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Nutrition Management in Patients With Traumatic Brain Injury: A Narrative Review

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HIGHLIGHTS

- Traumatic brain injury causes multiple gastrointestinal and nutritional complications.
- The assessment and multidisciplinary approach are essential for effective nutrition support.
- Route of access, glycemic control, and protein support are important considerations.

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ABSTRACT

Traumatic brain injury (TBI) is a major cause of long-term physical and psychological disability and death. In patients with TBI, undernutrition is associated with an increased mortality rate, more infectious complications, and worse neurologic outcomes. Therefore, timely and effective nutritional therapy is particularly crucial in the management of TBI to improve patients' prognoses. This narrative review summarizes the issues encountered in clinical practice for patients with neurotrauma who receive acute and post-acute in-patient rehabilitation services, and it comprehensively incorporates a wide range of studies, including recent clinical practice guidelines (CPGs), with the aim of better understanding the current evidence for optimal nutritional therapy focused on TBI patients. Recent CPGs were reviewed for 6 topics: 1) hypermetabolism and variation in energy expenditure in patients with TBI, 2) delayed gastric emptying and intolerance to enteral nutrition, 3) decision-making on the route and timing of access in patients with TBI who are unable to maintain volitional intake (enteral nutrition versus parenteral nutrition), 4) decision-making on the enteral formula (standard or immune-modulating formulas), 5) glycemic control, and 6) protein support. We also identified areas that need further research in the future.

Keywords: Traumatic Brain Injury; Nutrition Therapy; Enteral Nutrition; Parenteral Nutrition; Glycemic Control

INTRODUCTION

Traumatic brain injury (TBI) affects approximately 69 million people worldwide each year and has serious implications with regard to long-term physical and psychological disability and death [1-3]. In Korea, approximately 480,000 new TBI cases occur annually and the total medical costs for TBI steadily increased over the last decade [4]. Hypermetabolism and increased catabolism after TBI lead to hyperglycemia, protein wasting, and increased energy demand, which may be as high as 200% of the usual energy requirement [5,6]. A previous study reported that 68% of patients with acute TBI were malnourished [7]. This negative energy balance causes a decrease in body mass, especially skeletal muscle mass, and leads to a negative nitrogen balance. It is also associated with an increase in morbidity and mortality [8].

Nutrition in patients with TBI is pivotal for maintaining cellular homeostasis and reducing mortality and the incidence of infectious complications [9-11]. Therefore, timely and effective nutritional therapy is particularly crucial in the management of TBI to improve patients' prognoses, especially in more severe TBI cases. Although many previous studies have been conducted on nutrition in stroke patients, relatively few studies have explored nutrition in patients with TBI [12,13]. In this review, we summarize the difficulties or issues encountered in clinical practice and comprehensively incorporate previous studies and recent clinical practice guidelines (CPGs) to better understand the current evidence for optimal nutritional therapy in TBI patients. We also identify areas that need further research in the future.

TOPIC 1. HYPERMETABOLISM AND VARIATION IN ENERGY EXPENDITURE IN PATIENTS WITH TBI

The secondary response to trauma increases the secretion of catecholamines, which antagonize insulin, and inflammatory mediators. Hormonal changes after TBI can lead to hypermetabolism by increasing the secretion of corticosteroids, counterregulatory hormones, and cytokines. In the acute phase of TBI, energy requirements increase to 100%–200% of baseline-predicted resting energy expenditure (REE), which may persist for several weeks to several months, depending on the severity of the neurotrauma and level of recovery [5,14]. Hypercatabolism of brain injury is associated with increased morbidity and weight loss [15]. It generally stops and plateaus at 2 months postinjury, and this timing often coincides with admission to inpatient rehabilitation [16].

In the acute phase of TBI, factors including the patient's body temperature, use of sedatives, mechanical ventilation, and the severity of brain injury modify the REE, making it very challenging to predict an individual's nutritional requirements; this difficulty may lead to inadequate nutrition [17]. Moreover, since patients with severe TBI often have edema related to resuscitation, it is difficult to accurately predict energy requirements using body weight [18]. In the post-acute phase, calorie needs should be reassessed. Calorie demands decrease in the setting of limited mobility as the medical status normalizes [16]. Meanwhile, the process of rehabilitation therapy increases calorie needs and this may be 30-60% higher than control groups [16].

Recommendations from recent CPGs: Determination of energy expenditure

The American Society for Parenteral and Enteral Nutrition-Society of Critical Care Medicine (ASPEN-SCCM) and many clinicians recommend that indirect calorimetry is the current "gold standard" to measure energy requirements in patients with TBI whenever possible (quality of evidence: very low [ASPEN-SCCM]) [8,17]. However, using indirect calorimetry involves many practical difficulties, such as high costs and the requirement for a trained professional [19]. The ASPEN-SCCM guideline suggests that if indirect calorimetry is not available, a published predictive equation or a basic weight-based equation (25–30 kcal/kg/d) be applied to determine energy requirements in critically ill patients (quality of evidence: expert consensus) [17]. The Harris-Benedict, Ireton-Jones, and Penn State predictive equations are commonly used (**Table 1**) [20,21]. The Brain Trauma Foundation recommends that TBI patients be fed to achieve basal caloric replacement at least by the fifth day and at most, by the seventh day post-injury to lower risk of death (level IIA) [22].

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Table 1. Common equations for predicting resting energy expenditure

Equations
Equations derived from testing hospital patients
Penn State Equation
REE = (1.1 × value of HBE) + (140 × Tmax) + (32 × VE) − 5,340
Ireton-Jones Equation for ventilated patients
Male REE = 2,028 − 11 × A + 5 × W + 239 × T + 804 × B
Female REE = 1,784 − 11 × A + 5 × W + 239 × T + 804 × B
Equations derived from testing normal volunteers
Harris-Benedict Equations
Male REE = 66.47 + 13.75 × W + 5 × H − 6.755 × A
Female REE = 665.1 + 9.563 × W + 1.85 × H − 4.676 × A
Mifflin-St. Jeor Equations
Male BMR = 10 × W + 6.25 × H − 5 × A + 5
Female BMR = 10 × W + 6.25 × H − 5 × A − 161

REE, resting energy expenditure (kcal/day); HBE, REE calculated by Harris-Benedict method (kcal/day); Tmax, maximum body temperature in the past 24 hours (℃); VE, expired minute volume (L/min); A, ages (years); W, actual body weight (kg); T, trauma; B, burn; H, height (cm).

During inpatient rehabilitation, comprehensive information concerning limited mobility or paresis, progress in therapy and activities of daily living, and level of agitation is important for the nutrition reassessment [16]. Moreover, weekly monitoring for weight gain or loss is useful. In case of weight gain due to hyperphagia, it is important to apply behavioral strategies using a memory board or diary, and to encourage patients to follow a low-fat, well-balanced diet [16].

TOPIC 2. DELAYED GASTRIC EMPTYING AND INTOLERANCE TO ENTERAL NUTRITION

Gastroparesis, or delayed gastric emptying, is one of the major factors that cause feeding intolerance, which is exhibited in 45%–50% of TBI patients [6,23]. Previous studies showed that in patients with moderate-to-severe TBI, the gastric emptying half-life was delayed more than twice as compared to that of healthy control subjects. Gastrointestinal hypokinesia usually persisted during the first 1–2 weeks after TBI [14,24]. After the transfer to the general ward, the delay in emptying may continue depending on the severity of the TBI and if elevated intracranial pressure continues. Delayed gastric emptying may be assumed when there is feeding tube intolerance with large gastric residual volume. Ileus may be present, but it appears more commonly when brain injury is accompanied by the spinal cord injury [25].

There are numerous reasons for intolerance to enteral nutrition (EN) in patients with TBI (**Table 2**). Neurotrauma increases intracranial pressure and damages the autonomic nervous system [23,26]. Sedatives such as opioid agents delay gastric emptying, which consequently may increase gastric residual volume and the risk of vomiting [23]. Furthermore, several aspects of patients with TBI interrupt EN. For instance, pain from trauma, facial fractures, oral injury, and prolonged cervical immobilization may delay resumption of an oral diet. A previous study showed that surgery, extubation or intubation, or radiological exams interrupted approximately 30% of critically ill patients with TBI at least once during the observation period [27].

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Table 2. Reasons for intolerance to enteral nutrition in patients with TBI

Variables	Reasons
Central mechanism	Increased intracranial pressure
	Damage of the autonomic nervous system
Central and peripheral mechanism	Opioid agents
	Pain
Multiple trauma	Facial fractures
	Oral injury
	Prolonged cervical immobilization
Interruptions in healthcare	Surgery
	Extubation or intubation
	Radiologic exams
	Bedside procedures
	Large gastric residual volume
	Emesis

TBI, traumatic brain injury.

Recommendations from recent CPGs: Strategies to improve intolerance to EN in patients with TBI

There are several strategies to improve feeding tolerance in patients with TBI. First, the American Dietetic Association recommends positioning patients in a 45° head-of-bed elevation position to prevent aspiration pneumonia (grade II) and to minimize gastroesophageal or laryngopharyngeal reflux of gastric contents (grade I) [28]. Second, concentrated enteral formulas (≥ 1.5 kcal/mL) may reduce the risk of reflux or intolerance while meeting caloric requirements in less volume [20]. Thirdly, for EN, a continuous infusion is preferred rather than administration as a bolus. A recent randomized clinical trial (RCT) demonstrated that the continuous infusion had more positive effects on nitrogen balance and decreasing the hypercatabolic response in patients with TBI than intermittent EN and parenteral methods [29].

Since the enteric nervous system and intestinal smooth muscle are intact, motility-promoting agents should be useful. The ASPEN-SCCM guideline suggests that in patients at risk of swallowing aspiration, prokinetic medications (e.g., metoclopramide or erythromycin) be initiated where feasible [17]. Metoclopramide is currently the only FDA-approved promotility agent. However, the potential for central nervous system side effects due to antagonizing central dopamine D2 receptors may limit its use. It may also worsen the severity and frequency of seizures and should not be used in patients with TBI who have seizures. Also, patients taking medications that may increase the risk of extrapyramidal symptoms should avoid it. As a treatment for intolerance to EN, metoclopramide appears to be less effective in TBI than in other critically ill patients and combination therapy with erythromycin should be considered unless contraindicated [30,31]. Erythromycin is a macrolide antibiotic structurally similar to the GI hormone motilin. Although it does not have an FDA-approved indication, it is used as an effective promotility drug.

The European Society for Clinical Nutrition and Metabolism (ESPEN) guideline recommend that postpyloric feeding should be considered in critically ill patients whose gastric feeding intolerance has not been resolved with prokinetic agents (grade of recommendation B - strong consensus) or in patients whose risk for aspiration is high (grade of recommendation: good practice point [GPP] - strong consensus). Experts suggest that jejunal feeding should only be attempted in environments where the technique is readily available or if gastric akinesia persists despite appropriate attempts [6,32].

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After the transfer to the general ward, low fat (<30%) meals are preferred for gastroparesis because high fat meals may further prolong gastric emptying [16]. Antiemetcs may be suitable for nausea [16].

TOPIC 3. DECISION-MAKING ON THE ROUTE AND TIMING OF ACCESS IN PATIENTS WITH TBI WHO ARE UNABLE TO MAINTAIN VOLITIONAL INTAKE: EN VERSUS PN

According to meta-analyses of previous RCTs comparing early (within 24–48 hours) versus delayed EN, patients who received early EN showed lower mortality, reduced infection rates, and shorter hospital stays [33,34]. The advantages of EN over parenteral nutrition (PN) have been demonstrated in numerous previous RCTs regarding reduction of infection (e.g., pneumonia and central line infection in most patients, and abdominal abscess in trauma patients, in particular) and the length of stay in the intensive care unit [17]. In particular, EN preserves gut integrity, and stress and the immune response are physiologically regulated. Furthermore, access through the gut serves as a passageway for immune-modulating substances and is effective in preventing stress ulcers [35].

Recommendations from recent CPGs: Timing of the initiation of EN and PN in patients with acute TBI

Both the ASPEN-SCCM and ESPEN guidelines recommend initiating early EN (within 24-48 hours) instead of delaying EN (quality of evidence: very low [ASPEN-SCCM]; grade of recommendation: B - strong consensus [ESPEN]) [17,32]. Early EN therapy is more beneficial, especially in high-risk patients [17]. For hemodynamically stable patients, the use of EN over PN is recommended in both guidelines (quality of evidence-low to very low [ASPEN-SCCM]; grade of recommendation: A - strong consensus [ESPEN]) [17,32].

Gastric access is the standard method for initiating EN (quality of evidence: moderate to high [ASPEN-SCCM]; grade of recommendation: GPP - strong consensus [ESPEN]), and gradual increase of EN is necessary to avoid overfeeding in the early phase, especially in patients who are intolerant initially (grade of recommendation: A - strong consensus [ESPEN]) [17,32]. An initial EN rate of 20 mL/h is appropriate, and it is desirable to increase the amount by 10 to 20 mL/h every 6–8 hours to reach the target amount [20].

However, EN should be withheld in hemodynamically unstable patients [17]. If a patient receiving vasopressor therapy is provided with EN, close attention should be paid to intolerance signs such as abdominal distention, hypoactive bowel sounds, decrease in stool passing, and metabolic acidosis, which are early signs of gut ischemia. EN should be discontinued until stabilization of the symptoms and interventions.

Although early EN is recommended for most patients, there is no dispute about the necessity of supplementation with PN if malnutrition persists in order to minimize the detrimental effects of a negative energy balance [32]. However, the most appropriate time for prescribing supplemental PN has not yet been established. According to Casaer et al. [36], early PN was associated with an increased morbidity and infection rate. In particular, the potential side effects of overestimating the caloric target in the acute phase were discussed. Although the most appropriate timing of PN supplementation has not been determined, the ESPEN

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guideline recommends 4 to 7 days based on the results of previous studies [32]. Meanwhile, the ASPEN-SCCM guideline recommends considering the use of supplemental PN after 7–10 days if it is not possible to meet > 60% of energy and protein requirements by the enteral route alone [17]. Initiating PN prior to this 7- to 10-day period in critically ill brain-injured patients does not improve the outcome, and may even adversely affect the patient (quality of evidence: moderate [ASPEN-SCCM]) [17].

TOPIC 4. DECISION MAKING ON THE ENTERAL FORMULA: STANDARD OR IMMUNE-MODULATING FORMULAS

After brain injury, excessive release of glutamate and excitotoxic neurotransmitters increases the intracellular calcium and sodium influx and results in energy depletion. Formulas using immune-modulating nutrients such as glutamine, omega-3 fatty acids, arginine, and nucleotides have been proposed to promote neuroprotection from secondary brain insults [8]. Glutamine is one of the most abundant amino acids in the human body, and is mostly synthesized in muscles, where it is used for metabolism. In catabolic metabolism, which occurs after trauma, sepsis, or major surgery, more glutamine is metabolized than produced. Therefore, glutamine is categorized as a conditionally essential amino acid [37]. Previous studies have shown that glutamine-enriched enteral diets reduce infections and length of stay in patients with moderate-to-severe TBI [38-40]. However, when plasma glutamine levels are normal, excessive doses have the potential to cause adverse effects [41]. A proper dose of glutamine is between 0.3 to 0.5 g/kg body weight per day (i.e., 25–50 g/day) for 1 to 2 weeks during EN and PN [6].

Omega-3 polyunsaturated fatty acids (n-3 PUFA), which include eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are important for appropriate brain development and function. DHA is the most abundant n-3 PUFA in the brain and is involved in regeneration and repair in the central nervous system after TBI [42]. Previous studies showed that n-3 PUFA supplementation may decrease neuroinflammation after brain injury [43,44]; however, a larger clinical trial demonstrated that the administration of n-3 PUFA had little effect on quality of life in patients with TBI [45]. So far, there is no conclusive evidence supporting the use of n-3 PUFA [6]. DHA and EPA have promising effects in experimental studies, but no clinical data are convincing [46].

L-arginine is the precursor of several active compounds such as nitric oxide, proline, polyamines, ornithine, creatine, phosphocreatine, and agmatine [47]. Proper arginine supplementation is associated with improvements in the immune response and protein synthesis. Critical care formulas including arginine, fish oil, and various antioxidants have been shown to be effective at reducing infection in brain-injured patients [48].

Previous studies have shown that requirements for branched-chain amino acids (BCAAs; valine, isoleucine, and leucine) increase or BCAA levels decrease after TBI [49,50]. BCAAs are essential amino acids that act as important nitrogen donors for glutamate synthesis in the brain and are essential for neurotransmitter cycling [51]. BCAAs are also used in brain cells as a fuel source for the tricarboxylic acid cycle. BCAAs also act as major nitrogen donors through transamination in skeletal muscle. In particular, leucine activates mammalian target of rapamycin (mTOR) signaling and inhibits adenosine monophosphate kinase (AMPK) activity to promote protein synthesis and skeletal muscle growth [52]. Previous studies

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showed that intravenous BCAA (e.g., leucine) infusion reduced mortality and post-TBI disability by enhancing protein synthesis and homeostasis [53,54]. The effects of BCAAs on outcomes have mainly been studied in patients with severe TBI. Further investigations on the effect of BCAA supplementation on patients with mild TBI are needed. It is also necessary to explore the effects of supplementation according to patients' characteristics, such as age, sex, cognitive function, and emotional and behavioral state.

Recommendations from recent CPGs: Suggestions for immune-modulating enteral formulations

The use of an immune-modulating formulation containing arginine or EPA/DHA supplementation in addition to the standard enteral formula is suggested in patients with TBI (quality of evidence: very low [ASPEN-SCCM]) [17].

TOPIC 5. DECISION-MAKING ON GLYCEMIC CONTROL: TIGHT VERSUS PERMISSIVE

Although hyperglycemia after TBI is associated with injury severity and poorer outcomes, there is no consensus that strict blood glucose control has a positive effect on the outcomes of patients with TBI [8,55]. Intensive insulin therapy for strict glycemic control has been reported to increase energy crises in the brain (high lactate-to-pyruvate ratio and excessive glutamate) and the risk of reduced brain glucose concentration [56]. Hence, avoiding excessive hyperglycemia (> 10–11 mmol/L) and sustaining "permissive" glycemic control between 8 to 11 mmol/L are currently recommended [57]. Accumulating data have shown that during cerebral energetic crises, lactate, ketone bodies, and BCAAs may be favored substrates to reduce the potential detrimental effects of intensive insulin therapy [6].

Recommendations from recent CPGs: Suggestions for glycemic control in patients with TBI

The NICE-SUGAR study showed that patients with TBI randomly assigned to intensive (4.5–6.0 mmol/L) glucose control experienced moderate and severe hypoglycemia more frequently than the conventional glucose (< 10 mmol/L) control group. However, there was no significant difference between the two groups in clinically important outcomes [58]. Currently, it is recommended to avoid excessive hyperglycemia (more than 10–11mmol/l) and to sustain a moderate 'permissive' glucose control (8–11mmol/l) [6].

TOPIC 6. PROTEIN SUPPORT IN PATIENTS WITH TBI

The importance of protein goes beyond its role as a simple source of calories. It is the most important caloric nutrient for the recovery of brain damage, complementation of immune function, and maintenance of body mass. Most critically ill brain-injured patients have a high ratio of protein requirements to total energy requirements, and it is difficult to meet their requirements with general EN. Nitrogen excretion increases independently of the corresponding supplementation amount, and the steady loss of nitrogen can continue for up to 4 weeks. Therefore, it is important to maintain protein balance, and it may be difficult to balance nitrogen even in the post-acute phase [8]. For this reason, protein supplementation can be helpful in patients with insufficient EN, and regular evaluations of the adequacy of protein intake are necessary.

Recommendations from recent CPGs: Determination of adequate protein intake

The ASPEN-SCCM guideline suggests immediate implementation of EN with a high protein polymeric diet within 24–48 hours of trauma if the patient is hemodynamically stable (quality of evidence: very low) [17]. Protein requirements are estimated to be in the range of 1.2–2.0 g/kg actual body weight per day for trauma patients [17]. This requirement may be even higher in multitrauma patients. Most experts recommend that for patients with TBI, protein should account for 15%–20% of total calories, for which administration of at least 2 g/kg body weight per day is required [6]. Immune-modulating formulas may be an applicable option for achieving a sufficient protein supply in order to minimize negative nitrogen balance after TBI [17,59].

UNRESOLVED ISSUES AND FUTURE RESEARCH DIRECTIONS

Highlights of the topics discussed herein and recent recommendations for nutritional therapy in patients with TBI are listed in **Table 3**. Currently, some unresolved issues relate to a ketogenic diet and micronutrients (i.e., minerals, vitamins, and trace elements). A medium-chain triglyceride ketogenic diet might have a neuroprotective effect, and lactate and a ketogenic diet might be an alternative source of energy for patients with TBI [60]. However, related clinical data are insufficient to recommend ketogenic diets as a preferential nutritional strategy. A previous study showed that intravenous zinc supplementation for 2–4 weeks improved outcomes after TBI [60]. More research is needed to sharpen our understanding of the effects of zinc supplementation on recovery after TBI. Furthermore, prior studies demonstrated that intramuscular vitamin-D and vitamin-E injections enhanced cognitive symptoms and self-reported outcomes 6 months after severe TBI [61,62]. Further research is needed to clarify the effects of micronutrient supplementation on cognitive and physical outcomes in patients with TBI.

Table 3. Highlights of the issues and recommendations for nutrition therapy in patients with TBI

Issues	Recommendations
Determination of the energy expenditure	Increased energy demand after TBI may lead to hypermetabolsim and hypercatabolism which are associated with increased morbidity and weight loss [15,16]. Indirect calorimetry is the current "gold standard" for the determination of REE in patients with TBI, however, there are several practical difficulties [17,32]. A published predictive equation or a basic weight-based equation (25–30 kcal/kg/d) is an alternative measure [17]. Weekly monitoring for weight gain or loss is useful during inpatient rehabilitation [16].
Delayed gastric emptying and intolerance to EN	Gastric access is the standard method for initiating EN in patients with TBI. However, delayed gastric emptying is one of the major complications that may be observed in up to 50% of patients with TBI [6,23]. Proper positioning, continuous infusion, and motility promoting agents such as metoclopramide are recommended strategies for gastroparesis after TBI. Concentrated enteral formulas (≥ 1.5 kcal/mL) may reduce the intolerance [20].
Route and timing of access in patients who are unable to maintain volitional intake: EN versus PN	Early EN (within 24–48 hours) is recommended in patients with TBI. Use of supplemental PN be considered after 7–10 days if unable to meet > 60% of energy and protein requirements by the enteral route alone [17]. If EN is contraindicated in severely malnourished patients, PN should be implemented progressively within 3–7 days, rather than no nutrition [32].
Selecting immune-modulating enteral formulas	Immune-modulating formulation containing arginine or EPA/DHA supplementation in addition to standard enteral formula is suggested in patients with acute TBI [17]. Although not yet suggested in CPGs, previous studies showed that intravenous BCAA (e.g., leucine) infusion decreased mortality and disability in patients with severe TBI.
Glycemic control	Sustaining 'permissive' glycemic control between 8 to 11 mmol/l are currently recommended in patients with TBI [57].
Protein support	Maintaining protein balance during both acute and post-acute TBI is important. It is recommended that protein supply should account for 15%–20% of total calories, and administration at least 2 g/kg body weight per day in patients with TBI [6].

REE, resting energy expenditure; TBI, traumatic brain injury; EN, enteral nutrition; PN, parenteral nutrition; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; CPG, clinical practice guidelines; BCAA, branched-chain amino acids.

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The current literature on post-TBI nutritional therapy focuses largely on severe, acute TBI, making it difficult to generalize the findings to different subgroups, such as patients with mild or chronic TBI. Moreover, the relationship between nutrition and post-TBI functioning, and proper strategies to reduce mortality and morbidity have not been elucidated in geriatric or pediatric populations. Geriatric patients with TBI, on average, experience higher mortality and morbidity rates, slower recovery, and worse outcomes than younger patients [63]. A previous study showed that the Geriatric Nutritional Risk Index is a significant independent risk factor for mortality in geriatric patients with moderate to severe TBI [64]. Although malnutrition is closely related to poor outcomes during hospitalization in geriatric patients, it remains common and underdiagnosed [65]. Furthermore, nutrition is important in pediatric TBI for adequate repair and growth [20]. More high-quality evidence is needed to guide decision-making for clinical practice specific to geriatric or pediatric patients with TBI.

SUMMARY

Evidence-based and timely nutritional therapy is important in the management of TBI to improve patients' prognoses. The determination of REE is crucial, and indirect calorimetry is the current "gold standard" for the determination of REE in patients with TBI; however, due to several practical difficulties, using a published predictive equation or a basic weight-based equation is an alternative measure. Weekly monitoring for weight gain or loss is useful during inpatient rehabilitation. Early EN within 24–48 hours is beneficial. However, attention should be paid to delayed gastric emptying and strategies need to be discussed. If EN is contraindicated, PN should be given progressively within 3–7 days rather than no nutrition. An immune-modulating formulation containing arginine or EPA/DHA supplementation in addition to a standard enteral formula is suggested in patients with acute TBI. Intravenous BCAA (e.g., leucine) infusion may reduce mortality and disability in patients with severe TBI, but this possibility needs further investigation. Sustaining "permissive" glycemic control between 8 and 11 mmol/L and providing an adequate protein supply (15%–20% of total calories or administration at least 2 g/kg body weight per day) are currently recommended in patients with TBI. Ketogenic diets and micronutrients (i.e., minerals, vitamins, and trace elements) are unresolved issues and need future research. Furthermore, the relationship between nutrition and post-TBI functioning, as well as proper strategies to improve outcomes in different sub-groups, such as patients with mild TBI, chronic patients, geriatric patients, and pediatric patients with TBI need to be explored.

REFERENCES

1. GBD 2016 Traumatic Brain Injury and Spinal Cord Injury Collaborators. Global, regional, and national burden of traumatic brain injury and spinal cord injury, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol 2019;18:56-87.
PUBMED | CROSSREF
2. Lee YS, Lee HY, Leigh JH, Choi Y, Kim H, Oh BM. The Socioeconomic burden of acquired brain injury among the Korean patients over 20 years of age in 2015–2017: a prevalence-based approach. Brain Neurorehabil 2021;14:14.
CROSSREF
3. Kim HK, Leigh JH, Lee YS, Choi Y, Kim Y, Kim JE, Cho WS, Seo HG, Oh BM. Decreasing incidence and mortality in traumatic brain injury in Korea, 2008–2017: a population-based longitudinal study. Int J Environ Res Public Health 2020;17:6197.
PUBMED | CROSSREF

4. Kim HK, Leigh J, Kim TW, Oh BM. Epidemiological trends and rehabilitation utilization of traumatic brain injury in Korea (2008-2018). Brain Neurorehabil 2021;14:e25.
CROSSREF
5. Tavarez T, Roehl K, Koffman L. Nutrition in the neurocritical care unit: a new frontier. Curr Treat Options Neurol 2021;23:16.
PUBMED | CROSSREF
6. Quintard H, Ichai C. Nutritional and metabolic supplementation for the injured brain: an update. Curr Opin Crit Care 2019;25:126-131.
PUBMED | CROSSREF
7. Krakau K, Omne-Pontén M, Karlsson T, Borg J. Metabolism and nutrition in patients with moderate and severe traumatic brain injury: a systematic review. Brain Inj 2006;20:345-367.
PUBMED | CROSSREF
8. Kurtz P, Rocha EE. Nutrition therapy, glucose control, and brain metabolism in traumatic brain injury: a multimodal monitoring approach. Front Neurosci 2020;14:190.
PUBMED | CROSSREF
9. Bjørklund G, Chirumbolo S. Role of oxidative stress and antioxidants in daily nutrition and human health. Nutrition 2017;33:311-321.
PUBMED | CROSSREF
10. Markovic SJ, Fitzgerald M, Peiffer JJ, Scott BR, Rainey-Smith SR, Sohrabi HR, Brown BM. The impact of exercise, sleep, and diet on neurocognitive recovery from mild traumatic brain injury in older adults: a narrative review. Ageing Res Rev 2021;68:101322.
PUBMED | CROSSREF
11. Oddo M, Vespa P, Menon DK. Boosting the injured brain with supplemental energy fuels. Intensive Care Med 2019;45:872-875.
PUBMED | CROSSREF
12. Jung HJ, Lee YM, Kim M, Uhm KE, Lee J. Suggested assessments for sarcopenia in patients with stroke who can walk independently. Ann Rehabil Med 2020;44:20-37.
PUBMED | CROSSREF
13. Yi JH, Chun MH, Kim BR, Han EY, Park JY. Bowel function in acute stroke patients. Ann Rehabil Med 2011;35:337-343.
PUBMED | CROSSREF
14. 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 2007;23:308-317.
PUBMED | CROSSREF
15. Faisy C, Guerot E, Diehl JL, Labrousse J, Fagon JY. Assessment of resting energy expenditure in mechanically ventilated patients. Am J Clin Nutr 2003;78:241-249.
PUBMED | CROSSREF
16. Zasler ND, Katz DI, Zafonte RD, Arciniegas DB, Bullock RB, Kreutzer JS. Brain injury medicine: principles and practice. 2nd ed. New York, NY: Demos Medical Publishing; 2012:902-911.
17. McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, McCarthy MS, Davanos E, Rice TW, Cresci GA, Gervasio JM, Sacks GS, Roberts PR, Compher C; Society of Critical Care Medicine; American Society for Parenteral and Enteral Nutrition. 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 2016;40:159-211.
PUBMED | CROSSREF
18. Frankenfield D, Smith JS, Cooney RN. Validation of 2 approaches to predicting resting metabolic rate in critically ill patients. JPEN J Parenter Enteral Nutr 2004;28:259-264.
PUBMED | CROSSREF
19. Graf S, Karsegard VL, Viatte V, Heidegger CP, Fleury Y, Pichard C, Genton L. Evaluation of three indirect calorimetry devices in mechanically ventilated patients: which device compares best with the Deltatrac II®? A prospective observational study. Clin Nutr 2015;34:60-65.
PUBMED | CROSSREF
20. Cook AM, Peppard A, Magnuson B. Nutrition considerations in traumatic brain injury. Nutr Clin Pract 2008;23:608-620.
PUBMED | CROSSREF
21. Lee SJ, Lee HJ, Jung YJ, Han M, Lee SG, Hong SK. Comparison of measured energy expenditure using indirect calorimetry vs predictive equations for liver transplant recipients. JPEN J Parenter Enteral Nutr 2021;45:761-767.
PUBMED | CROSSREF

22. Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, Bratton SL, Chesnut R, Harris OA, Kissoon N, Rubiano AM, Shutter L, Tasker RC, Vavilala MS, Wilberger J, Wright DW, Ghajar J. Guidelines for the management of severe traumatic brain injury. Neurosurgery 2017;80:6-15.
PUBMED | CROSSREF
23. Ott L, Young B, Phillips R, McClain C, Adams L, Dempsey R, Tibbs P, Ryo UY. Altered gastric emptying in the head-injured patient: relationship to feeding intolerance. J Neurosurg 1991;74:738-742.
PUBMED | CROSSREF
24. Kao CH, ChangLai SP, Chieng PU, Yen TC. Gastric emptying in head-injured patients. Am J Gastroenterol 1998;93:1108-1112.
PUBMED | CROSSREF
25. Gore RM, Mintzer RA, Calenoff L. Gastrointestinal complications of spinal cord injury. Spine 1981;6:538-554.
PUBMED | CROSSREF
26. Abdelmalik PA, Dempsey S, Ziai W. Nutritional and bioenergetic considerations in critically ill patients with acute neurological injury. Neurocrit Care 2017;27:276-286.
PUBMED | CROSSREF
27. Chapple LA, Chapman MJ, Lange K, Deane AM, Heyland DK. Nutrition support practices in critically ill head-injured patients: a global perspective. Crit Care 2015;20:6.
PUBMED | CROSSREF
28. 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 2006;106:1226-1241.
PUBMED | CROSSREF
29. 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 2016;10:JC01-JC05.
PUBMED | CROSSREF
30. Dickerson RN, Mitchell JN, Morgan LM, Maish GO 3rd, Croce MA, Minard G, Brown RO. Disparate response to metoclopramide therapy for gastric feeding intolerance in trauma patients with and without traumatic brain injury. JPEN J Parenter Enteral Nutr 2009;33:646-655.
PUBMED | CROSSREF
31. 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 2007;14:344-348.
PUBMED | CROSSREF
32. Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP, Hiesmayr M, Mayer K, Montejo JC, Pichard C, Preiser JC, van Zanten ARH, Oczkowski S, Szczeklik W, Bischoff SC. ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr 2019;38:48-79.
PUBMED | CROSSREF
33. Heyland DK, Dhaliwal R, Drover JW, Gramlich L, Dodek P; Canadian Critical Care Clinical Practice Guidelines Committee. Canadian clinical practice guidelines for nutrition support in mechanically ventilated, critically ill adult patients. JPEN J Parenter Enteral Nutr 2003;27:355-373.
PUBMED | CROSSREF
34. Marik PE, Zaloga GP. Early enteral nutrition in acutely ill patients: a systematic review. Crit Care Med 2001;29:2264-2270.
PUBMED | CROSSREF
35. Kang W, Kudsk KA. Is there evidence that the gut contributes to mucosal immunity in humans? JPEN J Parenter Enteral Nutr 2007;31:246-258.
PUBMED | CROSSREF
36. Casaer MP, Mesotten D, Hermans G, Wouters PJ, Schetz M, Meyfroidt G, Van Cromphaut S, Ingels C, Meersseman P, Muller J, Vlasselaers D, Debaveye Y, Desmet L, Dubois J, Van Assche A, Vanderheyden S, Wilmer A, Van den Berghe G. Early versus late parenteral nutrition in critically ill adults. N Engl J Med 2011;365:506-517.
PUBMED | CROSSREF
37. Lacey JM, Wilmore DW. Is glutamine a conditionally essential amino acid? Nutr Rev 1990;48:297-309.
PUBMED | CROSSREF
38. Zeng J, Zhao XY, Huang Q, Wang ER. Effects of glutamine-enriched enteral nutrition on nutritional status and prognosis of patients with severe head injury. Zhonghua Shao Shang Za Zhi 2009;25:335-338.
PUBMED
39. Falcão de Arruda IS, de Aguilar-Nascimento JE. Benefits of early enteral nutrition with glutamine and probiotics in brain injury patients. Clin Sci (Lond) 2004;106:287-292.
PUBMED | CROSSREF

40. Yang DL, Xu JF. Effect of dipeptide of glutamine and alanine on severe traumatic brain injury. Chin J Traumatol 2007;10:145-149.
PUBMED
41. Heyland D, Muscedere J, Wischmeyer PE, Cook D, Jones G, Albert M, Elke G, Berger MM, Day AG; Canadian Critical Care Trials Group. A randomized trial of glutamine and antioxidants in critically ill patients. N Engl J Med 2013;368:1489-1497.
PUBMED | CROSSREF
42. Dyall SC. Long-chain omega-3 fatty acids and the brain: a review of the independent and shared effects of EPA, DPA and DHA. Front Aging Neurosci 2015;7:52.
PUBMED | CROSSREF
43. Bailes JE, Abusuwwa R, Arshad M, Chowdhry SA, Schleicher D, Hempeck N, Gandhi YN, Jaffa Z, Bokhari F, Karahalios D, Barkley J, Patel V, Sears B. Omega-3 fatty acid supplementation in severe brain trauma: case for a large multicenter trial. J Neurosurg 2020;133:1-5.
PUBMED | CROSSREF
44. Sears B, Bailes J, Asselin B. Therapeutic uses of high-dose omega-3 fatty acids to treat comatose patients with severe brain injury. PharmaNutrition 2013;1:86-89.
CROSSREF
45. Noguchi H, Nishi D, Matsumura K, Hamazaki K, Hamazaki T, Matsuoka YJ. Limited effect of omega-3 fatty acids on the quality of life in survivors of traumatic injury: a randomized, placebo-controlled trial. Prostaglandins Leukot Essent Fatty Acids 2017;127:1-5.
PUBMED | CROSSREF
46. Hasadsri L, Wang BH, Lee JV, Erdman JW, Llano DA, Barbey AK, Wszalek T, Sharrock MF, Wang HJ. Omega-3 fatty acids as a putative treatment for traumatic brain injury. J Neurotrauma 2013;30:897-906.
PUBMED | CROSSREF
47. Martí I Líndez AA, Reith W. Arginine-dependent immune responses. Cell Mol Life Sci 2021;78:5303-5324.
PUBMED | CROSSREF
48. Bower RH, Cerra FB, Bershadsky B, Licari JJ, Hoyt DB, Jensen GL, Van Buren CT, Rothkopf MM, Daly JM, Adelsberg BR. Early enteral administration of a formula (Impact) supplemented with arginine, nucleotides, and fish oil in intensive care unit patients: results of a multicenter, prospective, randomized, clinical trial. Crit Care Med 1995;23:436-449.
PUBMED | CROSSREF
49. Jeter CB, Hergenroeder GW, Ward NH 3rd, Moore AN, Dash PK. Human mild traumatic brain injury decreases circulating branched-chain amino acids and their metabolite levels. J Neurotrauma 2013;30:671-679.
PUBMED | CROSSREF
50. Elkind JA, Lim MM, Johnson BN, Palmer CP, Putnam BJ, Kirschen MP, Cohen AS. Efficacy, dosage, and duration of action of branched chain amino Acid therapy for traumatic brain injury. Front Neurol 2015;6:73.
PUBMED | CROSSREF
51. Yudkoff M. Interactions in the metabolism of glutamate and the branched-chain amino acids and ketoacids in the CNS. Neurochem Res 2017;42:10-18.
PUBMED | CROSSREF
52. Drummond MJ, Rasmussen BB. Leucine-enriched nutrients and the regulation of mammalian target of rapamycin signalling and human skeletal muscle protein synthesis. Curr Opin Clin Nutr Metab Care 2008;11:222-226.
PUBMED | CROSSREF
53. Aquilani R, Iadarola P, Contardi A, Boselli M, Verri M, Pastoris O, Boschi F, Arcidiaco P, Viglio S. Branched-chain amino acids enhance the cognitive recovery of patients with severe traumatic brain injury. Arch Phys Med Rehabil 2005;86:1729-1735.
PUBMED | CROSSREF
54. Sharma B, Lawrence DW, Hutchison MG. Branched chain amino acids (BCAAs) and traumatic brain injury: a systematic review. J Head Trauma Rehabil 2018;33:33-45.
PUBMED | CROSSREF
55. Hermanides J, Plummer MP, Finnis M, Deane AM, Coles JP, Menon DK. Glycaemic control targets after traumatic brain injury: a systematic review and meta-analysis. Crit Care 2018;22:11.
PUBMED | CROSSREF
56. Vespa P, McArthur DL, Stein N, Huang SC, Shao W, Filippou M, Etchepare M, Glenn T, Hovda DA. Tight glycemic control increases metabolic distress in traumatic brain injury: a randomized controlled within-subjects trial. Crit Care Med 2012;40:1923-1929.
PUBMED | CROSSREF

57. Oddo M, Schmidt JM, Carrera E, Badjatia N, Connolly ES, Presciutti M, Ostapkovich ND, Levine JM, Le Roux P, Mayer SA. Impact of tight glycemic control on cerebral glucose metabolism after severe brain injury: a microdialysis study. Crit Care Med 2008;36:3233-3238.
PUBMED | CROSSREF

58. NICE-SUGAR Study Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group and the Canadian Critical Care Trials Group, Finfer S, Chittock D, Li Y, Foster D, Dhingra V, Bellomo R, Cook D, Dodek P, Hebert P, Henderson W, Heyland D, Higgins A, McArthur C, Mitchell I, Myburgh J, Robinson B, Ronco J. Intensive versus conventional glucose control in critically ill patients with traumatic brain injury: long-term follow-up of a subgroup of patients from the NICE-SUGAR study. Intensive Care Med 2015;41:1037-1047.
PUBMED | CROSSREF

59. Rai VR, Phang LF, Sia SF, Amir A, Veerakumaran JS, Kassim MK, Othman R, Tah PC, Loh PS, Jailani MI, Ong G. Effects of immunonutrition on biomarkers in traumatic brain injury patients in Malaysia: a prospective randomized controlled trial. BMC Anesthesiol 2017;17:81.
PUBMED | CROSSREF

60. Young B, Ott L, Kasarskis E, Rapp R, Moles K, Dempsey RJ, Tibbs PA, Kryscio R, McClain C. Zinc supplementation is associated with improved neurologic recovery rate and visceral protein levels of patients with severe closed head injury. J Neurotrauma 1996;13:25-34.
PUBMED | CROSSREF

61. Lee JM, Jeong SW, Kim MY, Park JB, Kim MS. The effect of vitamin D supplementation in patients with acute traumatic brain injury. World Neurosurg 2019;126:e1421-e1426.
PUBMED | CROSSREF

62. Razmkon A, Sadidi A, Sherafat-Kazemzadeh E, Mehrafshan A, Jamali M, Malekpour B, Saghafinia M. Administration of vitamin C and vitamin E in severe head injury: a randomized double-blind controlled trial. Clin Neurosurg 2011;58:133-137.
PUBMED | CROSSREF

63. Gardner RC, Dams-O'Connor K, Morrissey MR, Manley GT. Geriatric traumatic brain injury: epidemiology, outcomes, knowledge gaps, and future directions. J Neurotrauma 2018;35:889-906.
PUBMED | CROSSREF

64. Su WT, Tsai CH, Huang CY, Chou SE, Li C, Hsu SY, Hsieh CH. Geriatric Nutritional Risk Index as a prognostic factor for mortality in elderly patients with moderate to severe traumatic brain injuries. Risk Manag Healthc Policy 2021;14:2465-2474.
PUBMED | CROSSREF

65. Gavazzi G, Krause KH. Ageing and infection. Lancet Infect Dis 2002;2:659-666.
PUBMED | CROSSREF