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Review Article

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Nutrition Therapy for Patients With Traumatic Brain Injury: A Narrative Review

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ABSTRACT

Traumatic brain injury (TBI) is a global health and socio-economic problem, resulting in significant disability and mortality. Malnutrition is common in TBI patients and is associated with increased vulnerability to infection, higher morbidity and mortality rates, as well as longer stays in the intensive care unit and hospital. Following TBI, various pathophysiological mechanisms, such as hypermetabolism and hypercatabolism, affect patient outcomes. It is crucial to provide adequate nutrition therapy to prevent secondary brain damage and promote optimal recovery. This review includes a literature review and discusses the challenges encountered in clinical practice regarding nutrition in TBI patients. The focus is on determining energy requirements, timing and methods of nutrition delivery, promoting enteral tolerance, providing enteral nutrition to patients receiving vasopressors, and implementing trophic enteral nutrition. Enhancing our understanding of the current evidence regarding appropriate nutrition practices will contribute to improving overall outcomes for TBI patients.

Keywords: Traumatic brain injury; Nutrition therapy; Enteral nutrition; Parenteral nutrition

INTRODUCTION

Traumatic brain injury (TBI) is a significant cause of death and severe disabilities. Globally, there are approximately 69 million cases of TBI each year, with over 24,000 cases reported in Korea.[7,20]

Following TBI, hypermetabolism and hypercatabolism occur due to the excessive secretion of endogenous catabolic hormones like catecholamines and corticosteroids. This leads to hyperglycemia, loss of lean body mass, and increased energy expenditure.[11,24,31,41] These metabolic changes can result in immune depression, heightened susceptibility to infections, increased morbidity and mortality rates, and prolonged stays in the intensive care unit (ICU) and hospital.[23] Consequently, optimal nutritional therapy is crucial for improving outcomes. However, approximately 68% of patients experience malnutrition within 2 months of head injury.[22]

Conflict of Interest
The authors have no financial conflicts of interest.

Despite extensive research on optimal nutritional therapy for TBI, the best approach remains unknown. This review aims to synthesize previous research findings and current clinical practice guidelines to summarize the challenges and issues surrounding nutritional therapy. By comprehensively incorporating previous studies and recent clinical practice guidelines, this review aims to provide insights into the optimal nutritional therapy for patients with TBI.

DETERMINATION OF ENERGY REQUIREMENTS

Previous studies have shown that severe trauma induces hypermetabolism and a catabolic state. The metabolic changes following TBI lead to an increased energy demand, which can range from 87% to 200% above usual values.[22] Resting energy expenditure reaches its peak within 4–5 days after trauma and remains elevated for 9–12 days.[29] However, accurately predicting energy requirements in the acute phase can be challenging due to various factors, including the patient's body temperature, accompanying injuries, infection, and the use of mechanical ventilation, sedatives, and muscle relaxants. To evaluate energy requirements, The American Society for Parenteral and Enteral Nutrition-Society of Critical Care Medicine (ASPEN-SCCM) and The European Society for Clinical Nutrition and Metabolism (ESPEN) recommend using indirect calorimetry whenever possible.[27,39] Indirect calorimetry provides a more accurate assessment. In cases where indirect calorimetry is not available, ASPEN-SCCM suggests using published predictive equations such as the Harris-Benedict, Ireton-Jones, Penn State, Mifflin-St. Jeor equations, or a basic weight-based equation (25–30 kcal/kg/day) to estimate energy requirements.[3,27]

TIMING AND ROUTES OF NUTRITION

Timing of initiation: early versus delayed

There is currently no Class I evidence available on optimal nutrition timing in TBI due to ethical concerns. However, several studies have indicated that early nutrition may lead to better outcomes.

A Cochrane review suggests that early feeding in head-injured patients may be associated with a lower risk of infections and a potential improvement in outcomes.[32]

Hartl et al.[16] demonstrated that patients who did not receive nutrition within 5 to 7 days after TBI had a significantly higher likelihood of death, while any nutrition within the first 5 days after TBI reduced the mortality rate. Furthermore, a decrease of 10 kcal/kg in caloric intake was associated with a 30%–40% increase in mortality.[16] Chourdakis et al.[6] found that early enteral feeding within 24 to 48 hours after TBI may improve the hormonal profile by reducing the downregulation of thyroid-stimulating hormone, thyroid hormones, and testosterone, which could attenuate the catabolic response.

Based on these findings, the Brain Trauma Foundation recommends providing basal caloric replacement to TBI patients by the 5th day post-injury, with a maximum delay until the 7th day.[4] Both the ASPEN-SCCM and ESPEN guidelines also recommend initiating early enteral nutrition (EN) within 24–48 hours in critically ill patients if oral intake is not possible.[27,39]

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TABLE 1. Advantages and disadvantages of nutritional routes

Nutritional routes	Detail
Enteral nutrition	
Advantages	Physiological route
	Cheaper
	No venous access required
	Safer and lower infection risk
	Maintenance of the integrity of the intestinal epithelium
	Promotion of an adequate IgA secretion
	Maintenance of the intestinal microbiome diversity
Disadvantages	Dependent of gastrointestinal function
	Feeding intolerance
	Frequent interruptions and suboptimal delivery rate
	Risk of pneumonia
Parenteral nutrition	
Advantages	Early calorie intake
	No dependence on gastrointestinal function
	Less interruptions
Disadvantages	Unphysiological route
	Expensive
	Requires venous access
	More risk of catheter-related infection
	Hyperglycemia
	Hypercholesterolemia
	Abnormalities in liver function tests

IgA: immunoglobulin A.

Routes of nutrition: EN versus parenteral nutrition (PN)

Several studies have demonstrated the advantages of EN compared to PN in various aspects, including preserving gut integrity, immune response, reducing infection rates, and shortening the length of stay in the ICU (**TABLE 1**).[10,12,13,33,35]

The intestine plays a crucial role in regulating the mucosal immune response by producing and secreting secretory immunoglobulin A through the gut-associated lymphoid tissue.[27,39]

Lack of enteral stimulation can lead to increased pro-inflammatory cytokines in the intestine, apoptosis, loss of tight junction proteins, dysfunction of the epithelial barrier, and alterations in the intestinal microbiome. Disruption of the intestinal epithelium, both functionally and anatomically, contributes to an increased risk of nosocomial infections, prolonged hospital stays, and higher mortality rates.[14,17,35] Therefore, PN, which bypasses a non-functional gastrointestinal tract, does not preserve the intestinal epithelial barrier and carries a higher risk of infection compared to EN.

However, there are certain situations in which EN should be withheld, including cases of hemodynamic instability, uncontrolled life-threatening hypoxemia, hypercapnia or acidosis, active gastrointestinal bleeding, and overt bowel ischemia.[27,39] EN, by increasing mesenteric blood flow, can elevate the oxygen demand on the intestine, thereby posing risks of bowel ischemia, necrosis, and perforation in hemodynamically unstable patients.[25,38] Therefore, both the ASPEN-SCCM and ESPEN guidelines recommend EN over PN for hemodynamically stable patients.[27,39]

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DECISION-MAKING FOR EN

Facilitating enteral tolerance

Despite the advantages of EN and recommendations for its use over parenteral nutrition PN, implementing EN in critically ill patients, especially those with TBI, can be challenging. It is common for EN in TBI patients to be associated with underfeeding and consequent malnutrition due to gastrointestinal (GI) intolerance and interruptions in EN delivery. Previous studies have reported that more than 30% of TBI patients do not receive sufficient enteral caloric intake, even in experienced and motivated intensive care units.[2] In patients with TBI, interruptions in feedings are common, with only 58% and 53% of energy and protein requirements, respectively, being met, despite the majority of patients being enterally fed,[5] Additionally, approximately 50% of TBI patients experience intolerance to EN.[34]

Several factors contribute to EN intolerance in TBI patients, including delayed gastric emptying due to elevated intracranial pressure, autonomic nervous system damage, and medications such as narcotics or pentobarbital. Delayed gastric emptying can result in large gastric residual volumes, increasing the risk of aspiration pneumonia.

To improve feeding tolerance in TBI patients, various strategies can be employed. First, elevating the head of the bed by 30 to 45 degrees helps reduce reflux of gastric contents and prevent aspiration pneumonia.[18] Second, transgastric jejunal feeding can decrease reflux and the incidence of ventilator-associated pneumonia.[4,15] Third, continuous infusion of EN has been found to be better tolerated and has a positive effect on nitrogen balance, reducing hypercatabolic response and maintaining total body protein compared to intermittent EN and PN.[26,37] Fourth, the use of concentrated enteral formulas (≥1.5 kcal/mL) can provide the required calories with less volume, reducing reflux. Finally, promotility agents such as metoclopramide or erythromycin may be considered to enhance GI motility and improve EN tolerance.[8,27,30,39]

These strategies aim to optimize EN delivery and minimize GI intolerance in TBI patients, ensuring they receive adequate nutrition to support their recovery and minimize complications.

Safety and tolerance of EN for patients receiving vasopressor

Ischemic bowel is a rare but potentially life-threatening complication associated with EN, with a high mortality rate.[25] The use of vasopressors, especially those with strong alpha-1 antagonism, can affect EN tolerance by reducing GI blood flow and splanchnic perfusion in a dose-dependent manner. However, there is limited research on the safety and tolerability of EN in patients requiring intravenous vasopressor support, making it difficult to estimate the risk of intestinal ischemia when combining different types of vasoactive drugs.[1,40]

A randomized clinical trial comparing EN versus PN in ventilated patients receiving vasopressor support showed a higher risk of bowel ischemia and colonic pseudo-obstruction in the EN group compared to the PN group.[36] However, there is also evidence suggesting that EN can be feasible in patients receiving vasopressors and may be associated with shorter ICU length of stay, lower need for renal replacement therapy, and decreased hospital mortality.[9,19,21]

Although there is currently no definitive guideline regarding the safe dose of vasopressors to initiate EN, some studies have reported certain dose ranges that are generally considered safe in terms of EN tolerance. For example, norepinephrine equivalents less than 0.14 mcg/kg/

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min or ≤12.5 mcg/min, dopamine at a dose of 3–10 mcg/kg/min, and dobutamine at a dose of 12 mcg/kg/min have been suggested as safe thresholds for EN initiation.[1,25,28]

It is important to note that the decision to initiate EN in patients receiving vasopressor support should be made on an individual basis, considering the patient's clinical condition, hemodynamic stability, and the presence of any contraindications or potential risks. Close monitoring and collaboration between the nutrition support team, critical care team, and gastroenterology specialists are essential in managing EN in patients requiring vasopressor support.

Trophic EN

Previous studies have indicated that providing more than 50% to 65% of the goal energy may be necessary to prevent intestinal permeability and systemic infection.[17,27] Trophic EN, typically defined as providing 10–20 kcal/hour, may be sufficient to prevent mucosal atrophy and maintain gut integrity. A single-center retrospective study focused on the effect of early trophic EN in mechanically ventilated patients with septic shock. The study found that patients who received less than 600 kcal/day within 48 hours (considered trophic EN, defined as 10 to 30 mL/h) had a shorter duration of mechanical ventilation and reduced length of stay without an increased risk of complications, compared to patients who did not receive EN or received 600 kcal/day or more within 48 hours.

These findings suggest that initiating trophic EN early on in critically ill patients, even at a low caloric intake, can have beneficial effects on clinical outcomes. However, it is important to note that individual patient factors and specific clinical contexts should be considered when determining the appropriate nutrition strategy, and further research is needed to establish optimal feeding practices in different patient populations.

CONCLUSION

Timely and effective nutritional therapy is essential in the management of TBI to improve patient outcomes. Accurately predicting energy requirements can be challenging, but indirect calorimetry is the preferred method, while published predictive equations or weight-based equations can be used as alternatives.

Early EN within 24–48 hours of trauma is recommended for hemodynamically stable TBI patients and has been associated with better outcomes. EN is preferred over PN due to its advantages in preserving gut integrity, immune response, reducing infections, and shortening ICU stays. However, EN should be withheld until patients are hemodynamically stable to avoid complications.

Implementing EN in TBI patients can be challenging due to factors like delayed gastric emptying and interruptions. Strategies to improve enteral tolerance include elevating the head of the bed, transgastric jejunal feeding, continuous infusion of EN, using concentrated formulas, and promotility agents.

The use of vasopressors can affect GI blood flow, and their impact on EN tolerance requires further investigation. Trophic EN, with low-calorie intake, can be considered for patients with enteral intolerance.

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TABLE 2. Recommendations for nutrition therapy in TBI

Issues	Recommendation
Energy expenditure	Indirect calorimetry is the gold standard for the determination of energy requirements
	If indirect calorimetry is not available, a published predictive equation or a basic weight-based equation can be applied
	Feeding patients to attain basal caloric replacement at 5 to 7 days after TBI
Timing and routes of nutrition	Initiating early EN within 24 to 48 hours instead of delaying enteral nutrition
	The use of EN over PN is recommended for hemodynamically stable patients
Facilitating enteral tolerance	Elevating the head of the bed by 30 to 45 degrees to prevent aspiration pneumonia
	Transgastric jejunal feeding reduce the incidence of ventilator-associated pneumonia
	Promotility agents such as metoclopramide or erythromycin may be considered
Safety and tolerance of EN for patients receiving vasopressor	It is unclear that the safe dose of vasopressor to initiate EN

TBI: traumatic brain injury, EN: enteral nutrition, PN: parenteral nutrition.

TABLE 2 summarizes the recommendations for nutrition therapy in TBI patients.

While there are recommendations for nutrition therapy in TBI, further studies are needed to identify the best approaches to improve outcomes in these patients.

REFERENCES

1. Allen JM. Vasoactive substances and their effects on nutrition in the critically ill patient. **Nutr Clin Pract** 27:335-339, 2012
PUBMED | CROSSREF
2. Barr J, Hecht M, Flavin KE, Khorana A, Gould MK. Outcomes in critically ill patients before and after the implementation of an evidence-based nutritional management protocol. **Chest** 125:1446-1457, 2004
PUBMED | CROSSREF
3. Bistrian BR, Askew W, Erdman JW Jr, Oria MP. Nutrition and traumatic brain injury: a perspective from the Institute of Medicine report. **JPEN J Parenter Enteral Nutr** 35:556-559, 2011
PUBMED | CROSSREF
4. Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. **Neurosurgery** 80:6-15, 2017
PUBMED
5. Chapple LA, Chapman MJ, Lange K, Deane AM, Heyland DK. Nutrition support practices in critically ill head-injured patients: a global perspective. **Crit Care** 20:6, 2016
PUBMED | CROSSREF
6. Chourdakis M, Kraus MM, Tzellos T, Sardeli C, Peftoulidou M, Vassilakos D, et al. Effect of early compared with delayed enteral nutrition on endocrine function in patients with traumatic brain injury: an open-labeled randomized trial. **JPEN J Parenter Enteral Nutr** 36:108-116, 2012
PUBMED | CROSSREF
7. Dewan MC, Rattani A, Gupta S, Baticulon RE, Hung YC, Punchak M, et al. Estimating the global incidence of traumatic brain injury. **J Neurosurg** 130:1080-1097, 2018
PUBMED | CROSSREF
8. Dickerson RN, Mitchell JN, Morgan LM, Maish GO 3rd, Croce MA, Minard G, et al. Disparate response to metoclopramide therapy for gastric feeding intolerance in trauma patients with and without traumatic brain injury. **JPEN J Parenter Enteral Nutr** 33:646-655, 2009
PUBMED | CROSSREF
9. Dorken Gallastegi A, Gebran A, Gaitanidis A, Naar L, Hwabejire JO, Parks J, et al. Early versus late enteral nutrition in critically ill patients receiving vasopressor support. **JPEN J Parenter Enteral Nutr** 46:130-140, 2022
PUBMED | CROSSREF
10. Elke G, van Zanten AR, Lemieux M, McCall M, Jeejeebhoy KN, Kott M, et al. Enteral versus parenteral nutrition in critically ill patients: an updated systematic review and meta-analysis of randomized controlled trials. **Crit Care** 20:117, 2016
PUBMED | CROSSREF
11. Foley N, Marshall S, Pikul J, Salter K, Teasell R. Hypermetabolism following moderate to severe traumatic acute brain injury: a systematic review. **J Neurotrauma** 25:1415-1431, 2008
PUBMED | CROSSREF

https://doi.org/10.13004/kjnt.2023.19.e31

12. Fukatsu K, Kudsk KA. Nutrition and gut immunity. **Surg Clin North Am** 91:755-770, 2011
PUBMED | CROSSREF
13. Fukatsu K. Impact of the feeding route on gut mucosal immunity. **Curr Opin Clin Nutr Metab Care** 17:164-170, 2014
PUBMED | CROSSREF
14. Fukatsu K. Role of nutrition in gastroenterological surgery. **Ann Gastroenterol Surg** 3:160-168, 2019
PUBMED | CROSSREF
15. Grahm TW, Zadrozny DB, Harrington T. The benefits of early jejunal hyperalimentation in the head-injured patient. **Neurosurgery** 25:729-735, 1989
PUBMED | CROSSREF
16. Härtl R, Gerber LM, Ni Q, Ghajar J. Effect of early nutrition on deaths due to severe traumatic brain injury. **J Neurosurg** 109:50-56, 2008
PUBMED | CROSSREF
17. Jabbar A, Chang WK, Dryden GW, McClave SA. Gut immunology and the differential response to feeding and starvation. **Nutr Clin Pract** 18:461-482, 2003
PUBMED | CROSSREF
18. Kattelmann KK, Hise M, Russell M, Charney P, Stokes M, Compher C. Preliminary evidence for a medical nutrition therapy protocol: enteral feedings for critically ill patients. **J Am Diet Assoc** 106:1226-1241, 2006
PUBMED | CROSSREF
19. Khalid I, Doshi P, DiGiovine B. Early enteral nutrition and outcomes of critically ill patients treated with vasopressors and mechanical ventilation. **Am J Crit Care** 19:261-268, 2010
PUBMED | CROSSREF
20. Kim HK, Leigh JH, Lee YS, Choi Y, Kim Y, Kim JE, et al. Decreasing incidence and mortality in traumatic brain injury in Korea, 2008-2017: a population-based longitudinal study. **Int J Environ Res Public Health** 17:17, 2020
PUBMED | CROSSREF
21. Kompan L, Kremzar B, Gadzijev E, Prosek M. Effects of early enteral nutrition on intestinal permeability and the development of multiple organ failure after multiple injury. **Intensive Care Med** 25:157-161, 1999
PUBMED | CROSSREF
22. Krakau K, Hansson A, Karlsson T, de Boussard CN, Tengvar C, Borg J. Nutritional treatment of patients with severe traumatic brain injury during the first six months after injury. **Nutrition** 23:308-317, 2007
PUBMED | CROSSREF
23. Kurtz P, Rocha EE. Nutrition therapy, glucose control, and brain metabolism in traumatic brain injury: a multimodal monitoring approach. **Front Neurosci** 14:190, 2020
PUBMED | CROSSREF
24. Lenz A, Franklin GA, Cheadle WG. Systemic inflammation after trauma. **Injury** 38:1336-1345, 2007
PUBMED | CROSSREF
25. Mancl EE, Muzevich KM. Tolerability and safety of enteral nutrition in critically ill patients receiving intravenous vasopressor therapy. **JPEN J Parenter Enteral Nutr** 37:641-651, 2013
PUBMED | CROSSREF
26. Mazaherpur S, Khatony A, Abdi A, Pasdar Y, Najafi F. The effect of continuous enteral nutrition on nutrition indices, compared to the intermittent and combination enteral nutrition in traumatic brain injury patients. **J Clin Diagn Res** 10:JC01-JC05, 2016
PUBMED | CROSSREF
27. McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, 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 Enteral Nutr** 40:159-211, 2016
PUBMED | CROSSREF
28. Merchan C, Altshuler D, Aberle C, Papadopoulos J, Schwartz D. Tolerability of enteral nutrition in mechanically ventilated patients with septic shock who require vasopressors. **J Intensive Care Med** 32:540-546, 2017
PUBMED | CROSSREF
29. Monk DN, Plank LD, Franch-Arcas G, Finn PJ, Streat SJ, Hill GL. Sequential changes in the metabolic response in critically injured patients during the first 25 days after blunt trauma. **Ann Surg** 223:395-405, 1996
PUBMED | CROSSREF
30. Nursal TZ, Erdogan B, Noyan T, Cekinmez M, Atalay B, Bilgin N. The effect of metoclopramide on gastric emptying in traumatic brain injury. **J Clin Neurosci** 14:344-348, 2007
PUBMED | CROSSREF

https://doi.org/10.13004/kjnt.2023.19.e31

31. Pepe JL, Barba CA. The metabolic response to acute traumatic brain injury and implications for nutritional support. **J Head Trauma Rehabil** 14:462-474, 1999
PUBMED | CROSSREF

32. Perel P, Yanagawa T, Bunn F, Roberts I, Wentz R, Pierro A. Nutritional support for head-injured patients. **Cochrane Database Syst Rev** 2006:CD001530, 2006
PUBMED | CROSSREF

33. Pierre JF. Gastrointestinal immune and microbiome changes during parenteral nutrition. **Am J Physiol Gastrointest Liver Physiol** 312:G246-G256, 2017
PUBMED | CROSSREF

34. Quintard H, Ichai C. Nutritional and metabolic supplementation for the injured brain: an update. **Curr Opin Crit Care** 25:126-131, 2019
PUBMED | CROSSREF

35. Quiroz-Olguín G, Gutiérrez-Salmeán G, Posadas-Calleja JG, Padilla-Rubio MF, Serralde-Zúñiga AE. The effect of enteral stimulation on the immune response of the intestinal mucosa and its application in nutritional support. **Eur J Clin Nutr** 75:1533-1539, 2021
PUBMED | CROSSREF

36. Reignier J, Boisramé-Helms J, Brisard L, Lascarrou JB, Ait Hssain A, Anguel N, et al. Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2). **Lancet** 391:133-143, 2018
PUBMED | CROSSREF

37. Rhoney DH, Parker D Jr, Formea CM, Yap C, Coplin WM. Tolerability of bolus versus continuous gastric feeding in brain-injured patients. **Neurol Res** 24:613-620, 2002
PUBMED | CROSSREF

38. Simo Es Covello LH, Gava-Brandolis MG, Castro MG, Dos Santos Netos MF, Manzanares W, Toledo DO. Vasopressors and nutrition therapy: Safe dose for the outset of enteral nutrition? **Crit Care Res Pract** 2020:1095693, 2020
PUBMED | CROSSREF

39. Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP, et al. ESPEN guideline on clinical nutrition in the intensive care unit. **Clin Nutr** 38:48-79, 2019
PUBMED | CROSSREF

40. Yang S, Wu X, Yu W, Li J. Early enteral nutrition in critically ill patients with hemodynamic instability: an evidence-based review and practical advice. **Nutr Clin Pract** 29:90-96, 2014
PUBMED | CROSSREF

41. Young B, Ott L, Dempsey R, Haack D, Tibbs P. Relationship between admission hyperglycemia and neurologic outcome of severely brain-injured patients. **Ann Surg** 210:466-472, 1989
PUBMED | CROSSREF