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Underfeeding Patients with Critical Illness: Making Sense of Recent Data

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Underfeeding Patients with Critical Illness: Making Sense of Recent Data

Jacklyn C. Hook, MS, RDN, LDN Patricia Sheean, PhD, RDN

Abstract

Nutrition support is an important component of care for patients with critical illness. Providing the estimated requirements of calories and protein is thought to prevent or decrease the likelihood of disease-related malnutrition. However, short-term calorie restriction may be advantageous in this setting. We searched PubMed for studies on permissive underfeeding or hypocaloric feeding for patients with critical illness to evaluate relevant outcomes. Of the initial 137 studies, 32 papers were evaluated, but only 16 met all eligibility criteria. The results support a beneficial or neutral impact of short-term calorie restriction on nutrition support–related complications, but also report conflicting findings on mortality and infection incidence when compared to patients who received higher calorie and protein targets. Across these studies, calorie and protein needs were calculated using different methods, and the specifications of underfeeding (i.e., the amount of protein administered and the percentage of estimated calorie needs) remain broad. To become common practice, a consensus must be reached on the definition of underfeeding in terms of percentage of calories and amount of protein.

Introduction

By definition, patients who are critically ill require care and treatment in an ICU. Nutrition support is recognized as an important aspect of care for these patients and has been a focused area of research over the past three decades.[1] Patients with critical illness experience catabolism, which involves cytokine, hormonal, and nervous system responses that alter temperature regulation, energy expenditure, and nutrient utilization in response to major injury or insult. Specifically, the catabolic response leads to the breakdown of lean mass to access amino acids needed for energy production and the acute-phase response. As a result, patients who

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are critically ill frequently experience significant depletion of lean mass and disease-related malnutrition, which occurs in 30% to 50% of hospitalized patients.[2]

Theoretically, providing calorie and protein needs at estimated requirements prevents or decreases the likelihood of malnutrition and therefore worse clinical outcomes.[3] However, the appropriate amount of calories for ICU patients remains clinically controversial. Previous observational research has indicated that underfeeding, or feeding less than the estimated needs, is associated with poor clinical outcomes.[4] Specifically, patients who receive lower levels of caloric delivery in the ICU setting experience negative clinical outcomes, including increased mortality, longer length of stay, and greater risk of nosocomial infections.[4,5] Conversely, overfeeding may be associated with hyperglycemia and refeeding syndrome.[6] However, an emerging body of research from randomized, controlled trials challenges these observations. The use of several different terms to describe underfeeding can contribute to confusion among clinicians. The term "permissive underfeeding" was first used in 1994 to describe a feeding strategy based on the idea that "short-term dietary restriction, but not elimination, could possibly limit pathological processes associated with overfeeding while minimally impairing organ function."[7] "Hypocaloric feeding" is a newer term used to describe underfeeding that means caloric intake is lower than the estimated calorie requirements.[8] This narrative review aims to examine the recent body of literature on the impact of underfeeding on specific clinical outcomes in critically ill patients.

Methodology

A complete search of the literature was conducted using the PubMed database. This search included papers that were published within the past 10 years, written in English, and limited to human studies. Combinations of keywords using medical subject headings included "underfeeding," "hypocaloric," "critically ill," "critical illness," and "intensive care unit." Through a secondary search, additional sources were identified by reviewing the references of relevant articles.

Screening Criteria

Papers were selected for review based on the following inclusion criteria: (1) an adult population deemed critically ill; (2) publication in a peer reviewed journal; (3) patients who were underfed, which is defined as having caloric or protein intakes lower than estimated requirements; and (4) reported clinical outcomes of interest, including mortality, incidence of infections, and nutrition support–related complications. Papers were omitted if they: (1) were meta-analyses and systematic reviews; (2) included a pediatric population; (3) excluded the critically ill population; or (4) excluded patients who were underfed. The computer-based preliminary search yielded 138 results. Abstracts and titles were reviewed for relevancy to the topic. If an abstract did not contain sufficient information to determine eligibility, the paper was reviewed for adequacy.

Results

Originally, 32 papers were reviewed, but only 16 papers met all inclusion criteria. Only studies that included patients who were critically ill and underfed and reported the impact of underfeeding on clinical outcomes were considered (Figure 1). This review is organized by the impact of underfeeding on clinical outcomes, specifically mortality, incidence of infections, and nutrition support–related complications. A summary of the studies is provided in Tables 1 and 2, which include key characteristics of the population,

Figure 1. Article screening and selection process for examining the impact of underfeeding on specific clinical outcomes

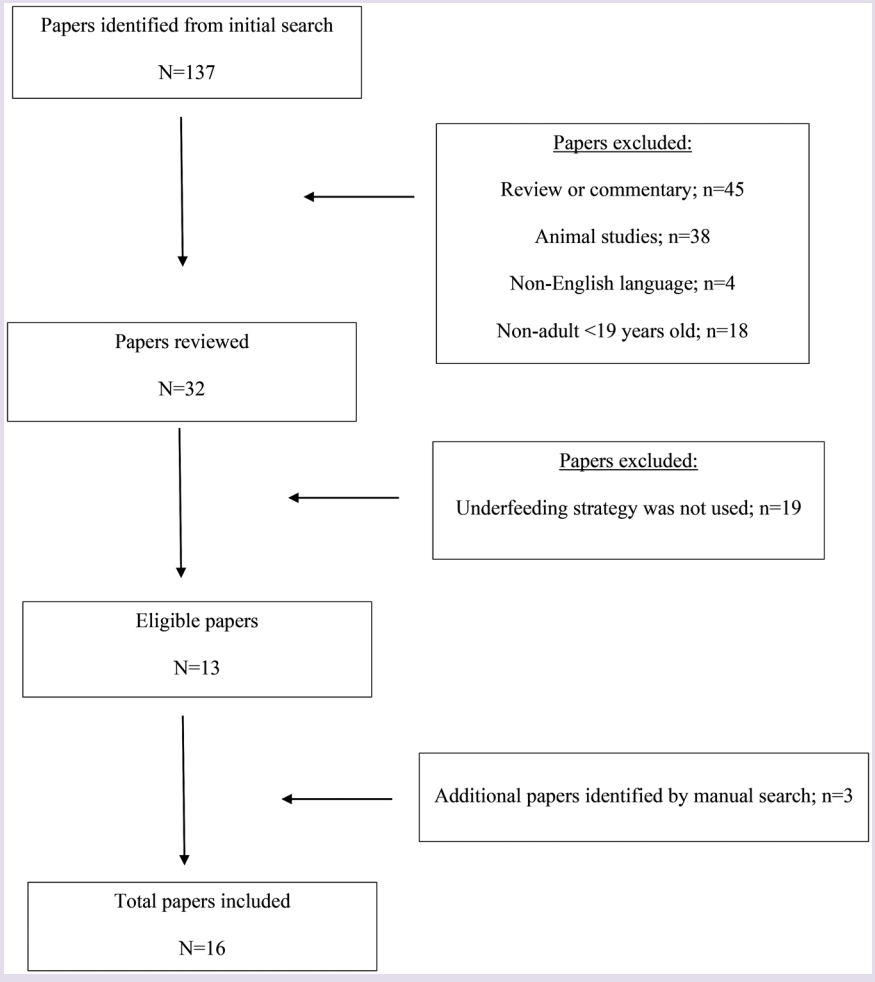

Table 1. Intervention studies reporting the practice of underfeeding in patients who are critically ill (n=10)

	Sample size/ population	Study design/ purpose	Calorie/protein goals	Exposure	Statistically significant outcomes (where *P* value ≤0.05)		
				Calories (kcal)/ protein (g) administered	Mortality	Infections	Nutrition support–related complications
Arabi et al (2011)	120; MICU and SICU patients	RCT; to examine effect of permissive underfeeding compared with target feeding and IIT compared with CIT	Target feeding group: 90% to 100% of EEN; Permissive underfeeding: 60% to 70% of EEN; Protein: 0.8 to 1.5 g/kg	Permissive underfeeding received fewer kcal 1,066.6+306.1 vs. 1,251.7+432.5 kcal (*P*=0.0.0002) (% of EEN: 59.0+16.1% vs. 71.4+22.8%) (*P*<0.0001). Protein was similar between groups (*P*=0.14).	Lower hospital mortality in underfeeding group (*P*=0.04)	None	None
Arabi et al (2015) PermiT trial	894; MICU and SICU patients	RCT; to evaluate effect of restriction of nonprotein calories compared with standard enteral feeding on 90-day mortality among critically ill adults	Standard feeding group: 100% of EEN; Permissive underfeeding group: 40% to 60% of EEN; Protein: 1.2 to 1.5 g/kg	Permissive underfeeding received fewer calories than standard 835+297 vs. 1,299+467 kcal (% of EEN: 46+14% vs. 71+22%) (*P*<0.001). Similar protein between groups (*P*=0.29).	None	None	None
Braunschweig et al INTACT study	78; ALI patients	RCT; to evaluate impact on outcomes of IMNT from diagnosis of ALI to hospital discharge compared with SNSC	Standard nutrition support vs. IMNT	IMNT group received more calories 1,798 vs 1,221 kcals (*P*<0.0001) (% of EEN: 84.7% vs. 55.4%) (*P*<0.0001). IMNT group received more protein 82 vs. 60.4 grams (*P*<0.0001) (% of needs: 76.1% vs 54.4%) (*P*<0.0001).	Mortality higher in IMNT (*P*=0.017), when adjusted for age and baseline SOFA score; risk of death in IMNT group was 5.67 times higher than in SNSC	Final sample size underpowered to detect differences in infection rates	None
Charles et al	83; SICU patients	RCT; to determine whether surgical infection outcomes in the ICU could be improved with the use of hypocaloric nutrition support	Eucaloric group: 100% of calculated daily caloric requirement (25 to 30 kcal/kg); Hypocaloric group: 50% of EEN (12.5 to 15 kcal/kg); Protein: 1.5 g/kg	Eucaloric group received more kcal/kg/d (12.3+0.7 vs. 17.1+1.1) (*P*<0.0002). Daily protein intake not different between groups.	None	None	None
Heidegger et al	153; MICU and SICU patients	RCT; to determine if optimizing calorie provision by SPN for 5 days after day 3 of ICU admission could improve clinical outcome in severely ill patients for whom EN alone is insufficient	Nutritional target set at 25 kcal/kg IBW for women and 30 kcal/kg IBW for men; Protein: 1.2 g/kg IBW	SPN group received more kcal/kg/d (mean calories daily between day 4 and day 8: 28 kcal/kg); EN group received less (20 kcal/kg/d) (% of needs: 103% vs. 77%) (*P*<0.0001). Mean protein between day 4 and 8: 1.2 g/kg per day SPN and 0.8 g/kg per day EN (% of needs: 100% vs. 71%) (*P*<0.0001).	None	Higher number of antibiotic days in EN for nosocomial infections (*P*=0.0298), antibiotic days (*P*=0.0257), lower number of antibiotic-free days EN group (*P*=0.0126)	None

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Table 1. **Intervention studies reporting the practice of underfeeding in patients who are critically ill (n=10) (*Continued*)**

	Sample size/ population	Study design/ purpose	Calorie/protein goals	Exposure	Statistically significant outcomes (where *P* value ≤0.05)		
				Calories (kcal)/ protein (g) administered	Mortality	Infections	Nutrition support–related complications
Petros et al	120; MICU patients	RCT; to compare impact of normocaloric vs. hypocaloric feeding in critically ill patients in first 7 days of ICU; rate of nosocomial infections during ICU stay	Normocaloric group: 100% of EEN (if 70% not met by day 3, received supplemental PN); Hypocaloric group: 50% of EEN	No differences of mean daily energy expenditure (1,773+333 vs. 1,837+321), taking total caloric supply, normocaloric group receive more calories (19.7+5.7 vs. 11.3+3.1 kcal/kg/d) (75.5% of target vs. 84.3% of targeted 50%) (*P*=0.001).	None	Hypocaloric group more nosocomial infections (*P*=0.046)	Daily insulin requirements higher in normocaloric group during half of study days, more episodes of hypoglycemia (*P*=0.03), diarrhea (more frequent in normocaloric day 4 [*P*=0.042] and 5 [*P*=0.024])
Rice et al EDEN trial	1,000; mechanically ventilated ALI patients	RCT; to determine if initial lower-volume trophic enteral feeding would increase ventilator-free days and decrease GI intolerances compared with initial full enteral feeding	Full-feeding group: initiated at 25 mL/h and advanced goal rates of 25 to 30 kcal/kg/d and 1.2 to 1.6 g/kg of protein calories; Initial trophic group: initiated at 10 mL/h to achieve goal of 10 to 20 kcal/h	Trophic feeding group received approx. 400 kcal/d (25% of calculated caloric goal) compared to approx. 1,300 kcal/d (80% of calculated caloric goal).	None	None	Full feeding group more days antidiarrheal (*P*<0.001) and prokinetic agents (*P*=0.001)
Rugeles et al (2013)	80; MICU patients	Double-blind RCT; to compare two EN regimens in the critically ill patient and their impact on development of severe organ failure, SOFA	Standard feeding group: 25 kcal/kg/d; Permissive underfeeding group: 15 kcal/kg/d with more than 1.5 g/kg of protein (60%)	Intervention group received 12 kcal/kg vs. 14 kcal/kg in control group. Both groups ended with caloric debt (17% in intervention and 40% in control). Protein delivery different (1.4 vs. 0.76 g/kg, *P*<0.0001).	Not reported	Not reported	Hyperglycemic events per day lower in hyperproteic (*P*=0.017)
Rugeles et al (2016)	120; ICU admission	RCT; to evaluate impact of different caloric regimens on severity of organ failure measured with SOFA	Hypocaloric group: 15 kcal/kg/d; Normocaloric group: 25 kcal/kg/d (60%); High protein scheme: 1.7 g/kg/d	Caloric intake higher in normocaloric group at 48 h (12.6 vs. 20.5 kcal/kg/d) and at 96 h (12.1 vs 19.2 kcal/kg/d). Protein intake same between groups at 48 h (1.2 vs. 1.4 g/kg/d) and at 96 h (1.3 vs. 1.3 g/kg/d).	None	Not reported	Lower average daily insulin requirements (*P*=0.27), as well as percentage patients requiring insulin (*P*=0.22) hypocaloric
Singer et al TICACOS	130; medical and surgical patients	RCT; to determine whether nutrition support guided by repeated measurements of resting energy compared to a single, initial weight-based measurement	Tight calorie group: calorie goal determined by repeated REE measurements using indirect calorimetry; Control group: calorie goal based on single determination of weight-based formula at time of recruitment (25 kcal/kg/d)	Mean calories delivered per day higher in study group (2,086+460 vs. 1,480+356) (*P*=0.01). Mean protein delivered per day higher in study group (76+16 vs 53+16) (*P*=0.001).	Hospital mortality lower in study group (*P*=0.023). Survival at 60 days higher in study group (*P*=0.023).	Total infection rate was higher in study group (*P*<0.05)	Not reported

IBW=ideal body weight, RCT=randomized, controlled trial, REE=resting energy expenditure

Table 2. **Observation studies reporting the practice of underfeeding in patients who are critically ill (n=6)**

	Sample size/ population	Study design/purpose	Nutritional intake measures	Exposure	Statistically significant outcomes		
				Calories (kcal)/ protein (g) administered	Mortality	Infections	Nutrition support–related complications
Alberda et al	2,884; medical and surgical patients	Observational study; to examine the relationship between the amount of calories and protein administered and clinical outcomes, and the extent to which premorbid nutritional status influenced relationship	Recorded type and amount of nutrients received daily for a maximum of 12 days or until death or discharge from the ICU	Calories and protein received per kg varied significantly across BMI groups; overall received 59.2% of calories and 56% of protein, with BMI <20 greater amounts than those with higher BMI	60-day mortality decreased for every 1,000 kcal/d provided 0.76 (*P*=0.014) (consistent at extremes of BMI and no association with BMI 25–35). Similar protein, 30 g 0.84 (*P*=0.008). Not significant in patients with a BMI>40	Not reported	Not reported
Arabi et al (2010)	523	Nested cohort patients enrolled in RCT; to determine whether the dose of caloric intake independently influences mortality and morbidity of critically ill patients	Caloric intake/target stratify patients into 3 tertiles: tertile I: caloric target <33.4%; tertile II: target 33.4% to 64.6%; tertile III: >64.6%	170 patients in tertile I, 181 patients in tertile II, 172 patients in tertile III	Tertile III associated with increased hospital mortality (*P*=0.0003), no differences in ICU mortality (*P*=0.08)	Tertile III associated with higher percentage of ICU-acquired infections (*P*<0.0001)	Not reported
Compher et al	2,853	Observational study; to investigate whether clinical outcomes vary by protein or calorie intake in patients with risk evaluated by the NUTRIC score	Delivery of protein and calories from feedings and calorie-containing medications for 12 consecutive days of patients who remained in ICU at least 4 days NUTRIC score ranged from 0 to 9: >5 high risk, <5 low risk	Patients achieved 59% goal protein and 62% of goal calorie intake (65% and 62% for 12-day subsample). Mean NUTRIC score is 4.8 for both samples	High-risk patients in 4-day sample odds of death increased 6.6% with each 10% increase protein. In 12-day sample odds, death increased 10.1% with each 10% increase in protein. TDA shorter for each 10% increase protein high-risk (4-day and 12-day).	Not reported	Not reported

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Table 2. **Observation studies reporting the practice of underfeeding in patients who are critically ill (n=6) (*Continued*)**

	Sample size/ population	Study design/purpose	Nutritional intake measures	Exposure	Statistically significant outcomes		
				Calories (kcal)/ protein (g) administered	Mortality	Infections	Nutrition support–related complications
Lee, Arini and Barakatun-Nisak	154; medical and surgical patients	Observational study; to investigate the relationship of calorie and protein intakes with 60-day mortality and the extent to which ICU length of stay and nutritional risk status influence this relationship	Max of 12 days, divided into 3 groups: received[a]	480; surgical patients	Observational before and after; to determine the effects of implementing an enteral feeding protocol on the nutrition delivery and outcomes of intensive care patients	Nurse-driven feeding protocol implemented. Caloric needs assessed on day 4 and 7, overfeeding receiving more than 110% of daily caloric needs via any route, underfeeding less than 80%	After implementation of protocol, fewer patients received enteral feeding (P=0.039). After group received more EN from day 3 onward and intake (enteral route) higher for days 3, 4, 6, and 7. After group received fewer overall calories for first 7 days (P<0.001).
Weijs et al	886; medical and surgical patients	Prospective observational cohort study; to investigate the effects of nutrition-targeted approach on clinical outcome	Protein target of 1.2 to 1.5 g/kg 4 groups: neither protein nor calories reached (NT), both protein and calorie target reached (PET), only calorie (ET), only protein (PT)	NT (75%+15%), ET (96%+5%), PET groups (99%+5%) for calories, and NT (72%+20%), ET (89%+10%), PET (112%+12%)	After making adjustments for number of confounders, reaching calorie and protein targets resulted in 50% decrease in 28-day mortality compared to those that reach neither target	Not reported	Not reported

NUTRIC=Nutrition Risk in the Critically Ill, TDA=Time to Discharge Alive

[a]Data from Padar M, Uusvel G, Starkopf L, Starkopf J, Blaser AR. Implementation of enteral feeding protocol in an intensive care unit:before-and-after study. *World J Crit Care Med*.2017;6(1):56–64. doi: 10.5492/wjccm.v6.i1.56

study design, study purpose, calorie and protein exposure, and findings of relevant outcomes.

Underfeeding and Mortality

Underfeeding has been associated with many different clinical outcomes in the ICU, most notably hospital and ICU mortality. Arabi et al conducted two separate studies to examine the effect of calorie delivery on mortality. Their first study compared target feeding of 90% to 100% of calorie requirements—calculated using the Harris–Benedict equation and adjusted for stress factors—to permissive underfeeding of 60% to 70% of calorie requirements in a randomized, controlled trial of 120 subjects. Protein requirements were calculated as 0.8 to 1.5 g/kg body weight/d, depending on patient and underlying conditions. No significant differences were found with 28-day all-cause mortality, ICU, and 180-day mortality. However, a significant survival benefit was found for those in the underfed group vs. the target feeding group with regard to hospital mortality (30% vs. 43%, respectively, *P*=0.04).[9] In the 2015 study, permissive underfeeding was compared to standard feeding, and the primary outcome of underfeeding was identified as 90-day all-cause mortality.[10] Patients in a sample of 894 participants were randomized to be either permissively underfed, with a goal of 40% to 60% of estimated energy needs (EEN), or standardly fed, with a goal of 70% to 100% of EEN. Caloric needs were calculated using the Penn State equation or the Ireton-Jones equation, depending on BMI and intubation status of the patient. Both groups received 1.2 to 1.5 g/kg/d of protein. No significant differences were found with the primary outcome, 90-day mortality (27% vs. 29%, *P*=0.58), or with in-hospital, ICU, 28-day, and 180-day mortality.[10]

In a 2014 study, a randomized, controlled trial was designed to compare intensive medical nutrition therapy (IMNT) with standard nutrition support care (SNSC) in patients with acute lung injury (ALI) from diagnosis to hospital discharge.[11] Patients in the IMNT group received significantly more calories, specifically 85% of EEN compared to 55% in the SNSC group. Prior to reaching enrollment goals, the trial was stopped when investigators found that the risk of death was 5.67 times higher in IMNT than in SNSC, after adjusting for age and baseline Sequential Organ Failure Assessment (SOFA) score.[11] In the Tight Calorie Control Study (TICACOS) in 2011, 65 patients were randomized to the control group, and 65 patients were randomized to the intervention, or tight calorie, group.[12] Patients in the tight calorie group received feedings based on estimated needs determined by repeated resting energy expenditure measurements using indirect calorimetry. Patients in the control group received feedings based on estimated needs determined by a weight-based formula. The two groups were comparable at baseline in terms of their SOFA scores on day 1, APACHE II score, and admission category. Patients in the tight calorie group received a mean of 2,086 calories and 76 g of protein per day, while patients in the control group received a mean of 1,480 calories (*P*=0.01) and 53 g of protein per day (*P*=0.001). There was a trend toward lower hospital mortality in the higher fed group compared to the lower fed group (32% vs. 48%, *P*=0.058). Survival at 60 days was also higher in the tight calorie group compared to the control group (58% vs 48%, *P*=0.023); however, ICU mortality was not significantly different between the two groups.[12]

A number of observational studies have examined the association between nutritional intake and mortality, as seen in Table 2. In an observational study of 2,884 critically ill patients who were mechanically ventilated, Alberda et al found that for every 1,000 calories provided per day, the adjusted odds ratio (OR) for 60-day mortality was 0.76 (95% confidence interval [CI] 0.61–0.95, *P*=0.014); however, the largest reduction was seen at the extremes of BMI, and no association was found for those who had a BMI between 25 and 35.[13] Similarly, with higher protein intake, 60-day mortality improved in patients with a BMI $\leq$25 and $\geq$35, but this benefit was not seen in those with a BMI $\geq$40. Calorie needs were calculated using a weight-based equation, and protein needs were decided by the individual provider.[13] In a multicenter, multinational observational study from 2017, 2,853 patients at high nutrition risk were identified using the Nutrition Risk in the Critically Ill, which assesses multiple clinical characteristics including BMI, previous dietary intake, age, and the severity of illness.[14] Calorie and protein goals were determined by participating sites and based on local practice patterns. High-risk patients who were in the ICU for four days had a 6.6% decreased risk of 60-day mortality with each 10% increase in protein intake, and a 7.1% decreased risk of mortality with each 10% increase in caloric intake. Of the patients who were in the ICU for 12 days, risk of mortality decreased in those who had an increased protein and caloric intake; however, these associations were not significant in patients who were classified as low nutrition risk.[14] A prospective observational cohort study analyzed the effects of achieving both calorie and protein targets, only calorie targets, and neither target in 886 patients who were mechanically ventilated.[15] Indirect calorimetry was performed to determine calorie needs, and protein was provided with a target of 1.2 to 1.5 g/kg of preadmission or adjusted body weight per day. Achieving both calorie and protein targets resulted in a 50% decrease in 28-day mortality compared to patients who did not reach either target.[15]

In contrast, an observational study by Arabi et al found that 2,884 critically ill patients who received >65% of calorie targets experienced higher hospital mortality than those who received <65% of calorie targets, although ICU mortality remained similar between groups.[16] Caloric targets were calculated using the Harris–Benedict equation adjusted for stress factors, and protein needs were calculated using 0.8 to 1.5 g/kg/d based on patient condition and disease status.[16] Padar et al evaluated the effect of a nurse-driven enteral feeding protocol on the amount of nutrients

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administered and on clinical outcomes in 480 patients admitted to the medical ICU (MICU) and surgical ICU (SICU).[17] The cumulative amount of calories was lower after the implementation of the protocol, with the Before group receiving a median of 7,030 calories and the After group receiving a median of 6,000 calories (P<0.001). Mortality levels at 90 and 120 days were found to be lower after the implementation of the protocol (37% vs. 29%, P=0.026; 39% vs. 30%, P=0.033), and the number of calories received via enteral route was higher following implementation. However, fewer total calories from both enteral nutrition (EN) and parenteral nutrition (PN) were received after implementation of the protocol.[17] Similar relationships were also found by Lee et al in 154 subjects, whose calorie and protein needs were estimated using 25 kcal/kg and 1.2 g/kg of actual, ideal, or adjusted body weight.[18] Mortality at 60 days was significantly higher in critically ill patients who received two-thirds or more of both calorie and protein needs when compared to those who received less than two-thirds (OR, 2.83; CI, 1.32–6.07; P=0.008).[18] However, when only the protein or calories received was two-thirds or more of the total needs, mortality was not affected.[18]

Five other randomized, controlled trials studied the effect of underfeeding on patients who were critically ill.[19–23] No differences were found between patients who were underfed and patients who were standardly fed with regard to mortality, including 28-day mortality, ICU mortality, and in-hospital mortality. Of the nine randomized, controlled trials[9–12,19–23] and six observational studies[13–18] in this mortality review, there were varying effects when comparing patients who were standardly fed to patients who were underfed.

Underfeeding and Infections

Nosocomial infections frequently occur in critically ill patients and are associated with increased mortality. The definition of infection may vary by hospital site, criteria used, and infection control services; definitions are reported per author. In a randomized, controlled trial of 83 patients, Charles et al did not detect a significant association in the mean number of infections per patient, the incidence of infection, or the distribution of infection type between patients in the eucaloric group (100% of EEN) and the hypocaloric group (50% of EEN).[19] Calorie needs were determined using a weight-based equation of either 25 to 30 kcal/kg/d in the eucaloric group or 12.5 to 15 kcal/kg/d for the hypocaloric group, while protein goals were the same for both groups.[19] The EDEN trial, a randomized, controlled trial, compared initial trophic enteral feedings of 10 to 20 kcal/h via an omega-3 or control supplement to full enteral feedings of 25 to 30 kcal/kg/d and 1.2 to 1.6 g/kg/d in 1,000 patients with ALI.[22] Similar to the previous studies, no significant differences were found in the incidence of infections and the amount of nutrients received.[22]

An intervention study completed by Heidegger et al used indirect calorimetry on day 3 of admission to the ICU to adjust calorie targets.[20] The 305 patients were assigned to receive either EN only or EN with supplemental parenteral nutrition (SPN). Patients assigned to the SPN group received 103% of their calorie target and 1.2 g/kg/d of protein, compared to 77% of the calorie target and 0.8 g/kg/d in the EN group. Data were obtained from days 1 to 28 for cumulative caloric balance and follow-up variables. During the follow-up period, 41 (27%) patients in the SPN group and 58 (38%) in the EN group developed nosocomial infections (P=0.0338).[20] Petros et al randomized critically ill patients into a normocaloric and a hypocaloric feeding group to receive either 100% or 50% of total daily calorie requirements, respectively.[21] Caloric needs were measured by either indirect calorimetry or the Ireton-Jones predictive equation using ideal body weight. In the normocaloric group, SPN was used on day 3 if at least 70% of the target caloric supply was not achieved. The normocaloric group received 76% of their 100% target, whereas the hypocaloric group received 84% of their 50% target during the seven-day study period. Admission diagnosis, APACHE-II score, age, and body weight were similar between each group. Patients in the hypocaloric group had significantly more patients with nosocomial infections (26%) when compared to the normocaloric group (11%).[21]

Four other randomized, controlled trials and one observational study examined the effect of underfeeding on the incidence of infections.[9,10,12,16,24] In two studies by Arabi et al, no differences with infection incidence and feeding amount were found (P=0.89; P=0.54).[9,10] Owais et al found more episodes of systemic inflammatory response syndrome in the normocaloric group (P=0.017).[24] Singer et al found total infection rate to be greater in the higher fed group (P<0.05),[12] which is similar to Arabi et al, where a higher percentage of ICU-acquired infections was associated with the higher fed group (P<0.0001).[16] Results varied among the eight randomized, controlled trials[9,10,12,19–22,24] and one observational study[16] that discussed feeding amount and infection incidence.

Underfeeding and Nutrition Support–Related Complications

In critically ill patients, glucose control can be difficult to achieve, and both hyper- and hypoglycemia have been associated with increased morbidity and mortality.[25] Nutrition support frequently impacts glucose control, and the total amount of nutrients administered can impact blood glucose levels and the risk of hyper- and hypoglycemia.[25] Arabi et al found no significant difference between the underfed and standard feeding groups regarding hypoglycemia, although the use of insulin and its dose amount was significantly higher in the standard feeding group.[10] In the 2011 study by Arabi et al, patients who were randomly assigned to the permissive underfeeding group also received intensive insulin therapy (IIT) to maintain a blood glucose level of 80 to 110 mg/dL, compared to the conventional insulin therapy (CIT) given to the target feeding group who maintained a blood glucose level of 180 to 200 mg/dL.

Similarly, no significant differences were observed between the two feeding groups, although 38 patients (32%) in the IIT group experienced hypoglycemia compared to eight patients (7%) in the CIT group ($P<0.0001$).[9] In the 2013 study by Rugeles et al of 80 patients, the intervention group received a higher percentage of calories from carbohydrates, whereas the control group received a higher percentage of calories from protein.[26] The number of hyperglycemic events per day ($P=0.017$) and the amount of insulin required ($P>0.05$) was higher in the control group.[26] In the 2016 study by Rugeles et al, patients received either 15 kcal/kg/d or 25 kcal/kg/d of calories, but both groups received a high amount of protein at 1.5 g/kg/d. The number of hyperglycemic episodes did not differ between groups, but average daily insulin requirements and the percentage of patients who required insulin were lower in the hypocaloric group.[23]

Aspiration, fluid imbalance, and gastrointestinal complications including diarrhea and constipation are all considered nutrition support–related complications. In the study by Rice et al, patients who received initial trophic feeds of 20 kcal/h experienced less gastrointestinal intolerances, significantly on days 2 and 3 of the study period.[22] Patients in the trophic feeding group had fewer days of regurgitation, vomiting, elevated gastric residual volumes, and constipation, as well as a lower administration of antidiarrheal and prokinetic agents. However, no differences were seen with diarrhea, aspiration, or abdominal distension and cramping.[22] Padar et al showed that after the implementation of a nurse-driven feeding protocol, patients received fewer total calories compared to infusion rates.[17] Despite this decrease, the daily occurrence of vomiting, bowel distension, large gastric residual volumes, and diarrhea were similar between groups.[17]

Four other randomized, controlled trials evaluated the impact of feeding amount on nutrition support–related complications.[11,19–21] In three studies, there were no differences in hypo- and hyperglycemia or in the amount of insulin required.[11,19,20] Petros et al found daily insulin requirements to be higher in the standardly fed group for half of the study ($P=0.03$).[21] Of the nine randomized, controlled trials[9–11,19–23,26] and one observational study,[17] underfeeding was found to have either a beneficial or neutral impact on complications including hyper- and hypoglycemia, aspiration, and gastrointestinal issues.

Discussion

This narrative review focused on the impact of underfeeding on clinically relevant outcomes for critically ill patients. In general, we found that underfeeding had mixed effects on mortality, infections, and nutrition outcomes, as no consistent relationship could be observed across studies. Several factors may have impeded our abilities to make definitive conclusions that merit consideration.

First, clinical outcomes related to underfeeding may be affected by body weight, specifically if a patient is classified as normal weight or obese. In a study completed in 2002, 40 patients who were critically ill and obese were assigned to either a eucaloric or hypocaloric feeding group, where patients achieved 25 to 30 kcal/kg of adjusted body weight per day or less than 20 kcal/kg of adjusted body weight per day.[27] Both groups had a protein goal of 2 g/kg of ideal body weight per day. Those in the hypocaloric group were on antibiotics for a significantly decreased duration by day 10 ($P<0.03$); however, the incidence of infectious complications, including pneumonia, sepsis, and empyema, was not significantly different between groups.[27] Patients who are critically ill and obese may lose existing lean body mass at a faster rate than normal weight patients due to their inability to use free fatty acids for resting energy expenditure.[28] This issue has contributed to the consensus of recommending hypocaloric, hyperproteic feedings for patients who are classified as obese and in the ICU.[29] However, this recommendation is based on limited research, and little is known about the differences between metabolic reactions to critical illness in normal weight patients and patients who are overweight or obese.

Second, the outcomes related to underfeeding may be affected by which macronutrients, either calories or protein, are being restricted. Studies varied on the amount of protein that was administered, as protein intake was intentionally different between groups in some cases but similar in others. Rugeles et al researched this issue in two separate studies where groups received different and similar calorie and protein infusions.[23,26] In the 2016 study, there were improvements in SOFA score changes and blood glucose levels in the hyperproteic group,[26] but no improvements were seen in the hypocaloric group with regard to clinical outcomes.[23] The studies also varied in the methods used to determine patients' calorie needs or targets. Indirect calorimetry was used in some studies,[12,21] while predictive equations were used in others,[9,10,24] including Ireton-Jones, Penn State, Harris–Benedict, Schofield's, and other weight-based equations.[19,20,22,23,26] The prescribed calorie administration to patients in the permissive underfeeding or hypocaloric group also differed among studies, ranging anywhere from 20% to 70% of estimated calorie requirements. In a number of studies reviewed by Weijs and Wischmeyer, trials achieving protein delivery of around 1.0 g/kg/d or more were associated with better outcomes. This association was not seen in trials where protein was not addressed.[30] These findings imply that optimization of protein may be an important factor to improve outcomes.[30]

Third, the outcomes may vary depending on whether critically ill patients are in the MICU or SICU. In 2010, two international, prospective, observational studies collected data to compare how nutrients are delivered in the MICU and SICU.[31] In total, 5,497 patients were included, and 38% of the sample was comprised of patients in the SICU. Surgical patients undergoing cardiovascular and gastrointestinal

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surgery used PN more frequently, while cardiovascular surgery patients received the least overall nutrition support. Therefore, patients admitted to the SICU may be more likely to experience a dysfunctional GI tract or hemodynamic instability, which affects the amount of nutrients administered and received.[31] Patients in the SICU experience frequent interruptions due to scheduled tests and procedures, intolerance, ventilator-weaning trials, and necessary care.[32] Currently, feeding recommendations for patients in the MICU and SICU are similar, although the use of an immune-modulating formula is recommended for patients in the SICU.[29] However, surgical patients receive EN less frequently and later than patients in the MICU. They may also receive fewer overall nutrients due to their disease or clinical status. These factors support crucial differences between these two populations, which may have implications on the responses and evaluations concerning standard feeding vs. underfeeding.

Finally, many of the studies included in this review focused on ICU, hospital, or other short-term mortality end points. While these short-term end points are important, examining the effects of underfeeding on other long-term outcomes beyond mortality may be more relevant for ICU survivors. Post–intensive care syndrome (PICS) is a grouping of post–critical care complications that include persistent cognitive dysfunction, acquired weakness, and intrusive memory akin to post-traumatic stress disorder.[33] Patients affected by PICS are often unable to return to work, and family members are needed to stay home to care for these patients.[33] Needham et al completed a prospective follow-up to the EDEN trial to assess numerous long-term outcomes at six and 12 months following ALI and either normo- or hypocaloric feedings.[34] Feeding amount did not significantly impact most long-term outcomes, including physical function, survival rate, and admission to a health-care or skilled nursing facility. However, mental health measures favored those who were underfed, and more patients in the trophic group were admitted to a physical rehabilitation center.[34] In a study by Wei et al, patients with low nutritional adequacy had higher mortality at three and six months.[35] Patients who were administered adequate calories within the first eight days of their ICU stay had improved functional aspects of health-related quality of life at three months, but this association was no longer significant at six months.[35] Based on these results, feeding amount may affect physical function, mortality, quality of life, and, as a result, the occurrence of PICS. However, more research is needed to better investigate these important outcomes in long-term survivors of critical illness, as it relates to underfeeding.

Future Directions

Unfortunately, the current definition of underfeeding includes a broad range of both calorie and protein goals. In order to truly assess the impact of underfeeding on important and relevant outcomes, a consensus on the amount of calories that constitutes underfeeding, as well as the most accurate and feasible methods of calculating caloric needs, protein needs, and energy expenditure, is required. To allow for more accurate nutrition support dosing, studies are needed that compare MICU and SICU populations, metabolic differences, and their impact on clinical outcomes. Lastly, short-term outcomes are the focus of current research. Further trials should determine the impact of underfeeding on long-term outcomes to consider how quality of life and mental, physical, and financial status are impacted following discharge.

CPEU Codes

5170 - Critical care, trauma
5440 - Enteral and parenteral nutrition support

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Advanced Practice Dietetics: The RDN-AP, An Evolution

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ABSTRACT

The registered dietitian nutritionist (RDN) profession has changed and evolved over the past 100 years. The profession continues to evolve with the recent recognition of the advanced practice RDN role. The emerging role of interdisciplinary team management in health care will provide the opportunity for RDNs, especially advanced dietetics professionals, to expand their scope of practice. Leadership and communication skills are key components of the future education of RDN professionals. Development of an advanced practice curriculum as a component in RDN advancement will provide RDNs with the skill sets needed to become critical leaders in the health-care environment.

Introduction

The United States is entering a new era of health-care delivery in which changes in health-care policy are driving an increased focus on cost, quality, and transparency of care.[1] At the same time, the aging population and increasing rate of chronic illness are coupled with a decreasing number of primary care physicians. The role of advanced practice professionals in addressing these disparities has led to advanced practice roles that can contribute to improved quality of and access to health care.[2] This new era will require a deliberately more holistic and interdisciplinary care process.

The World Health Organization maintains that interprofessional collaborative

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