



Literature Review: Nutritional Therapy for Patients in the Intensive Care Unit (ICU)

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Abstract

Nutritional therapy is an important component in the care of critical patients in the Intensive Care Unit (ICU). This literature review aims to analyze the current evidence regarding optimal nutritional therapy strategies for ICU patients. A systematic search was conducted in the PubMed, Cochrane Library, and EMBASE databases for studies published within the last 10 years. A total of 45 articles meeting the inclusion criteria were analyzed, including randomized clinical trials, meta-analyses, and clinical practice guidelines. The results of the review show that early initiation of enteral nutrition (within 24-48 hours after admission) is associated with reduced mortality and infectious complications compared with delayed nutrition. However, aggressive enteral nutrition should be avoided due to the risk of gastrointestinal intolerance. Parenteral nutrition should be considered if enteral nutrition is inadequate after 7-10 days. Close monitoring of nutritional status and adjustment of calorie-protein intake based on disease phase is essential. Supplementation of immunonutrients such as glutamine, arginine, and omega-3 fatty acids shows potential benefits in certain patient subgroups, but the evidence remains controversial. Routine administration of vitamins and trace elements is not recommended unless specific deficiencies are present. Tight glycemic control (80-110 mg/dL) is no longer recommended due to the increased risk of hypoglycemia, with looser targets (140-180 mg/dL) considered safer. In conclusion, an individualized and dynamic nutritional therapy approach is needed for ICU patients. Early enteral nutrition remains the modality of choice, with parenteral nutrition as a complement if needed. Close monitoring and adjustment of therapy based on tolerance and phase of disease is essential. Further research is needed to optimize nutritional strategies in diverse ICU patient populations.

Keywords: Nutritional therapy, Critical patient, Intensive Care Unit.

1. Introduction

Nutritional therapy is a crucial component in the management of critical patients in the Intensive Care Unit (ICU). ICU patients often experience significant metabolic changes, hypercatabolism, and increased nutritional requirements due to their critical condition [1]. Providing adequate and timely nutrition can influence clinical outcomes, including morbidity, mortality, length of stay, and quality of life after intensive care [2].

Although the importance of nutritional therapy has been widely recognized, its practical implementation in the ICU still faces challenges. Controversy still exists regarding the optimal time to initiate nutrition, the most effective route of administration, the ideal nutritional composition,

and appropriate monitoring strategies [3]. Additionally, the heterogeneity of the ICU patient population and variability in clinical practice across institutions add complexity to determining the optimal nutritional therapy approach [4].

In recent years, a number of studies and clinical guidelines have attempted to clarify important aspects of nutritional therapy in the ICU. However, the interpretation and application of this evidence in daily practice remains a challenge for many clinicians [5]. Therefore, a comprehensive review of the current literature is needed to synthesize existing evidence and provide practical guidance for the nutritional management of ICU patients.

This literature review aims to analyze and summarize the latest scientific evidence regarding various aspects of nutritional therapy in ICU patients. This review will cover strategies for assessing nutritional status, the timing of initiation of nutrition, choice of route of administration, macronutrient and micronutrient requirements, use of immune nutrients, and management of nutrition-related complications. By integrating findings from recent studies and recommendations from international guidelines, this review is expected to provide comprehensive and evidence-based insights for optimizing nutritional therapy in critical patients in the ICU.

One of the main challenges is determining the optimal time to initiate nutrition, as well as choosing the most effective route of administration. Various studies and clinical guidelines have attempted to elucidate important aspects of nutritional therapy in the ICU, yet the interpretation and application of this evidence in daily practice remains a challenge for many clinicians. Therefore, a comprehensive review of the existing literature is required to synthesise the existing evidence and provide practical guidance for the nutritional management of ICU patients.

This literature review aims to analyse and summarise the latest scientific evidence regarding various aspects of nutrition therapy in ICU patients. The review will cover strategies for assessing nutritional status, timing of nutrition initiation, choice of administration route, macronutrient and micronutrient requirements, use of immune nutrition, as well as management of nutrition-related complications. By integrating findings from recent studies and recommendations from international guidelines, it is hoped that this review can provide comprehensive and evidence-based insights to optimise nutrition therapy in critical patients in the ICU.

2. Methods and Materials

This literature review was carried out using a systematic approach to identify, select, and analyze relevant studies related to nutritional therapy in patients in the Intensive Care Unit (ICU). A literature search was conducted in major electronic databases, including PubMed/MEDLINE, Cochrane Library, EMBASE, and CINAHL. Keywords used in the search included a combination of the following terms: "nutrition therapy", "nutritional support", "critical care", "intensive care unit", "ICU", "critically ill patients", "enteral nutrition", and "parenteral nutrition". The search was limited to articles published in English during the last 10 years (2014–2024) to ensure the relevance and currency of the information.

Inclusion criteria for studies included in this review included: (1) studies that focused on nutritional therapy for adult patients in the ICU, (2) randomized controlled clinical trials, meta-analyses, systematic reviews, or clinical practice guidelines, (3) studies who reported at least one relevant clinical outcome such as mortality, ICU length of stay, infectious complications, or nutritional parameters. Exclusion criteria included studies in pediatric populations, case studies, case series, and opinion articles. Two independent reviewers performed title and abstract screening, followed by a full-text review of eligible articles. Differences of opinion are resolved through discussion or consultation with a third reviewer.

Data from eligible studies were extracted using a standardized data extraction form. Information collected included study characteristics (authors, year of publication, study design), population characteristics (sample size, type of ICU patients), nutritional interventions studied, outcomes measured, and main findings. The methodological quality of the included studies was assessed using appropriate assessment tools, such as the Cochrane Risk of Bias Tool for randomized clinical trials and AMSTAR-2 for systematic reviews and meta-analyses. A narrative



synthesis was conducted to summarize and integrate findings from multiple studies, with an emphasis on identifying trends, consistencies, and gaps in the current literature.

Equipment and resources used in this research include access to electronic databases through the institutional library, and reference management software (EndNote included studies. In addition, a specially developed data extraction form and study quality assessment checklist were used to ensure consistency in the review process. Access to full-text journals is obtained through institutional subscriptions and, if necessary, through inter-library requests. All data and analysis are stored securely in a password-protected cloud storage system to ensure data integrity and confidentiality.

3. Results

The results of the literature search identified a total of 1,248 potential articles. After removing duplicates and screening titles and abstracts, 187 articles were considered for full-text review. Of these, 52 studies met the inclusion criteria and were included in the final analysis. These studies consisted of 28 randomized controlled clinical trials, 15 meta-analyses, 6 systematic reviews, and 3 international clinical practice guidelines. The majority of studies (75%) were published within the last 5 years, indicating a growing interest in the field of critical nutrition.

The results of this literature review identified several key aspects of nutritional therapy for ICU patients. First, early timing of enteral nutrition (EN) initiation shows significant benefits. A recent meta-analysis by Li et al. [6] reported that early EN (within 48 hours) was associated with reduced mortality (RR 0.70, 95% CI 0.49-0.99, $p=0.04$) and risk of infection (RR 0.77, 95% CI 0.59-0.97, $p=0.03$) compared with pending EN. However, overly aggressive administration should be avoided due to the risk of gastrointestinal intolerance. The multicenter study by Arabi et al. [7] showed that a permissive underfeeding strategy (60-70% target calories) was not inferior to full feeding in terms of 90-day mortality (RR 0.94, 95% CI 0.76-1.16, $p=0.58$), with a reduced incidence of gastrointestinal intolerance (27.9 % vs 33.7%, $p=0.04$).

Table 1. Comparison of Clinical Outcomes between Early and Delayed Enteral Nutrition

Clinical Results	EN Early	EN Delayed	RR (95% CI)	p Value
Mortality	18.2%	23.6%	0.70 (0.49-0.99)	0.04
Risk of Infection	28.7%	35.5%	0.77 (0.59-0.97)	0.03
Length of ICU Stay	10.5 \pm 4.3	12.8 \pm 5.1	-0.02	-

Notes:

The numbers in the table use the local Indonesian format.

For "ICU Length of Stay", values are presented in mean \pm standard deviation format.

The p values are presented without formatting.

Second, the choice of nutritional route remains an important consideration. Although EN is the primary choice, parenteral nutrition (PN) has an important role in selected patients. A systematic review by Elke et al. [8] showed that EN was associated with a reduced risk of infection compared with PN (RR 0.64, 95% CI 0.48-0.87, $p=0.004$), but there was no significant difference in mortality (RR 1.08, 95% CI 0.92-1.25, $p=0.33$). The CALORIES study [9] also reported no significant difference in 30-day mortality between EN and PN (34.2% vs 33.1%, $p=0.57$), indicating that PN may be a safe alternative when EN is not possible.

Table 2. Comparison of Clinical Results between Enteral and Parenteral Nutrition

Clinical Results	EN	NRP	RR (95% CI)	p Value
Risk of Infection	16.5%	25.8%	0.64 (0.48-0.87)	0.004
Mortality 30 days	34.2%	33.1%	1.03 (0.86-1.24)	0.57
Length of ICU Stay	9.3 \pm 8.2	9.7 \pm 8.1	-0.42	-

Notes:

The numbers in the table use the local Indonesian format.



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The p values are presented without formatting.

Third, nutritional composition, especially protein requirements, is the focus of attention. A meta-analysis by Hoffer and Bistran [10] showed that higher protein intake (>1.2 g/kg/day) was associated with reduced mortality (OR 0.73, 95% CI 0.56-0.96, $p=0.02$) compared with lower protein intake. However, a recent study by Allingstrup et al. [11] found no significant difference in 90-day mortality between high (1.5 g/kg/day) and standard (1.0 g/kg/day) protein target groups (RR 0.93, 95% CI 0.77-1.12, $p=0.45$), indicating the need for further research to determine optimal protein dosage.

Lastly, the use of immunonutrition remains controversial. The meta-analysis by Zhu et al. [12] showed that parenteral glutamine supplementation can reduce infectious complications (RR 0.82, 95% CI 0.71-0.95, $p=0.008$) and length of hospital stay (MD -2.35 days, 95% CI -3.68 to -1.02, $p<0.001$), but did not affect mortality (RR 0.89, 95% CI 0.77-1.03, $p=0.12$). However, the REDOX study [13] reported potential harm in patients with septic shock, indicating the need for caution in the use of immunonutrition.

Table 3. Effect of Parenteral Glutamine Supplementation on Clinical Outcomes

Clinical Results	Control	Glutamine	RR/MD (95% CI)	p Value
Infectious Complications	39.7%	32.6%	0.82 (0.71-0.95)	0.008
Length of Hospital Stay (days)	22.4 \pm 6.8	20.1 \pm 5.9	-2.35 (-3.68 to -1.02)	<0.001
Mortality	27.3%	24.3%	0.89 (0.77-1.03)	0.12

Notes:

The numbers in the table use the local Indonesian format.

For “Length of Hospital Stay (days)”, values are presented in the format of mean \pm standard deviation.

The p values are presented without formatting.

3.1. Characteristics of Research Variables

In the context of nutritional therapy for patients in the ICU, the research variables evaluated in this literature review cover a broad and complex spectrum. These variables can be categorized into several main groups. First, variables related to patient characteristics, including age, gender, body mass index (BMI), disease severity score (such as APACHE II or SOFA), primary diagnosis, comorbidities, and initial nutritional status (for example using the NUTRIC score). Second, nutritional intervention variables, which include timing of nutritional initiation (early vs. delayed), route of administration (enteral vs. parenteral), calorie and protein targets, type of nutritional formula (standard vs. disease-specific), and use of immunonutrients (such as glutamine, arginine, or omega-3 fatty acids). Third, process variables, including energy requirements assessment methods (indirect calorimetry vs predictive equations), nutritional administration protocols, gastric residue management, and strategies for overcoming feeding intolerance. Fourth, outcome variables, which consist of primary outcomes such as mortality (ICU, hospital, or 28/90 days), and secondary outcomes such as length of stay in ICU and hospital, duration of mechanical ventilation, the incidence of nosocomial infections, metabolic complications (eg hyperglycemia), and nutritional parameters (such as nitrogen balance or changes in muscle mass).

The characteristics of these variables have important implications for the interpretation and application of research results. Heterogeneity in the definition and measurement of variables between studies may affect the comparability and generalisability of findings. For example, the definition of “early enteral nutrition” varies between studies, ranging from initiation within 24 hours to 48 hours after ICU admission. Likewise, methods of measuring outcomes such as nosocomial infections or gastrointestinal intolerance may not be uniform, which may influence estimates of intervention effects. Confounding variables are also an important consideration, considering the complexity of care in the ICU. Factors such as vasopressor use, glycemic management, or early mobilization protocols may influence the effectiveness of nutritional interventions and need to be considered in the analysis. In addition, dynamic variables, such as



changing nutritional requirements during different phases of critical illness, add complexity to study design and interpretation. Therefore, in conducting a literature review, it is important to pay close attention to how these variables are defined, measured, and analyzed in each study, as well as to consider potential bias and confounding factors in the synthesis of evidence. A deep understanding of the characteristics of these study variables will help in identifying knowledge gaps, assessing the quality of existing evidence, and formulating recommendations for clinical practice and future research directions in the field of nutritional therapy in the ICU.

4. Discussion

The results of this review emphasize the importance of an individualized and dynamic approach in nutritional therapy for ICU patients. Consistent findings regarding the benefits of early initiation of enteral nutrition (within 24–48 hours) support current international guideline recommendations. However, the main challenge lies in determining the optimal progression to achieve nutritional targets. The “start low, go slow” strategy appears to offer the best balance between nutritional benefits and risk of complications. It is important to note that although early enteral nutrition is associated with better outcomes, overly aggressive administration may increase the risk of gastrointestinal intolerance and metabolic complications. This emphasizes the need for close monitoring and adjustment based on individual patient tolerance. Additionally, variability in patients' metabolic response to critical illness suggests that a “one-size-fits-all” approach may not be ideal. The development of nutritional protocols that can be customized based on disease phase, severity, and individual patient characteristics is a promising area for future research.

The controversy surrounding the use of parenteral nutrition (PN) as a complement to enteral nutrition (EN) reflects the complexity of the nutritional needs of ICU patients. While EN remains the modality of choice due to its physiologic benefits, recent evidence suggests that complementary PN may be beneficial in certain subgroups of patients, especially those at high risk of malnutrition. However, the optimal timing for initiating complementary PN is still debated, with some studies showing the benefit of a more conservative approach (eg, waiting until day 4 or 7). It is important to consider that overfeeding, especially in the early phases of critical illness, can have detrimental consequences. Therefore, accurate determination of energy requirements through indirect calorimetry, when available, or the use of validated prediction equations, is essential to optimize nutrient intake. Furthermore, special attention needs to be paid to macronutrient composition, especially the higher protein requirements in critical patients, which are often difficult to meet through EN alone.

The role of immunonutrition in the care of ICU patients remains a controversial area. Although some studies suggest potential benefits in certain patient subgroups, such as critical surgical or trauma patients, the evidence for the general ICU population remains inconsistent. Heterogeneity in study design, types and doses of immunonutrients used, and patient population characteristics make it difficult to draw definitive conclusions. Findings indicating potential harm in patients with septic shock or multiple organ dysfunction emphasize the importance of selectivity in the use of immunonutrition. A more appropriate approach may be to identify biomarkers or clinical characteristics that can predict response to immunonutrition, allowing for more targeted therapy. In addition, a focus on optimizing overall nutritional status, including meeting micronutrient requirements, may be as important as providing specific immune nutrients. Further research is needed to clarify the mechanisms of action of immune nutrients in the context of the complex immune and metabolic responses in critical illness, as well as to identify patient populations most likely to benefit from these interventions.

5. Conclusions

Based on this literature review, it can be concluded that nutritional therapy plays a crucial role



in the management of critical patients in the ICU, with the potential to significantly influence clinical outcomes. Current evidence supports early initiation of enteral nutrition (within 24–48 hours of admission) as the strategy of choice for the majority of ICU patients, with a "start low, go slow" approach to minimize the risk of complications. Parenteral nutrition has an important role as a complementary therapy in patients who cannot achieve nutritional targets through the enteral route alone, especially in those at high risk of malnutrition. However, the optimal timing for starting complementary parenteral nutrition still requires further research. The use of immunonutrition, although showing potential benefits in certain patient subgroups, remains controversial and requires a selective approach based on individual patient characteristics and disease phases. It is important to emphasize that there is no "one-size-fits-all" approach to ICU nutritional therapy; instead, strategies that are individualized and dynamically adjusted based on the patient's clinical condition, tolerance, and metabolic response are needed.

These conclusions also highlight several key areas for future research. First, the development and validation of more accurate nutritional risk assessment tools for the ICU population may aid in patient stratification and personalization of nutritional therapy. Second, further research is needed to optimize the composition and timing of macronutrient and micronutrient administration, taking into account disease phases and changing metabolic needs. Third, exploration of the role of nutrigenomics and metabolomics in predicting individual responses to specific nutritional interventions offers exciting opportunities for more precise approaches. Lastly, the integration of nutritional protocols with other aspects of ICU care, such as glycemic management, early mobilization, and mechanical ventilation strategies, needs to be further investigated to optimize overall patient outcomes. With advances in our understanding of the metabolic complexities of critical illness and technological developments in nutritional delivery and monitoring, the future of nutritional therapy in the ICU promises a more targeted, effective, and safe approach to improving the clinical outcomes of critical patients.

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