Original Article

Non-nutritional calories in critically ill patients using enteral and/or parenteral nutritional therapy

Calorias não nutricionais em pacientes críticos em uso de terapia nutricional enteral e/ou parenteral

DOI: 10.37111/braspenj.2025.40.2.17-en

Monique Vanessa de Azevedo Proença[1]
Silmara Rodrigues Machado[2]
Caroline Valverde Pereira[3]
Luma Kagueyama[4]
Gabriela Duarte Dias[5]
Érika Suiter[6]
Ariane Nadólskis Severine[7]

Keywords:
Non-nutritional calories. Critical patient. Enteral nutrition. Parenteral nutrition.

Unitermos:
Calorias não nutricionais. Paciente crítico. Nutrição enteral. Nutrição parenteral.

Address for correspondence:
Monique Vanessa de Azevedo Proença
Hospital Sírio Libanês – Nutrição – Rua Dona Adma Jafet, 91 – São Paulo, SP, Brasil – CEP: 01308-050
E-mail: monique.vproenca@hsl.org.br

Date of submission:
February 6th, 2025

Accepted for publication:
November 4th, 2025

Date of publication:
November 20th, 2025

ABSTRACT
Introduction: Critically ill patients experience intense metabolic stress and inflammation, increasing the risk of complications and mortality. Adequate nutritional therapy is essential to prevent underfeeding and overfeeding, particularly by accounting for non-nutritional calories (NNCs) from propofol, dextrose, and citrate. This study evaluated the association between NNC use, overfeeding occurrence, and clinical outcomes in adult intensive care unit (ICU) patients. Methods: A cross-sectional, prospective study was conducted in the ICUs of a tertiary hospital in São Paulo, Brazil, including 36 adult patients (≥18 years) between July and November 2023. Participants were divided into two groups: Group 1 (with NNCs) and Group 2 (without NNCs). Clinical, nutritional, and outcome data were collected and analyzed using SPSS 24, with a significance level of 5%. Results: The mean age was 69.6±15.6 years, with predominance of males (75%) and nutritional risk (94.4%). The NNC group (55.6%) showed higher SOFA scores (median 7.0 vs. 4.5; p=0.018) and a greater proportion of non-malnourished patients according to GLIM (p=0.047). Citrate was the main NNC source, providing an average of 245.7 kcal/day. No significant difference was found in caloric adequacy (p=0.896), but the NNC group had longer ICU stays and recorded deaths. Conclusion: NNC use was associated with greater clinical severity and worse outcomes, although no significant difference in overfeeding was observed. These findings underscore the importance of including NNCs in total energy calculations to ensure safer and more individualized nutritional management among critically ill patients.

RESUMO
Introdução: Pacientes críticos apresentam intenso estresse metabólico e inflamação, aumentando o risco de complicações e mortalidade. A adequada terapia nutricional é essencial para prevenir a subalimentação e a hiperalimentação, especialmente considerando o aporte de calorias não nutricionais (CNN) provenientes de propofol, dextrose e citrato. Este estudo avaliou a associação entre o uso de CNN, a ocorrência de hiperalimentação e os desfechos clínicos em pacientes adultos internados em unidades de terapia intensiva (UTI). Método: Estudo transversal e prospectivo realizado em UTIs de um hospital terciário em São Paulo, Brasil, incluindo 36 pacientes adultos (≥18 anos) entre julho e novembro de 2023. Os participantes foram divididos em dois grupos: Grupo 1 (uso de CNN) e Grupo 2 (sem CNN). Foram coletados dados clínicos, nutricionais e de desfecho, analisados pelo software SPSS 24, com nível de significância de 5%. Resultados: A média de idade foi de 69,6 ± 15,6 anos, predominando o sexo masculino (75%) e o risco nutricional (94,4%). O grupo com CNN (55,6%) apresentou maior escore SOFA (mediana 7,0 vs. 4,5; p=0,018) e maior proporção de pacientes não desnutridos segundo o GLIM (p=0,047). O citrato foi a principal fonte de CNN, com média de 245,7 kcal/dia. Não houve diferença significativa na adequação calórica (p=0,896), mas observou-se maior tempo médio de internação e presença de óbitos no grupo com CNN. Conclusão: O uso de CNN esteve associado à maior gravidade clínica e piores desfechos, embora sem diferença significativa na hiperalimentação. Os resultados reforçam a necessidade de incluir as CNN no cálculo energético total, promovendo condutas nutricionais mais seguras e individualizadas em pacientes críticos.

1. Nutricionista, Especialista em Paciente Crítico pelo Programa de Residência Multiprofissional no Cuidado ao Paciente Crítico do Hospital Sírio Libanês, Pós-graduada em Nutrição Clínica com ênfase em Funcional, Ortomolecular e Fitoterapia, Hospital Sírio-Libanês, São Paulo, SP, Brasil.
2. Nutricionista, Mestre em Ciências da Saúde pela Universidade Federal de São Paulo, Hospital Sírio-Libanês, São Paulo, SP, Brasil.
3. Nutricionista, Especialista em Paciente Crítico pelo Programa de Residência Multiprofissional no Cuidado ao Paciente Crítico do Hospital Sírio Libanês, São Paulo, SP, Brasil.
4. Nutricionista, Especialista em Paciente Crítico pelo Programa de Residência Multiprofissional no Cuidado ao Paciente Crítico do Hospital Sírio Libanês, Especialista em Nutrição Clínica pelo Programa de Aprimoramento Profissional em Nutrição Clínica pelo Instituto Central do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (ICHC-FMUSP), Hospital Sírio-Libanês, São Paulo, SP, Brasil.
5. Nutricionista, Especialista em Nutrição Clínica em Gastroenterologia pelo Instituto Central do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, Pós-Graduação em Equipe Multidisciplinar de Terapia Nutricional: Protocolos para Manejo Clínico pelo Curso de Terapia Nutricional da Universidade de São Paulo, Especialista em Nutrição Parenteral e Enteral pela Sociedade Brasileira de Nutrição Parenteral e Enteral, Hospital Sírio-Libanês, São Paulo, SP, Brasil.
6. Nutricionista Coordenadora do Serviço de Alimentação do Hospital Sírio-Libanês, Especialista em Nutrição Clínica pela Associação Brasileira de Nutrição, Especialista em Terapia Ortomolecular, Nutrição Celular e Longevidade pela Faculdade de Ciências da Saúde de São Paulo, Especialista Preceptores do Sistema Único de Saúde pelo Sírio-Libanês Ensino e Pesquisa- Hospital Sírio-Libanês, Especialista em Gestão de Atenção à Saúde pelo Sírio-Libanês Ensino e Pesquisa, Hospital Sírio-Libanês, São Paulo, SP, Brasil.
7. Nutricionista Gerente do Serviço de Alimentação, Especialista em Gestão de Atenção à Saúde pelo Hospital Sírio-Libanês, Mestre em Ciências da Saúde pela Universidade Federal de São Paulo, Especialista em Nutrição Clínica pela Associação Brasileira de Nutrição, Hospital Sírio-Libanês, São Paulo, SP, Brasil.

INTRODUCTION

Critically ill patients admitted to intensive care units (ICU) present a high state of metabolic stress and inflammation, which increases the risk of complications and mortality. In this context, adequate nutritional therapy is fundamental to mitigate catabolism, modulate the immune response, and improve clinical outcomes. Guidelines recommend initiating enteral nutrition between 24 and 48 hours after admission. However, nutritional management requires caution to avoid both underfeeding and overfeeding[1-4].

Overfeeding, characterized by an excess of calories, can lead to serious complications such as hyperglycemia, hepatic steatosis, increased risk of infections, and prolonged mechanical ventilation and ICU stay. Furthermore, the risk of refeeding syndrome, a dangerous metabolic and electrolytic condition, also needs to be carefully managed[5,6].

In this scenario, it is crucial to consider all caloric sources the patient receives, including non-nutritional calories (NNC). NNC such as propofol, dextrose, and trisodium citrate are often infused in critically ill patients for sedation, fluid maintenance, or anticoagulation. The caloric contribution of these compounds is often neglected in clinical practice, which can result in an inadequate calculation of the total caloric offer[7,8]. The majority of studies on nutritional management in the ICU focus only on enteral or parenteral nutrition, without evaluating the combined impact of NNC on clinical outcomes. Therefore, this study sought to evaluate whether the use of non-nutritional calories is associated with the occurrence of overfeeding and clinical outcomes in adult patients admitted to the ICU who received enteral and/or parenteral nutritional therapy.

METHODS

The present study is a cross-sectional and prospective study, conducted in the general and cardiology ICUs of a tertiary and philanthropic hospital in São Paulo, SP, Brazil. The sample consisted of adult patients (≥18 years) admitted to the ICU between July and November 2023, who received enteral nutritional therapy (EN) and/or parenteral nutritional therapy (PN).

The participants were divided into two groups: Group 1, in which individuals used EN and/or PN associated with at least one NNC and Group 2, in which individuals received only EN and/or PN.

Patients with a minimum stay of 48 hours in the ICU, using exclusive EN and/or PN were included. Cases with incomplete data, readmissions, use of oral diet (exclusive or initiated at any time), fasting patients, pregnant women, patients in imminent death, and those transferred to other institutions were excluded.

After approval by the Research Ethics Committee for Human Beings (CAAE: 70722223.5.0000.5461), the variables age, sex, diagnosis (clinical or surgical), body mass index (BMI), Nutritional Risk Score 2002 (NRS-2002), Global Leadership Initiative on Malnutrition (GLIM), Sequential Organ Failure Assessment (SOFA), Simplified Acute Physiology Score III (SAPS III), alternative feeding route (NE/NP) , volume and calories of enteral and/or parenteral diet, percentage of caloric adequacy calculated through the ratio between total caloric intake and estimated caloric needs using the pocket formula, according to the European Society for Clinical Nutrition and Metabolism (ESPEN) recommendations for critically ill patients, volume of propofol 1% (1.1 kcal/ml), dextrose (3.4 kcal/g) and/or citrate (0.59 kcal/mmol), length of stay, and clinical outcomes (ICU discharge, death, or transfer to another institution) were collected from the patients' medical records.

The collected data were analyzed using the IBM-SPSS Statistics® version 24 software. For descriptive data analysis, simple and cross tables were used for qualitative or categorized variables. Quantitative variables were represented by absolute and relative frequency, measures of central tendency, and dispersion. The normality of quantitative variables was verified by the Shapiro-Wilk test.

In the inferential analysis, Fisher's Exact test was used for categorical variables, Student's T-test for continuous variables with normal distribution, the Mann-Whitney test for non-normal distributions between two groups, the Kruskal-Wallis test for more than two independent groups, and Spearman's coefficient for correlation between non-parametric continuous variables[9-11]. The level of significance considered for the inferential analyses was 5%.

RESULTS

The convenience sample was composed of 36 patients who met the inclusion criteria during the collection period, with a mean age of 69.6 years (standard deviation; SD=15.6). The majority of patients were male (75%) and classified as having nutritional risk according to NRS-2002 (94.4%).

In the group that received NNC (Group 1), 55.6% (n=20) were included, and 44.4% (n=16) in Group 2, which did not receive NNC.

In the comparison of age between the groups, using the Mann-Whitney test, it was observed that individuals in

Group 1 were significantly younger compared to Group 2 (median age: 71 vs. 73 years; p=0.045). Though there was no statistical difference, a trend towards a higher BMI in Group 1 (median of 27.9 kg/m^2) was observed when compared to Group 2 (median of 24.5 kg/m^2; p=0.078).

Furthermore, using Fisher's Exact test, Group 1 presented a significantly higher proportion of patients without malnutrition according to the GLIM criteria (p=0.047) (Table 1).

In the analysis of clinical scores, there was no significant difference between the groups regarding SAPS III (median of 35.1 vs. 36.2; p=0.947), which evaluates clinical instability and severity at admission. However, Group 1 presented a significantly higher SOFA score (median of 7.0 vs. 4.5; p=0.018), indicating greater organ dysfunction, since SOFA is an indicator of clinical severity in critically ill patients, based on multiple system failure.

Regarding NCC, citrate was the most frequently used source, with a mean use of 11 days, compared to 10 days for the others, in addition to presenting the highest caloric intake with a mean of 245.74 (SD=63.87) kcal according to Table 2.

In relation to overfeeding, the mean percentage of daily caloric adequacy over the seven days showed no significant difference between the groups (p=0.896). The daily evolution of consumption can be visualized in Figure 1.

Table 2 – Number of calories derived from propofol, dextrose, and citrate to patients in Group 1.

Source	Mean calories (SD)
Propofol	236.96 (62.21)
Dextrose	170.10 (122.48)
Citrate	245.74 (63.87)

SD = standard deviation.

In relation to clinical outcomes, we found that Group 1 patients had a longer length of stay in the ICU and slightly more than half were discharged from the ICU (55%) compared to Group 2, where all received ICU discharge. It is noteworthy that, from an inferential point of view, both groups stayed for the same amount of time in the ICU (p=0.165), but had distinct patterns of outcome (Table 3).

DISCUSSION

The present study evidenced that the majority of patients were elderly males with nutritional risk according to NRS-2002. These findings align with previous studies, such as those by Pereira et al.[12] and Santos et al.[13], who reported a high prevalence of elderly individuals and a predominance of the male sex among critically ill patients using enteral

Table 1 – Characterization of patients in Groups 1 and 2.

Variable		Group 1 (n=20)	Group 2 (n=16)	p-value
Sex, n (%)	Female	4 (20)	11 (68.8)	0.470[a]
	Male	16 (80)	5 (31.3)	
Diagnosis, n (%)	Clinical	16 (80)	14 (87.5)	0.295[b]
	Surgical	3 (15)	2 (12.5)	
NRS-2002, n (%)	Without risk	1(5)	1 (63)	>0.999[a]
	With risk	19 (95)	15 (93.8)	
GLIM, n (%)	Non malnourished	12 (60)	3 (18.8)	
	Moderate malnutrition	2 (10)	6 (16.7)	0.047[a]
	Severe malnutrition,	4 (20)	8 (50)	
Feeding route, n (%)	Enteral nutrition EMN)	9 (45)	10 (62.5)	0.395[a]
	Parenteral nutrition (PN)	6 (30)	11 (30.6)	
	EN + PN	5 (25)	6 (16.7)	
SOFA, median (min-max)		7 (0.0-17.0)	4.6 (1.0-10.0)	0.018[b]
SAPS III, median (min-max)		35.1 (5.4-94.8)	36.2 (8.0-93.9)	0.947[b]

n = sample size; [a] = Fisher's Exact test; [b] = Student's T-Test.

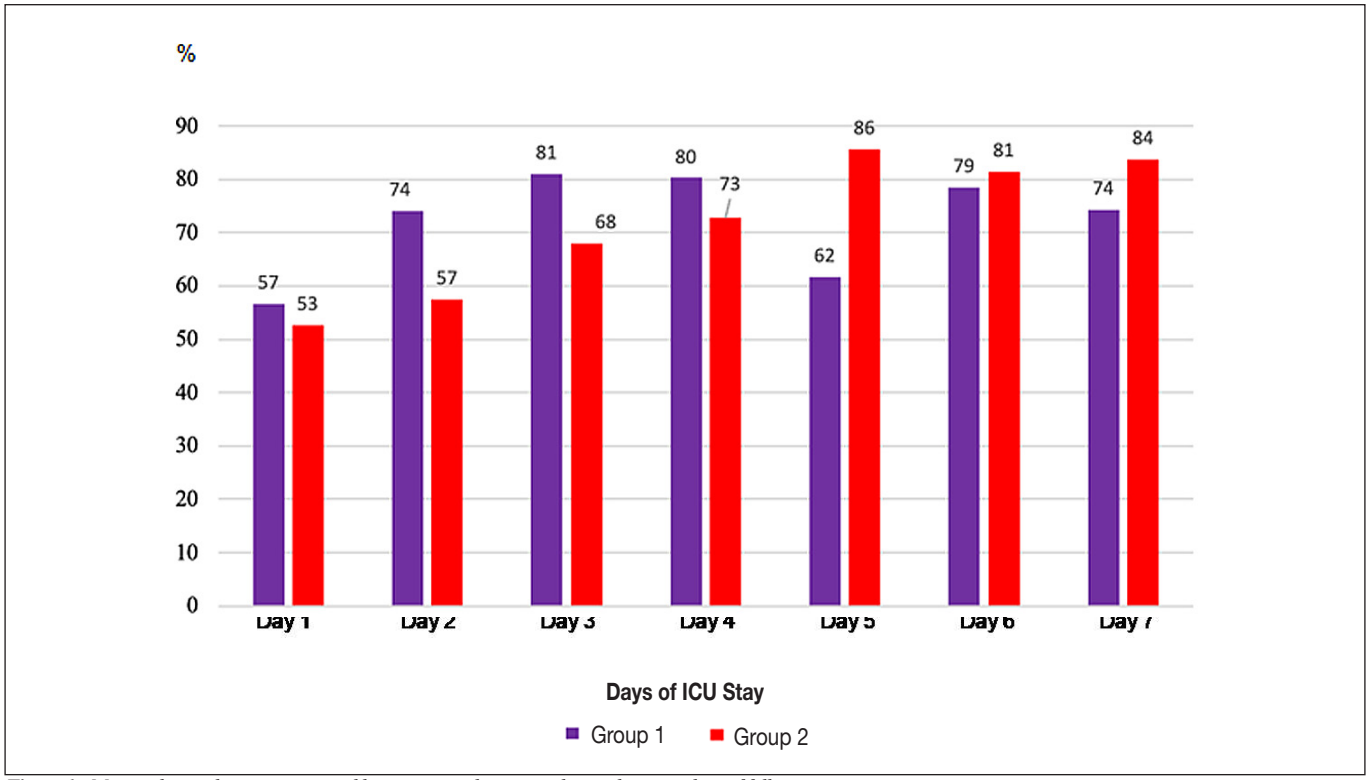

Figure 1 - *Mean caloric adequacy consumed by patients in the groups during the seven days of follow-up.*

Table 3 – Distribution of ICU stay time and outcome of patients in groups with and without NNC.

	Group 1	Group 2	Total	p-value
ICU length of stay (days), mean (SD)	23.4 (16.1)	16,9 (16,3)	20.5 (16.3)	0.165[a]
ICU discharge, n (%)	11 (55)	16 (100)	27 (75)	0.004[b]
Death, n (%)	3 (15)	0 (-)	3 (8.3)	
Remaining in the ICU, n (%)	6 (30)	0 (-)	6 (16.7)	

SD = standard deviation; [a] = Mann-Whitney Test; [b] = Extension of Fisher's Exact test.

nutritional therapy. The greater frequency of the elderly can be explained by the greater vulnerability of this age group to the development of critical illnesses, due to the presence of chronic comorbidities, functional decline, and increased susceptibility to metabolic stress. Furthermore, the male sex has been associated with worse outcomes in the ICU, related both to biological factors, such as a higher prevalence of cardiovascular and respiratory diseases, and behavioral factors, such as lower adherence to preventive care and medical follow-up[12-16].

Curiously, despite the lower median age in the group that received NNC, greater clinical severity was observed, reflected by significantly higher SOFA scores. This finding contrasts with the expectation of greater organ dysfunction in the elderly, suggesting that the indication of therapies with NNC may have been directed to the most critically ill patients, regardless of age. It is important to emphasize that the higher SOFA score is a reflection of the patient's initial clinical condition severity, and not a consequence of the presence of non-nutritional calories in itself[17,18].

Group 1 showed a tendency towards a higher BMI, although without statistical significance, which may indicate a more preserved nutritional status. This became more evident with the application of the GLIM criteria, which revealed a significantly higher proportion of non-malnourished patients in this group. This data is relevant, given that malnutrition in critically ill patients is associated with worse outcomes, such as prolonged ICU stay, a fact corroborated by our analysis and previous studies[8,19].

Among the NNC studied, citrate was the most used, being responsible for the largest caloric contributions. Studies

by Rogers & Jenkins[19] and Bousie et al.[5] demonstrated that patients on continuous renal replacement therapy (CRRT) can receive between 191 and 263 kcal/day from citrate. When these calories are not accounted for in the nutritional prescription, there is a risk of overfeeding, which can lead to significant metabolic complications, such as hyperglycemia, hepatic steatosis, infections, and increased mortality. Furthermore, overfeeding can prolong the time of ICU stay, especially in patients dependent on mechanical ventilation[2,3,5,20].

In the analysis of caloric adequacy over the seven days of follow-up, there was no statistically significant difference between the groups. However, it was observed that Group 1 reached 70% of the caloric goal already on the second day, while Group 2 only reached this mark on the fourth day. This temporal difference is clinically relevant, especially based on the BRASPEN guidelines[4], which recommend offering between 15–20 kcal/kg up to the fourth day and 25–30 kcal/kg when the patient is in the acute phase of critical illness.

Braunschweig et al.[20] evaluated different caloric offers in critically ill patients with acute lung injury and identified that patients who received 80% of the caloric goal had worse outcomes compared to patients who received 55% of the goal during the first week of ICU stay. Zusman et al.[21] found that patients who received up to 70% of caloric needs had better outcomes compared to patients who received a greater caloric offer. One of the justifications for these findings is that critically ill patients, during the initial phases of acute injury, present significant endogenous energy production, and by offering large amounts of energy in this phase, the risk of overfeeding increases, especially when CNN is not considered, bringing worse outcomes to the patients, such as longer length of stay, greater risk of death, and others[5,20-23].

Although the mean ICU stay time was longer in Group 1, the difference was not statistically significant. However, it is striking that all patients in Group 2 were discharged from the ICU, while in Group 1, deaths and cases of prolonged stay occurred, which suggests a possible unfavorable clinical impact related, directly or indirectly, to the more critical profile or nutritional management[24].

CONCLUSION

The presence of NNC in critically ill patients was associated with greater clinical severity and worse outcomes, such as a longer length of stay in the ICU and the occurrence of deaths. Despite the lack of a significant difference in overfeeding between the groups, the findings reinforce the importance of considering NNC in the calculation of nutritional therapy, aiming for a safer and more individualized approach. It is also concluded that more studies are needed to deepen the understanding of the impacts of non-nutritional calories on relevant clinical outcomes.

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Study location: Hospital Sírio Libanês, São Paulo, SP, Brazil.

Conflict of interest: The authors declare there are none.