Assessing the Nutritional Status and Adequacy of Energy and Protein Intakes of Children Admitted to the Pediatric Intensive Care Unit

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ABSTRACT

Children admitted to the pediatric intensive care unit (PICU) are at high risk of malnutrition due to the stress of critical illness, and challenges with meeting nutrient needs. The objectives of this study were to describe the prevalence of malnutrition (undernutrition) at admission and discharge from the PICU and the adequacy of dietary intakes during PICU stay according to current practice guidelines. Sixty patients (median age 1.8y) were enrolled. Malnutrition (moderate-severe) was identified in 12% of patients at admission and 15% at discharge using weight-for-length and BMI-for-age z scores. Mid-upper arm circumference z score declined significantly (p=0.002) during PICU stay. Median (IQR) delivery of enteral energy and protein during the first 10 days was 64 (50-73)% and 62 (40-82)%, respectively, of prescribed goal. A total of 174 feeding interruptions were noted in 36 enterally fed patients. Malnutrition was present in the PICU and areas for improvement in nutrient delivery were identified.

Les enfants admis à l'unité de soins intensifs pédiatriques (USIP) sont à risque élevé de malnutrition en raison du stress métabolique causé par une maladie grave et des difficultés à répondre aux besoins en nutriments. Les objectifs de l'étude étaient de décrire la prévalence de la malnutrition (dénutrition) à l'admission et à la sortie de l'USIP et décrire l'apport alimentaire pendant le séjour à l'USIP, conformément aux lignes directrices actuelles de pratique. Soixante patients (âge médian 1.8) ont participé à cette étude. La malnutrition (modérée à sévère) a été identifiée chez 12% des patients à l'admission et 15% à la sortie en utilisant les scores z du poids pour la longueur et de l'IMC pour l'âge. Le score z de la circonférence médio-supérieure du bras a diminué de manière significative (p = 0,002) pendant le séjour à l'USIP. L'apport médian (IQR) en énergie et protéine sous forme de nutrition entérale au cours des 10 premiers jours était respectivement de 64 (50-73)% et 62 (40-82)% de l'objectif prescrit. Un total de 174 interruptions d'alimentation ont été notées chez 36 patients nourris par voie entérale. La malnutrition était présente dans l'USIP et des aspects à améliorer pour augmenter l'apport nutritionnel ont été identifiés.

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List of Abbreviations

Abx: Antibiotics

AND: Academy of Nutrition and Dietetics

ASPEN: American Society for Parenteral and Enteral Nutrition

BMI: Body mass index

BMIA: Body mass index for age/ BMI-for-age

CDC: Center for Disease Control and Prevention

CHEO: Children's Hospital of Eastern Ontario

CI: Confidence Interval

CPEG: Canadian Pediatric Endocrine Group

EN: Enteral Nutrition

HGS: Handgrip strength

ICU: Intensive Care Unit

IQR: Interquartile Range

LFA: Length-for-age

LOS: Length of stay

MUAC: Mid-upper arm circumference

OR: Odds Ratio

PELOD: Pediatric Logistic Organ Dysfunction

PICU: Pediatric Intensive Care Unit

PN: Parenteral Nutrition

PRISM: Pediatric Risk of Mortality

SCCM: Society of Critical Care Medicine

SD: Standard Deviation

SPSS: Statistical Package for Social Sciences

US: United-States

WFA: Weight-for-age

WFL: Weight-for-length

WHO: World Health Organization

CHAPTER I: INTRODUCTION

Every year, over 240,000 patients are admitted to intensive care units in Canada, approximately 10,000 of these patients being children and adolescents (CIHI, 2016). Patients who suffer from critical illness will present with metabolic stress which can have deleterious effects on their overall health (Nelms, Sucher, & Lacey, 2016; Preiser, et al., 2014). The metabolic response to critical illness involves multiple mechanisms with primary goal of mobilizing nutrients to respond to the increased demand in energy (Nelms et al., 2016). This metabolic adaptation may eventually lead to a loss of lean muscle mass and hospital-acquired weakness (Hill, 1992; Pichard et al., 2004). Achieving adequate delivery of nutrients is essential to prevent the loss of lean muscle mass. This is especially important in children as they have both higher energy demand for growth and limited energy reserves which puts them at higher risk for malnutrition (Joosten & Hulst, 2011; Mehta & Duggan, 2009).

In 2015 and 2017, new guidelines were published for the identification of malnutrition in the pediatric population (Becker et al., 2015) and for the provision of nutrition support in the pediatric intensive care unit (PICU) (Mehta et al., 2017). These guidelines state the importance of a full nutrition assessment upon admission to the PICU to identify the presence of malnutrition. In addition, they also state the importance of accurately estimating energy and protein requirements and optimizing intakes (Becker et al., 2015; Mehta et al., 2017). In past studies, malnutrition has been associated with increased dependency of mechanical ventilation, increased risk of infection, longer length of PICU stay and longer length of hospital stay (Daskalou, et al., 2016; de Souza Menezes, et al., 2012). There is currently a lack of data on the prevalence of malnutrition and how nutritional status evolve in Canadian PICUs as well as the possible associations with malnutrition

and adverse outcomes. Furthermore, additional research is needed to describe the current feeding practices in the pediatric intensive care unit, looking into the adequacy of feeding over the course of PICU stay.

This study aims to examine the prevalence of malnutrition at admission and discharge from a Canadian PICU, as well as describe the adequacy of energy and protein intakes in a population of critically ill pediatric patients.

CHAPTER II: LITERATURE REVIEW

2.1 CRITICAL ILLNESS AND ITS METABOLIC IMPLICATIONS

2.1.1 Defining Critical Illness

Patients who have sustained life threatening, single or multi-organ system failure due to disease or injury (Canadian Medical Association, 2018), are likely to be admitted to an intensive care unit (ICU). ICUs are staffed with multidisciplinary care teams that "seek to provide for the needs of these patients through immediate and continuous observation and intervention in order to restore health and prevent complications" (Canadian Medical Association, 2018:3). In Canada, there is a total of 286 hospitals with 3170 ICU beds and 4982 mechanical ventilators available for the care of critically ill patients (Fowler et al., 2015). Of all acute care hospitals (n=286) in Canada, 22 (7.7%) have an ICU that routinely cares for children and 15 (5.2%) hospitals have dedicated pediatric ICUs (Fowler et al., 2015). Furthermore, among hospitals capable of providing invasive mechanical ventilation there is an average of nine ICU beds per hospital (interquartile range 5-18) (Fowler et al. 2015). Four types of intensive care units exist in Canada including, general ICUs, specialized ICUs (for burn, cardiac, neurosurgery, trauma, and respirology patients), as well as pediatric and neonatal ICUs (CIHI, 2016). According to research conducted by the Canadian Institute for Health Information (CIHI), in 2013-2014, the 10 most common reasons for being admitted in a general ICU were myocardial infarction/ shock/cardiac arrest, arrhythmia, heart failure, chronic obstructive pulmonary disease, sepsis, poisoning/toxic effect of drug, respiratory failure, unstable angina/arteriosclerotic heart disease, other cardiac disorders and diabetes (CIHI, 2016). On the other hand, when looking at pediatric admissions to the ICU an Australian study found that the main reasons for being admitted were respiratory illnesses, congenital anomalies, neurological disorders, injuries, neoplasms, endocrine/metabolic diseases, circulatory system

disorders, infections, musculoskeletal disorders, and chronic disease conditions (Ibiebele, Algert, Bowen, & Roberts, 2018). In 2013-2014, over 230 800 adults were admitted to an ICU in Canada, with 80% of these admissions resulting from urgent hospital admissions, representing a 12% increase in ICU admissions compared to 2007-2008 (CIHI, 2016).

In 2018, total health expenditure was expected to reach $253.5 billion, which is approximately $6,839 per person (CIHI, 2018). ICUs represent a costly resource due to higher staff-to-patient ratios for intensive monitoring and complex treatment. Therefore, ICU beds tend to be consistently more expensive than general ward beds. For instance, the average cost per bed per day in an ICU was $3,592 compared to $1,135 on a general ward (CIHI, 2016).

An intensive care unit is an environment filled with challenges that requires multiple resources to care for critically ill patients. These resources include, ventilators, heart monitors, increased imaging, and sample analysis, increased medication and increased need for nutrition support which are all supported by the interdisciplinary health team in the ICU. In order to appropriately care for these patients, it is also very important to consider metabolic changes in response to the stress of critical illness. As mentioned by Mehta and Duggan in their article *Nutritional Deficiencies during Critical Illness*:

> *The caloric burden imposed by the metabolic response to injury, surgery or inflammation may be proportional to the severity and duration of the stress but cannot be accurately estimated. Nutritional support cannot reverse or prevent the metabolic stress response. However, failure to provide optimal calories and protein during the acute stage of illness could result in exaggeration of existing nutritional deficiencies or result in new onset malnutrition (Mehta & Duggan, 2009 :2)*

2.1.2 Metabolic Implications of Critical Illness

The knowledge and understanding of the metabolic response to critical illness has changed in last decades compared to how it was previously appreciated in the 19th and 20th century (Cuesta & Singer, 2012). David Cuthbertson is considered a scientific pioneer in regard to the metabolic response to critical illness. He described the metabolic changes occurring in patients following a major trauma as the increased utilization of body protein recognized that the body uses protein from lean tissue when under traumatic stress (Cuesta & Singer, 2012). Indeed, he described the response to critical illness as the Ebb phase and the Flow phase (Cuthbertson, 1942; Cuthbertson, 1982). The Ebb phase which occurs immediately after injury, starts with a decrease in metabolic activity, subnormal oxygen consumption and body temperature, increases in blood glucose, sodium retention, and tissue edema related to increased vascular permeability (Mahan, Escott-Stump, & Raymond, 2012). The flow phase, on the other hand, comprises an acute phase and an adaptive phase and is characterized by increased cardiac output, oxygen consumption, body temperature, energy expenditure and total body protein catabolism (Mahan et al., 2012). In his studies, Cuthbertson described the flow phase as starting 3 to 10 days after trauma and lasting until the patient begins to heal, with metabolism returning to the anabolic state (Cuthbertson, 1942; Cuthbertson, 1982; Cuthbertson & Zagreb, 1979).

During critical illness, multiple metabolic adaptations occur with the primary goal of mobilizing nutrients in response to the increased and immediate demand for energy (Nelms, Sucher, & Lacey, 2016). In response to the energy demand, there is activation of various hormones including, glucagon, cortisol, epinephrine and norepinephrine which are all considered catabolic hormones (Rolfes, Pinna, & Whitney, 2009). In the early phase of critical illness, oxidation of glucose is increased following the increased breakdown of glycogen (glycogenolysis) as a result of the

secretion of epinephrine and glucagon, increasing the production of renal and hepatic glucose (Cartwright, 2004; Marik & Bellomo, 2013). Cortisol is also involved in the altered substrate utilization by increasing free fatty acid mobilization (lipolysis) and increasing protein catabolism. Therefore, the increased concentration of amino acids leads to the increase of protein synthesis that act as inflammatory response mediators that are used for tissue repair, and conversion of amino acids to glucose in the liver (gluconeogenesis) (Nelms et al., 2016; Rolfes et al., 2009). Thus, the combined effects of these hormones cause hyperglycemia which often accompanies critical illness. Insulin resistance contributes to stress hyperglycemia and may be an adaptive response to increase glucose uptake in non-insulin dependent vital organs unable to use other substrates in stress conditions (Preiser, Ichai, Orban, & Groeneveld, 2014). Furthermore, during critical illness gluconeogenesis persists despite hyperglycemia and dietary glucose intake because of continuous release of glucagon, cortisol and pro-inflammatory cytokines, therefore, interfering with the release of insulin and its action. (Cartwright, 2004). In addition, the response to stress is also regulated by cytokines (pro-inflammatory proteins) such as interleukine-1 (IL-1), IL-6, tumor necrosis factor alpha (TNF-a) and interferons (Mahan et al., 2012; Nelms et al., 2016). These cytokines have different metabolic effects such as increasing catabolism, activating and releasing cellular mediators, thereby increasing acute-phase protein synthesis causing hypermetabolism, fever, and damage to respiratory monocytes (Marik & Flemmer, 2012; Nelms et al., 2016).

2.1.3 Nutrient Utilization during Critical Illness

Under normal conditions, substrate utilisation is determined by diet composition and time since last meal. In critically ill individuals, substrate utilisation is determined by the endogenous stores (glycogen, fat, amino acids) which become depleted following various processes as described above. For instance, as glycogen stores are depleted, free fatty acids and proteins are used as energy

substrates. Under hypermetabolic conditions, lipolysis is unable to provide adequate energy substrate due to the high oxygen demand to convert lipids into ATP, and mitochondrial dysfunction that is common during the early phase of critical illness (Tappy et al., 1998). As a result, muscle protein is broken down allowing amino acids to be used for wound healing, immune defense and hepatic gluconeogenesis (Cartwright, 2004). Furthermore, substrate utilization varies depending on which phase of critical illness the patient is in (ebb or flow). Indeed, the oxidation of carbohydrates is increased during the early phase of critical illness (ebb) over the oxidation of lipids and proteins (Tappy et al., 1998). Later on, during the flow phase, with the depletion of glycogen stores, the body will experience a decrease in glucose utilization, an increase in lipolysis, and loss of lean body mass through increased protein catabolism (Tappy et al., 1998). Under these conditions, having the appropriate nutrition support is essential in order to maintain muscle mass and avoid nutritional deficiencies (Mehta & Duggan, 2009).

2.1.4 Clinical manifestations during Critical Illness

When a patient is in a critical state, it is highly likely that there will be a negative impact on lean muscle mass and gut microbiota due to the metabolic alterations mentioned above. Muscle loss is one of the major consequences of metabolic stress during critical illness (Valla et al., 2017). Studies of body composition have shown that patients under metabolic stress can lose up to 5% or 750-1000g of lean body mass every day causing a rapid depletion of muscle mass and increased muscle weakness (Hill, 1992; Pichard et al., 2004). Indeed, the loss of muscle mass due to critical illness may be followed by multiple negative consequences. For instance, a 10% loss of lean muscle mass may be associated with impaired immunity and increased infections; a 20% loss may be associated with decreased wound healing, weakness and increased infections; 30% loss may cause increased weakness which manifests as not being able to sit, development of pressure sores,

pneumonia, and cessation of healing; a 40% loss of lean muscle mass may result in death mainly from pneumonia (Nelms et al., 2016). Furthermore, when nutrient intake is inadequate and there is depletion of energy stores, leading to loss of lean muscle mass, there is also reduction in respiratory muscle weakness due to an altered strength and endurance of muscle contraction (Benotti, & Bistrian, 1989). Respiratory muscle weakness may prolong respiratory failure in patients and increase the length of time required for mechanical ventilation (de Souza Menezes, Leite, & Koch Nogueira, 2012), which may ultimately lead to a longer length of hospital stay (de Souza Menezes et al., 2012; Grippa et al., 2017).

In addition, critical illness may also affect gut health by causing a near ecological collapse, where more than 90% of the protective commensal bacteria are lost within the first 6h of onset of critical illness (McClave, Lowen, & Martindale, 2017). The loss of commensal bacteria leads to the loss of cytoprotective exoproducts of short chain fatty acids, and to low biodiversity, which promotes resistance to multiple antibiotics, the emergence of pathogens and complications from secondary infections (McClave et al., 2017). Therefore, achieving adequate delivery of macronutrients is essential under these conditions, in order to prevent a negative nitrogen balance, thus preventing the loss of lean muscle mass and to prevent the loss of commensal bacteria. This is especially important in the pediatric population as children have both a higher energy demand per unit of body mass in view of growth, and limited energy reserves which puts them at a particularly high risk for malnutrition (Joosten & Hulst, 2008; Mehta & Duggan, 2009).

2.2 PEDIATRIC MALNUTRITION IN HOSPITALS

2.2.1 Defining Pediatric Malnutrition

The *American Society of Enteral and Parenteral Nutrition* (ASPEN) defines pediatric malnutrition (undernutrition) as "a state of imbalance between the intake and the requirements of nutrients which results in cumulative deficits of energy, protein, or micronutrients that may negatively affect growth, development and other relevant outcomes'' (Mehta et al., 2013:19). Malnutrition may be non-illness related such as with behavior, unfavorable environment or socioeconomic status or may be illness related (Mehta et al., 2013). When malnutrition is acquired in the hospital (hospital-acquired malnutrition) or illness related it may result from a loss of nutrients (caused by malabsorption or exudate), increased energy expenditure, decreased nutrient intake or an altered utilization of nutrients (Mehta et al., 2013). These factors are frequently seen in acute illnesses such as traumas, burns, and infections, and can also be seen in chronic diseases such as cystic fibrosis, chronic renal failure, congenital heart failure, gastrointestinal diseases and neuromuscular diseases (Mehta et al., 2013). Malnutrition is often the term used to define undernutrition; however, children can be considered malnourished if they are overnourished (i.e. consume too much energy)[1]. Furthermore, malnutrition is characterized as being acute or chronic, depending on the duration. Acute malnutrition usually lasts less than 3 months and is identified as a decreased weight-for-height ratio which will manifest as lean body mass depletion (Mehta et al., 2013). On the other hand, chronic malnutrition, either moderate or severe, usually lasts for more than 3 months and is identified as a decreased height-for-age, also known as stunting. Moderate chronic malnutrition impacts cognitive development and severe chronic malnutrition also causes immune dysfunctions (Mehta et al., 2013).

[1] For the purpose of this review, malnutrition will refer to undernutrition unless otherwise specified

2.2.2 Indicators of Pediatric Malnutrition (Undernutrition)

In 2015, the Academy of Nutrition and Dietetics (AND) and ASPEN (AND-ASPEN) published the recommended indicators for identifying and diagnosing pediatric malnutrition (Becker et al., 2015). According to AND-ASPEN, these indicators should be "evidence informed, universally available and validated, be applied inexpensively in multiple settings, be properly used with minimal training, be able to reproducibly identify undernutrition, be able to quantify the severity of undernutrition, and be used to monitor changes in nutritional status" (Becker et al., 2015:149). These indicators were put in place as a standardized approach to identify and diagnose pediatric undernutrition was missing, especially in children older than 60 months (Becker et al., 2015). There is currently controversy around what would be the best approach to use in this population. In hospitals, if there is no prior screening in place, assessment of nutritional status is usually preceded by a referral from the attending physician to the dietitian. Therefore, children at risk for malnutrition may be overlooked, given that nutritional assessments tend to be sporadic, and the degree to which dietitians are consulted varies from one institution to another. As discussed in the review by Bouma (2017): "Malnutrition must be identified before it can be addressed. A uniform set of indicators allows for children to be diagnosed with pediatric malnutrition, to receive the intervention that they need to optimize nutrition in the setting of their current medical therapy, and to continue to achieve growth once the medical condition has resolved or is under control" (Bouma, 2017: 32). Therefore, based on the latest evidence, the consensus statement recommends that clinicians assess all indicators, however, only 1 indicator is needed to diagnose pediatric malnutrition. The recommended indicators include Food/Nutrient intake, Assessment of Energy and Protein Needs, Growth Parameters, Weight Gain Velocity, Mid-Upper Arm Circumference, and Handgrip Strength.

Food/Nutrient Intake

During hospitalization, it is of great importance that children maintain an adequate intake of food and nutrients in order to prevent the deterioration of their nutritional status. Measuring the actual intake of energy and protein in order to verify if needs are met should be regularly performed for all patients especially those at high risk for malnutrition (Becker et al., 2015). Evaluating the adequacy of dietary intake can be done by obtaining history or direct observation of food and nutrients consumed. It is also essential to verify that the energy and protein requirements calculated by the dietitian are met when patient needs nutritional support to prevent further deterioration of nutritional status.

Assessment of Energy and Protein Requirements

Indirect calorimetry or standard predictive equations can be used to estimate energy requirements. Although both of these methods provide an estimation of energy requirements, indirect calorimetry (IC) is preferred over predictive equations to estimate the child's actual energy requirements and guide the prescription of daily energy goals. As discussed in clinical guidelines "Energy expenditure measured by IC for critically ill children is independent of nutritional status, initial diagnosis, or severity of the acute illness" (Mehta et al., 2017). When indirect calorimetry is not feasible or unavailable, there is a variety of predictive equations that can be used. For hospitalized patients, AND-APSEN recommends using The Food and Agriculture Organization and The World Health Organization (FAO/WHO) or the Schofield predictive equations (Becker et al., 2015; Mehta et al., 2017). Although these equations are imprecise, they are the most commonly used equations to estimate energy requirements in healthy and hospitalized children (Becker et al., 2015).

Protein requirements are usually estimated using the Dietary Reference Intake (DRI) for protein in both healthy and hospitalized children. The child's clinical condition should be considered when estimating protein needs as some situations may warrant a greater protein intake (i.e. critical illness, wound healing, infection) while other situations might warrant a lower protein intake (i.e. acute renal failure) (Becker et al., 2015; Mehta et al., 2017). Health Canada (DRIs) recommends between 0.8-1.0 g/kg/day of protein in healthy children from 6mo – 18yo (Canada, 2006.). However, randomized controlled trials and observational studies of protein supplementation in critically ill children have shown that these requirements can reach up to 2.0-3.0g/kg/day to account for increased energy expenditure and prevent the loss of lean body mass (Mehta et al., 2017).

Growth Parameters

Growth is the primary outcome parameter when assessing the nutritional status of children. It is recommended by WHO and the Dietitians of Canada to monitor growth at regular intervals throughout childhood and adolescence, and every time a child is admitted to a healthcare setting (Becker et al., 2015). Anthropometric measurements (weight, height/length, head circumference) are usually compared to a population standard to evaluate the adequacy of growth. When the child's growth is being monitored, timely intervention may be put in place to reverse the deficit and bring the child back to the appropriate growth trajectory (Dietitians of Canada & Canadian Paediatric Society, 2010). Traditionally, the anthropometric measurements were plotted and compared using percentiles, the 50^{th} percentile being the median growth trajectory of the population. These specific growth charts are useful in identifying if a child is growing adequately and following a specific growth curve (using the percentiles), however these growth charts do not depict with precision how far away the data point is, in standard deviations (SD), from the median. The WHO recommends the use of z scores for describing anthropometric measures, especially in

groups as z scores are more precise in describing anthropometrics than the percentile on a standard growth curve (de Onis & Blössner, 1997). Z scores can be used to assess weight-for-age, weight-for-height, height-for-age and BMI-for-age (Mehta et al., 2013). Concisely, "a z score is a statistical measure that tells how a single data point compares with normal data and, if above or below "average", how atypical the measurement is" (Becker et al., 2015:30). Percentiles are usually used in the clinical or community setting to clearly indicate the child's position within the reference population, while z scores are more commonly used in population-based applications and research reporting (Dietitians of Canada & Canadian Paediatric Society, 2010). Furthermore, a child who is developing and growing normally will be on or between -1 and 1 z scores for a given indicator (Dietitians of Canada & Canadian Paediatric Society, 2010). In March 2014, the first revised set of the WHO growth charts for Canada was released, and the second set was released in September the same year. Both sets of growth charts released in 2014 continue to stay in line with the recommendations from the Collaborative statement published in 2010 by the Dietitians of Canada where it is recommended to use the same growth charts nationally while assessing growth. The WHO growth charts "represent the best description of physiological growth for children from birth to five years of age. They embody optimal growth and, as such, depict the rate of growth that should serve as a goal or prescription for all healthy Canadian infants and children to achieve, regardless of ethnicity" (Dietitians of Canada & Canadian Paediatric Society, 2010:7). It is for that reason the Canadian Pediatric Endocrine Group (CPEG) endorsed the 2014 revisions and archived the CPEG growth charts (« WHO Growth Charts for Canada | Canadian Pediatric Endocrine Group », s. d.).

Weight gain Velocity

Growth can be defined as undergoing natural development by increasing in size and changing physically and progressing to maturity (Oxford Dictionaries, s. d.-a). Velocity on the other hand is defined as the speed of something in a given direction (Oxford Dictionaries, s. d.-b). Therefore, growth velocity is the rate at which weight or height/length is changing over time. A regression or stagnation of the growth velocity is an early indicator of the deterioration of the nutritional status (Becker et al., 2015). When food and nutrient intake is adequate, the average daily/monthly rates of weight gain are sufficient to maintain the child on the growth curve. The rate of growth will vary depending on the age of the child and the period of development (Becker et al., 2015). The WHO has guidelines available for the assessment of weight gain velocity that can be used in children from birth to 24 months (« WHO | Weight velocity », s. d.).

Mid-Upper Arm Circumference

Mid-upper arm circumference (MUAC) is an indicator of muscle and subcutaneous adipose tissue and is an accepted measure of nutritional status (Lee & Nieman, 2013). Therefore, MUAC should be measured when assessing the nutritional status of patients as recommended by AND-ASPEN guidelines (Becker et al., 2015; Mehta et al., 2013). This measurement was also shown to be useful in patients with fluid shifts such as edema in the lower extremities, ascites or in patients receiving steroids, as MUAC is less affected by fluid status or hydration (Green Corkins & Teague, 2017) and under these conditions, may be a more sensitive indicator than weight-for-height for classification of acute malnutrition and prediction of mortality (Mehta et al., 2013). In these situations, weight trends alone are not accurate indicators for malnutrition in relation to fluid status. MUAC also correlates with body mass index (BMI) in children, which is a numerical value of a person's weight in relation to their height (Stephens et al., 2018). In children and teenagers, BMI

is age and sex specific and is often referred to as BMI-for-age (CDC, 2018). After calculating BMI, it is expressed as a percentile and assessed in the following manor: underweight (< 5^{th} percentile), healthy weight (5^{th} to < 85^{th} percentile), overweight (85^{th} to < 95^{th}), and obese (≥ 95^{th} percentile) (CDC, 2018). Following the WHO Multicenter Growth Reference Study from 1997 to 2003 (« WHO | The WHO Multicentre Growth Reference Study (MGRS) », s. d.), growth standards for MUAC were developed with the release of new international growth charts. There are currently MUAC standards that can be found through the WHO for children aged 3-60 months (« WHO | Arm circumference-for-age », s. d.). In the United-States, the Center for Disease Control (CDC) uses the 1999-2012 CDC Child Growth Standards for mid-upper arm circumference-for-age, to report percentiles and z-scores on children from 2 months to 18 years of age (Abdel-Rahman, Bi, & Thaete, 2017).

Skinfold thicknesses are measurements that are used to determine body fat stores. These measurements are often used in a research setting and may also be useful in determining the nutritional status (Green Corkins & Teague, 2017). References range for triceps and subscapular skinfolds for children aged 1.5-19 years have been published by Addo and Himes (2010) and used by the CDC. These reference ranges can be used to assess a child's nutrition status in relation to the percentiles on a growth curve (Addo & Himes, 2010). Skinfolds, especially triceps skinfold, are better used in combination with other measurements like the MUAC, than as a sole indicator of nutrition status. As fat stores change during growth and development, the usefulness of these measurements is often debated in pediatric populations (Green Corkins & Teague, 2017).

Handgrip strength

Handgrip strength (HGS) is a simple non-invasive measurement that is commonly used to test muscle function and track progress throughout hospitalization. HGS is measured using a handheld dynamometer where patients apply maximal pressure on the instrument. Handgrip strength has been shown to predict post-operative complications, length of hospital stay, readmission and mortality in patients aged 16-95 years old (Webb, Newman, Taylor, & Keogh, 1989). Muscle function reacts earlier to changes in nutritional status than muscle mass and can therefore be used as a measurement to evaluate the response to nutritional interventions in children ages 6 and older (Secker & Jeejeebhoy, 2007). In the previously sited study by Secker and JeeJeebhoy, handgrip strength correlated with BMI z scores independent of gender, age, disease severity or anthropometric characteristics (Secker & Jeejeebhoy, 2007). In pediatric populations, handgrip strength has been proven feasible and reliable when used in children 6 years and older as these children are more likely able to follow instructions and perform the test adequately. Normal reference ranges for large populations have not yet been established and therefore the use of the appropriate reference range provided with the dynamometer is warranted (Becker et al., 2015).

2.2.3 Malnutrition risk screening tool

To evaluate malnutrition in children, nutritional screening followed by a complete nutritional assessment is performed on children deemed at nutritional risk. It is important to understand that being at risk of malnutrition and being malnourished is not the same, as a patient at risk of malnutrition will not necessarily become malnourished over the course of a hospital stay. Nutrition screening is performed to identify patients who are at risk for malnutrition and is a tool that is quick and easy to use by all healthcare professionals during the admission process of the patient. A nutritional assessment is a more thorough evaluation of the nutritional status and is able to

establish the presence of malnutrition and the degree as low, moderate or severe (McCarthy, Dixon, Crabtree, Eaton-Evans, & McNulty, 2012). Pediatric nutritional screening tools to identify patients at risk of malnutrition have been developed for non-ICU patients over the past few years and include the Screening Tool for the Assessment of Malnutrition in Peadiatrics (STAMP), the Screening Tool for Risk on Nutritional Status and Growth (STRONGkids), Paediatric Yorkhill Malnutrition Score (PYMS), Nutritional Risk Score (NRS), the Pediatric Nutrition Screening Tool (PNST), and the Subjective Global Nutrition Assessment for Children (SGNA). When a patient is identified as at risk for malnutrition with a screening tool, there seems to be a positive association with length of hospital stay and rate of infection (Hulst, et al., 2010; Huysentruyt et al., 2015; McCarthy, et al., 2012; Secker & Jeejeebhoy, 2007). Furthermore, there is currently no ‘’Gold Standard’’ among these pediatric nutrition screening tools as there is insufficient evidence to choose one tool over another based on their predictive accuracy (Huysentruyt et al., 2015). The Canadian Malnutrition Task Force (CMTF) established a Pediatric Working Group in spring of 2018 that will be working on the detection, prevention and treatment of malnutrition with a particular focus on in-patient populations (CMTF, n/a).

2.2.4 Prevalence of malnutrition in the general hospital setting

In the general pediatric hospital setting, there are numerous studies that have been conducted internationally to estimate the prevalence of malnutrition, however, rarely has it been done nationally. Three Canadian studies were identified to have evaluated the prevalence of malnutrition in a general hospital setting. A multicenter study that included hospitals from 5 Canadian provinces (Alberta, Nova-scotia, Ontario, Quebec, Vancouver), evaluated the prevalence of malnutrition as well as the deterioration in nutrition status in patients aged 1 month to 18 years of age admitted to a medical, surgical, or oncology wards (Bélanger et al., 2019). Both the $STRONG_{kids}$ and SGNA

screening tools were applied at admission and malnutrition was defined as weight-for-age, height-for-age, BMI-for-age, or weight-for-height/length z-score <-2 SD. The results of this study showed that 19.5% of children were malnourished upon admission and that half of the children lost weight during hospital stay (Bélanger et al., 2019). In a second Canadian study conducted in a tertiary-care pediatric teaching-hospital, which evaluated the prevalence of malnutrition at admission while excluding critically ill patients, it was estimated that in children aged from 1 month to 18 years there was a malnutrition prevalence of 8.8% when using BMI-for-age (<-2 SD) (Baxter et al., 2014). However, a different prevalence estimate was found when using weight-for-age, weight-for-length, and height-for-age as the malnutrition identification criteria, identifying 6.9% of children as acutely malnourished and 13.4% as chronically malnourished (Baxter et al., 2014). The third identified Canadian study conducted in a general pediatric unit using a pediatric nutritional risk score, found the prevalence of malnutrition in children from 0 months to 18 years to be at 11% and 6.3% for acute and chronic malnutrition respectively (Groleau et al., 2014). In different countries around the world, such as Australia, Brazil, France, Germany, Holland, The Netherlands, Turkey, the UK, and USA the prevalence of acute malnutrition has been estimated between 1.9% to 48.6% in children aged 0-18 years (Daskalou, Galli-Tsinopoulou, Karagiozoglou-Lampoudi, & Augoustides-Savvopoulou, 2016; Groleau et al., 2014). The wide variation in the prevalence of malnutrition seems to be due to the inconsistency in the criteria used to define malnutrition in this population and the different countries in which the studies were conducted as socioeconomic conditions vary from one country to another which might affect nutritional status.

2.3.0 Pediatric Malnutrition During Critical Illness

2.3.1 Nutritional assessment in the intensive care unit

Maintaining an adequate nutritional status while suffering from a critical illness is of great importance in order to recover promptly by reducing the loss of lean muscle mass, reducing the rate of infections, and reducing the length of hospital stay. In July 2017, The American Society for Parenteral and Enteral Nutrition (ASPEN) and the Society of Critical Care Medicine (SCCM) (SCCM-ASPEN) published *The Guidelines for the provision and assessment of nutrition support therapy in the pediatric critically ill patient* (Mehta et al., 2017). These guidelines reiterate the importance of nutrition assessment particularly in the detection of the malnourished patients as timely intervention is important in their recovery. The recommendations in these guidelines encompass a detailed nutritional assessment of all patients within 48h of admissions to the PICU including measurement of height/length and weight and that BMI z score be used for patients at extreme values (Mehta et al., 2017). Unfortunately, the measurement of height/length and weight within the first 48 h of PICU admission is often lacking as there can be many perceived barriers to obtaining anthropometric measurements (Irving et al., 2015). The results from an international survey on perceived barriers to anthropometric measurements in critically ill children, completed by ordering providers (n=119) and nurses (n=139), showed that the most commonly perceived patient-specific barriers were presence of medical devices (57%), need for extracorporeal life support (54%), and unstable hemodynamic status (52%) (Irving et al., 2015). Furthermore, although 84% of the respondents agreed that anthropometric measurements were important, only 3% indicated that measurements were always obtained during patient's admission to PICU (Irving et al., 2015). In 2004, an Australian study conducted in a tertiary pediatric hospital showed that 12% of patients did not have a weight measured, 73% had no height/length recorded and 12% had

neither (O'Connor, Youde, Allen, Hanson, & Baur, 2004). As children are at risk for rapid deterioration while in the PICU, a uniform approach to defining pediatric malnutrition may allow for more timely interventions aimed at reducing the rate of nutrition deterioration (Mehta et al., 2017).

As previously mentioned, there is currently no "Gold standard" in regard to nutritional screening tools to be used in the general hospital setting. There is also no consensus as to which tool could be used in the pediatric intensive care unit as these malnutrition screening tools have not been validated with critically ill children. In 2013, Vermilyea et al. conducted a study in the PICU of a Wisconsin hospital using the SGNA to compare the rate of malnutrition with commonly used objective anthropometric and laboratory measurements in 150 children aged 31 days to 5 years. This study showed that the ratings (well-nourished, moderately malnourished, severely malnourished) of the SGNA had a moderate to strong correlation with standard anthropometric measurements such as, mid upper arm circumference (MUAC), weight, length, weight-for-height, triceps skinfold (TSF), and percent ideal body weight (IBW). However, the SGNA could not predict the outcome for LOS, rate of infection and mortality as there were no significant associations between SGNA rating and outcome across the three different groups (Vermilyea et al., 2013). This was the first study to evaluate the use of a subjective nutritional assessment method for use in critically ill children. These results question the usefulness or utility of the SGNA for a nutritional assessment with the critically ill children and therefore, there is currently no consensus as to which tool could be used in the pediatric intensive care unit as no other malnutrition screening tool has been validated with critically ill children. Therefore, SCCM-ASPEN recommends a nutritional assessment to identify malnourished patients, which includes a dietary history, detection of changes in anthropometry, measurement of functional status, and a nutrition-focused

physical examination of all critically ill infants and children (Mehta et al., 2017).

2.3.2 Prevalence of malnutrition in the pediatric intensive care unit

ASPEN and SCCM acknowledge the fact that high-level evidence for nutrition practices in the PICU environment is scarce (Mehta et al., 2017). Few studies have looked at the prevalence of malnutrition in the pediatric intensive care unit, and of these only two studies were found to include a Canadian population. One study included 1622 mechanically ventilated patients, aged 1 month to 18 years, from 6 different country/regions (90 patients from Canada). The aim of this study was to determine the influence of admission nutritional status on clinical outcomes in mechanically ventilated children (Bechard et al., 2016). Nutritional status was defined using admission BMI z scores where patients were classified as underweight (BMI z score <-2), normal weight (BMI z score ≥-2 and ≤1), overweight (BMI z score >1 and ≤2), or obese (BMI z score 2). Two hundred ninety-one patients (18%) were found to be underweight at admission to the PICU, 235 (15%) were overweight, 217 (13%) were obese and 879 (54%) were of normal weight (Bechard et al., 2016). In 2009, a study conducted in Montreal aimed to assess the nutritional status of mechanically ventilated children upon admission and to evaluate the prescribed and delivered calories from nutrition support during PICU stay (Bockenkamp, Jouvet, Arsenault, et al, 2009). This study included 49 patients aged 0-17 years with a length of stay of more than 3 days who were mechanically ventilated. Nutritional status was defined as a weight-for-age z score of -2 or lower. Ten patients (20%) were found to be moderately or severely malnourished at admission to the ICU (Bockenkamp et al., 2009).

Internationally, there have been multiple studies conducted in Brazil. A study by de Souza Menezes (2012) aimed to determine the nutritional status of children admitted to a PICU and to

assess the effect of malnutrition as an independent risk factor affecting outcome in this patient group (de Souza Menezes et al., 2012). The authors report that 45.5% of patients were malnourished at admission. Malnutrition was identified when weight-for-age in children less than 2 years old or BMI z scores in children older than 2 were of -2 SD or lower (de Souza Menezes et al., 2012). Furthermore, a study by Leite (n=221) that aimed to determine whether hyperglycemia and hypoglycemia were associated with higher mortality, longer LOS, and fewer ventilator-free days found the prevalence of malnutrition to be 47% (weight-for-age z score in children less than 2 and BMI z score in children over 2 less than -2 SD) (Leite, de Lima, et al., 2013).

2.3.3 Change in nutritional status during PICU stay

Few studies have assessed the evolution of nutritional status over the course of PICU stay. In 2004, Hulst et al. conducted a prospective observational study to determine the nutritional status of critically ill children (preterm to term neonates and older children) from admission to 6 months after discharge from the PICU (Hulst et al, 2004). A child (0-17y of age) was classified as malnourished when weight-for-age z score was <-2 SD. A total of 293 children were enrolled and were measured at 4 time points, namely, at admission and discharge from the PICU and at 6 weeks and 6 months after PICU discharge. 15% of the children were identified as being acutely malnourished (14% of the preterm neonates [n=104], 9% of the term neonates [n=96], and 24% of the older children [n=93]). Furthermore, 20% of the children were found to be chronically malnourished (26% of the preterm neonates, 11% of the term neonates and 22% of the older children). Therefore, a total of 70 children showed signs of acute and/or chronic malnutrition upon admission (Hulst et al., 2004). From admission to discharge the proportion of children classified as acutely malnourished increased, from 14 to 32% in the preterm neonates, and from 9 to 23% in

the term neonates. There was no significant difference in the proportion of malnourished older children between admission and discharge, however there was a small but significant decrease in calf circumference (CC), mid-upper arm circumference (MUAC) and triceps skinfold (TSF) measurements in this age group (Hulst et al., 2004). Moreover, 6 months after discharge, almost all children showed complete recovery of their nutrition status, meaning that they had attained or surpassed the parameters (WFA, MUAC, TSF, CC) measured at PICU admission (Hulst et al., 2004).

A study by Delgado et al. (2008) aimed to evaluate the incidence of hospital malnutrition during the first 72h of admission the PICU (Delgado et al., 2008). A total of 1077 patients aged between 2 months and 16 years, were enrolled in this retrospective study. Malnutrition was identified when weight-for-age z score was -2 or lower. With this indicator, as much as 53% of patients were found to be malnourished at admission. Z scores of weight-for-age only worsened in the well-nourished patients during the study period, while it seemed to improve between study day 1 and 10 in the malnourished group (Delgado et al., 2008).

In 2015, de Betue et al. conducted an observational study to determine whether patients achieved their energy goals at day 4 after PICU admission and measured the difference in weight-for-age SD between admission and discharge as a secondary outcome (de Betue et al., 2015). Like previously mentioned studies, malnutrition was identified when WFA z score was < -2 SD. A total of 325 children aged 0-18 years were enrolled in this study and 19% (n=62) were identified as malnourished at admission. Among the patients having their body weight measured at PICU discharge (n=223), 50 (22%) were malnourished at admission. There were significant changes in the proportion of children classified as malnourished and as well-nourished based on WFA z score.

At PICU discharge 8 out of the 50 malnourished patients became well-nourished (admission -3.34 [-11.08 to -2.01]; discharge -3.10 [-7.28 to 0.46]; p = 0.007). On the other hand, some of the well-nourished patients showed a decrease in WFA SD at discharge where 17 out of 173 well-nourished patients were malnourished at PICU discharge (admission -0.36 [-1.98 to 4.55]; discharge -0.53 [-4.58 to 4.46]; p = 0.009) (de Betue et al., 2015).

A French study by Valla et al (2019) described the occurrence of faltering growth (previously named failure to thrive) during PICU stay in critically ill children aged 0-18 years, with length of stay greater than 5 days (n=579 patients). Weight and height/length were measured at admission and weight was monitored every day throughout PICU stay in order to calculate BMI-for-age z score. Faltering growth and risk of faltering growth were identified as a decline of at least 1SD in BMI z score during PICU stay, and between 0.5 and 1 SD, respectively. Malnutrition (undernutrition) was identified when BMI z score was < -2 SD. At admission, undernutrition was identified in 15% of the population. Furthermore, 10.2% of children presented with a BMI z score decline greater than 1SD and 27.8% of children presented with a BMI z score decline greater than 0.5 SD during their PICU stay (Valla et al., 2019).

The most common indicator for the identification of malnutrition in most of the studies cited above is WFA <-2 SD. Hoçwever, as it is explained in the *Health's Professional's Guide for using the WHO growth charts for Canada:*

> Weight-for-age alone is not recommended as a nutritional parameter for any age, and especially beyond 10 years of age because of the wide variability in age at onset of puberty and its associated changes in body composition. When weight-for-age alone is used to screen for over nutrition, pubertal children may appear as having excess weight by weight-for-age when in fact they are just tall; at the other extreme, overweight children that are short or stunted would appear to be normal. The WHO recommends that weight continue to be measured for children beyond 10 years of age, for the purpose

> of calculating, plotting and monitoring BMI-for-age (Dietitians of Canada & Canadian Paediatric Society, 2014:9)

Therefore, BMI-for-age and weight-for-length/height may be more appropriate and comparable indicators for the identification of malnutrition in the PICU in regard to the different age groups (0 to less than 24 months and 2 to 18 years of age). Furthermore, anthropometric measurements were always performed by multiple observers during the study period of past studies. The inter-rater variability that is often seen with anthropometric measurements, introduces a source of error in the results that may be difficult to control for.

2.3.4 Associated Outcomes

Malnutrition can lead to many adverse outcomes on the child's health such as delayed recovery, increased frequency of infections, higher ventilator dependency (meaning the child will need help with breathing for a longer period of time), and increased risk of morbidity and mortality which may ultimately lead to a prolonged length of stay (LOS) in the hospital (Daskalou et al., 2013).

Infections

Malnutrition and infection may be prone to a vicious cycle as malnutrition may lead to an increased risk of infection, and infection may affect the nutritional status leading to malnutrition (Inadequate dietary intake – lowered immunity – may increase disease severity and duration – appetite loss, nutrient loss, altered metabolism which may cause malnutrition…) (Katona & Katona-Apte, 2008). An inadequate dietary intake may also affect the immune system as it may impair the immune response, thus reducing protection against pathogen invasion and increasing the frequency of infections (Joosten & Hulst, 2008). In a multi-center European study (Hecht et al., 2015), a higher proportion of malnourished patients had adverse complications such as diarrhea and

vomiting compared to the well-nourished patients (22% vs 12% and 26% vs 14%, respectively). Furthermore, a study evaluating three pediatric malnutrition risk tools, on the general and surgery units, and used in children from 1 month to 18 years, found that patients who were identified at high risk of malnutrition by all three tools experienced fever more frequently and were prescribed more antibiotics than the medium and low-risk patients (Chourdakis et al., 2016). In addition, underweight and obese children had higher odds of acquiring an infection while hospitalized than children with an adequate nutritional status (Bechard et al., 2016).

Mechanical Ventilation

Patients who are malnourished are at higher risk of increased ventilator dependency (Joosten & Hulst, 2008). A study by de Souza Menezes et al. (2012) conducted in the pediatric intensive care unit with critically ill children aged 3 months to 5 years, found that a greater proportion of malnourished children were dependent on mechanical ventilation after the first 10 days of hospitalization compared with well-nourished children (de Souza Menezes et al., 2012). In addition, underweight children were seen to have fewer (1.3 and 1.6) ventilator-free days compared to normal weight and overweight children respectively (Bechard et al., 2016).

Length of Stay

Multiple studies have evaluated the effects of malnutrition on length of stay (LOS). A multi-center European study (Hecht et al., 2015) found that 7% (n=167) of the population (n=2410; 1month to 18years) was moderately (BMI ≥ -3 to ≤ -2 SDS) or severely (<-3 SDS) malnourished, and concluded that the patients who were malnourished (moderate and severe) had a longer LOS than the well-nourished patients. The median LOS was 5 days for the moderately malnourished and 7 days for the severely malnourished patients, compared to a median LOS of 4 days for the well-

nourished patients (Hecht et al., 2015). Furthermore, another study in which LOS was measured in children aged at least 12 months excluding the ones who were critically ill, found that there was a significant association between nutritional status and length of stay as undernourished patients were more likely to demonstrate a prolonged length of stay regardless of age (O'Connor, Youde, Allen, & Baur, 2004). In addition, Campanozzi et al. described that a length of stay of >5 days was a risk factor for nutrition deterioration (decrease in BMI-for age z-score from admission) while hospitalized, and that undernourished children (1mo – 16y) had a longer length of stay compared to children with a normal nutritional status (Campanozzi et al., 2009). Furthermore, in an international multi-center study by Bechard et al. (2016) assessing the influence of nutritional status at PICU admission (BMI z-score) on important clinical outcomes in mechanically ventilated children, underweight children had a 29% lower chance of being discharged than those who were normal weight over the 60 day study period (Bechard et al., 2016).

We can see in the previously discussed studies, that the prevalence of malnutrition varies from one institution to another and one country to another. Malnutrition at admission to the PICU varies from 15 to 53% and nutrition status deterioration occurs in 4-18% of patients during PICU stay which could lead to adverse outcomes. In these conditions, achieving an adequate nutritional intake to prevent the deterioration in nutritional status and minimize adverse outcomes is essential (Becker et al., 2015; Mehta et al., 2017).

2.3.5 Adequacy of feeding in the pediatric intensive care unit

The *Guidelines for the provision and assessment of nutrition support in the pediatric critically ill* (Mehta et al., 2017), mention that enteral nutrition is the preferred method of nutrient delivery over parenteral nutrition in critically ill children as past studies have demonstrated beneficial effects for

gastrointestinal mucosal integrity and motility (Ikeda et al., 2003; Sano et al., 2007). Furthermore, it is emphasized that early initiation of EN (within 24-48 hours) and achievement of 25% of goal calories within 48 hours and more than 66% of energy and protein goal within the first week of PICU admission was associated with improved clinical outcomes such as reduced PICU mortality and 60-day mortality (Mehta et al., 2012; Mehta, Bechard, Zurakowski, et al, 2015).

Many studies have evaluated the actual dietary intake of children admitted to a PICU, as well as the possible associations with clinical outcomes. One Canadian study aimed to assess the nutritional status of mechanically ventilated children and to evaluate prescribed and delivered enteral and parenteral calories during PICU stay (Bockenkamp et al., 2009). All mechanically ventilated patients with an estimated length of PICU stay of more than 72h were eligible for enrollment. Estimated energy requirements (EER) were based on ASPEN guidelines (American Society for Parenteral and Enteral Nutrition, 2002) and compared to prescribed calories which were determined by the attending medical team. The delivered calories were then compared to the EER. The median estimated energy requirements per patient were 90 kcal/kg/day, the prescribed calories were 75kcal/kg/day and delivered calories 58kcal/kg/day (Bockenkamp et al., 2009). Fifty percent of patients met goal energy intake by the 9th day of admission. The main reasons for feeding interruptions were also recorded with undergoing procedures as the most common reason, followed by intolerances. There was a median of 3 (1-5) interruption days per patient (Bockenkamp et al., 2009).

In 2012, Mehta et al conducted a multi-center prospective cohort study where they examined the factors influencing the adequacy of energy and protein intakes in mechanically ventilated children (ages 1 month to 18 years) in the PICU (Mehta et al., 2012). Nutritional practices including

prescribed and actual energy and protein intakes, route of delivery, frequency and duration of feeding interruptions, and use of adjunctive drugs were recorded for a maximum of 10 days or until PICU discharge (Mehta et al., 2012). A total of 500 patients from 31 PICUs and 8 different countries participated in the study. Nutrition was provided in the form of enteral nutrition (EN), parenteral nutrition (PN) and mixed (EN+ PN). Mean (SD) prescribed goals for daily energy and protein intake were 64 (29) kcal/kg and 1.7 (0.7) g/kg respectively. Actual mean daily intakes for energy and protein were 28 kcal/kg and 0.8g/kg (Mehta et al., 2012). Adequacy of feeding was inadequate over the course of PICU stay with mean daily enteral adequacy of 38% for energy and 43% for protein (Mehta et al., 2012). Intake of a higher percentage of prescribed dietary goals was associated with younger age, shorter duration of mechanical ventilation, medical vs surgical diagnosis, non-use of PN, and shorter interruptions to EN (Mehta et al., 2012). Fluid restriction, feeding intolerance and procedures were the most common reasons for interrupting feeds and the reasons responsible for inadequate energy and protein intakes during PICU stay (Mehta et al., 2012).

In continuation with the previous study and using the same methodology, Mehta et al conducted another international study where they examined the association of protein intake on outcomes such as 60-day mortality in mechanically ventilated children (Mehta, et al, 2015). One thousand two-hundred and forty-five patients were enrolled from 59 PICUs across 15 countries. Mean (SD) prescribed goals for energy and protein were 69 (28) kcal/kg/day and 1.9 (0.7) g/kg/day, respectively (Mehta et al., 2015). When comparing to the ASPEN recommendations (Mehta, et al., 2009) for the age-based daily protein intake goal, protein was under prescribed in 466 patients (37%) (Mehta et al., 2015). Furthermore, the percentage of adequacy for nutrient intake was 36 ±

35% for energy and 37 ± 38% for protein. Intake of a higher percentage of prescribed dietary goals was associated with lower rates of 60-day mortality (Mehta et al., 2015).

As most results show inadequate dietary intake during PICU stay, a few studies concentrated their efforts on identifying the possible reasons why energy and protein goals were not met. A Canadian study conducted in Edmonton in 2015, aimed at describing current practices surrounding nutrition delivery, specifically time to nutrition initiation as well as reasons and duration for feeding interruptions (Keehn et al., 2015). One hundred consecutively admitted patients were enrolled in this study. The mean time to initiation of nutrition support was 22.8 hours. Furthermore, a total of 118 interruptions were identified, with at least 1 interruption occurring per admission in 42% of patients (Keehn et al., 2015). Patients on enteral nutrition had a higher occurrence of feeding interruptions compared to those who received PN as PN does not need to be interrupted for certain procedures. In addition, patients less than 6 months had a higher mean number of interruptions (2.4) compared to patients more than 6 months and also spent the longest duration of time without nutrition (23h) (Keehn et al., 2015). The most frequent single cause for interrupting nutrition support was a planned extubation (24%). Other reasons included procedures (15%), risk for aspiration (15%), medication administration (13%), and unknown reason in 19% of the interruptions (Keehn et al., 2015).

Moreover, de Betue et al (2015) and de Souza Menezes et al (2013), came to similar conclusions following their studies where patients who were admitted to the pediatric intensive care unit with malnutrition (WFA <-2), had significantly higher energy intakes during their PICU stay compared to patients admitted without malnutrition (de Betue et al., 2015; de Souza Menezes et al., 2013). In the study by de Betue et al. (2015), malnourished patients on enteral nutrition were more likely

to be fed above the target range (de Betue et al., 2015) and in the study by de Souza Menezes et al. (2013), malnourished patients were more likely to reach 90% of basal metabolic rate at least one day during PICU stay (de Souza Menezes, et al., 2013).

Achieving adequacy of feeding in the pediatric intensive care unit, is a global challenge. Few studies have reported feeding practices that achieve or surpass energy and protein goals. It is therefore of great importance to continue to identify adequacy of feeding and reasons for this in order to find solutions to overcome this challenge and prevent the development of malnutrition during PICU stay.

CHAPTER III: RESEARCH RATIONAL AND STUDY OBJECTIVES

3.1 RESEARCH RATIONAL

Children admitted to the pediatric intensive care unit (PICU) are at high risk of malnutrition due to the stress of critical illness, treatment, and challenges with meeting energy and protein needs. As discussed in the previous chapter, malnourished patients are at higher risk of being affected by negative outcomes such as prolonged length of mechanical ventilation, increased risk of infection, delayed recovery, longer length of PICU stay and longer length of hospital stay (Daskalou, et al, 2016). Despite the numerous studies describing the prevalence of malnutrition in PICUs, only 2 studies were found to have included a Canadian population (Bechard et al., 2016; Bockenkamp, et al., 2009). Furthermore, most studies used weight-for-age (WFA) as the primary indicator to identify malnutrition which is not in line with current guidelines for the identification of pediatric malnutrition from the Academy of Nutrition and Dietetics (AND) and the American Society of Parenteral and Enteral Nutrition (ASPEN) (AND-ASPEN), and is also not an appropriate indicator for children of 10 years of age and older (Dietitians of Canada & Canadian Paediatric Society, 2010). Moreover, Valla mentioned (2019) that few studies described the evolution of the nutritional status during PICU stay, while multiple studies described the high frequency of malnutrition at PICU admission and its association to adverse outcomes. To our knowledge, this will be the first Canadian study to describe the change in nutritional status over the course of PICU stay using the most recent indicators for the identification of malnutrition (AND-ASPEN). Furthermore, Valla also mentions:

> *PICU healthcare professionals have limited impact on pre-PICU nutritional status; however, they can increase the awareness of their pediatric colleagues to the risks of malnutrition in PICU, especially in surgical wards responsible for children planned for elective surgery that will require PICU admission. PICU*

healthcare professionals could eventually play a greater role preventing or minimizing faltering growth occurrence during PICU stay (Valla et al., 2019:7)

Therefore, knowing the prevalence of malnutrition in the setting of pediatric critical illness and also understanding the changes or deterioration in nutritional status that occur during PICU stay is of great importance to address this problem accordingly. Moreover, given that inadequate nutrient delivery contributes to malnutrition and poor outcome, it is important to describe current feeding practice and actual energy and protein intakes relative to prescribed goal intake according to the latest nutrition practice guidelines (Mehta et al., 2017).

3.2 STUDY OBJECTIVES

Primary Objectives

The primary objectives of this study are to:

1. Describe the prevalence of malnutrition (according to AND-ASPEN guidelines) at admission and discharge from the PICU
2. Describe adequacy of energy and protein intakes over the course of the PICU admission and describe the duration and reason for feeding interruptions

Secondary Objectives

- To compare weight, height/length, z scores, mid-upper arm circumference, skinfolds, handgrip strength and presence of malnutrition (AND-ASPEN guidelines) at admission and discharge from the PICU
- To describe associations between malnutrition status and following factors: adequacy of protein and energy intakes, demographic data (age, sex, ethnicity), diagnosis, co-morbidities, disease severity, number of days on mechanical ventilation, length of PICU stay, length of hospital stay, rate of hospital-acquired infection, presence of pressure sores

CHAPTER IV: ASSESSING THE NUTRITIONAL STATUS OF CHILDREN ADMITTED TO THE PEDIATRIC INTENSIVE CARE UNIT

Introduction

Critically ill children are at high risk of malnutrition due to the stress of critical illness, treatment, and challenges with meeting energy and protein needs (Martinez & Mehta, 2016). At admission to the pediatric intensive care unit (PICU), children commonly present with hemodynamic instability, as well as metabolic and immunologic alterations. During critical illness, multiple metabolic adaptations occur with primary goal of mobilizing nutrients in response to the increased and immediate demand for energy (Nelms, Sucher, & Lacey, 2016). Therefore, in response to various hormonal changes, protein catabolism is increased, and free amino acids are used for wound healing, immune defense, and hepatic gluconeogenesis (Cartwright, 2004). This mechanism may lead to the loss of lean body mass which is one of the major consequences of metabolic stress during critical illness (Valla et al., 2017). Malnourished patients are at higher risk for adverse outcomes during PICU stay, such as, increased dependency on mechanical ventilation, increased risk of infection, slower recovery, longer length of PICU stay and longer length of hospital stay (Daskalou et al, 2016).

Prevalence estimates of moderate to severe malnutrition at PICU admission vary widely as 15 to 53% of patients have been identified as malnourished (Bechard et al., 2016; Bockenkamp, et al., 2009; de Souza Menezes, et al., 2012; Grippa et al., 2017; Leite, et al., 2013). These marked differences in prevalence estimates of malnutrition among these studies may be due to inconsistency in the reference ranges and cut-off values used to assess malnutrition, the type of pediatric indicators used to identify malnutrition (weight-for-age, weight-for-length or BMI-for-age) as well as studies performed in various countries where malnutrition or more or less prevalent.

Little is known about the change in nutritional status of critically ill children during PICU stay and its potential impact on adverse outcomes. To our knowledge, only four studies have evaluated the change in nutrition status over the course of PICU stay. In all studies evaluating nutritional status change, it was found that between 10 and 37% of patients experienced a decline in weight-for-age or BMI-for-age z scores and that this decline was mostly prevalent in patients who were well-nourished at PICU admission (de Betue et al., 2015; Delgado et al., 2008; Hulst et al., 2004; Valla et al., 2019). In one study, children that presented with a decline in BMI-for-age z score were more dependant of mechanical ventilation, had a longer length of stay and acquired more infections (Valla et al., 2019).

In 2015, the Academy of Nutrition and Dietetics and the American Society of Parenteral and Enteral Nutrition (AND-ASPEN) published a consensus statement outlining the recommended indicators for identifying pediatric malnutrition (Becker et al., 2015). These indicators include the assessment of food and nutrient intake, the assessment of energy and protein requirements, and the monitoring of growth parameters, weight gain velocity, mid-upper arm circumference and handgrip strength (Becker et al., 2015). In 2017, *the guidelines for the provision and assessment of nutrition support therapy in the pediatric critically ill patient* from ASPEN and the Society of Critical Care Medicine (SCCM) (SCCM-ASPEN) were updated (Mehta et al., 2017). These guidelines state the importance of nutrition assessment with respect to the early detection and treatment of malnutrition in children given the known negative impact of malnutrition on recovery. These guidelines recommend that all patients should undergo a detailed nutritional assessment within 48h of admissions to the PICU, including measurement of height/length and weight (Mehta et al., 2017). However, the consistent measurement of height/length and weight within the first 48 h of PICU admission is often not done given the many perceived barriers to obtaining

anthropometric measurements, such as, presence of medical devices and unstable hemodynamic status (Irving et al., 2015).

The prevalence of malnutrition in Canadian PICUs has not been adequately reported as only two studies were conducted in Canadian PICUs (Bechard et al., 2016; Bockenkamp, et al., 2009) and the most recent recommended indicators for identifying malnutrition (Becker et al., 2015) were not used. In order to gain insight into the extent of the problem and its potential impact in a Canadian setting, the primary objective of the present study was to describe the prevalence of malnutrition at admission and discharge from the PICU in Ottawa, Canada, according to current guidelines (Becker et al., 2015). As secondary objectives, we aimed to evaluate the change in nutritional status indicators over the course of the PICU stay, and to describe associations between presence of malnutrition and patient demographic and clinical characteristics, adequacy of feeding, and patient outcomes.

Methods

Study population and design

This prospective cohort study was conducted between August 2018 and April 2019 in a 10-bed mixed surgical-medical-cardiac PICU at the Children's Hospital of Eastern Ontario (CHEO), which is a university teaching hospital located in Ottawa, Canada. All consecutively admitted patients who were between 1 month and <18 years of age at the time of admission, admitted for less than 24 hours and had an estimated length of PICU stay of ≥ 48hours were eligible for enrolment. In cases of readmission, patients were not included if they had already been enrolled in the study. Research ethics approval for this study was obtained from the Children's Hospital of Eastern Ontario (CHEO) Research Ethics Board and the University of Ottawa's Office of Research

Ethics and Integrity. A deferred consent model was approved by the CHEO Research Ethics Board and informed written consent was obtained from parents or legal guardians.

Data collection

Study data were collected and managed using REDCap®, which is an electronic data capture tools hosted at CHEO (Harris et al., 2019, 2009). REDCap® was used in this study to prospectively record, for each patient, demographic and clinical characteristics, severity of illness score (PRISM III), Pediatric Logistic Organ Dysfunction score (PELOD-2), duration of mechanical ventilation and non-invasive ventilation, use of vasoactive infusion, length of PICU stay, length of hospital stay, rate of infection[2], presence of pressure sores, anthropometric measurements including weight, length/height, mid-upper arm circumference, skinfold thickness and handgrip strength and nutritional status. The nutritional variables including daily energy and protein goals and actual intake, frequency of feeding interruption, and reasons for interruptions were also recorded and are reported elsewhere (Chapter 5).

Anthropometric measurements

Anthropometric measurements were taken at two time points while admitted to the PICU, namely at admission and at discharge. The following measurements (weight, length/height, mid-upper arm circumference, skinfold thickness and handgrip strength) were taken in order to assess nutritional status of patients according to AND-ASPEN guidelines (Becker et al., 2015).

Prior to starting study patient enrollment, all PICU bed scales (Versa Care, Hill-Rom, Chicago, IL) and infant weighing scales (Pediatric Scale 4802, Scaletronix, White Plains, NY) were verified

[2] Infection was noted if there was a positive culture from blood, urine or other specimens, and if antibiotics were given for ≥4 days. The number of days on antibiotics will be used as a proxy for hospital acquired infections.

and calibrated by the CHEO medical engineering team. In accordance with the latest SSCM-ASPEN 2017 practice guidelines (Mehta et al., 2017), a clinical protocol was put in place for nursing and medical staff of the PICU to measure weight and height for all patients at admission to the PICU (no protocol was implemented for discharge weights).

In order to reinforce this protocol during the period of study, team meetings were held, and a poster was placed in every PICU room to remind patient care team members to weigh every patient at PICU admission. Once a patient was enrolled in the study, the admission PICU weight was extracted from the patient's medical chart and recorded in the case report form in RedCap®. When possible, the patient was reweighed to ensure most accurate weight possible. Patients were weighed using an infant scale (≤2 years of age), bed scale (>2 years), or chair scale (Seca 952, Seca, Hanover, MD), as appropriate. At PICU discharge, patients were reweighed using the same scale.

Recumbent height was measured using a length board (PED LB 35-107-X, Ellard Instrumentation, Monroe, WA for < 2years old; or with REC LB-6X, Ellard Instrumentation, Monroe, WA for patients >110 cm in length) or a measuring tape when use of length board was not possible due to the medical condition of the patient. When a measuring tape could not be used because of patient condition, height was predicted using knee height in children ≥6y (Chumlea, et al., 1994). Mid-upper arm circumference (MUAC) was measured using a flexible measuring tape (Seca 218, Seca, Hanover, MD) and skinfolds (triceps, suprailiac, thigh, subscapular) were measured using Lange skinfold calipers (Nutriactiva, Minneapolis, MN). Handgrip strength was measured, when possible in children over 6 years of age, who were able to follow instructions, at admission and discharge

from the PICU using the Jamar plus digital dynamometer (563213, Patterson Medical, Warrenville, IL).

All measurements were performed by the same investigator to prevent inter-rater variability in measurements.

Assessing nutritional status

The nutritional status of patients was determined by assessing the indicators of pediatric malnutrition, according to the AND-ASPEN consensus statement (2015). When there was only one time point available, the indicators used were: weight-for-length (WFL) z-score for infants and children <2 years of age, BMI-for-age z-score (BMIA) for those ≥ 2 years of age, height/length-for-age z-score and MUAC-for-age z-score for those 2 months - 18 years of age. A patient was classified as being mildly malnourished when weight-for-length, BMI-for-age or MUAC-for-age z-score was ≤ -1 SD; and moderately or severely malnourished when weight-for-length, BMI-for-age or MUAC-for-age z-scores was ≤-2 or ≤-3, respectively. When two data points were available (i.e. at admission and discharge from the PICU), weight gain velocity (<2 years of age), weight loss (2-18 years of age), and adequacy of nutrient intake (data reported in chapter V) were used as indicators for malnutrition (Becker et al., 2015). Z-scores were calculated using the *Canadian Pediatric Endocrine Group*'*s* Growth Chart Plotter App (Canadian Pediatric Endocrine Group, 2014) for weight-for-length, BMI-for-age and length-for-age. Mid-upper arm circumference z scores were assessed using the Center for Disease Control and Prevention's Peditool, that can be used in children from 2 months to 18 years. This tool is based on a study where z score values were computed for US children aged 2 months to 18 years (Abdel-Rahman, Bi, & Thaete, 2017).

Statistical analysis

All statistical analysis was performed on IBM SPSS version 26 software. Continuous data was described as mean and standard deviation or median and interquartile range while discrete data was described as frequency and percent.

The sample size is based on the estimation of a 20% prevalence of undernutrition in critically ill children. We have based this estimated prevalence on previous studies done in industrialized countries where the prevalence of malnutrition in the PICU was between 15% and 24% (Bechard et al., 2016; Hulst et al., 2004; Valla et al., 2019). Based on this estimated prevalence, a sample size of 60 was calculated utilizing an alpha level of 0.05 (95% confidence level) and a total width of confidence interval of 20% (Browner et al., 2001).

The prevalence of malnutrition (as undernutrition) at admission and at discharge from the PICU was described as the percent of the total number of children meeting the AND-ASPEN criteria for mild to severe malnutrition. The percent (%) of children who were overweight and obese (Weight-for-length z score >2, or BMI- for age z score >2) (Bechard et al., 2016) was also described. Adequacy of feeding is presented as percent of goal as described in chapter 5.

Comparison of anthropometric measurements between admission and discharge from the PICU was performed using a paired t-test. Associations between continuous variables were tested using the Spearman rank-order correlation coefficient. Adequacy of feeding as a percent of prescribed in relation to admission and discharge z scores was tested using Spearman rank-order correlation coefficient. Adequacy of feeding in relation to malnutrition category was analyzed with Kruskal-Wallis' H test. Association between categorical variables was analyzed using a chi-square or

Fisher's exact test, and association between categorical and continuous variables was analyzed with Mann-Whitney's U test or Kruskal-Wallis' H test.

A p value of < 0.05 was considered statistically significant.

Results

Of the 295 patients admitted to the PICU during the study period, 128 were eligible and 60 were enrolled. Figure 1 illustrates the patient enrollment flow chart. Table 1 describes the demographic and clinical characteristics of the sample population studied. The median (IQR 25^{th} - 75^{th}) age of the study cohort was 1.8 (IQR: 0.4-8.4) years, 42% were female, 61% were of Western European descent and 11% were North American Aboriginal. A majority of this cohort was admitted for medical illnesses (83%), particularly for infectious disease (43%), respiratory conditions (17%), cardiovascular conditions (15%) and neurological conditions (15%). Forty-four patients were in need of ventilatory support (invasive and/or non-invasive) during PICU stay and the median duration of mechanical ventilation was 6.0 (IQR: 2.4-11.1) days. Median PICU length of stay (LOS) was 5.4 (IQR: 3.6-9.4) days and 55% of cohort had a PICU LOS of more than 5 days.

Table 2 shows the prevalence of malnutrition (undernutrition) at admission and at discharge from the PICU based on the AND-ASPEN nutritional indicators when one data point is available (Becker et al., 2015). Based on combined weight-for-length (WFL for children < 2y) and BMI-for-age (BMIA for 2-18 years) z scores, the prevalence of malnutrition was 27% at admission and 23% at discharge. When using mid-upper arm circumference z scores, 24% and 42% of children were identified as malnourished at PICU admission and discharge, respectively. The proportion of malnourished children changed significantly from admission to discharge when using MUAC z

score as a nutritional indicator (p=0.031), this did not occur when using BMIA and WFL as indicators (p=0.125).

At admission to the PICU, 8 (13%) patients were overweight/obese using WFL/BMIA z scores (>2 SD), and 4 (8%) patients were overweight/obese when using MUAC z scores (>2SD).

Table 3 shows the prevalence of malnutrition using the AND-ASPEN nutritional indicators when two data points were available (i.e. at admission and discharge from the PICU). Forty-eight percent of patients below two years of age presented with mild-moderate-severe malnutrition indicated by weight gain velocity, with 34% of these patients presenting with severe malnutrition. Furthermore, 62% of patients between 2 and 18 years of age were categorized as adequately nourished, as their weight loss was less than 5% of their usual body weight during PICU stay.

Between admission and discharge from the PICU, MUAC z-score was the only nutritional indicator to decline significantly (p=0.002) (Table 4). Twenty-seven patients had a mean ± SD decrease in MUAC z-score of -0.71 ± 0.59 during PICU stay. MUAC includes adipose tissue, muscle tissue and bone. In order to gain more insight on this change we examined the change in triceps skinfold thickness, which is a measure of subcutaneous adipose tissue, and found that it did not decline significantly over the course of PICU stay. The decline in MUAC z-score along with unchanged skinfold thickness may suggest a loss of lean muscle mass, which deserves further investigation. Although WFL z score in children < 2 years of age increased somewhat (p=0.01) during the PICU stay, many children in this age group (48%) failed to achieve their expected weight gain.

Combined weight-for-length and BMI-for-age admission z scores were not associated with age,

ethnicity, admission diagnosis, presence of co-morbidities, PRISM III and PELOD admission scores (results not shown), nor were they associated with clinical outcomes such as, length of PICU stay, length of hospital stay, and the number of days on ventilatory support (Table 5). As shown in Figures 2 and 3, there were significant correlations between the number of antibiotic days (in relation to hospital-acquired infection) and combined WFL and BMIA z scores at admission and at discharge. Overweight patients tended to be on antibiotics for more days than underweight and normal weight patients (admission: $r=0.54$ $p=0.021$; discharge: $r=0.635$ $p=0.006$). These results align with the findings of Bechard et al. (2016), where there was a higher likelihood of acquiring an infection for obese PICU patients (OR, 1.64; 95% CI, 1.33-2.03; $p<0.001$) (Bechard et al., 2016). Furthermore, adequacy of energy and protein intakes as percent of prescribed were not associated with admission and discharge nutritional status (WFL and BMIA), nor were they related to change in z-score during PICU stay (results not shown). MUAC z-score was not associated with gender, age, admission diagnosis, presence of co-morbidities, PRISM and PELOD admission scores (results not shown), nor was it associated with length of PICU stay, hospital length of stay, and days on antibiotics as shown in Table 6. MUAC admission z score and change in MUAC z score during PICU stay was also not associated with adequacy of feeding during PICU stay (results not shown).

Furthermore, as shown in Figure 5, non-Western European/non-Aboriginal ethnicities (other) seemed to have a greater change in MUAC z-scores from admission to discharge compared to Western European patients, and to Aboriginal ethnicity ($p=0.011$). There was no significant difference between non-Western European/non-Aboriginal and Aboriginal patients.

Discussion

This is one of the first studies done in a Canadian PICU that assessed nutritional status based of the most recent guidelines from the Academy of Nutrition and Dietetics and the American Society of Parenteral and Enteral Nutrition (Becker et al., 2015). Second, this study is also the first Canadian study to provide insight on nutritional status change that occurs during PICU stay in relation to adequacy of nutritional intake. In addition, this is one of the first studies to include self-reported ethnicity to describe patients admitted to PICU and to compare ethnicity with change in nutritional status.

This study aimed to describe the prevalence of malnutrition at admission and discharge from the PICU according to the criteria specified by the 2015 consensus statement (Becker et al., 2015). Assessment of nutritional status using WFL/BMIA or MUAC z scores showed that a relatively large proportion of children suffered from malnutrition (mild, moderate, or severe) during PICU stay. Overall, when looking at WFL/BMIA 27% and 23% were identified as malnourished at admission and discharge, respectively. When looking at the MUAC indicator 24% and 42% were identified as malnourished at admission and discharge. In terms of moderate and severe malnutrition (<-2 SD or <-3SD for given indicator), the prevalence was 12% based on WFL/BMIA and 16% based on MUAC at admission; 15% based on WFL\BMIA and 22% based on MUAC at discharge. The proportion of malnourished (moderate-severe) children at PICU discharge, in our study, compares to findings of previous studies where between 15 and 25% of patients were identified as malnourished although different methodologies were used to identify malnutrition (Bockenkamp et al., 2009; de Souza Menezes et al., 2012; Hulst et al., 2004; Valla et al., 2019). Past studies have reported malnutrition as being moderate or severe (<-2SD or <-3SD), therefore, mild malnutrition was usually not included in the prevalence value. With the consensus statement

from AND-ASPEN using indicators to identify mild malnutrition, we thought it was of interest and saw it as a strength to include the information from this indicator (mild malnutrition) in our results. As described in the consensus statement (Becker et al., 2015), "mild malnutrition related to undernutrition, is usually the result of an acute event, either due to economic circumstances or acute illness, and presents with unintentional weight loss or weight gain velocity less than expected" (Becker et al., 2015:157). Valla et al (2019), found that faltering growth was frequent in the PICU with more than 25% of patients presenting with a BMI z score decline greater than 0.5 SD, and 24% of patients with more than 5% weight loss (Valla et al., 2019). Our study yielded similar findings where 38% of patients over 2 years of age presented with a weight loss of more than 5%. In our cohort, however, only 5 (10%) patients presented with a z score decline of more than 0.5 SD, even though, 48% of patients less than 2 years of age did not reach 75% of the norm for expected weight gain during PICU stay. Due to their higher growth rates and higher energy and protein needs, younger children may be more vulnerable to the development of malnutrition.

MUAC has rarely been used in the assessment of nutritional status of children during their PICU or hospital stay in past studies. However, in the publication of the recommended indicators for the identification of malnutrition by AND-ASPEN in 2015, MUAC was considered to be a more useful and easily obtained measurement to assess nutritional status, especially important in those whose weight may be affected by lower extremity edema, ascites or steroids (Becker et al., 2015). Furthermore, MUAC has been indicated as a more sensitive prognostic indicator for mortality than weight-for-length in malnourished patients (Rasmussen et al., 2012; Schwinger, et al., 2019; Taneja et al., 2018). During critical illness, nutrient mobilization is increased in order to account for the immediate energy demand (Nelms, Sucher, & Lacey, 2016). Therefore, protein catabolism is increased, and free amino acids are used for wound healing and immune defense, which may

lead to the loss of lean muscle mass (Cartwright, 2004; Valla et al., 2017). Mid-upper arm circumference may be a more sensitive measurement to assess the deterioration of nutritional status as it was the only nutritional indicator to decrease significantly over the course of PICU stay while triceps skinfold thickness did not vary significantly. These results may reflect that muscle mass is lost more rapidly than adipose tissue during critical illness (Marques & Langouche, 2013; Pichard et al., 2004). In addition, these results align with those of Hulst et al. (2004) where calf circumference and mid-upper arm circumference declined significantly during PICU stay (Hulst et al., 2004). Identifying and quantifying loss of lean muscle mass in critically ill children would be important in order to target optimal nutrition and physical interventions to reduce muscle wasting and possibly reduce the risk of poor outcomes (Ong, Lee, Leow, & Puthucheary, 2017). In critically ill patients, the pathophysiology of ICU-acquired weakness is multifactorial and involves peripheral nerve alteration (neuropathy) that can lead to muscle wasting (Puthucheary et al., 2013; Valla et al., 2017). In addition, in bedridden patients and those under sedation or neuroblocking agents, disuse atrophy may occur (Valla et al., 2017). In the adult population, ICU-acquired weakness was associated with prolonged length of stay, as well as post-ICU rehabilitation, resulting in increased healthcare costs (Kress & Hall, 2014; Ong, Lee, Leow, & Puthucheary, 2017).

This study has some limitations that need to be acknowledge. First, there are errors associated with anthropometric measurements in terms of techniques and equipment. To minimize these errors, all anthropometric measurements were performed by a single trained investigator according to standardized procedure, in order to decrease inter-rater variability and increase accuracy of anthropometric measurements. To ensure accuracy of equipment, all weighing scales were

calibrated and verified by the hospital's biomedical engineering team prior to the start of the study. Calibration of skinfold calipers was verified prior to each measurement using a calibration block. Interpretation of anthropometric measurements, especially weight, in a PICU setting may be questionable due to potential fluid overload (or dehydration) that is common in critically ill children at admission. It is for that very reason that patients were only enrolled in the study if they had been admitted to the PICU for less than 24 hours, and that a new protocol for measuring weight at PICU admission was initiated before commencement of recruitment. Patients were weighed using the same scale at admission and discharge from the PICU and were weighed wearing minimal clothing (or naked). Mid-upper arm circumference is suggested to be a more accurate indicator to assess nutritional status during critical illness as unlike weight, it is less influenced by fluid shifts or hydration status (Green Corkins & Teague, 2017; Mehta et al., 2013). However, as there are no Canadian reference standards and that the World Health Organization (WHO) only has reference standards for children from 3 months to 5 years, the Center for Disease Control and Prevention reference standards were used (Abdel-Rahman, Bi, & Thaete, 2017). As these references are for American children, they may not accurately portray mid-upper arm circumference measures of Canadian children population. Second, sample size was relatively small for this study. Sixty patients provided sufficient power to assess the prevalence of malnutrition at admission to the PICU, however it may not provide sufficient power to draw conclusions about weight decline during PICU stay and associations between nutritional status and adverse outcomes. Furthermore, as this is a single-center study, results may not be generalizable to all Canadian PICUs.

Conclusion

In summary, we found that 12% and 27% of our cohort was admitted to the PICU with moderate-

severe and with mild-moderate-severe malnutrition, respectively. We also found that this prevalence changed at PICU discharge when looking at MUAC z score as 27 patients presented with a decline MUAC z score, bringing the prevalence of malnutrition up to 42% (mild-moderate-severe). In our cohort, we were able to demonstrate a correlation between admission and discharge WFL/BMIA z scores and hospital-acquired infections. Furthermore, we were also able to demonstrate the association between ethnicity and change in MUAC z scores during PICU stay. More research is needed in Canadian pediatric intensive care units to further describe the extent of malnutrition and change in nutritional status and to describe associations between malnutrition and outcomes. In addition, we should investigate in more depth the change in mid-upper arm circumference over the course of PICU stay by evaluating the change in tissue stores.

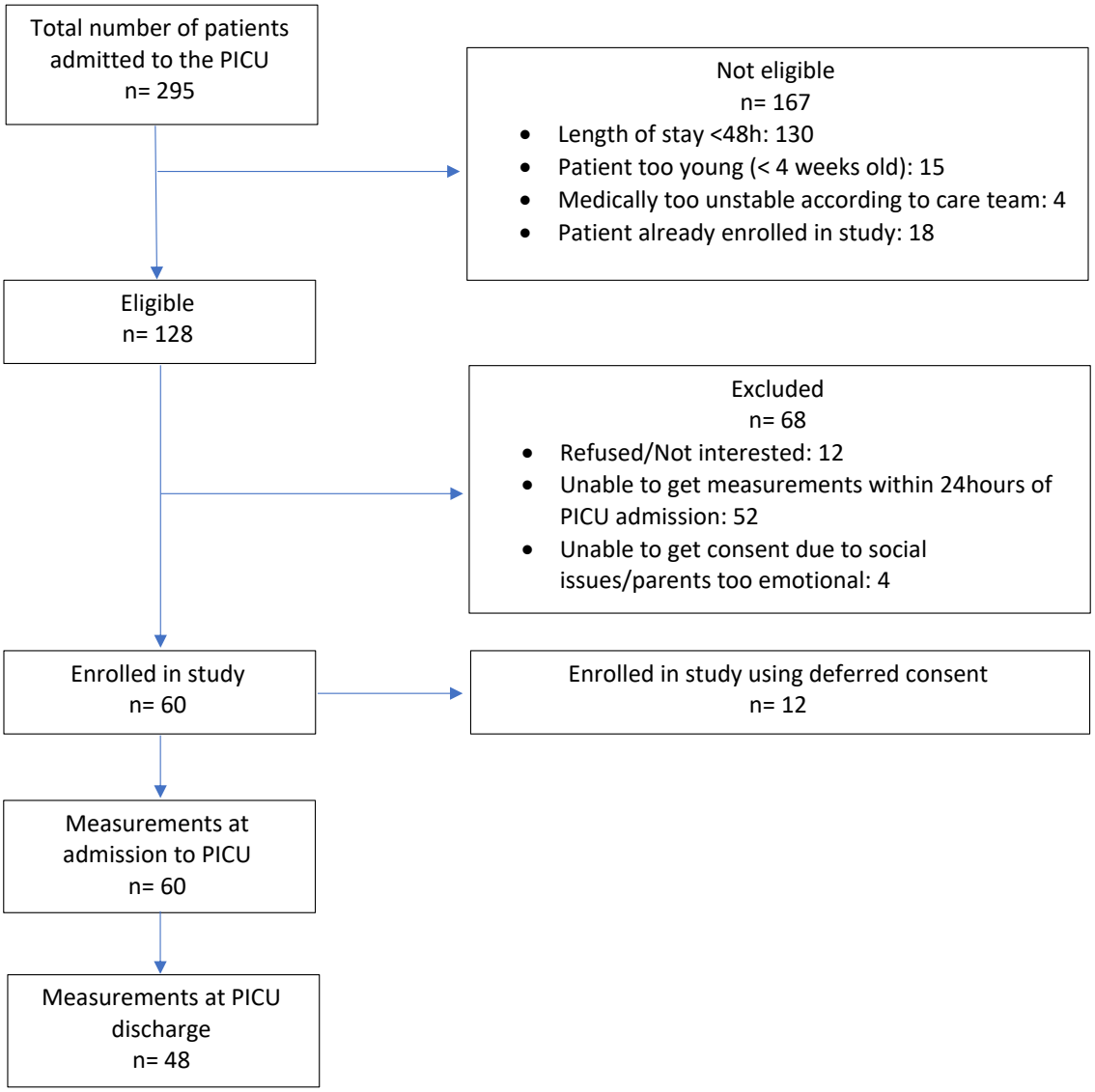

Fig. 4.1. Enrollment flowchart of critically ill children admitted to the PICU (n=60). PICU, pediatric intensive care unit;

Table 4.1
Demographic and clinical characteristics of children admitted to PICU (n= 60)

Variables	Median (IQR) or n (%)
Age (y)	1.8 (0.4-8.4)
Age Categories	
1 to <24 months	33 (55)
2 to 5 years	9 (15)
6 to < 12 years	10 (16.7)
≥ 12 to 18 years	8 (13.3)
Sex (Female)	25 (42)
Patient Ethnicity (Father /Mother)	
Western European/Western European	37 (61)
East Asian/ East Asian	1 (2)
Southeast Asian/ Southeast Asian	1 (2)
West Asian/West Asian	3(5)
Central African/Central African	3 (5)
Northern African/Northern African	2 (3)
Northern African/Western African	1 (2)
Latin American/Latin American	1 (2)
North American Aboriginal/North American Aboriginal	7 (11)
Unknown/West Asian	1 (2)
Unknown/Unknown	3 (5)
Admission Category	
Medical	50 (83)
Surgical: Elective	10 (17)
Diagnosis at admission	
Cardiac	9 (15)
Respiratory	10 (17)
Infectious disease	26 (43)
Neurology	9 (15)
Trauma	4 (7)
Hematology/Oncology	2 (3)
Presence of chronic disease (n=36)	
Prematurity	13 (36)
Cardiovascular disease	8 (22)
Neurological disorder [a]	8 (22)
Chromosomal anomaly [b]	12 (33)
Musculoskeletal disease [c]	8 (22)
Developmental delay [d]	9 (25)

Continued…

Number of chronic conditions per patient (n=36)	
One	22 (61)
Two	8 (22)
Three	5 (14)
Four	1 (3)
PRISM III	3.0 (1.0-6.0)
PELOD	
Day 1 (n=60)	3.0 (2.0-7.0)
Day 3 (n=48)	4.5 (0-7.0)
Day 7 (n=26)	3.0 (1.0-6.0)
PICU Discharge (n=60)	0 (0-1.0)
Days on ventilatory support [e] (n=44)	4.0 (2-8)
Invasive (n=33)	6.0 (2.4-11.1)
Non-invasive (n=36)	3.0 (1.3-8.1)
Vasoactive infusion (Yes) (n=17)	
Dopamine	1 (6)
Epinephrine	13 (76)
Norepinephrine	11 (65)
Milrinone	7 (12)
Vasopressin	2 (3)
Length of PICU stay (days)	5.4 (3.6-9.4)
Patients with LOS of >5days	33 (55%)
Length of Hospital stay (days)	14.2 (6.4-40.4)

[a] includes seizure disorders, Rett syndrome, Microcephaly
[b] includes chromosomal duplication, Trisomy 21, Molybdenum cofactor deficiency, Miller-Dieker syndrome, Coffin-Siris syndrome, Sickle cell disease
[c] includes cerebral palsy/Worster-Drougth syndrome, Congenital hypotonia, Scoliosis, spinal muscular atrophy
[d] includes Smith-Magenis syndrome
[e] Patients could have received invasive and non-invasive ventilation during PICU stay

Table 4.2
Prevalence of malnutrition (undernutrition) at admission and at discharge from the PICU according to primary indicators at single time point (Becker et al. 2015)

Weight-for-length/BMI-for-age*	**Admission (n=60)**	**Discharge (n=48)**	**P value**
Mild, moderate and severe malnutrition	16 (27%)	11 (23%)	0.125
Moderate and severe malnutrition	7 (12%)	7 (15%)	1.0
Mid-upper arm circumference	**Admission (n=51)**	**Discharge (n=36)**	**P value**
Mild, moderate and severe malnutrition	12 (24%)	15 (42%)	0.031
Moderate and severe malnutrition	8 (16%)	8 (22%)	0.250

*Using 2014 WHO growth charts adapted for Canada (set 2) as reference standards for infants from birth to 24 months of age and children from 2 to 19 years of age

Table 4.3
Prevalence of malnutrition according to primary indicators calculated from two time points (Becker et al. 2015) n (%)

	Adequate nutrition status	**Mild malnutrition**	**Moderate malnutrition**	**Severe malnutrition**
Weight gain velocity (<2 years of age) (n=27)[a]	*75% or more of the norm for expected weight gain[d]*	*>50% to < 75% of the norm for expected weight gain*	*>25% to <50% of the norm for expected weight gain*	*Less than 25% of the norm for expected weight gain*
	14 (52)	2 (7)	2 (7)	9 (34)
Weight loss (2-18 years of age) (n=21)[b]	*Less than 5% of usual body weight[e]*	*5% to < 7.5% usual body weight*	*7.5% to <10% usual body weight*	*10% usual body weight*
	13 (62)	5 (24)	2 (10)	1 (4)
Deceleration in weight-for-length/height z score (<2 years of age)	*No Decline in z-scores*	*Decline of 1 z-score*	*Decline of 2 z-scores*	*Decline of 3 z-scores*
	48 (100)	0	0	0
Adequacy of Dietary intake (n=50)[c]	*More than 75% estimated energy/protein need*	*51-75% estimated energy/protein need*	*26%-50% estimated energy/protein need*	*≤25% estimated energy/protein need*
	19 (38)	15 (30)	13 (26)	3 (6)

[a] Missing 6 patients from admission to discharge; [b] Missing 6 patients from admission to discharge; [c] Missing data for 10 patients
[d] Using 2014 WHO growth charts adapted for Canada (set 2) as reference standards for infants from birth to 24 months of age, and WHO norms for weight gain velocity; [e] Admission weight was used as reference for usual body weight

Table 4.4
Difference in nutritional status indicators over the course of PICU stay

Nutritional status indicators	n*	Admission	n	Discharge	Mean paired difference (95% CI), p value
Weight (kg)	48	22.3 (27.5)	48	22.2 (27.4)	-0.079 (-0.49; 0.34), 0.703
Height (cm)	47	96.9 (42.9)	47	96.6 (42.9)	-
Head Circumference (cm)	21	40.7 (4.7)	-	41.6 (4.7)	-
WFL z-score	27	-0.26 (1.59)	27	-0.07 (1.50)	0.19 (0.05; 0.33), 0.01
>2 SD	2	2.55 (0.35)	2	2.40 (0.57)	
-0.9 to 1.9 SD	15	0.42 (0.74)	19	0.34 (0.82)	
-1 to -1.9 SD	6	-1.18 (0.55)	3	-1.47 (0.25)	
-2 to -2.9 SD	2	-2.15 (0.21)	1	-	
< -3 SD	2	-3.54 (0.23)	2	-3.21 (0.15)	
BMIA z-score	21	0.03 (2.4)	21	-0.14 (2.51)	-0.17 (-0.44; 0.09), 0.192
>2 SD	5	2.5 (0.36)	4	2.50 (0.39)	
-0.9 to 1.9 SD	11	0.50 (0.75)	12	0.56 (0.91)	
-1 to -1.9 SD	2	-1.40 (0.29)	1	-	
-2 to -2.9 SD	-	-	1	-	
< -3 SD	3	-4.83 (0.76)	3	-5.13 (0.51)	
LFA z-score	48	0.07 (0.2)	48	0.05 (1.76)	-
< -3 SD	3	-4.87 (1.88)	3	-4.32 (1.63)	
MUAC z-score	36	-0.09 (1.66)	36	-0.475 (1.68)	-0.43 (-0.68; -0.18), 0.002
>2 SD	4	2.63 (0.49)	1	-	
-0.9 to 1.9 SD	23	0.37 (0.78)	20	0.58 (0.68)	
-1 to -1.9 SD	4	-1.51 (0.24)	7	-1.45 (0.32)	
-2 to -2.9 SD	3	-2.38 (0.20)	6	-2.35 (0.31)	
< -3 SD	2	-3.72 (0.38)	2	-3.92 (0.08)	
MUAC (cm)	44	18.3 (7.9)	44	17.6 (7.8)	-0.72 (-1.14; -0.30), 0.002
Triceps skinfold (mm)	42	11.8 (7.2)	42	11.6 (7.4)	-0.22 (-1.02; 0.58), 0.578
Suprailliac skinfold (mm)	18	7.3 (8.4)	18	6.3 (5.5)	-0.97 (-3.0; 1.0), 0.316
Thigh Skinfold (mm)	38	16.4 (7.6)	38	16.0 (8.5)	-0.26 (-1.05; 0.53), 0.510
Subscapular (mm)	4	13.8 (16.0)	4	16.4 (16.5)	-
Handgrip strength	1	11.77	1	9.3 (4.1)	-

Values are mean (SD)
*Only those patients with available values for both admission and discharge are included

Table 4.5
Association between clinical outcomes and admission nutritional status classification based on combined weight-for-length and BMI-for-age z scores (n=60)

Clinical Outcomes	Overweight/Obese (n=8)	Adequate nutrition status (n=36)	Underweight* (n=16)	P value
PICU LOS (days)	5 (2-10)	5 (6-13)	7 (2-24)	0.342
Hospital LOS (days)	17 (-9; 112)	10 (16-51)	15 (15-58)	0.470
Number of days on abx *n*	8 (-12; 27) 2	5 (4-9) 11	5 (3-6) 5	0.447
Days on ventilatory support *n*	5 (-7; 46) 7	4 (3-10) 24	5 (-1; 27) 13	0.531
Days on nutrition support *n*	6 (3-10) 5	5 (5-7) 31	8 (5-9) 14	0.696
Presence of pressure sores (n)	0	1	2	-
Death (n)	0	0	2	-

* Includes mild moderate and severe malnutrition

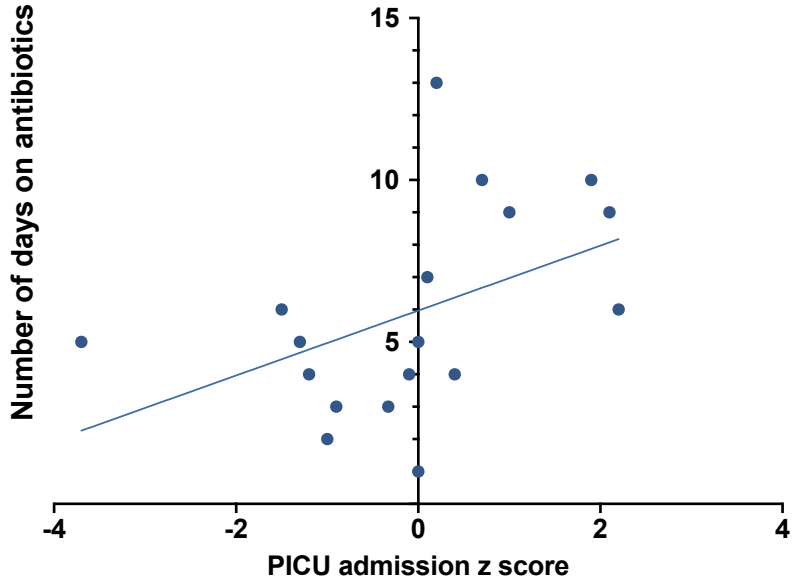

Fig 4.2: Number of days on antibiotics (acquired infection) in relation to admission z score (Weight-for-length/BMI-for-age); (r_o=0.54 p=0.021)

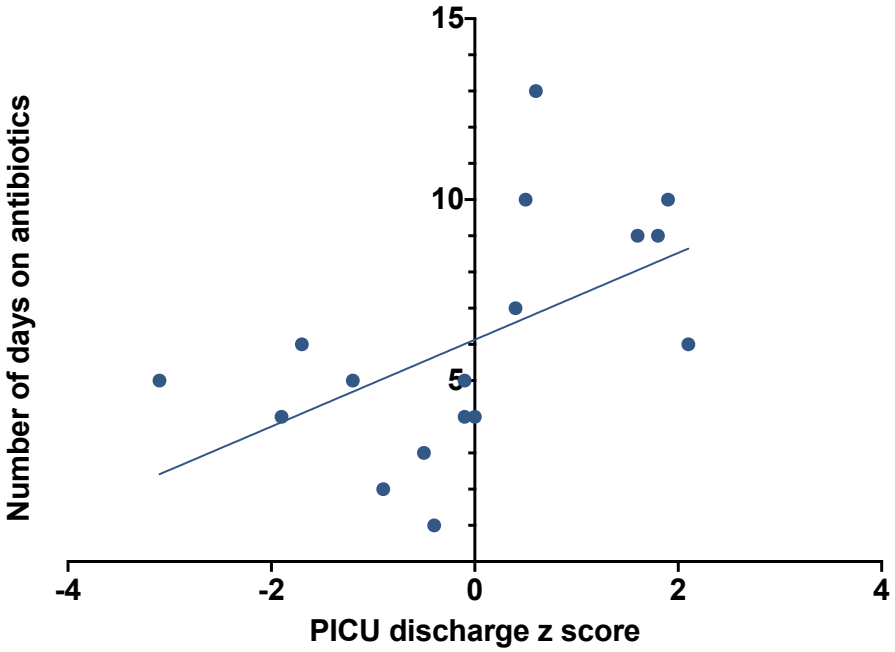

Fig 4.3: Number of days on antibiotics (acquired infection) in relation to discharge z score (Weight-for-length/BMI-for-age); (r_o=0.635; p=0.006)

Table 4.6
Association between clinical outcomes and admission nutritional status classification based on MUAC z scores (n=51)

Clinical Outcomes	Overweight/Obese (n=4)	Adequate nutrition status (n=35)	Underweight* (n=12)	P value
PICU LOS (days)	7 (-2; 20)	5 (5-17)	5 (2-16)	0.907
Hospital LOS (days)	18 (1-38)	15 (22-59)	12 (7-91)	0.988
Number of days on abx *n*	10 (3-15) 2	5 (4-8) 13	- 1	0.246
Days on ventilatory support *n*	7 (-11; 27) 3	4 (3-18) 26	3 (-9; 42) 7	0.772
Days on nutrition support *n*	10 (3-16) 2	7 (5-8) 29	5 (4-8) 10	0.329
Presence of pressure sores (n)	0	1	1	-
Death (n)	0	1	1	-

**Includes mild, moderate and severe malnutrition*

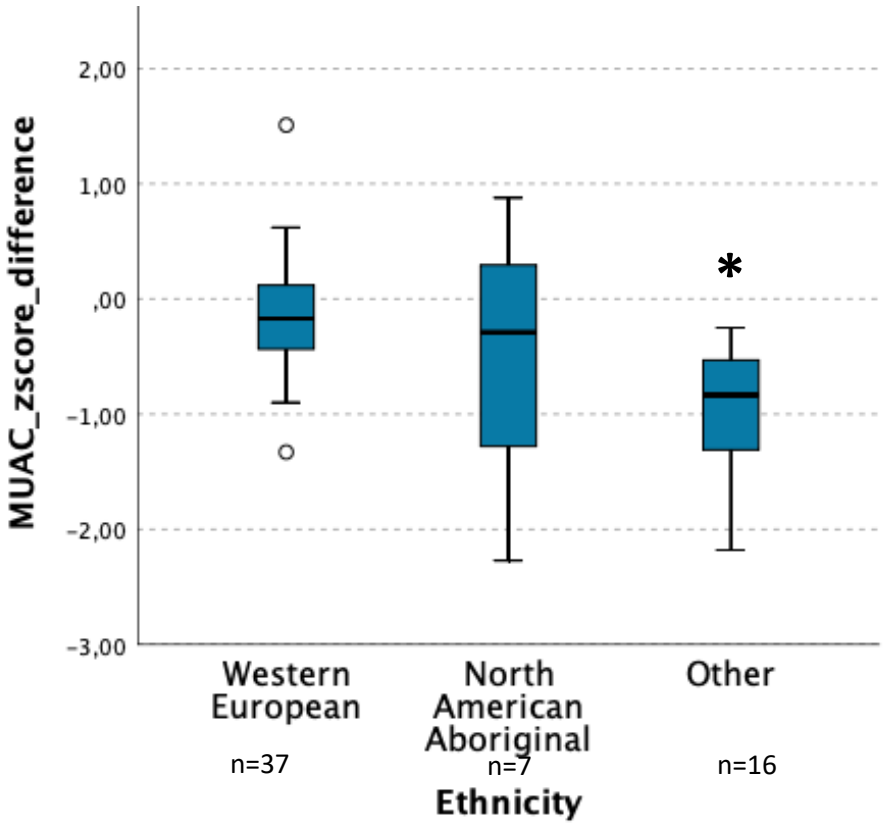

Fig 4.4: Change in MUAC z score over PICU stay according to ethnicity, Statistical analysis comparing median change in MUAC z scores over PICU stay among ethnicity groups was done using Kruskal-Wallis test (H=9.048, p=0.011), *Denotes the median statistically significant differences with Western European group (p=0.008, adjusted by the Bonferroni correction for multiple tests)

CHAPTER V: ADEQUACY OF ENERGY AND PROTEIN INTAKES OF CHILDREN ADMITTED TO THE PEDIATRIC INTENSIVE CARE UNIT

Introduction

Critically ill children are at high risk of developing nutritional deficiencies due to the metabolic stress of critical illness causing an imbalance between dietary intake and energy expenditure (Martinez & Mehta, 2016; Mehta et al., 2017). Studies that have been done over the past years to identify the prevalence of malnutrition in the pediatric intensive care unit (PICU), have found that between 15 and 53% of children presenting with malnutrition at PICU admission (Bechard et al., 2016; Bockenkamp, et al., 2009; de Souza Menezes, et al., 2012; Grippa et al., 2017; Leite, et al., 2013). Additionally, a few studies have shown that the nutritional status of these children deteriorates during PICU stay (de Betue et al., 2015; Delgado et al., 2008; Hulst et al., 2004; Valla et al., 2019). Furthermore, malnutrition has been associated with poor outcome during hospitalization, such as mortality and morbidity, including increased risk of infection, higher dependency of mechanical ventilation, poor wound healing, and longer length of PICU and hospital stay (Costa, Tonial, & Garcia, 2016; Martinez & Mehta, 2016).

Adequate nutrition is essential for complete recovery and normal growth of the child (Becker et al., 2015; Mehta et al., 2017). Clinicians are challenged to provide adequate nutrition for optimal immune function and recovery while avoiding the complications of under or overfeeding (Flaring & Finkel, 2009). Many factors may lead to an inadequate delivery of energy and protein during PICU stay. Those identified include, delayed enteral nutrition (EN), fluid restriction, intolerance, intubation or extubation, bedside procedures and radiological or surgical procedures (Rogers, et al., 2003). These frequent and potentially avoidable interruptions often result in large deficits over

the course of patient hospitalization (Hulst et al., 2004; Hulst, et al. 2006) which may exacerbate the deterioration of nutritional status of these children.

In July 2017, The American Society for Parenteral and Enteral Nutrition (ASPEN) and the Society of Critical Care Medicine (SCCM) (SCCM-ASPEN), published the new *Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Pediatric Critically Ill Patient* (Mehta et al., 2017). These guidelines provide insight on the optimal ways to assess energy and protein requirements as well as on the most favorable practices in regard to enteral and parenteral nutrition support with critically ill pediatric patients. Given that inadequate nutrient intake contributes to malnutrition (Mehta et al., 2017), it is essential to understand the current feeding practices that occur in Canadian PICUs and verify if they align with the most recent practice guidelines.

The objectives of this study were to 1) describe the adequacy of energy and protein intakes in children during PICU stay at the Children's Hospital of Eastern Ontario (Ottawa, Canada) and 2) describe the duration and reason for feeding interruptions

Methods

Study population and design

This prospective cohort study was conducted between August 2018 and April 2019 in a 10-bed mixed surgical-medical-cardiac PICU in the Children's Hospital of Eastern Ontario (CHEO), a teaching hospital located in Ottawa, Canada. All consecutively admitted patients who were 1 month to <18 years of age at admission who had been admitted for less than 24 hours and had an estimated length of PICU stay of ≥ 48hours. In cases of readmission, patients were not included if they were already enrolled in study. Research ethics approval for this study was obtained from the

Children's Hospital of Eastern Ontario (CHEO) Research Ethics Board and the University of Ottawa's Office of Research Ethics and Integrity. A deferred consent model was approved by the CHEO Research Ethics Board and written informed consent was obtained from parents or children capable of doing so.

Data collection

Study data were collected and managed using REDCap® an electronic data capture tools hosted at CHEO (Harris et al., 2019, 2009). REDCap® was used in this study to prospectively record, for each patient, demographic and clinical characteristics, Pediatric risk of mortality score (PRISM III), Pediatric Logistic Organ Dysfunction score (PELOD-2), duration of mechanical ventilation and non-invasive ventilation, use of vasoactive infusion, length of PICU stay, length of hospital stay, rate of infection[3], presence of pressure sores, anthropometric measurements and nutritional status. Nutritional variables including daily energy and protein goals and actual intake, volume of formula, type of formula, feeding route, feeding mode, frequency and duration of feeding interruption, and reasons for interruptions were also recorded.

As described in chapter 4, nutritional status was assessed at admission and at discharge from the PICU and was based on the 2015 consensus statement regarding the recommended indicators for the identification of pediatric malnutrition (Becker et al., 2015).

Estimating total energy and protein intake through nutrition support

To assess total energy and protein intake received by nutrition support (enteral and parenteral nutrition), a prospective chart review was conducted. The feeding route, feeding mode, total

[3] Infection was noted if there was a positive culture from blood, urine or other specimens, and if antibiotics were given for ≥4 days.

volume, reasons for interrupting feeding, and total time feeds were held were extracted from medical chart and recorded. Total energy and protein intakes were estimated based on daily volume of formula provided along with supplements and other nutrition support, when applicable, as described in medical chart. The daily goal intake as well as the type of formula and its concentration (see Appendix XIV for macronutrient composition of formulas) were extracted from the dietitian's chart note which enabled the calculation of estimated energy and protein intakes. In cases where patients were fed by parenteral nutrition, total volume received was recorded in case report form and the PICU dietitian provided the study investigator with the actual energy and protein concentration received (kcal/kg/day and g/kg/day). This information was provided to study investigator as actual concentrations of nutrients from PN were not easily available for study investigator in patient charts. For oral nutrition, data was only collected for patients who were bottle fed and had intake recorded in their medical chart. Nutrition intake variables were collected for a maximum of 10 days or until PICU discharge, whichever came sooner.

Assessment of adequacy of energy and protein intakes

The estimation of energy and protein requirements for patients admitted to the PICU were determined by the PICU's clinical dietitian according to the SCCM-ASPEN clinical practice guidelines in the absence of indirect calorimetry (Mehta et al., 2017). The "WHO equation" was used to determine energy requirements for patients (Joint FAO/WHO/UNU Expert Consultation on Energy and Protein Requirements, 1985). A stress factor was added to the equation according to the medical status of the patient (i.e. traumatic brain injury, or other). Protein requirements were calculated using the recommendations from the latest SCCM-ASPEN practice guidelines indicating that a minimum intake of 1.5g/kg/day must be ensured to avoid cumulative protein deficits in critically ill children and that protein intakes may reach 2-3g/kg/day in children 0-2

years of age (Mehta et al., 2017). Prescribed goal was equal to the estimated requirements for energy and protein. When a range was provided as the goal for energy and protein the median value was used as the goal.

For the purpose of this study, daily energy and protein intakes were deemed adequate when actual intake was ≥75% of estimated goal energy and protein intakes (Becker et al., 2015). Adequacy of intake is expressed as a percentage of goal intakes ([Delivered ÷ Prescribed] x 100).

Statistical analysis

All statistical analysis was performed on IBM SPSS version 26 software. Continuous data is described as mean and standard deviation or median and interquartile range while discrete data is described as frequency and percent.

The prevalence of inadequate intakes of energy and protein was described as the percent of the patients with mean daily energy intakes and daily mean protein intakes that were below 75% of goal intakes. Adequacy of feeding was evaluated over a maximum of 10 days (or until PICU discharge, if earlier) by determining the average daily amount of calories and protein received by EN or by EN plus parenteral nutrition (PN) or by PN alone. Evaluable nutrition days started on the first day any form of nutrition was received and ended at day ten of PICU admission or at PICU discharge. When feeds were interrupted, the duration and reason for the interruptions were recorded. Feeding interruptions were expressed as frequencies and percent. The median (IQR) number of hours feeding interruptions occurred per day is expressed as the number of interrupted hours per evaluable nutrition days and number of interrupted hours per interrupted days (median

of interrupted hours per day calculated using only the number of days there were feeding interruptions). Feeding interruptions are expressed in two ways to better compare to other studies.

A p value of < 0.05 was considered statistically significant.

Results

Subject characteristics and enrollment flow chart are shown in chapter 4. Briefly, of the 295 patients admitted to the PICU during this period, 60 were enrolled in the study. The median (IQR 25^{th} and 75^{th}) age of the study cohort was 1.8 (IQR: 0.4-8.4) years, 42% were female, 61% were of Western European descent and 11% were North American Aboriginal. A majority of this cohort was admitted for medical illnesses (infectious disease, respiratory conditions, cardiovascular conditions) (83%). Forty-four patients were in need of ventilatory support (invasive and/or non-invasive) during PICU stay and the median duration of mechanical ventilation was 6.0 (IQR: 2.4-11.1) days. Median PICU length of stay (LOS) was 5.4 (IQR: 3.6-9.4) days and 55% of cohort had a PICU LOS of more than 5 days.

During the study period, we were able to collect data on nutrition variables for 50 patients who were either bottle fed or received enteral and-or parenteral nutrition. The 10 remaining patients were orally fed during their PICU admission and were not included in this analysis. For oral nutrition, we only included children who were bottle fed and had the volume of intake and type of formula recorded in their medical chart.

Enteral nutrition was the primary mode of feeding. Forty patients (80%) were fed solely by EN, 6 (12%) patients were fed by a combination of EN and PN, 2 (4%) patients were fed exclusively by PN, and 2 (4%) patients were exclusively bottle fed. In approximately 50% of enterally fed patients, the nasogastric route was used. Initiation of enteral nutrition occurred on the first day of

PICU admission for 49% of patients with a median of 18 (IQR: 7-33) hours. Seven patients (15%), were tube fed prior to PICU admission. Five were on homemade blenderized diets and 2 were using Nestle's Compleat formulas. We were not able to assess dietary intake for 2 patients on a homemade blenderized diet as parents did not have a standardized recipe for the feeds. These patients are included in the total of 10 patients with missing information on nutritional intakes. Table 1 describes the feeding information of enrolled patients.

As demonstrated in Table 2, median prescribed goals for energy and protein were 82 (IQR: 55-100) kcal/kg/day and 2.5 (IQR: 1.8-2.5) g/kg/day, respectively. We were able to evaluate actual dietary intake for a median of 6.5 (IQR: 4-10) days. Actual energy and protein intakes for this cohort were 57 (IQR: 32-81) kcal/kg/day and 1.4 (IQR: 0.9-1.9) g/kg/day, respectively, which shows an actual median intake below prescribed. The median percentage of adequacy was 64% (IQR: 50-73%) for energy and 62% (IQR: 40-82%) for protein when patients received EN alone, which fell below the adequacy level set at 75% (Becker et al., 2015), suggesting inadequate energy and protein intakes during PICU stay(Becker et al., 2015). When patients were fed solely by PN or bottle, adequacy of energy and protein intakes (≥ 75% of goals) was also not met. However, when patients received a combination of EN + PN, percentage of adequacy was higher reaching a median of 85% (IQR: 54-104%) for energy and 96% (IQR: 73-108%) for protein. Figure 1 shows the median adequacy of energy and protein intakes over the first 10 days of PICU stay for patients who were enterally fed.

Feeding interruptions occurred in 36 (78%) patients on enteral nutrition and the frequency of EN interruptions, expressed as the number of days with at least one interruption, during the evaluable nutrition days was 4 days (IQR: 2-7). Delivery of enteral nutrition was held for a median of 5.9

(IQR: 3.3-7.9) hours per interrupted day or a median of 2.8 (IQR: 1.8-4.6) hours per evaluable nutrition days. A total of 174 interruptions were identified. The most frequent reason for interruption was procedures (49%) which included, intubations, planned extubations, MRIs, CT scans and physiotherapy. Additionally, 26% of interruptions were caused by intolerances and 19% of interruptions were for unknown reasons as there was no documentation of reason for interruption in medical chart (Table 3).

Discussion

This study investigated the actual intakes of energy and protein in relation to nutrient needs of children during their PICU stay and the main reasons for feeding interruptions. The major findings were that adequacy of feeding was not reached in a majority of patients during PICU stay (62%), especially in those children who did not receive a combination of enteral and parenteral nutrition. The main route of feeding for children in the PICU was enteral nutrition given the importance of maintaining gut integrity and function in this population (Mehta et al., 2017). In patients receiving enteral nutrition as sole source of nutrition (n=40), approximately 60% of their energy and protein needs were met. It was only possible to reach adequacy of feeding when using a combination of enteral and parenteral (n=6). These patients received a combination of EN and PN as they were unable to receive enough formula through the enteral route to meet their needs because of their medical condition and reduced gastrointestinal function. Furthermore, feeding interruptions were very frequent in the PICU as 174 interruptions were noted and 78% of patients had at least one interruption during a median of 6.5 (IQR: 4-10) evaluable nutrition days with procedures being the main reason children did not meet their nutritional requirements.

On the basis of observational cohort studies, the 2017 SCCM-ASPEN *Guidelines for the provision and assessment of nutrition support therapy in the pediatric critically ill patient*, early initiation of enteral nutrition (within 24-48 hours) and achievement of up to two-thirds of nutrient goal in the first week of critical illness was associated with improved clinical outcomes (Mehta et al., 2012, 2017; Wong, et al., 2017). In 2015, Keehn et al. found that the mean time of delay to initiate any form of nutrition support was 22.8 hours (Keehn et al., 2015), which is similar to what was observed in our study as mean time to nutrition initiation was 23.8 hours. The results of this study are also in line with two international studies by Mehta et al. (2012, 2015) where initiation of EN was done within the first 24 hours of PICU admission in 50 to 60% of patients (Mehta et al., 2012; Mehta, et al., 2015). Implementation of a nutrition support protocol has been shown to reduce the delay of initiating nutrition support. Tume et al. (2010) reported that the time to initiation of nutrition support was reduced by a mean of 11.9 hours with a 35% adherence to the protocol (Tume, Latten, & Darbyshire, 2010). Additionally, Meyer et al. (2009) audited nutrition practices after the implementation of a nutrition support protocol and found that time to initiation of nutrition support was reduced from 15 hours to 4.5 hours from the first to the fourth audit (Meyer et al., 2009). The findings from the present study are similar to other centers before the implementation of a nutrition support protocol and suggests that the adoption of a protocol in the future may improve nutrient delivery during PICU stay.

Adequate energy and protein intakes representing at least 75% of the estimated requirements were not met in the majority (62%) of children in our cohort. Median prescribed goals for energy were 82 (IQR: 55-100) kcal/kg/day and median prescribed goals for protein were 2.5 (IQR: 1.8-2.5) g/kg/day. Actual energy and protein intakes reached approximately 60% of goal when patients were fed solely by enteral nutrition and were over 85% when patients received a combination of

EN and PN. The achievement of nutrient intakes according to the estimated requirements is challenging in the PICU. Other studies have reported inadequacy of feeding in the PICU such as the two international multi-center studies by Mehta et al. (2012; 2015), where actual energy and protein intakes were between 36-51% and 37-61% (range) of prescribed goal, respectively (Mehta et al., 2012, 2015). Compared to these studies, our cohort reached a slightly higher adequacy of intake as a percent of prescribed, as median adequacy was approximately 60%. A study by Hulst et al. (2004) showed that cumulative nutritional deficits, when compared to recommended dietary allowance (RDA), were associated with a decline in SD-scores for weight and mid-upper arm circumference (Hulst et al., 2004). Future studies should examine the association between adequacy of feeding and nutritional status indicators.

Feeding interruptions were frequent in our study (174 interruptions), over the 10 ten days that were evaluated and occurred in 78% of patients who were fed by enteral nutrition. Procedures (intubation, extubation, CT scan, MRI, physiotherapy)) were the primary cause of interruption and resulted in more time without nutrition for patient's whose feeds were held. These results compare to previous studies that described nutritional practices in the PICU and recorded reasons for feeding interruptions. Keehn et al. (2015) identified 118 interruptions during their study period (41 days) and procedures were also the main reason for interruption as they accounted for 54% of the interruptions (Keehn et al., 2015). In addition, Mehta et al. (2010) observed feeding interruptions in 30% of patients where 58% of these were deemed avoidable (Mehta et al., 2010). We did not describe the frequency of avoidable interruptions during our study. It is possible that a large proportion of the 174 observed interruptions could have been avoidable which would have reduced the time without nutrition for many patients.

This study does have some limitations that should be acknowledged. Even though the main diagnosis encountered were infectious diseases and respiratory illnesses, our recruitment was not limited to winter months where the prevalence of respiratory illnesses is higher. Recruitment was performed over 8 months which enabled us to get a wide array of diagnosis over this period. In addition, all data collection was performed by a single investigator, including anthropometric measurements, which prevents inter-rater variability. Nutrition practices were not recorded for the entire length of PICU stay. Therefore, evaluating nutritional intake for only the first 10 days of PICU admission, might have prevented us from collecting an accurate depiction of total energy and protein intake. Additionally, energy requirements were estimated using the WHO equation (Becker et al., 2015), which might have resulted in an over or under-estimation of energy requirements for some patients and prevented us from accurately estimating adequacy of energy intake. This equation is, however, recommended in the 2017 SCCM-ASPEN guidelines when indirect calorimetry is not available in the unit (Mehta et al., 2017). Moreover, we did not analyze nitrogen balance during our study, which prevents us from evaluating more accurately the protein status of our study sample. Furthermore, this study is a single center, therefore, results might not be generalizable to other PICUs.

Conclusion

This study found that a majority of study participants were not meeting their energy and protein requirements during the first 10 days of PICU stay. Prolonged delay to initiate nutrition support and frequent feeding interruptions contributed to patients not meeting these requirements. Past studies have shown that over half of the interruptions may be avoidable and that the implementation of a nutrition support protocol may have a positive impact in improving nutrient delivery and prevent caloric and nutrient deficits. Future research should focus on finding solutions

to reduce feeding interruptions and audit nutrition practices once a nutrition support protocol is implemented.

Table 5.1
Feeding information of study cohort (n=60)

Route of delivery n (%)	
Patients who received any EN	46 (77%)
Nasogastric	24 (52%)
Orogastric	3 (7%)
Post pyloric	5 (11%)
G-tube	14 (30%)
Patients who received any PN	8 (13%)
Patients who received oral nutrition only	6 (10%)
Mode of EN delivery n (%) (n=46)	
Continuous	39 (85%)
Bolus	7 (15%)
Initiation of EN n (%) (n=46)	
Prior to PICU admission	6 (13%)
On the first PICU day	23 (50%)
On the second PICU day	12 (26%)
On the third PICU day	3 (7%)
On the fourth PICU day or later	2 (4%)

Table 5.2
Prescribed and actual energy and protein intakes over the first ten days of PICU stay (n=50)

Nutrient goals (prescribed)*	
Prescribed energy intake (kcal/day)	822 (627-1337)
Prescribed protein intake (g/day)	24 (15-44)
Prescribed energy intake by weight (kcal/kg/day)	82 (52-100)
Prescribed protein intake by weight (g/kg/day)	2.5 (1.8-2.5)
Nutrient delivery	
Evaluable nutrition days (d)	6.5 (4-10)
Actual energy intake (kcal/day)	510 (327-970)
Actual protein intake (g/day)	13 (8-35)
Actual energy intake by weight (kcal/kg/day)	57 (32-81)
Actual protein intake by weight (g/kg/day)	1.4 (0.9-1.9)
Actual energy intake (EN only) as % of prescribed	64 (50-73)
Actual protein intake (EN only) as % of prescribed	62 (40-82)
Actual energy intake (EN + parenteral nutrition) as % of prescribed (n=6)	85 (54-104)
Actual protein intake (EN + parenteral nutrition) as % of prescribed (n=6)	96 (73-108)
Actual energy intake (PN only) as % of prescribed (n=2)	10 (4.0- -)
Actual protein intake (PN only) as % of prescribed (n=2)	65 (52.0- -)
Actual energy intake (oral only) as % of prescribed (n=2)	49 (24- -)
Actual protein intake (oral only) as % of prescribed (n=2)	44 (23- -)

*Nutrient goals were equal to requirements
Values are median (IQR)
Values for 10 patients receiving oral (food) intake or blenderized homemade formula not captured

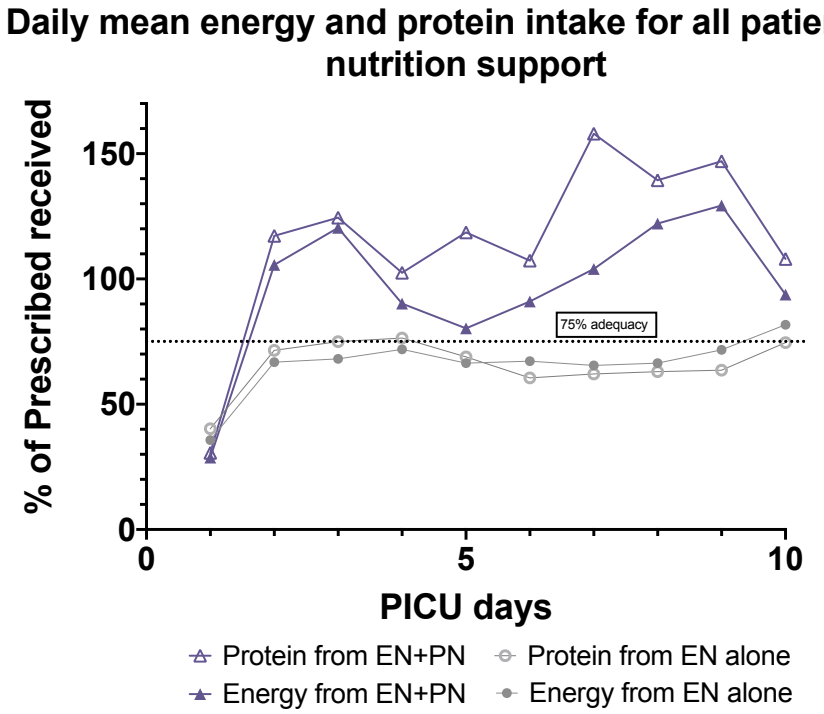

Fig 5.1: Daily mean energy and protein intakes for patients receiving EN (enteral nutrition), n=40, or a combination of EN and PN (parenteral nutrition), n=6

Table 5.3
Frequency and main reasons for feeding interruptions in enterally fed patients over the first ten days of PICU stay (n=36)

Frequency of EN interruptions (days)	4.0 (2.0-7.0)
Duration of EN interruptions (hours/ interrupted day)	5.9 (3.3-7.9)
Duration of EN interruption (hours/evaluable nutrition days)	2.8 (1.8-4.6)
Main reasons for EN interruptions (n=174)	
Medication	3 (2)
Mechanical problem	2 (1)
Intolerance	45 (26)
Tube Misplacement	4 (3)
Procedure [a]	86 (49)
Unknown	34 (19)

[a] Includes intubation, extubation, MRI, CT scan and physiotherapy
Values are median (IQR)

CHAPTER VI: DISCUSSION

Our study is the first Canadian study, to our knowledge, to evaluate nutritional status of critically ill children according to the most recent nutrition practice guidelines (Mehta et al., 2017) and definition of pediatric malnutrition (Becker et al., 2015). To our knowledge we are also one of the first Canadian studies to describe the deterioration of the nutritional status over the course of PICU stay in relation to the adequacy of nutritional intake during the first 10 days of PICU stay. Moreover, rarely did previous studies report ethnicity of enrolled patients. We found that ethnicity may have been a contributing factor to the change in nutritional status during PICU stay. We are one of the first studies to include self-reported ethnicity to describe patients and to compare ethnicity with nutritional status. Patients who were of non-Western European/non-Aboriginal ethnicities (i.e. Other) seemed to have a greater change in MUAC z-scores from admission to discharge compared to Western European patients.

In terms of prevalence of malnutrition, we were able to show that a relatively large proportion of children were malnourished at PICU admission and discharge. The prevalence of malnutrition when using weight-for-length (WFL) z scores and BMI-for-age (BMIA) z scores as indicators for malnutrition was 27% at admission to the PICU and 23% at discharge from the PICU. When using mid-upper arm circumference (MUAC) z score as an indicator for the identification of malnutrition, 24% of patients were admitted with malnutrition and this prevalence increased to 42% at discharge. Furthermore, MUAC z score was the only nutritional indicator to decrease significantly during PICU stay, as twenty-seven patients (75%) presented with a decline in MUAC z score between admission and discharge from the PICU. When identifying the presence of malnutrition using two time points, we found that 48% of children <24 months did not meet 75%

of the norm for expected weight gain and 38% of children >2 years or age lost more than 5% of their usual body weight.

Furthermore, we showed that 62% of patients did not meet adequacy of feeding as they did not meet 75% or more of their energy and protein requirements. Our results showed that patients who did not receive a combination of enteral nutrition and parenteral nutrition received approximately 60% of energy and protein requirements. Of the 6 patients who received a combination of EN and PN a median of 85% (IQR: 54-104) of prescribed for energy and 96% (IQR: 73-108) of prescribed for protein was delivered. In addition, feeding interruptions were frequent with 174 interruptions occurring during the evaluable nutrition days. This resulted in 78% of patients on EN having at least one feeding interruption during their evaluable nutrition days.

In past studies evaluating the adequacy of feeding, it was shown that patients reached approximately 36-51% of their prescribed goal for energy and 37-61% for protein during the first 10 days of PICU admission (Mehta et al., 2012; Mehta, et al., 2015). Adequacy of feeding was mostly not met due to feeding interruptions which are common in the intensive care setting (Keehn et al., 2015; Martinez & Mehta, 2016). As mentioned, we recorded a total of 174 interruptions in 36 (78%) patients on enteral nutrition and the main reasons for feeding interruptions were procedures (Intubation, extubation, CT scan, MRI, physiotherapy) and perceived intolerances. We found that the median time feeds were held was 5.9 (IQR: 3.3-7.9) hours per day during which feeding interruptions occurred. In a past study by Metha et al. (2010), it was found that approximately 50% of EN interruptions were avoidable in critically ill patients (Mehta et al., 2010). Furthermore, multiple feeding interruptions could result in up to 42% of time without nutrition in the PICU, which could impact nutrient delivery and prevent adequacy of feeding from

being met (Keehn et al., 2015; Martinez & Mehta, 2016; Mehta et al., 2010). Not reaching prescribed goals for energy and protein could potentially impact nutritional status over the course of PICU stay. As previously mentioned, patients receiving a combination of EN and PN were more likely to reach energy and protein prescribed goals. However, this may not be an appropriate course of action for feeding patients in the PICU as PN poses a greater risk for infection and is a more costly approach. Although no associations were found in our study between adequacy of feeding and nutritional status, mainly due to insufficient sample size, we observed a decrease in MUAC z score in 27 patients over PICU stay. As discussed in previous chapters, the metabolic response to stress during critical illness is predominantly characterized by loss of lean muscle mass (Preiser, et al., 2014). As no significant change in triceps skinfold thickness (measure of subcutaneous adipose tissue) between admission and discharge from the PICU was found, the decline in mid-upper arm circumference z score may represent a decrease in muscle mass.

Limitations

As discussed in chapter 4 and 5, our study does have some limitations. The use of anthropometric measurements is challenging and not always reliable depending on the level of training of the personnel and equipment used. During data collection, we minimized these errors to the best of our abilities by calibrating the equipment, having all measurements performed by a sole investigator, initiating a protocol for measuring weight at PICU admission and enrolling patients who had been admitted to the PICU for less than 24 hours. Furthermore, nutritional practices were not recorded for the entire length of PICU stay, which could prevent an accurate estimation of adequacy of intake. Energy requirements were estimated using the WHO equation which could cause an over or under-estimation of requirements. In addition, we did not analyze nitrogen balance which prevents us from accurately evaluating the protein status of enrolled patients. Furthermore,

the approach used to identify malnutrition (undernutrition) in this study did not include the assessment of micronutrient deficiencies; nor did it include a nutrition-focused physical exam which has been used by others as an additional parameter in the assessment of malnutrition (Bouma, 2017). Of note, the use of biomarkers such as serum proteins (albumin, prealbumin, transferrin) are no longer considered meaningful biomarkers to identify malnutrition, given that their serum concentrations are affected by other factors such as inflammation and fluid shifts (Bouma, 2017).Finally, our sample size is relatively small, and this was a single center study, therefore, results may not be generalizable to other institutions with different characteristics. Future studies will need to include a larger sample size to increase accuracy of results and have sufficient power to analyze differences among groups in relation to adverse outcomes.

Significance for practice

This study provides new descriptive data on the current prevalence of malnutrition at admission and discharge from a Canadian PICU, as well as describe the adequacy of energy and protein intakes in a population of critically ill pediatric patients. This study also provides descriptive data regarding changes in anthropometric measurements – specifically weight and mid-upper arm circumference – and how these changes relate to outcomes and feeding practices. To our knowledge, we are the first Canadian study that uses the most recent recommendations for the identification of malnutrition.

Mid-upper arm circumference could be recognized as a more sensitive measure to evaluate change in nutritional status over the course of PICU stay compared to weight-for-length or BMI-for-age, as it is less influenced by fluid shifts or hydration status (Green Corkins & Teague, 2017; Mehta et al., 2013). We hypothesized that the decline in MUAC z score, in our cohort, could potentially

be the result of a loss of lean muscle mass, as there was no significant change in triceps skinfold thickness. Therefore, future studies should re-evaluate the change in MUAC z scores over the course of PICU stay. The use of ultrasound to quantify the change in muscle size may be of interest. Although there is currently a lack of studies investigating the use of muscle ultrasound in critically ill children, this technique could prove to be a useful and non-invasive tool to detect change in muscle size (Ong, Lee, Leow, & Puthucheary, 2017). As discussed by Ong et al. (2017), it would be of interest to investigate the association between muscle change, functional ability and nutritional intake "to further increase the utility of muscle ultrasound as a nutrition and functional assessment tool in critically ill children" (Ong et al., 2017:1097).

Moreover, this study will hopefully inform health care practitioners on current practices and areas where improvements may be necessary, such as improving adequacy of feeding and preventing the deterioration of nutritional status. In the summer of 2019, a feeding protocol for the initiation and advancement of nutrition support was implemented in CHEO's PICU. Future research should re-evaluate adequacy of energy and protein intakes following the initiation of this protocol and verify if time to initiation of nutrition support is reduced and if this measure helped reach prescribed energy and protein goals. In addition, in order to increase precision in estimation of adequacy of feeding, future studies should assess energy requirements using indirect calorimetry and analyze nitrogen balance to accurately evaluate protein intakes and requirements.

CHAPTER VII: CONCLUSION AND FUTURE DIRECTIONS

This study aimed to describe the prevalence of malnutrition at admission and discharge from the pediatric intensive care unit (PICU) using the most current clinical practice guidelines, and to describe the adequacy of energy and protein intakes over the first 10 days of PICU stay. We assessed the presence of malnutrition at admission and at discharge from the PICU using either weight-for-length and BMI-for-age z scores (depending on the age of the child), and mid-upper arm circumference (MUAC) z scores. We can conclude that approximately a quarter of the patients admitted to the intensive care unit present with malnutrition (mild, moderate or severe malnutrition), and a tenth of patients presented with moderate-severe malnutrition. MUAC z score decreased significantly ($p=0.002$) over the course of PICU stay, which may reflect decreased muscle mass. Our results suggest that MUAC together with triceps skinfolds are useful indicators of nutritional status deterioration. The results also showed that expected weight gain during the PICU stay, was below 75% of the norm in 48% of children less than 24 months of age. In older children 38% experienced weight loss greater than 5% of their usual body weight. Due to their higher growth rates and higher energy and protein needs, younger children appear to be more vulnerable to the development of malnutrition.

In terms of feeding adequacy, we conclude that a majority of study participants (62%) did not achieve goal intakes when set at 75% of estimated energy and protein requirements. Feeding interruptions were frequent in our cohort, with 174 interruptions occurring in 78% of patients on EN.

To better understand the implications of these results in terms of patient outcomes, future studies should include a larger sample size and include multiple centers. Future studies could evaluate nutritional strategies aimed at preventing the deterioration of nutritional status using MUAC and triceps skinfolds and other techniques aimed at measuring lean muscle mass. Based on these conclusions, practitioners should consider implementing a protocol to evaluate the nutritional status of all patients admitted and reassess nutritional status weekly to prevent nutritional status deterioration. In addition, practitioners should consider implementing a protocol for the initiation and advancement of nutrition support to reduce the time to initiation, prevent avoidable interruptions, and increase adequacy of feeding.

As previously mentioned, critically ill children are at higher risk of malnutrition due to the stress of critical illness, treatment, and difficulties achieving adequacy of intake. Malnutrition has also been associated with adverse outcomes (Daskalou et al., 2016). Our findings have addressed a gap in knowledge by providing insight on the current prevalence of malnutrition and describing current feeding practices in a Canadian PICU. Future studies are needed to evaluate the efforts at improving nutrient care delivery and its impact on nutritional status and patient outcomes.

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APPENDICES

APPENDIX I: ETHICS APPROVAL FROM THE CHILDREN'S HOSPITAL OF EASTERN ONTARIO

CHEO Research Ethics Board Approval - Delegated Review

Principal Investigator: Dr. Dayre McNally
REB Protocol No: 18/61X
Romeo File No: 20180245
Project Title: CHEOREB# 18/61X - Assessing nutritional status of children admitted to the pediatric intensive care unit
Primary Affiliation: Clinical Research\Pediatric Intensive Care
Protocol Status: Active
Approval Date*: July 19, 2018
Approval Expiry Date:** July 15, 2019

Documents Reviewed & Approved:

Document Name	Comments	Version Date
Investigator Response	Investigator Response Letter	7/12/2018
Recruitment Materials	Telephone Consent Script, Version 1, 02-May-2018	5/2/2018
Consent Form	Protocol 18-61X McNally Consent Form (v12-Jul-2018)	7/12/2018
Consent Form	Protocol 18-61X McNally Deferred Consent Form (v12-Jul-2018)	7/12/2018
Assent Form	Protocol 18-61X McNally Assent Form 7-11y (v12-Jul-2018)	7/12/2018
Assent Form	Protocol 18-61X McNally Assent Form for Very Young Children (v12-Jul-2018)	7/12/2018
Case Report Form	Malnutrition Case Report Form (v12-Jul-2018)	7/12/2018
Other Document	Bedside Poster (v12-Jul-2018)	7/12/2018
Protocol	Malnutrition Protocol (v1,12-Jul-2018)	7/12/2018
Questionnaire/Survey	Ethnicity Questionnaire (v12-Jul-2018)	7/12/2018
Recruitment Materials	Deferred Consent Pamphlet (v12-Jul-2018)	7/12/2018

This is to notify you that the Children's Hospital of Eastern Ontario Research Ethics Board has granted approval to the above named research study on the date noted above. Your project was reviewed within the delegated stream, which is reserved for projects that involve no more than minimal risk to human participants.

Final approval is granted for the above noted study, with the understanding that the investigator agrees to comply with the following requirements:

1. The investigator must conduct the study in compliance with the protocol and any additional conditions set out by the Board.
2. The investigator is responsible for complying with all applicable guidelines and regulations regarding the ethical conduct of research with humans, as applicable to the research project.
3. Approval for studies that include an investigational device(s) is contingent upon the investigator securing an Investigational Testing Authorization notice from Health Canada.
4. Investigators must obtain annual renewal approval prior to the expiration date stated above.
5. The investigator must not implement any deviation from, or changes to, the protocol, consents or assents without the approval of the REB except where necessary to eliminate hazard to the research subject, or when the change involves only logistical or administrative aspects of the study (e.g., change of telephone number or research staff). As soon as possible, however, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendment(s) should be submitted to the Board for review and approval.
6. The investigator must, prior to use, obtain approval from the Board for changes to the study documentation, e.g., changes to the informed consent letters, recruitment materials.
7. Investigators must obtain approval from the Board of French version(s) of the consent/assent form(s), unless a waiver has been granted. An interpreter should be offered to participants as required or at the request of the participant throughout the course of research.
8. The investigator must promptly report to the REB all unexpected and untoward occurrences (including the loss or theft of study data and other such privacy breaches).
9. Investigators must notify the REB of any change in study status (closed to accrual, temporary, premature or permanent).
10. Investigators must submit a study closure event form at the conclusion of the study.

Should you have any questions or concerns, please do not hesitate to contact the Research Ethics Board Office at 613-737-7600 ext. 3350 or 2128.

Regards,

Richard Carpentier, PhD
Chair, Research Ethics Board
Président, Comité d'éthique de la recherche

* The final approval date for initial delegated study applications approved with or without modifications will be the date the REB has determined that the conditions of approval have been satisfied.

** The expiry date of REB approval for initial study applications will be as follows:
- If the date of approval was **on or before** the 15th of the month, the expiry date will be the 15th of the month prior to the date of review and approval by the Chair and/or delegate *in the following year*;
- If the date of review and approval was **after** the 15th of the month, the expiry date will be the 15th of the month in which the date of review and approval by the REB *in the following year*.

APPENDIX II: ETHICS APPROVAL FROM THE UNIVERSITY OF OTTAWA

02/07/2019

Université d'Ottawa
Bureau d'éthique et d'intégrité de la recherche

University of Ottawa
Office of Research Ethics and Integrity

CERTIFICAT D'APPROBATION ÉTHIQUE I CERTIFICATE OF ETHICS APPROVAL

Numéro du dossier / Ethics File Number	H-08-18-751
Titre du projet / Project Title	Assessing the nutritional status of children admitted to the pediatric intensive care unit
Type de projet / Project Type	Thèse de maîtrise / Master's thesis
Statut du projet / Project Status	Renouvelé / Renewed
Date d'approbation (jj/mm/aaaa) / Approval Date (dd/mm/yyyy)	02/07/2019
Date d'expiration (jj/mm/aaaa) / Expiry Date (dd/mm/yyyy)	15/07/2020

Équipe de recherche / Research Team

Chercheur / Researcher	Affiliation	Role
Alexandra DUBUC	École interdisciplinaire des sciences de la santé / Interdisciplinary School of Health Sciences	Chercheur Principal / Principal Investigator
Pauline DARLING	École des sciences de la nutrition / School of Nutrition Sciences	Superviseur / Supervisor

Conditions spéciales ou commentaires / Special conditions or comments

02/07/2019

Université d'Ottawa
Bureau d'éthique et d'intégrité de la recherche

University of Ottawa
Office of Research Ethics and Integrity

Le Comité d'éthique de la recherche (CÉR) de l'Université d'Ottawa, opérant conformément à l'*Énoncé de politique des Trois conseils* (2014) et toutes autres lois et tous règlements applicables, a examiné et approuvé la demande d'éthique du projet de recherche ci-nommé.

L'approbation est valide pour la durée indiquée plus haut et est sujette aux conditions énumérées dans la section intitulée "Conditions Spéciales ou Commentaires". Le formulaire « Renouvellement ou Fermeture de Projet » doit être complété quatre semaines avant la date d'échéance indiquée ci-haut afin de demander un renouvellement de cette approbation éthique ou afin de fermer le dossier.

Toutes modifications apportées au projet doivent être approuvées par le CÉR avant leur mise en place, sauf si le participant doit être retiré en raison d'un danger immédiat ou s'il s'agit d'un changement ayant trait à des éléments administratifs ou logistiques du projet. Les chercheurs doivent aviser le CÉR dans les plus brefs délais de tout changement pouvant augmenter le niveau de risque aux participants ou pouvant affecter considérablement le déroulement du projet, rapporter tout évènement imprévu ou indésirable et soumettre toute nouvelle information pouvant nuire à la conduite du projet ou à la sécurité des participants.

The University of Ottawa Research Ethics Board, which operates in accordance with the *Tri-Council Policy Statement* (2014) and other applicable laws and regulations, has examined and approved the ethics application for the above-named research project.

Ethics approval is valid for the period indicated above and is subject to the conditions listed in the section entitled "Special Conditions or Comments". The "Renewal/Project Closure" form must be completedfour weeks before the above-referenced expiry date to request a renewal of this ethics approval or closure of the file.

Any changes made to the project must be approved by the REB before being implemented, except when necessary to remove participants from immediate endangerment or when the modification(s) only pertain to administrative or logistical components of the project. Investigators must also promptly alert the REB of any changes that increase the risk to participant(s), any changes that considerably affect the conduct of the project, all unanticipated and harmful events that occur, and new information that may negatively affect the conduct of the project or the safety of the participant(s).

Marc Alain BONENFANT
Coordonnateur de l'éthique / Ethics Coordinator
Pour/For **Daniel LAGAREC** Président(e) du/ Chair of the **Comité d'éthique de la recherche en sciences sociales et humanités / Social Sciences and Humanities Research Ethics Board**

APPENDIX III: JUSTIFICATION FOR DEFERRED CONSENT

A Deferred consent model was used for the following reasons:

1. The CHEO PICU has a large referral area, meaning many patients are transferred urgently from outlying areas. Legal guardians do not always accompany the patients during transfer and arrive to CHEO at a later time. In cases where the legal guardian does accompany the patient, transfers often occur overnight and once the patient is stable (the ideal time to approach for consent), the legal guardians leave the PICU to eat, sleep, arrange accommodations, and sometimes travel home to attend to affairs.
2. Many of the patients admitted to the CHEO PICU suffer from chronic illness and are in and out of hospital frequently. The guardians of these patients are often very comfortable with the hospital environment and continue to work during their child's hospitalization, only visiting during the evenings or weekends when study staff are not available.
3. Generally, the first part of PICU admission is when patients are most unstable and require active resuscitation. During this time, legal guardians are very distressed, particularly in acute cases, and it is difficult to approach them for consent. Distress has been shown to impact the ability of legal guardians to comprehend or even remember giving consent (Menon et al., 2012), thus approaching during this delicate time has implications for the « informed » aspect of informed consent.
4. Many patients are in isolation, making it difficult to speak with both the circle of care to obtain permission to approach, and difficult to approach and follow up with the legal guardian to see what they have decided regarding participation.

APPENDIX IV: ENGLISH CONSENT FORM

Information & consent form

Protocol Title: Assessing nutritional status of children admitted to the pediatric intensive care unit

Site Investigator: Dr. Dayre McNally, MD

Children's Hospital of Eastern Ontario (CHEO), Department of Pediatric Intensive Care, 401 Smyth Road, Ottawa, ON K1H 8L1,

Other investigators:
Alexandra Dubuc, RD, MSc candidate
Graduate Studies University of Ottawa, (

Pauline B. Darling, PhD, RD
Assistant professor, School of Nutrition Sciences, University of Ottawa,

Julie Larocque, RD
Clinical dietitian, Pediatric Intensive Care Unit, Children's Hospital of Eastern Ontario,

Solange Lamont, RD, CDE
Coordinator and professional practice leader- Dietitians, Children's Hospital of Eastern Ontario,

Katie O'Hearn, MSc
Research Coordinator, Pediatric Intensive Care Unit, Children's Hospital of Eastern Ontario,

For more simplicity, the word "you", when used in this form, means "yourself" or "your child".

You are being invited to join a research study about assessing the nutritional status of children at the beginning and at the end of their stay in the pediatric intensive care unit (PICU). You are being invited to join this study because you have been admitted to the PICU) and your doctor thinks that you will stay in the PICU for more than 48 hours.

Before agreeing to take part in this study, it is important that you read and understand this document. Taking part in this study is voluntary. Your decision to participate or not in this study will not affect the care you receive at CHEO. You are free to withdraw from the study at any time and there will be no penalty to you or your child.

Why is this study being done?

Nutrition is very important for children in the PICU and we do not know the number of children who arrive at the hospital with malnutrition. Malnutrition can be caused by many factors, such as

infection, chronic illness, inflammation, or not taking in enough nutrients. In the PICU, children with malnutrition may take a longer time to get better, need more help with their breathing, stay in the hospital longer, or get more frequent or more serious infections.

This study is being done because we do not know for certain how many children are admitted to the PICU in Canada with malnutrition. This information will help us to find out if children are being fed properly while they are in the PICU and what the care team can do to improve the nutrition of children admitted to the PICU in the future.

How many people will participate?

At CHEO, we expect to have 81 people participate. The study is expected to be recruiting for 8 to 12 months.

What will I have to do?

- At the beginning of your stay in the PICU, we will measure:
    - How much you weigh by using the scale that is attached to your bed or a chair that can measure how much you weigh. (5 minutes)
    - How tall you are by sliding a measuring board under you while you lie in bed. If you can't lie flat on the bed because of a medical condition, the height between your foot and your knee will be measured using a measuring tape. (5 minutes)
    - The length around the middle of your upper arm using a measuring tape. The measurement will be repeated twice. (10 minutes)
    - The length around your head if you are less than 3 years old, using a tape measure.
    - Your body fat at four areas on your body: your arm, your thigh, under your waist and on your back. These measurements will be made by using a special instrument to gently grasp your skin for a few seconds. Each of these areas will be measured twice. (15 minutes)
    - When possible, the strength of your hand muscles will be measured by having you squeeze a handle as hard as you can for a few seconds. Measurement will be repeated 3 times. (10 minutes)
- All the above measurements should take a maximum of 45 minutes.
- All of these measurements will be repeated again just before you leave the pediatric intensive care unit.
- Your health records will be looked at to see other weights documented, the amount of food you eat, other conditions you may have, the reason why you are in the hospital, if you have an infection and pressure sores, medications prescribed, the number of days you may need help breathing, the number of days you stay in the PICU and the hospital, and where you are going after you leave the hospital
- You will also be asked to fill out a short questionnaire regarding your ethnicity. You do not have to fill out this questionnaire if you do not wish to.

- After you leave the PICU, if you are still in the hospital, and if you agree, we will come see you once every week on the general ward and perform the same measurements to see if there are changes.

These measurements are being done for research purposes but will not interfere with the care provided.

When?	Content of visit	Duration of visit
Admission to PICU	Weight How tall you are Length around your arm Length around your head Amount of fat on your body The strength of your hand	45 minutes
Discharge from PICU	Weight How tall you are Length around your arm Length around your head Amount of fat on your body The strength of your hand	45 minutes
Weekly after PICU discharge, if child is still in the hospital until hospital discharge	Weight How tall you are Length around your arm Length around your head Amount of fat on your body The strength of your hand	45 minutes

If you decide to participate in this study, you will be asked to let the researcher do the measurements listed above when you arrive and just before you leave the PICU and once per week on the general ward if you stay at the hospital. If you are eating normal food and have food brought to you from outside the hospital, you will also be asked to keep a food journal for 2-week days and 1 weekend day every week until you leave the hospital. We will also ask you to keep your food wrappers and place them in the envelope placed on the bed side table.

Are there any risks to participating?

There are no foreseeable risks to participate in this study. The only discomfort might be related to measurements of the amount of fat on your body as they may cause redness at the area where the special instrument will be placed. Redness will disappear within a few seconds after the measurements are done. To minimize redness, measurements will be performed by alternating between the three sites and by waiting at least 15 seconds before performing another skinfold measurement.

Are there any benefits to participating?

If you decide to participate, you may or may not benefit from participating in this study; However, with this study we hope to improve future care of children in the PICU.

Will I be paid to participate?

You will not be paid to take part in this study.

Can I Withdraw?

You can withdraw from the study at any time without any impact to your current or future care at CHEO. Please discuss with your investigator if you would like to withdraw. If you withdraw your consent, the investigator will no longer collect, and disclose your health information for the purpose of this study. Information that was already collected will still be used by the Investigator.

What if I get injured?

In the event that you or your child suffers injury as a direct result of participating in this study, normal legal rules on compensation will apply. Medical care will be provided to you or your child. By signing this consent form you are in no way waiving your legal rights or releasing the investigator from their legal and professional responsibilities.

Will I be told about new information?

We will inform you of any new information that might change your decision to continue to participate in this research project. We will ask you again if you still want to be in the study.

The results of the PICU admission assessment (i.e. child's nutrition status) will be fed back to the Most Responsible Physician (MRP) and the care team. The MRP will be free to use this information to guide the child's care as they see fit, and can make a determination whether the malnutrition is related to disease or caregiver factors.

You can receive a copy of the study results at the end of the study. Please let the study team know if you like to receive a copy.

What about confidentiality and privacy?

Your personal information will be kept strictly confidential except as required or permitted by law. Any information that would indicate that a child was being harmed or at risk of such harm, would not be kept confidential and instead be disclosed as appropriate to the appropriate authorities.

For this study we will be collecting these personal identifiers: name, sex, date of birth, medical record number, and ethnicity for the research purposes described in this consent form. Your personal identifiers will be kept in a document that links this information with a study ID, called a master list. The study ID will be used in all of the research documents instead of your name to protect your privacy. The master list will be stored separately from the research data. It will be stored in a locked office at CHEO with access restricted to researcher and supervisor.

Representatives from the CHEO Research Ethics Board, a quality reviewer from CHEO Research Institute, and University of Ottawa Research Ethics Board may look at your records at the site where these records are held, to check that the study is following the proper laws and guidelines.

The research data produced from this study will be stored in a secure cabinet in a locked office at Roger-Guidon at the University of Ottawa. Before leaving CHEO, study data will be de-identified, this means that any personal information (i.e name, date of birth, medical record number) will be coded with a study ID so that you cannot be identified by name. Only members of the research team and the individuals described above will have access to the data. Following completion of the study the research data and master list will be kept for 7 years after the last publication of this study. They will then be destroyed. You will not be identified in any publication or presentation of this study.

A copy of the signed consent form will be provided to you.

Is the research team benefiting from the study?

- The research team members are not benefiting personally, financially or in some other way from this study.

What if I have questions?

If you have any questions concerning participation in this study contact:

Dr. Dayre McNally at phone number OR

Alexandra Dubuc, RD at phone number

This study has been reviewed and approved by the CHEO Research Ethics Board. The CHEO Research Ethics Board is a committee of the hospital that includes individuals from different professional backgrounds. The Board reviews all human research that takes place at the hospital. Its goal is to ensure the safety of people taking part in research. The Board's work is

not meant to replace a parent or child's decisions and choices that are best for them. You may contact the Research Ethics Board for information regarding a patient's rights in research studies at (613) 737-7600 (3272), although this person cannot provide any health-related information about the study.

Consent form Signatures

By signing this consent form I agree that:

- I am voluntarily agreeing to participate in this research study;
- I understand the information within this consent form;
- All of the risks and benefits of participation have been explained to me;
- All of my questions have been answered;
- I agree that the research team visit me weekly on a general ward following my PICU discharge to take my measurements, if I am still in the hospital;
- I allow access to my medical records and/or personal information as described in this consent form;
- I do not give up my legal rights by signing this form.

Pre-enrollment from cardiovascular clinic:

☐ Verbal consent was obtained. Participant will sign consent form at pre-surgical appointment (or next visit at CHEO).

A copy of the signed Information Sheet and/or Consent Form will be provided to me.

Signatures

Obtain the appropriate signatures, which should be based on capacity.

Printed Participant's Name	Participant's Signature	Date

Printed Parent's Name	Parental Signature	Date

Printed Name of Person Who Conducted Consent Discussion	Signature of Person Who Conducted Consent Discussion	Date

Use this section if a translator or impartial witness is required.

If the consent discussion has been conducted in a language other than English, and an impartial qualified translator is required.

Printed Name of Translator	Translator Signature	Date

The “Signature of the Witness” line is intended for an impartial witness which is necessary when either the subject or the subject’s legally authorized representative (LAR) speaks and understands English, but cannot read and write or is visually impaired

Printed Witness Name	Signature of Witness	Date

APPENDIX V: FRENCH CONSENT FORM

Formulaire d'information et de consentement

Titre du protocole : Évaluation de l'état nutritionnel des patients admis à l'unité de soins intensifs pédiatrique

Investigateur principal : Dr. Dayre McNally

Centre Hospitalier pour Enfants de l'Est Ontarien (CHEO), Département pédiatrique des soins intensifs, 401 Smyth Road, Ottawa, ON, K1H 8L1,

Autres Investigateurs :

Alexandra Dubuc, RD, MSc candidate
Étude Gradué à l'Université d'Ottawa,

Pauline B. Darling, PhD, RD
Professeure adjointe, École des sciences de la nutrition, Université d'Ottawa,

Julie Larocque, RD
Diététiste clinique, Unité des soins intensifs, Centre Hospitalier pour Enfants de l'Est Ontarien,

Solange Lamont, RD, CDE
Coordonnatrice et leader de la pratique professionnelle – Diététiste, Centre Hospitalier pour Enfants de l'Est Ontarien,

Katie O'Hearn, MSc
Coordonnatrice de recherche, Unité des soins intensifs, Centre Hospitalier pour Enfants de l'Est Ontarien,

Lorsque le mot « vous » est utilisé dans ce document, cela implique « vous-même » ou « votre enfant ».

Vous êtes invités à participer à une étude sur l'évaluation de l'état nutritionnel des enfants au début et à la fin de leur séjour à l'unité de soins intensifs pédiatriques (USIP). Vous êtes invité à

vous joindre à cette étude parce que vous avez été admis à l'USIP et votre médecin pense que vous demeurerez à l'USIP pendant plus de 48 heures.

Avant d'accepter de participer à cette étude, il est important que vous lisiez et compreniez ce document. Participer à cette étude est volontaire. Votre décision de participer ou non à cette étude n'affectera pas les soins que vous recevez à CHEO. Vous êtes libre de vous retirer de l'étude à tout moment et il n'y aura pas de pénalité pour vous ou votre enfant.

Le but de l'étude

La nutrition est très importante pour les enfants de l'USIP et présentement, nous ne connaissons pas le nombre d'enfants qui arrivent à l'hôpital en état de malnutrition. La malnutrition peut être causée par de nombreux facteurs, comme une infection, une maladie chronique, une inflammation, ou ne pas absorber suffisamment de nutriments. À l'USIP, les enfants souffrant de malnutrition peuvent prendre plus de temps pour se rétablir, avoir besoin d'une plus grande aide pour respirer, rester plus longtemps à l'hôpital ou contracter des infections plus fréquentes ou plus graves.

Nous effectuons cette étude parce que nous ne savons pas avec certitude combien d'enfants sont admis à l'USIP au Canada avec la malnutrition. Cette information nous aidera afin de déterminer si les enfants sont bien nourris pendant qu'ils sont admis à l'USIP et ce que l'équipe de soins peut faire pour améliorer la nutrition des enfants admis à l'USIP à l'avenir.

Combien de personnes vont participer à cette étude ?

À CHEO, nous prévoyons que 81 personnes participent à cette étude. L'étude devrait recruter des participants pendant 8 à 12 mois.

Qu'est-ce que je vais devoir faire ?

- Au début de votre séjour à l'USIP, nous mesurerons :
    - Combien vous pesez en utilisant la balance qui est intégrée à votre lit ou une chaise qui peut mesurer combien vous pesez. (5 minutes)
    - Votre taille en glissant une planche de mesure en-dessous de vous pendant que vous êtes au lit. Si vous ne pouvez pas vous allonger sur le lit à cause d'un problème de santé, la hauteur entre votre pied et votre genou sera mesurée à l'aide d'un ruban à mesurer. (5 minutes)
    - La circonférence du milieu de votre bras en utilisant un ruban à mesurer. La mesure sera répétée deux fois. (10 minutes)

- La circonférence autour de votre tête si vous avez moins de 3 ans, en utilisant un ruban à mesurer.
- La quantité de gras à quatre endroits sur votre corps: votre bras, votre cuisse, votre taille et votre dos. Ces mesures seront faites en utilisant un instrument spécial pour saisir doucement votre peau pendant quelques secondes. Chacune de ces zones sera mesurée deux fois. (15 minutes)
- Lorsque ce sera possible, la force des muscles de votre main sera mesurée en serrant la poignée d'un instrument aussi fort que vous le pouvez pendant quelques secondes. La mesure sera répétée 3 fois. (10 minutes)

- Toutes les mesures ci-dessus devraient durer au maximum 45 minutes.
- Toutes ces mesures seront répétées juste avant de quitter l'unité de soins intensifs pédiatriques.
- Vos dossiers de santé seront examinés pour voir d'autres poids documentés, la quantité de nourriture que vous mangez, d'autres conditions que vous pourriez avoir, la raison pour laquelle vous êtes à l'hôpital, si vous avez une infection ou des plaies de lit, les médicaments prescrits, le nombre de jours où vous pourriez avoir besoin d'aide pour respirer, le nombre de jours où vous demeurez à l'USIP ainsi qu'à l'hôpital, et où vous allez après votre départ de l'hôpital
- Il vous sera également demandé de remplir un court questionnaire concernant votre ethnicité. Vous n'êtes pas obligé de remplir ce questionnaire si vous ne le souhaitez pas.
- Après votre départ de l'USIP, si vous êtes encore à l'hôpital, et si vous êtes d'accord, nous viendrons vous voir une fois par semaine dans l'unité de médecine générale et effectuerons les mêmes mesures pour voir s'il y a des changements.

Ces mesures sont effectuées à des fins de recherche mais n'interféreront pas avec les soins fournis.

Quand?	**Contenu de la visite**	**Durée de la visite**
Admission à l'USIP	Poids Taille/longueur Circonférence autour du bras Circonférence autour de la tête Quantité de graisse sur le corps La force de la main	45 minutes
Départ de l'USIP	Poids Taille/longueur Circonférence autour du bras Circonférence autour de la tête Quantité de graisse sur le corps La force de la main	45 minutes

Chaque semaine suivant le congé des soins intensifs, si vous êtes toujours admis à l'hôpital	Poids Taille/longueur Circonférence autour du bras Circonférence autour de la tête Quantité de graisse sur le corps La force de la main	45 minutes

Si vous décidez de participer à cette étude, on vous demandera de laisser le chercheur faire les mesures énumérées ci-dessus à votre arrivée, juste avant de quitter l'USIP, et une fois par semaine dans l'unité de médecine générale si vous êtes toujours à l'hôpital. Si vous mangez de la nourriture normale et que vous recevez de la nourriture de l'extérieur de l'hôpital, on vous demandera de tenir un journal alimentaire pour 2 jours de semaine et 1 jour de fin de semaine, et ce, chaque semaine jusqu'à ce que vous quittiez l'hôpital. Nous vous demanderons également de conserver vos emballages de nourriture et de les placer dans l'enveloppe placée sur votre table de chevet.

Y-a-t-il des risques à participer à cette étude?

Il n'y a pas de risques prévisibles à participer à cette étude. Le seul inconfort pourrait être lié aux mesures de la quantité de graisse sur votre corps, car ils peuvent provoquer des rougeurs à la zone où l'instrument spécial sera placé. La rougeur disparaîtra quelques secondes après que les mesures aient été effectuées. Pour minimiser les rougeurs, les mesures seront effectuées en alternant entre les quatre sites et en attendant au moins 15 secondes avant d'effectuer une autre mesure de pli cutané.

Y-a-t-il des bénéfices à participer à cette étude?

Si vous décidez de participer, vous pouvez ou non bénéficier de votre participation à cette étude; Cependant, avec cette étude, nous espérons améliorer les soins futurs des enfants de l'USIP.

Serai-je payé pour participer?

Vous ne serez pas payé pour participer à cette étude.

Puis-je me retirer de l'étude?

Vous pouvez vous retirer de l'étude à tout moment sans que cela ait un impact sur vos soins actuels ou futurs à CHEO. S'il vous plaît discuter avec l'investigateur si vous souhaitez vous retirer. Si vous retirez votre consentement, l'investigateur ne recueillera plus et ne divulguera pas vos informations de santé aux fins de cette étude. Les informations déjà recueillies seront toujours utilisées par l'investigateur.

Qu'arrivera-t-il si je me blesse ?
Dans le cas où vous ou votre enfant subissiez une blessure résultant directement de sa participation à cette étude, les règles légales normales en matière d'indemnisation s'appliqueront. Des soins médicaux vous seront prodigués à vous ou à votre enfant. En signant ce formulaire de consentement, vous ne renoncez en aucun cas à vos droits légaux ou libérez l'investigateur de ses responsabilités légales et professionnelles.

Serai-je informé de nouvelles informations?
Nous vous informerons de toute nouvelle information susceptible de changer votre décision de continuer à participer à ce projet de recherche. Nous vous demanderons à nouveau si vous voulez toujours participer à l'étude.

Les résultats de l'évaluation d'admission à l'USIP (c'est-à-dire l'état nutritionnel de l'enfant) seront communiqués au médecin responsable (MR) et à l'équipe de soins. Le MR sera libre d'utiliser cette information pour guider les soins de l'enfant comme bon lui semble, et pourra déterminer si la malnutrition est liée à la maladie ou aux facteurs du soignant.

Vous pouvez recevoir une copie des résultats de l'étude à la fin de l'étude. Veuillez indiquer à l'équipe de recherche si vous souhaitez en recevoir une copie.

Qu'en est-il de la confidentialité et de la vie privée?

Vos informations personnelles resteront strictement confidentielles sauf si requis ou permis par la loi. Toute information qui indiquerait qu'un enfant a été blessé ou risque de subir un tel préjudice ne serait pas gardée confidentielle et serait plutôt divulguée aux autorités compétentes.

Pour cette étude, nous allons recueillir ces identifiants personnels: nom, sexe, date de naissance, numéro de dossier médical et origine ethnique aux fins de recherche décrites dans ce formulaire de consentement. Vos identifiants personnels seront conservés dans un document qui lie ces informations avec un ID d'étude, appelé liste principale. L'identifiant de l'étude sera utilisé dans tous les documents de recherche au lieu de votre nom pour protéger votre vie privée. La liste principale sera stockée séparément des données de recherche. Il sera entreposé dans un bureau fermé à CHEO avec un accès restreint au chercheur et au superviseur.

Des représentants du Comité d'éthique de la recherche de CHEO, un examinateur de la qualité de l'institut de recherche de CHEO et le Comité d'éthique de la recherche de l'Université d'Ottawa peuvent consulter vos dossiers sur le site où ces documents sont conservés afin de vérifier que l'étude respecte les lois et les lignes directrices.

Les données de recherche produites dans le cadre de cette étude seront conservées dans une armoire sécurisée dans un bureau fermé à clé à Roger-Guidon, à l'Université d'Ottawa. Avant de

quitter CHEO, les données de l'étude seront anonymisées, ce qui signifie que toute information personnelle (nom, date de naissance, numéro d'enregistrement médical) sera codée avec un numéro d'identification de sorte que vous ne pouvez pas être identifié par votre nom. Seuls les membres de l'équipe de recherche et les personnes décrites ci-dessus auront accès aux données. Une fois l'étude terminée, les données de recherche et la liste principale seront conservées pendant 7 ans après la dernière publication de cette étude. Ils seront ensuite détruits. Vous ne serez identifié dans aucune publication ou présentation de cette étude.

Une copie du formulaire de consentement signé vous sera fournie.

L'équipe de recherche bénéficie-t-elle de l'étude ?
Les membres de l'équipe de recherche ne bénéficient pas personnellement, financièrement ou d'une autre manière de cette étude.

Et si j'ai des questions?

Si vous avez des questions concernant la participation à cette étude, contactez: Dr. Dayre McNally au numéro de téléphone OU

Alexandra Dubuc, RD au numéro de téléphone

Cette étude a été examinée et approuvée par le comité d'éthique de la recherche de CHEO. Le comité d'éthique de la recherche de CHEO est un comité de l'hôpital qui comprend des personnes de différents milieux professionnels. Le conseil examine toutes les recherches sur les humains qui ont lieu à l'hôpital. Son objectif est d'assurer la sécurité des personnes participant à la recherche. Le travail du Conseil n'a pas pour but de remplacer les décisions et les choix des parents ou des enfants qui leur conviennent le mieux. Vous pouvez communiquer avec le Comité d'éthique de la recherche pour obtenir des renseignements sur les droits d'un patient en matière de recherche au (613) 737-7600 (3272), bien que cette personne ne puisse fournir aucune information sur la santé concernant l'étude.

Signature du formulaire de consentement
En signant ce formulaire de consentement, j'accepte que :
• J'accepte volontairement de participer à cette étude de recherche ;
• Je comprends l'information contenue dans ce formulaire de consentement.
• Tous les risques et avantages de la participation m'ont été expliqués ;
• Toutes mes questions ont été répondues ;

• Je suis d'accord que l'équipe de recherche me rende visite chaque semaine dans une unité de médecine général après mon congé de l'USIP pour prendre mes mesures, si je suis encore à l'hôpital ;
• J'autorise l'accès à mes dossiers médicaux et / ou à mes renseignements personnels tel que décrit dans le présent formulaire de consentement ;
• Je n'abandonne pas mes droits légaux en signant ce formulaire.

Pré-inscription de la clinique cardiovasculaire :

☐ Le consentement verbal a été obtenu. Le participant doit signer le formulaire de consentement à un rendez-vous pré-chirurgical (ou la prochaine visite au CHEO).

Une copie de la feuille d'information signée et / ou du formulaire de consentement me sera fournie.

Signatures

Obtenir les signatures appropriées, qui devraient être basées sur la capacité.

Nom du participant en lettres moulues	Signature du participant	Date

Nom du parent en lettres moulues	Signature du parent	Date

Nom en lettres moulues de la personne qui a mené la discussion sur le consentement	Signature de la personne qui a mené la discussion sur le consentement	Date

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Utiliser cette section si un traducteur ou témoin impartial est requis

Si la discussion sur le consentement a été menée dans une langue autre que le français, un traducteur qualifié impartial est requis.

Nom en lettres moulues du traducteur	Signature du traducteur	Date

La ligne «Signature du témoin» est destinée à un témoin impartial qui est nécessaire lorsque le sujet ou son représentant légal (RL) parle et comprend le français, mais ne sait ni lire ni écrire, ou est malvoyant

Nom en lettres moulues du témoin	Signature du témoin	Date

APPENDIX VI: ENGLISH DEFERRED CONSENT FORM

Information & deferred consent form

Protocol Title: Assessing nutritional status of children admitted to the pediatric intensive care unit

Site Investigator: Dr. Dayre McNally, MD

Children's Hospital of Eastern Ontario (CHEO), Department of Pediatric Intensive Care, 401 Smyth Road, Ottawa, ON K1H 8L1

Other investigators:
Alexandra Dubuc, RD, MSc candidate
Graduate Studies University of Ottawa

Pauline B. Darling, PhD, RD
Assistant professor, School of Nutrition Sciences, University of Ottawa

Julie Larocque, RD
Clinical dietitian, Pediatric Intensive Care Unit, Children's Hospital of Eastern Ontario

Solange Lamont, RD, CDE
Coordinator and professional practice leader- Dietitians, Children's Hospital of Eastern Ontario

Katie O'Hearn, MSc
Research Coordinator, Pediatric Intensive Care Unit, Children's Hospital of Eastern Ontario

For more simplicity, the word "you", when used in this form, means "yourself" or "your child".

Introduction

While your child was very sick and receiving emergency treatment, your child's doctor agreed to enter your child into a research study called the NUTRIPIC Study. This study is being led by Dr. Dayre McNally, MD at CHEO and includes all patients from 1 month to less than 18 years of age being admitted to the pediatric intensive care unit (PICU) with an estimated stay of more than 48h. A participant's consent is typically obtained prior to any study procedures being completed however in certain situations this is not possible which was the case for your child. Because your child was extremely ill and receiving emergency treatment at the time that they became eligible to enter this study, it was not possible to obtain informed consent from you before completing this study's first set of research assessments on your child. This process of allowing your doctor to decide if your child is appropriate for this study, enrolling your child first, and then getting your permission later, is accepted by families, healthcare teams and research ethics boards and is used in research in emergency settings.

However, your decision to continue participating in this study is voluntary. We will now inform you about the details of the study so that you understand what the NUTRIPIC Study is about, have an opportunity to ask us questions, and if you agree, for you to give us permission for your child's ongoing participation in the study. The decision to allow for your child's continued participation in this study is fully voluntary (your choice). If you decide not to participate, any data collected so far about your child will be deleted at your request.

We realise that this is a very stressful time for you and we thank you for taking the time to consider ongoing participation in this study.

Before agreeing to take part in this study, it is important that you read and understand this document. Taking part in this study is voluntary. Your decision to participate or not in this study will not affect the care you receive at CHEO. You are free to withdraw from the study at any time and there will be no penalty to you or your child. However, data that has been collected with your child after you have given your consent will be kept for the purpose of this study and no other measurements will be taken. If you do not agree that your child participate in this study, data that has already been taken will be destroyed.

Why is this study being done?

Nutrition is very important for children in the PICU and we do not know the number of children who arrive at the hospital with malnutrition. Malnutrition can be caused by many factors, such as infection, chronic illness, inflammation, or not taking in enough nutrients In the PICU, children with malnutrition may take a longer time to get better, need more help with their breathing, stay in the hospital longer, or get more frequent or more serious infections.

This study is being done because we do not know for certain how many children are admitted to the PICU in Canada with malnutrition. This information will help us to find out if children are being fed properly while they are in the PICU and what the care team can do to improve the nutrition of children admitted to the PICU in the future.

How many people will participate?

At CHEO, we expect to have 81 people participate. The study is expected to be recruiting for 8 to 12 months.

What will I have to do?

When you arrived in the PICU, we measured:

- How much you weighed by using the scale that is attached to your bed or a chair that can measure how much you weight. (5 minutes)

- How tall you are by sliding a measuring board under you while you laid in bed. If you could not lie flat on the bed because of a medical condition, the height between your foot and your knee was measured using a measuring tape. (5 minutes)
- The length around the middle of your upper arm using a measuring tape in the middle of your arm. The measurement was repeated twice. (10 minutes)
- The length around your head if you were less than 3 years old, using a tape measure.
- Your body fat at four areas on your body: your arm, your thigh, under your waist and on your back. These measurements were done by using a special instrument that gently grasps your skin for a few seconds. Each of these areas will be measured twice. (15 minutes)
- If possible, the strength of your hand muscle was measured by having you squeeze a handle as hard as you could for a few seconds. Measurement was repeated 3 times. (10 minutes)

- All the above procedures took a maximum of 45 minutes.

As part of your participation in this study, we would ask you to:

- Let us repeat all measurements that were performed when you arrived in the PICU, just before you leave the PICU.
- Permit the collection of information from your medical chart. Your health records will be looked at to see other weights documented, the amount of food you eat, other conditions you may have, the reason why you are in the hospital, if you have an infection and pressure sores, medications prescribed, the number of days you may need help breathing, the number of days you stay in the PICU and the hospital, and where you are going after you leave the hospital
- Fill out a short questionnaire regarding your ethnicity. You do not have to fill out this questionnaire if you do not wish to.

- After you leave the PICU, if you are still in the hospital, and if you agree, we will come see you once every week on the general ward and perform the same measurements to see if there are changes.

These procedures are being done for research purposes but will not interfere with the care provided.

When?	Content of visit	Duration of visit
Admission to PICU (Before consent was obtained)	Weight How tall you are Length around your arm Length around your head Amount of fat on your body	45 minutes

	The strength of your hand	
Discharge from PICU (After consent is obtained)	Weight How tall you are Length around your arm Length around your head Amount of fat on your body The strength of your hand	45 minutes
Weekly after PICU discharge, if child is still in the hospital until hospital discharge	Weight How tall you are Length around your arm Length around your head Amount of fat on your body The strength of your hand	45 minutes

If you decide to participate in this study, you will be asked to let the researcher use the information from the measurements listed above completed when you arrived and to have the measurements completed just before you leave the PICU and once per week on the general ward if you stay at the hospital. If you are eating normal food and have food brought to you from outside the hospital, you will also be asked to keep a food journal for 2-week days and 1 weekend day every week until you leave the hospital. We will also ask you to keep your food wrappers and place them in the envelope placed on the bed side table.

Are there any risks to participating?

There are no foreseeable risks to participate in this study. The only discomfort might be related to measurements of the amount of fat on your body as they may cause redness at the area where the special instrument will be placed. Redness will disappear within a few seconds after the measurements are done. To minimize redness, measurements will be performed by alternating between the three sites and by waiting at least 15 seconds before performing another skinfold measurement.

Are there any benefits to participating?

If you decide to participate, you may or may not benefit from participating in this study; However, with this study we hope to improve future care of children in the PICU

Will I be paid to participate?

You will not be paid to take part in this study.

Can I Withdraw?

You can withdraw from the study at any time without any impact to your current or future care at CHEO. Please discuss with your investigator if you would like to withdraw. If you withdraw your consent, the investigator will no longer collect, and disclose your health information for the purpose of this study. Information that was already collected will still be used by the Investigator.

What if I get injured?

In the event that you or your child suffers injury as a direct result of participating in this study, normal legal rules on compensation will apply. Medical care will be provided to you or your child. By signing this consent form you are in no way waiving your legal rights or releasing the investigator from their legal and professional responsibilities.

Will I be told about new information?

We will inform you of any new information that might change your decision to continue to participate in this research project. We will ask you again if you still want to be in the study.

You can receive a copy of the study results at the end of the study. Please let the study team know if you like to receive a copy.

What about confidentiality and privacy?

Your personal information will be kept strictly confidential except as required or permitted by law. Any information that would indicate that a child was being harmed or at risk of such harm, would not be kept confidential and instead be disclosed as appropriate to the appropriate authorities.

For this study we will be collecting these personal identifiers: name, sex, date of birth, medical record number, and ethnicity for the research purposes described in this consent form. Your personal identifiers will be kept in a document that links this information with a study ID, called a master list. The study ID will be used in all of the research documents instead of your name to protect your privacy. The master list will be stored separately from the research data. It will be stored in a locked office at CHEO with access restricted to researcher and supervisor.

Representatives from the CHEO Research Ethics Board, a quality reviewer from CHEO Research Institute, and the University of Ottawa Research Ethics Board may look at your records at the site where these records are held, to check that the study is following the proper laws and guidelines.

The research data produced from this study will be stored in a secure cabinet in a locked office at Roger-Guidon at the University of Ottawa. Before leaving CHEO, study data will be de-identified, this means that any personal information (i.e. name, date of birth, medical record

number) will be coded with a study ID so that you cannot be identified by name. Only members of the research team and the individuals described above will have access to the data. Following completion of the study the research data and master list will be kept for 7 years after the last publication of this study. They will then be destroyed. You will not be identified in any publication or presentation of this study.

A copy of the signed consent form will be provided to you.

Is the research team benefiting from the study?

The research team members are not benefiting personally, financially or in some other way from this study.

What if I have questions?

If you have any questions concerning participation in this study contact:

Dr. Dayre McNally at phone number OR

Alexandra Dubuc, RD at phone number

This study has been reviewed and approved by the CHEO Research Ethics Board. The CHEO Research Ethics Board is a committee of the hospital that includes individuals from different professional backgrounds. The Board reviews all human research that takes place at the hospital. Its goal is to ensure the safety of people taking part in research. The Board's work is not meant to replace a parent or child's decisions and choices that are best for them. You may contact the Research Ethics Board, for information regarding a patient's rights in research studies at (613) 737-7600 (3272), although this person cannot provide any health-related information about the study.

Consent form Signatures

By signing this consent form I agree that:

- I am voluntarily agreeing to participate in this research study;
- I understand the information within this consent form;
- All of the risks and benefits of participation have been explained to me;
- All of my questions have been answered;
- I agree that the research team visit me weekly on a general ward following my PICU discharge to take my measurements, if I am still in the hospital;
- I allow access to my medical records and/or personal information as described in this consent form;
- I do not give up my legal rights by signing this form.

A copy of the signed Information Sheet and/or Consent Form will be provided to me.

Signatures

Obtain the appropriate signatures, which should be based on capacity.

Printed Participant's Name	Participant's Signature	Date
Printed Parent's Name	Parental Signature	Date
Printed Name of Person Who Conducted Consent Discussion	Signature of Person Who Conducted Consent Discussion	Date

Use this section if a translator or impartial witness is required.

If the consent discussion has been conducted in a language other than English, and an impartial qualified translator is required.

Printed Name of Translator	Translator Signature	Date

The “Signature of the Witness” line is intended for an impartial witness which is necessary when either the subject or the subject’s legally authorized representative (LAR) speaks and understands English, but cannot read and write or is visually impaired

Printed Witness Name	Signature of Witness	Date

APPENDIX VII: FRENCH DEFERRED CONSENT FORM

Formulaire d'information et de consentement différé

Titre du protocole : Évaluation de l'état nutritionnel des patients admis à l'unité de soins intensifs pédiatrique

Investigateur principal : Dr. Dayre McNally

Centre Hospitalier pour Enfants de l'Est Ontarien (CHEO), Département pédiatrique des soins intensifs, 401 Smyth Road, Ottawa, ON, K1H 8L1

Autres Investigateurs :

Alexandra Dubuc, RD, MSc candidate
Étude Gradué à l'Université d'Ottawa

Pauline B. Darling, PhD, RD
Professeure adjointe, École des sciences de la nutrition, Université d'Ottawa

Julie Larocque, RD
Diététiste clinique, Unité des soins intensifs, Centre Hospitalier pour Enfants de l'Est Ontarien

Solange Lamont, RD, CDE
Coordonnatrice et leader de la pratique professionnelle – Diététiste, Centre Hospitalier pour Enfants de l'Est Ontarien

Katie O'Hearn, MSc
Coordonnatrice de recherche, Unité des soins intensifs, Centre Hospitalier pour Enfants de l'Est Ontarien

Lorsque le mot « vous » est utilisé dans ce document, cela implique « vous-même » ou « votre enfant ».

Introduction

Pendant que votre enfant était très malade et recevait un traitement d'urgence, le médecin de votre enfant a accepté de faire participer votre enfant à une étude de recherche appelée étude NUTRIPIC. Cette étude est menée par le Dr Dayre McNally, MD au CHEO et comprend tous les patients de 1 mois à moins de 18 ans admis à l'unité de soins intensifs pédiatriques (USIP) avec un séjour estimé de plus de 48h. Le consentement d'un participant est généralement obtenu avant l'achèvement de toute procédure d'étude, mais dans certaines situations, cela n'est pas possible, ce qui était le cas pour votre enfant. Parce que votre enfant était extrêmement malade et recevait un traitement d'urgence au moment où il est devenu admissible à cette étude, il n'a pas été possible d'obtenir un consentement éclairé de votre part avant de remplir la première série d'évaluations de votre enfant. Ce processus permettant à votre médecin de décider si votre enfant convient à cette étude, d'inscrire votre enfant en premier et d'obtenir votre permission plus tard, est accepté par les familles, les équipes de soins et les comités d'éthique de la recherche.

Cependant, votre décision de continuer à participer à cette étude est volontaire. Nous allons maintenant vous informer des détails de l'étude afin que vous compreniez l'objet de l'étude NUTRIPIC, que vous ayez l'occasion de nous poser des questions et, si vous êtes d'accord, d'autoriser la participation de votre enfant à l'étude. La décision de permettre à votre enfant de continuer à participer à cette étude est entièrement volontaire (votre choix). Si vous décidez de ne pas participer, toutes les données collectées à ce jour concernant votre enfant seront supprimées à votre demande.

Nous réalisons que c'est une période très stressante pour vous et nous vous remercions d'avoir pris le temps d'envisager une participation continue à cette étude.

Avant d'accepter de participer à cette étude, il est important que vous lisiez et compreniez ce document. Participer à cette étude est volontaire. Votre décision de participer ou non à cette étude n'affectera pas les soins que vous recevez à CHEO. Vous êtes libre de vous retirer de l'étude à tout moment et il n'y aura aucune pénalité pour vous ou votre enfant. Cependant, les données qui ont été recueillies avec votre enfant après que vous avez donné votre consentement seront conservées aux fins de cette étude, par contre aucune autre mesure ne sera prise. Si vous n'êtes pas d'accord à ce que votre enfant participe à cette étude, les données qui ont déjà été prises seront détruites.

Le but de l'étude

La nutrition est très importante pour les enfants de l'USIP et présentement, nous ne connaissons pas le nombre d'enfants qui arrivent à l'hôpital en état de malnutrition. La malnutrition peut être causée par de nombreux facteurs, comme une infection, une maladie chronique, une inflammation, ou ne pas absorber suffisamment de nutriments. À l'USIP, les enfants souffrant de malnutrition peuvent prendre plus de temps pour se rétablir, avoir besoin d'une plus grande aide pour respirer, rester plus longtemps à l'hôpital ou contracter des infections plus fréquentes ou plus graves.

Nous effectuons cette étude parce que nous ne savons pas avec certitude combien d'enfants sont admis à l'USIP au Canada avec la malnutrition. Cette information nous aidera afin de déterminer si les enfants sont bien nourris pendant qu'ils sont admis à l'USIP et ce que l'équipe de soins peut faire pour améliorer la nutrition des enfants admis à l'USIP à l'avenir.

Combien de personnes vont participer à cette étude ?

À CHEO, nous prévoyons que 81 personnes participent à cette étude. L'étude devrait recruter des participants pendant 8 à 12 mois.

Qu'est-ce que je vais devoir faire ?

Lorsque vous êtes arrivé à l'USIP, nous avons mesuré:

- Votre poids en utilisant la balance qui est attachée à votre lit ou une chaise qui peut mesurer combien vous pesez. (5 minutes)
- Votre taille en glissant une planche sous vous pendant que vous étiez au lit. Si vous ne pouviez pas vous allonger à plat sur le lit à cause d'un problème médical, la hauteur entre votre pied et votre genou a été mesurée à l'aide d'un ruban à mesurer. (5 minutes)
- La longueur autour du milieu de votre bras en utilisant un ruban à mesurer. La mesure a été répétée deux fois. (10 minutes)
- La longueur autour de votre tête si vous aviez moins de 3 ans, en utilisant un ruban à mesurer.
- La quantité de graisse corporelle à quatre endroits sur votre corps: votre bras, votre cuisse, votre taille et votre dos. Ces mesures ont été faites en utilisant un instrument spécial qui saisit doucement votre peau pendant quelques secondes. Chacune de ces zones a été mesurées deux fois. (15 minutes)
- Si possible, la force des muscles de votre main a été mesurée en serrant la poignée d'un instrument aussi fort que vous le pouviez pendant quelques secondes. La mesure a été répétée 3 fois. (10 minutes)

• Toutes les procédures ci-dessus ont duré au maximum 45 minutes.

Dans le cadre de votre participation à cette étude, nous vous demandons de:

- Nous laisser répéter toutes les mesures qui ont été effectuées lorsque vous êtes arrivé à l'USIP, et ce, juste avant de quitter l'USIP.
- Permettre la collecte d'informations de votre dossier médical. Votre dossier de santé sera examiné pour voir d'autres poids documentés, la quantité de nourriture que vous mangez, d'autres conditions que vous pourriez avoir, la raison pour

laquelle vous êtes à l'hôpital, si vous avez une infection et des plais de lits, les médicaments prescrits, le nombre de jours où vous pourriez avoir besoin d'aide pour respirer, le nombre de jours où vous demeurez à l'USIP et à l'hôpital, et où vous allez après votre départ de l'hôpital

- Remplir un court questionnaire concernant votre ethnicité. Vous n'êtes pas obligé de remplir ce questionnaire si vous ne le souhaitez pas.

- Après votre départ de l'USIP, si vous êtes encore à l'hôpital, et si vous êtes d'accord, nous viendrons vous voir une fois par semaine dans l'unité de médecine générale et effectuerons les mêmes mesures pour voir s'il y a des changements.

Ces mesures sont effectuées à des fins de recherche mais n'interféreront pas avec les soins fournis.

Quand?	**Contenu de la visite**	**Durée de la visite**
Admission à l'USIP (Avant d'obtenir le consentement)	Poids Taille/longueur Circonférence autour du bras Circonférence autour de la tête Quantité de graisse sur le corps La force de la main	45 minutes
Départ de l'USIP (Après avoir obtenu le consentement)	Poids Taille/longueur Circonférence autour du bras Circonférence autour de la tête Quantité de graisse sur le corps La force de la main	45 minutes
Chaque semaine suivant le congé des soins intensifs, si vous êtes toujours admis à l'hôpital	Poids Taille/longueur Circonférence autour du bras Circonférence autour de la tête Quantité de graisse sur le corps La force de la main	45 minutes

Si vous décidez de participer à cette étude, on vous demandera de laisser le chercheur faire les mesures énumérées ci-dessus à votre arrivée, juste avant de quitter l'USIP, et une fois par semaine dans l'unité de médecine générale si vous êtes toujours à l'hôpital. Si vous mangez de la nourriture normale et que vous recevez de la nourriture de l'extérieur de l'hôpital, on vous demandera de tenir un journal alimentaire pour 2 jours de semaine et 1 jour de fin de semaine, et ce, chaque semaine jusqu'à ce que vous quittiez l'hôpital. Nous vous demanderons également de conserver vos emballages de nourriture et de les placer dans l'enveloppe placée sur votre table de chevet.

Y-a-t-il des risques à participer à cette étude?

Il n'y a pas de risques prévisibles à participer à cette étude. Le seul inconfort pourrait être lié aux mesures de la quantité de graisse sur votre corps, car ils peuvent provoquer des rougeurs à la zone où l'instrument spécial sera placé. La rougeur disparaîtra quelques secondes après que les mesures aient été effectuées. Pour minimiser les rougeurs, les mesures seront effectuées en alternant entre les quatre sites et en attendant au moins 15 secondes avant d'effectuer une autre mesure de pli cutané.

Y-a-t-il des bénéfices à participer à cette étude?

Si vous décidez de participer, vous pouvez ou non bénéficier de votre participation à cette étude; Cependant, avec cette étude, nous espérons améliorer les soins futurs des enfants de l'USIP.

Serai-je payé pour participer?

Vous ne serez pas payé pour participer à cette étude.

Puis-je me retirer de l'étude?

Vous pouvez vous retirer de l'étude à tout moment sans que cela ait un impact sur vos soins actuels ou futurs à CHEO. S'il vous plaît discuter avec l'investigateur si vous souhaitez vous retirer. Si vous retirez votre consentement, l'investigateur ne recueillera plus et ne divulguera pas vos informations de santé aux fins de cette étude. Les informations déjà recueillies seront toujours utilisées par l'investigateur.

Qu'arrivera-t-il si je me blesse ?

Dans le cas où vous ou votre enfant subissiez une blessure résultant directement de sa participation à cette étude, les règles légales normales en matière d'indemnisation s'appliqueront. Des soins médicaux vous seront prodigués à vous ou à votre enfant. En signant ce formulaire de consentement, vous ne renoncez en aucun cas à vos droits légaux ou libérez l'investigateur de ses responsabilités légales et professionnelles.

Serai-je informé de nouvelles informations?

Nous vous informerons de toute nouvelle information susceptible de changer votre décision de continuer à participer à ce projet de recherche. Nous vous demanderons à nouveau si vous voulez toujours participer à l'étude.

Les résultats de l'évaluation d'admission à l'USIP (c'est-à-dire l'état nutritionnel de l'enfant) seront communiqués au médecin responsable (MR) et à l'équipe de soins. Le MR sera libre d'utiliser cette information pour guider les soins de l'enfant comme bon lui semble, et pourra déterminer si la malnutrition est liée à la maladie ou aux facteurs du soignant.

Vous pouvez recevoir une copie des résultats de l'étude à la fin de l'étude. Veuillez indiquer à l'équipe de recherche si vous souhaitez en recevoir une copie.

Qu'en est-il de la confidentialité et de la vie privée?

Vos informations personnelles resteront strictement confidentielles sauf si requis ou permis par la loi. Toute information qui indiquerait qu'un enfant a été blessé ou risque de subir un tel préjudice ne serait pas gardée confidentielle et serait plutôt divulguée aux autorités compétentes.

Pour cette étude, nous allons recueillir ces identifiants personnels: nom, sexe, date de naissance, numéro de dossier médical et origine ethnique aux fins de recherche décrites dans ce formulaire de consentement. Vos identifiants personnels seront conservés dans un document qui lie ces informations avec un ID d'étude, appelé liste principale. L'identifiant de l'étude sera utilisé dans tous les documents de recherche au lieu de votre nom pour protéger votre vie privée. La liste principale sera stockée séparément des données de recherche. Il sera entreposé dans un bureau fermé à CHEO avec un accès restreint au chercheur et au superviseur.

Des représentants du Comité d'éthique de la recherche de CHEO, un examinateur de la qualité de l'institut de recherche de CHEO et le Comité d'éthique de la recherche de l'Université d'Ottawa peuvent consulter vos dossiers sur le site où ces documents sont conservés afin de vérifier que l'étude respecte les lois et les lignes directrices.

Les données de recherche produites dans le cadre de cette étude seront conservées dans une armoire sécurisée dans un bureau fermé à clé à Roger-Guidon, à l'Université d'Ottawa. Avant de quitter CHEO, les données de l'étude seront anonymisées, ce qui signifie que toute information personnelle (nom, date de naissance, numéro d'enregistrement médical) sera codée avec un numéro d'identification de sorte que vous ne pouvez pas être identifié par votre nom. Seuls les membres de l'équipe de recherche et les personnes décrites ci-dessus auront accès aux données. Une fois l'étude terminée, les données de recherche et la liste principale seront conservées pendant 7 ans après la dernière publication de cette étude. Ils seront ensuite détruits. Vous ne serez identifié dans aucune publication ou présentation de cette étude.

Une copie du formulaire de consentement signé vous sera fournie.

L'équipe de recherche bénéficie-t-elle de l'étude ?
Les membres de l'équipe de recherche ne bénéficient pas personnellement, financièrement ou d'une autre manière de cette étude.

Et si j'ai des questions?

Si vous avez des questions concernant la participation à cette étude, contactez: Dr. Dayre McNally au numéro de téléphone OU

Alexandra Dubuc, RD au numéro de téléphone

Cette étude a été examinée et approuvée par le comité d'éthique de la recherche de CHEO. Le comité d'éthique de la recherche de CHEO est un comité de l'hôpital qui comprend des personnes de différents milieux professionnels. Le conseil examine toutes les recherches sur les humains qui ont lieu à l'hôpital. Son objectif est d'assurer la sécurité des personnes participant à la recherche. Le travail du Conseil n'a pas pour but de remplacer les décisions et les choix des parents ou des enfants qui leur conviennent le mieux. Vous pouvez communiquer avec le Comité d'éthique de la recherche pour obtenir des renseignements sur les droits d'un patient en matière de recherche au (613) 737-7600 (3272), bien que cette personne ne puisse fournir aucune information sur la santé concernant l'étude.

Signature du formulaire de consentement

En signant ce formulaire de consentement, j'accepte que :

• J'accepte volontairement de participer à cette étude de recherche ;
• Je comprends l'information contenue dans ce formulaire de consentement.
• Tous les risques et avantages de la participation m'ont été expliqués ;
• Toutes mes questions ont été répondues ;
• Je suis d'accord que l'équipe de recherche me rende visite chaque semaine dans une unité de médecine général après mon congé de l'USIP pour prendre mes mesures, si je suis encore à l'hôpital ;
• J'autorise l'accès à mes dossiers médicaux et / ou à mes renseignements personnels tel que décrit dans le présent formulaire de consentement ;
• Je n'abandonne pas mes droits légaux en signant ce formulaire.

Une copie de la feuille d'information signée et / ou du formulaire de consentement me sera fournie.

Signatures

Obtenir les signatures appropriées, qui devraient être basées sur la capacité.

Nom du participant en lettres moulues	Signature du participant	Date

Nom du parent en lettres moulues	Signature du parent	Date

Nom en lettres moulues de la personne qui a mené la discussion sur le consentement	Signature de la personne qui a mené la discussion sur le consentement	Date

---

Utiliser cette section si un traducteur ou témoin impartial est requis

Si la discussion sur le consentement a été menée dans une langue autre que le français, un traducteur qualifié impartial est requis.

Nom en lettres moulues du traducteur	Signature du traducteur	Date

La ligne «Signature du témoin» est destinée à un témoin impartial qui est nécessaire lorsque le sujet ou son représentant légal (RL) parle et comprend le français, mais ne sait ni lire ni écrire, ou est malvoyant

Nom en lettres moulues du témoin	Signature du témoin	Date

APPENDIX VIII: ENGLISH STUDY PAMPHLET

NUTRIPIC

Pediatric Intensive Care Unit Nutrition Status Study

Where can I get more information?

If you have questions about the study, please contact

- **Dr. Dayre McNally, MD** (Study Doctor), at the Children's Hospital of Eastern Ontario at *phone number*
- **Alexandra Dubuc, RD** (co-Investigator), at the Children's Hospital of Eastern Ontario and Master's Student at the University of Ottawa at *phone number*
- **Julie Larocque, RD** (co-investigator), at the Children's Hospital of Eastern Ontario at *phone number*
- **Katie O'Hearn, MSc** (Study coordinator), at the Children's Hospital of Eastern Ontario at *phone number*

If you have questions about the rights of a research participant, please contact the CHEO Research Ethics Board at *phone number*

P.4

Version date : 12-07-2018

NUTRIPIC

Pediatric Intensive Care Unit Nutrition Status Study

Why did I receive this?

Your child has a severe condition that required an admission to the pediatric intensive care unit (PICU).

During critical illness, your child will undergo a large amount of stress which may cause a deterioration in their nutritional status. If your child is malnourished there may be a higher risk of infection, a higher dependency of mechanical ventilation, loss of muscle mass, and a longer length of hospital stay.

This study is being done to evaluate how many children are malnourished when admitted to the PICU and how many children are malnourished when discharged from the PICU. This study will also evaluate the nutritional status of your child after discharged from the PICU if your child is staying in the hospital.

P.1

Version date : 12-07-2018

NUTRIPIC

Pediatric Intensive Care Unit Nutrition Status Study

What is the study?

This study will evaluate the number of children who are affected by malnutrition at admission and discharge from the pediatric intensive care unit by measuring your child's weight, height/length, mid-upper arm circumference, skinfolds (to measure the amount of fat on your body) and handgrip strength.

We will also be looking into the disease severity, comorbidities, and the amount of food your child is actually eating/being fed.

We are doing this study because we are unsure about the number of children affected by malnutrition in a Canadian PICU. Knowing this information will help improve patient care and help understand how to prevent children from having their nutritional status deteriorate while in the hospital.

What are the Risks and Benefits of participating in this study?

- If you decide to participate, you may or may not benefit from participating in this study; However, with this study we hope to improve future care of children in the PICU.
- There are no foreseeable risks to participate in this study. The only discomfort might be related to measurements of the amount of fat on your body as they may cause redness at the area where the special instrument will be placed. Redness will disappear within a few seconds after the measurements are done.

P.2

Version date : 12-07-2018

NUTRIPIC

Pediatric Intensive Care Unit Nutrition Status Study

What's next?

A participant's consent is typically obtained prior to any study procedures being completed, however in certain situations this is not possible which was the case for your child. Because your child was critically ill and needed to be treated quickly, the research team could not obtain your consent before starting this study's first set of research assessments on your child. It was important for us to complete the study measurements on your as soon as possible upon admission to the PICU.

However, your decision to continue participating in this study is voluntary. You can decide to continue to participate or you can decide to withdraw and remove all of the data that was collected for the study. The decision is yours to make. A member of the research team will come by to answer your questions and ask you about continuing in the study as soon as is convenient for you.

We encourage you to have the healthcare team page the study staff if you are ready to speak to them about the study before the study team comes to speak with you.

The study was designed by doctors and dietitians at CHEO and has been approved by the CHEO Research Ethics Board

P.3

Version date : 12-07-2018

APPENDIX IX: FRENCH STUDY PAMPHLET

NUTRIPIC

Étude sur l'État Nutritionnel des Enfants dans l'Unité de Soins Intensifs Pédiatrique

Où puis-je obtenir plus d'informations?

Si vous avez des questions sur l'étude, veuillez contacter:

- **Dr Dayre McNally, MD** (Médecin en charge de l'étude), au Centre Hospitalier pour Enfants de l'Est Ontarien, au # téléphone
- **Alexandra Dubuc, RD** (co-investigatrice), au Centre Hospitalier pour Enfants de l'Est Ontarien et Étudiante Graduée à l'Université d'Ottawa, au # téléphone
- **Julie Larocques, RD** (co-investigatrice), au Centre Hospitalier pour Enfants de l'Est Ontarien, au # téléphone
- **Katie O'Hearn** (Coordonnatrice de recherche), au Centre Hospitalier pour Enfants de l'Est Ontarien, au # téléphone

Si vous avez des questions sur les droits d'un participant à la recherche, veuillez communiquer avec le Comité d'éthique de la recherche de CHEO au # téléphone

P.4

Version date : 24-07-2018

NUTRIPIC

Étude sur l'État Nutritionnel des Enfants dans l'Unité de Soins Intensifs Pédiatrique

Pourquoi ai-je reçu ce pamphlet?

Votre enfant souffre d'une maladie grave nécessitant une admission à l'unité de soins intensifs pédiatriques (USIP).

Pendant une maladie grave, votre enfant subira une grande quantité de stress qui peut entraîner une détérioration de son état nutritionnel. Si votre enfant est sous-alimenté, il peut y avoir un risque plus élevé d'infection, une plus grande dépendance de la ventilation mécanique, une perte de masse musculaire et une durée d'hospitalisation plus longue.

Cette étude vise à évaluer combien d'enfants sont en état de malnutrition lorsqu'ils sont admis à l'USIP et combien d'enfants souffrent de malnutrition lorsqu'ils obtiennent leur congé de l'USIP. Cette étude évaluera également le changement de l'état nutritionnel de votre enfant après son congé de l'USIP si votre enfant est toujours à l'hôpital.

P.1

Version date : 24-07-2018

NUTRIPIC

Étude sur l'État Nutritionnel des Enfants dans l'Unité de Soins Intensifs Pédiatrique

Quelle est le but de cette étude?

Cette étude évaluera le nombre d'enfants affectés par la malnutrition à l'admission et à la sortie de l'unité de soins intensifs pédiatriques en mesurant le poids, la taille / longueur, la circonférence du bras, les plis cutanés (pour mesurer la quantité de graisse sur votre corps) et la force de la main.

Nous examinerons également la gravité de la maladie, les comorbidités et la quantité de nourriture que votre enfant consomme ou nourrit.

Nous faisons cette étude parce que nous ne sommes pas certains du nombre d'enfants touchés par la malnutrition dans une USIP canadienne. Connaître cette information aidera à améliorer les soins aux patients et aidera à comprendre comment empêcher les enfants d'avoir leur état nutritionnel se détériorer pendant qu'ils sont à l'hôpital.

Quels sont les risques et les avantages de participer à cette étude?

- Si vous décidez de participer, vous pouvez ou non bénéficier de votre participation à cette étude; Cependant, avec cette étude, nous espérons améliorer les soins futurs des enfants de l'USIP.
- Il n'y a pas de risques prévisibles à participer à cette étude. Le seul inconfort pourrait être lié aux mesures de la quantité de graisse sur votre corps car ils peuvent provoquer des rougeurs à la zone où l'instrument spécial sera placé. La rougeur disparaîtra dans quelques secondes après que les mesures sont faites

P.2

NUTRIPIC

Étude sur l'État Nutritionnel des Enfants dans l'Unité de Soins Intensifs Pédiatrique

Quels sont les prochaines étapes?

Le consentement d'un participant est généralement obtenu avant l'achèvement de toute procédure d'étude, mais dans certaines situations, cela n'est pas possible, ce qui était le cas pour votre enfant. Puisque votre enfant était gravement malade et devait être traité rapidement, l'équipe de recherche n'a pas pu obtenir votre consentement avant de commencer la première série de mesures sur votre enfant. Il était important pour nous de compléter les mesures d'étude le plus tôt possible lors de votre admission à l'USIP.

Cependant, votre décision de continuer à participer à cette étude est volontaire. Vous pouvez décider de continuer à participer ou vous pouvez décider de retirer et de supprimer toutes les données collectées pour l'étude. La décision est à vous. Un membre de l'équipe de recherche viendra répondre à vos questions et vous demander de poursuivre l'étude dès que possible.

Nous vous encourageons à demander à l'équipe de soins de santé de consulter le personnel de l'étude si vous êtes prêt à leur parler de l'étude avant que l'équipe d'étude ne vienne vous parler.

L'étude a été conçue par des médecins et des diététistes du CHEO et a été approuvée par le Comité d'éthique de la recherche du CHEO

Version date : 12-07-2018

P.3

APPENDIX X : ENGLISH ETHNICITY QUESTIONNAIRE

Study ID: _____

Date: _____

Ethnicity

What were the ethnic or cultural origins of your child's ancestors?

An ancestor is usually more distant than a grandparent
You can provide more than one answer.

Biological Mother

- ☐ Eastern European (Polish, Russian, Croatian, etc.)
- ☐ Western European (English, French, Portuguese, etc.)
- ☐ East Asian (Chinese)
- ☐ East Asian (Korean)
- ☐ East Asian (Japanese)
- ☐ South Asian (East Indian, Pakistani, Sri Lankan, etc.)
- ☐ Southeast Asian (Vietnamese, Malaysian, Filipino, etc.)
- ☐ West Asian (Iranian, Afghan, Palestinian, etc.)
- ☐ East African (Ethiopian, Kenyan, Somali, etc.)
- ☐ Middle African (Cameroonian, Chadian, Congolese, etc.)
- ☐ Northern African (Moroccan, Algerian, Egyptian, Sudanese, etc.)
- ☐ Southern African (Botswana, South African, etc.)
- ☐ Western African (Ghanaian, Nigerian, Guinean, etc.)
- ☐ Latin American (Argentinean, Costa Rican, Mexican, etc.)
- ☐ Caribbean Region (Jamaican, Trinidadian/Tobagonian, etc.)
- ☐ Indian-Caribbean (Guyana with origins in India)
- ☐ North American Aboriginal (Inuit, Métis, First Nations, etc.)
- ☐ Oceania (Samoan, Fijian, etc.)
- ☐ Australian or New Zealander
- ☐ Other (please specify) _____

- ☐ Unknown

Biological Father

- ☐ Eastern European (Polish, Russian, Croatian, etc.)

- Western European (English, French, Portuguese, etc.)
- East Asian (Chinese)
- East Asian (Korean)
- East Asian (Japanese)
- South Asian (East Indian, Pakistani, Sri Lankan, etc.)
- Southeast Asian (Vietnamese, Malaysian, Filipino, etc.)
- West Asian (Iranian, Afghan, Palestinian, etc.)
- East African (Ethiopian, Kenyan, Somali, etc.)
- Middle African (Cameroonian, Chadian, Congolese, etc.)
- Northern African (Moroccan, Algerian, Egyptian, Sudanese, etc.)
- Southern African (Botswana, South African, etc.)
- Western African (Ghanaian, Nigerian, Guinean, etc.)
- Latin American (Argentinean, Costa Rican, Mexican, etc.)
- Caribbean Region (Jamaican, Trinidadian/Tobagonian, etc.)
- Indian-Caribbean (Guyana with origins in India)
- North American Aboriginal (Inuit, Métis, First Nations, etc.)
- Oceania (Samoan, Fijian, etc.)
- Australian or New Zealander
- Other (please specify) _____

☐ Unknown

Adapted from Omand et al. 2014

☐ **I do not want to respond to this question**

APPENDIX XI : FRENCH ETHNICITY QUESTIONNAIRE

Identifiant : _____

Date : _____

Questionnaire sur l'Ethnicité

Quelles étaient les origines ethniques ou culturelles des ancêtres de votre enfant?

Un ancêtre est habituellement plus éloigné qu'un grands-parents
Vous pouvez fournir plus d'une réponse.

Mère Biologique

- ☐ Européen de l'Est (polonais, russe, croate, etc.)
- ☐ Européen de l'Ouest (Anglais, Français, Portugais, etc.)
- ☐ Asiatique de l'Est (Chinois)
- ☐ Asiatique de l'Est (Coréen)
- ☐ Asiatique de l'Est (Japonais)
- ☐ Asiatique du Sud (Indien de l'Est, Pakistanais, Sri Lankais, etc.)
- ☐ Asiatique du Sud-est (Vietnamien, Malaisien, philippin, etc.)
- ☐ Asiatique de l'Ouest (Iranien, Afghan, Palestinien, etc.)
- ☐ Africain de l'Est (Ethiopien, Kenyan, Somalien, etc.)
- ☐ Africain du Centre (Camerounais, Tchadien, Congolais, etc.)
- ☐ Africain du Nord (Marocain, Algérien, Égyptien, Soudanais, etc.)
- ☐ Africain du Sud (Botswana, Afrique du Sud, etc.)
- ☐ Africain de l'Ouest (Ghanéen, nigérian, guinéen, etc.)
- ☐ Amérique latine (Argentine, Costa Rica, Mexique, etc.)
- ☐ Région des Caraïbes (Jamaïcain, Trinidadien / Tobago, etc.)
- ☐ Indien-Caraïbes (Guyana avec des origines en Inde)
- ☐ Autochtone nord-américain (Inuit, Métis, Premières Nations, etc.)
- ☐ Océanie (Samoan, Fidjien, etc.)
- ☐ Australien ou Néo-Zélandais
- ☐ Autre (veuillez préciser) _____

- ☐ Inconnu

Père Biologique

- ☐ Européen de l'Est (polonais, russe, croate, etc.)

☐ Européen de l'Ouest (Anglais, Français, Portugais, etc.)
☐ Asiatique de l'Est (Chinois)
☐ Asiatique de l'Est (Coréen)
☐ Asiatique de l'Est (Japonais)
☐ Asiatique du Sud (Indien de l'Est, Pakistanais, Sri Lankais, etc.)
☐ Asiatique du Sud-est (Vietnamien, Malaisien, philippin, etc.)
☐ Asiatique de l'Ouest (Iranien, Afghan, Palestinien, etc.)
☐ Africain de l'Est (Ethiopien, Kenyan, Somalien, etc.)
☐ Africain du Centre (Camerounais, Tchadien, Congolais, etc.)
☐ Africain du Nord (Marocain, Algérien, Égyptien, Soudanais, etc.)
☐ Africain du Sud (Botswana, Afrique du Sud, etc.)
☐ Africain de l'Ouest (Ghanéen, nigérian, guinéen, etc.)
☐ Amérique latine (Argentine, Costa Rica, Mexique, etc.)
☐ Région des Caraïbes (Jamaïcain, Trinidadien / Tobago, etc.)
☐ Indien-Caraïbes (Guyana avec des origines en Inde)
☐ Autochtone nord-américain (Inuit, Métis, Premières Nations, etc.)
☐ Océanie (Samoan, Fidjien, etc.)
☐ Australien ou Néo-Zélandais
☐ Autre (veuillez préciser) _____

☐ Inconnu

Adapté de Omand et al. 2014

☐ **Je souhaite ne pas répondre à cette question**

APPENDIX XII : PRISM III SCORE CALCULATION

PRISM III score – severity points (Modified from: Pollack MM, Patel KM, Ruttimann UE. *PRISM III: An updated pediatric risk of mortality score*. Crit Care Med 1996;24:743-52)

Variable	*Neonate < 1 month*	*Infant 1-12 months*	*Child 12-144 months*	*Adolescent >144 months*	*Score*
Systolic BP (mmHg)	40-55	45-65	55-75	65-85	3
	< 40	< 45	< 55	< 65	7
Heart rate (beats per min)[1]	215-225	215-225	185-205	145-155	3
	> 225	> 225	> 205	> 155	4
Creatinine (mg/dL)	> 0,85 or	> 0,90 or	> 0,90 or	> 1,30 or	2
or (μmol/L)	> 75	> 80	> 80	> 115	
Blood urea nitrogen (mg/dL)	> 11,9 or	> 14,9 or	> 14,9 or	> 14,9 or	3
or (mmol/L)	> 4,3	> 5,4	> 5,4	> 5,4	
Prothrombin time (PT) (seconds)	> 22 or	> 22 or	> 22 or	> 22 or	3
or Partial thromboplastin time (PTT) (seconds)	> 85	> 57	> 57	> 57	

Variable	*All other ages*	*Score*
Temperature [2]	< 33°C (91,4°F) **or**> 40,0°C (104,0°F)	3
Mental status (Glasgow coma score) [3]	< 8	5
Pupillary reflexes [4]	One fixed, one reactive	7
	Both fixed	11
PaO_2: mmHg (kPa) [5]	42,0-49,9 (5,6-6,7)	3
	< 42,0 (5,6)	6
PCO_2 : mmHg (kPa) [6]	50,0-75,0 (6,7-10,0)	1
	> 75,0 (10,0)	3
Acidosis (pH or total CO_2) [6]	pH 7,0-7,28 **or** totalCO_2 5-16,9 mmol/L	2
	pH < 7,0 **or** totalCO_2< 5 mmol/L	6
Alcalosis (pH and total CO_2) [6]	pH 7,48-7,55	2
	pH > 7,55	3
	total CO_2> 34,0 mmol/L	4
Potassium : mmol/L = mEq/L	> 6,9	3
Glucose : mmol/L (mg/dL)	> 11,0 (200)	2
White blood cell count (cells/mm^3)	< 3000	4
Platelet count (cells/mm^3)	100 000-200 000	2
	50 000-99 999	4
	< 50 000	5

APPENDIX XIII: PELOD SCORE CALCULATION

Organ dysfunctions and variables[a]	Points by severity levels						
	0	1	2	3	4	5	6
Neurological[b]							
Glasgow coma score	≥11	5-10			3-4		
Pupillary reaction	Both reactive					Both fixed	
Cardiovascular[c]							
Lactemia (mmol/L)	<5.0	5.0-10.9			≥11.0		
Mean arterial pressure (mmHg)							
0 to < 1 month	≥46		31-45	17-30			≤16
1 to 11 months	≥55		39-54	25-38			≤24
12 to 23 months	≥60		44-59	31-43			≤30
24 to 59 months	≥62		46-61	32-44			≤31
60 to 143 months	≥65		49-64	69-48			≤35
≥144 months	≥67		52-66	38-51			≤37
Renal							
Creatinine (μmoL/L)							
0 to < 1 month	≤69		≥70				
1 to 11 months	≤22		≥23				
12 to 23 months	≤34		≥35				
24 to 59 months	≤50		≥51				
60 to 143 months	≤58		≥59				
≥144 months	≤92		≥93				
Respiratory[d]							
PaO_2 (mmHg) /FiO_2	≥61		≤60				
$PaCO_2$ (mmHg)	≤58	59-94		≥95			
Invasive ventilation	no			yes			
Hematological							
White blood cell count ($x10^9$/L)	>2		≤2				
Platelets ($x10^9$/L)	≥142	77-141	≤76				

Reference:
Leteurtre S, Duhamel A, Salleron, J, Grandbastien B, Lacroix J, Leclerc F on behalf of the Groupe Francophone de Reanimation et d'Urgences Pediatriques (GFRUP), PELOD 2: An Update of the PEdiatric Logistic Organ Dysfunction Score. DOI: 10.1097/CCM.0b013e31828a2bbd

APPENDIX XIV: NUTRITIONAL INFORMATION OF ENTERAL FORMULAS PRESCRIBED IN THE PICU

Type of formula	Energy (kcal/mL)	Protein (g/mL)
Expressed Breast Milk	0.67	0.012
Enfamil A+ 20	0.68	0.0135
Enfamil A+ Lactose free	0.68	0.0142
Good Start stage 1 20	0.67	0.015
Good start stage 1 24	0.81	0.0182
Alimentum 20	0.68	0.0186
Puramino 24	0.81	0.023
Neocate Splash	1.0	0.029
Nutren Junior	1.0	0.030
Peptamen Junior	1.0	0.030
Peptamen AF	1.2	0.076
Peptamen w/prebio	1.0	0.040
Peptamen 1.5	1.5	0.068
Compleat	1.0	0.038
Compleat Pediatric	0.42	0.038
Jevity 1.5	1.5	0.064
Peidasure plus fibre	1.5	0.042

APPENDIX XV: ANTHROPOMETRIC MEASUREMENTS DATA COLLECTION FORM

Study ID (Randomization Number)	_____
Date	_____
Weight (kg):	_____
Source	◯ Bed scale ◯ Infant scale ◯ Chair scale ◯ Estimate ◯ Weight from emergency
Bed number	_____
Height (cm)	_____
Height source	◯ Length board ◯ Measuring tape ◯ Estimate ◯ Height from emergency
Type of Length board	◯ Pediatric board ◯ Adult board
Knee Height (cm)	_____
Side (Knee height)	◯ Right ◯ Left
Head circumference (cm)	_____
Mid-Upper Arm Circumference #1 (cm)	_____
Mid-Upper Arm Circumference #2 (cm)	_____
Mid-Upper Arm Circumference Mean (cm)	_____
Side (MUAC)	◯ Right ◯ Left
Tricep skinfold #1 (mm)	_____

Tricep skinfold #2 (mm)	_____
Triceps skinfold Mean (mm)	_____
Side (Triceps SF)	◯ Right ◯ Left
Subscaplar skinfold #1 (mm)	_____
Subscaplar skinfold #2 (mm)	_____
Subscapular skinfold Mean (mm)	_____
Side (subscapular SF)	◯ Right ◯ Left
Suprailiac skinfold #1 (mm)	_____
Suprailiac skinfold #2 (mm)	_____
Suprailiac skinfold Mean (mm)	_____
Side (Suprailiac SF)	◯ Right ◯ Left
Thigh skinfold #1 (mm)	_____
Thigh skinfold #2 (mm)	_____
Thigh skinfold Mean (mm)	_____
Side (thigh SF)	◯ Right ◯ Left
Handgrip strength #1	_____
Handgrip strength #2	_____
Handgrip strength #3	_____

Handgrip strength Mean (kg)	_____
Side (Handgrip strength)	◯ Right ◯ Left

APPENDIX XVI: MALNUTRITION STATUS DATA COLLECTION FORM

Primary indicators when single data point available	
Weight-for-height	_____
Malnutrition status	◯ Mild malnutrition ◯ Moderate malnutrition ◯ Severe malnutrition ◯ Overweight ◯ Normal
BMI-for-age	_____
Malnutrition status	◯ Mild malnutrition ◯ Moderate malnutrition ◯ Severe malnutrition ◯ Overweight ◯ Normal
Length/height-for-age	_____
Malnutrition status	◯ Mild malnutrition ◯ Moderate malnutrition ◯ Severe malnutrition ◯ Overweight ◯ Normal
Mid-upper arm circumference	_____
Malnutrition status	◯ Mild malnutrition ◯ Moderate malnutrition ◯ Severe malnutrition ◯ Overweight ◯ Normal

Primary indicators when 2 data points available	
Weight gain velocity (< 2 years of age)	◯ Mild Malnutrition (Less than 75% of the norm for expected weight gain) ◯ Moderate malnutrition (Less than 50% of the norm for expected weight gain) ◯ Severe malnutrition (Less than 25% of the norm for expected weight gain) ◯ Overweight ◯ Normal

Weight loss (2-20 years of age)	◯ Mild malnutrition (5% usual body weight) ◯ Moderate malnutrition (7.5% usual body weight) ◯ Severe malnutrition (10% usual body weight) ◯ Overweight ◯ Normal
Deceleration in weight for height/length z-score	◯ Mild malnutrition (Decline in 1 z-score) ◯ Moderate malnutrition (Decline in 2 z-score) ◯ Severe malnutrition (Decline in 3 z-score) ◯ Overweight ◯ Normal
Inadequate nutrient intake	◯ Mild malnutrition (51-75% estimated energy/protein need) ◯ Moderate malnutrition (26-50% estimated energy/protein need) ◯ Severe malnutrition (< or = 25% estimated energy/protein need) ◯ Overweight ◯ Normal

APPENDIX XVII: SAMPLE OF ENTERAL NUTRITION DATA COLLECTION FORM

Study ID (Randomization Number)	_____
Enteral feed Start date	_____
Enteral feed start time	_____
Enteral feed end date	_____
Enteral feed end time	_____
Patient discharged from PICU on Enteral feeds?	◯ Yes ◯ No
Day 1	
Date day 1	_____
Feeding route	◯ Nasogastric ◯ Nasoduodenal ◯ Nasojejunal ◯ Orogastric ◯ PEG ◯ PEG-J ◯ Gastric tube (G-Tube)
Feeding mode	◯ Continuous ◯ Cyclic ◯ Intermittent ◯ Bolus
Type of formula	_____
Formula concentration (kcal/mL)	_____
Formula protein content (g/mL)	_____
Total volume provided for 24hours (mL)	_____
Total volume provided for 24h (mL/kg)	_____
Energy provided for 24 hours (kcal)	_____

Energy provided for 24 hours (kcal/kg)	_____
Protein provided for 24 hours (g)	_____
Protein provided for 24 hours (g/kg)	_____
Goal energy intake- dietitian (kcal)	_____
Goal energy intake- dietitian (kcal/kg)	_____
Goal protein intake- dietitian (g)	_____
Goal protein intake- dietitian (g/kg)	_____
Were the feeds held?	◯ Yes ◯ No
Reasons feeds were held	☐ Medication ☐ Mechanical problem (tube obstruction, broken pump) ☐ Intolerance ☐ Aspiration ☐ Tube misplacement ☐ Procedure ☐ Other
How long were feeds held? (hours)	_____
Were any supplements provided?	◯ Yes ◯ No
Supplements provided	☐ ONS ☐ Protein powder ☐ Breastmilk
Volume of supplement provided (mL)	_____
Energy from supplement (kcal)	_____
Protein from supplement (g)	_____