Nutrition in intensive care in adults: review of the literature and development of evidence-based feeding protocols

Sarah Ikram, Erfan Hussain, Ali Bin Sarwar Zubairi

Abstract
The subject of nutrition in intensive care is broad. Thenutrition support therapy plays a crucial role in the management of critically ill patients. This review was carried out to address the existing controversies and to recognise the current practice guidelines for the management of nutrition in intensive care units (ICUs) in adults. A PubMed search was carried out for clinical trials addressing the current nutrition practice in ICUs, recommendations for calculating energy requirements and efficacy of an algorithmic approach to nutritional delivery in an ICU setting. Algorithms were developed and modified for the practice of nutrition in an adult ICU in a quaternary care hospital in Pakistan.

Keywords: Intensive care unit, Enteral nutrition, Parenteral nutrition, Ideal body weight, Body mass index, Gastric residual volume.

Introduction
Critical illness, stress, sepsis, trauma, surgery and burns have the potential to induce a systemic inflammatory response that places an additional demand on the body's nutritional requirements. Extensive muscle protein wasting, alteration in hormonal secretion, decreased level of physical activity, increased inflammatory mediators and hindrance in tissue perfusion have been seen in critically ill patients and prolong the need for mechanical ventilation. Anorexia is more pronounced in patients who are malnourished prior to admission in an intensive care unit (ICU) and these patients demonstrate an inability to feed themselves by mouth ranging from days to months. The documentation and prevalence of malnutrition in hospitalised patients is available in the medical literature since the 1970s and is hypothesised to have a significant role in the development of infections, pressure ulcers, impaired ventilator drive and immunosuppression resulting in increased risk of death.

Methods
For the purpose of this paper, we focused on review articles, clinical trials, consensus statements and guidelines. The review was conducted utilizing the Pub Med/Medline, Cochrane and CINAHL databases. The search resulted in a total of 1759 articles, using a Mesh word strategy specifically for: intensive care enteral and parenteral nutrition, nutritional protocols, guidelines, systematic reviews and randomised control trials. Additional limits were applied for age 18 years and above, and publications over the last 10 years. Upon screening for relevance to this paper, 48 articles were identified. Duplicate studies, case reports, animal studies, editorials and evaluation studies of the guidelines were excluded, leaving 10 relevant papers for final referencing. The remaining references were integrated from newer evidences, trials and review articles that specifically addressed variations in the existing trials and provided guidelines and methods to improve the current nutrition practice in intensive care.

To the best of our knowledge there are no nutritional support guidelines for intensive care patients in Pakistan. Furthermore there have been no studies in Pakistan to evaluate the development and efficacy of implementation of nutritional management protocols in the ICU.

An interdisciplinary working group, including a dietician and intensivist, was given a task to develop evidence-based nutrition algorithms at our university hospital. The working group also reviewed the guidelines published by Society of Critical Care Medicine (SCCM) for nutritional management of the intensive care patient. The protocols specifically address the limitations of current guidelines in...
the relevant patient population. They are not intended for the paediatric intensive care population. Protocol development took almost a year, involving literature review, readjustments of the algorithms and finally approval from the institutional critical care committee which includes intensivists from Medicine and Surgery, and representatives from Nutritional Services, Pharmacy and Nursing.

The transition of nutritional support from adjunctive to a definitive therapy
ICU patients requiring mechanical ventilation are unable to feed themselves. Therefore, patients are dependent on nutrition support therapy (also known as artificial or specialised nutrition therapy) to meet their nutritional requirement during the course of a critical illness.3 In the recent decade the role of ICU nutrition support has been rejuvenated and its status has progressed from being an adjunctive therapy to definitive therapy in the sicker population.3 The use of timely and appropriate nutritional support therapy in critically ill patients has been shown to decrease infection, bacterial translocation, incidence of pressure ulcers, ICU length of stay, and in the preservation of gastrointestinal mucosal integrity.7 Enteral nutrition (EN) has been defined as feeding provided through the gastrointestinal tract via a tube, catheter or stoma that delivers nutrients distal to the oral cavity, and Parenteral nutrition (PN) is defined as the intravenous administration of nutrients which is further divided into two categories; central and peripheral.8 Several clinical practice guidelines recommend the use of EN over PN due to its associated benefits.3,9 Controversies exist in some areas of nutrition practice and are still open to debate. The controversial areas identified are:

- Body Mass Index (BMI) Values: Caucasians vs. Asians
- Estimation of Energy Requirements
- Markers of Nutritional Status
- Enteral vs. Parenteral Nutrition in the critically ill
- Trophic versus Full Feeding
- Immunonutrition: Arginine versus Glutamine
- Gastric Residual Volume
- Nutrition in Pancreatitis: To feed or to rest the pancreas

Alteration of Body Mass Index (BMI)
BMI compares weight to height and is utilised to determine the incidence of obesity and malnutrition. Cut-off values are recommended by the World Health Organisation (WHO) and include underweight and

Table: WHO recommendations for Body Mass Index in Asians.11

<table>
<thead>
<tr>
<th>Classification</th>
<th>BMI kg/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under Weight</td>
<td>&lt; 18.5</td>
</tr>
<tr>
<td>Normal Weight</td>
<td>18.5-22.9</td>
</tr>
<tr>
<td>Over Weight</td>
<td>&gt; 23</td>
</tr>
<tr>
<td>At Risk</td>
<td>23-24.9</td>
</tr>
<tr>
<td>Obesity Class I</td>
<td>25-29.9</td>
</tr>
<tr>
<td>Obesity Class II</td>
<td>&gt;30</td>
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WHO: World Health Organisation.

gradations of excess weight that have been shown to be linked with increased risk of developing non-communicable diseases. However, these recommendations were intended for international use which reflected increased risk for development of cardiovascular diseases and Type 2 diabetes. On the basis of the available data from Asia, WHO concluded that Asians generally have a higher percentage of body fat than white people of the same age, gender and BMI (Table), and that substantial risk factors were present below the cut-offs defined by WHO.10 Therefore, the WHO expert consultation committee proposed different values for the Asian population.11 Hence, there is a need to use appropriate BMI values in our population to effectively evaluate nutritional status.

Estimation of Energy Requirements
The calculation of calories i.e. the estimation of daily expenditure remains the cornerstone of nutritional assessment. To date, indirect calorimetry remains the gold standard for the calculation of the metabolic rate.12 Multiple equations to estimate energy requirements have been cited in the literature. Guidelines have recommended the use of indirect calorimetry, if available, or use of predictive equations to calculate the calorie requirements of the ICU population.3 A recent study subjected patients on mechanical ventilator with the estimations provided by the indirect calorimetry as the intervention group and the control group was formed on the basis of calculated energy targets. The intervention group had decreased hospital mortality but increased length of stay and infections than in patients whose calorie requirement were calculated with the indirect calorimetry.13

Nonetheless, the Penn State Equation 2003 (b) has recently been validated and recommended for patients less than 60 years with a BMI 25kg/m² or higher.14,15 For the subset of obese critically ill patients aged 60 years and older, the Penn State Equation (Modified) has been validated and recommended as the preferred equation
for patients requiring mechanical ventilation.\textsuperscript{16}

**Markers of Nutritional Status**

Serum proteins such as albumin, pre-albumin and transferrin have been used as markers of adequacy of nutritional support. Low levels of these serum proteins were thought to be reflective of poor nutritional status. These surrogate markers are still considered markers of nutritional status probably due to the old belief that they reflect clinical outcomes. To address the issue, a number of studies investigated the accuracy and reliability of these serum nutritional markers and found them as reflectors of acute phase response and indicators of inflammatory process.\textsuperscript{17} Koretz analyzed 99 randomised control trials (RCTs) and studied the relationship of 12 nutritional parameters with clinical outcomes but failed to demonstrate improved clinical outcomes with changes in nutritional markers.\textsuperscript{18} The SCCM guidelines recommend that alterations in serum proteins should not be considered representative of the nutritional status of ICU patients.\textsuperscript{3}

**Enteral vs. Parenteral Nutrition in the Critically Ill: Which One to Prefer?**

The rationale that EN is cost-effective, and provides immune enhancing benefits and decreases infections laid the foundations for preference of EN over PN.\textsuperscript{3,9} Despite various clinical trials and innovation in methods, route and techniques to feed patients, controversy and uncertainty still surround the debate as to which feeding regimen is the best for the critically ill patients.\textsuperscript{19}

Cesaer et al. has addressed the timing of initiation of parenteral feeding in the critically ill population when caloric targets could not be achieved with enteral feeding alone. The study found that late initiation of PN was found to be cost saving and resulted in enhanced recovery and lesser complications.\textsuperscript{20} Another study by Heidegger et al. has addressed the concern of feeding patients who were unable to tolerate EN. The patients in this study were supplemented with parenteral nutrition when they were unable to achieve their caloric goals with EN alone during their course of critical illness. The study demonstrated that the initiation of PN 4 days after ICU admission was associated with decreased risk of hospital-acquired infections.\textsuperscript{21} The authors suggested that the lack of increase of infection with PN may be due to measures to prevent hospital-acquired infections. In the light of the presenting evidence, the question is, whether early PN support should be provided to patients to whom early EN was contraindicated. This was addressed by the investigators in the Early and Parenteral Nutrition Study.\textsuperscript{22}

In this study patients undergoing mechanical ventilation received either PN within 24 hours or standard nutritional therapy upon admission in intensive care. The results of the trial found patients had shorter mechanical ventilation days, but had no effect on 60-day mortality. However, the best time of initiation of PN still remains unknown.

In conclusion, the decision to use either EN or PN needs to be made at the bedside, based on individualised patient needs, availability of nutritional formulation and cost. However, the practice of using early total PN (TPN) in Pakistan may be problematic because of the associated cost and low level of adoption of hospital-acquired infection preventive measures which are crucial to safe delivery of PN, and to limit the possible infection risks associated with PN.

**Trophic versus Full Feeding**

Calculating and defining caloric goals has become an integral part of nutritional support therapy with the belief that it attenuates malnutrition. The right dosage of enteral feeding during the course of intensive care still remains unknown. Despite conflicting results from the findings of observational studies, older guidelines recommended the use of full feeding close to caloric goals, as the desired approach for mechanically ventilated patients.\textsuperscript{3,9} This approach depends on the concept that full caloric intake improves clinical outcomes. Contrary to the practice, investigators have found prolonged life span in species that underwent caloric restriction during critical illness.\textsuperscript{23} This observation was demonstrated in humans when results from a recent study suggested that underfeeding may reduce mechanical ventilation days and may improve mortality among ICU patients.\textsuperscript{24} Therefore, low dose feedings also called "trophic" nutrition (10-30 cc/hour or 25\% of total caloric intake) has gained momentum in practice for patients upon admission to the ICU. The Initial Trophic vs. Full Enteral Feeding in patients with Acute Lung Injury (EDEN trial) randomised medical ICU patients with acute lung injury into trophic feeding without protein supplementation versus full feeding.\textsuperscript{25} The study demonstrated similar outcomes with both regimens and the patients fed with trophic feeding had no increase in ventilator-free days in comparison to full feeding and was associated with less gastrointestinal (GI) intolerance. Arabi et al. has addressed whether caloric restriction with preservation of full protein supplementation could improve outcomes in the intensive care patients.\textsuperscript{26} The caloric goal of permissive underfeeding was set to be 40-60\% and the standard requirement was 70-100\% of prescribed calories. The results of this trial found no changes in mortality in both groups. Therefore, the utilisation of trophic feeding does not appear to affect
Figure 1: Intensive care enteral and parenteral feeding.

mortality and hence can be provided to patients during the initial course of critical illness. In conclusion, we recommend that the decision to use either trophic or full feeding regimen should be based on individualised needs, and especially on severity of malnutrition.

**Immunonutrition: Arginine versus Glutamine**

Immunonutrition is defined as "the ability of nutrients to alter, or attenuate the systemic inflammatory response in the critically ill patient". These immune-modulating formulas constitute nutrients such as omega-3 fatty acids, arginine, glutamine and antioxidants. Low levels of glutamine, a non-essential amino-acid, have been linked with adverse clinical outcomes. With the potential therapeutic benefits of these nutrients, previous guidelines have recommended the routine use of these nutrients to aid in survival. However, the

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**Figure-2: Selection of enteral formulation.**

TPN: Total parenteral nutrition.
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Figure 3: Intensive care enteral feeding: gastric residual volume protocol.

ICU: Intensive care unit. GRV: Gastric residual volumes. EN: Enteral nutrition. TPN: Total parenteral nutrition.
results of recent randomised control trials have discouraged the administration of immunonutrition in critically ill patients due to increased mortality.\textsuperscript{27}

**Gastric Residual Volume**

Intensive care patients often experience intestinal dysfunction, which includes delayed gastric emptying and dysmotility. The clinical manifestations of intestinal dysfunction commonly result in high gastric residual volumes (GRV) and vomiting, and it may place the patient at a high risk for aspiration.\textsuperscript{28} Over time, different GRV limits and thresholds were defined which led to
Figure 5: Intensive care enteral feeding: constipation protocol.
conspicuous variation and different practice algorithms throughout the world. Recently two randomised controlled trials have addressed the current practice and made recommendations for holding EN in the face of high GRVs. A study by Montejo et al. has demonstrated that gastric residual volume of up to 500ml could be well tolerated and did not increase the incidence of ventilator associated pneumonia. Furthermore, the investigators from another trial revealed that the exclusion of measuring GRV did not increase complications and affect clinical outcomes. The result of these trials weaved an important thread in the existing evidence and questions the current practice of measuring GRV in the clinical setup. This led the recommendation of a GRV threshold of up to 500mL and an evaluation of signs of physical intolerance should be made before withholding enteral feeding in intensive care as suggested by the current clinical guidelines. Also, utilisation of prokinetic agent such as erythromycin and metoclopramide has been recommended to aid in gastric emptying.

**Nutrition in Pancreatitis: To feed or to rest the pancreas**

Acute pancreatitis in its severe form can initiate a Systemic Inflammatory Response Syndrome (SIRS), and promotes catabolism. Total parenteral nutrition has been the standard of care for these patients. Growing evidence suggests that feeding through the gut may play an important role in SIRS accompanied with pancreatitis. However, controversy exists with which feeding regimens should be used (TPN vs. EN) and what route to utilise with enteral nutrition i.e. Naso-Gastric (NG) vs. Naso-Jejunal (NJ). After analysing the data, current guidelines recommend the use of enteral nutrition in patients with severe acute pancreatitis. Nally et al, in a systemic review, found NG feeding to be effective in patients with acute severe pancreatitis.
Factors Impeding Delivery of Nutritional Therapy in ICU and the Need for Feeding Algorithms

Nutrition support therapy in intensive care is suboptimal and differs between medical and surgical patients. Interruption of nutritional delivery for diagnostic procedures, cessation of feeding for the management of high GRV, underestimation of the nutritional requirement, and delayed initiation of nutritional support are some of the factors that can lead to the inadequate delivery of enteral feeding in the ICU. Studies document that a gap exists between the estimated nutritional need of the ICU patient which leads to a greater caloric deficit during their course of critical illness. The development and implementation of guidelines has been documented to be the most effective tools to ensure efficacy of treatment. A study by McClave et al. showed that only 51.6% of the nutrition therapy goal was achieved compared to the planned or prescribed therapy in intensive care patient. Guidelines published by the SCCM and American Society for Parenteral and Enteral Nutrition (ASPEN) recommend the use of feeding algorithms. The literature to date reveals several studies that have evaluated the positive impact of implementation of nutrition support algorithms on nutrition care outcomes in mechanically ventilated patients. The evidence supports the use of feeding protocols that have been shown to maximise the efficacy, and minimise the errors associated with the delivery of EN support regimens in the ICU. An algorithm is defined as a practical step-by-step version of the guideline and is a detailed sequence of action to produce a desired outcome (Figures 1-6). Ideally, translation of research findings with evidence-based protocols should define best medical practices serving as a tool to better educate patients and medical providers who are administering the protocols.

Conclusion

For many years, the importance of nutrition has been highlighted in the critical care setting. However, the appropriate selection of enteral formulation, calculation of energy requirements, the role of immunonutrition etc. have all gone through the process of evaluation and revision within the nutrition literature in ICU. This article presents the latest recommendations and controversies for the nutritional management of the critically ill adult population. As an adjunct to the paper, algorithms are provided that were modified and developed for our quaternary care hospital for the interested reader.

Acknowledgment

We are grateful to Ms. Faiza Jamal and Ms. Mozamila Mughal from the Department of Nutrition and Food Services, for editorial assistance.

Conflict of Interest: All authors disclose that we do not any financial and personal relationships with other people or organizations that could inappropriately influence (bias) our work.

Funding Source: There is no funding source for the study design, collection, analysis and interpretation of data, writing of the manuscript or decision to submit the manuscript for publication.

Ethical Approval: Not required.

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