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Commentary regarding the impact of malnutrition (nutritional imbalance) on pediatric surgical outcome

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Over the past several years, a number of reports have been published which evaluate the relationship between nutritional status and clinical outcome using the American College of Surgeons' Pediatric National Surgical Quality Improvement Program (NSQIP-P) database. In this issue of the Journal of Pediatric Surgery, Robison et al. [1], using this database to identify the presence of malnutrition, report a significantly increased incidence of post-operative infection associated with children who were receiving nutritional support, had stunted growth, and/or were hypoalbuminemic prior to surgical intervention. The authors should be congratulated for their considerable effort to adapt this database for the purpose of relating pediatric malnutrition to clinical outcome; however, several factors which have bearing on these findings are important to consider.

Traditionally, pediatric malnutrition, like adult malnutrition, has been viewed through the prism of body composition losses based on anthropometric assessment along with a documented history of inadequate protein-calorie intake. Pediatric anthropometric indices include weight-for height (length), height-for-age, mid-upper arm muscle circumference, and body mass index-for-age. When multiple measurement data points are available, dynamic assessment tools including weight gain/growth velocity (particularly useful for infant evaluation), deceleration in weight-for-height, and weight loss can help to establish the degree and duration of malnutrition. Other modalities, such as diminished grip strength, which reflects reduced muscle mass and correlates with loss of total body protein, can be used to assess functional compromise. When applied to general pediatric populations, particularly in developing countries, quantitative protein-calorie malnutrition (starvation-related) has been considered to be accurately and reliably established using these anthropometric assessment tools [2], and has been strongly linked with an increased risk of mortality and morbidity, especially related to infection [3]. In contrast, the reported frequency of malnutrition in pediatric patients requiring illness-related hospitalization ranges broadly from less than 5% to greater than 50% in various studies [4]. As much of this inconsistency in reported malnutrition prevalence among children (and adults) is thought to be owing to lack of standardized definitions and uniform nutritional screening practices, an endeavor has been underway for the past decade to better conceptualize malnutrition.

The evolution of this initiative derives from an improved understanding of the impact that cytokine-induced inflammation can have on nutritional status assessment and related clinical outcomes, especially in circumstances of pre-existing poor nutrient intake-based malnutrition, and has led to a re-evaluation of criteria for characterizing malnutrition in both adult and pediatric patients [5–8]. This represents a change in focus toward a broader concept of malnutrition to include nutritional imbalances created by acute and chronic illness as well as inappropriate therapy resulting in protein undernutrition and caloric overnutrition. This expanded concept now includes acute (for example - trauma, sepsis or burns) and chronic (for example - cancer, Crohn disease or cystic fibrosis) inflammatory conditions which, through cytokine-induced protein catabolism, deplete lean body mass, promote muscle weakness and ventilator dependency, cause immune dysfunction and increased sepsis risk, delay wound healing, prolong hospital length of stay, and increase mortality.

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Recognition of inflammation in the hospital setting can be established by assessing the acute phase and visceral (constitutive) protein pools, accomplished by measuring serum concentrations of C-reactive protein (CRP) and prealbumin (transthyretin) respectively. Albumin is also a visceral protein indicator but is somewhat less sensitive to acute change owing to a substantially longer half-life and much larger pool size than prealbumin. In addition, the intravenous administration of albumin-containing blood products can lead to assessment inaccuracies. The cytokine (inflammatory) response to acute injury induces hepatic CRP synthesis as well as a metabolic response, mediated by counter-regulatory hormones (catecholamines, glucagon and cortisol), resulting in protein catabolism with a subsequent reduction of the visceral protein pool. The magnitude and duration of the injury insult can thus be assessed by serial measurement of serum CRP and prealbumin concentrations, and these data can be used to appropriately optimize protein-calorie administration to promote wound healing, spare muscle loss, support immunologic function, and avoid overfeeding during the acute metabolic stress period [9,10]. These indices can also be used to predict mortality and morbidity in critically ill infants and children [11,12]. Keeping in mind the caveats noted above, albumin can be used as a prealbumin surrogate; however, hypoalbuminemia in the setting of acute injury cannot reliably be ascribed to, nor be a measure of, starvation-induced undernutrition [13] but instead primarily reflects metabolic stress response-mediated protein catabolism proportionate to the severity of the injury [9–11]. In fact, low serum albumin values have been shown to independently predict mortality and functional outcome in critically ill pediatric patients [14].

In this study [14], malnutrition and serum CRP were independently associated with hypoalbuminemia , but 55% of the study patients were determined to be well-nourished upon admission to the Pediatric Intensive Care Unit (PICU) based on anthropometric assessment. While it is certainly possible that children with pre-hospital starvation-induced malnutrition were included in the study group Robison et al. [1] evaluated, the authors were unable to establish which study patients were preoperatively malnourished versus those who were well-nourished but acutely ill with injury-induced protein catabolism prior to surgery using the NSQIP-P database. In the absence of any direct injury severity preoperative evaluation (such as serum C-reactive protein levels), these two patient groups can be easily conflated. According to the data presented [1], nearly 10% of the patients were septic, in septic shock, or had SIRS, and 28% had an ASA designation of >/= 3. It is, therefore, likely that the hypoalbuminemia observed actually reflected acute injury metabolism rather than malnutrition in a substantial number of study patients. The fact that albumin data were missing in the great majority of patients included for evaluation further confounds this analysis.

In their report, Robison et al. [1] identify the presence of nutritional support as a predictor of post-operative infection. This association is potentially problematic for several reasons. As the authors themselves note, the NSQIP-P database does not allow for children who are well-nourished but are receiving nutritional support, such as gastrostomy-fed patients, to be distinguished from nutritionally-supported malnourished patients who may be at higher risk for post-operative infection owing to malnutrition. Furthermore, since NSQIP-P data do not include the nature of the nutritional support administered (e.g. initiation timing, route, protein-calorie amount given, duration), it is not possible to evaluate the quality or likely efficacy of the supplementation provided, potentially leading to inaccurate risk stratification, outcome assessment, and even the erroneous assumption that nutritional intervention may be counter-productive. Although many issues regarding optimal pediatric nutritional strategies have yet to be adequately addressed, on the basis of data currently available, there is general consensus that early versus delayed nutritional intervention results in decreased mortality, improved morbidity, and improved physiologic function, particularly in critically ill patients [15,16]. Enteral administration is preferred but parenteral supplementation is beneficial if nutritional goals cannot be met via enteral delivery alone [17,18]. Caloric overfeeding and protein underfeeding are associated with increased mortality and morbidity [19-21]. Since skeletal muscle, the major protein repository in the body, is substantially depleted in starvation-related malnutrition and protein stores are further (and rapidly) catabolized in response to injury, adequate repletion of protein is the crucial nutritional goal in critically ill patients [8] to diminish endogenous losses and supplement the circulating pool of free amino acids, facilitate muscle sparing, support immunologic function, fuel the inflammatory response, and promote wound healing. Optimization of protein administration in critically ill children has been shown to increase serum free amino acid concentrations and visceral protein pool size while decreasing infection and mortality, indicative of improved immunologic function [22-24].

In summary, malnutrition is a complex, multifaceted clinical phenomenon. Its impact on clinical outcome must be evaluated in terms of its type and severity, the causes and pathophysiologic mechanisms which contributed to it, and whether an appropriate therapeutic strategy was applied. Critically ill children with antecedent starvation-related malnutrition are at substantially greater risk of a poor outcome than those who are well nourished. Nutritional imbalances caused by injury vary dependent on the type of injury as well as the magnitude and duration of the resulting metabolic insult. These data are crucial to ascertain in selecting among an ever-growing multitude of available nutritional therapeutic options. Determining which options are most appropriate to specific clinical situations are issues best addressed through the agency of multi-institutional randomized clinical trials (RCT), which remain regrettably few to date in both adult and pediatric populations [8,17]. Unfortunately, NSQIP-P, which does not allow for a more granular evaluation, is a much less effective substitute in this regard. One of its major limitations, given the expanded concept of malnutrition discussed above, is the inability to assess and quantify inflammation. Adding serum CRP to the database would constitute a substantial improvement, both in terms of the etiology of malnutrition as well as the severity assessment of injury insult.

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