

Characteristics	N (%)
EN start within 48 hours	58 (63.0)
Reasons for not starting within 48 hours (N=34)	
Terminality	1 (2.9)
Hemodynamic instability	11 (32.3)
GT complications	12 (35.3)
Others	10 (29.4)
Reasons for discontinuation (N=34)	
Procedures	15 (44.1)
Terminality	2 (5.9)
Hemodynamic instability	3 (8.8)
GT complications	7 (20.6)
Others	7 (20.6)
EER compliance	
D3=50% of EER (N=85)	43 (50.5)
D7=100% of EER (N=72)	18 (33.3)
Protein compliance	
D3=50% of PTN (N=85)	40 (47.0)
D7=100% of PTN (N=72)	11 (15.2)

EN - enteral nutrition; GT - gastrointestinal tract; EER - estimated energy requirement; PTN - protein. D3 - day 3; D7 - day 7.

**Table 3** - Characteristics according to early or late start of enteral nutrition

Characteristics	Early enteral nutrition		p value
	Yes N (%)	No N (%)	
LOS (days)	(N=56)	(N=26)	
≤7	9 (16.1)	4 (15.4)	
8-14	25 (44.6)	10 (38.5)	0.72
15-21	12 (21.4)	4 (15.4)	
22-28	7 (12.5)	5 (19.2)	
>28	3 (5.4)	3 (11.5)	
MV	(N=58)	(N=34)	
Yes	54 (93.1)	34 (100)	0.29
No	4 (6.9)	0 (0)	
Mortality	(N=58)	(N=34)	
Yes	19 (32.8)	17 (50)	0.10
No	39(67.2)	17 (50)	
Severity	(N=58)	(N=34)	
Sepsis	11(19)	12 (35.3)	0.21
Severe sepsis	12 (20.7)	5(14.7)	
Septic shock	35 (60.3)	17 (50.0)	
Nutritional status (BMI)	(N=56)	(N=33)	
Malnutrition	13 (23.2)	5 (15.2)	0.63
Normal	22(39.3)	13 (39.4)	
Overweight	21 (37.5)	15 (45.5)	
APACHE II*	24.10±8.75	23.94±11.07	0.96
SOFA*	7.79±3.76	8.82±4.77	0.25

LOS - length of stay; MV - mechanical ventilation; BMI - body mass index; APACHE II - Acute Physiology and Chronic Health Evaluation II; SOFA - Sequential Organ Failure Assessment. \*Student's t-test for scores represented as means±standard deviation. Chi-squared test for the other variables represented as N (%).



**Table 4** - Characteristics according to compliance with calorie goals at Day 3 and Day 7

Characteristics	EER					
	D3			D7		
	Yes N (%)	No N (%)	p value	Yes N (%)	No N (%)	p value
LOS (days)	(N=42)	(N=40)		(N=18)	(N=54)	
≤7	7 (16.7)	6 (15.0)	0.82	1 (5.6)	6 (11.1)	0.65
8-14	19 (45.2)	16 (40)		10 (55.6)	22 (40.7)	
15-21	9 (21.4)	7 (17.5)		4 (22.2)	11 (20.4)	
22-28	5 (11.9)	7 (17.5)		3 (16.7)	9 (16.7)	
>28	2 (4.8)	4 (10)		0 (0.0)	6 (11.1)	
MV	(N=43)	(N=42)		(N=18)	(N=54)	
Yes	40 (93.0)	41 (97.6)	0.72	15 (83.3)	53 (98.1)	0.09
No	3 (7.0)	1 (2.4)		3 (16.7)	1 (1.9)	
Mortality	(N=43)	(N=42)		(N=18)	(N=54)	
Yes	16 (37.2)	13 (31.0)	0.54	7 (38.9)	19 (35.2)	0.77
No	27 (62.8)	29 (69.0)		11 (61.1)	35 (64.8)	
Severity	(N=43)	(N=42)		(N=18)	(N=54)	
Sepsis	10 (23.3)	12 (28.6)	0.81	6 (33.3)	14 (25.9)	0.82
Severe sepsis	9 (20.9)	7 (6.7)		3 (16.7)	11 (20.4)	
Septic shock	24 (55.8)	23 (54.8)		9 (50.0)	29 (53.1)	
Nutritional status (BMI)	(N= 42)	(N=40)		(N=17)	(N=53)	
Malnutrition	9 (50)	9 (50)	0.15	2 (11.1)	15 (83.3)	0.81
Normal	18 (51.4)	16 (45.7)		7 (20)	22 (62.9)	
Overweight	15 (41.7)	15 (41.7)		8 (22.2)	16 (44.4)	
APACHE II*	24.0±7.2	25.1±9.8	0.55	25.2±6.4	25.0±9.0	0.76
SOFA*	7.8±3.6	8.7±4.2	0.33	7.8±3.3	8.0±3.7	0.89

EER - estimated energy requirement; D3 - day 3 following admission to the intensive care unit; D7 - day 7 following admission to the intensive care unit; LOS - length of stay, MV - mechanical ventilation; BMI - body mass index; APACHE II - Acute Physiology and Chronic Health Evaluation II; SOFA - Sequential Organ Failure Assessment. \* Student's t-test for scores represented as means±standard deviation. Chi-squared test for the other variables represented as N (%).

was 143.5% (83.3 to 201.5%), 76% (59.4 to 109.2%), and 73.3% (45.2 to 102.3%) in patients with sepsis, severe sepsis, and septic shock, respectively ( $p=0.50$ ). At D7, the compliance was 81.3% (47.1 to 118.9%), 76% (59.4 to 109.2%), and 73.3% (45.2 to 102.3%) in patients with sepsis, severe sepsis, and septic shock, respectively ( $p=0.86$ , Kruskal-Wallis test).

## DISCUSSION

Patients who are hemodynamically stable and have a functioning GT should receive early enteral nutrition, within 24 to 48 hours of hospital admission, as recommended by the DITEN, ESPEN, and ASPEN guidelines.<sup>(8-10)</sup> The start of nutrition in that period decreases the LOS, incidence of infectious complications,<sup>(17)</sup> and patient mortality.<sup>(17,18)</sup>

As in the study by Khalid et al.,<sup>(18)</sup> wherein 60% of the critically ill patients studied received early EN, in the present study, most patients (63%) also started EN within 48 hours of hospital admission.

However, EN start time was not associated with the patients' nutritional status or outcomes, such as LOS or mortality, in contrast to the results of Khalid et al.,<sup>(18)</sup> who showed that early EN was positively associated with a lower risk of in-hospital mortality. However, it must be noted that theirs was an observational study. Two meta-analyses also showed no effect of EN start time on mortality.<sup>(17,19)</sup> Our sample's homogeneity, mainly regarding severity, presumably affected the lack of such associations. However, the number of ICU-discharged patients receiving early EN was significant.

The association of early EN with low mortality in the study by Kahlid et al.<sup>(18)</sup> was more evident in the more severe patients, that is, patients who depended on multiple vasopressors for more than 2 days. Although that variable was not evaluated in the present study, it is interesting to note that 60.3% of our patients with septic shock received early EN, although the prognostic scores did not differ between patients receiving and not receiving early EN, and no stratified severity association was found between patients with sepsis, severe sepsis, and septic shock ( $p=0.21$ ). Considering only this percentage, severity does not appear to have been instrumental in the decision to start or not start EN. As in a previous study,<sup>(16)</sup> gastrointestinal causes were the main reason for delaying the start of EN in our patients. These causes are also often responsible for recurrent interruptions in enteral nutrition in the ICU.<sup>(16)</sup> GT symptoms are common in the ICU, and up to 62% of patients show at least one GT symptom for at least 1 day. There is also increasing evidence that the development of GT problems is related to worse outcomes, including increased time under MV and higher mortality in critically ill patients.<sup>(20-22)</sup> As expected, because our patients were critically ill, hemodynamic instability was also a decisive reason for delaying the start of EN, as suggested by the guidelines.<sup>(8-10)</sup>

Guidelines recommend that EN be quantitatively adequate in terms of nutrients, in addition to starting early. Patients should receive 50-65% of the energy requirements in the first 3 days of hospitalization and must meet all of the outlined goals within the first 7 days.<sup>(10)</sup> In critically ill patients, low calorie intake during the first week in the ICU is associated with higher mortality risk,<sup>(23)</sup> while a negative energy balance is associated with increased infections,<sup>(24)</sup> increased time under MV, and LOS in the ICU.<sup>(5,25)</sup> In contrast, time under MV and ICU LOS are not identifiably associated with low calorie intake during the first week of ICU stay.<sup>(23)</sup>

**Table 5** - Characteristics according to compliance with protein goals at Day 3 and Day 7

Characteristics	PTN					
	D3		p value	D7		p value
	Yes N (%)	No N (%)		Yes N (%)	No N (%)	
LOS (days)	(N =39)	(N =43)		(N =11)	(N =61)	
≤7	7 (17.9)	6 (14.0)	0.17	1 (9.1)	6 (9.8)	0.93
8-14	19 (48.7)	16 (37.2)		6 (54.5)	26 (42.6)	
15-21	9 (23.1)	7 (16.3)		2 (18.2)	13 (21.3)	
22-28	2 (5.1)	10 (23.3)		2 (18.2)	10 (16.4)	
>28	2 (5.1)	4 (9.3)		0 (0.0)	6 (9.8)	
MV	(N =40)	(N =45)		(N =11)	(N =61)	
Yes	37 (92.5)	44 (97.8)	0.52	10 (90.9)	58 (95.1)	0.81
No	3 (7.5)	1 (2.2)		1 (9.1)	3 (4.9)	
Mortality	(N =40)	(N =45)		(N =11)	(N =61)	
Yes	16 (40.4)	13 (28.9)	0.28	5 (45.5)	21 (34.4)	0.51
No	24 (60.0)	32 (71.1)		6 (54.5)	40 (65.6)	
Severity	(N =40)	(N =45)		(N =11)	(N =61)	
Sepsis	9 (22.5)	13 (28.9)	0.64	5 (45.5)	15 (24.6)	0.37
Severe sepsis	9 (22.5)	7 (15.6)		2 (18.2)	12 (19.7)	
Septic shock	22 (55.0)	25 (55.6)		4 (36.4)	34 (55.7)	
Nutritional status*	(N = 39)	(N =43)		(N =10)	(N =60)	
Malnutrition	9 (50)	9 (50)	0.15	2 (11.1)	15 (83.3)	0.18
Normal	16 (45.7)	18 (51.4)		4 (11.4)	25 (71.4)	
Overweight	14 (38.9)	16 (44.4)		4 (11.1)	20 (55.6)	
APACHE II**	24.0±7.4	25.1±9.5	0.56	26.9±5.1	24.0 ±8.8	0.47
SOFA**,**	8.0±3.6	8.4±4.2	0.63	8.4±8.8	7.9±3.7	0.64

PTN - protein; D3 - day 3 following admission to the intensive care unit; D7 - day 7 following admission to the intensive care unit; LOS - length of stay, MV - mechanical ventilation; SOFA - Sequential Organ Failure Assessment; APACHE II - Acute Physiology and Chronic Health Evaluation II. \* Nutritional status according to body mass index.<sup>(15)</sup> \*\* Student's *t*-test for scores represented as means±standard deviation. \*\*\* Chi-squared test for the other variables represented as N (%).

However, negative energy balance is common during severe critical illness, despite the application of nutrition protocols.<sup>(24)</sup> The current study evaluated whether patients received up to 50% of energy and protein requirements at D3 of EN, and approximately 50% were able to meet those goals. The achievement of the recommended goals for the first week of EN were also evaluated, and the success rate decreased to approximately 30% regarding the calorie goals and was even lower regarding the protein goals (approximately 15% patients) at D7 of ICU stay. Over time, meeting the goals most likely becomes more complex because they are higher, that is, 100% of the planned nutrition. The protein requirements are even more difficult to meet because they depend on the kilocalories/gram of nitrogen ratio in routinely used enteral formulations, which protein modulation could counteract. The deficit condition at D7 extends to all classes of nutritional status, although overweight patients require a greater amount of protein.<sup>(10)</sup> The other reason for not meeting the goals at D7 could be the patients'

severity. Thirty-four of the 63 patients who received EN at D7 were in septic shock, with medians of compliance with calorie and protein goals below the other patients studied.

Based on prognostic scores, the sample consisted of patients whose severity most likely caused increased ICU LOS and, consequently, increased the number of procedures and EN nutrition interruptions. It was not possible, however, to show a statistically significant association between meeting the goals and the length of hospital stay, mortality, or use of MV. One of the study's limitations is that most patients were under MV, restricting our ability to interpret the data regarding the associations between compliance and the estimated calorie and protein requirements and the data regarding the early start of EN.

Factors contributing to a patient's energy deficit also include the lack of nutrition protocols and physical factors, such as deficient gastric motility, diarrhea, and the procedures performed, including surgery and radiological examinations.<sup>(26,27)</sup> In the present study, 44.1% of patients suffered discontinued administration of enteral nutrition to undergo procedures. A study conducted by Cartolano et al.<sup>(16)</sup> also found that external procedures were the most significant cause of discontinued EN. Given that the present study considered only patients who received EN at D3 and D7; who met, on average, the energy and protein goals at D3; and who had 75% compliance with the goals at D7, the impact of the several causes of EN discontinuation can be seen clearly, especially the impact of external procedures. That is, patients in whom it was possible to administer EN on the days evaluated came closer to achieving the predefined goals, as in the study of Franzosi et al.,<sup>(28)</sup> who treated critically ill patients in the same ICU and observed that the patients reached 84% and 75% compliance with the energy goals and protein goals at D7 of EN, respectively. However, analyzing only D7 in the present study, the results indicate the need to evaluate the patients' individual outlook regarding EN and the need for compliance with the guidelines, which recommend considering supplemental parenteral nutrition when unable to meet the requirements (100% of kcal) after 7 to 10 days of EN alone.<sup>(9,10)</sup> Despite the recommendations, studies have shown that permissive underfeeding, that is, meeting approximately 60 to 70% of the estimated requirements for basal energy expenditure, reduces ICU-admitted patients' time under MV<sup>(29)</sup> and mortality<sup>(30)</sup>, which also settles an unresolved controversy regarding

the minimum EN required to affect the outcome of critically ill patients.<sup>(28)</sup>

Another issue that must be addressed is that in the present study, 86.4% of patients who did not receive early EN did not meet both calorie and protein goals at D7, corroborating the previous finding that delaying the start of nutritional support exposes patients to energy deficits that cannot be offset during the remaining ICU stay.<sup>(5)</sup>

The patients' sporadic monitoring at preset days, minimizing any variations in the administration of EN between these preset days and after 7 days, is a limitation of the present study.

## CONCLUSION

Although most ICU-admitted septic patients started EN early, calorie and protein goals at D3 of the ICU stay were only met by half the patients, and this percentage was even lower at D7. The main reasons for starting EN after 48 hours were GT complications and hemodynamic instability. Procedures were the most common reason for EN discontinuation. There was no association between early EN or compliance with calorie and protein goals and the patients' nutritional status, LOS, progress, or severity.

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## RESUMO

**Objetivo:** Avaliar a adequação do manejo nutricional do paciente séptico a diretrizes de nutrição enteral para pacientes críticos.

**Métodos:** Estudo de coorte prospectivo com 92 pacientes sépticos, idade  $\geq 18$  anos, internados em unidade de terapia intensiva, em uso de nutrição enteral, avaliados segundo diretrizes para pacientes críticos quanto à nutrição enteral precoce, adequação calórica e proteica, e motivos para não início da nutrição enteral precoce bem como de interrupção da mesma. Escores prognósticos, tempo de internação, evolução clínica e estado nutricional também foram analisados.

**Resultados:** Pacientes com idade média de  $63,4 \pm 15,1$  anos, predominantemente masculinos, diagnóstico de choque séptico (56,5%), tempo de internação na unidade de terapia intensiva de 11 (7,2 a 18,0) dias, escores SOFA de  $8,2 \pm 4,2$  e APACHE II de  $24,1 \pm 9,6$  e mortalidade de 39,1%. Em 63% dos pacientes, a nutrição enteral foi iniciada precocemente. Cerca de 50% atingiu as metas calóricas e proteicas no 3º dia de internação na unidade de terapia intensiva, percentual que foi reduzido para 30% no 7º dia. Motivos para início da nutrição enteral tardia foram complicações do trato gastrointestinal (35,3%) e instabilidade hemodinâmica (32,3%). Procedimentos foram o motivo mais frequente para interrupção da nutrição enteral (44,1%). Não houve associação entre a adequação às diretrizes com estado nutricional, tempo de internação, gravidade ou evolução.

**Conclusão:** Embora expressivo o número de pacientes sépticos que iniciaram a nutrição enteral precocemente, metas calóricas e proteicas no 3º dia da internação foram atingidas apenas pela metade destes, percentual que diminuiu no 7º dia.

**Descritores:** Sepsis; Unidades de terapia intensiva; Terapia intensiva; Terapia nutricional; Guias como assunto; Nutrição enteral

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