Propofol Sedation

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Propofol is a commonly used intravenous sedative for ventilator-dependent patients. Its advantage over other sedative agents, such as benzodiazepines, is in its rapid onset and short half-life which allows for daily awakening and spontaneous breathing trials. The use of propofol is recommended by the Brain Trauma Foundation for the treatment of elevated intracranial pressure and sometimes prolonged continuous large doses are required.

propofol enteral nutrition parenteral nutrition fat emulsions critical illness nutritional requirements hypnotics and sedatives food–drug interactions

1. Introduction

The use of propofol is recommended by the Brain Trauma Foundation for the treatment of elevated intracranial pressure [1] and sometimes prolonged continuous large doses are required. Prolonged use of large doses can be problematic in the nutritional management of these patients since propofol is formulated in a 10% lipid emulsion as either soybean oil in the United States or available in a mixed oil formulation internationally. As a result, complications associated with caloric overfeeding, hypertriglyceridemia, and inadequate protein intake may occur for patients receiving propofol therapy [2]. The intent of this entry is to examine caloric intake associated with propofol therapy and to describe some strategies to avoid overfeeding that will still meet the increased protein needs of critically ill patients who require enteral nutrition (EN) or parenteral nutrition (PN) therapy.

2. Complications Associated with Hypertriglyceridemia and Caloric Overfeeding

Those with conditions susceptible to impaired exogenous lipid clearance due to decreased lipoprotein lipase activity (e.g., diabetes mellitus, pancreatitis, and renal failure); liver failure; or a history of hyperlipidemia, obesity, corticosteroid therapy, human immunodeficiency virus disease, or multisystem organ failure are at risk for hypertriglyceridemia during the administration of intravenous lipid emulsion [3][4]. Higher doses of intravenous propofol (lipid emulsion) can result in hypertriglyceridemia as lipoprotein lipase becomes saturated at a serum triglyceride concentration of ~300 to 400 mg/dL resulting in non-enzymatic means of elimination (e.g., from first order kinetics to zero order kinetics) with the lipid emulsion and its remnants being eliminated via the reticuloendothelial system [4]. Excessive serum triglyceride concentrations and increased appearance of chylomicron-like remnants from intravenous lipid emulsion can result in reticuloendothelial system clogging, compromised immune function, as well as pancreatitis [4][5][6]. However, some patients at risk for impaired

clearance may also require a lower dosage of propofol for effective sedation, which could potentially dampen the appearance of hypertriglyceridemia.

Caloric overfeeding is also an issue particularly when high doses of propofol are combined with calories derived from enteral or parenteral nutrition [2][7][8][9]. PN, which is comprised of 60% glucose, 20% lipid, and 20% protein, given at a total caloric intake equal to the estimated basal energy expenditure and then increased to 1.5 times the estimated basal energy expenditure in ventilator dependent patients significantly increased carbon dioxide production by 35% [10]; this could potentially impair ventilator weaning. Caloric overfeeding, especially when the carbohydrate or glucose intake is in excess of 4 to 5 mg/kg/min, can also result in hyperglycemia [11]. Caloric excess, in general, has been associated with poorer outcomes. In a retrospective analysis of 1171 ICU patients from a mixed medical/surgical/trauma population with an ICU length of stay greater than 4 days, increased mortality was associated with a total caloric intake that exceeded about 1.2 to 1.3 times the measured resting energy expenditure [12].

Another potential option to reduce caloric and triglyceride intake is to employ a 2% (20 mg/mL) propofol emulsion instead of 1% (10 mg/mL), which would result in delivery of half the amount of lipid emulsion at an equivalent propofol dose. The 2% propofol emulsion is available in Europe and other international countries but has not been approved for use by the Food and Drug Administration (FDA) in the United States. However, in response to the COVID-19 pandemic, the FDA has issued an emergency use authorization to permit the use of this unapproved product. Despite this authorization, many institutions in the United States do not have the 2% product.

These data provide sufficient evidence that patients who receive concurrent propofol and EN or PN may need to have their nutrition regimens adjusted to provide less calories to prevent overfeeding. Serum triglycerides should also be routinely monitored while the patient is receiving propofol therapy.

3. The Rationale and Dilemma for Providing Sufficient Protein Intake

Recent studies have indicated an association between improved mortality, shorter ventilation days, and shorter duration of ICU and hospital stays with increases in protein intake for critically ill patients [12][13][14][15][16]. This is particularly relevant for those critically ill patients with a prolonged ICU stay, such as those with multiple traumatic injuries and TBI [14]. It is recommended by the Society of Critical Care Medicine (American Society for Parenteral and Enteral Nutrition) guidelines that critically ill patients receive 1.2 to 2 g/kg/d [5]. However, they also indicate that certain critically ill subpopulations such as those with trauma, obesity, and those who require continuous renal replacement therapy may need a greater protein intake (e.g., 2 to 2.5 g/kg/d) [5][17][18][19][20][21]. In order to overcome the anabolic resistance associated with aging, a greater protein intake may be required for those older than 59 years of age compared to younger adults to achieve the same nitrogen balance [22]. However, it should be acknowledged that the current literature is lacking in randomized prospective clinical trials to ascertain exactly how much protein is required or if an improvement in nitrogen balance for various homogenous populations will result in improved clinical outcomes; all require further study.

Most studies provided less than 1.2 g/kg/d of protein, which is inadequate for critically ill patients. This reduced protein intake may have been due to the concept of reducing the infusion rate of EN to avoid overfeeding or for patient conditions requiring fluid restriction [23][9][24]. Since EN formulas have a fixed composition, the macronutrient components cannot be altered unlike PN. Thus, reducing the rate of the continuous EN formula will also reduce the protein intake. Patients with traumatic injuries and TBI are among the most likely populations to receive prolonged, high dose propofol therapy [25][7][26] and require a greater protein intake than many other critically ill patients [5][19]. Therefore, a simple reduction in EN rate to decrease calories will result in decreased protein intake which could potentially be detrimental to clinical outcomes. Patients with TBI tended to receive greater protein intakes than other ICU populations when receiving propofol; however, average protein intakes were still less than target goals. The reason for this inadequacy in achieving ideal protein intake was likely related to multiple factors, including interruptions in EN due to various surgical, interventional, and diagnostic procedures [27], as well as an increased incidence of gastric feeding intolerance and a greater amount of tachyphylaxis to metoclopramide therapy when compared to those without TBI [28].

4. Strategies to Avoid Overfeeding with Calories and to Maintain or Improve Protein Intake

4.1. Parenteral Nutrition

For those institutions where PN solutions are compounded by the pharmacy, it is easy to adjust the individual components to meet energy and protein requirements. A typical approach is to either omit or decrease the amount of lipid emulsion, particularly for those receiving high dose soybean-oil based propofol therapy. If lipid calories beyond what is provided with the propofol infusion are desired, a mixed oil lipid emulsion could be added to the parenteral nutrition solution to avoid excessive intakes of long-chain omega-6 fatty acids. This approach also gives the prescriber flexibility in avoiding excessive lipid intake as the propofol rate may be increased and decreased throughout the day as the patient is titrated to the target Richmond-Agitation Sedation Scale score of −2 for light sedation [29]. The clinician will also need to assess if the patient is receiving the appropriate caloric intake based on previously established targets. Depending on the target caloric intake, the amount of dextrose in the dextrose-amino acid PN solution may need to be increased or decreased accordingly. Dextrose contributes 3.4 kcal/g and amino acids are 4 kcal/g. Some practitioners might find it confusing that a 10% lipid emulsion (propofol) contributes 11 kcal/g (1.1 kcal/mL), whereas intravenous lipids (20% or 30%) used in compounding PN solutions contribute 10 kcal/g (2 or 3 kcal/mL, respectively). This is because fat contributes 9 kcal/g, which would render the caloric content from only the fat component for a 10% intravenous lipid emulsion solution at 0.9 kcal/mL. However, to produce a lipid emulsion, egg phosphatides are used as the emulsifying agent and glycerol is also added to make the solution isotonic. Both components also contribute calories amounting to ~0.2 kcal/mL or 2 kcal/g of the 10% lipid emulsion. Thus, the 10% intravenous lipid emulsion product will contribute 11 kcal/g or 1.1 kcal/mL.

It is recommended that the dextrose intake not exceed 4 to 5 mg/kg/minute amounting to 20 to 25 kcal/kg/d to avoid overfeeding complications [11][30]. The brain and other glucose-dependent tissues require ~130 g of glucose daily [31]. For surgical, trauma, and thermally injured patients, glucose consumption of the wound may require an

additional glucose intake of ~80 to 150 g daily depending on the extent of the wound [32][33]. Thus, it is our current practice to provide at least ~200 g of dextrose daily for surgical, trauma, and thermally injured patients if the patient is not experiencing significant hyperglycemia.

Accomplishing these goals for the institutions that use multi-chamber bag PN solutions, particularly for those patients with high protein needs, may be more challenging. The recent expansion of available products to include a 10% dextrose/8% amino acid and 14% dextrose/8% amino acid solutions may facilitate ease in meeting these goals. For the institutions that only have fat-containing multi (three)-chamber bags, breaking the seal between only the glucose-amino acid compartments will only allow the fat free components of the PN solution to be used. Another alternative solution is to piggyback an amino acid solution via a separate central venous catheter port (or via a Y-site, albeit less desirable if a separate port is not available) to be co-infused with the multi-chamber bag PN preparation if greater protein intake is desired beyond what is available in the multi-chamber bag PN.

4.2. Enteral Nutrition

Avoiding overfeeding and providing sufficient protein for those who receive enteral nutrition concurrently with an intravenous propofol infusion can be very challenging, especially for highly catabolic and critically ill patients. The primary challenge results from EN formulations that are only available with fixed components and the macronutrients cannot be altered unlike PN solutions. Adult EN formulas range from 1 kcal/mL to 2 kcal/mL and the protein content can range from ~34 g/L to 94 g/L. The macronutrient components of various EN formulations vary based on the population for its intended use such as “standard formulas” for malnourished and unstressed or mildly stressed patients or disease/condition-specific formulas for those who require volume restriction or have renal, hepatic, or pulmonary impairment/failure; elevated protein needs; diabetes/hyperglycemia; or obesity. Additionally, there are EN formulas fortified with “immune modulating” ingredients or predigested/elemental diets. Liquid and powder modular protein supplements are also commercially available.

To avoid overfeeding, some clinicians have recommended adjusting the EN regimen or reducing the rate of the EN formulation [23][34][9][24]. Others suggested the use of a high protein (20%) containing formula at a reduced rate but admitted that the patient may not achieve target energy and protein needs [9]. Unfortunately, the use of volume restricted (2 kcal/mL) EN formulas for patients requiring fluid restriction are low in protein content when used for patients with high protein requirements. Most studies examining EN regimens resulted in inadequate protein intakes and often provided less than 1.2 g/kg/d [35][23][34][8][36][9][37].

Researchers have recently published our approach to this dilemma in 51 critically ill patients with multiple traumatic injuries with severe TBI or with isolated severe TBI who received high doses of propofol requiring caloric restriction [7]. Our approach entailed the use of a “very high protein” enteral formula (92 g protein/L, 1 kcal/mL) at a reduced rate along with supplemental 15, 30, or 45 g liquid protein boluses multiple times throughout the day. One exception to this enteral formula selection was for patients with greater severity of injury (estimated Injury Severity Score > 20), whereby an immune-modulating formula (94 g of protein/L and 1.5 kcal/mL) with an enteral glutamine supplement and liquid protein doses were given [38]. The liquid protein supplements should be diluted to half

strength for ease in administration via a small bore feeding tube but can be effectively delivered at full strength when administered via a larger bore tube (e.g., nasogastric suction tube or gastrostomy) [39]. If the EN infusion rate did not provide enough daily volume of feeding to meet the recommended dietary intake for vitamins (i.e., 1000 mL or 1500 mL depending on the formula), a liquid multivitamin preparation was provided daily.

The assigned target caloric intake (from both propofol and enteral nutrition) was 30 to 32 kcal/kg/d for those without obesity [19]. For those with obesity, a caloric goal of 22 to 25 kcal/kg ideal body weight (IBW)/d [21][40] was assigned. Patients received an average of 356 ± 243 kcals/d or 5 ± 3 kcal/kg/d from propofol but the caloric intake was widely variable among the patients and ranged from 1 kcal/kg/d to 15 kcal/kg/d. Caloric intake from EN ranged from 7 ± 4 kcal/kg/d on the first day of feeding to 16 ± 9 kcal/kg/d by the fifth day of EN. Caloric intake from large-volume dextrose-containing solutions averaged < 1 kcal/kg/d. The daily total caloric intakes using our approach to EN with concurrent propofol therapy during the study observation period are given in **Figure 1**.

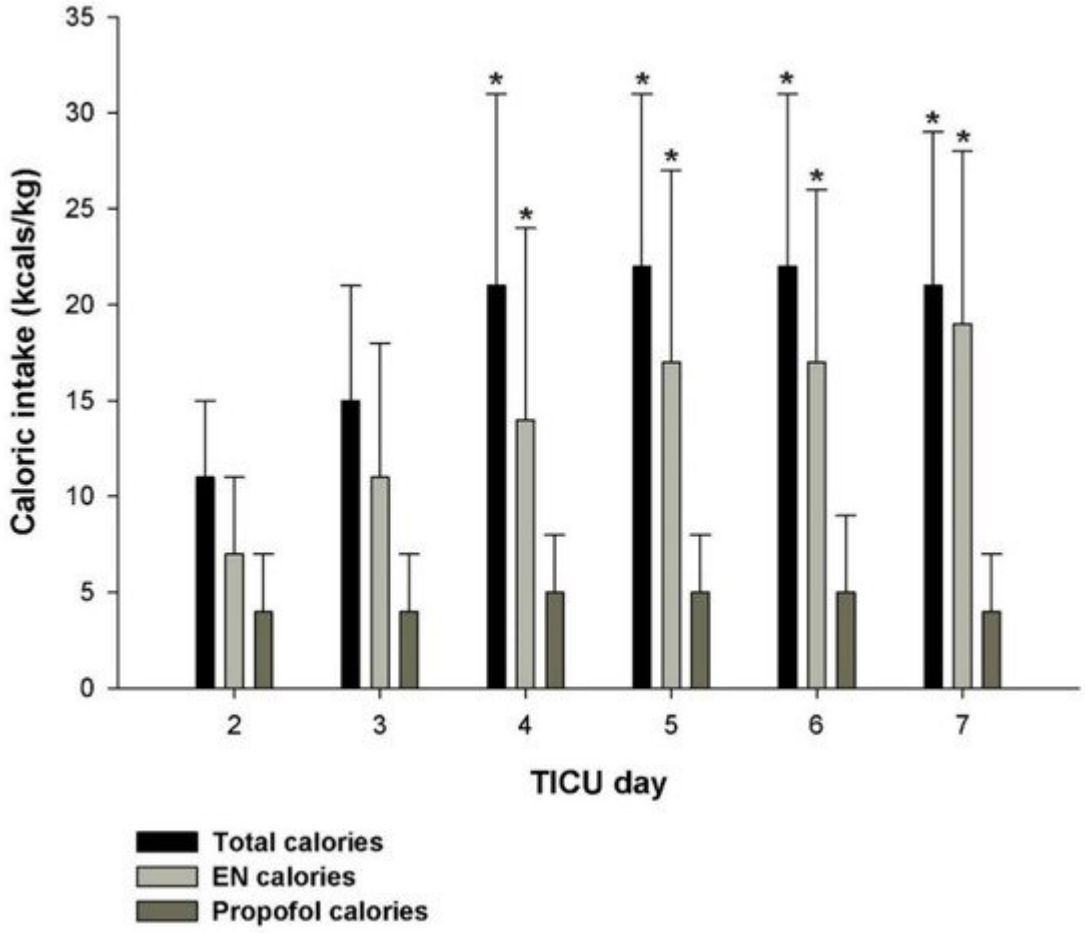

Figure 1. Total caloric intake, enteral nutrition calories, and propofol calories over days 2 to 7 for patients who received concurrent enteral nutrition and propofol [7]. One-way ANOVA indicated a significant difference in total caloric intake ($p < 0.001$) and enteral nutrition caloric intake ($p < 0.001$), but not propofol caloric intake ($p = 0.076$). * $p < 0.05$ from day 2. Day 1 represents a partial day upon admission to the TICU and was not included in the analysis. TICU, trauma intensive care unit.

Critically ill patients with traumatic injuries have high protein requirements of 2 to 2.5 g/kg/d [5][19] and providing a high protein intake with caloric restriction during propofol therapy is difficult. This is even more so for the obese patient who receives hypocaloric high protein nutrition therapy during propofol therapy and especially for those with a body mass index > 39.9 kg/m^2 because it is recommended to provide 2.5 g/kg IBW/d of protein [5][17][18]. **Figure 2** illustrates the advantage of increased delivery of protein with our approach as opposed to a simple reduction in EN feeding rate (without protein boluses). If the actual energy intake provided by use of this technique was met with either a “high protein” or standard enteral formula containing either 64 or 44 g of protein per liter, patients would have received 24% to 38% less protein despite receiving the same amount of calories. In addition, use of a “very high protein” containing EN formula with a reduced rate and supplemented with protein boluses resulted in the highest reported protein intake when compared with other studies. Despite this improvement, we were still unable to meet protein goals for some patients because of interruptions in EN delivery due to feeding intolerance, multiple surgical procedures, inability to provide intravenous erythromycin (due to drug shortage, prolonged QTc interval, or significant drug-interaction) despite tachyphylaxis to metoclopramide therapy, and hemodynamic instability [27][28].

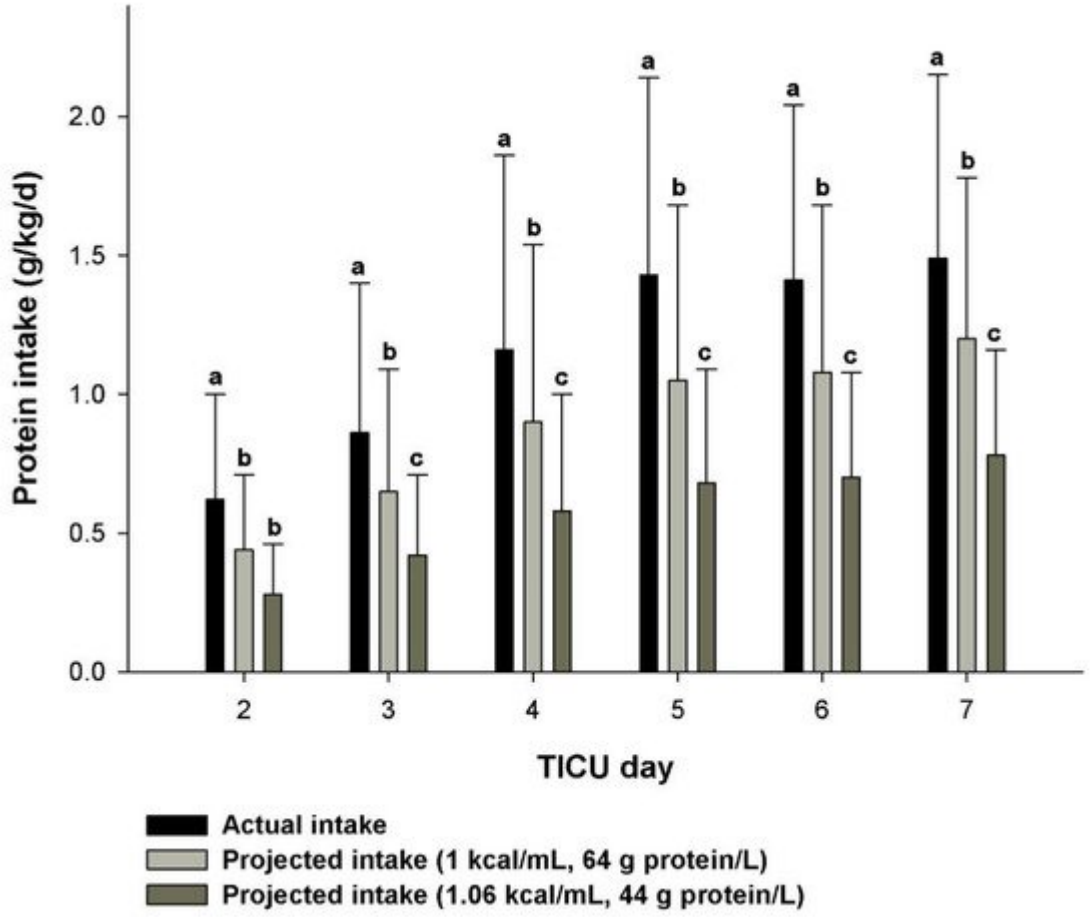

Figure 2. Actual protein intake from the modified EN regimen compared to projected protein intakes with “standard” formulas when given at an isocaloric intake as the modified EN regimen ($p < 0.001$) for patients who received concurrent enteral nutrition and propofol [7]. Daily protein intakes for each regimen that contain a different letter (e.g., a, b, or c) are significantly different from one another ($p < 0.05$). Day 1 represents a partial day upon admission to the TICU and was not included in the analysis. TICU, trauma intensive care unit.

References

1. Carney, N.; Totten, A.M.; O'Reilly, C.; Ullman, J.S.; Hawryluk, G.W.; Bell, M.J.; Bratton, S.L.; Chesnut, R.; Harris, O.A.; Kissoon, N.; et al. Guidelines for the management of severe traumatic brain injury. Neurosurgery 2017, 80, 6–15.
2. Buckley, C.T.; Dickerson, R.N. Propofol: A risk factor for caloric overfeeding and inadequate protein delivery. Hosp. Pharm. 2020, 55, 151–152.
3. Llop, J.; Sabin, P.; Garau, M.; Burgos, R.; Perez, M.; Masso, J.; Cardona, D.; Sanchez Segura, J.M.; Garriga, R.; Redondo, S.; et al. The importance of clinical factors in parenteral nutrition-associated hypertriglyceridemia. Clin. Nutr. 2003, 22, 577–583.
4. Miles, J.M.; Park, Y.; Harris, W.S. Lipoprotein liapse and triglyceride-rich lipoprotein metabolism. Nutr. Clin. Pract. 2001, 16, 273–279.
5. McClave, S.A.; Taylor, B.E.; Martindale, R.G.; Warren, M.M.; Johnson, D.R.; Braunschweig, C.; McCarthy, M.S.; Davanos, E.; Rice, T.W.; Cresci, G.A.; 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, 159–211.
6. Seidner, D.L.; Mascioli, E.A.; Istfan, N.W.; Porter, K.A.; Selleck, K.; Blackburn, G.L.; Bistrian, B.R. Effects of long-chain triglyceride emulsions on reticuloendothelial system function in humans. JPEN J. Parenter Enter. Nutr. 1989, 13, 614–619.
7. Buckley, C.T.; Van Matre, E.T.; Fischer, P.E.; Minard, G.; Dickerson, R.N. Improvement in protein delivery for critically ill patients requiring high-dose propofol therapy and enteral nutrition. Nutr. Clin. Pract. 2021, 36, 212–218.
8. Ibarra-Pastrana, E.; Serralde-Zuniga, A.; Calderon de la Barca, A.M. Critical energy and protein deficits with high contribution of non-nutrient calories after one week into an intensive care unit. Clin. Nutr. 2020, 40, 632.
9. Taylor, S.J.; Bowles, J.; Jewkes, C. Propofol use precludes prescription of estimated nitrogen requirements. J. Intensive Care Med. 2005, 20, 111–117.
10. Talpers, S.S.; Romberger, D.J.; Bunce, S.B.; Pingleton, S.K. Nutritionally associated increased carbon dioxide production. Excess total calories vs high proportion of carbohydrate calories. Chest 1992, 102, 551–555.
11. Rosmarin, D.K.; Wardlaw, G.M.; Mirtallo, J. Hyperglycemia associated with high, continuous infusion rates of total parenteral nutrition dextrose. Nutr. Clin. Pract. 1996, 11, 151–156.

12. Zusman, O.; Theilla, M.; Cohen, J.; Kagan, I.; Bendavid, I.; Singer, P. Resting energy expenditure, calorie and protein consumption in critically ill patients: A retrospective cohort study. Crit. Care 2016, 20, 367.
13. Allingstrup, M.J.; Esmailzadeh, N.; Wilkens Knudsen, A.; Espersen, K.; Hartvig Jensen, T.; Wiis, J.; Perner, A.; Kondrup, J. Provision of protein and energy in relation to measured requirements in intensive care patients. Clin. Nutr. 2012, 31, 462–468.
14. Yeh, D.D.; Fuentes, E.; Quraishi, S.A.; Lee, J.; Kaafarani, H.M.A.; Fagenholz, P.; Butler, K.; DeMoya, M.; Chang, Y.; Velmahos, G. Early protein inadequacy is associated with longer intensive care unit stay and fewer ventilator-free days: A retrospective analysis of patients with prolonged surgical intensive care unit stay. JPEN J. Parenter Enter. Nutr. 2018, 42, 212–218.
15. Nicolo, M.; Heyland, D.K.; 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. 2016, 40, 45–51.
16. Berger, M.M.; Soguel, L.; Charriere, M.; Theriault, B.; Pralong, F.; Schaller, M.D. Impact of the reduction of the recommended energy target in the ICU on protein delivery and clinical outcomes. Clin. Nutr. 2017, 36, 281–287.
17. Choban, P.; Dickerson, R.; Malone, A.; Worthington, P.; Compher, C. American Society for, Parenteral and Enteral Nutrition, ASPEN Clinical guidelines: Nutrition support of hospitalized adult patients with obesity. JPEN J. Parenter Enter. Nutr. 2013, 37, 714–744.
18. Choban, P.S.; Dickerson, R.N. Morbid obesity and nutrition support: Is bigger different? Nutr. Clin. Pract. 2005, 20, 480–487.
19. Dickerson, R.N.; Pitts, S.L.; Maish, G.O., 3rd; Schroeppel, T.J.; Magnotti, L.J.; Croce, M.A.; Minard, G.; Brown, R.O. A reappraisal of nitrogen requirements for patients with critical illness and trauma. J. Trauma. Acute Care Surg. 2012, 73, 549–557.
20. Scheinkestel, C.D.; Kar, L.; Marshall, K.; Bailey, M.; Davies, A.; Nyulasi, I.; Tuxen, D.V. Prospective randomized trial to assess caloric and protein needs of critically Ill, anuric, ventilated patients requiring continuous renal replacement therapy. Nutrition 2003, 19, 909–916.
21. Dickerson, R.N.; Medling, T.L.; Smith, A.C.; Maish, G.O., 3rd; Croce, M.A.; Minard, G.; Brown, R.O. Hypocaloric, high-protein nutrition therapy in older vs younger critically ill patients with obesity. JPEN J. Parenter Enter. Nutr. 2013, 37, 342–351.
22. Dickerson, R.N.; Maish, G.O., 3rd; Croce, M.A.; Minard, G.; Brown, R.O. Influence of aging on nitrogen accretion during critical illness. JPEN J. Parenter Enter. Nutr. 2015, 39, 282–290.
23. Ferrie, S.; Herkes, R.; Forrest, P. Nutrition support during extracorporeal membrane oxygenation (ECMO) in adults: A retrospective audit of 86 patients. Intensive Care Med. 2013, 39, 1989–1994.

24. Minnelli, N.; Gibbs, L.; Larrivee, J.; Sahu, K.K. Challenges of maintaining optimal nutrition dtatus in COVID-19 patients in intensive care settings. JPEN J. Parenter Enter. Nutr. 2020, 44, 1439–1446.
25. Bousie, E.; van Blokland, D.; Lammers, H.J.; van Zanten, A.R. Relevance of non-nutritional calories in mechanically ventilated critically ill patients. Eur. J. Clin. Nutr. 2016, 70, 1443–1450.
26. DeChicco, R.; Materese, L.; Hummell, A.C.; Speerhas, R.; Seidner, D.; Steiger, E. Contribution of calories from propofol to total energy intake. J. Am. Diet. Assoc. 1995, 95, A25.
27. Morgan, L.M.; Dickerson, R.N.; Alexander, K.H.; Brown, R.O.; Minard, G. Factors causing interrupted delivery of enteral nutrition in trauma intensive care unit patients. Nutr. Clin. Pract. 2004, 19, 511–517.
28. Dickerson, R.N.; Mitchell, J.N.; Morgan, L.M.; Maish, G.O., 3rd; Croce, M.A.; Minard, G.; Brown, R.O. Disparate response to metoclopramide therapy for gastric feeding intolerance in trauma patients with and without traumatic brain injury. JPEN J. Parenter Enter. Nutr. 2009, 33, 646–655.
29. Sessler, C.N.; Gosnell, M.S.; Grap, M.J.; Brophy, G.M.; O'Neal, P.V.; Keane, K.A.; Tesoro, E.P.; Elswick, R.K. The Richmond Agitation-Sedation Scale: Validity and reliability in adult intensive care unit patients. Am. J. Respir. Crit. Care Med. 2002, 166, 1338–1344.
30. Burke, J.F.; Wolfe, R.R.; Mullany, C.J.; Mathews, D.E.; Bier, D.M. Glucose requirements following burn injury. Parameters of optimal glucose infusion and possible hepatic and respiratory abnormalities following excessive glucose intake. Ann. Surg. 1979, 190, 274–285.
31. Elwyn, D.H. Nutritional requirements of adult surgical patients. Crit. Care Med. 1980, 8, 9–20.
32. Dickerson, R.N.; Rosato, E.F.; Mullen, J.L. Net protein anabolism with hypocaloric parenteral nutrition in obese stressed patients. Am. J. Clin. Nutr. 1986, 44, 747–755.
33. Wilmore, D.W.; Aulick, L.H.; Mason, A.D.; Pruitt, B.A., Jr. Influence of the burn wound on local and systemic responses to injury. Ann. Surg. 1977, 186, 444–458.
34. Hastings, J.; Ridley, E.J.; Bianchet, O.; Roodenburg, O.; Levkovich, B.; Scheinkestel, C.; Pilcher, D.; Udy, A. Does propofol sedation contribute to overall energy provision in mechanically ventilated critically ill adults? A retrospective observational study. JPEN J. Parenter Enter. Nutr. 2018, 42, 748–757.
35. Castro, M.; Nogueira, P.B.; Ribeiro, F.A.; Bottairi, D.S.; Piovacari, S.F.; Assis, T.; Laselva, C.R.; Toledo, D.O. Relevance of non-nutritional calories by propofol in Covid-19 critically ill patients. Clin. Nutr. 2020, 40, 509.
36. Richardson, M.; Saunders, J.; Quinn, C.; Halloran, T.O.; Riain, S.O. Improvements in goal protein achieved following a change from propofol 1% to propofol 2% and a change in enteral feeding protocol in the ICU. Clin. Nutr. 2018, 37, S55.

37. Terblanche, E.; Remmington, C. Observational study evaluating the nutritional impact of changing from 1% to 2% propofol in a cardiothoracic adult critical care unit. J. Hum. Nutr. Diet. 2020, 34, 413–419.
38. Kudsk, K.A.; Minard, G.; Croce, M.A.; Brown, R.O.; Lowrey, T.S.; Pritchard, F.E.; Dickerson, R.N.; Fabian, T.C. A randomized trial of isonitrogenous enteral diets after severe trauma. An immune-enhancing diet reduces septic complications. Ann. Surg. 1996, 224, 531–540, discussion 540-533.
39. Dickerson, R.N.; Harris, S.L. Difficulty in administration of liquid protein solution via an enteral feeding tube. Am. J. Health Syst. Pharm. 2009, 66, 796–797.
40. Dickerson, R.N.; Boschert, K.J.; Kudsk, K.A.; Brown, R.O. Hypocaloric enteral tube feeding in critically ill obese patients. Nutrition 2002, 18, 241–246.