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UNSUPERVISED MACHINE LEARNING MODEL FOR ANALYZING NUTRITIONAL SUPPORT IN MECHANICALLY VENTILATED PATIENTS

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Highlights: (1) Unsupervised analysis revealed patterns in the nutrition of critically ill patients. (2) Achieving caloric-protein goals in less than 5 days was linked to mortality. (3) Vasopressor use was a strong predictor of poor clinical outcomes. (4) Qualitative analysis showed 23% of deaths were explained by studied variables. (5) Early nutrition (24-48h) and BMI 25-29.9 kg/m² were associated with mortality.

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UNSUPERVISED MACHINE LEARNING MODEL FOR ANALYZING NUTRITIONAL SUPPORT IN MECHANICALLY VENTILATED PATIENTS

ABSTRACT

Nutritional support is essential for critically ill patients on mechanical ventilation, helping to prevent malnutrition, optimize clinical outcomes, and reduce mortality. However, there is still no consensus on the ideal timing for achieving caloric and protein goals, highlighting the need for further studies to guide evidence-based practices. This study aimed to model, in an unsupervised manner, nutritional intervention in critically ill patients on mechanical ventilation admitted to an Intensive Care Unit (ICU). A retrospective study was conducted using data from 260 patients treated in the ICU of a tertiary hospital in Maringá, Paraná, Brazil, through multiple correspondence analysis (MCA) and qualitative comparative analysis (QCA). The MCA explained approximately 21.8% of the variation in mortality outcomes, where being male, having no clinical complications or associated comorbidities, using vasopressors, initiating early nutritional therapy within 24 to 48 hours, having a body mass index between 25 and 29.9 kg/m², and achieving caloric and protein goals within five days were more prominently associated with mortality. QCA, in turn, demonstrated that, on average, 23% of deaths could be explained by the combination of dependent variables analyzed in this study, primarily body mass index, timing of enteral therapy initiation, caloric and protein goals, and vasopressor use. These findings suggest that, in the studied population, the combination of adequate nutritional supply and timely management was associated with better clinical outcomes, underscoring the need for care protocols that prioritize early nutritional assessment and intervention in critically ill patients on mechanical ventilation and enteral support.

Keywords: Nutritional therapy, Mechanical ventilation, Critical care.

MODELO NÃO SUPERVISIONADO DE *MACHINE LEARNING* PARA ANÁLISE DE SUPORTE NUTRICIONAL EM PACIENTES SOB VENTILAÇÃO MECÂNICA

RESUMO

O suporte nutricional é essencial para pacientes graves em ventilação mecânica, ajudando a prevenir desnutrição, otimizar desfechos clínicos e reduzir mortalidade. Entretanto, ainda não há consenso sobre o momento ideal para atingir as metas calóricas e proteicas, evidenciando a necessidade de mais estudos para orientar práticas baseadas em evidências. O objetivo deste estudo foi modelar de maneira não supervisionada a intervenção nutricional em pacientes criticamente doentes sob ventilação mecânica internados em Centro de Terapia Intensiva (CTI). Para analisar esses pacientes foi desenvolvido uma pesquisa retrospectiva, com dados de 260 pacientes atendidos no CTI de um hospital terciário da cidade de Maringá, Paraná, Brasil, por meio da análise de correspondência múltipla (ACM) e análise comparativa qualitativa (QCA). A ACM explicou aproximadamente 21,8% da variação em relação ao desfecho de óbito, onde ser do sexo masculino, não ter complicações clínicas e comorbidades associadas, utilizar vasopressor, iniciar a terapia nutricional precoce entre 24 e 48 horas, ter índice de massa corporal entre 25 até 29,9 kg/m² e atingir a meta calórica proteica em menos de cinco dias, estiveram associados de forma mais proeminente à ocorrência de óbitos. A QCA por sua vez, demonstrou que, em média, 23% dos óbitos podem ser explicados pela combinação das variáveis dependentes analisadas neste trabalho, principalmente pelo índice de massa corporal, tempo de início da terapia enteral, meta calórica proteica e uso de vasopressor. Esses achados sugerem que, na população estudada, a combinação entre oferta nutricional adequada e manejo oportuno esteve associada a melhores indicadores clínicos, reforçando a necessidade de protocolos assistenciais que priorizem a avaliação e intervenção nutricional precoce em pacientes críticos sob ventilação mecânica e suporte enteral.

Palavras-chave: Terapia nutricional, Ventilação mecânica, Cuidado crítico.

INTRODUCTION

Critically ill patients requiring mechanical ventilation are among the most complex and vulnerable populations in the Intensive Care Unit (ICU)[1]. Managing these individuals requires a multifaceted approach, integrating advanced medical interventions and supportive therapies[2]. Nutritional support is paramount in this context, as it plays a vital role in preventing malnutrition and improving survival outcomes. Understanding its interaction with clinical factors is essential to optimize care and reduce mortality[2]. As a result, several studies have investigated the efficacy and benefits of different nutritional strategies ICU[3].

Research indicates that the early introduction of nutritional support in critically ill patients can reduce hospital stay duration and contribute to better clinical outcomes [4]. For those on mechanical ventilation, the challenges are even more complex, including malnutrition, neuroendocrine disorders, and increased susceptibility to hospital-acquired infections, in addition to cellular hypermetabolism[4]. Thus, the assessment of baseline skeletal muscle mass and its quality can serve as mortality indicators in critically ill patients, highlighting the importance of nutritional intervention while considering other factors that may affect prognosis and treatment in hospitalized patients to prevent malnutrition and improve patient survival[5].

The guidelines of the European Society of Intensive Medicine (ESICM) and the Brazilian Society of Parenteral and Enteral Nutrition (BRASPEN/SBNPE)[6] recommend the initiation of early nutritional support within the first 48 hours after mechanical ventilation, unless contraindications such as uncontrolled shock, hypoxemia, uncontrolled acidosis, uncontrolled upper gastrointestinal bleeding, abdominal bleeding, compartment syndrome, among others, are present, and achieving the caloric-protein goal after the fourth day of nutritional support[7].

However, to the best of our knowledge, there is no consensus in the literature regarding the initiation of nutritional support and the ideal time to achieve caloric-protein goals in patients with severe pulmonary function impairment in ICU, nor whether independent variables are related to mortality. In this context, the aim of this study was to apply an unsupervised machine learning model to analyze the nutritional intervention in critically ill patients on mechanical ventilation without prior malnutrition.

MATERIALS AND METHODS

Study Design and Location

A retrospective cross-sectional study was conducted following the recommendations of Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)[8], using data from patients treated at a tertiary hospital located in Maringá, Paraná, Brazil. This institution, with 300 beds including 29 in the ICU, was selected due to its role as a regional referral center for high-complexity care, encompassing critical care and mechanical ventilation, and for its robust electronic health records system (MV Soul), which enabled the accurate retrieval of comprehensive clinical and nutritional support data.

Data Source

Secondary data available in the MV Soul system (MV Informática Nordeste Ltda, São Paulo, Brazil) were used.

Initially, the database comprised 333 patients over 18 years old with severe respiratory impairment and no prior malnutrition, treated in the ICU of the aforementioned hospital between January and December 2021. From the initial sample, patients who were not subjected to mechanical ventilation, those who died within 24 hours after mechanical ventilation, and/or those transferred to other hospitals in Maringá and the surrounding region were excluded, totaling 260 patients for study continuation (Figure 1).

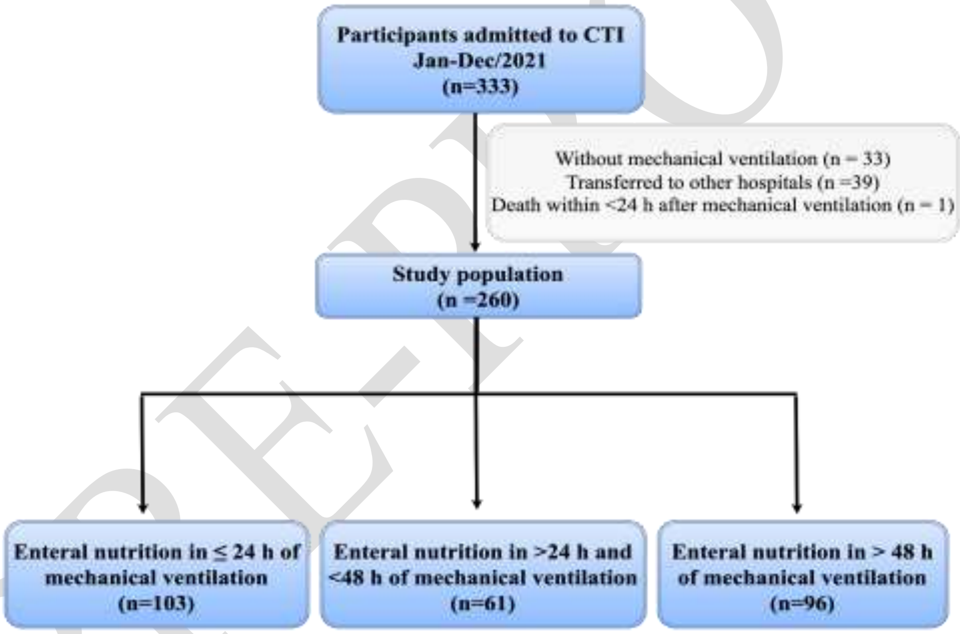

Figure 1. Flowchart of patient selection for the study. NE = enteral nutrition, MV = mechanical ventilation

Source: The authors

Study Variables

The dependent variable was mortality. The independent variables analyzed were: age, sex, body mass index (BMI), initiation of nutritional support, achieved caloric-protein goal, type of comorbidity and complications, use of hemodialysis, use of vasopressors, and use of mechanical ventilation, as described in the supplementary material (Annexes I and II), and were categorized into three distinct groups.

The first group comprised demographic variables (e.g., sex, age, BMI) associated with the presence of pre-existing comorbidities (e.g., systemic arterial hypertension, diabetes mellitus, dyslipidemia, chronic kidney dysfunction, chronic obstructive pulmonary disease, and smoking).

The second group referred to the nutritional support provided to patients, including variables such as the initiation of nutritional support, established caloric and protein goals, the time required to achieve these goals, and complications. The third group encompassed the therapeutic support provided to patients, represented by the use of vasopressors, the need for hemodialysis, and mechanical ventilation.

Multiple Correspondence Analysis (MCA)

A multiple correspondence analysis (MCA) was conducted using the FactorMineR package in the RStudio software (version 4.3.1), adopting a preprocessing approach that involved transforming the independent and dependent variables into binary form, where "0" indicates the absence of the event and "1" represents the presence of the event[9].

MCA is a multivariate statistical approach applied to the analysis and graphical representation of multivariate categorical data in complex datasets [7]. This methodology is based on the following fundamental principles: a profile point in a dimensional space, a weight (or mass) assigned to each point, and a distance function between points known as the chi-square distance[7]. The method optimally reduces the dimensionality of the points by projecting them into a subspace (typically a two-dimensional plane), adjusted to the points by weighted least squares, where each point is weighted according to its respective mass, and the distances between points and the subspace are measured in terms of chi-square distances[9-10].

Thus, in the present study, the variables that were statistically significant according to the chi-square test (see Annex II) were used in the MCA, extracting the eigenvalues of the measured distance through their cosine values. The obtained results were interpreted and plotted in the construction of a perceptual map with the two main dimensions, "death" and "no death," which explain the highest proportion of variance[9].

Qualitative Comparative Analysis (QCA)

In the next stage, a qualitative comparative analysis (QCA) was performed using the QCA package in the RStudio software (version 4.3.1). The analysis employed logical minimization to identify the simplest combination of causal conditions associated with the outcome of interest. This process was based on a previously constructed truth table, which is a necessary prerequisite for minimization. A graph was subsequently generated to visualize the results[11].

The truth table is structured as a matrix with k columns, corresponding to the number of causal conditions included in the analysis and 2^k rows representing all possible configurations of these conditions. Individual cases are assigned to the appropriate rows based on their specific characteristics[11].

Several measures were applied in the QCA to evaluate the strength of relationship between causal conditions and the outcome, including necessity inclusion (inclN), ratio of necessary consistency (RoN), and necessary covariance (covN). The InclN metric reflects the proportion of cases in which a condition is present when the outcome occurs, ranging from 0 to 1. Values closer to 1 indicate a highly necessary condition for the outcome, whereas values below 0.5 suggest that the condition is not essential for the result[11].

The ratio of necessary consistency (RoN) is another fundamental measure in QCA analysis, indicating the proportion of cases in which both the necessary condition and the outcome are present compared to cases in which both are absent. Values close to 1 suggest a weak relationship, while values above 1 indicate a stronger relationship. Values below 0.5 suggest that the necessary condition alone is not sufficient to produce the outcome[11].

Finally, necessary covariance (covN) assesses the strength of the relationship between the necessary condition and the outcome, controlling for the effect of other variables. It ranges from -1 to 1, with values close to 1 indicating a strong positive relationship, values close to -1 indicating a strong negative relationship, and values near 0 suggesting a weak or nonexistent relationship[12].

Based on the combinations of conditions identified in the QCA analysis, it is possible to determine which ones are associated with the outcome of death in critically ill patients. These findings were displayed to observe the influence of each data set on the final outcome[12,14]. This analysis involved comparing variable categories concerning the results obtained from MCA, as well as the qualitative interpretation of the results.

The qualitative comparative analysis (QCA) was performed using a set of latent variables (which are not directly observed but inferred through a mathematical model based on other directly measured variables)[15].

Ethical Aspects

This study was approved by the Permanent Committee on Ethics in Research with Human Beings of the State University of Maringá (UEM), under protocol number 5.658.055/2022. CAAE: 62023522.0.0000.0104. Since we used secondary data, in accordance with Resolution No 466/2012 of the Brazilian Ministry of Health the requirement of informed consent was waived. All data were anonymized to ensure confidentiality, and ethical principles were strictly respected.

RESULTS

Patient Characterization

Among the 260 selected patients, 59.6% were up to 64 years old, 30.7% were between 65 and 74 years old, and 9.6% were over 75 years old. The average age was 59.5 years. Regarding sex, 57.6% were male, and 30% of them had comorbidities. Nutritional support initiated within 24 hours was provided to 39.6% (103/260) of the patients, while 23.4% (61/260) received enteral nutrition between 24 and 48 hours, and 37% (96/260) received it after 48 hours.

Outcome

It was observed that the mortality rate was 96% for elderly individuals aged 75 years or older and 88% for males. Regarding the presence of more than one comorbidity, 52.3% of patients had this condition, which showed a strong association with lethality, reaching 93.4%. Additionally, the need for hemodialysis was identified in 38% of patients, and among them, 93.1% progressed to death. The use of vasopressors was noted in 96.1% of cases, of which 88.4% were associated with a fatal outcome.

Regarding body mass index (BMI), those with a BMI between 30.0 and 34.9 kg/m² had a higher lethality rate compared to other groups. Concerning the timing of enteral support initiation, the mortality rate was 82.5% for those who started within 24 hours, 88.5% for 24 to 48 hours, and 90.6% for those who started after 48 hours, culminating in an overall lethality rate of 87% among all studied patients. Notably, the decision to initiate nutritional therapy after 48 hours was particularly relevant for patients with a BMI of 40 kg/m² or higher, as it represented 62.5% of deaths in this group.

All patients who did not meet the caloric and protein target established by the hospital protocol progressed to death. Among those who met the target, 86.6% did so in less than five days and passed away, while 66.7% achieved the target in more than five days and also died.

In the evaluated sample, variations in age, body mass index, and adherence to nutritional goals were observed among critically ill patients undergoing mechanical ventilation and enteral nutritional support.

Clinical Outcomes

For a more detailed understanding of these results, the predictors of mortality were sex, age, body mass index, caloric-protein target, early initiation of nutritional support, and complications. In the univariate analysis, sex, age, body mass index, caloric-protein target, early initiation of nutritional support, and nutritional complications were associated, as shown in Table 1.

Table 1. Demographic and baseline characteristics

Group	Category	Survived n (%)	Non-survivors n (%)
Sex	Male	18 (14.7%)	132 (85.3%)
Sex	Female	16 (15.5%)	94 (84.5%)
Age	≥75	1 (4.0%)	24 (96.0%)
Age	65–74	5 (10.0%)	75 (90.0%)
Age	≤64	28 (19.4%)	127 (80.6%)*
BMI	≥35	3 (18.8%)	13 (81.2%)
BMI	25–29.9	5 (31.2%)	11 (68.8%)
BMI	18.5–24.9	3 (9.8%)	38 (90.2%)
BMI	<18.5	16 (13.0%)	121 (87.0%)
BMI	Missing	7 (18.4%)	43 (81.6%)
Energy goal_3	>100%	23 (37.7%)	46 (62.3%)*
Energy goal_2	80–100%	11 (14.6%)	71 (85.4%)
Energy goal_1	<80%	0 (9.0%)	109 (99.1%)*
Early nutrition	>48 h	9 (10.4%)	87 (89.6%)
Early nutrition	24–48 h	7 (13.1%)	54 (86.9%)
Early nutrition	≤24 h	18 (20.4%)	85 (79.6%)
Nutritional complication	Yes	2 (21.4%)	32 (78.6%)
Nutritional complication	No	12 (14.6%)	214 (85.4%)

Source: The authors

BMI = Body Mass Index

Energy goal = target of 25 to 30 kcal/kg/day and 1.5 to 2.0 g/protein/kg/day

*p < 0,05 **

The logistic regression results indicate which independent variables are most strongly associated with mortality (Figure 2). It is observed that failing to meet the caloric-protein target is more strongly associated with mortality, while achieving the caloric-protein target after five days is more associated with survival.

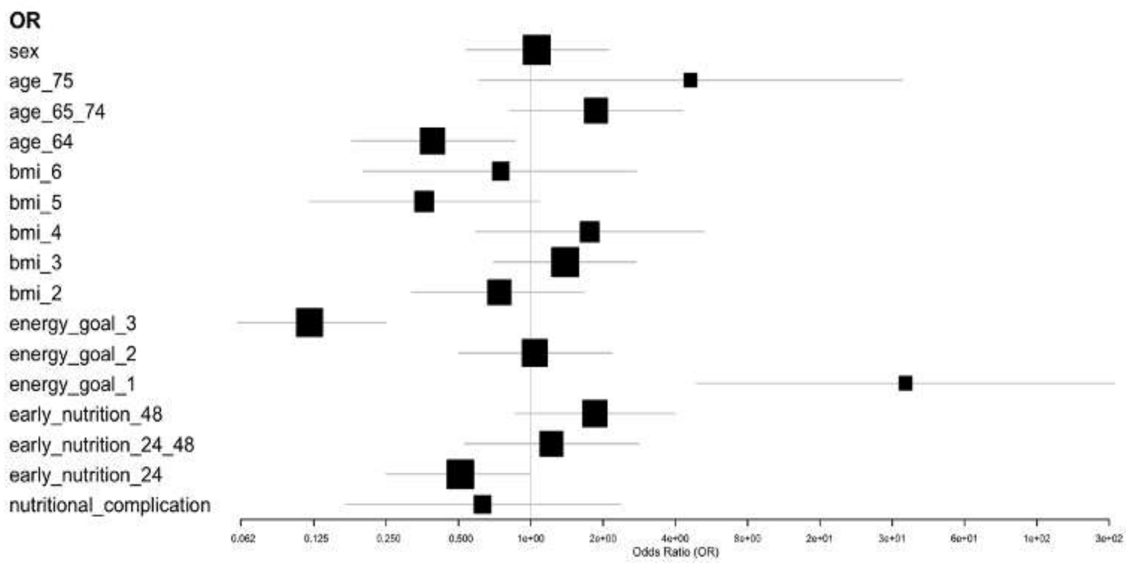

Figure 2. Forest plot of the odds ratio from logistic regression between the independent explanatory variables ("sex; age; BMI; energy goal; early nutrition; nutrition complication") and the dependent variable "death".
Source: The authors

For a deeper understanding of these results, multiple correspondence analysis (MCA) was used to create a two-dimensional perceptual map. Analyzing these dimensions together, we can observe that the variables used in this study explain approximately 21.8% of the variation related to mortality outcomes.

It is possible to note that being male (sex_1), having no complications (n_comp_0), having comorbidities (comor_1; comor_2), using vasopressors (vp_1), initiating early nutritional support between 24 and 48 hours (e_nut_24_48), belonging to the BMI group of 30 to 34.9 kg/m² (bmi_4) classified as obese class I, failing to reach the caloric-protein target (e_goal), and not achieving the caloric-protein target within five days (e_goal2) were more prominently associated with mortality.

On the other hand, the absence of the need for vasopressors (vp_0) and reaching the caloric-protein target in more than five days (e_goal3) were more closely related to the survival of critically ill patients undergoing mechanical ventilation and enteral nutrition (Figure 3).

The sum of the axes explored in the scatter plot helps us understand the total data variation and identify the variables that have the greatest impact on the outcome. These variables are those that are farther from the center of the graph and contribute most significantly to group formation (Figure 3). These results indicate that caloric-protein target achievement, age, male sex, timing of nutritional support initiation, comorbidities, and nutritional complications are important predictors of mortality in these patients.

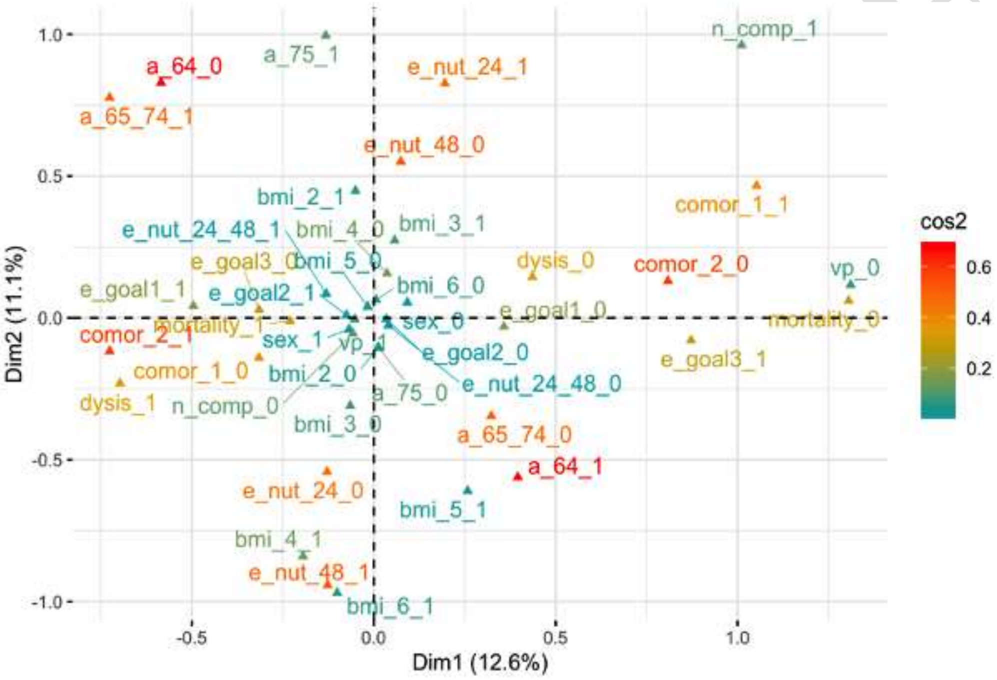

Figure 3. Perceptual map of the position of variables in relation to dimensions 1 and 2 and their relationship with the groups forming the variable "death," extracted through multiple correspondence analysis.

Dimension 1: (comor_2_0; como_2_1; mortality_0; como_1_1; e_goal3_1; dysis_1; a_65_74_1; a_64_0; dysis_0; e_goal1_1; a_64_1; comor_1_0; e_goal1_0; e_goal3_0; a_65_74_0)

Dimension 2: (e_nut_48_1; a_64_0; e_nut_48_0; a_64_1; a_65_74_1; e_nut_24_0; bmi_4_1; a_75_1; a_65_74_0; bmi_6_1; comor_1_1; n_comp_1; bmi_3_0; bmi_3_1)

0 = absence of mortality (survival)

1 = mortality

age= age; age_64= age up to 64 years; age_65_74 = age 65 to 74 years; age_75 = age 75 years or older; female = female gender; male = male gender; bmi = body mass index in kg/m²; bmi_1 = bmi group ≤18.5 kg/m²; bmi_2 = bmi group 18.6 to 24.9kg/m²; bmi_3 = bmi group 25 to 29.9kg/m²; bmi_4 = bmi group 30 to 34.9kg/m²; bmi_5 = bmi group 35 to 39.9kg/m²; bmi_6 = bmi group ≥ 40 kg/m²; energy_goal (e_goal) = caloric-protein goal; energy_goal1 (e_goal1) = caloric-protein goal not achieved; energy_goal2 (e_goal2) = caloric-protein goal achieved within 5 days; energy_goal3 (e_goal3) = caloric-protein goal achieved after 5 days; early_nutrition_1 (e_nut_24) = enteral nutritional support initiation before 24 hours; early_nutrition_2 (e_nut_24_48) = enteral nutritional support initiation between 24 and 48 hours; early_nutrition_3 (e_nut_48)= enteral nutritional support initiation after 48 hours; mortality_0 = absence of death; mortality_1 = presence of death; comorbity_1 (comor_1) = one comorbidity; comorbity_2 (comor_2) = more than one comorbidity; nutrition_complication (n_comp) = nutritional complication; nutrition_complication_0 (n_comp_0) = absence of complication; nutrition_complication_1 (n_comp_1) = presence of complication; dialysis (dysis_0) = absence of hemodialysis; dialysis (dysis_1) = presence of hemodialysis; vasopressor_0 (vp_0) = absence of vasopressor use; vasopressor_1 (vp_1) = presence of vasopressor use

Source: The authors

Through QCA, it was possible to identify those six variables and three combinations (sets) generated by the intermediate solution algorithm that leads to a higher chance of the mortality outcome. It produced the following expressions that highlight the relationship between mortality and these factor (bmi*early_nutrition*˜energy_goal*comorbidity*vasopressor), dimension 2 (bmi*˜early_nutrition*˜energy_goal*hemodialysis*˜vasopressor) and dimension 3 (bmi*˜energy_goal*hemodialysis*comorbidity). For example, 11 participants were explained by **set** 1, 10 participants by **set** 2, 14 by **set** 3, and 16 by the combination of **set** 1 with **set** 3. Therefore, it can be concluded that 51 deaths could be explained by these **sets** of latent variables (Figure 4)

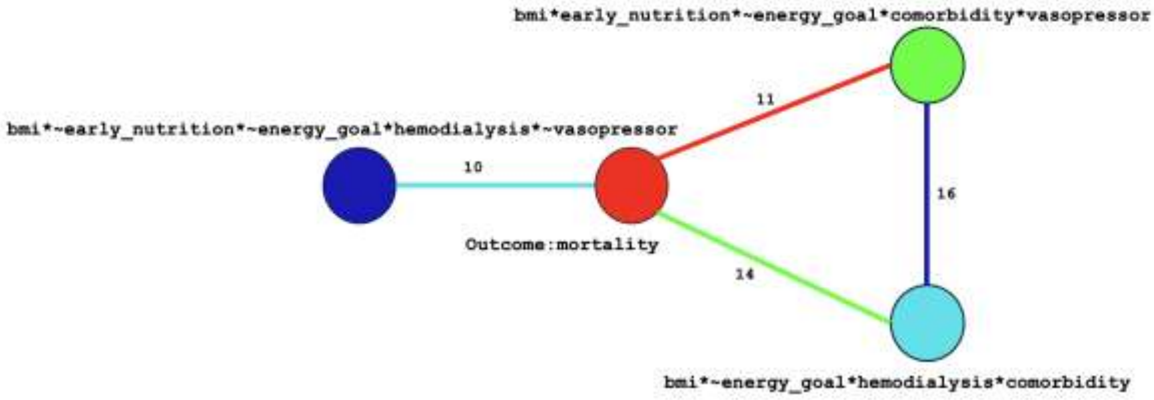

Figure 4. Qualitative comparative analysis showing treatment sets and their association with mortality.

Source: The authors

DISCUSSION

Our unsupervised analysis revealed that, in critically ill, mechanically ventilated without prior malnutrition and at high risk of death, initiating nutritional support within 24–48 hours and rapidly achieving caloric-protein targets (within less than five days) were associated with worse prognosis, rather than favorable outcomes. Previous studies highlight the relevance of nutritional support in critically ill patients[16 -17]. However, to the best of our knowledge, there is still no consensus on the ideal timing for initiating nutritional support and the time required to achieve caloric and protein targets in these individuals, especially in those with severe pulmonary dysfunction and no prior malnutrition.

In addition to the MCA and QCA findings, the logistic regression model summarized in Figure 2 provides further insight into the independent predictors of mortality. The plot highlights that failure to achieve caloric-protein targets (<80%) was the strongest factor associated with death, with an odds ratio markedly higher compared to other variables.

Conversely, patients who reached nutritional goals after five days had increased odds of survival, suggesting that a slower achievement of targets may be protective in this population. Although variables such as age, BMI, and early nutrition initiation showed trends toward association, their confidence intervals crossed the null value, indicating weaker or non-significant independent effects. These results reinforce that, beyond demographic and clinical factors, the dynamics of nutritional adequacy play a central role in prognosis. The logistic regression analysis thus complements the unsupervised machine learning approach, emphasizing that nutritional goals should not be pursued uniformly but tailored to the patient's risk profile and clinical condition[18].

Early initiation of nutritional support within 24–48 hours is widely recommended by international guidelines such as ESPEN and ASPEN, aiming to reduce infectious complications and preserve muscle function in critically ill patients. However, recent large, randomized trials and systematic reviews have shown that delivering high-dose nutrition—both calories and protein—within the first 24–48 hours of ICU admission may be detrimental, regardless of the feeding route[16, 19-21].

This potential harm has been linked to the suppression of essential cellular repair pathways, including autophagy, as well as to increased risk of hyperglycemia and metabolic overload[22]. These effects appear to be particularly pronounced in patients without prior malnutrition and at high risk of death, in whom an excessive early nutrient load may exacerbate metabolic stress and impair recovery[23].

In critically ill patients, inadequate nutritional management can worsen prognosis, prolong mechanical ventilation, and extend ICU length of stay. Our Multiple Correspondence Analysis (MCA) explained 21.8% of the variance in mortality and revealed distinct clinical–nutritional profiles associated with outcomes (Figure 3). Mortality was associated with male sex, absence of nutritional complications, presence of comorbidities, vasopressor use, initiation of enteral nutrition within 24–48 hours, BMI between 30–34.9 kg/m², and failure to achieve nutritional targets. In contrast, survival was associated with absence of vasopressor use and achieving nutritional targets after five days. While MCA identified individual clinical–nutritional variables associated with mortality or survival, QCA explored how these factors interact in specific configurations to influence outcomes. This complementary approach allowed us to capture both isolated patterns and the combined effects of metabolic, hemodynamic, and nutritional variables.

These findings are consistent with recent cohort studies showing that failure to reach nutritional targets, in combination with other risk factors, is linked to increased mortality[23]. Other factors independently associated with higher mortality include male sex, presence of comorbidities, vasopressor use, and BMI in the 30–34.9 kg/m² range, underscoring the complexity of delivering optimal nutrition in the ICU. Increasingly, the evidence supports an individualized nutritional approach rather than a “one-size-fits-all” strategy. Adjusting the timing, route, and caloric–protein goals based on patient risk factors, comorbidities, and disease[24].

Critical illness induces a profound inflammatory and catabolic response, leading to rapid loss of lean body mass, immune dysfunction, and increased risk of infection and adverse outcomes[26]. Appropriately timed and individualized nutritional therapy can help mitigate these effects by modulating inflammation through bioactive nutrients (e.g., omega-3 fatty acids, vitamin D, antioxidants, probiotics) and preserving lean mass through adequate protein and energy provision. Such strategies also support immune function, enhance tissue repair, and may improve tolerance to mechanical ventilation, ultimately contributing to better recovery trajectories in critically ill patients[25-27].

The evidence highlights that the impact of nutrition is not uniform; it depends on the broader clinical constellation. Our Qualitative Comparative Analysis identified three configurational pathways that together accounted for 51 deaths (23% of all fatalities), indicating that mortality in this cohort arose from specific combinations rather than single variables acting in isolation. Across these pathways (Figure 4), the most influential conditions were elevated BMI (30–34.9 kg/m²), failure to reach nutritional targets, need for hemodialysis, vasopressor use, and early initiation of enteral nutrition. These factors clustered in different constellations—with organ failure markers (vasopressors, hemodialysis) amplifying risk when coupled with inadequate nutritional achievement or accelerated feeding—highlighting that the prognostic impact of nutrition depends on the broader clinical context [24,28]. Collectively, the QCA results reinforce a configurational view of risk: in critically ill, mechanically ventilated patients without prior malnutrition, mortality is best explained by the co-occurrence of metabolic stress, organ dysfunction, and how (and how fast) nutrition is delivered, supporting individualized strategies over uniform protocols[29].

Our results also demonstrated that mortality was directly correlated with elderly male individuals, with a body mass index between 25 and 29 kg/m², associated comorbidities, and the need for vasopressors and hemodialysis. This is because aging is associated with a reduction in physiological reserve and an increased prevalence of comorbidities such as diabetes and hypertension, which worsen the body's response to critical situations[30]. Additionally, excess weight (BMI between 25 and 29 kg/m²) may be related to chronic low-grade inflammation, which impairs recovery. The use of vasopressors indicates severe hemodynamic instability, while the need for hemodialysis reflects kidney failure, both of which are associated with higher hospital mortality[31].

Recent literature supports that aging, male sex, and overweight are linked to worse ICU outcomes due to reduced physiological reserve and chronic low-grade inflammation[32-33]. The requirement for vasopressors reflects severe hemodynamic instability, and the necessity of hemodialysis indicates renal failure, both associated with increased hospital mortality[34-35].

It is also important to consider that our data were collected during the second year of the COVID-19 pandemic, a period characterized by hyperinflammatory and hypermetabolic states in ventilated patients, as well as potential resource limitations that could have influenced nutritional practices[36]. This context reinforces the importance of interpreting our results within a unique clinical scenario that may differ from non-pandemic ICU populations.

This single-center observational design limits external validity and precludes establishing causal relationships. The absence of detailed laboratory parameters and post-discharge follow-up may have introduced residual confounding. Nonetheless, applying multiple correspondence analysis and qualitative comparative analysis enabled the identification of clinically relevant associations that can inform future investigations in hospital nutrition and critical care[37].

CONCLUSION

The study highlights the importance of initiating nutritional support at the appropriate time, between 24 and 48 hours, specifically in critically ill patients at risk of death. The research suggests that rapidly achieving nutritional targets in these patients may directly influence mortality, emphasizing that a personalized approach is essential for this high-complexity profile. Furthermore, this personalization of nutritional support proves to be relevant not only for critically ill patients but also for other emerging diseases, reinforcing the need for targeted strategies based on the patient's critical condition.

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Annex I. Selected variables of critically ill patients admitted to the Intensive Care Unit (ICU) and subjected to mechanical ventilation with nutritional support.

Variable	Definition
Age	Age of the patient at the time of admission to the intensive care unit.
Sex	Male / Female
BMI	Body mass index in kg/m².
Caloric-Protein Target	Evaluates how many days the patient needed to reach the caloric-protein target of 25 to 30 kcal/kg/day and 1.5 to 2.0 g/protein/kg/day.
Initiation of Nutritional Support	Evaluates the time in hours between admission to the intensive care unit and the initiation of enteral nutritional support.
Outcome (Mortality)	Evaluates the patient's outcome after admission to the intensive care unit.
Comorbidity	Hypertension, Kidney failure, Diabetes, Chronic Obstructive Pulmonary Disease, Dyslipidemia, Smoking
Nutritional Complication	Fever, Mechanical ventilation, Diarrhea, Constipation, Hemodialysis, Use of vasopressors

Annex II. List of variables and abbreviations.

Abbreviation	Variable/Meaning
age	Age
age_64	Age up to 64 years
age_65_74	Age from 65 to 74 years
age_75	Age 75 years or older
male (sex_1)	Male
female (sex_2)	Female
bmi	Body mass index in kg/m²
bmi_1	BMI group ≤18.5 kg/m²
bmi_2	BMI group 18.6 to 24.9 kg/m²
bmi_3	BMI group 25 to 29.9 kg/m²
bmi_4	BMI group 30 to 34.9 kg/m²
bmi_5	BMI group 35 to 39.9 kg/m²
bmi_6	BMI group ≥ 40 kg/m²
energy_goal (e_goal)	Caloric-protein target
energy_goal1 (e_goal1)	Caloric-protein target not achieved
energy_goal2 (e_goal2)	Caloric-protein target achieved within 5 days
energy_goal3 (e_goal3)	Caloric-protein target achieved in more than 5 days
early_nutrition_1 (e_nut_24)	Enteral nutritional support initiation before 24 hours
early_nutrition_2 (e_nut_24_48)	Enteral nutritional support initiation between 24 and 48 hours
early_nutrition_3 (e_nut_48)	Enteral nutritional support initiation after 48 hours
mortality_0	No death
mortality_1	Death
comorbity_1 (comor_1)	One comorbidity
comorbity_2 (comor_2)	More than one comorbidity
nutrition_complication (n_comp)	Nutritional complication
nutrition_complication_0 (n_comp_0)	No complication

nutrition_complication_1 (n_comp_1)	Complication present
dialysis (dysis_0)	No dialysis
dialysis (dysis_1)	Dialysis present
vasopressor_0 (vp_0)	No vasopressor use
vasopressor_1 (vp_1)	Vasopressor use present