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The Change in Nutritional Status in Traumatic Brain Injury Patients: A Retrospective Descriptive A Retrospective Descriptive Study

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The Change in Nutritional Status in Traumatic Brain Injury Patients:

A Retrospective Descriptive Study

by

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A dissertation submitted in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy
College of Nursing
University of South Florida

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Expenditure

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Dedication

I dedicate this work to my family, friends, and teachers who supported me throughout the years. Thank you for your prayers, encouragement, advice, and mentorship. The journey was easier because of you.

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The completion of this work would not have been possible without a number of individuals. I would like to thank my husband, friends, and family, your love and care powered me to fulfill my dream!

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Abstract

There is a high prevalence in malnutrition among traumatic brain injury (TBI) due to the hypermetabolism and hypercatabolism which develop post injury. Traumatic brain injury patients are different, even among themselves, in their energy requirements and response to nutritional therapy. This implies that there are other factors that affect the energy intake of these patients and enhance the incidence of malnutrition.

This dissertation study examines the nutritional status of TBI patients upon admission to the intensive care unit (ICU) and during their hospital stay to describe baseline status, detect changes in nutritional status over 7 days, and identify the factors affecting the adequacy of energy intake and the change in nutritional status as a consequence. Anthropometric measurements, biomedical measurements, measures of severity of illness, daily health status, level of brain injury severity, and other data were collected from the medical records of 50 patients, who were ≥ 18 years old, mechanically ventilated in the first 24 hours of ICU admission, and had a Glasgow Coma Scale score between 3-12. These data were used to examine the previous relationships.

Although there was no statistically significant change found in body mass index and weight, there was a significant change detected in other nutritional markers, including hemoglobin, albumin, and total lymphocyte levels over the 7 days of ICU and hospital stay. No significant relationship was found between the adequacy of energy intake and total prescribed energy, severity of illness, level of brain injury severity, daily health status, patient age, intracranial pressure, or time of feeding initiation.

Findings may be used to develop and test interventions to improve nutritional status during the acute phase of TBI. This will lay a foundation for health care providers, including nurses, to establish standards for practice and nutrition protocols to assure optimal nutrition assessment and intervention in a timely manner.

Chapter I: Introduction

Malnutrition is a state of losing muscle protein and/or lean tissue related to inadequate nutrition intake, impaired absorption, affected transport or nutrient utilization, or all of these factors combined (Jensen, Bistran, Roubenoff, & Heimbürger, 2009; Sheean et al., 2013). Malnutrition has devastating effects on critically ill patients, and can lead to increased morbidity, mortality, length of hospital stay (da Cunha, da Rocha, & Hissa, 2013), length of mechanical ventilation (Adrie et al., 2014; Barr, Hecht, Flavin, Khorana, & Gould, 2004), and prolonged rehabilitation (Dénes, 2004). These effects have economic implications as well (Chakravarty, Hazarika, Goswami, & Ramasubban, 2013).

The prevalence of malnutrition in hospitals is estimated to range from 40 to 57% (Beghetto, Luft, Mello, & Polanczyk, 2009; Chakravarty et al., 2013; Mercadal-Orfila, Lluch-Taltavull, Campillo-Artero, & Torrent-Quetglas, 2012). More than 35% of patients in Intensive Care Units (ICUs) are reported to be malnourished on admission (Nisim & Allins, 2005; Sungurtekin, Sungurtekin, Oner, & Okke, 2008). Most of the ICU patients' nutritional status worsens over time, even when they receive nutritional therapy. This worsening was found to be related to the patients' nutritional status before admission and underfeeding during hospitalization (Barr et al., 2004; Kim & Choi-Kwon, 2011). Among patients with Traumatic Brain Injury (TBI), 75% show clinical markers of malnutrition at 3 weeks (Dhandapani, Manju, Sharma, & Mahapatra, 2007).

According to the World Health Organization (WHO), TBI is predicted to be the main cause of death and disability by 2020 (Hyder, Wunderlich, Puvanachandra, Gururaj, &

Kobusingye, 2007). More than 200 out of every 100,000 people experience TBI annually (Hui et al., 2013). Traumatic brain injury involves direct insult to the brain which results in direct and permanent damage to the tissues and blood vessels. However, the damage of TBI does not stop with the initial injury; a secondary injury cascade occurs days or weeks after initial injury (Cook, Peppard, & Magnuson, 2008; Krakau, Omne-Pontén, Karlsson, & Borg, 2006). Secondary injury can be avoided or reduced by early treatment of TBI (Krakau et al., 2006). Nutrition-based interventions have the potential to enhance recovery (Costello, Lithander, Gruen, & Williams, 2014), but additional research is needed. The Brain Trauma Foundation (2007) identified nutrition therapy as a priority research area and one of the 15 key intervention types likely to influence outcomes in TBI patients.

Patients who experience TBI are at high risk of malnutrition because of the metabolic changes they develop post-injury. A systematic review found that the mean of energy expenditure following TBI ranged from 87% to 200% above normal and may continue to be elevated for 30 days (Foley, Marshall, Pikul, Salter, & Teasell, 2008). High production of corticosteroids, counter-regulation hormones and cytokines are responsible for this hyper-metabolic status (Pepe & Barba, 1999; Anthony, Couch, Losey, & Evans, 2012; Dhandapani et al., 2007; Lenz, Franklin, & Cheadle, 2007; Charrueau et al., 2009; Woodcock & Morganti-Kossmann, 2013). Furthermore, TBI patients are prone to develop a hyper-catabolic state, which results in negative nitrogen balance and increased requirements of protein and energy (Dickerson et al., 2012; Foley et al., 2008). These physiological challenges of TBI patients make their energy expenditure and calorie requirements unique (Cook et al., 2008), and their response to nutritional therapy different from other patients in the ICU (Costello et al., 2014; Heyland, Dhaliwal, Jiang, & Day, 2011)

The high prevalence of malnutrition in TBI patients could be related to the high energy demand and fast protein breakdown. Other factors influencing estimates of prevalence include how patients were assessed for nutritional requirements, what nutritional therapy goals were set for them, and if achievement of those goals was monitored (Krakau et al., 2010). For these reasons, it is very important to describe the baseline nutritional status of TBI patients and the changes on nutritional status that will occur during ICU and hospital stay. Furthermore, it is important to identify the factors that affect this change during ICU stay and hospitalization.

Statement of the Problem

There are few reports describing baseline nutritional status in TBI patients and their nutritional trajectory during early ICU care and hospital stay. Also, there is a scarcity of data about the factors that affect the nutritional change in this particular cohort.

Purpose of the Study

The purpose of this study was to examine the nutritional status of TBI patients upon admission to ICU and during hospital stay to describe baseline status, detect changes in nutritional status over 7 days, and identify the factors affecting the adequacy of energy intake and the change in nutritional status as a consequence. Evaluating the changes in nutritional status in TBI patients is essential in order to develop interventions to improve TBI patients' nutritional status in hospital, including evidence based nutritional protocols.

Specific Aims

This study had two specific aims. The aims and hypotheses of the study are described here:

Aim1: To compare Body Mass Index (BMI) of TBI patients at admission to ICU to BMI at day 7 of the hospital stay.

Hypothesis 1: BMI over 7 days of ICU and hospital stay will deteriorate compared to BMI calculated at admission.

Aim 2: To investigate the effect of total energy prescription, time of feeding initiation, severity of illness, level of brain injury severity, daily health status, patients age, and ICP on the adequacy of energy intake among TBI patients during ICU and hospital stay.

Hypothesis a: Under -prescription of energy, delayed time of feeding initiation are factors decrease energy intake.

Hypothesis b: Severity of illness, daily health status, age, level of brain injury severity, and intracranial pressure (ICP) are factors increase energy expenditure.

Definition of Relevant Terms

Malnutrition is a decrease in lean body mass which may be associated with functional impairment (Jensen et al., 2009). Traumatic brain injury is a change in brain function or an evidence of brain pathology related to an external force (Menon, Schwab, Wright, & Maas, 2010). Hyper-metabolism is an elevation in metabolic rate that is associated with physiological signs such as elevation in body temperature, minute ventilation, and heart rate (Frankenfield, 2006). Hyper-catabolism is elevated break down of muscle mass in order to preserve visceral mass which lead to changes in the body composition and appears in the form of weight loss (Frankenfield, 2006; Vizzini & Aranda-Michel, 2011). Nutritional therapy is providing oral, enteral, or parenteral nutrition as part of medical treatment in order to maintain or restore the optimal nutritional status (American Society for Parenteral and Enteral Nutrition (A. S. P. E.), 2013). Energy expenditure is the sum of basal metabolic rate, physical work expended energy, and thermogenesis (Mongardon & Singer, 2010). Negative nitrogen balance is a state when

nitrogen excretion is more than nitrogen ingestion related to protein break down (Vizzini & Aranda-Michel, 2011). Adequacy of energy intake is the ratio of calculated patient energy requirement to energy intake.

Significance to Nursing

The results of this study will shed light on the effect of nutritional status of TBI patients upon admission and over the first 7 days of hospital stay. Showing the deterioration of nutritional status of TBI patients in ICU and identification of factors that influence this change will enable development and testing of interventions to improve nutritional status during the acute phase of TBI. This will lay a foundation for health care providers, including nurses, to establish standards for practice and nutrition protocols to assure optimal nutrition assessment and intervention in a timely manner.

Chapter II: Review of Literature

This chapter presents a review of literature. The chapter starts with a conceptual framework followed by a discussion about the metabolic changes in traumatic brain injury (TBI) patients. Also, the chapter discusses factors decrease energy intake and other factors increase energy expenditure during TBI patients intensive care unit (ICU) and hospital stay.

Conceptual Framework

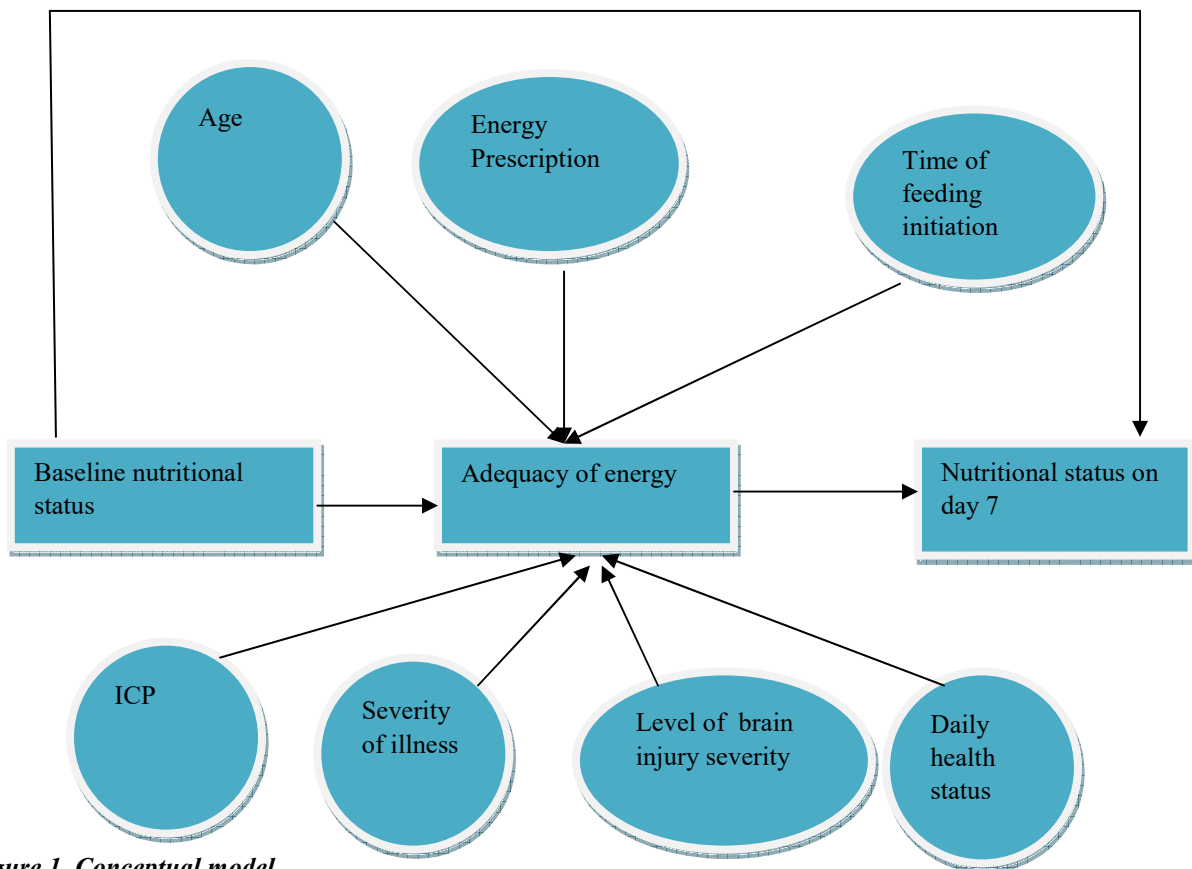


Figure 1. Conceptual model

This conceptual model (Figure 1) represents the change in nutritional status of TBI patients over 7 days in the ICU and the hospital stay. The trajectory is affected by factors increase or decrease patients' energy intake. These factors are, and not limited to, energy prescription, time of feeding initiation, patient's age, daily health status, level of brain injury severity, severity of illness, and intracranial pressure (ICP). These factors have an influence on the adequacy of energy intake of TBI patients that may lead to the change in nutritional status. The indirect relationship between the baseline nutritional status and the nutritional status on day 7 that is mediated by the adequacy of energy intake has not be studied in this dissertation. This relationship will be examined in future data analyses.

Metabolic Changes Following Injury

Moderate to severe TBI patients experience hypermetabolism in the early period following injury (Krakau et al., 2006) which lasts up to 30 days (Foley et al., 2008), and may persist up to one year following injury (Pepe & Barba, 1999). This hypermetabolic state is thought to result from high production of counter regulatory hormones such as epinephrine, norepinephrine, glucagon, and cortisol (Pepe & Barba, 1999). High production directly following injury of corticosteroids and cytokines, such as tumor necrosis factor-alpha (TNF- α), interleukine-1 (IL-1) and interleukine-6 (IL-6), is thought to have a role in this hypermetabolic state as well (Pepe & Barba, 1999).

The metabolic rate of TBI patients is affected by many factors, including: the type and extent of injury; the degree of inflammatory response; age; and the types and dosages of sedative, narcotic, and paralytic medications (Frankenfield, 2006). The metabolic rate in non-sedated TBI patients ranges from 105-160% and from 96-132% in sedated patients (Krakau et al., 2006). Even with paralysis, energy expenditure remains elevated by 20-30% (Brain Trauma

Foundation, 2007). Other investigators found that the mean energy expenditure of moderate to severe TBI patients ranged from 75% to 200%, and the administration of sedatives or barbiturates reduced the metabolic rate by 13-32% and paralyzing agents by 12-28%, while propranolol and morphine administration was associated with a smaller reduction in metabolic rate (Foley et al., 2008).

Hypercatabolism is a state characterized by high break down of skeletal muscle protein into carbon skeletons and nitrogen. Counterregulatory hormones also have a role in catabolism. They increase utilization of glucose by the brain, blood cells and bone marrow, which leads to depletion of hepatic glycogen stores within 24 hours following injury (Pepe & Barba, 1999). Gluconeogenesis then becomes the major mechanism of providing glucose. Amino acids, which come from the breakdown of skeletal muscles, become the source of carbon skeletons necessary to drive gluconeogenesis (Pepe & Barba, 1999). Traumatic brain injury patients can lose up to 1000 grams of muscle tissue per day due to the metabolic preferences for amino acids as a source of energy rather than use of ketone bodies, which result from fat break down. Also, acute phase reactant proteins, prolonged immobilization, and steroid use, all further increase protein break down in TBI patients (Pepe & Barba, 1999).

Resting energy expenditure (REE) can be predicted by a variety of different equations, none of which are specific for TBI, or can be estimated by using indirect calorimetry (Cook et al., 2008; Krakau et al., 2006). Resting energy expenditure formulas depend on the body weight that can be changed dramatically in acute illness due to edema (Vizzini & Aranda-Michel, 2011). So far, indirect calorimetry is the gold standard to measure the metabolic rate in critically ill patients (Cook et al., 2008; Krakau et al., 2006). However, indirect calorimetry can't measure metabolic rate accurately for TBI patients with intermittent muscle contractions, sympathetic

storming, or fever (Cook et al., 2008). Furthermore, indirect calorimetry is not routinely performed in the ICU because it requires specialized equipment and is costly.

There are some studies that have been conducted to evaluate the accuracy of using formulas to predict REE relative to the REE that is measured by indirect calorimetry. McEvoy, Cran, Cooke, & Young (2009) found that FAO/WHO/UNU and Harris-Benedict equations have predicted REE poorly compared to indirect calorimetry in patients recovering from TBI. Another study, included 94 mechanically ventilated patients, used the original Harris-Benedict equations and those corrected for usual stress factors, the Swinamer equation, the Fusco equation, the Ireton-Jones equation, and Faisy equation to identify the most accurate resting energy expenditure (REE) prediction formula in comparison with indirect calorimetry (Savard et al., 2008). The authors found that the Faisy equation, which depends on height, weight, temperature, and minute ventilation is the most accurate formula to estimate REE in mechanically ventilated patients (Savard et al., 2008).

Nitrogen balance is an important measure of adequacy of caloric intake and metabolism. Internal protein dynamics can be monitored and interpreted using urinary creatinine excretion and serum urea nitrogen concentration (Dickerson et al., 2012). Although there is no significant difference in the nitrogen balance between TBI and trauma patients without TBI (Dickerson et al., 2012), TBI patients suffer from a negative nitrogen balance due to high protein break down and low protein synthesis at the same time (Dickerson et al., 2012; Krakau et al., 2006). The nitrogen balance varies depending on the amount of protein the patients receive (Dickerson et al., 2012). Previous investigations found that the daily nitrogen balance in TBI patients ranged from -3g to -16g (Krakau et al., 2006). Dickerson et al. (2012) found that trauma injured patients' daily

nitrogen balance ranged from -11g with a mean of 1.3g/day of protein intake to -20g without protein intake.

Full caloric replacement can be achieved within 7 days by starting nutritional therapy for TBI within the first 72 hours post injury (Brain Trauma Foundation, 2007). An intake of 1.2-1.5 g/kg/day of protein is generally sufficient for nitrogen equilibrium in critically ill patients (Frankenfield, 2006; Hoffer & Bistran, 2012). However, Dickerson et al. (2012) found that 54% of the patients who received 2g/kg/day achieved nitrogen balance, while just 38% and 29% of patients who received 1.5-1.99 g/kg/day and 1-1.49 g/kg/day respectively achieved nitrogen equilibrium. The literature shows that 2.0–2.5 g /kg/day of protein substrate is safe and sufficient for most critically ill adults (Hoffer & Bistran, 2012). The Brain Trauma Foundation (2007) recommends that 15–20% of total calories should be provided as nitrogen calories to reduce nitrogen loss. Nevertheless, most critically ill patients receive less than half of the commonest current recommendation, 1.5 g /kg/day of protein, for the first week or longer of their ICU stay (Hoffer & Bistran, 2012).

According to the Society of Critical Care Medicine (SCCM) and the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) (SCCM /ASPEN),critically ill patients should receive > 50-65% of energy requirements to achieve clinical benefits of EN during the first week of hospitalization (McClave et al., 2009). In patients with a body mass index (BMI) <30, protein requirements range from 1.2-2.0 g/kg actual body weight per day, and energy requirements range from 25-30 Kcal/kg actual weight. Obese patients who have a BMI> 30 have to receive 60-70% of target energy requirements. If they have BMI >30-40, they have to receive protein ≥ 2.0 g/kg ideal body weight per day, and ≥ 2.5 g/kg ideal body weight per day if they have BM I ≥ 40

(McClave et al., 2009). For TBI patients in particular, the Brain Trauma Foundation (2007) define adequacy of nutrition therapy as receiving 100-140% of energy requirements.

Prescription of Energy

Up to two thirds of hospitalized malnourished patients remain untreated because of poor assessment (Bajwa & Kulshrestha, 2012). Krakau et al. (2010) found that nutritional guidelines were not used in 50% of 78 hospital units in Sweden. Also, nutrition screening was not done for every patient upon admission, and nutritional data in 64 nursing and medical records were incomplete. The records included information about energy requirements for only 16 % of the patients, and information about weight development and body mass index for 7% and 2% of the patients respectively (Krakau et al., 2010).

The nutrition knowledge base and the interest in nutritional treatment, the accurate evaluation of patients' energy requirements, and the anticipation of problems during delivery all play major roles in the prescription and delivery of nutritional therapy, as well as the success of these processes (De Jonghe et al., 2001). In some clinical settings, enteral nutrition (EN) is not prescribed based on protocols or guidelines, but based on the physician's opinion (Kim & Choi-Kwon, 2011). Poor assessment and poor treatment could be related to the lack of knowledge and clinical skills in the nutrition field among physicians and nurses (Sheean, Peterson, Zhao, Gurka, & Braunschweig, 2012; Soguel, Revelly, Schaller, Longchamp, & Berger, 2012). As a result, physicians lack the confidence and ability to prescribe adequate and effective nutritional interventions. Physicians prescribe only about 66%-78% of the goal requirements of enteral tube feeding, and only 71- 78% of the prescribed volume is delivered to the patients in ICU (McClave et al., 1999; De Jonghe et al., 2001). Thus, McClave et al. (1999) found that patients received a

mean volume of only 52% of the nutritional goal resulting in weight loss among 54% of the patients while receiving EN (McClave et al., 1999).

Unfortunately, over-feeding can result in metabolic complications as well. It can cause hyperglycemia, refeeding-like syndrome with electrolyte derangements, hepatic steatosis, pulmonary compromise with difficulty weaning from the ventilator, and even obesity in the long-term patient (Cook et al., 2008).

Route of Feeding

There are debates regarding the route of feeding in TBI patients (Brain Trauma Foundation, 2007). In practice, EN is the first choice whenever critically ill patients have a functioning gastrointestinal tract (Ukleja, 2010). EN supports cells and organs' function, has a lower risk of hyperglycemia or hyperosmolarity, and supports the gut mass and barrier function (Zaloga, 2006; Justo Meirelles & Aguilar-Nascimento, 2011). However, using EN in patients with gastrointestinal intolerance is associated with underfeeding and malnutrition as a consequence (Zaloga, 2006; Justo Meirelles & Aguilar-Nascimento, 2011), and EN increases the risk of aspiration and pneumonia in TBI patients (Justo Meirelles & Aguilar-Nascimento, 2011; Kuppinger et al., 2013; Wang et al., 2013).

On the other hand, parenteral nutrition (PN) is associated with infectious complications, hyperglycemia, and overfeeding (Dissanaike, Shelton, Warner, & O'Keefe, 2007). However, some studies found PN to be superior to EN due to reduction in mortality rate and infectious complications (Harvey et al., 2014; Wang et al., 2013), length of stay in the ICU and hospital, and in rates of adverse effects (Harvey et al., 2014). There is no difference in the amount of calories and proteins that can be delivered using either route (Justo Meirelles & Aguilar-Nascimento, 2011; Harvey et al., 2014). Although PN delivers nitrogen more efficiently,

nitrogen excretion in patients fed parenterally is greater than EN, so that similar nitrogen balance is achieved by either route (Justo Meirelles & Aguilar-Nascimento, 2011).

Feeding Interruption

Feeding interruption is more common in EN. Insufficient delivery of EN may be related to interruptions for clinical procedures, including diagnostic imaging studies, airway management, mechanical problems, high residual volumes, tube displacement, events related to routine nursing care, and other causes such as hemodynamic instability or patient intolerance (McClave et al., 1999.; De Jonghe et al., 2001; Passier et al., 2013; Peev et al., 2014). Peev et al. (2014) studied 94 critically ill patients in a surgical ICU and found that patients who have experienced feeding interruption at least once have higher mean daily and cumulative caloric deficits, and have 3-fold higher risk of being underfed compared to patients have not experienced any feeding interruption during ICU stay.

Patients experience feeding interruption for 19.6%-32% of total infusion time (McClave et al., 1999). Passier et al. (2013) found that 90% of ICU patients had their EN interrupted for 30.8 hour/ patient during their ICU admission, which is equivalent to a mean of 7.9% of the patients' total ICU length of stay (De Jonghe et al., 2001; Passier et al., 2013). Compounding the problem, feedings may be interrupted for planned procedures that are postponed, for GRV < 500 ml, or for an imaging study in which the radiologist did not request fasting, resulting in unnecessary feeding interruptions which led to a nutrition deficit (Passier et al., 2013; Peev et al., 2014). About 26% of feeding interruptions episodes are considered avoidable (Peev et al., 2014), which may have significant negative impacts on clinical outcomes.

High Gastric Residual Volume

Traumatic brain injury patients develop impairment in gastric motility that can cause intolerance to EN, especially in the first two weeks following injury (Bochicchio et al., 2006). Delayed gastric emptying has been found in 50% of patients on mechanical ventilators and in 80% of traumatic brain injury patients (Ukleja, 2010). Prolonged gastric motility can be exacerbated by sedatives that are used in TBI to decrease ICP (Bochicchio et al., 2006; Pinto, Rocha, Paula, & de Jesus, 2012). High Gastric Residual Volume (GRV) is the most common manifestation of EN intolerance (Kuppinger, Rittler, Hartl, & Rüttinger, 2013; Pinto et al., 2012); high GRV is responsible for 83% of EN intolerance (Pinto et al., 2012). High GRV prevents patients from starting EN within the first 48-72 hours, especially if they are sedated (Bochicchio et al., 2006; Pinto et al., 2012).

The definition of high GRV varies in the literature. It commonly is identified as between 200 to 250 ml (Bochicchio et al., 2006; Kuppinger et al., 2013; Metheny, Mills, & Stewart, 2012). Acosta-Escribano et al. (2010) defined increased GRV as the recovery of more than 500 ml of feeding formula. However, about 25% of nurses interrupt EN for residual volume of less than or equal to 150ml (McClave et al., 1999; Metheny et al., 2012), which leads to unnecessarily diminishing the delivery of calories to patients, especially when EN is checked every 4-6 hours and held for 4 hours each time the patients show high GRV (McClave et al., 1999; Metheny et al., 2012).

Time of Feeding Initiation

Early feeding enhances immunity, reduces incidence of infections, protects visceral protein, enhances neurological recovery, and decreases mortality (Chiang et al., 2012). In a study conducted on rats to determine the optimal time for nutrition support after TBI, Aydin et al.

(2005) found that delayed EN resulted in deleterious changes in the gut, including thinning of the intestinal mucosa with villous shortening, loss of DNA and protein, and reduction in enzymatic activity. Thus, it is recommended that feeding begin within the first 8 hours of TBI to avoid these outcomes (Aydin et al., 2005). Enteral nutrition provided within 48 hours increases the survival rate and GCS among TBI patients over the first 7 days of ICU care, and improves clinical outcomes 1 month after injury (Chiang et al., 2012). Also, providing PN to TBI patients within 48 hours was found to increase immunological markers CD4, CD4 and CD8 ratios, and T-lymphocyte function in response to Concanavalin A (Sacks et al., 1995), indicating that early nutrition support improve immune function in patients sustaining TBI. Delayed EN has correlated significantly with anthropometric, biochemical, and clinical markers of nutritional depletion (Dhandapani et al., 2012). Early nutrition provides a steady supply of glucose to the brain, which otherwise must depend on the glucose that results from muscle protein breakdown (Härtl, Gerber, Ni, & Ghajar, 2008).

Level of Brain Injury Severity

Traumatic brain injury patients with lower GCS scores (4-5) show greater energy expenditure than those with higher scores (6-11), (Foley et al., 2008). Development of malnutrition is more common among TBI patients with poorer GCS scores, who have poor prognoses and lower rates of survival (Chiang et al., 2012). Unfavorable neurological outcomes are associated with delayed nutrition therapy following TBI (Dhandapani et al., 2012).Chiang et al. (2012) found that in the first 7 days of ICU care, patients with GCS scores of 6-8 who received EN had significant improvement in the scores of GCS compared to patients with GCS scores in the same range who did not receive EN; patients with a GCS score of 6-8 who received EN also showed better GCS scores compared to those who received EN but had lower initial

GCS scores (4-5). In another study, the combination of GCS>5 and early EN improved patients' GCS scores and improved disability compared to lower GCS or delayed EN (Dhandapani et al., 2012).

Severity of Illness

The relationship between severity of illness and malnutrition has not been well elucidated. In a study which included 119 elderly patients, two severity of illness scores (Acute Physiological And Chronic Health Evaluation, APACHE II ; and Simplified Acute Physiology Score II, SAPS II) were found to be higher among malnourished patients, but the differences were not significant (Atalay, Yagmur, Nursal, Atalay, & Noyan, 2008). A significant increase in APACHE II and SAPS II scores were found in malnourished patients (47 patients) compared with the well-nourished patients (77 patients) in another study (Sungurtekin et al., 2008).

Intracranial Pressure

Optimization of nutritional intake and ICP management in the first week following TBI is one of the three topics that were recently identified as the highest priority knowledge translation projects in the area of TBI (Bayley et al., 2014). Nutrition support and ICP monitoring and management have a demonstrated evidence-practice gap (Bayley et al., 2014). However, focusing on these areas in research may improve clinical care and outcomes of TBI patients. We did not identify any studies in the literature about the relationship between ICP and nutrition or malnutrition in TBI patients.

SCCM/ A.S.P.E.N and other Guidelines

Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) (SCCM /ASPEN) recommend assessment of weight loss, previous nutrient intake prior to admission, level of disease severity, co-morbid conditions, and function

of the gastrointestinal tract before initiation of nutrition therapy in critically ill patients (McClave et al., 2009). EN is recommended over PN by SCCM /ASPEN and the Canadian clinical practice guidelines (McClave et al., 2009; Heyland, Dhaliwal, Drover, Gramlich, & Dodek, 2003). They recommend starting EN within 24-48 hours after admission. The Brain Trauma Foundation (2007) recommend initiation of nutritional therapy no later than 72 hours after TBI in order to achieve full caloric replacement within 7 days of injury. If EN is not available or feasible, PN should not be used before the 7th day of hospitalization, in case the critically ill patient has no evidence of protein-calorie malnutrition. Otherwise, PN should start as soon as possible (McClave et al., 2009). If energy requirements have not been achieved after 7-10 days with EN, PN could be added to the EN (McClave et al., 2009). Holding EN related to GRV<500 should be avoided in the absence of other signs of intolerance such as: vomiting, diarrhea, and bloating. Keeping a patient nil per os (NPO) prior to, during, and immediately following diagnostic tests or procedures should be minimized to prevent inadequate delivery of nutrients (McClave et al., 2009).

Summary

This research program's long term goal is to reduce the prevalence of malnutrition in TBI patients during ICU and hospital stay. The literature is very scarce about the change in nutritional status of TBI patients while admitted to the ICU and remainder of the hospital stay following injury. Baseline nutritional status needs to be assessed accurately due to the uniqueness and individuality of TBI patients' energy expenditure and calorie requirements. Many factors affect the development of malnutrition in TBI patients besides the metabolic changes that the patients develop. Some of these factors have been studied, however, it is not clear which factor has the greatest effect on malnutrition development. This study highlights the gaps in the literature about

those factors and also will shed light on some other factors that may have an effect that have not been studied before.

Chapter III: Methods

A retrospective descriptive study was conducted to examine the change in nutritional status in traumatic brain injury (TBI) patients over 7 days beginning with admission to the intensive care unit (ICU). This section addresses the study design, setting, sample, instruments, procedures, and data analysis plan for the specific aims of the study.

Design, Sample, and Setting

This retrospective descriptive study explored changes in nutritional status of TBI patients over the first 7 days beginning with admission to the ICU. Five hundred and eighty one records were reviewed to identify patients ≥ 18 years old with documented TBI who were admitted to the ICU at Tampa General Hospital (TGH), were mechanically ventilated in the first 24 hours of admission, and had a GCS score between 3-12 on Emergency Room (ER) admission. Fifty records met the inclusion/exclusion criteria and were included in the study.

Tampa General Hospital in Tampa, Florida, is one of the largest hospitals in Florida. It is licensed for 1,004 beds. Approximately 73.6% of admissions are White, 20.7% are African-American, and 17.2% are Hispanic. Tampa General Hospital is the area's only level 1 trauma center and one of just four burn centers in Florida. The primary investigator, Dina Masha'al, co-investigator/faculty advisor Dr. Munro, and study coordinator Paula Cairns are all credentialed by the TGH Office of Clinical Research.

Instruments

Demographic Data and Co-morbidities were collected from the hospital admission record. Demographic data included: age, gender, ethnicity, race, marital status, and co-morbid conditions.

The Acute Physiology, Age, and Chronic Health Evaluation III (APACHE III) was used to assess severity of illness upon admission. The scale total score ranges from 0 to 299 and consists of five sub-scores: vital signs/laboratories, pH/pCO₂, neurological, age, and chronic health. The level of measurement is ratio. The highest score indicates the more severe disease. Interclass correlation of inter-rater reliability was 0.90. Higher APACHE III score is significantly associated with increase in relative risk of hospital death. The scale is specific to patient status at one point in time (within the first 24 hours of ICU admission). As patient status changes, risk prediction will also change (Knaus et al., 1991). The APACHE III was used to describe the study population, to document the initial level of illness severity in the participants, and to explore the predictors that affect the change in nutritional status.

The Glasgow Coma Scale (GCS) was used to assess patients' level of brain injury severity as well as level of consciousness. The scale scores can range from 3 to 15, with 3 being the lowest consciousness state (no response to pain, no verbalization, and no eye opening). The level of measurement for the scale is interval. The scale has three components: eye opening, motor response, and verbal response. The agreement percentage for the exact total GCS in an emergency department using 116 trauma patients with altered level of consciousness was 32% (τ -b=0.739; Spearman ρ =0.864; Spearman ρ^2 =75%) (Gill, Reiley, & Green, 2004). Kevric, Jelinek, Knott & Weiland (2011) examined 140 patients in the emergency department, and found that the inter-rater reliability of the GCS was moderate (κ =0.59). This scale was used to assess

the level of brain injury severity at emergency room (ER) admission, and level of consciousness during hospitalization. See Appendix A for GCS components.

The Sequential Organ Failure Assessment (SOFA) score was used to assess daily health status of the patients. This tool has six items: respiratory, coagulation, hepatic, cardiovascular, central nervous, and renal. A score of 0 indicates normal function, while a 4 is the most abnormal (Vincent, Ferreira & Moreno, 2000). The scale level of measurement is ratio. The intraclass correlation coefficient was .89 for the total SOFA score. Kappa values were (0.552), (0.634), and (>0.8) for the central nervous system, respiratory system, and for the other organ systems respectively (Arts, de Keizer, Vroom, & de Jonge, 2005). See Appendix B for SOFA scale.

Measures of the Intracranial Pressure (ICP) of the patients was obtained from the medical records. The average of the daily ICP readings was calculated for each day. Types of EN Formulas were obtained for the first 7 days of hospitalization from patients' records and used to assess the prescribed energy.

Anthropometric Measurements and Biomedical Measurements were used to assess the change in nutritional status at admission and 7 days after that. Anthropometric measurements included height (in meters), weight (in kilograms), and body mass index (BMI). Biochemical measurements included serum albumin, hemoglobin, and total lymphocyte count (TLC).

Feeding Tube Type and Site, Route of Feeding, Time of Feeding Initiation, were obtained from the medical records.

The Faisy Equation was used to predict the patients' energy requirement (Savard et al., 2008). Adequacy of Energy Intake was defined as the ratio of calculated patient energy requirement to energy intake; the Brain Trauma Foundation (2007) defines adequate intake as

receiving 100-140% of energy requirements. Key variables, instruments and their measurement intervals are summarized in Table 1.

Table 1: Key Variables

Aims	Variable/Instrument	Measurement interval
Aim1	Baseline nutritional status: -Anthropometric measurements: height, weight, BMI -Biochemical measurements: serum albumin, hemoglobin, and TLC Nutritional status after 7 days: -Anthropometric measurements: height, weight, BMI-Biochemical measurements: serum albumin, hemoglobin, TLC.	within 24 hours of admission After 7 days of admission
Aim2	-Adequacy of energy intake: REE, total energy intake -Energy prescription: Type of EN formula -Route of feeding: PN vs. EN -Time of feeding initiation -Severity of illness: APACHEIII -Level of brain injury severity/ level of consciousness: GCS -Daily health status -Age -ICP: average	Daily for 7 days Daily Daily At time of feeding initiation At admission At ER admission/daily average Daily At admission Daily

Medical Record Review Procedure

The study protocol was implemented in accordance with the ethical standards of the institutional review board (IRB) and approved by the University of South Florida (USF) and TGH. The IRB approval was obtained before the initiation of the study. All required approvals from TGH were obtained before the beginning of the study. All policies from the USF and TGH were adhered to. Medical records of trauma patients admitted to the ICU during 2013 or 2014 were reviewed for documentation of TBI. If there was no documentation of TBI, no further review took place. If TBI was documented in the medical record, the hospital admission date, the

patient demographics, and GCS at ER admission were collected, and APACHE III data was calculated.

On a daily basis for the first 7 days of admission, SOFA score was calculated to assess daily health status. The total average of the ICP results and GCS results were calculated each day. Values of serum albumin, hemoglobin, and TLC were collected at admission and on day 7, and the results were compared to the reference values used by TGH laboratory. Patients' energy requirements were predicted using Faisy equation: $REE(KG/day) = 8 \times \text{body weight (Kg)} + 14 \times \text{height (Cm)} + 23 \times \text{minute ventilation (L/min)} + 94 \times \text{body temperature (C}^\circ\text{)} - 4834$ (Savard et al., 2008). Energy prescription was obtained from the medical record as well as the total energy the patient received each day. Adequacy of energy intake was calculated daily for 7 days based on the amount of calories that the patient received and the calculated energy requirement. Patients were considered adequately fed if they received 100% or more of their energy requirements (Brain Trauma Foundation, 2007). Types of formulas, route of feeding (enteral nutrition(EN) or parenteral nutrition (PN)), feeding tube type, time of feeding initiation were collected from the patients' medical records.

Body mass index was calculated once at admission and once after 7 days of ICU or hospital stay to evaluate the change in nutritional status. Height and weight were obtained from the patient's medical record as well. Weight and height were used to calculate BMI (kg/m^2), and the values obtained were evaluated according to World Health Organization (WHO) standards. Data were collected starting from patient admission to the ICU, and continued for 7 days even patients were transported to other wards.

Data Analysis Plan

Descriptive analysis was used to characterize the sample at admission. Aim 1: **To describe the change in BMI of TBI patients at day 7 in the ICU and hospital stay.** Paired t-test was used to describe the change in BMI of TBI patients at day 7 in ICU and hospital stay. Aim 2: **to investigate the effect of energy prescription, time of feeding initiation, severity of illness, daily health status, age level of coma, and ICP on the adequacy of energy intake among TBI patients during ICU and hospital stay.** A multiple regression analysis was conducted to identify the influence of these factors on the adequacy of energy intake in TBI patients during the ICU and hospital stay.

Chapter IV: Results

A description of the study findings are presented in this chapter. Outcomes of preliminary data analyses, descriptive statistics for the variables, and analysis for specific aims are presented in this chapter.

Preliminary Analyses

Because of the retrospective nature of the data collection, there were missing values among the data of this study. Missing values were missing completely at random. This means that missing values were randomly distributed throughout the data set (Acock, 2005). Some of the parameters were collected for 7 days, and used to calculate other parameters. There were 350 instances of missing data. Missing data in some parameters (weight, height, temperature, mean blood pressure, tidal volume, Fio2, Pao2, respiratory rate, platelet number, bilirubin, creatinine, etc..) resulted in 21% of SOFA scores, and 50% of adequacy of energy intake results missing. Also, about 32% of total prescribed energy and 36% of daily average intracranial pressure were missing as well.

Missing data among the variables that were collected at admission, and those that were collected at admission and on day 7 were smaller. There were three missing values in APACHE III scores, two missing values in albumin at admission results, 20 missing values in albumin on day 7. Also, there were two missing values in TLC at admission and one missing value in hemoglobin on day 7.

Casewise deletion was used to manage missing values in the data set. Casewise deletion may result in loss of 20-50% of the data, and it often addresses the missing values in a systematic

way. In case of having values missing completely at random, casewise deletion is conservative according to Acock (2005). Figure 2 illustrates the number of patients that were included in specific aims analysis.

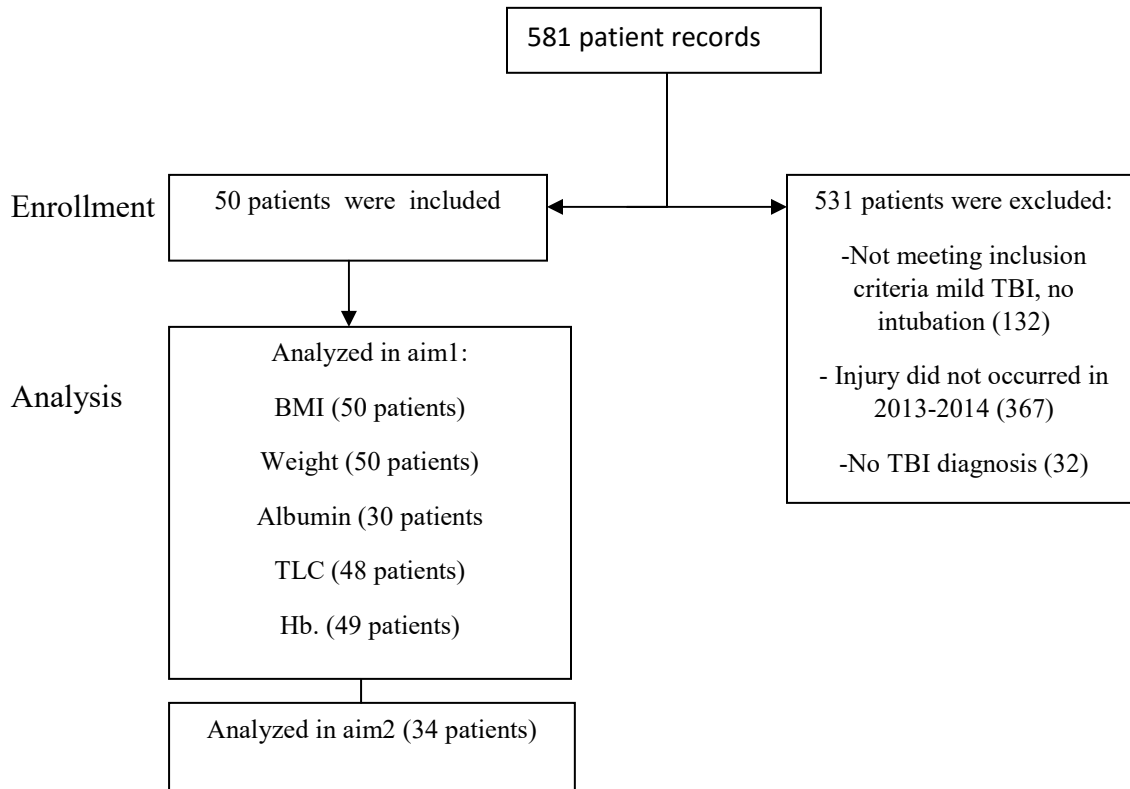


Figure 2. Consort enrollment and analysis flowchart

Data were screened for outliers using standardized scores. Standardized scores, or z scores, represent the distance a participant lies from the average score on any given variable, and are measured in standard deviations. According to Tabachnick and Fidell (2007), scores on any variable which are more than 3.29 standard deviations from the mean are considered outliers. However, not all of the outliers were removed. Four outlying values were found for the same patient in total prescribed energy. Three outlying values were found in daily average of ICP, two of them were for the same patient. Five outlying values were found in SOFA scores, four of them for the same patient. Three outlying values were found for three different patients in IV therapy

values. Two patients were found to have an outlying values for age. Other two patients were found to have an outlying values for number of ICU days. One patient was found to have an outlying values for number of ventilation days, and another patient for time of feeding initiation.

Also, an outlying value was found in the data of weight, height, BMI, hemoglobin, TLC, and albumin that were collected at admission. Outlying values of weight and height were found for the same patients at day 7. Body mass index at day 7 had 3 outlying values. There were two outlying values for albumin, hemoglobin, and TLC at day 7. Outlying values of these variables did not change the normality of the distribution except for TLC on day 7, IV therapy, number of ventilation days, and number of ICU days. Outlying values for IV therapy were excluded.

Skewness is a lack of symmetry in the distribution, with the bulk of the scores clustered at one end of the distribution. Kurtosis describes the “peakedness” of the distribution of scores (Tabachnick & Fidell, 2007). Distribution was normal for the parameters except for TLC at day 7, number of ventilation days, and number of ICU days. TLC at day 7 was positively skewed, therefore, a transformation was done to correct for skewness. No action was taken to treat the skewness of number of ventilation and ICU days parameters because these data were not included in any further statistical analysis.

Adequacy of energy intake difference, ICP difference, total prescribed energy difference, and SOFA difference were calculated by taking the difference between the first and last available value of each variable. There was no skewness in these variables. SOFA difference and total prescribed energy variables had kurtosis. Linearity and multicollinearity assumptions were tested for the variables that were included in the regression analysis. Bivariate correlation was used to examine the relationships among the total prescribed energy, ICP, daily health status, age, level of brain injury severity, severity of illness, time of feeding initiation and the adequacy of energy

intake. The results showed low to moderate correlation among these variables. Also, partial regression plots were created to check for linearity. The plots showed linear relationships between the dependent and the independent variables.

Descriptive Statistics

Demographic Characteristics: The results of the demographic characteristics for the sample (N = 50) included in this analysis are presented in Table 2. The age of the patients ranged from 18 to 77 years. The majority of the sample were male (82%) and single (60%). Seventy-four percent of the patients were not Hispanic. The majority (58%) were White, 20% were Black/AA, and 22% were other races. The cause of TBI for the majority of them (58%) was motor vehicle accidents (MVA), followed by motor cycle accidents (MCA) (16%), and falls (16%). The majority of the patients (62%) had no co-morbidities, probably related to the young ages of the participants.

Nutritional Characteristics: Patients' baseline nutritional characteristics included weight, height, albumin, TLC, and hemoglobin, as well as BMI which was calculated. Table 3 illustrates these variables' means and standard deviations.

Eighty-eight percent of the patient were fed enterally. Six patients did not receive any type of nutrition; four of these did not have an EN or PN prescription. Lack of nutrition for those patients was due to the short intubation period (less than four days), or to multiple failed attempts of feeding tube initiation, or to death within the first 72 hours from ICU admission. The majority of the patients received EN via Dobhoff Tube (DHT) (38%). Twenty-eight percent received EN via naso-gastric (NG) tubes, and twenty percent via oro-gastric (OG) tubes. The mean of time of feeding initiation was 35.5 hours.

Table 2. Descriptive Characteristics of the Participants

Variable	N	Mean	SD	%
Age	50	34	16.3	
Gender				
Male	41			82
Female	9			18
Marital Status				
Married	10			20
Divorced	3			6
Separated	2			4
Single	30			60
Unknown	5			10
Ethnicity				
Hispanic	11			22
Non-Hispanic	37			74
Unknown	2			4
Race				
White	29			58
Black/AA	10			20
West Indian	1			2
Other	8			16
Unknown	2			4
Cause of TBI				
MVA	29			58
MCA	8			16
Fall	8			16
Assault	3			6
GSW	2			4

MVA, motor vehicle accident; MCA, motor vehicle accident; GSW, gunshot wound

Table 3. Baseline Nutritional Characteristics

Variable	N	Mean	SD
Weight (KG)	50	82.444	18.438
Height (m)	50	1.758	.079
BMI	50	26.525	4.793
Albumin	48	3.435	.729
TLC	50	2.893	2.119
Hb.	50	13.024	2.741

Sample size (N) varies due to missing data. BMI, body mass index; TLC, total lymphocyte count; Hb, hemoglobin.

There were seven types of formula prescribed for the patients. Some of the patients used the same formula over the seven days, some of them were switched to other types of formulas. Some of the patients stopped EN before day7 or did not start it on day one or did not start it at all. Four of the patients did not have a prescription for EN.

Fibersource HN was the most prescribed formula. This formula was prescribed for 76% of the patients. Isosource 1.5 was prescribed for 10% of the patients, followed by Diabetisource AC and Replet w/Fiber that each of them were prescribed for 6% of the patients. Finally each of Peptamen 1.5, Peptamen AF, and Nutren 2.0 were prescribed for 4% of the patients.

Daily estimated energy, daily prescribed energy, and daily energy intake, resting energy requirement (REE), and adequacy of energy intake (AEI) was collected and calculated for 7 days. Table 5 and Figure 3 present the means of daily estimated energy, daily prescribed energy, daily energy intake, resting energy expenditure (REE), and adequacy of energy intake (AEI) for the sample as a whole.

Table 4. Percentages of Patients who had EN Prescription, and Percentage of Patients with Prescription who were Receiving EN Each Day.

Day Number	% of Patients who had EN Prescription	% of Patients with prescription who were Receiving EN
Day1	6%	66.7%
Day2	56%	57%
Day3	80%	77.5%
Day4	82%	90%
Day5	84%	93%
Day6	78%	95%
Day7	78%	97.4%

Table 5. The Means in KCal of Daily Estimated Energy, Daily Prescribed Energy, Daily Energy Intake, Resting Energy Expenditure (REE), and Adequacy of Energy Intake (AEI).

Variable	Estimated Energy	Prescribed Energy	Energy Intake	REE	AEI
Day Number					
Day 1	2133	1987	191	7654	2.6%
Day 2	2143	2141	515	7818	6.6%
Day 3	2105	2153	722	7759	9.5%
Day 4	2093	2113	1368	7829	8.9%
Day 5	2093	2114	1393	7778	17.9%
Day 6	2090	2097	1272	7819	16.5%
Day7	2090	2092	1427	7807	18.5%

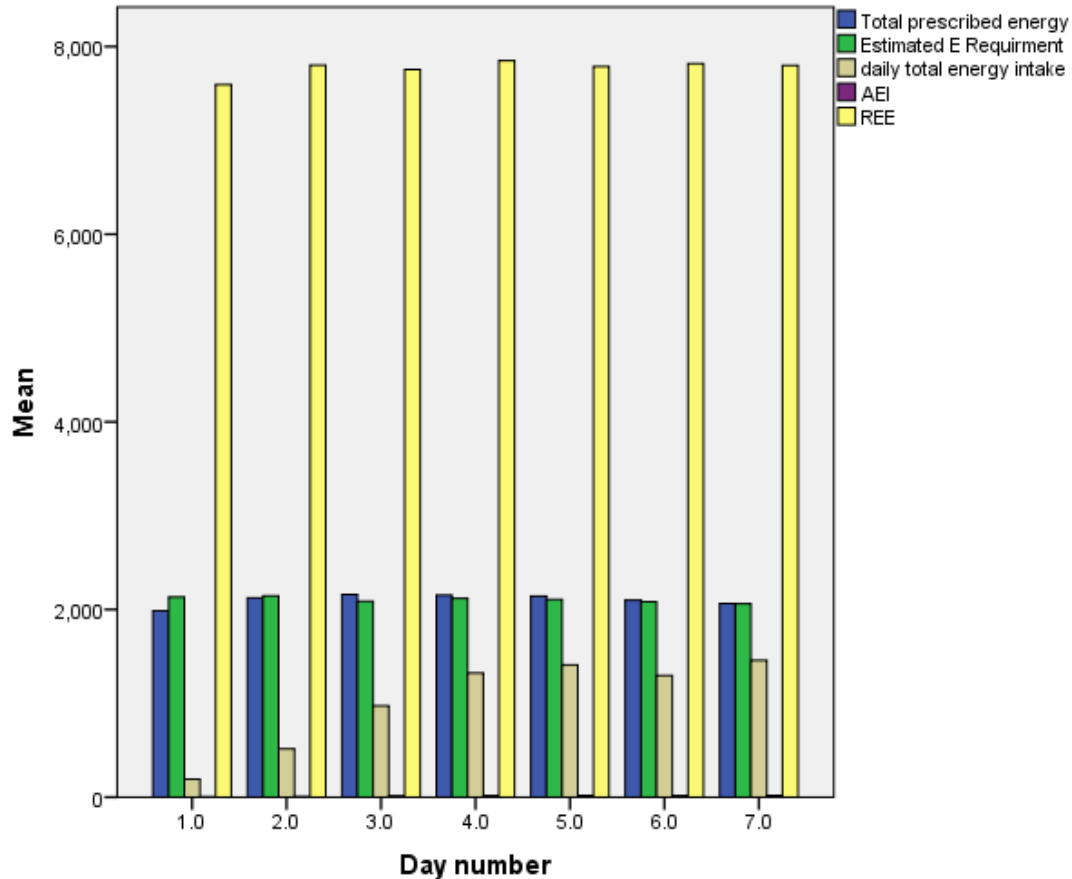


Figure 3. The Means of daily estimated energy, daily prescribed energy, daily energy intake, resting energy expenditure (REE), and adequacy of energy intake (AEI).

Other Characteristics: Patients' APACHE III scores mean was 70.851. The GCS(ER) mean was 4.740. Patients' ICU stay period and ventilation days ranged from 2 to 119 days and 2 to 65 days respectively. The average length of mechanical ventilation in the first 7 days was 5.8 days. Daily average ICP, daily average GCS, and SOFA were collected and calculated for 7 days. Figure 4 shows the means of these variables over seven days.

Analyses for the Specific Study Aims

Aim1: The first aim of this study was to compare BMI of TBI patients at admission to ICU to BMI at day 7 of the hospital stay. Paired t-test was calculated for BMI, weight, albumin, hemoglobin, and total lymphocyte count. The results showed (Table 6) that there were no significant differences between BMI at ICU admission and BMI at day 7 of the hospital stay, as

well as weight at ICU admission and weight on day 7. The results showed that there was a significant difference between ICU admission values and values at day 7 for albumin, hemoglobin and TLC.

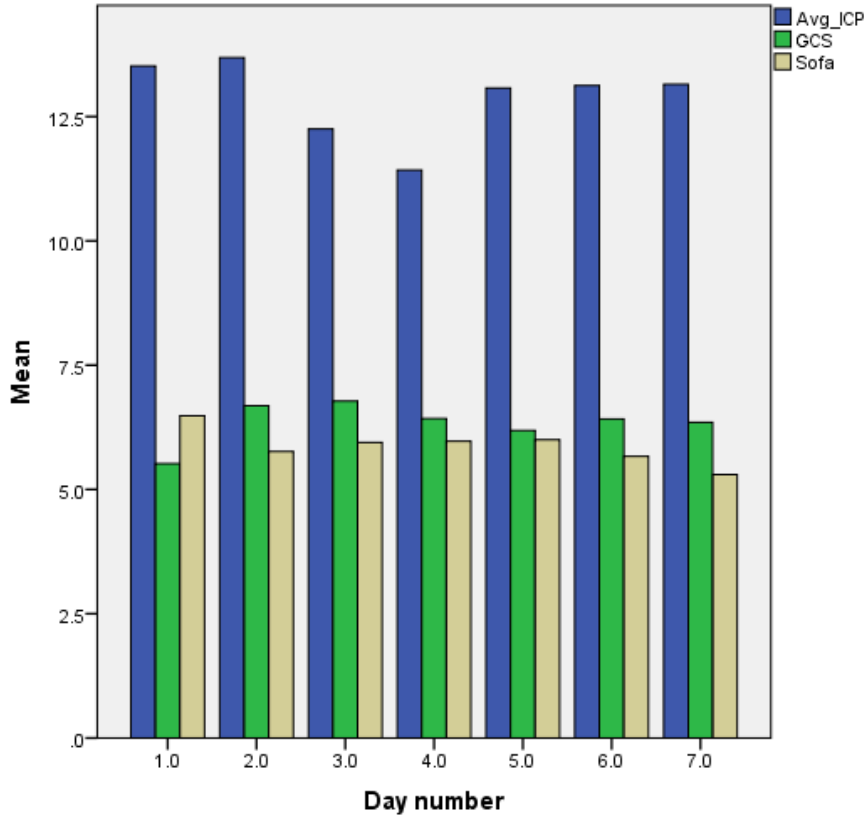


Figure 4. Mean of daily intracranial pressure (ICP), Glasgow Coma Scale (GCS), and the sequential organ failure assessment (SOFA) scores averages.

The mean of albumin, TLC, and hemoglobin changed from 3.357 to 2.557, from 2.7069 to 1.4785, and from 12.994 to 9.784 respectively. Looking at the means of these variables, we conclude that there were significant decreases in albumin, TLC, and hemoglobin from day 1 of ICU admission to day 7 of hospital stay. The effect size (Cohen's d) was large: for albumin it was 0.9053, for TLC it was 0.58077, and for hemoglobin it was 1.2003. Using another formula ($\eta^2 = t^2 / (t^2 + N - 1)$, where N is the number of participants) the effect size of albumin was 0.45887, TLC was 0.25624, and hemoglobin was 0.59531, confirming the large effect size.

Table 6: Results of Paired t-test of ICU Admission and Day 7 Data for Aim 1 Nutritional Variables

	Mean	SD	t-test	Sig. (2-tailed)
Weight1- Weight2	-.518	7.602	-.482	.632
BMI1- BMI2	-.155	2.539	-.432	.668
Albumin1-Albumin2	.800	.884	4.959	.000
TLC1- TLC2	2.635	1.884	9.684	.000
Hb1-Hb2	3.210	2.674	8.403	.000

The number 1 represent the result within 24 hours of ICU admission; The number 2 represent the result on day 7; BMI, body mass index; TLC, total lymphocyte count; Hb, hemoglobin.

Seventeen patients (34%) received blood at admission or within the first 7 days of ICU and hospital admission. The average amount of blood transfused was 2217.88 ml. The mean intravenous (IV) therapy volume was calculated daily to assess the effect of fluid resuscitation on hemodilution for this cohort. The minimum daily mean of IV therapy was 868.2 ml/day, and the maximum was 3371.7 ml/day. Figure 5 illustrates the mean and standard deviation of IV therapy over 7 days.

A bivariate correlation was calculated to assess the relationship between the change in hemoglobin over 7 days and the mean of total IV intake during hospitalization. The results showed a weak correlation between them ($r = .213$).

Aim2: The second aim of this study was to investigate the effect of age, energy prescription, time of feeding initiation, severity of illness, daily health status, level of brain injury severity, and ICP on the adequacy of energy intake among TBI patients during ICU and hospital stay. Bivariate correlation was used to examine the relationships among these variables. The results showed (Table 7) low to moderate correlations.

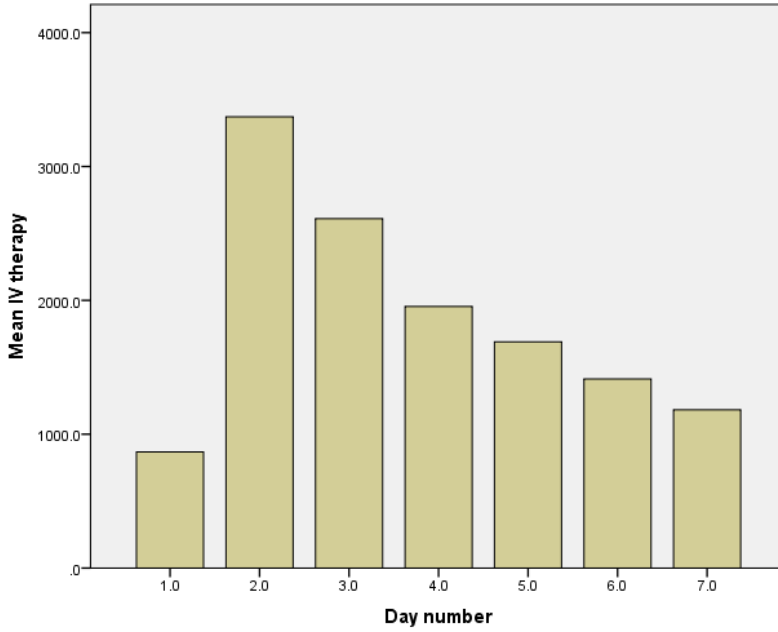


Figure 5. Mean volume of IV therapy

Table 7: Correlations of Aim 2 Variables

	AEI	Age	APACHEIII	TFI	GCS (ER)	PE	SOFA	ICP
AEI difference	1.000	-.135	.187	-.023	-.001	.081	.002	-.037
Age		1.000	.140	-.157	.489	-.101	-.045	.395
APACHEIII			1.000	-.097	-.355	.217	.261	.133
TFI				1.000	.016	.108	-.359	-.067
GCS(ER)					1.000	-.285	-.260	-.022
PE difference						1.000	.145	.298
SOFA							1.000	-.041
difference								
ICP difference								1.000

AEI, adequacy of energy intake; TFI, Time of Feeding Initiation; GCS(ER), Glasgow Coma Scale at emergency room admission; PE, Prescribed Energy

A multiple linear regression was performed to evaluate the effect of total prescribed energy, ICP, daily health status, age, level of brain injury severity, severity of illness, time of feeding initiation on the adequacy of energy intake. Preliminary analysis was performed to ensure there was no violation of the assumption of linearity, normality, and multicollinearity. There was no significant regression found ($F(7, 33) = .474, p = .844$), with an R^2 of .113, and adjusted R^2 of -.125. Table 8 shows the results of multiple regression analysis.

Table 8. Results of Multiple Regression

Model	B	Standard Error	Standardized Coefficients (Beta)	T	Significance	Zero-Order	Part
Constant	-15.455	7.192		-2.149	.041		
Age	-.169	.129	-.344	-1.308	.202	-.135	-.242
APACHEIII	.107	.071	.328	1.496	.147	.187	.276
Time of Feeding Initiation	-.030	.081	-.076	-.372	.713	-.023	-.069
GCS(ER)	.961	.857	.288	1.121	.272	-.001	.207
TPdifference	.002	.006	.064	.305	.763	.081	.056
SOFAdifference	-.201	.718	-.059	-.279	.782	.002	-.052
ICPdifference	.035	.224	.035	.156	.877	-.037	.029

N=34; TPdifference, total prescribed energy difference

Statistically significant (<0.05) positive relationships were found between the difference of total prescribed energy and the difference of ICP, the difference of ICP and age, and GCS(ER) and age. Also, negative relationships were found between time of feeding initiation and the difference in SOFA scores and GCS(ER) and APACHEIII.

Chapter V: Discussion

In this section, the results of the study are discussed. The content includes the following: a discussion of the study findings, study limitations, recommendation and conclusions. The purpose of this study was to examine the nutritional status of traumatic brain injury (TBI) patients upon admission to intensive care unit (ICU) and during hospital stay to describe baseline nutritional status, detect changes in nutritional status over 7 days, and identify the factors affecting the adequacy of energy intake and the change in nutritional status as a consequence. This study is an important foundation for development of interventions to improve TBI patients' nutritional status in hospital, including evidence based nutritional protocols.

This study had two specific aims: 1) To compare body mass index (BMI) of TBI patients at admission to ICU to BMI at day 7 of the hospital stay. 2) To investigate the effect of energy prescription, time of feeding initiation, severity of illness, level of brain injury severity, daily health status, age, and intracranial pressure (ICP) on the adequacy of energy intake among TBI patients during ICU and hospital stay. To our knowledge, this is the first study to demonstrate the changes of nutritional status over time during ICU and hospital stay in TBI patients as well as the factors affecting adequacy of energy intake.

Our study included 50 patients who met the inclusion/exclusion criteria. Those patients were identified from review of 581 patients' records in Tampa General Hospital (TGH). The majority of the sample were males, single and young. Traffic accidents were the main causes of TBI among the younger patients, followed by falls which were mainly among older patients. Falls and motor vehicle accidents are the two most common causes of TBI. Motor vehicle

accidents are the leading cause of TBI-related death; Falls constitute 35.2% of all TBI, and account for 60.7% of TBI in adults older than 65 years (Warden et al., 2006). The majority of the patients were non-Hispanic and 58% of them were White. This was expected, given the demographics of Hillsborough County, where 76.6% of people are non-Hispanic or Latino, and 71.2% of them are White. At TGH, 73.6% of the hospital inpatients are White. Further research need to be conducted in different areas and states in order to understand the most common cause of TBI in each area and find the appropriate intervention. Also, these numbers could be a good indicator for the driving schools in Hillsborough county to give more safety courses, especially for young and new drivers (and motorcyclists), before providing any driving license.

In general, tests of the specific aims and hypotheses did not all yield expected outcomes but there were some encouraging findings. We were surprised that there were no significant change in BMI or weight over the course of the first 7 days of ICU admission among TBI patients. This could be related to the young ages of the patients (M=34 years old) and their relatively healthy status at admission, or/and possibly to the development of edema, which is a clinical marker of malnutrition (Dhandapani et al., 2007).

These results are not consistent with Kim & Choi-Kwon (2011) study results, where BMI showed a significant decrease in ICU patients, especially who were severely malnourished at admission. Severe TBI patients are at high risk of significant weight loss due to the complex nutritional needs that they develop, secondary to the severity and time span of hypermetabolism and hypercatabolism (Aadal, Mortensen & Nielsen, 2015). A recent study found that patients with acquired brain injury (TBI, stroke, and other diagnoses) lose weight in acute phase after injury, and those with TBI in particular lose more weight than patients with stroke and they are at higher risk of malnutrition (Aadal et al., 2015). Allard et al. (2015) studied 373 patients, who had

their weight and nutritional status assessed using the Subjective Global Assessment (SGA) tool at admission. Twenty-five percent of the patients had weight loss of $\geq 5\%$, which was defined as nutritional deterioration. Fifty-one percent of them were classified as having SGA deterioration (Allard et al., 2015). Unfortunately, nutritional status for TBI patients could not be classified in this dissertation study due to the retrospective study design, which was one of the limitations.

In our current study a significant reduction was found in the values of hemoglobin, TLC, and albumin. A high effect size was noted, indicating a substantial difference in the results obtained on day 1 and day 7. Kim & Choi-Kwon (2011) found no significant changes in hemoglobin, TLC, and albumin results over 7 days for critically ill patients who received EN. According to Salim et al. (2008) about half of patients with severe TBI develop anemia during the first week of admission. One might argue that the significant decrease in hemoglobin level could be related to hemodilution. A bivariate correlation was done to examine this. There was a weak correlation ($r=.213$) between the difference in hemoglobin level between day 1 and day 7 and the average of intravenous (IV) therapy for each patient. This weak correlation rules out hemodilution as an explanation for the change in hemoglobin values. In our results, hemoglobin change is significant although 34% of the patients received 2217.88 ml of blood in average.

In 2011 González Madroño, Mancha, Rodríguez, de Ulibarri, & Culebras analyzed the relationship between weight loss, BMI, TLC, and albumin level for 101 patients. They observed that the mean level of albumin and TLC were higher for individuals with a BMI >18.5 or with no weight loss compared to those with BMI <18.5 and some weight loss. Also, they found that as albumin and TLC levels became lower, the probability of a patient being malnourished was higher (González Madroño et al., 2011). In addition, Sungurtekin et al. (2008) found that hemoglobin, hematocrit, and serum albumin values were significantly higher in well-nourished

and moderately malnourished groups than in severely malnourished groups. Singh, Gupta, Aggarwal, Agarwal, & Jindal (2009) found that the patients who were discharged alive from the respiratory ICU had higher baseline serum albumin than the nonsurvivors.

Although albumin, TLC, and hemoglobin could be considered less strong indicators of nutritional status in the literature, they might be more meaningful for TBI patients than those without TBI. These laboratory values, along with weight and BMI, are clinically relevant and easy to obtain for nutrition assessment and screening. Missing data were found while collecting these variables, indicating that they are not uniformly collected in critically ill TBI patients (Krakau et al., 2010). Nurses and dietitians should be trained to assess and document these variables routinely to keep health care providers updated on the patient's nutritional health status. In addition more research needs to be done on the change of nutritional status of TBI patients over longer periods of time and with larger sample.

In order to investigate the factors that affect the adequacy of energy intake and the development or worsening of malnutrition among TBI patients, we analyzed the relationship between selected variables including the energy prescription, time of feeding initiation, severity of illness, level of brain injury severity, age, daily health status, and ICP and the adequacy of energy intake among TBI patients during ICU and hospital stay.

The results of the study showed no effect from any of the independent variables on the dependent variable. These results are in contrast with other studies, where they found that underprescription (Kim & Choi-Kwon, 2011) and feeding interruption (O'Leary-Kelley, Puntillo, Barr, Stotts, & Douglas, 2005) were contributing factors to inadequate energy intake. The results of this study could be affected by the small sample size and the short period of patients' tracking which reduced the variability in the factors. Also, other factors we planned to test could not be

reliably obtained from the medical record, such as gastric residual volume (GRV) and total hours of feeding interruption; this is again a limitation of the retrospective study design. Future research should include additional variables such as GRV and be done with larger sample and over a longer period. Again, precise prospective documentation of GRV, hours of feeding interruption, and causes of feeding interruption would be a good way to know exactly how these factors affect the delivery of nutrition to the patients.

Kim & Choi-Kwon (2011) noted that the nutritional status of ICU patients was deteriorated in adequately fed and not malnourished patients, as well as not adequately fed patients. This may be related to the underestimation of energy requirements for those patients. In this study, the Faisy equation was used to estimate the energy requirements, and the estimate of energy requirements it generated diverged from estimates used by the dietitians. It was found that the dietitians prescribed only 27% of the patients' energy requirements required as calculated based on Faisy equation, and patients received only 12% of their requirements. Based on the dietitians' estimated energy requirements, dietitians' prescribed 99.7% of the requirements, but the patients received only 46.9% of the prescribed energy. These results are even lower than what McClave et al. (1999) and De Jonghe et al. (2001) found. They found that physicians prescribe only about 66 -78% of the goal requirements of EN, and only 71- 78% of the prescribed volume delivered to the patients in ICU. In another study including 60 mechanically ventilated patients, 68% of the patients received less than 90% of their energy requirements, and half of them received less than 50% of their energy requirement during the 3 days study period (O'Leary-Kelley et al., 2005).

Prescribed energy depends on the formulas that have been used to calculate energy requirements, since calorimetry is not routinely used and is not considered cost effective.

O'Leary-Kelley et al. (2005) selected 25 patients from a larger sample (N= 60) to have their energy requirement measured using calorimetry and simultaneously calculated using Harris-Benedict's equation. The values obtained for energy requirements differed significantly, where the mean of Harris-Benedict's equation estimate was 488 kcal greater than the mean of calorimetry resting energy expenditure (REE) (O'Leary-Kelley et al., 2005). McEvoy et al. (2009) found that both FAO/WHO/UNU and Harris-Benedict equations have predicted REE poorly compared to indirect calorimetry in patients recovering from TBI. O'Leary-Kelley et al. (2005) found that the Harris-Benedict equation was more practical and effective than indirect calorimetry for estimating energy requirements in ICU patients due to the clinical and technical limitation that prevented using calorimetry in the ICU. These limitations included inaccurate measurement as a result of gas leaks or water vapor in the ventilator system, instability of delivered oxygen concentration, and fraction of inspired oxygen more than 0.60 (O'Leary-Kelley et al., 2005). The Faisy equation was used to calculate energy requirement in this study because Savard et al. (2008) found it to be the most accurate formula to estimate energy requirements in mechanically ventilated patients in comparison with indirect calorimetry. Further research need to be done to compare the difference between formulas in predicting REE among mechanically ventilated TBI patients. This would help health care providers to prescribe adequate amount of nutrition and energy for TBI patients in particular.

Enteral nutrition was the feeding method of choice for all patients who received nutritional support in this study. That is consistent with SCCM /ASPEN guidelines. They recommend the use of EN only, and avoidance of PN unless EN is not available or feasible and not before day 7 of hospital stay (McClave et al., 2009). Also, the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines recommend complementary TPN only when EN

is contraindicated or if EN is not tolerated by the 3rd day (Kreymann et al., 2006). It is well known that EN supports cells and organs' function, has a lower risk of hyperglycemia or hyperosmolarity, and supports the gut mass and barrier function (Zaloga, 2006; Justo Meirelles & Aguilar-Nascimento, 2011). Future research should include TBI patients who have been fed parenterally as well as enterally, in order to compare between both methods. This could be accomplished by extending the period of patient tracking and the sample size. This will be essential for developing an evidence based protocol to improve nutritional status in TBI patients.

The time of feeding initiation average was 35.5 hours (0-96 hours), where zero indicates no initiation for feeding. There was only one patient who started EN after 96 hours of ICU admission. Time of feeding initiation was harmonious with SCCM /ASPEN, Canadian clinical practice guidelines, and Brain Trauma Foundation recommendations, all of which recommend initiating EN in the first 24 to 72 hours of admission (McClave et al., 2009; Heyland et al., 2003; Brain Trauma Foundation, 2007). Early feeding enhances immunity, reduces incidence of infections, protects visceral protein, enhances neurological recovery, and decreases mortality (Chiang et al., 2012). Chiang et al. (2012) found that providing EN within 48 hours increased the survival rate and GCS among TBI patients over the first 7 days of ICU care, and improved clinical outcomes 1 month after injury (Chiang et al., 2012). Dhandapani et al. (2012) found that delayed EN is associated with clinical markers of nutritional depletion.

In this study, patients did not receive the adequate amount of energy they needed based on the Faisy equation, or the amount of energy that was estimated by the dietitians. This was the case in many other studies. Kim, Shin, Shin, & Cho (2010) reported that 52.2% of 47 patients who were enterally fed experienced underfeeding. On the other hand, the adequacy of energy intake has been achieved in other studies after a period of time. Franzosi, Abrahao, & Loss

(2012) reported that adequacy of energy has been achieved on the 7th day of hospitalization and it was 84% of the estimated energy requirement. In an Indian study that included 258 patients admitted to the respiratory ICU, the calorie prescription increased from a median of 88.9% of the recommended value on day 1 to 114.4% on day 21 (Singh et al., 2009). In the same study, the calorie delivery took 28 days to increase from 55.1% to 92.0% of the recommended value (Singh et al., 2009). Roberts, Kennerly, Keane, & George (2003) found that only 28% of the patients, out of 50 patients, received 20-35 Kcal/Kg by day 3 of nutrition support, which was considered adequate in that study. In our study, adequacy of energy intake was found to be the highest in day 7, but it was only 18.5% of the required energy that was calculated using the Faisy equation.

The cause of not achieving the adequate energy in this study, based on the dietitians' estimation and prescription, could be related to frequent feeding interruptions that could not be assessed. Feedings were withheld a mean of 7 hours/day; 70% of the lost feeding time was related to ICU related factors, including scheduled surgeries and planned extubations (O'Leary-Kelley et al., 2005). High gastric residual volume, surgeries and procedures, airway management, tube displacement, routine nursing care, and hemodynamic instability are also common causes of feeding interruption (McClave et al., 1999.; De Jonghe et al., 2001; Passier et al., 2013; Peev et al., 2014).

According to McClave et al. (1999), patients experience feeding interruption for 19.6 - 32% of the total infusion time. As previously mentioned, Peev et al. (2014) found that patients who have experienced feeding interruption at least once have higher mean daily and cumulative caloric deficits, and have 3-fold higher risk of being underfed compared to patients who have not experienced any feeding interruption during ICU stay. It is estimated that about 26% of feeding interruptions episodes can be avoided, which can improve the feeding delivery (Peev et al.,

2014). In terms of GRV in particular, Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) (SCCM /ASPEN) recommend not holding EN with GRV < 500 ml in the absence of other signs of intolerance, such as vomiting, diarrhea, and bloating (McClave et al., 2009). This is not the case in practice. McClave et al. (1999) and Metheny et al. (2012) found that about 25% of nurses interrupt EN for GRV of less than or equal to 150ml. Unfortunately, causes of feeding interruption and total hours of feeding interruption could not be collected in this study due to the retrospective study design and a lack of documentation about GVR in the medical record. This leads us back to the importance of documenting nutritional variables that help clinicians to assess and evaluate every patient's nutritional status and evaluate their nutritional delivery.

Level of brain injury severity measured by Glasgow Coma Scale (GCS) at emergency room(ER) admission, severity of illness measured by the Acute Physiology, Age, and Chronic Health Evaluation (APACHEIII), daily health status measured by the Sequential Organ Failure Assessment (SOFA), patients' age, ICP were independent variables that were not found to affect the adequacy of energy intake in this study. To our knowledge, there are no studies yet published that test the relationship between all of these variables and the adequacy of energy intake; thus, we cannot compare our findings to others. Some studies have examined the relationship between limited sets of these variables and malnutrition. Foley et al. (2008) noted that TBI patients with low GCS (4-5) experienced greater REE than TBI patients with higher GCS (6-11). Based on that, it is expected that patients with lower GCS scores and more severe illness need more energy, so they are more likely to be inadequately fed and to develop malnutrition. Development of malnutrition among patients with poor GCS scores was documented in the Chiang et al. (2012) study as well. It was found that the GCS scores improved in patients who were receiving

EN and had a relatively high initial GCS score (GCS >5) (Chiang et al., 2012; Dhandapani et al., 2012).

In terms of severity of illness and malnutrition, Sungurtekin et al. (2008) found a significant increase in APACHE II and Simplified Acute Physiology Score II (SAPS II) scores among malnourished patients (N=47) compared to well nourished (N=77). Another study of 119 elderly patients found that APACHE II and SAPS II were higher among malnourished patients, but the differences were not significant (Atalay et al., 2008).

Although daily health status, ICP, and patients' age have not been discussed in the literature as factors affecting the adequacy of energy intake, they are factors which affect the nutritional requirements of patients, and ICU patients in particular considering the hypermetabolism and catabolism they experience. Nutritional needs differ from person to person and from disease to another. Young people definitely have nutritional requirements different from older people. Those who have deteriorated organ function and health status differ in nutritional requirements from those in good health. Patient age, daily health status, and ICP could be good indicators for the amount of energy the patients' need to avoid deterioration of nutritional status or development of malnutrition. More research about these variables would help health care providers to consider patient characteristics while prescribing their patients' nutritional support. Also, these factors could be part of evidence based nutritional protocol to improve nutritional status of TBI patients.

Baseline nutritional status of TBI patients has been assessed using clinically relevant parameters. A direct relationship has been found between some of the baseline nutritional status parameters (hemoglobin, albumin, and TLC) of TBI patients and these parameters on day 7. This relationship indicates that the nutritional status of TBI patients has deteriorated, supported by the

significant change in hemoglobin, albumin, and TLC levels over 7 days of ICU and hospital stay. In addition, the conceptual model of this study (Figure 1) posits that this change can be mediated by adequacy of energy intake. This indirect relationship has not been studied in this dissertation. Although the model failed to confirm any significant relationship between the adequacy of energy intake and any of the independent variables, future research with larger sample size, prospective design, and follow-up for longer period should explore these relationships.

Limitation and Strength

The retrospective design of the study restricted the direct collection of many anthropometric variables informative about nutritional status, such as patients' triceps skinfold thickness, mid-arm circumference, and mid-arm muscle circumference. Directly collected anthropomorphic data would have enhanced baseline nutritional status assessment. The retrospective design also precluded us from classifying patients' nutritional status using nutritional assessment and screening scales. However, we were able to expand the sample size of the study, and the variables that have been used to assess the baseline nutritional status were clinically relevant and easily obtainable by providers. Missing data all over the variables were a limitation as well. Many variables could not be collected from the patient's record because of unavailability such as GRV, total hours of feeding interruption and causes of feeding interruption; this limits the ability to understand causality. Due to the small sample size of this study, sample variability was increased and the statistical power was reduced. The study included patient data over 7 days of hospitalization, which is a relatively short period for TBI patients. This led to flattening of the data and inability to obtain significant results.

Recommendation

Longitudinal prospective studies, including larger sample sizes, are needed in order to detect the change in nutritional status among TBI patients using BMI, weight loss, and other anthropometric measurements. Future studies should be designed to include using nutritional screening and assessment tools that enable the researchers to classify patients' nutritional status at admission. Factors that affect adequacy of energy intake need to be expanded to include GRV and total time of feeding interruption. Also, factors affecting adequacy of energy intake such as severity of illness, daily health status, ICP and level of consciousness need to be repeated, since no previous research has been published evaluating these factors in TBI. Furthermore, the future aims should test the relationship between the baseline nutritional status and the length of ICU, hospital and rehabilitation center stay, and the length of ventilation days.

Conclusion

Malnutrition is an increasing problem in the ICU. Traumatic brain injury patients are not an exception due to hypermetabolism and hypercatabolism experienced after injury. Few studies have been done to assess the change in nutritional status in this cohort over early hospitalization, and multiple factors likely affect the deterioration of their nutritional status. The current study sought to track the change in nutritional status of TBI patients and explore the relationship between adequacy of energy intake and prescribed energy, daily health status, level of consciousness, ICP, severity of illness, and age. Although no significant change was found in weight and BMI, there were significant changes in hemoglobin, albumin, and TLC levels over the first 7 days of hospitalization. Furthermore, no significant relationship was found between adequacy of energy intake and any of the independent variables, but future research over longer period of time with a larger sample size may detect such relationships. Nutritional status of TBI

patients during their ICU stay and hospitalization period should be one of the collaborative treatment goals. Establishing a standardized nutritional protocol including prescription and delivery of nutrition is essential to meet the nutritional requirements of TBI patients during their treatment journey. Future research need to focus on the development of nutritional protocol that depends on the assessment of patients' nutritional status, and on the factors that affect the nutrition delivery.

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Appendices

Appendix A: Glasgow Coma Scale (GCS)

Glasgow Come Scale

Eye opening:	Spontaneous	=4
	To speech	=3
	To pain	=2
	None	=1
Verbal response:	Oriented	=5
	Confused	=4
	Inappropriate	=3
	Incomprehensible sounds	=2
	None	=1
Motor response:	Obeys	=6
	Localizing	=5
	Normal Flexion	=4
	Abnormal Flexion (decorticate)	=3
	Extension (decerebrate)	=2
	None	=1

Total =15



(Jennett et al., 1977)

Appendix B: GCS Use Permission

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