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Impact of Calorie and Protein Deficits on Clinical Outcomes in Critically Ill Patients: Insights from an Indian Intensive Care Unit

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ABSTRACT

Background: Critical illness triggers metabolic alterations, predisposing patients to calorie/protein deficits, which are further exacerbated by nutritional delivery barriers. Nutrition inadequacy is linked to adverse outcomes. Despite guideline recommendations emphasizing early and adequate nutrition support, prescribed calorie and protein targets are frequently not achieved in routine intensive care unit (ICU) practice, particularly in resource-variable settings. This study evaluates the impact of calorie and protein deficits on clinical outcomes, including mortality and length of stay, among critically ill patients.

Methods: This retrospective observational study included 1,073 adult critically ill patients. Nutritional requirements were estimated using European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines. Daily calorie and protein deficits were calculated as difference between prescribed and delivered intake, and cumulative deficits were derived by summing daily deficits over the ICU stay. Patients were stratified into low- and high-deficit groups (<2000 vs. ≥2000 kcal; <75 vs. ≥75 g protein). Clinical outcomes were compared using Mann-Whitney U, χ^2, and Kaplan-Meier survival analysis, and multivariable logistic regression was performed to identify independent associations with mortality.

Results: Calorie deficit ≥2000 kcal was associated with longer ICU stay [median (IQR): 10 (7-15) vs. 8 (6-12) days; p<0.001], longer duration of mechanical ventilation [5 (2-9.75) vs. 4 (0-7); p<0.001], and higher mortality (31.3% vs. 22.2%; OR 1.60, 95% CI 1.22-2.11; p=0.001). Protein deficit ≥75 g was associated with longer ICU stay [10 (7–14) vs. 9 (6–13) days; p=0.001] and increased duration of mechanical ventilation [5 (2–9) vs. 4 (1–8) days; p=0.014]. Survival was significantly lower in high-deficit groups. Baseline characteristics and severity/nutritional risk scores were comparable, suggesting an association independent of baseline differences.

Conclusions: This study identified critical nutritional deficit thresholds (calorie ≥2000 kcal, protein ≥75 g) associated with adverse outcomes in critically ill patients. These findings suggest that the impact of nutritional deficits may occur early during ICU stay and at lower thresholds than previously recognized. Given that nutrition represents a modifiable component of ICU care, early, individualized, and protocolized nutritional strategies aimed at minimizing cumulative deficits may help improve clinical outcomes.

Keywords: Calorie deficit; Clinical outcomes; Critical illness; Early nutritional support; Enteral nutrition; Feeding strategy; Malnutrition; Parenteral nutrition; Mechanical ventilation; Protein deficit

Introduction

Critical illness is characterized by profound metabolic alterations that predispose patients to nutritional deficits. The acute response to severe injury or infection follows a biphasic course: an initial ebb phase, lasting 24–48 hours, marked by hypometabolism, reduced energy expenditure, and impaired tissue perfusion; followed by the flow phase, during which catabolism and hypermetabolism predominate.[1] During the flow phase, increased energy expenditure and protein breakdown result in rapid depletion of lean body mass, accentuated by the proinflammatory and neuroendocrine response. These metabolic shifts, compounded by the practical challenges of delivering adequate nutrition in the intensive care unit (ICU), such as gastrointestinal intolerance, interruptions for procedures, and delayed initiation of feeding, contribute to significant cumulative calorie and protein deficits.[1,2]

Inadequate nutrition in critically ill patients can have severe consequences, leading to worsened health, longer hospitalization, and higher healthcare costs.[3-7] Malnutrition in critically ill patients has been consistently linked to impaired wound healing, increased infection risk, prolonged mechanical ventilation, higher ICU length of stay, and increased mortality. [3-7] Alarmingly, malnutrition prevalence among ICU patients can reach as high as 78%.[8] Thus, nutrition represents a critical component of ICU care, with substantial implications for patient outcomes and resource utilization.[9-13] Multiple observational studies have demonstrated a strong association between nutritional status and their clinical outcomes, with adequate nutrition linked to reduced mortality rates and shorter duration of ICU stay.[9,12,13]

Numerous international guidelines emphasize the importance of timely and adequate delivery of calories and protein to critically ill patients to support recovery and mitigate complications.[14-16] The joint clinical practice guidelines of the American Society for Parenteral and Enteral Nutrition (ASPEN) and the Society of Critical Care Medicine (SCCM) specifically address critically ill adults (≥18 years) who are anticipated to remain in a medical or surgical ICU for more than 2–3 days. These guidelines recommend assessing patients' nutritional risk upon admission and estimating energy and protein requirements to guide individualized nutrition therapy goals.[16] Despite these recommendations, the optimal caloric and protein targets remain an area of active investigation, with ongoing debate regarding both the quantity and timing of nutritional interventions. Current consensus statements from both the European Society for Clinical Nutrition and Metabolism (ESPEN) and ASPEN recommend hypocaloric feeding, targeting approximately 70% of calculated energy requirements during the first week, unless indirect calorimetry is available to measure true energy expenditure.[14-16] This strategy is intended to reduce the risks of overfeeding, which may worsen outcomes through hyperglycemia, hypercapnia, or hepatic steatosis.[17-19] However, more recent studies have questioned the universality of this recommendation. Evidence suggests that both underfeeding and overfeeding can be harmful, and that the ideal energy intake may vary according to the phase of illness and the patient's metabolic status.[14,19-21]

Despite international guidelines advocating early enteral nutrition and adequate protein supplementation, real-world observational studies show that recommended nutritional targets are rarely achieved in routine ICU practice.[2,22,23] In Indian ICUs, where resource limitations and practice heterogeneity are common, local data on the magnitude of nutrition deficits and their impact on outcomes remain scarce.[23] The need for effective nutritional assessment and intervention strategies is critical to improving patient recovery and minimizing complications.[10] Therefore, the present study aimed to to evaluate the impact of nutritional status, specifically calorie and protein deficits, on clinical outcomes and the length of ICU and hospital stay among critically ill patients.

Methods

STUDY POPULATION

This retrospective observational study was conducted in the ICU of a tertiary healthcare centre in Mumbai, India. This study included all adult patients (>18 years of age) admitted to the ICU between February 2022 and June 2025. Informed consent was obtained from all participants or their guardians. The patients were followed up till their discharge or death. The study was approved by the institutional ethics committee of the hospital (approval number: HNH/IEC/2023/OCS/CCM/122).

ENERGY AND DEFICIT CALCULATIONS

Nutritional requirements were determined for each patient based on their clinical condition, in accordance with the ESPEN guidelines. Daily nutrition deficits were calculated as the difference between prescribed targets (calorie and protein requirements) and the actual (calorie and protein) delivered intake. Cumulative deficits were obtained by summing daily deficits over the duration of ICU stay.

Because cumulative deficits are inherently influenced by ICU length of stay and may therefore introduce time-dependent bias, time-adjusted deficit measures were additionally calculated. Mean daily calorie deficit was defined as total cumulative calorie deficit divided by ICU length of stay, and mean daily protein deficit was calculated similarly. These variables were analyzed as continuous predictors in regression modeling to better reflect sustained underdelivery independent of duration of ICU exposure.

NUTRITION DELIVERY PRACTICES

Nutrition support was provided as part of routine ICU care and individualized according to identified barriers to feeding in critically ill patients. At our institution, four strategies are routinely employed to address barriers to adequate nutrition delivery: (1) Catch-up and match-up feeding was implemented for patients experiencing feeding interruptions due to surgical/therapeutic procedures; (2) Parenteral nutrition was initiated in patients with gastrointestinal intolerance or contraindications to enteral feeding; (3) Hypercaloric feeds (>1 kcal/mL) and/or supplemental parenteral nutrition were provided to patients with fluid restrictions to ensure adequate energy and protein delivery. In addition, structured nursing education and training sessions were conducted to enhance awareness of malnutrition and ensure adherence to feeding protocols.

DATA COLLECTION

Demographic characteristics and the presence of co-morbidities were retrieved from the electronic medical records of the hospital. Severity and nutritional risk were assessed for all patients using the Acute Physiology and Chronic Health Evaluation (APACHE), Sequential Organ Failure Assessment (SOFA), Nutritional Risk Screening (NRS), Nutrition Risk in the Critically Ill (NUTRIC), and Nutrition Reassessment Scores. Clinical outcomes, including the duration of mechanical ventilation, length of stay in the ICU, and total duration of hospitalization, were recorded for each patient.

STATISTICAL ANALYSIS

The normality of the data was tested using the Shapiro-Wilk test. Numerical variables were expressed as median and interquartile range (IQR), and categorical data were expressed as numbers and percentages. Patients were stratified retrospectively into groups based on mean calorie and protein deficits using *a priori*, clinically relevant thresholds (<2000 vs. ≥2000 kcal for calorie deficit and <75 vs. ≥75 g for protein deficit). Numerical variables in the two groups were compared using the independent Mann-Whitney U test. Categorical variables were compared using the $\chi2$ test. Fisher's exact test was employed instead of the $\chi2$ test when >20% of cells had expected frequencies <5. Further, survival in the two groups was plotted using the Kaplan-Meier survival curves and were compared using the log-rank test.

To evaluate whether nutritional deficits were independently associated with ICU mortality, multivariable logistic regression analysis was performed. Covariates were selected based on clinical relevance and/or statistical significance on univariate analysis ($p<0.05$). Covariates included age, APACHE-II score, SOFA score, NUTRIC score, and the presence of chronic liver disease. Two regression models were constructed. In the first model, cumulative calorie and protein deficit groups were entered as categorical predictors. In the second model, mean daily calorie and protein deficits were analyzed as continuous variables. Effect sizes were reported as adjusted odds ratios (OR) with 95% confidence intervals (CI), expressed per 100 kcal/day increase in mean daily calorie deficit and per 10 g/day increase in mean daily protein deficit. Model discrimination was assessed using the area under the receiver operating characteristic curve (AUC).

A two-tailed p-value of <0.05 for all analyses was considered statistically significant. All statistical analyses were performed using STATA 17.0 (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC).

Results

DEMOGRAPHIC CHARACTERISTICS

A total of 1073 patients were included in the study, of which 65.1% (N=700) were males. The mean age of the cohort was 63.04±14.87 [age range: 19-97 years; median: 65 (53-74)] and the body mass index (BMI) was 25.67±9.32 kg/m² [median: 24.6 (21.5-28.3)]. Based on cumulative calorie and protein deficits calculated retrospectively, patients were categorized into two groups using *a priori*, clinically relevant thresholds: those with a calorie deficit of <2000 kcal and those with a deficit of ≥2000 kcal; those with protein deficit <75 g and ≥75 g. There were no statistically significant differences in age, BMI, severity scores, or nutritional risk scores between the groups stratified by calorie deficit (<2000 vs. ≥2000 kcal) or by protein deficit (<75 vs. ≥75 g) (Table 1).

Table 1: Comparison of demographic details, severity scores and nutrition risk scores between the calorie and protein deficit groups.

Covariates	Calorie deficit [Median (IQR)]			Protein deficit [Median (IQR)]		
	<2000	**≥2000**	**p-value**	**<75**	**≥75**	**p-value**
Age (years)	66 (54-75)	63 (52-73)	0.057	66 (54-75)	63 (52-72)	0.058
BMI (kg/m²)	24.75 (21.6-28.6)	24.6 (21.3-25.1)	0.071	24.3 (21.2-28.1)	25.1 (21.9-28.6)	0.066
APACHE-II	18 (13-23)	19 (13-23)	0.928	18 (13-23)	19 (13-23)	0.938
SOFA	7 (4-11)	7 (3-11)	0.206	7 (4-11)	7 (3-11)	0.478
NRS score	3 (3-4)	3 (3-4)	0.5	4 (3-4)	3 (3-4)	0.163
Nutrition reassessment score	3 (3-4)	3 (3-4)	0.567	4 (3-4)	3 (3-4)	0.106
NUTRIC score	5 (3-6)	4 (3-6)	0.573	5 (3-6)	4 (3-6)	0.450

APACHE, Acute Physiology and Chronic Health Evaluation; BMI, Body Mass Index; NRS, Nutritional Risk Screening; NUTRIC, Nutrition Risk in the Critically Ill; SOFA, Sequential Organ Failure Assessment

DISTRIBUTION OF COMORBIDITIES

The distribution of comorbidities was comparable between the calorie (<2000 vs. ≥2000 kcal) and protein (<75 vs. ≥75 g) deficit groups, except for chronic liver disease (Table 2).

Table 2: Comparison of comorbidities between calorie deficit groups

Covariates	Calorie deficit [N (%)]			Protein deficit [N (%)]		
	<2000 (N=492)	≥2000 (N=581)	p-value	<75 (N=566)	≥75 (N=507)	p-value
Diabetes Mellitus	238 (48.37)	275 (47.33)	0.801	280 (49.47)	232 (45.76)	0.249
Hypertension	307 (62.40)	345 (59.38)	0.344	342 (60.42)	311 (61.34)	0.807
Chronic Kidney Disease	80 (16.26)	89 (15.32)	0.735	98 (17.31)	71 (14.00)	0.161
Chronic Liver Disease	63 (12.80)	101 (17.38)	**0.046**	72 (12.72)	92 (18.15)	**0.017**
Ischemic Heart Disease	118 (23.98)	125 (21.51)	0.721	137 (24.20)	106 (20.91)	0.224

IMPACT OF CALORIE AND PROTEIN DEFICIT ON CLINICAL OUTCOMES

Patients in the ≥2000 kcal deficit group had significantly longer ICU and hospital stays, as well as a prolonged duration of mechanical ventilation compared with those in the <2000 kcal group. Similarly, higher protein deficit was significantly associated with longer ICU stay and duration of mechanical ventilation; however, no significant difference in total hospital stay was observed between the protein deficit groups (Table 3).

Table 3: Comparison of clinical outcomes between the calorie and protein deficit groups

LOS	Calorie deficit [Median (IQR)]			Protein deficit [Median (IQR)]		
	<2000	≥2000	p-value	<75	≥75	p-value
Ventilator	4 (0-7)	5 (2-9.75)	**<0.001**	4 (1-8)	5 (2-9)	**0.014**
ICU	8 (6-12)	10 (7-15)	**<0.001**	9 (6-13)	10 (7-14)	**0.001**
Hospital	15 (10-24)	16 (11-24)	**0.02**	16 (11-24)	16 (11-24)	0.461

LOS, length of stay; ICU, intensive care unit; IQR, interquartile range

The mortality rates in the <2000 and ≥2000 calorie deficit groups were 22.2% (109/492) and 31.3% (182/581), respectively. The mortality rates in the <75 and ≥75 protein deficit groups were 24.7% (140/566) and 29.8% (151/507), respectively. The odds of survival in the <2000 groups was higher than that in the ≥2000 group (3.514 vs. 2.192), with OR of 1.603 (95% CI, 1.217-2.112). A similar trend was observed in the protein deficit groups; however, the difference was not statistically significant (Table 4).

Table 4: Association of calorie (<2000 vs. ≥2000 kcal) and protein (<75 vs. ≥75 g) deficit groups with survival in critically ill patients.

Group		Mortality rate	Odds of Survival	Odds Ratio (95% CI) Group 1 vs Group 2	p-value	χ^2
Calorie deficit	**<2000**	22.2%	3.514	1.603 (1.217-2.112)	**0.001**	10.877
	≥2000	31.3%	2.192			
Protein deficit	**<75**	24.7%	3.043	1.291 (0.986-1.690)	0.063	3.197
	≥75	29.8%	2.358			

CI, confidence interval

Additionally, Kaplan-Meier analysis revealed a statistically significant difference in survival between the two calorie deficit (Log-rank test, χ^2=4.0358, p-value=0.002) and protein deficit groups (Log-rank test, χ^2=4.685, p-value=0.008; Figures 1 and 2).

Figure 1: Kaplan-Meier survival plot between the calorie deficit groups.

Comparison between groups with a calorie deficit ≥2000 kcal versus <2000 kcal revealed significantly lower survival probability in the high-deficit group (log-rank test, p=0.002).

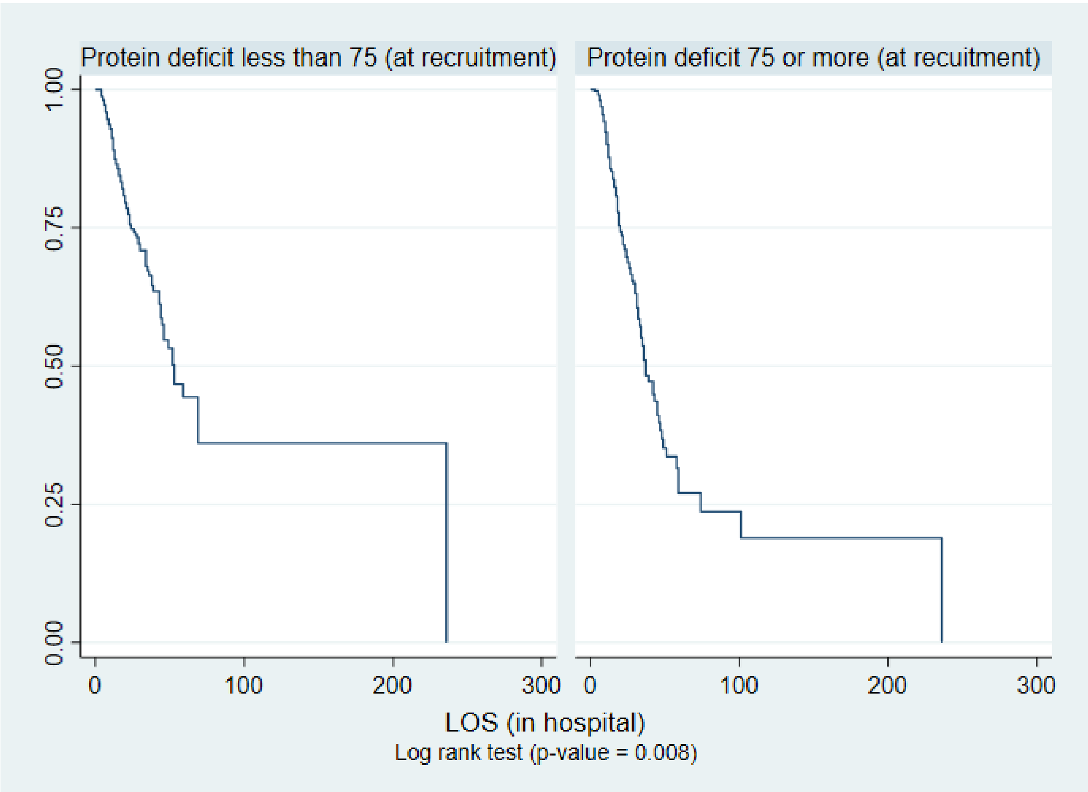

Figure 2: Kaplan-Meier survival plot between the protein deficit groups.
Comparison between groups with a protein deficit ≥75 g versus <75 g revealed significantly lower survival probability in the high-deficit group (log-rank test, p=0.008).

MULTIVARIABLE ANALYSIS OF ICU MORTALITY
After adjustment for age, APACHE-II score, SOFA score, NUTRIC score, and chronic liver disease, cumulative calorie deficit ≥2000 kcal remained independently associated with ICU mortality (adjusted OR 1.54; 95% CI 1.12–2.10; p=0.008). In contrast, cumulative protein deficit ≥75 g was not independently associated with mortality after adjustment (adjusted OR 1.19; 95% CI 0.89–1.60; p=0.23).

TIME-ADJUSTED DEFICIT ANALYSIS
When mean daily deficits were analyzed to mitigate time-dependent bias, mean daily calorie deficit remained independently associated with ICU mortality, with an adjusted OR of 1.05 per 100 kcal/day increase (95% CI 1.00–1.09; p=0.044). Mean daily protein deficit did not retain statistical significance after adjustment (adjusted OR 1.07 per 10 g/day increase;

95% CI 0.96–1.20; p=0.21). The multivariable model demonstrated moderate discrimination (AUC=0.68).

Discussion

The present study adds to the growing body of evidence suggesting that caloric and protein deficits in critically ill patients are not merely passive indicators of baseline disease severity but may reflect clinically relevant nutritional inadequacy associated with adverse outcomes. We observed that a cumulative energy deficit of ≥2000 kcal during ICU stay was significantly associated with increased mortality, prolonged ICU and hospital stay, and extended duration of mechanical ventilation. These findings, although associative rather than causal, underscore that nutritional deficits—even those considered modest relative to previously reported thresholds[17,18,24]—can carry serious clinical consequences when accrued early during critical illness. Nutritional deficits likely reflect a complex interaction between illness severity, feeding intolerance, and interruptions in nutrition delivery.

We observed notably higher unadjusted mortality rate in the group with a calorie deficit ≥2000 kcal (31.3%) compared to those with deficits <2000 kcal (22.2%), corresponding to significantly higher odds of survival in the lower-deficit group (OR=1.603; 95% CI, 1.217–2.112; p=0.001). Importantly, after multivariable adjustment for age, severity scores, and chronic liver disease, cumulative calorie deficit ≥2000 kcal remained independently associated with ICU mortality. Similar trends were observed in relation to protein deficits; however, the association between protein deficit and mortality did not remain statistically significant after adjustment, suggesting that calorie deficit may represent the more robust predictor in this cohort. Notably, baseline characteristics, comorbidities, severity scores (APACHE II, SOFA), and nutritional risk scores did not differ significantly between deficit (calorie and protein) groups, indicating that the observed associations were unlikely to be confounded by illness severity or underlying risk profiles. Instead, nutritional deficits appear to be a potentially modifiable factor that may influence clinical trajectory in this population, although these associations should be interpreted in the context of the complex interplay between illness severity, ICU length of stay, and duration of nutritional exposure.

Nutritional deficits are relevant in ICU patients because critical illness induces a hypermetabolic and catabolic state characterized by rapid proteolysis and energy expenditure. Without adequate nutritional support, the body preferentially breaks down skeletal and respiratory muscle to meet energy demands. This leads to ICU-acquired weakness, delays in weaning from mechanical ventilation, and functional impairment post-discharge.[1,20] In addition to muscular catabolism, energy and protein deficits blunt both innate and adaptive immune responses, predisposing patients to infections, sepsis, and slower recovery from surgical or traumatic insults.[1,2,25,26] Protein is particularly essential for wound healing, collagen synthesis, and maintenance of tissue integrity. This increases the risk of in-hospital complications as well as poor rehabilitation and functional disability post-discharge. Furthermore, prolonged underfeeding exacerbates systemic inflammation, impairs organ perfusion, and contributes to metabolic derangements that hinder recovery of cardiac, renal, and pulmonary function.[2,14,20] These biological mechanisms provide a robust explanatory framework for our findings and align with prior studies demonstrating that underfeeding has been associated with increased morbidity and mortality in the ICU.

Our identification of 2000 kcal and 75 g as thresholds for defining high versus low caloric and protein deficits was based on a data-driven, hypothesis-generating approach, guided by deficit ranges previously reported in observational studies to be associated with adverse outcomes. Prior studies have demonstrated that lower energy and protein delivery, particularly when intake falls below prescribed targets, is associated with higher mortality and prolonged ICU stay,[12,22] while cumulative deficits of ≥6000 kcal and ≥300 g protein have been linked to poorer functional status at ICU discharge.[27] These ranges provide clinically relevant benchmarks in an observational context and should be interpreted as exploratory markers rather than definitive cutoffs. Although exploratory, this threshold is physiologically relevant: it approximates the daily energy requirement of critically ill adults, which ranges from 1900 to 2500 kcal/day depending on body weight and metabolic demand.[14-16] In a hypercatabolic state, failure to meet even one day of requirements can lead to rapid cumulative deficits with systemic consequences. In critically ill patients with elevated metabolic demands, such an energy shortfall may rapidly precipitate catabolism, immune dysfunction, impaired wound healing, and prolonged organ dysfunction, delaying recovery.[10,28-30]

Importantly, because cumulative nutritional deficits are inherently influenced by ICU length of stay, which itself is closely linked to illness severity and outcomes, we performed additional time-adjusted analyses using mean daily calorie and protein deficits to mitigate duration-dependent bias. Mean daily calorie deficit remained independently associated with ICU mortality after adjustment, although the magnitude of effect was modest (adjusted OR 1.05 per 100 kcal/day increase). This suggests that sustained underdelivery of energy, rather than duration of ICU exposure alone, may contribute to adverse outcomes. However, the relatively small effect size indicates that nutritional deficit likely represents one of multiple interacting determinants of ICU mortality. Mean daily protein deficit did not retain statistical significance after adjustment.

Our findings are consistent with prior observational data showing that delivery of <70% of estimated caloric needs during early days (day 3–7) of ICU stay is associated with higher 28-day mortality; patients who achieved ≥70% of their caloric targets in this early window had significantly lower mortality, emphasizing the importance of timely and adequate feeding.[22] Similarly, Puruhita et al. reported that an energy deficit of 2,000 kcal by day 3 increased mortality risk more than eightfold in critically ill patients.[31] Previous studies have reported even higher thresholds for adverse outcomes—Villet et al. found that patients with a cumulative energy deficit of −12,600 ± 10,520 kcal experienced substantially higher complication rates,[17] while Dvir et al. observed similar associations at weekly deficits >4,700 kcal.[18] The comparatively lower threshold identified in our study suggests that physiologic tolerance to underfeeding may be narrower than previously considered, and adverse effects may begin earlier in the course of critical illness. This underscores the need for more proactive monitoring and timely correction of nutritional deficits in critically ill patients.

Protein remains an overlooked aspect of the nutritional equation. While the focus in critical care nutrition has historically centered on calorie adequacy, growing evidence supports protein as a distinct and critical determinant of clinical outcome.[12,14,15,21,25] Critically ill patients often receive calorie-dense yet protein-poor regimens, which may preserve energy intake while allowing muscle loss to progress unchecked, ultimately attenuating the potential benefits of nutritional therapy. Observational data and post-hoc analyses of randomized trials suggest that protein intakes of 1.2–2.0 g/kg/day are associated with improved nitrogen balance, reduced ICU-acquired weakness, and better post-discharge functionality, even in the absence of full calorie delivery.[11,14,15,30]

Calorie and protein deficits are biologically and clinically interrelated, as patients who fail to meet energy targets are also likely to receive inadequate protein. While combined analyses may further refine risk stratification, we analyzed calorie and protein deficits separately to reflect real-world ICU practice, where energy and protein prescriptions, formulations, and barriers often differ. In our cohort, protein deficits paralleled caloric shortfalls and were similarly associated with increased mortality, suggesting the need for equal emphasis on meeting protein targets. This aligns with the mechanistic role of protein in immune function, tissue repair, and preservation of lean mass, which are critical factors in ICU recovery,[12,21,25] and supports guideline recommendations for early and prioritized protein delivery.[14,15] Moreover, emerging randomized and post-hoc trial data suggest that early high protein intake may improve recovery-related outcomes, with potential effects on mechanical ventilation duration, underscoring the importance of early nutrition delivery.[32] This calls for a shift in clinical focus from solely caloric adequacy to balanced macronutrient targets, with specific attention to protein goals during critical illness. Future studies should also explore the joint impact of combined deficits.

In our institution, a structured "catch-up and match-up" strategy is routinely employed to address interruptions in nutritional delivery. This includes early initiation of enteral or parenteral nutrition, daily monitoring of actual versus prescribed intake, and timely supplementation tailored to individual requirements. Despite these interventions, nutritional needs remained unmet in a subset of patients due to feeding intolerance, interruptions for procedures, or other barriers. A large international cohort data from 63 countries (NutritionDay ICU) reported variability in nutrition support that is often delayed and rarely reaches the recommended targets.[33] This highlights the ongoing challenges in achieving nutritional goals and underscores the importance of ongoing evaluation, proactive and flexible feeding strategies, and multidisciplinary collaboration in optimizing nutrition delivery in the ICU.

In general, these guidelines advocate a progressive approach to nutrition delivery, aiming to achieve approximately 70–100% of estimated energy requirements during the first week of ICU stay while avoiding both significant underfeeding and overfeeding. Observational data from European ICU cohorts, including the EuroPN ICU nutrition cohort study, further support this approach, demonstrating that moderate energy and protein delivery is associated with improved survival and successful ventilator weaning.[34] Conversely, excessive energy delivery in the acute phase has been associated with adverse metabolic consequences, including hyperglycemia, increased CO_2 production, and hepatic steatosis, which may negatively impact clinical outcomes.[17,18,34] Recent high-quality reviews further emphasize individualized, phase-specific nutritional strategies in critically ill patients.[35] The multivariable model in our study demonstrated moderate discrimination (AUC=0.68), indicating that nutritional deficit represents only one component of a multifactorial risk profile in critically ill patients.

This study has several limitations. The single-center design may limit generalizability, and the exclusion of patients with incomplete nutritional data may have introduced potential selection bias. However, the observed associations are consistent with prior studies, including international and Indian ICU cohorts, suggesting external validity.[21,23] Nevertheless, a major strength of this study lies in the use of a large, comprehensive electronic health record dataset that enabled precise quantification of cumulative caloric and protein deficits over time, and their relationship with robust outcome measures. Additionally, cumulative nutritional deficits are inherently influenced by ICU length of stay, introducing time-dependent bias. Patients with prolonged ICU courses are more likely to accrue larger deficits, even with similar daily feeding practices, and also have a higher baseline risk of adverse outcomes, making it difficult to fully disentangle the independent effect of nutritional deficits from duration of illness. Thus, cumulative deficit serves as a clinically relevant marker of sustained nutritional inadequacy during critical illness, particularly when early deficits are not adequately corrected. Therefore, nutritional deficits should be considered risk markers rather than independent drivers of outcomes.

Conclusion

This study underscores the critical role of early and adequate nutritional support in improving outcomes for critically ill patients. Our study identified clinically relevant thresholds—calorie deficit ≥2000 kcal and protein deficit ≥75 g—and found that these are strongly and consistently associated with adverse clinical outcomes, including increased mortality, longer ICU stay, and greater mechanical ventilation requirements. Thus, calorie and protein deficits may manifest clinical consequences much earlier and at lower thresholds than previously assumed. Nutrition, unlike clinical variables, represents a modifiable aspect of care and an actionable domain. Nutritional adequacy can be influenced and optimized through timely intervention, targeted supplementation, and individualized planning. Our findings support the implementation of structured nutrition protocols that prioritize early initiation, frequent monitoring, and adaptive supplementation to meet individualized energy and protein requirements. Importantly, the identified nutritional deficit thresholds may serve as early clinical warning markers, helping to identify patients at risk for prolonged ICU stay and poorer prognosis, thereby facilitating timely recognition and targeted nutritional intervention. Future prospective studies should seek to validate the early nutritional thresholds and define phase-specific macronutrient requirements across different ICU populations.

Conflicts of Interest Statement

The authors have no conflicts of interest to declare.

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