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Review Article

Feeding adequacy among Critically Ill Patients in the Intensive Care Unit and Its Association with Clinical Outcomes: A Narrative Review

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Abstract

The Intensive Care Unit (ICU) is one of the disciplines in the hospital that provides close monitoring to the seriously ill or injured patients, also known as the critically ill patients. Critically ill patients in the ICU are usually unable to maintain volitional oral nutrition intake and therefore require nutritional therapy. Nutritional therapy can be delivered via the enteral or parenteral route. Optimal nutrition adequacy (i.e. neither underfeeding nor overfeeding) is very important for better clinical outcome. However, the problem of suboptimal feeding adequacy continues to be reported over the years. This article attempts to give an overview of the literature on feeding adequacy and the relationship of feeding adequacy with clinical outcomes among the critically ill patients in the ICU.

Keywords: *Critical Illness, Intensive Care Unit, Nutritional therapy, Feeding Adequacy*

Introduction

The Intensive Care Unit (ICU) is one of the disciplines in the hospital that provides close monitoring to the seriously ill or injured patients,[1] also known as the critically ill patients. Critically ill patients are often unconscious and may not be able to breathe adequately by themselves. Their respiratory function is often compromised and presents with low blood pressure, leading to poor oxygen perfusion to the vital organs.[2] Therefore, they are usually intubated and mechanically ventilated, given inotropes and vasopressors (drugs to support their blood pressure) and sedated. Their hemodynamic status is frequently unstable. Such conditions commonly predispose to multiorgan dysfunction as a complication, with a higher mortality rate seen in those with a higher number of organ failure.[3]

Critical illness is defined as "A life-threatening process…that ultimately involves respiratory, cardiovascular and neurological compromise".[4] Oral intake is almost always impossible in these patients,[5] necessitating the provision of artificial nutrition (i.e. feeding). Feeding the critically ill patients was previously regarded as adjunctive care (known as nutritional support). However, feeding is now regarded as nutritional therapy that may help to attenuate stress response, prevent oxidative cellular injury and favorably modulate immune responses.[6]

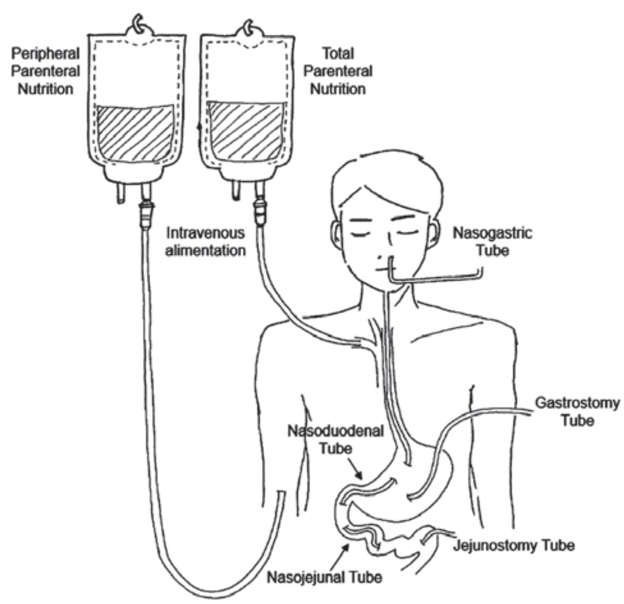

Figure-1: Enteral and Parenteral Nutrition

Enteral nutrition delivers nutrients into the gastrointestinal tract via a feeding tube. Depending on where the tube ends and how the tube is inserted into the gastrointestinal tract, enteral nutrition can be in the form of nasogastric tube, nasoduodenal tube, nasojejunal tube, gastrostomy tube and jejunostomy tube. Parenteral nutrition, also known as intravenous alimentation, delivers nutrients directly into the bloodstream. Total parenteral nutrition and peripheral parenteral nutrition delivers nutrients via the central and peripheral line, respectively.

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Nutritional therapy can be delivered via the enteral or parenteral routes (Figure 1). Enteral nutrition (EN) delivers nutrients into the gastrointestinal tract via a feeding tube for patients who are unable to maintain volitional intake. Parenteral nutrition (PN) delivers nutrients directly into the bloodstream, via central or peripheral line. Compare to PN, EN has additional benefits of maintaining gut structural and functional integrity, modulating metabolic response, and attenuating oxidative stress and the inflammatory response while supporting the humoral immune system.[7] Therefore, EN (i.e. tube feeding) acts as the first line nutritional therapy in mechanically ventilated critically ill patients who are unable to maintain volitional intake.

While the rational of initiating feeding to patients who are unable to maintain oral intake is justified, the effort to ensure patients are fed optimally based on nutrition prescription are often neglected. Studies have reported that critically ill patients receiving inadequate energy and protein are presented with poor clinical outcomes such as increased risk of infections, length of mechanical ventilations, morbidities and mortality.[7] Although the definition of underfeeding differs in various studies, but it was generally recognized that 80% of prescribed energy and protein represent adequate feeding.[8] It may be more important to ensure protein adequacy as studies have shown that improvement of clinical outcomes is associated with adequate protein intake, even after adjustment for energy adequacy.[9,10]. However, caution also need to be taken to avoid overfeeding patients, which is usually defined as feeding over 110% of energy prescribed,[11] as it is associated with complications such as hyperglycemia, azotemia, hypertriglyceridemia, electrolyte imbalance, immunosuppression, alteration in hydration status, hepatic steatosis, and difficulty waning from mechanical ventilation.[12]

Over the years, suboptimal feeding continues to be a major concern in the critically ill patient population [8,13] despite various studies reporting on the relationship between nutritional adequacy and clinical outcomes. Factors associated with suboptimal feeding need to be investigated and action is needed to address this issue. This paper aims to review the literature that reported on feeding adequacy and studies that investigated on the relationship between feeding adequacy and clinical outcomes.

Methods

The literature search was conducted in electronic databases i.e. PubMed and Google Scholars up to December 2016, limited to articles published in English language. Studies included in this narrative review are adult (≥18 years old), critically ill patients who were admitted into the ICU, and nutritional therapy (EN or PN) initiated during the ICU stay.

For prevalence of underfeeding, studies must report energy and/or protein adequacy; while for studies reporting on the relationship between nutritional adequacy and clinical outcomes, at least one of the important clinical outcomes such as mortality, infectious complications, length of ICU and/or hospital stay or duration of mechanical ventilation must be reported. Studies in non-critically ill patients were excluded. In addition, studies that investigated on PN route and timing were also excluded.

Results

Feeding Adequacy in the World, Asia & Malaysia

Several single-center studies had reported the energy and/or protein adequacy among critically ill patients (Table 1). McClave et al[13] showed that ICU patients (n=44) received about 51.6% of their targeted calorie requirement, while De Jonghe and colleagues[14] found that 71% of calorie requirement was effectively delivered by both EN and PN route. On the other hand, Binnekade et al[15] reported on average about 66% and 54% of energy and protein respectively was delivered among the 403 critically ill patients investigated.

On the global level, two international, prospective, observational study was conducted in year 2007 and 2008. In 2007, 158 ICUs from 20 countries with 2946 mechanically ventilated patients who stayed in ICU for at least 72 hours showed that average nutritional adequacy across sites was 59% (range, 20.5%-94.4%) for energy and 60.3% (range, 18.6%-152.5%) for protein.[16] In year 2008, the second study involved 179 ICU from 18 countries with the same patient population (n=2956) showed that the average energy adequacy across sites was 56.2% (range, 20.3%-90.1%).[17]

The most recent international multi-center observational study across 6 different geographic regions (Europe & South Africa, Canada, Australia & New Zealand, Latin America, Asia & USA) from 26 countries, 201 ICUs and 3390 patients showed that on average, patients receive 61.2% ± 29.4% and 57.6% ± 29.6% of prescribed energy and protein, respectively, with a mean energy balance of - 695 ± 532 kcal/day.[8] When zoomed into Asia, a result lower than the international average was seen. On average, patients received 53.5% ± 28.0% and 51.9% ± 30.1% of prescribed energy and protein, respectively, with a mean energy balance of -736 ± 480 kcal/day. The prevalence of iatrogenic underfeeding (defined as received <80% of prescribed energy) was 74% at the international level, and 82% for Asia region.[8]

In Malaysia, three single-center studies had been conducted to investigate feeding adequacy among critically ill patients. A small cross-sectional study in Hospital Selayang among critically ill patients on total enteral nutrition (n=67) presented by Mageswary et al[18] showed that before appropriate feeding protocol was implemented, about 69.0% of patients achieved goal calorie (>70% of prescribed calorie) on day 5 after feeding initiation. Yip et al[19] showed that 66% of patients achieved 80% of prescribed energy within 3 days of admission at Universiti Malaya Medical Center. Lee et al[20] in their preliminary study in a Malaysian public hospital showed that the average energy and protein adequacy was 71.8% and 62.4%; while patients with high nutrition risk had lower adequacy, with average adequacy of 67.9% and 60.3% for energy and protein, respectively.

In summary, critically ill patients received approximately 50-70% of their energy and protein requirements.

Table 1: Studies investigated feeding adequacy among critically ill patients

First Author, year (country)	Population	Sample Size	Route	ER and/or PR	Energy and/or Protein delivered
McClave et al., 1999[13] (USA)	Mixed ICU	44	EN	ER: 25-35 kcal/kg/d	51% of ER
De Jonghe et al., 2001[14] (France)	Medical ICU	51	EN (12%), PN (28.3%), or Mixed (58.7%)	ER: Harris-Benedict Equation	71% of ER
Binnekade et al., 2005[15] (Netherlands)	Medical ICU	403	EN	ER: 25 kcal/kg/d PR: 1.5 g/kg/d	66% of ER 54% of PR
Cahill et al., 2010[16] (20 countries)	Mixed ICU	2946	EN (61.7%), PN (11.8%), or Mixed (6.7%)	Determined by attending healthcare professionals	59% of ER 60.3% of PR
Heyland et al., 2010[17] (18 countries)	Mixed ICU	2956	EN (71.6%), PN (6.0%), or Mixed (14.0%)	Determined by attending healthcare professionals	56.2% of ER
Heyland et al., 2014[8] (26 countries)	Mixed ICU	3390	EN (77%), PN (6%), Mixed (15%)	Determined by attending healthcare professionals	61.2% of ER 57.6% of PR Asia: 53.5% of ER 51.9% of PR
Malaysia					
Mageswary et al., 2013[18] (Malaysia)	N.R	67	EN	Determined by attending dietitian	69.0% of ICU patients achieved 70% of ER on day 5 after feeding initiation
Yip et al., 2014[19] (Malaysia)	Mixed	77	EN	ER: 25 kcal/kg/d	66% of patients achieved 80% of ER within 3 days of ICU admission
Lee et al., 2016[20] (Malaysia)	Mixed	25	EN	ER: 25 kcal/kg/d PR: 1.2 g/kg/d	78.2% of ER 62.4% of PR High nutrition risk: 67.9% of ER 60.3% of PR

ICU: Intensive Care Unit, EN: Enteral Nutrition, PN: Parenteral Nutrition, ER: Energy Requirement, PR: Protein Requirement

Feeding adequacy and its implication to clinical outcomes

Inadequate feeding among critically ill patients is associated with poorer clinical outcomes such as increased infectious complication, length of ICU and hospital stay, duration of mechanical ventilation, and mortality, although such association was not consistently demonstrated in recent studies. The association between feeding adequacy and clinical outcomes are reviewed.

Small observational studies

About eight small observational studies (Table 2) among critically ill patients conducted in various countries demonstrated the association between underfeeding and poorer clinical outcome. In 2005, Villet et al[21] conducted a prospective observational study on 48 surgical patients who stayed in ICU for ≥5 days. It was shown that negative energy balance correlated with increase length of stay (p=0.0001), infections (p=0.0042) and length of mechanical ventilation (p=0.0002). Rubinson et al[22] studied 138 medical ICU patients who was nil by mouth for ≥96 hours and showed that after adjustment for potential confounders, patients who received ≥25% of recommended calories was associated with a significantly lower risk of bloodstream infection [relative hazard 0.27, 95% confidence interval (CI), 0.11-0.68]. Dvir et al (2006) in a prospective study of 50 ICU patients also found that patients with negative energy balance of >4000 kcal has strong association with complications such as respiratory distress syndrome (p=0.0003), sepsis (p=0.0035) and renal failure (p=0.0001).

In a retrospective study of 295 patients, Tsai et al[23] demonstrated that patients receiving lower energy delivery was 2.43 times at risk of ICU mortality than high energy

Table 2: Observational Studies investigating the relationship between feeding adequacy and clinical outcomes.

First Author, year (country)	Study Design	Population	Sample Size	Main Findings
Small Observational Studies				
Rubinson et al. 2004[22] (USA)	Prospective	Medical ICU	138	Patients who received ≥25% of ER compared with <25% of ER had significant lower risk of bloodstream infection after adjustment for SAPS II
Villet et al., 2005[21] (Switzerland)	Prospective	Surgical ICU	48	Cumulated energy deficit after 7 days correlated with both total and infectious complications
Petros et al., 2006[41] (Germany)	Prospective	Medical ICU	61	Patients who took longer time to achieve target ER (≥4 days) compared with shorter time (<4 days) had significant higher mortality rate (73.3% vs 26.1%)
Dvir et al., 2006[42] (Israel)	Prospective	Mixed ICU	50	Maximum negative energy balance is associated with ARDS, sepsis, renal failure, pressure sores, need for surgery and total complications rate
Faisy et al., 2009[43] (France)	Retrospective	Medical ICU	38	Patients with mean energy deficit ≥1200 kcal/d had a higher ICU mortality rate than patients with lower deficit after the 14th ICU day
Tsai et al., 2011[23] (Taiwan)	Retrospective	Medical ICU	295	Patients who received <60% of ER had 2.43 times higher ICU mortality than ≥ 60% of ER
Heyland et al., 2011[24] (Canada)	Prospective	Mixed ICU	207	Increase 1000 kcal/d of energy and 30g/d of protein is associated with lower risk of developing at least 1 probable infection after >96 h of ICU admission
Allingstrup et at., (Denmark)	Prospective	Mixed ICU	113	Increased protein provision was associated with significant 2012[9] decrease hazard ratio of death, even after adjusted for baseline APACHE II, SOFA and age
Large Observational Studies				
Alberda et al., 2009[25] (37 countries)	Prospective	Mixed ICU	2772	Increased 1000 kcal/d of energy and 30g/day of protein is associated with significant reduced 60-d mortality and increased ventilator-free days. This association is only present in patients with BMI <25 and ≥35
Arabi et al., 2010[29] (Saudi Arabia)	Prospective	Mixed ICU	523	A dose-effect relationship between increasing calorie intake and higher hospital mortality, risk of ICU-acquired infections, ventilator-associated pneumonia, duration of mechanical ventilation, and length of stay in ICU and hospital.
Heyland et al., 2011[30] (33 countries)	Prospective	Mixed ICU	7872	After excluding days after permanent progression to oral intake and number of evaluable days, achieving approximate 80% of ER is associated with significant reduction in mortality in patients who stay >96 h in ICU
Elke et al., 2014[26] (33 countries)	Prospective	Mixed ICU	2270	In ICU patients with sepsis and/or pneumonia, increased 1000 kcal/d of energy and 30g/day of protein is associated with significant reduced 60-d mortality and increased ventilator-free days.
Wei et al., 2015[27] (ICUs in Canada, Europe and US)	Secondary analysis of a prospective RCT	Mixed ICU	475	- Survival time was significantly shorter in patients with low than high nutritional adequacy - At 3-month follow-up, every 25% increase in nutritional adequacy was associated with improvement of physical functioning and role physical score
Nicolo et al., 2015[10] (202 ICUs from INS 2013)	Prospective	Mixed ICU	2828	≥80% of prescribed protein intake was associated with reduced mortality. ≥80% of prescribed protein intake was associated with shorter time-to-discharge alive in adjusted 12-day sample

ICU: Intensive Care Unit, ER: Energy requirement, PR: Protein requirement, d: day, h: hour, SAPS II: Simplified Acute Physiology Score II, APACHE II: Acute Physiology and Chronic Health Evaluation II, SOFA: Sequential Organ-failure Assessment, INS: International Nutrition Survey delivery after adjusting for confounders (p=0.020). Furthermore, a study in 3 medical/surgical ICUs among mechanically ventilated patients who stayed in the ICU for more than 72 hours and received EN showed that successful EN may be associated with reduction in infectious complications, particularly after 96 hour of ICU admission.[24] For protein, Allingstrup et al[9] also found that increased protein provision was associated with significant decrease in hazard ratio of death, even after adjusted for baseline prognostic factors.

Large Multicenter observational studies

Large multicenter observational studies (Table 2) was conducted since the commencement of the International Nutrition Survey (INS) in year 2007. Since then, about 5 analyses were conducted based on the international sample.

In year 2009, a large international observational study on 2772 mechanical ventilated patients by Alberda et al[25] showed an increase of 1000 kcal and 30 g protein per day was associated with reduced 60-days mortality [odds ratio (OR) 0.76, 95% CI 0.61-0.95, p=0.014] and an increased in number of ventilator free days (VFD) (3.5 VFD, 95% CI 1.2-5.9, p=0.003). Elke et al[26] selected a sample of 2270 ICU patients with sepsis and/or pneumonia from the database of the INS from year 2007 to 2011 also showed that an increase of 1000 kcal and 30 g protein per day was associated with reduced 60-day mortality (OR 0.61, 95% CI 0.48-0.77, p<0.001), and more ventilator-free days (2.81 days, 95% CI 0.53-5.08, p=0.02).

The relationship between nutritional adequacy and long-term outcome was also investigated. In a large sample (n=475) of patients who were mechanical ventilated for >8 days in ICU and had at least 2 organ failures related to their acute illness, survival time with low nutritional adequacy was significantly shorter than high nutritional adequacy (Hazard Ratio 1.7, 95% CI 1.1-2.6) and health-related quality of life was significantly higher with every 25% increase nutritional adequacy at 3 month follow up.[27]

On the contrary, Krishnan et al[28] showed that lower adequacy was associated with better outcomes than higher levels of calorie intake. Arabi et al[29] also showed that there was a dose-effect relationship between increasing calorie intake and higher hospital mortality, risk of ICU-acquired infections, rate of ventilator-associated pneumonia (VAP), increase duration of mechanical ventilation and length of stay in hospital and ICU. However, these associations were shown to be influenced by the statistical methodology used. Heyland et al[30] found that analyses that do not account for the progression to oral intake and the number of ICU days used in the calculation of the proportion calories received will lead to a potentially erroneous finding whereby higher calories intake is associated with increased mortality, whereas analyses that account for these key factors showed that better fed patients have reduced mortality.

In fact, Heyland et al[30] in the same study of an international sample of 7872 mechanically ventilated, critically ill patients who remained in the ICU for at least 96 hours showed that the overall association between percentage of the caloric prescription received and mortality is highly statistically significant with increasing calories associated with decreasing mortality (p<0.0001), and it appears that approximating goal of 80% of prescribed calories (and not more than 100% of prescribed calories) is associated with the best survival, regardless of body mass index. Similar results for protein was also demonstrated by Nicolo et al[10] among 2828 patients in ICU for at least 4 days, whereby patients who received ≥80% of prescribed protein had reduced mortality and shorter time-to-discharge alive, after adjusted for covariates and energy intake.

Randomized controlled trial (RCT)

Beside observational studies, several RCTs had been conducted in recent years (Table 3). Rice et al conducted the EDEN pilot (2011, n=200)[31] and multicenter RCT (2012, n=1000)[32] to investigate the effect of initial lower volume trophic or full enteral feeding for the first 6 days since ICU admission among patients with acute lung injury. Both studies achieved significant difference in calories and protein intake between the full and trophic feeding groups. The pilot study showed that the VFD to day-28, hospital mortality rate and ICU-free days were similar between groups. The multicenter RCT confirmed the results of the pilot study and showed no significant different between groups on VFD to day-28, 60-day mortality, development of infections and organ failure-free days.

The TICACOS study[33] is currently the only RCT that uses indirect calorimetry to calculate energy requirement, shows that there is a trend towards reduction of hospital mortality (p=0.058) and significant lower organ failure score at day 3 (p=0.027) in the intervention group who received significantly more calories and protein than the control group. However, the control group had a significant lower length of mechanical ventilation (p=0.03), length of stay in ICU (p=0.04), and trend towards reduce VAP (p=0.08) and infectious complications (p=0.05). These contradicting results is most probably due to calorie overfeeding as the study investigators did not consider intravenous non-nutrition energy intake (such as dextrose-containing fluids and propofol), which corresponds to an additional 10-15% calories.[34] Similar problem exists in a trial by Braunschweig et al[35] which showed 5.67 times higher hospital mortality in the full feeding group. The possibility of overfeeding is noted in their figure 2 that from day 5 onwards patients consistently received ≥100% of their energy prescription and almost reaching 120% on day 13 and day 14, probably contributing to the high mortality of the full feeding group.

In year 2014, Peake et al[36] randomized patients to receive isonitrogenous enteral formula with caloric density 1.5 kcal/ml and 1.0 kcal/ml. It was found that the 1.5 kcal/ml group who received significantly more calories had trend toward improved duration of survival (p=0.057), although there was no difference on VFD to day-28 and ICU & hospital length of stay. In the same year, Petros et al[37] also found that patients who are fed more adequately had reduced nosocomial infection, despite no difference in mortality rate.

Table 3: Randomized controlled trials comparing clinical outcomes between full feeding and underfeeding

First Author, year (country)	Population	Sample Size	Energy (E) and Protein (P) received Full feeding group	 Underfeeding group	Outcome (Full feeding compare with underfeeding)
Taylor et al., 1999[44] (UK)	Head injured and MV	82	E: 59.21% P: 68.7%	E: 36.8% P: 37.9%	- Good neurologic outcome at 3 months: ↑ trend (p=0.08) - At least 1 infection: ↓ - At least 1 complication: =
Desachy et al.,	Mixed ICU	100	E: 1715 ± 331 kcal/d P: unknown	E: 1297 ± 331 kcal/d P: unknown	- ICU LOS: = - Hospital LOS: = - ICU mortality: = - Hospital mortality: =
Arabi et al., 2011[38] (Saudi Arabia)	Mixed ICU	240	E: 1251.7 ± 432.5 kcal/d (71.4 ± 22.8%) P: 43.6 ± 18.9 g/d (63.7 ± 25.0%)	E: 1066.6 ± 306.1 kcal/d (59.0 ± 16.1%) P: 47.5 ± 21.2 g/d (65.2 ± 25.7%)	- ICU LOS: ↑ trend (p=0.09) - Hospital LOS:= - MV duration: ↑ trend (p=0.10) - 28-d mortality: = - 180-d mortality: ↑ trend (p=0.07) - ICU mortality: = - Hospital mortality: ↑
Singer et al., 2011[33] (Israel)^	Mixed ICU	130	E: 2086 ± 460 kcal/d P: 76 ± 16 g/d	E: 1480 ± 356 kcal/d P: 53 ± 16 g/d	- Length of MV: ↑ - ICU LOS: ↑ - Hospital LOS: = - ICU mortality: = - VAP: ↑ trend (p=0.08) - Infectious complications: ↑ trend (p=0.05) - Hospital Mortality: ↓ trend (p=0.058) - SOFA at Day 3: ↓
Rice et al., 2011[31] (USA)	Acute Lung Injury	200	E: 1418 ± 868 kcal/d (74.8 ± 38.5%) P: 54.4 ± 3.2g/d	E: 300 ± 149 kcal/d (15.8 ± 11.0%) P: 10.9 ± 6.8g/d	- VFD to d-28: = - Hospital Mortality: = - ICU-free day: = - Hospital-free day: =
Rice et al., 2012[32] (USA)	Acute Lung Injury	1000	E: ~1300 kcal/d (~80%) P: Unknown	E: ~400 kcal/d (~25%) P: Unknown	- VFD to d-28: = - 60-d Mortality: = - VAP: = - Infections: =
Charles et al., 2014[46] (USA)	Surgical ICU	83	E: 1338 ± 92 kcal/d (17.1 ± 1.1 kcal/kg) P: 83 ± 6 g/d (1.1 ± 0.1 g/kg)	E: 982 ± 61 kcal/d (12.3 ± 0.7 kcal/kg) P: 86 ± 6 g/d (1.1 ± 0.1 g/kg)	- Total no. of infections: = - ICU LOS: = - Hospital LOS: = - Mortality: =
Petros et al., 2014[37] (Germany)	Medical ICU	100	E: 19.7 ± 5.7 kcal/kg (75.5%) P: ~0.8 g/kg	E: 11.3 ± 3.1 kcal/kg (42.2%) P: ~0.5 g/kg	- Nosocomial infection: ↓ - ICU mortality: = - Hospital mortality: = - 28-d mortality: =
Peake et al., 2014[36] 0(Australia)	Mixed ICU	112	E: 2040 ± 578 kcal/d P: 70 ± 20 g/d	E: 1504 ± 573 kcal/g P: 74 ± 30 g/d	- VFD to d-28: = - ICU LOS: = - Hospital LOS: = - ICU mortality: = - Hospital Mortality: = - 90-d mortality: ↓ trend (p=0.057)

Arabi et al., 2015[39] (Saudi Arabia & Canada)	Mixed ICU	894	E: 1299 ± 467 kcal/d (71 ± 22%) P: 59 ± 25 g/d (69 ± 25%)	E: 835 ± 297 kcal/d (46 ± 14%) P: 57 ± 24 g/d (68±24%)	- ICU mortality: = - Hospital mortality: = - 28-d, 90-d, 180-d mortality: = - Incident of RRT: ↑
Braunschweig et al., 2015[35] (USA)	Mixed ICU	78	E: 1798 ± 509 kcal/d (84.7 ± 22%) P: 82 ± 23 g/d (76.1%)	E: 1221 ± 423 kcal/g (55.4 ± 19%) P: 60.4 ± 24 g/d (54.4%)	- Nosocomial infections: = - Length of MV: = - ICU LOS: = - Hospital LOS: = - Hospital mortality: ↑

^The intention-to-treat results were presented for Singer et al., 2011
MV: Mechanically-ventilated, ICU: Intensive Care Unit, LOS: Length of stay, d: day, VFD: ventilator-free day, SOFA: sequential organ failure assessment, VAP: ventilator-associated pneumonia. =: No significant difference, ↑: significantly increased, ↓: significantly reduced

Arabi et al[38] in year 2011 found that the full feeding group in their study had higher hospital mortality, and trend towards longer ICU length of stay, duration of mechanical ventilation as well as higher 180-d mortality. However, it must be noted that the absolute caloric intake between group were small (~184 kcal/d) despite reaching statistical difference, and the protein intake of the underfeeding group was higher than the full feeding group. Therefore, it is hard to attribute the poorer clinical outcome in the full feeding group to greater nutritional intake. The same authors in year 2015 conducted the PERMIT multicenter trial[39] which randomized patients to receive permissive underfeeding (40-60% of caloric requirement) or full-feeding (70-100% of caloric requirement) with similar protein intake. It was shown that there was no significant difference in all important clinical outcomes (mortality, length of stay, VAP) except that the permissive underfeeding group had a lower incident of renal replacement therapy (p=0.04).

In a nutshell, results from RCTs tend to show there is no significant difference in clinical outcomes between patients who received more calorie and/or protein, although some of them did show a trend towards better survival in patients who received more nutrition. Findings from RCTs combined with the signal of improved clinical outcomes in better fed patients shown in various multicenter prospective observational studies should allow us to conclude that optimal calories and protein provided to critically ill patients may improve patients' outcomes, provided overfeeding is avoided. The use of nutritional screening tools such as the NUTRIC score[40] in stratifying patients who require full or hypocaloric feeding is an important consideration but is out of the scope of this review.

Recommendation and Conclusion

The relationship between optimal feeding adequacy (neither underfeeding nor overfeeding) and better clinical outcomes (improved survival, reduced length of stay and infectious complications) is shown in many observational studies, while some RCTs showed reduced infections and mortality with better feeding adequacy. Despite this relationship, feeding adequacy was suboptimal, which warrants further investigation on the contributing factors so that a more informed action can be taken to address this issue.

In Malaysia, data regarding feeding adequacy and the factors associated with suboptimal feeding adequacy among the critically ill patients are still lacking. It is suggested that these factors are investigated in future research. This is because it is imperative to first discover the scope of the problem and factors associated with poor feeding practices, which then acts as a 'stepping stone' for the implementation of effective solution to improve nutritional delivery and status, ultimately leading to better overall clinical outcome and cost-saving in the Malaysian ICU.

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References

1. Vincent J-L. Critical care – where have we been and where are we going? *Crit Care*. 2013;17(Suppl 1):S2. doi:10.1186/cc11500.
2. Sakka SG. Hemodynamic Monitoring in the Critically Ill Patient - Current Status and Perspective. *Front Med*. 2015;2(August):44. doi:10.3389/fmed.2015.00044.
3. Bilevicius E, Dragosavac D, Dragosavac S, Araújo S, Falcão ALE, Terzi RGG. Multiple Organ Failure in Septic Patients. *Braz J Infect Dis*. 2001;5(3):103-110. doi:10.1590/S1413-86702001000300001.
4. Robertson LC, Al-Haddad M. Recognizing the critically ill patient. *Anaesth Intensive Care Med*. 2013;14(1):11-14. doi:10.1016/j.mpaic.2012.11.010.
5. Kreymann KG, Berger MM, Deutz NEP, et al. ESPEN Guidelines on Enteral Nutrition: Intensive care. *Clin Nutr*. 2006;25(2):210-223. doi:10.1016/j.clnu.2006.01.021.
6. McClave SA, Taylor BE, Martindale RG, et al. Guidelines for the

Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *JPEN J Parenter Enter Nutr*. 2016;40(2):159-211. doi:10.1177/0148607115621863.

7. McClave, Martindale RG, Rice TW, Heyland DK. Feeding the Critically Ill Patient. *Crit Care Med*. 2014. doi:10.1097/CCM.0000000000000654.

8. Heyland DK, Dhaliwal R, Wang M, Day AG. The prevalence of iatrogenic underfeeding in the nutritionally "at-risk" critically ill patient: Results of an international, multicenter, prospective study. *Clin Nutr*. 2014. doi:10.1016/j.clnu.2014.07.008.

9. Allingstrup MJ, Esmailzadeh N, Wilkens Knudsen A, et al. Provision of protein and energy in relation to measured requirements in intensive care patients. *Clin Nutr*. 2012;31(4):462-468. doi:10.1016/j.clnu.2011.12.006.

10. Nicolo M, Heyland DK, Chittams J, Sammarco T, Compher C. Clinical Outcomes Related to Protein Delivery in a Critically Ill Population: A Multicenter, Multinational Observation Study. *JPEN J Parenter Enter Nutr*. 2015. doi:10.1177/0148607115583675.

11. Reid C. Frequency of under- and overfeeding in mechanically ventilated ICU patients: causes and possible consequences. *J Hum Nutr Diet*. 2006;19:13-22.

12. Schlein KM, Coulter SP. Best Practices for Determining Resting Energy Expenditure in Critically Ill Adults. *Nutr Clin Pr*. 2014;29(1):44-55. doi:10.1177/0884533613515002.

13. Mcclave SA, Sexton LK, Spain DA, et al. Enteral tube feeding in the intensive care unit: Factors impeding adequate delivery. *Crit Care Med*. 1999;27(7):1252-1256.

14. De Jonghe B, Appere-De-Vechi C, Fournier M, et al. A prospective survey of nutritional support practices in intensive care unit patients: What is prescribed? What is delivered? *Crit Care Med*. 2001;29(1):8-12.

15. Binnekade J, Tepaske R, Bruynzeel P, Mathus-vliegen E, de Haan R. Daily enteral feeding practice on the ICU : attainment of goals and interfering factors. *Crit Care*. 2005;9(3):R218-R225. doi:10.1186/cc3504.

16. Cahill NE, Dhaliwal R, Day AG, Jiang X, Heyland DK. Nutrition therapy in the critical care setting: What is "best achievable" practice? An international multicenter observational study. *Crit Care Med*. 2010;38(2):395-401. doi:10.1097/CCM.0b013e3181c0263d.

17. Heyland DK, Heyland RD, Cahill NE, et al. Creating a Culture of Clinical Excellence in Critical Care Nutrition: The 2008 Best of the Best'' Award. *JPEN J Parenter Enter Nutr*. 2010;34(6):707-715. doi:10.1177/0148607110361901.

18. Mageswary LL, Adlin Natasya MS, Fathiyah Noor O, Lee Fang T, Sing Ean T. Improving Enteral Nutrition Support Practice Among ICU Patietns at Hospital Selayang. 2013:29. http://www.slideshare.net/lionelchewvunliung/l-mageswary-lapchmanan-improving-nutrition-support-practices-among-intensive-care-unit-patients-at-selayang-hospital.

19. Yip KF, Rai V, Wong KK. Evaluation of delivery of enteral nutrition in mechanically ventilated Malaysian ICU patients. *BMC Anesthesiol*. 2014;14(1):127. doi:10.1186/1471-2253-14-127.

20. Lee ZY, Barakatun-nisak MY, Airini IN. Enteral Nutrition Feeding Adequacy among Mechanically Ventilated Critically Ill Patients with High Nutrition Risk in a selected Public Hospital in Malaysia : A preliminary study. *Bangladesh Crit Care J*. 2016;4(1):9-13.

21. Villet S, Chiolero L, Bollmann MD, et al. Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients. *Clin Nutr*. 2005;24:502-509. doi:10.1016/j.clnu.2005.03.006.

22. Rubinson L, Diette GB, Song X, Brower RG, Krishnan J a. Low caloric intake is associated with nosocomial bloodstream infections in patients in the medical intensive care unit. *Crit Care Med*. 2004;32(2):350-357. doi:10.1097/01.CCM.0000089641.06306.68.

23. Tsai J, Chang W, Sheu C, et al. Inadequate energy delivery during early critical illness correlates with increased risk of mortality in patients who survive at least seven days: A retrospective study. *Clin Nutr*. 2011;30:209-214. doi:10.1016/j.clnu.2010.09.003.

24. Heyland DK, Stephens KE, Day AG, McClave SA. The success of enteral nutrition and ICU-acquired infections : A multicenter observational study. *Clin Nutr*. 2011;30(2):148-155. doi:10.1016/j.clnu.2010.09.011.

25. Alberda C, Gramlich L, Jones NE, et al. The relationship between nutritional intake and clinical outcomes in critically ill patients : results of an international multicenter observational study. *Intensive Care Med*. 2009;35:1728-1737. doi:10.1007/s00134-009-1567-4.

26. Elke G, Wang M, Weiler N, Day AG, Heyland DK. Close to recommended caloric and protein intake by enteral nutrition is associated with better clinical outcome of critically ill septic patients: secondary analysis of a large international nutrition database. *Crit Care*. 2014;18(1):R29. doi:10.1186/cc13720.

27. Wei X, Day AG, Ouelette-Kuntz H, Heyland DK. The Association Between Nutritional Adequacy and Long-Term Outcomes in Critically Ill Patients Requiring Prolonged Mechanical Ventilation: A Multicenter Cohort Study. *Crit Care Med*. 2015. doi:10.1097/CCM.0000000000001000.

28. Krishnan JA, Parce PB, Martinez A, Diette GB, Brower RG. Caloric Intake in Medical ICU Patients : Consistency of Care With Guidelines and Relationship to Clinical Outcomes Caloric Intake in Medical ICU Patients. *Chest*. 2003;124(1):297-305. doi:10.1378/chest.124.1.297.

29. Arabi YM, Haddad SH, Tamim HM, et al. Near-Target Caloric Intake in Critically III Medical-Surgical Patients Is Associated With Adverse Outcomes. *JPEN J Parenter Enter Nutr*. 2010;34(3):280-288. doi:10.1177/0148607109353439.

30. Heyland DK, Cahill N, Day AG. Optimal amount of calories for critically ill patients: Depends on how you slice the cake! *Crit Care Med*. 2011;39(12):1. doi:10.1097/CCM.0b013e318226641d.

31. Rice TW, Mogan S, Hays MA, Bernard GR, Jensen GL, Wheeler AP. Randomized trial of initial trophic versus full-energy enteral nutrition in mechanically ventilated patients with acute respiratory failure. *Crit Care Med*. 2011;39(5):967-974. doi:10.1097/CCM.0b013e31820a905a.

32. Rice TW, Wheeler AP, Thompson BT, et al. Initial Trophic vs Full Enteral Feeding in Patients With Acute Lung Injury: The EDEN Randomized Trial. *JAMA*. 2012;307(8):795-803. doi:10.1001/jama.2012.137.

33. Singer P, Anbar R, Cohen J, et al. The tight calorie control study (TICACOS): A prospective, randomized, controlled pilot study of nutritional support in critically ill patients. *Intensive Care Med*. 2011;37(4):601-609. doi:10.1007/s00134-011-2146-z.

34. Berger MM, Pichard C. Understanding the causes of death in INTACT by Braunschweig et al. *JPEN J Parenter Enter Nutr*. 2015;39(2):144. doi:10.1177/0148607114542831.

35. Braunschweig CA, Sheean PM, Peterson SJ, et al. Intensive nutrition in acute lung injury: a clinical trial (INTACT). *JPEN J Parenter Enter Nutr*. 2015;39(1):13-20. doi:10.1177/0148607114528541.

36. Peake SL, Davies AR, Deane AM, et al. Use of a concentrated enteral nutrition solution to increase calorie delivery to critically ill

patients: a randomized, double-blind, clinical trial. *Am J Clin Nutr*. 2014;100:616-625. doi:10.3945/ajcn.114.086322.

37. Petros S, Horbach M, Seidel F, Weidhase L. Hypocaloric vs Normocaloric Nutrition in Critically Ill Patients: A Prospective Randomized Pilot Trial. *JPEN J Parenter Enter Nutr*. 2014. doi:10.1177/0148607114528980.

38. Arabi YM, Tamim HM, Dhar GS, et al. Permissive underfeeding and intensive insulin therapy in critically ill patients: a randomized controlled trial. *Am J Clin Nutr*. 2011;93:569-577. doi:10.3945/ajcn.110.005074.

39. Arabi YM, Aldawood AS, Haddad SH, et al. Permissive Underfeeding or Standard Enteral Feeding in Critically Ill Adults (supp). *N Engl J Med*. 2015;372(25):2398-2408. doi:10.1056/NEJMoa1502826.

40. Heyland DK, Dhaliwal R, Jiang X, Day AG. Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. *Crit Care*. 2011;15(6):R268. doi:10.1186/cc10546.

41. Petros S, Engelmann L. Enteral nutrition delivery and energy expenditure in medical intensive care patients. *Clin Nutr*. 2006;25(1):51-59. doi:10.1016/j.clnu.2005.08.013.

42. Dvir D, Cohen J, Singer P. Computerized energy balance and complications in critically ill patients: An observational study. *Clin Nutr*. 2006;25:37-44. doi:10.1016/j.clnu.2005.10.010.

43. Faisy C, Lerolle N, Dachraoui F, et al. Impact of energy deficit calculated by a predictive method on outcome in medical patients requiring prolonged acute mechanical ventilation. *Br J Nutr*. 2009;101:1079-1087. doi:10.1017/S0007114508055669.

44. Taylor SJ, Fettes SB, Jewkes C, Nelson RJ. Prospective, randomized, controlled trial to determine the effect of early enhanced enteral nutrition on clinical outcome in mechanically ventilated patients suffering head injury. *Crit Care Med*. 1999;27(11):2252-2531.

45. Desachy A, Clavel M, Vuagnat A, Normand S, Gissot V, Francois B. Initial efficacy and tolerability of early enteral nutrition with immediate or gradual introduction in intubated patients. *Intensive Care Med*. 2008;34:1054-1059. doi:10.1007/s00134-007-0983-6.

46. Charles EJ, Petroze RT, Metzger R, et al. Hypocaloric compared with eucaloric nutritional support and its effect on infection rates in a surgical intensive care unit: a randomized controlled trial. *Am J Clin Nutr*. 2014;100(5):1337-1343. doi:10.3945/ajcn.114.088609.1.