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Defining Fluid Restriction in the Management of Infants Following Cardiac Surgery and Understanding the Subsequent Impact on Nutrient Delivery and Growth Outcomes

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DEFINING FLUID RESTRICTION IN THE MANAGEMENT OF INFANTS FOLLOWING CARDIAC SURGERY AND UNDERSTANDING THE SUBSEQUENT IMPACT ON NUTRIENT DELIVERY AND GROWTH OUTCOMES

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Melissa Li

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To: Interim Dean Mark L. Williams
R.Stempel College of Public Health and Social Work

This dissertation, written by Melissa Li, and entitled Defining Fluid Restriction in the Management of Infants Following Cardiac Surgery and Understanding the Subsequent Impact on Nutrient Delivery and Growth Outcomes, having been approved in respect to style and intellectual content, is referred to you for judgment.

We have read this dissertation and recommend that it be approved.

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DEDICATION

This dissertation is dedicated to the little ones who are faced with adversity early on in life, to those who are committed to giving them the best chance of living fulfilling and healthy lives, and to my parents for instilling the importance of education, work ethic and resolve in me.

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ABSTRACT OF THE DISSERTATION

DEFINING FLUID RESTRICTION IN THE MANAGEMENT OF INFANTS FOLLOWING CARDIAC SURGERY AND UNDERSTANDING THE SUBSEQUENT IMPACT ON NUTRIENT DELIVERY AND GROWTH OUTCOMES

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Professor Adriana Campa, Major Professor

Adequacy of nutritional intake during the postoperative period, as measured by a change in weight-for-age z-scores from surgery to the time of discharge, was evaluated in infants (n = 58) diagnosed with a congenital heart defect and admitted for surgical intervention at Miami Children's Hospital using a prospective observational study design. Parental consent was obtained for all infants who participated in the study.

Forty patients had a weight available at hospital discharge. The mean preoperative weight-for-age z-score was -1.3 ±1.43 and the mean weight-for-age z-score at hospital discharge was -1.89 ±1.35 with a mean difference of 0.58 ±0.5 ($P < 0.001$). Fluid volume during the early postoperative period was approximately 12% higher than the postoperative protocol of 4 mL/kg/hr. Patients received significantly less calories (43 ±17.9 vs. 46 ±17.9, $P<0.001$) and protein (1.72±0.76 vs. 1.81 ±0.74, $P=0.001$) than ordered for parenteral nutrition (PN)

and significantly less calories (98 ±30 vs. 101 ±28.5, $P<0.001$) and protein (2.07 ±0.78 vs. 2.18±0.79, $P<0.001$) for oral/enteral nutrition (EN) diet orders. The difference in volume received from nutrition in patients who received nutrition on postoperative day 1, compared to patients who had nutrition initiated after postoperative day 1, were significantly different until postoperative day 6 when volume received was no longer different between groups ($p= 0.2$).

Nutritional intake during the postoperative period was inadequate based on a decrease in weight-for-age z-scores from the time of surgery until discharged home. Our findings suggested that limited fluid volume for nutrition likely contributes to suboptimal nutritional delivery during the postoperative period; however, inadequate nutrition prescription may also be an important contributing factor. Development of a nutrition protocol for initiation and advancement of nutrition support may reduce the delay in achieving patient's nutritional goals and may attenuate the observed decrease in z-scores during the postoperative period.

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ABBREVIATIONS AND ACRONYMS

APEM	Acute Protein Energy Malnutrition
BMR	Basal Metabolic Rate
CHD	Congenital Heart Defects
CPEM	Chronic Protein Energy Malnutrition
CPS	Cardiopulmonary Support
EN	Enteral Nutrition
FTT	Failure to Thrive
ICU	Intensive Care Unit
IL	Intralipids
IV	Intravenous
NPO	Nothing by Mouth
PICU	Pediatric Intensive Care Unit
PN	Parenteral Nutrition
RACHS-1	Risk Adjustment for Congenital Heart Surgery 1
REE	Resting Energy Expenditure
TEE	Total Energy Expenditure
WHO	World Health Organization

I. INTRODUCTION

Congenital heart defects (CHD) are structural abnormalities of the heart or major blood vessels that vary in severity and either resolve spontaneously or require surgical intervention. In 2008 the incidence of CHD confirmed by echocardiography in the United States is reported as 10.8 per 1,000 live births (Egbe et al., 2014). The infant mortality rate from CHD in the United States has steadily declined from 92.16 per 100,000 live births in 1979-1981 to 37.69 per 100,000 live births in 2006 (Boneva et al., 2001; Gilboa, Salemi, Nembhard, Fixler, & Correa, 2010). Improvement in survival rates to one year of age over the past 30 years has brought to the forefront a population that requires support in the management of co-morbidities associated with CHD.

A comprehensive understanding of what is known about healthy infants and the challenges faced by infants diagnosed with CHD is essential to identify ways to minimize co-morbidities associated with CHD. The first year of life is marked by a rapid rate of growth and development in the healthy infant. According to World Health Organization (WHO) growth standards, infants double their birth weight by four months of age and almost triple their birth weight by 14 to 15 months of age (WHO, 2006). During this time internal organs mature and neurodevelopmental milestones are achieved. Infants have limited nutritional reserves and are dependent on adequate nutritional intake to meet the demands for growth and development (Fomon, Haschke, Ziegler, & Nelson, 1982).

Infants diagnosed with critical CHD that require surgical intervention within the first year of life are at a disadvantage compared to their healthy counterparts.

The heart is the organ that delivers nourishment to the body by delivering oxygenated blood and nutrients to perfuse organs and tissues. Oxygenation of blood follows an efficient circuit of carbon dioxide rich blood returning from the body to the right side of the heart via the superior and inferior vena cava to be pumped to the lungs via the pulmonary artery for oxygenation. The blood returns back to the left side of the heart via the pulmonary veins to be pumped out to the body via the aorta. CHD causes a disruption to the effectiveness of this process to varying degrees (Steltzer, Rudd, & Pick, 2005). Critical consequences include reduced perfusion to organs, increased work demand on the heart muscle, and compromised respiratory status. The increased demand of a compromised heart function can compound the nutritional requirements of a growing infant.

The growth of infants diagnosed with CHD has long been described as a challenge in the literature. Early investigations into growth failure in infants with CHD centered on the idea of a "hypermetabolic" state and measured resting energy expenditure (REE) via indirect calorimetry in an attempt to explain the observed failure-to-thrive (FTT) with mixed results (Huse, Feldt, Nelson, & Novak, 1975; Krauss & Auld, 1975; Krieger, 1970; Lees, Bristow, Griswold, & Olmsted, 1965). Lees et al. (1965) observed a higher mean oxygen consumption in infants with CHD compared to healthy controls, however, this difference appeared to be related to nutritional status as those whose weight was greater than 60% of the median weight-for-age had a mean oxygen consumption similar to healthy controls. Comparing infants with CHD to a control group of infants with growth failure in the absence of organic disease resulted in no significant difference in basal metabolic rate (BMR) and oxygen consumption (Krieger, 1970). Huse et al. (1975) did not find a significant difference in oxygen consumption between infants with CHD and controls which was the opposite of findings by Krauss & Auld (1975) who looked at the neonate with CHD.

These findings led some researchers to suggest that the growth failure was result of a combination of factors which may include inadequate nutritional intake and gastrointestinal malabsorption (Huse et al., 1975; Krieger, 1970; Lees et al., 1965). Infants with CHD were reported to have growth failure due to inadequate calorie intake to meet their energy requirements (Huse et al., 1975; Mennon & Poskitt, 1986). When provided supplemental feedings via a gastric tube, infants demonstrated weight gain indicating that infants with CHD grow when their energy requirement are met (Bougle, Iselin, Kahyat, & Duhamel, 1986; Krieger, 1970). Investigations into malabsorption as a potential factor for FTT has not revealed significant differences in energy loss via stool when comparing infants with CHD to healthy infants (Menon & Poskitt, 1985; Vaisman et al., 1994; van der Kuip et al., 2003).

More contemporary studies have reported observing no difference in REE between infants with CHD and healthy controls; however, it is suggested that total energy expenditure (TEE), as determined by doubly labelled water technique, is responsible for growth failure rather than REE (Ackerman, Karn, Denne, Ensing, & Leitch, 1998; Farrell, Schamberger, Olson, & Leitch, 2001; Leitch et al., 1998; van der Kuip et al., 2003).

In some instances surgical intervention is described to positively impact growth outcomes; however, timing of surgical intervention is important, as age and weight status at time of surgery are factors associated with outcomes (Natarajan, Anne, & Aggarwal, 2011; Polito et al., 2011; Srinivasan et al., 2010; Vaidyanathan et al, 2009; Winch et al., 2009). A younger age is associated with prolonged mechanical ventilation (Polito et al., 2011). A lower weight-for-age z-score is associated with a longer hospital stay (Anderson et al., 2009). Surgery itself poses challenges to the growing infant as it brings about a stress response including hemodynamic instability and alterations in hormonal and cytokine responses (Finnerty, Mabvuure, Ali, Kozar & Herndon, 2013; Mehta & Duggan, 2009). Nutrition is important to attenuate the catabolic state and promote recovery (Finnerty et al., 2013; Mehta & Duggan, 2009).

Water is a central component in the management of hospitalized patients as it is the vehicle for which patients receive electrolytes, medications and nutrition. Maintenance fluid restriction is common practice in the postoperative management of infants following cardiac surgery (Owens & Musa, 2009). However, fluid restriction is poorly defined in the literature and varies between institutions and physicians. Additionally fluid restriction has been identified as a main barrier to providing adequate nutrition in critically ill children (Lambe, Hubert, Jouvet, Cosnes, & Colomb, 2007; Rogers, Gilbertson, Heine, & Henning, 2003).

Objectives

The objectives of this study were to: 1) evaluate the adequacy of nutrition as measured by a change in weight-for-age z-scores, 2) describe fluid volumes received by infants following cardiac surgery, 3) examine fluid utilization to provide essential products including intravenous fluids, medications, blood products, and nutrition and identify route/method of delivery, 4) evaluate the amount of energy and protein delivered, and 5) compare energy and protein intakes to nutritional provisions ordered.

Significance

Defining fluid restriction and identifying its impact on the postoperative course is important for establishing a foundation for future research to make advancements in establishing evidenced based practice in the nutritional management of infants following cardiac surgery.

Specific Aims and Hypotheses

Specific Aim 1: Evaluate adequacy of nutritional intake during the postoperative period by comparing preoperative weight status as measured by weight-for-age z-scores to weight status at discharge home.

> *Hypothesis 1*: Nutritional intake during the postoperative period will be less than optimal as reflected by a decrease in weight-for-age z-scores of ≥ 0.5 from the time of surgery to the time of discharge home.

Specific Aim 2: Describe fluid volumes received by infants during the postoperative period following cardiac surgery to identify actual fluid volumes provided in current practice.

Specific Aim 3: Describe how fluid volume is utilized and delivered to infants during the postoperative period following cardiac surgery to categorize how fluid volume is distributed in current practice to provide essential products, such as, intravenous fluids, medications, blood products, and nutrition, and identify routes/method of delivery.

Specific Aim 4: Describe the amount of Calories and protein delivered to infants during the postoperative period following cardiac surgery to identify actual Calories and protein delivered in current practice.

Specific Aim 5: Compare Calories and protein delivered to infants during the postoperative period following cardiac surgery to Calories and protein prescribed with estimates expressed as Calories per kilogram body weight and grams of protein per kilogram body weight.

> *Hypothesis 2*: Calories and protein delivered to infants during the postoperative period following cardiac surgery will be less than the intended nutrition ordered.

Investigation of the specific aims is presented in three chapters. Chapter III presents findings on defining fluid restriction in infants diagnosed with a congenital heart defect recovering from cardiac surgery at Miami Children's Hospital from a retrospective study data (n = 303) and includes descriptive findings of trends in delivery of calories and protein. Chapter IV explores the adequacy of nutritional intake via a prospective study design and evaluates nutritional delivery in 58 infants diagnosed with a congenital heart defect recovering from cardiac surgery. Chapter V focuses on comparing nutritional orders with what is actually received to better understand potential gaps in nutritional delivery.

II. REVIEW OF LITERATURE

Fluid restriction evolved as a way to minimize complications associated with fluid overload in postoperative patients with cardiovascular disease. Fluid retention raises concerns for postoperative complications, such as, the inability to wean from mechanical ventilatory support and acute kidney injury (Boschee et al., 2014; Hazel, Gajarski, Yu, Donohue, & Blatt, 2013; Valentine et al., 2012). A longer duration on ventilator support has been associated with prolonged intensive care unit stay following cardiac surgery (Gillespie et al., 2006). Fluid restriction remains general practice even with advancements in surgical techniques, improved postoperative measures to address inflammation through the use of steroids, and improved fluid management of patients through the use of diuretics (Li et al., 2008; Nicholson, Clabby, & Mahle, 2014).

Maintenance Fluid Requirements in Infants

The formula proposed by Holliday and Segar (1957) is widely accepted as the means to estimate maintenance fluid requirements delivered parenterally. Holliday and Segar acknowledged limitations of the proposed formula. The formula addresses maintenance and does not include the need to correct for water deficits or abnormal losses of water (Holliday & Segar, 1957). Therefore, adjustments may be needed depending on specific clinical presentations. Fluid restriction is suggested based on this formula. In reviewing the literature, the exact origin of these recommendations is unclear. Researchers reporting the need for fluid restriction cite books as references and the books do not have references justifying this information (Owens & Musa, 2009; Elliot & Delius, 1998; Rogers et al., 2003).

It should be noted that the proposed volume for maintenance by Holliday and Segar (1957) has been modified for ease of calculation in clinical practice to 4 mL/kg/hr resulting in an actual intake of 96 mL/kg/day due to rounding to the nearest whole number. It is unclear who proposed this adjustment, however, it is written as standard practice in the postoperative orders at Miami Children's Hosptial.

Postoperative Fluid Volumes in Clinical Practice

A limited number of studies have evaluated fluid intake in infants with congenital heart defects who are recovering from cardiac surgery (Hazel et al., 2013; Nicholson, Clabby, & Mahle, 2014; Nicholson, Clabby, Kanter, & Mahle, 2013; Rogers et al., 2003; Szekely, Sapi, Kiraly, Szatmari, & Dinya, 2006). Rogers et al. (2003) identified fluid restriction as the major barrier to providing adequate nutrition, with fluid restriction defined as less than 80% of daily maintenance fluid requirements.

In a retrospective study, Nicholson et al. (2013) evaluated fluid volume at three time points during hospital admission demonstrating the progression in fluid volume during the postoperative course in 65 neonates who underwent modified systemic-to-pulmonary artery shunt palliation. Findings include a median total fluid intake of 95 mL/kg/day (IQR 81-103.3 mL/kg/day) while receiving parenteral nutrition support in the cardiac intensive care unit, 133.5 mL/kg/day (IQR 121.9-

145 mL/kg/day) at time of transfer to the cardiac satellite unit, and 147 mL/kg/day (IQR 137.8-155.3 mL/kg/day) at time of discharge home (Nicholson et al., 2013).

Nicholson et al. (2014) report a policy of total fluid restriction to as little as 40-50 mL/kg/day during the early postoperative period and observed a median total fluid intake on postoperative day one, two, and three of 43.9 mL/kg/day (IQR 32.9-61.0 mL/kg/day), 56.7 mL/kg/day (IQR 48.0-76.1 mL/kg/day), and 66.7 mL/kg/day (IQR 56.6-75.5 mL/kg/day), respectively. Hazel et al. (2013) report routine standard of care during the first 24-48 hours after surgery as providing 75-100 mL/kg/day of dextrose-containing crystalloid solutions. Based on the literature, many institutions follow a fluid restriction less than or equal to full maintenance as proposed by Holliday and Segar (1957) during the early postoperative period. Fluid restriction is variable as there is lack of studies in the literature to provide evidence to support what is the best practice. The philosophy of an institution regarding the degree of fluid restriction is based on a consensus of the physicians' expert opinion (Nicholson et al., 2014).

Fluid Intake Volume and Postoperative Outcomes

Studies have reported mixed findings regarding the association of higher fluid intake volumes and longer duration of mechanical ventilation (Hazel et al., 2013; Nicholson et al., 2014; Szekely et al., 2006). Szekely et al. (2006) prospectively evaluated risk factors for prolonged mechanical ventilation in 411 children admitted to the cardiac intensive care unit. Medium mechanical ventilation was defined as >61 hours representing the 75th percentile of the study population and long mechanical ventilation was defined as >7 days representing the 90th percentile of the study population (Szekely et al., 2006). A mean input volume of 4.3 mL/kg/hr during the first 24 hours following surgery was associated with medium mechanical ventilation but not long mechanical ventilation (Szekely et al., 2006).

Nicholson et al. (2014) retrospectively looked at 65 neonates who underwent modified systemic-to-pulmonary artery shunt palliation to compare infants who achieved negative fluid balance ≤24 hours to those who achieved negative fluid balance >24 hours. It was found that duration of mechanical ventilation, cardiac intensive care unit (CICU) length of stay, and total hospital length of stay were not associated with postoperative fluid restriction management (Nicholson et al., 2014).

In a prospective observational study, Hazel et al. (2013) focused on fluid overload in the postoperative period as measured by two methods: 1) total fluid in minus total fluid out and 2) current weight minus preoperative weight. Poor outcomes were defined as follows: a) need for continuous renal replacement therapy, b) time to first extubation >6.5 days, c) intensive care length of stay >9.9 days, or d) death within 30 days of surgery (Hazel et al., 2013). Total fluid volumes received by patients were not reported. Fluid overload when expressed as a percentage of daily weight was a predictor of poor outcomes during multivariate analysis when controlling for peak serum creatinine (OR 1.07; 95% CI 1.01-1.14; p=0.03) (Hazel et al, 2013).

There is inconclusive evidence as to whether or not volume of intake or fluid balance contributes to poor outcomes. Fluid volume is likely a contributing factor to patient outcomes. However, until the optimal volume allowance can be defined variable reports may continue to persist.

Perioperative Nutritional Status and Postoperative Outcomes

Nutritional status at the time of surgery is an important factor especially in undernourished infants that are faced with the additional burden of the stressed state following cardiac surgery. Radman et al. (2014) utilized tricep skin-fold as a measurement of total body fat mass and found that lower preoperative tricep skin-fold measurements were associated with increased duration of mechanical ventilation, length of ICU stay, and duration of inotropic infusion.

Toole et al. (2014) attempted to correlate nutritional status with hospital outcomes in 121 infants and children undergoing cardiac surgery utilizing Waterlow criteria for acute and chronic malnutrition classification. The authors found 51.2% of patients had acute protein energy malnutrition (APEM) and 40.5% of patients had chronic protein energy malnutrition (CPEM) (Toole et al., 2014). By day 7 following cardiac surgery, mean calorie and protein intake met less than 70% of the estimated requirements and this trend was not significantly different between patients with and without malnutrition (Toole et al., 2014). Patients with mild CPEM had a significantly longer length of hospital stay compared to patients without CPEM ($p<0.005$) (Toole et al., 2014).

Less than optimal nutritional status at the time of surgery can delay recovery and prolong hospitalization. It is critical to ensure that patients, especially those who present with malnutrition, are adequately supported nutritionally to minimize the negative outcomes resulting from malnutrition.

Adequacy of Postoperative Nutritional Intake

Understanding how well patients are nutritionally supported during the postoperative period is another important factor in determining the impact of fluid restriction on nutritional intake. Li et al. (2008) measured REE using indirect calorimetry in 17 infants following the Norwood procedure and compared Calorie intake to measured REE. Measured REE on postoperative day 0, 1, 2, and 3 were (mean ±SD) 43 (±11), 39 (±8), 39 (±7), and 41 (±6) kcal/kg/day, respectively (Li et. al, 2008). An important finding is that caloric intake did not meet REE until postoperative day 3. Additionally mean (±SD) protein intake was less than dietary recommended intakes (DRI) for age and were reported as 0, 0.2 (±0.2), 0.6 (±0.5), and 0.9 (±0.5) g/kg/day on days 0, 1, 2, and 3 respectively (Li et. al, 2008).

De Wit and colleagues (2010) studied 21 children who were admitted to the pediatric ICU and ventilated following cardiac surgery. REE was measured using indirect calorimetry. The mean REE was 67.8 (±15.4) kcal/kg/day and patients were reported to receive a mean (±SD) intake of 15.9 kcals/kg/day indicating that energy intake was inadequate to meet estimated needs on the day of measurement (De Wit et. al, 2010).

In examining the energy intake during the postoperative course, Nicholson et al. (2013) found that patients received a median caloric intake of 50.4 kcals/kg/day (IQR 41.6-63.6 kcals/kg/day), while exclusively receiving parenteral nutrition support in the cardiac intensive care unit. Children received 94 kcals/kg/day (IQR 85-103 kcals/kg/day) at the time of transfer to the cardiac satellite unit, and 119 kcals/kg/day (IQR 111-125 kcals/kg/day) at time of discharge home. Of importance is that the median weight-for-age *z*-scores from the time of surgery to discharge home was decreased by -1.3 z-scores (IQR -1.7 to -0.7) (Nicholson et al., 2013).

Several other studies have observed decreases in weight-for-age z-scores during the postoperative stay (Anderson et al., 2011; Medoff-Cooper et al., 2011; Nicholson et al., 2014; Rogers et al., 2003). Rogers et al. (2003) observed a decrease in median weight-for-age *z*-scores from -1.44 (range -2.7 to 1.52) prior to admission to -2.24 (range -3.13 to 0.96) at hospital discharge. The change in median weight-for-age z-score was significant when comparing weight prior to admission to the PICU to weight at the time of discharge from the PICU ($p<0.001$) (Rogers et al., 2003). Nicholson et al., (2014) reported a significant decrease in weight-for-age z-scores between patients who achieved negative fluid balance <24 hours postoperatively and those who achieved negative balance >24 hours postoperatively ($p=0.47$) with the latter having a higher weight-for-age z-score suggesting that caloric intake may be compromised due to fluid restriction.

A study by Medoff-Cooper et al. (2011) conducted on neonates with functionally univentricular physiology compared the change in weight-for-age z-score from surgery to hospital discharge and found a mean change in weight-for-age z-score of -1.5 (±0.8). The authors also noted a significant difference in change in weight-for-age z-score between those who were exclusively fed orally compared to those who were tube fed with the latter experiencing a greater decrease in weight-for-age z-scores (Medoff-Cooper et al., 2011).

Anderson et al. (2011) found a decrease in median weight-for-age z-scores of -1.0 (range -2.3 to 0.2) from time of surgery to discharge home. A decrease in weight-for-age z-scores was associated with failed initial postoperative extubation ($p = 0.001$) and delayed initiation of postoperative nutrition support ($p < 0.001$) (Anderson et al., 2011).

Although studies conducted are observational in nature and reflect single institution experiences often consisting of limited observations there appears to be a common trend in the observed decline in weight-for-age z-scores from the time of surgery to hospital discharge. These findings illustrate the inadequacy of nutritional intake during the postoperative period, however, the events that lead to this decline remains unclear. Inadequate energy intake is described early in the postoperative period at which time point fluid restriction is suggested to be the limiting factor. A potential confounder or contributing factor can be the philosophy of individual institutions regarding the practice of nutrition support. Only recently the literature has started to recognize the need to fully explore nutritional practice, nutritional intake, and weight concurrently in the postoperative infant recovering from cardiac surgery (Costello, Gellatly, Daniel, Justo, & Weir, 2014; Lambert et al., 2014). The lack of a comprehensive understanding of fluid restriction and nutritional delivery makes it difficult to determine if the decline in weight-for-age z-scores can be prevented or attenuated. Fluid restriction can have a direct impact on nutritional delivery. The magnitude to which it contributes to inadequate intake during the postoperative period should be explored to potentially identify other contributing factors.

Nutrition Prescription vs. Nutrition Delivery

The primary focus of this study was to describe current practices regarding fluid allowance and the subsequent impact on nutritional delivery and growth. However, it is important to be cognizant of other potential issues with nutritional delivery aside from fluid restriction.

In an observational study, de Neef et al. (2008) compared nutrition delivery to nutrition prescription in a pediatric intensive care unit setting. A statistically significant but clinically irrelevant disparity between prescribed and delivered nutrition was observed and inadequate prescription was implicated as the variable responsible for malnutrition (de Neef et al., 2008). It is important to investigate if a discrepancy between nutrition ordered and nutrition delivered exists in the postoperative cardiac patient to better identify areas for improvement in the management of infants following cardiac surgery.

In summary, less than optimal nutritional delivery is well documented in the critical care setting (de Menezes, Leite, & Nogueira, 2013; de Neef et al., 2008; Kyle, Jaimon, & Coss-Bu, 2012; Larsen et al., 2013; Mehta et al. 2012). Adequate nutrition is important for recovery, as malnutrition in the critical care setting is associated with poor clinical outcomes (Li et al., 2008; de Neef et al., 2008; Larsen et al., 2013; Mehta et al. 2012). Fluid restriction is a barrier to providing adequate nutrition as allocation of restricted volume to infusion of necessary medications typically results in a limited volume available for nutrition support and insufficient energy intake (Lambe et al., 2007; Li et al., 2008; Rogers et al., 2003). Variability in fluid allowance following cardiac surgery makes it difficult to clearly define best practices and identify ways to minimize delays in patient recovery. A comprehensive analysis of fluid restriction during the postoperative period and the subsequent impact on nutrient delivery and growth is lacking in the literature. The findings of the present study are expected to provide a foundation for further research in the development of nutrition protocols that are supported by evidenced based practice and improve clinical outcomes in infants following cardiac surgery.

III. DEFINING FLUID RESTRICTION IN THE MANAGEMENT OF INFANTS FOLLOWING CARDIAC SURGERY

Abstract

Background: Fluid restriction is reported to be a barrier to providing adequate nutrition to children following cardiac surgery. However, fluid restriction is poorly defined and the degree of restriction varies amongst institutions. While our institution has a postoperative protocol for fluid restriction, it is unknown how much fluid patients tolerate in actual practice. The aim of this study was to describe fluid volumes received by infants following cardiac surgery at Miami Children's Hospital.

Methods: Retrospective chart reviews were conducted for infants from birth to 12 months of age who underwent cardiac surgery. Total fluid intake, subcomponents of total fluid intake, and output were recorded in 24-hour increments for a maximum of 14 days. Energy and protein intakes were also calculated for each day.

Results: A total of 293 patients had complete data available for analysis of fluid intake. On postoperative day 1 through 4 the medians of volume received were from 103 to 106 mL/kg/day. Patients who received less than 90 mL/kg/day or more than 120 mL/kg/day on postoperative day 1 tended to be older and were successfully extubated from the mechanical ventilator sooner than patients who received 90-120 mL/kg/day. However, despite these differences, the median length of postoperative stay were similar (9 days for patients who received 90-

120 mL/kg/day and 8 days for patients who received greater than 120 mL/kg/day or less than 90 mL/kg/day).

Conclusions: Following cardiac surgery, infants received 10% more volume than the postoperative protocol of 4 mL/kg/day on postoperative day 1. Mean energy intake did not exceed 80 kcals/kg/day by postoperative day 7 and mean protein intake did not meet reference intakes for healthy children until postoperative day 5. Further investigations into fluid volume utilization, nutrition support practices during the postoperative period, and growth outcomes are needed to better identify strategies to optimize the nutritional management of infants following cardiac surgery.

Introduction

Fluid restriction in the postoperative pediatric cardiac patient evolved as a way to minimize complications associated with fluid overload, such as dependence on mechanical ventilation and acute kidney injury (Boschee et al., 2014; Hazel, Gajarski, Yu, Donohue, & Blatt, 2013; Valentine et al., 2012). This remains as general practice even with advancements in surgical techniques and improved postoperative measures to address inflammation and fluid balance with medications (Li et al., 2008; Nicholson, Clabby, & Mahle, 2014). However, the definition of fluid restriction varies in practice and is influenced by physicians' individual training and the philosophies of individual institutions.

Fluid restriction was found to be a main barrier to providing adequate nutrition, especially in patients with cardiac conditions (Rogers, Gilbertson, Heine, & Henning, 2003). Allocation of restricted volume to infusion of necessary medications typically results in a limited volume available for nutrition support and insufficient energy intake (Lambe et al., 2007; Li et al., 2008; Rogers et al., 2003).

Variability in the amount of fluid volume provided to infants following cardiac surgery makes it difficult to clearly define the best practice and identify ways to improve clinical practice in infants following cardiac surgery. The primary goal of this study was to determine the fluid volumes patients actually receive in current practice, describe the nutritional intake received during the postoperative period, and identify patient outcomes at Miami Children's Hospital.

Methods

Study Design and Subjects

The research design was a retrospective cohort study conducted at Miami Children's Hospital. Infants from birth to 12 months of age, who underwent cardiac surgery between January 1, 2008 and June 30, 2010, were identified from hospital medical records. Exclusion criteria included: a) infants less than 34 weeks post-conceptional age at time of surgery, b) weight less than 2500 g at time of surgery, and c) diagnosis of other non-cardiac conditions which may affect the ability to regulate fluid (i.e. acute or chronic renal dysfunction). The cut-off post-conceptional age was based on the estimated completion time of nephrogenesis (Shaffer & Weismann, 1992). The study was approved by the Institutional Review Boards of Florida International University and Miami Children's Hospital (Western Institutional Review Board).

Measurements

Data were collected by chart review from the hospital's electronic medical record. The following baseline information was obtained: gestational age at birth, weight (kg), length (cm) and head circumference (cm) at birth, most recent weight (kg), length (cm) and head circumference (cm) prior to surgery, age at time of surgery, gender, race/ethnicity, cardiac diagnosis, other medical diagnosis, surgical history, and cardiopulmonary bypass time (if applicable) of current surgical intervention. Fluid intake volume was measured as a continuous variable. Intake and output were recorded in 24-hour increments.

Subcomponents of total fluid were also recorded in 24-hour increments, including intravenous (IV) fluids, medications/drips, blood/blood products, parenteral nutrition support (PN), enteral nutrition support (EN), and oral food intake.

Collection of continuous data was discontinued when the patient was discharged from the hospital, expired or if there was a change in patient status that affected standard fluid management in the postoperative course (i.e. requiring cardiopulmonary support or further surgical intervention). Weight was recorded as a continuous variable as available. Data on calorie and protein intakes were calculated by a Registered Dietitian. The data were documented as kilocalories per kilogram body weight per day (kcals/kg/day) and grams of protein per kilogram body weight per day (g protein/kg/day) using the most recent weight available. To minimize error in the collection of these data, documented nutritional intake from oral intake, EN, and PN were cross referenced with physician orders. Additional outcome variables of interest included length of postoperative stay and duration of mechanical ventilation. Documentation of continuous variables began with postoperative day "0" until the patient was discharged home, or up to 14 days following surgery.

Data Analysis

Since the study was a preliminary pilot study, a sample size calculation was not performed. Continuous variables were assessed for normality of distribution. Univariate analyses were expressed as percentages, medians with interquartile ranges (IQR), and means with standard deviations (SD). Fluid volume was divided into 3 groups based on volume received on postoperative day 1 (<90 mL/kg/day, 90-120 mL/kg/day, and >120 mL/kg/day). The ranges for each group were empirically determined based on how the data for fluid volume on postoperative day 1 appeared. Nonparametric analyses were conducted for differences between groups. Age at the time of surgery and duration of mechanical ventilation were the only variables that met criteria of homogeneity of variance and were chosen for further analysis. Kruskal- Wallis test was used to test for differences between the three groups. Mann-Whitney U Test was used to test for differences between each of the groups. Statistical significance was defined as $p<0.05$. The data were analyzed using PASW Statistics 18 (SPSS Inc, Chicago, IL).

Results

A total of 303 patients met inclusion criteria. On postoperative day 1, five patients were breast fed, four were on cardiopulmonary bypass support, and one was taken to surgery. A total of 293 had complete data available for analysis of fluid intake on postoperative day 1. The demographic profile of the cohort was as follows: 55% were male (n = 162), 45% female (n = 131), 22% were Whites (non-Hispanic), 17% Blacks (non-Hispanic), 42% White or Black Hispanics, and 19% others. The median age of the cohort at the time of surgery was 80 days (IQR 8-167 days) and the median weight was 4.1 kg (IQR 3.2 - 6 kg). The median length of hospital stay was 12 days (IQR 6-22 days) and median length of postoperative stay was 8.5 days (IQR 5-14 days). The median duration of mechanical ventilation was 47 hrs (IQR 21-94 hrs). Table 1 outlines the median (IQR) volumes of intake and fluid balance for postoperative days 1 to 14. Negative fluid balance was greatest on postoperative days 1 and 2.

The routes of nutritional provisions on postoperative day 1 were as follows: 193 patients (65.9%) only received dextrose intravenously, 3.4% received either parenteral and/or enteral nutrition support and 30.7% were fed by mouth. Patients who only received dextrose from IV fluids on postoperative day 1 had total fluid intake distributed as follows: 71% IV fluid, 27% medication/drips, and 2% blood products.

A total of 281 patients had complete data available for analysis of nutritional intake. Data for the median kilocalorie and protein intakes for each of the 14 days are presented in Table 2. Mean energy intake did not exceed 80 kcals/kg/day by postoperative day 7 and did not exceed 100 kcals/kg/day by postoperative day 14 in patients who remained hospitalized (Figure 2). Mean protein intake did not meet reference intakes for healthy children until postoperative day 5 (Figure 3).

Patient characteristics based on volume of intake on postoperative day 1 are presented in Table 3. Age and duration of mechanical ventilation were significantly different between patients who received <90 mL/kg/day on postoperative day 1 and those who received 90-120 mL/kg/day. Patients who received <90 mL/kg/day were older than patients who received 90-120 mL/kg/day (median of 107 days vs. 61 days, p=0.001) and had a shorter duration of postoperative intubation (median of 27 hours vs. 70 hours, p=0.006). Patients who received 90-120 mL/kg/day had a longer duration of mechanical ventilation than those who received >120 mL/kg/day on postoperative day 1 (median of 70 hours vs. 24 hours respectively, p=0.001). However, despite these differences the median length of postoperative stay was similar. Those who received <90 mL/kg/day or >120 mL/kg/day on postoperative day 1 were not significantly different with respect to age or duration of mechanical ventilation.

Discussion

Fluid intake volume during the first 4 days of the postoperative period was about 10% higher than the postoperative protocol of 4 mL/kg/hr. Total fluid intake volume was also higher than values reported at other institutions during the early postoperative period (Hazel, 2013; Nicholson, 2014; Rogers, 2003).

While our institution has reported higher volume of intakes during the early postoperative period, outcome measures of length of hospital stay and duration of mechanical ventilation were similar to reports at other institutions (Anderson et al., 2011; Toole et al., 2014). In a cohort of infants with two-ventricle physiology Anderson et al. (2011), reported a median hospital length of stay of 11 days (range 2-54 days) and a median postoperative ventilator time of 48 hours (range 3 to 1176 hours). In children less than 24 months of age, Toole et al. (2014) reported a median hospital length of stay following cardiac surgery of 15 days (IQR 9-30 days) and a median length of mechanical ventilation of 2 days. It should be noted that, independent of fluid intake and energy restriction, the duration of ventilation support and length of hospital stay may be influenced by the complexity of the cardiac defect being addressed. Gillespie et al. (2006) reported a median postoperative mechanical ventilation time of 9.5 hours (range 0-260 hours) in patients who underwent elective surgery and 72 hours (range 0-5304 hours) in patients who underwent non-elective surgery. In infants with univentricular physiology, Medoff-Cooper et al. (2011) reported a median mechanical ventilation time of 72 hours (range 3-624 hours) and a median length of hospital stay of 20 days (range 8-138 days).

Regardless of the volume received on postoperative day 1, the volume of fluid intake between groups converged between postoperative days 3 and 4. Along with this observation, the difference between groups relative to energy and protein intakes was narrowed by postoperative days 3 to 4. Conversely, Larsen et al. (2013) observed differences in energy intake and found that patients with lower cumulative energy intake during postoperative days 0-10 had an increased duration of ventilation support (5±1.2 days, $p=0.01$) and longer hospital length of stay (25±6.4 days, $p=0.001$). Fluid received early in the postoperative period may be driven by the clinical status of the patient, resulting in deviation from the postoperative protocol, and accounting for the observed variations in volumes received by patients. Additionally, the observed convergence of the intakes of fluid volume, energy, and protein may be representative of a more homogenous sample within the cohort, as patients who have a quicker recovery time are discharged home. Patients who remain hospitalized for a longer duration may have a more complex cardiac diagnosis. The institution’s practice regarding providing nutrition support during the critical state and recovery phase may account for the observed alignment of nutritional provisions among the three initial fluid intake categories. Findings of suboptimal energy and protein intakes warrant further investigation.

Limitations of the study include those inherent with a retrospective design. The study variables were limited to available documented data and the accuracy of this information could not be verified. Another limitation is that the data collected are reflective of clinical practice in the past. As advancements in patient care evolve, the outcomes of the retrospective study may not be entirely representative of current practice. Although energy and protein intakes were described in this cohort, it is unclear how weight status is affected during the postoperative period. Additionally, documentation on the complexity of the cases were not obtained, therefore, we could not determine if fluid volume received, and observed outcomes, were associated with complexity of the cardiac defects being addressed.

Conclusion

In this study, following cardiac surgery, infants received slightly more volume than the postoperative protocol of full maintenance on postoperative day 1. Mean energy intake did not exceed 80 kcals/kg/day by postoperative day 7 and mean protein intake did not meet reference intakes for healthy children until postoperative day 5. Further investigations into fluid volume utilization, nutrition support practices during the postoperative period, and growth outcomes are needed to better identify strategies to optimize the nutritional management of infants following cardiac surgery.

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Table 1. Median (IQR) Fluid Intake and Fluid Balance on Postoperative Days 1-14

	Day 1 (n = 293)	Day 2 (n = 277)	Day 3 (n = 258)	Day 4 (n = 234)	Day 5 (n = 202)	Day 6 (n = 178)	Day 7 (n = 155)
Fluid Intake (mL/kg/day)	105 (93-125)	103 (91-121)	105 (91-123)	106 (91-131)	111 (96-135)	116 (95-136)	117 (103-140)
Fluid Balance (mL/day)	-125 (-252-55)	-109 (-279-60)	-19 (-144-103)	40 (-56-146)	71 (-34-178)	75 (-14-157)	104 (7-185)

	Day 8 (n = 131)	Day 9 (n = 102)	Day 10 (n = 93)	Day 11 (n = 82)	Day 12 (n = 73)	Day 13 (n = 62)	Day 14 (n = 51)
Fluid Intake (mL/kg/day)	120 (102-139)	122 (100-144)	124 (106-144)	123 (107-143)	123 (100-146)	119 (99-134)	124 (111-135)
Fluid Balance (mL/day)	97 (-9-183)	89 (13-151)	81 (14-182)	85 (38-169)	108 (68-183)	93 (33-156)	76 (-9-187)

Table 2. Median (IQR) Calorie and Protein Intake on Postoperative Days 1-14

	Day 1 (n = 281)	Day 2 (n = 255)	Day 3 (n = 238)	Day 4 (n = 211)	Day 5 (n = 179)	Day 6 (n = 153)	Day 7 (n = 137)
Calorie Intake (kcal/kg/day)	12 (9-17)	19 (11-43)	38 (16-59)	53 (30-74)	62 (41-82)	65 (50-87)	76 (61-97)
Protein Intake (g/kg/day)	0 (0-0)	0 (0-1)	0.84 (0-1.5)	1.32 (0.5-1.9)	1.54 (0.9-2.2)	1.54 (1.1-2.1)	1.66 (1.3-2.3)

	Day 8 (n = 119)	Day 9 (n = 97)	Day 10 (n = 84)	Day 11 (n = 75)	Day 12 (n = 67)	Day 13 (n = 58)	Day 14 (n = 48)
Calorie Intake (kcal/kg/day)	78 (59-98)	77 (60-99)	82 (71-106)	87 (69-102)	87 (72-103)	84 (69-97)	85 (69-104)
Protein Intake (g/kg/day)	1.69 (1.2-2)	1.76 (1.2-2.3)	1.83 (1.4-2.5)	1.83 (1.4-2.3)	1.82 (1.5-2.4)	1.78 (1.4-2.3)	1.95 (1.4-2.4)

Table 3. Patient Characteristics categorized by volume received on postoperative day 1

Variable	< 90 mL/kg/day	90-120 mL/kg/day	>120 mL/kg/day
n (%)	56 (19%)	146 (50%)	91 (31%)
Age (days)*	107(34-197)	61 (8-151)	100 (8-177)
Weight (kg)*	4.64 (3.43-6.6)	3.8 (3.2-5.25)	4.8 (3.1-6.3)
Post-op stay (days)*	8 (5-13)	9 (6.5-14)	8 (4-14)
Intubation (hours)*	27 (21-70)	70 (27-96)	24 (1-95)
Initiation of nutrition (days)*	2 (2-3)	2 (0-3)	0 (0-3)
Calories received on day 1 (kcals/kg/day)*†	10 (8-12)	11 (9-13)	20 (12-58)
Protein received on day 1 (g/kg/day)*†	0 (0-0)	0 (0-0)	0 (0-1.06)

*Median (interquartile range)
†Adequate intake 0-6 months of age: 1.52 g/kg/day; Dietary reference intake 6-12 months of age: 1.2 g/kg/day

Figure 1. Comparison of mean fluid intake between groups categorized by volume received on postoperative day 1 for postoperative days 1 through 14

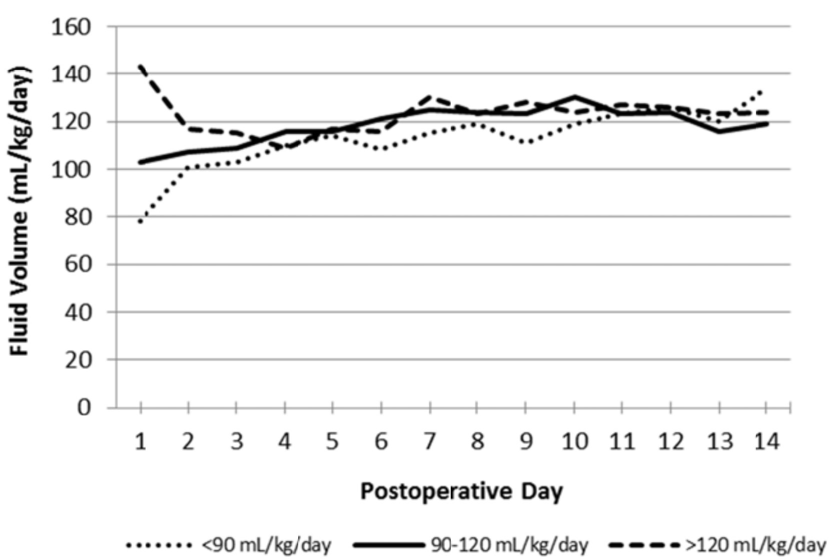


Figure 2. Comparison of mean calorie intake between groups categorized by volume received on postoperative day 1 for postoperative days 1 through 14

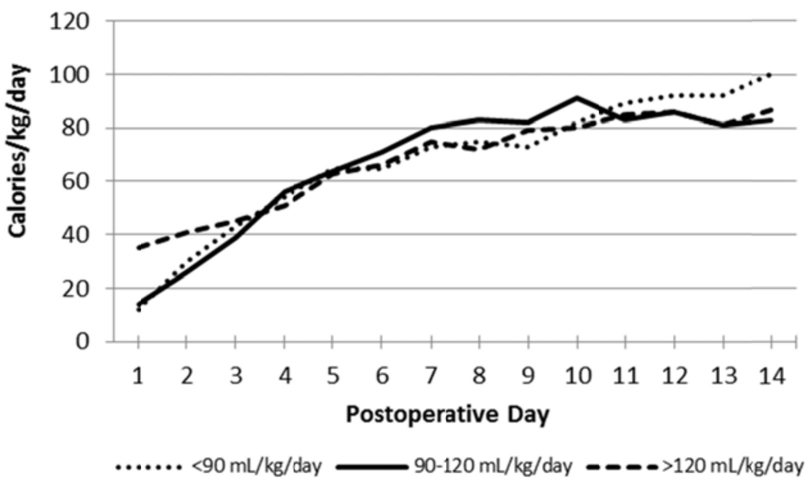
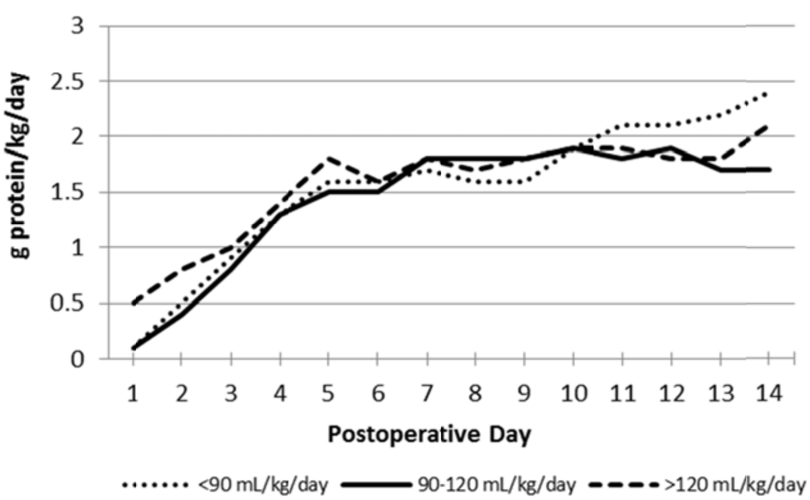


Figure 3. Comparison of mean protein intake between groups categorized by volume received on postoperative day 1 for postoperative days 1 through 14



IV. UNDERSTANDING THE IMPACT OF FLUID RESTRICTION ON NUTRIENT DELIVERY AND GROWTH OUTCOMES IN INFANTS FOLLOWING CARDIAC SURGERY

Abstract

Background: Fluid restriction is reported to be a barrier in providing adequate nutrition following cardiac surgery. The specific aim of this study was to evaluate the adequacy of nutritional status during the postoperative period using anthropometries by comparing preoperative weight status, as measured by weight-for-age z-scores, to weight status at discharge home.

Methods: Infants from birth to 12 months of age who were scheduled for cardiac surgery at Miami Children's Hospital between December 2013 and September 2014 were followed during the postoperative stay. Total fluid intake, subcomponents of total fluid intake, and output were recorded in 24-hour increments for a maximum of 28 days. Preoperative and discharge weight-for-age z-scores were analyzed.

Results: Parental consent was obtained for a total of 58 infants who participated in the study. Forty patients had a weight available at hospital discharge. The median discharge weight-for-age z-score was -1.8 (IQR -2.78 to -0.65). The mean (SD±) preoperative weight-for-age z-score was -1.3 ±1.43 and the mean weight-for-age z-score at hospital discharge was -1.89 ±1.35 with a mean difference of 0.58 ±0.5 (P <0.001). Patients with increased risk categories were associated with a greater length of mechanical ventilation (r= 0.624, P<0.001) and greater decrease in weight-for-age z-scores (r= -0.597, P=0.002).

Conclusions: Nutritional status during the postoperative period was found inadequate through the use of objective anthropometric measures and comparing them with normal growth curves. Increase in risk categories predicted increased length of mechanical ventilation and a greater decrease in weight-for-age z-scores. Further investigations are warranted to better understand the relationship of fluid restriction with nutrient intake following cardiac surgery to determine if the decline in weight-for-age z-scores can be attenuated, and if strategies for nutrient concentration are tolerated. The development of future protocols for nutritional intervention need to have in consideration surgical risk categories.

Introduction

Fluid restriction in the postoperative pediatric cardiac patient evolved as a way to minimize complications associated with fluid overload, such as dependence on mechanical ventilation and acute kidney injury (Boschee et al., 2014; Hazel, Gajarski, Yu, Donohue, & Blatt, 2013; Valentine et al., 2012). Fluid restriction, however, was found to be an important barrier to providing adequate nutrition, especially in patients with cardiac conditions (Rogers, Gilbertson, Heine, & Henning, 2003). Allocation of restricted volume to infusion of necessary medications typically results in a limited volume available for nutrition support and in insufficient energy intake (Lambe et al., 2007; Li et al., 2008; Rogers et al., 2003).

Several studies have observed decreases in weight-for-age z-scores during the postoperative stay. This measure compares weight-for-age of one child to a healthy population of children. In examining the energy intake during the postoperative course, Nicholson et al. (2013) found that the median weight-for-age *z*-scores from the time of surgery to discharge home was decreased by -1.3 (IQR -1.7 to -0.7). Rogers et al. (2003) observed a decrease in median weight-for-age *z*-scores from -1.44 (range -2.7 to 1.52) prior to admission to -2.24 (range -3.13 to 0.96) at hospital discharge. The change in median weight-for-age z-score was significant when comparing weight prior to admission to the pediatric intensive care unit (PICU) to weight at the time of discharge from the PICU ($p<0.001$) (Rogers et al., 2003). Nicholson et al., (2014) reported a significant decrease in weight-for-age z-scores between patients who achieved negative fluid balance <24 hours postoperatively and those who achieve negative balance >24 hours postoperatively (p=0.47) with the latter having a higher weight-for-age z-score suggesting that caloric intake may be compromised due to fluid restriction.

A study by Medoff-Cooper et al. (2011) on neonates with functionally univentricular physiology compared the change in weight-for-age z-score from surgery to hospital discharge and found a mean change in weight-for-age z-score of -1.5 (±0.8). The authors also noted a significant difference in change in weight-for-age z-score between those who were exclusively fed orally compared to those who were tube fed with the latter experiencing a greater decrease in weight for age z-scores (Medoff-Cooper et al., 2011).

Anderson et al. (2011) found a decrease in median weight-for-age *z*-scores of -1.0 (range -2.3 to 0.2) from time of surgery to discharge home. A decrease in weight-for-age *z*-scores was associated with failed initial postoperative extubation (P= 0.001) and delayed initiation of postoperative nutrition support (P<0.001) (Anderson et al., 2011).

Although studies conducted are mostly observational with limited observations and reflect single institution experiences, there appears to be a common trend in the observed decline in weight-for-age z-scores from the time of surgery to hospital discharge. These findings suggest that the nutritional intake during the postoperative period is inadequate; however, the events that lead to this decline remain unclear. In these studies, inadequate energy intake is described early in the postoperative period, and fluid restriction is suggested to be the limiting factor.

The specific aim of this study was to evaluate nutritional status during the postoperative period by comparing preoperative weight status, as measured by weight-for-age z-scores, to weight status at discharge home. It was hypothesized that nutritional intake during the postoperative period was less than optimal, as reflected by a decrease in weight-for-age z-scores of ≥0.5, which is clinically relevant, from the time of surgery to the time of discharge home. Additionally, the fluid volumes received by the patients in this cohort, and how they were utilized and delivered to infants during the postoperative period, following cardiac surgery were described.

Methods

Study Design and Subjects

The research design was a prospective cohort study conducted at Miami Children's Hospital. Infants from birth to 12 months of age who were diagnosed with a congenital heart defect and were admitted for surgical intervention between December 2013 and September 2014 were eligible for the study. Infants with a gestational age of less than 36 weeks at the time of surgery or with a diagnosis of renal dysfunction prior to surgery were excluded. The cut-off gestational age was determined based on the estimated completion time of nephrogenesis (Shaffer & Weismann, 1992). The study was approved by the Institutional Review Boards of Florida International University and Miami

Children's Hospital (Western Institutional Review Board). Parental informed consent was obtained prior to enrollment into the study.

Measurements

The following baseline information was collected from the medical record: chronological age, gestational age at birth, weight (kg), length (cm) and head circumference (cm) at birth, current weight (kg), length (cm) and head circumference (cm), gender, race/ethnicity, cardiac diagnosis, other medical diagnosis, surgical intervention, whether or not the patient was placed on cardiopulmonary bypass during the surgery and the duration in minutes that support was received, and surgical history (if applicable). If a patient received nutrition preoperatively the route was documented as oral, enteral (EN), and parenteral (PN).

The World Health Organization (WHO) Child Growth Standards were used to obtain weight-for-age, length-for-age, head circumference-for-age and weight-for-length z-scores. The z-scores were calculated using the WHO's software, WHO Anthro (version 3.2.2, January 2011; WHO, Geneva, Switzerland). A 3.15% error rate was determined after performing the calculation only once. Since a change in weight-for-age z-scores was the primary outcome of interest, and accuracy was of great importance, calculations were performed at least twice for each patient. If there was a discrepancy between outputs, the calculation was done a third time for confirmation of the correct value. A decline of 0.5 weight-for-age z-score during hospital stay was considered clinically relevant (Burch et al., 2014).

The Risk Adjustment for Congenital Heart Surgery 1 (RACHS-1) method is a tool created by a panel of experts that utilized variables, such as in-hospital mortality, surgical procedure codes, age, prematurity, and major non-cardiac structural anomaly to categorize in-hospital mortality risk in children younger than 18 years undergoing surgery for congenital heart disease (Jenkins et al., 2002). RACHS-1 categories were obtained to account for the individual complexity of each case.

Continuous data were collected on each patient, including total fluid intake volume, total fluid output volume, and fluid balance recorded in milliliters (mL) per 24-hour period. Postoperative day “0” included volume received during the pre-operative and intraoperative period. The composition of total intake was documented under the categories of: intravenous fluids, medications, blood products, parenteral nutrition, enteral nutrition, and oral nutrition. Route of delivery was documented. Volume of output was categorized as urine output, drainage (chest tubes, gastric secretions), and stool. For infants who had a Foley catheter, urine was collected into a collection container. For infants who did not have a catheter, the diaper was weighed to quantify output.

Laboratory values that affect nutritional management of patients were recorded as available. Laboratory values of interest included glucose, BUN, creatinine, triglycerides, liver function tests, and lactate levels. Acute kidney injury was determined based on the Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group practice guidelines (2012). Acute kidney injury stage 1 is defined as having a serum creatinine 1.5-1.9 times baseline or an increase in serum creatinine by ≥0.3 mg/dl increase within 48 hours (KDIGO Acute Kidney Injury Work Group, 2012). Receipt of diuretics, vasoactive medications, and paralytic agents were documented as categorical variables.

Weights while intubated were obtained as deemed necessary by the attending physician. Following extubation, patients were expected to be weighed daily unless otherwise specified by the attending physician. Therefore, weights were recorded as available. Duration of postoperative intubation was recorded in hours. Length of postoperative intensive care unit stay and length of postoperative hospital stay were documented in days.

Continuous data were collected until discharged home or up to a maximum of 28 days. After 28 days patients were discontinued from the study. Research Electronic Data Capture (REDCap) tools hosted at Florida International University were used to manage the study data (Harris et al., 2009). REDCap is a secure web application designed to capture data for research studies. Forms were designed to calculate Calorie and protein intake based on data inputs.

Data Analysis

Based on preliminary data, the standard deviation of the mean difference in preoperative weight-for-age z-scores and weight-for-age z-scores at hospital discharge was estimated as 0.55. The value for standard deviation used to calculate the sample size was 20% above 0.55 given the high variability of estimates of standard deviations. A sample size of 70 patients was selected based on what was estimated to be affordable to conduct the study. The selected sample size allowed the ability to detect a mean difference as small as 0.22 with a power of 80%.

Descriptive statistics for continuous variables were reported as percentages, means, and medians with interquartile ranges. Data were tested for normality. Paired t-test was used to compare preoperative and discharge weight-for-age z-scores. Statistical significance was defined as $p<0.05$. The data was analyzed using IBM SPSS Statistics 22 (SPSS Inc, Chicago, IL).

Results

A total of 82 patients met inclusion criteria during the study period. Thirteen parents declined participation, 8 parents were not available to provide consent and it was determined inappropriate to approach 3 parents for informed consent. A total of 58 patients were enrolled in the study.

During the study period 44 patients were discharged home, 7 patients had a length of stay greater than 28 days, 5 patients required surgical intervention, and 2 patients expired. The distribution of patients is shown in Figure 1.

Patient Characteristics

The demographic profile of the cohort were as follows: 60% male (n = 35), 40% female (n = 23), 28% were Whites (non-Hispanic), 52% were Whites (Hispanic), 10% were Blacks (non-Hispanic), 8% were others (Hispanic), and 2% others (non-Hispanic). The median age of the cohort was 37 days (IQR 7-138 days) and the median preoperative weight was 3.7 kg (IQR 3.21 – 5.53 kg). The RACHS-1 risk categories of the cases are provided in Table 1. There were no patients with a risk category of 1 or 5. The median z-scores for anthropometric measurements collected at birth and preoperatively are presented in Table 2.

Ninety percent of patients received nutrition preoperatively. Of those patients who received nutrition preoperatively, 73% received nutrition by mouth, 8% received a combination of nutrition by mouth and enteral nutrition (EN), 2% received a combination of nutrition by mouth and parenteral nutrition (PN), 13% received only EN, and 4% received only PN.

Postoperative Outcomes

Ninety-seven percent of patients were placed on cardiopulmonary support (CPS) for surgery. The median duration of CPS was 119 minutes (IQR 86.5-176 minutes). Thirty-one percent of patients (n = 18) developed acute kidney injury. None of the patients required dialysis. On postoperative day 0, 78% of patients returned to the unit intubated. The median duration of mechanical ventilator support was 65.5 hrs (IQR 23.3 – 91.6 hrs). The median length of postoperative stay was 9 days (IQR 5-14.5 days). Duration of mechanical ventilation was positively correlated with length of postoperative stay (r= 0.393, P=0.029). Table 3 provides the median volumes of intake and fluid balance for postoperative days 1 to 28. Fluid volumes based on RACHS-1 categories are delineated in Table 4.

Growth Outcomes

Forty patients had a weight available at hospital discharge. The median weight at discharge was 4.02 kg (3.34 to 6.02 kg) and the discharge weight-for-age z-score was -1.8 (IQR -2.78 to -0.65). In patients who had pre-operative and discharge weights (n = 40), the mean preoperative weight-for-age z-score was -

1.3 ±1.43 and the mean weight-for-age z-score at hospital discharge was -1.89 ±1.35 with a mean difference of 0.58 ±0.5 ($p < 0.001$). When stratified based on RACHS-1, patients classified as category 2 (n = 16) had a mean preoperative weight-for-age z-score of -1.27 ±1.43 and a mean weight-for-age z-score at hospital discharge of -1.58 ±1.44 with a mean difference of 0.31 ±0.29 (p= 0.001). Patients classified as category 3 (n = 11) had a mean preoperative weight-for-age z-score of -1.51 ±1.6 and a mean weight-for-age z-score at hospital discharge of -2.14 ±1.4 with a mean difference of 0.63 ±0.56 (p= 0.004). Patients classified as category 4 (n = 7) had a mean preoperative weight-for-age z-score of -1.33 ±1.2 and a mean weight-for-age z-score at hospital discharge of -2.06 ±1.2 with a mean difference of 0.73 ±0.46 (p= 0.006). Patients classified as category 6 (n = 6) had a mean preoperative weight-for-age z-score was -0.97 ±1.69 and weight-for-age z-score at hospital discharge was -2.03 ±1.2 z-score with mean difference of 1.06 ±0.54 (p= 0.005). A higher RACHS-1 category was correlated with a greater decrease in weight-for-age z-scores (r= -0.597, P=0.002)

In patients who had birth and preoperative weights available (n = 52), the mean birth weight-for-age z-score was -0.46 ±1.04 and the mean preoperative weight-for-age z-score was -1.33 ±1.34 with a mean difference of 0.87 ±1.04 (P<0.001). In patients who had birth and preoperative head circumference measurements available (n = 30), the mean birth head circumference-for-age z-score was -0.33 ±1.47 and the mean preoperative head circumference-for-age z-score was -1.28 ±1.96 with a mean difference of 0.96 ±1.31 (P<0.001).

In patients who were born full term and had birth and preoperative lengths available (n = 19), there were no significant differences observed in changes in length-for-age z-scores. In patients who were born full term and had birth and preoperative weight and lengths available (n = 15) the mean weight-for-length z-score at birth was -0.4 ±1.14 and the mean preoperative weight-for-length z-score was -1.89 ±2.38 with a mean difference of 1.49 ±1.97 (P= 0.011). Baseline weight-for-age z-scores were not correlated with duration of intubation, length of postoperative stay, or change in weight-for-age z-scores.

Fluid Volume Distribution

Fluid volume allocated to nutrition gradually increased as volume for IV fluid, medications and drips and blood products decreased. The trend in fluid volume distribution is shown in Figure 2. Volume allocated to nutrition reached maintenance fluid needs (100 mL/kg/day) on postoperative day 6.

In comparing patients who experienced a change in z-score of <0.5 and patients who experienced a change in z-score of ≥0.5, mean total volume received (113±17.1 vs 119±13, P=0.38) and mean total volume received for nutrition (86±30.2 vs 76±22.4, P=0.36) were not significantly different between groups.

Discussion

The observed decrease in weight-for-age z-score from time of surgery to hospital discharge is in agreement with previous studies (Anderson et al., 2011; Medoff-Cooper et al., 2011; Nicholson et al., 2013). Although the change observed in this study was smaller, the decrease in weight-for-age z-score is clinically relevant. The nutritional goal is weight maintenance during the critical state and appropriate weight gain during the recovery phase. In theory, a male infant with an age of 37 days and a weight of 3.7 kg would present with a decrease in weight-for-age z-score of 0.56, if weight maintenance was observed for 10 days. A female infant of the same age and weight would theoretically experience a similar change in weight-for-age z-score if weight was maintained for 11 days. The findings of this study demonstrated that infants undergoing cardiac surgery are faced with adversity during a critical period of growth and development, which may result in impaired growth during the postoperative period.

Fluid volume during the early postoperative period was about 12% higher than the postoperative protocol of 4 mL/kg/hr. Total fluid intake volume was also higher than values reported at other institutions during the early postoperative period (Hazel, 2013; Nicholson, 2014; Rogers, 2003).

While we observed a higher volume of intakes during the early postoperative period and the median duration of mechanical ventilation was slightly longer than other studies, median length of hospital stay was shorter than reported at other institutions (Anderson et al., 2011; Toole et al., 2014). It should be acknowledged that duration of ventilation support and length of hospital stay is influenced by the complexity of the cardiac defect being addressed. Gillespie et al. (2006) reported a median postoperative mechanical ventilation time of 9.5 hours (range 0-260 hours) in patients who underwent elective surgery and 72 hours (range 0-5304 hours) in patients who underwent non-elective surgery. In infants with univentricular physiology, Medoff-Cooper et al. (2011) report a median mechanical ventilation time of 72 hours (range 3-624 hours) and a median length of stay of 20 days (range 8-138 days). The variation in mechanical ventilation time and length of postoperative stay was observed within our cohort when the variables were stratified based on RACHS-1 categorization. Duration of mechanical ventilation and postoperative length of stay increased as the risk category increased which coincide with what the risk categories are intended to predict. When mean differences in weight-for-age z-scores were estimated by RACHS-1 categories, every category showed increasing deterioration from category 2 to 6, which became clinically relevant (>0.5 change in z-score) in risk categories 3, 4 and 6.

A decrease in weight-for-age z-scores and a slow progression of nutritional intake during the postoperative period provides some insight into the inadequacy of nutritional intake. Researching the relationship of the characteristics and changes in nutritional intake with z-scores is the natural progression of this investigation. It is from these data that we can infer that the delay in meeting EERs explain the observed decrease in weight-for-age z-scores. The question that remains is if the slow progression of nutritional intake can be improved, either by accelerating the process or by concentrating nutrients without increasing surgical risk, to optimize nutritional intake and positively influence nutritional status.

In addition to suboptimal growth during the postoperative period, growth is impaired in some patients from birth to surgical intervention. Weight-for-age, length-for-age, head circumference-for-age and weight-for-length z-scores decreasing below -2 from birth to surgical intervention classifies some infants as underweight, stunted and wasted. Preoperative growth failure is a factor that requires further investigation as minimizing this may improve the postoperative course as adequate nutritional status at baseline is known to be associated with better outcomes (Radman et al., 2014; Toole et al., 2014).

Adequate nutritional status before surgery has demonstrated to improve the outcomes of surgery (Radman et al., 2014; Toole et al., 2014). Clinical practice is continually evolving to achieve better outcomes. The intent of this study was to obtain a baseline of current practice, which is lacking in the literature, to be able to make educated decisions to improve practice.

Limitations of this study include a small sample size and some missing data. The medical team was aware that a Nutrition study was being conducted on the postoperative infants; however, specific outcomes of interest were not disclosed. The number of eligible patients and the observed enrollment rate was less than anticipated. Although a prospective design was chosen to improve the quality of data collected, it was not possible to have all data points collected as some baseline variables were not available in the electronic medical record.

Conclusion

Nutritional status was objectively measured by anthropometrics during the postoperative period in infants recovering from cardiac surgery, as evidenced by the magnitude of a declining weight-for-age z-score. Increased in risk categories predicted increased length of mechanical ventilation and a greater decrease in weight-for-age z-scores. Further investigations are warranted to better understand the relationship of fluid restriction with nutrient intake following cardiac surgery to determine if the decline in weight-for-age z-scores can be attenuated, and if strategies for nutrient concentration may be tolerated. The development of future protocols for nutritional intervention need to have in consideration surgical risk categories.

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Figure 1. Patient Enrollment and Reason for Discontinuation from the Study

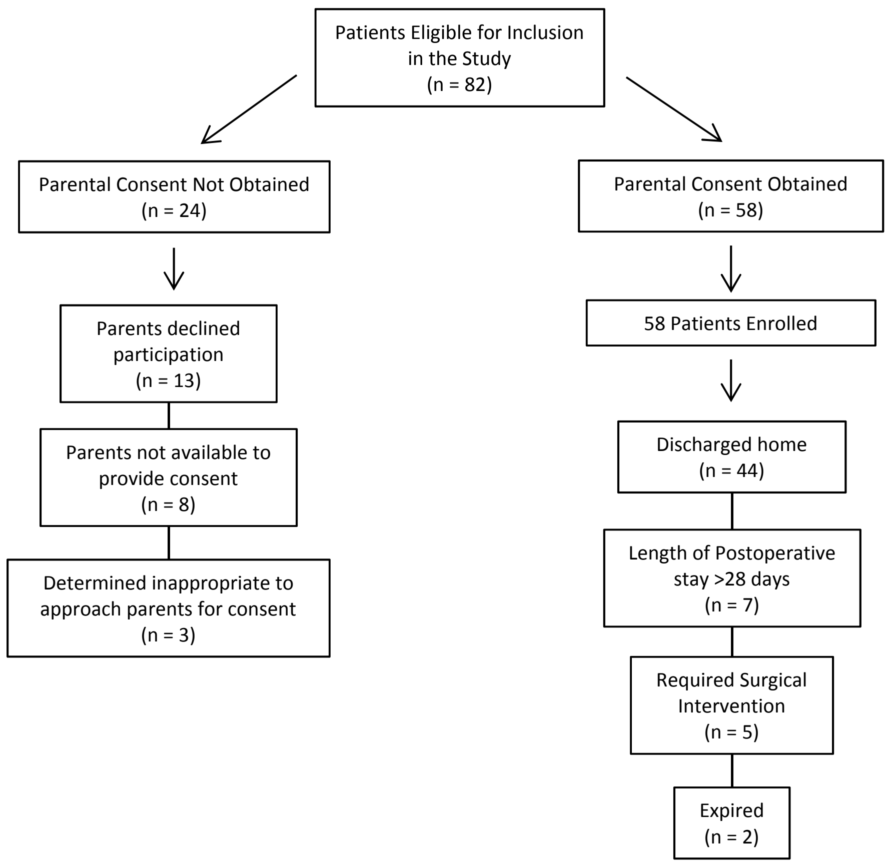


Table 1. RACHS-1 Categories

Risk Category	n (%)	Pre-operative Weight-for-age z-score	Intubated (hrs)	CPS time (min)	POS (days)	Discharge Weight-for-age z-score
2	20 (34.5)	-1.42 (IQR -2.33 to -0.26)	25 (4-29)	95 (81-114)	7 (5-15)	-1.51 (IQR -2.64 to -0.39)
3	16 (27.6)	-1.58 (IQR -3.37 to -0.36)	35 (6-75)	116 (84-124)	6 (4-12)	-2.18 (IQR -2.99 to -0.72)
4	10 (17.2)	-1.42 (IQR -2.5 to -0.25)	71 (44-128)	133 (90-184)	8 (7-13)	-1.93 (IQR -2.89 to -1.42)
6	12 (20.7)	-1.2 (IQR -1.8 to -0.1)	91 (71-120)	236 (196-250)	14 (11-24)	-1.59 (IQR -3.14 to -1.04)

Table 2. Anthropometric Growth Measure z-scores Expressed as Median and Interquartile Ranges

Growth Measure	z-score
Birth Weight-for-Age (n = 52)	-0.38 (IQR -1.27 to 0.28)
Birth Length-for-Age (n = 43)	-0.19 (IQR -1.26 to 0.67)
Birth Head Circumference-for-Age (n = 40)	-0.34 (IQR -1.16 to 1.21)
Birth Weight-for-Length (n = 31)	-0.27 (IQR -1.18 to 0.68)
Preoperative Weight-for-Age (n = 58)	-1.42 (IQR -2.33 to -0.29)
Preoperative Length-for-Age (n = 31)	-1.38 (IQR -2.25 to -0.8)
Preoperative Head Circumference-for-Age (n = 44)	-1.31 (IQR -2.28 to -0.8)
Preoperative Weight-for-Length (n = 31)	-1.49 (IQR -2.83 to 0.38)

Table 3. Median (IQR) Fluid Intake and Fluid Balance on Postoperative Days 1-28

	Day 1 (n = 58)	Day 2 (n = 57)	Day 3 (n = 54)	Day 4 (n = 46)	Day 5 (n = 41)	Day 6 (n = 40)	Day 7 (n = 36)	Day 8 (n = 34)	Day 9 (n = 31)	Day 10 (n = 29)
Fluid Intake (mL/kg/day)	109 (96-144)	104 (92-122)	110 (94-129)	112 (100-126)	115 (97-134)	115 (97-143)	128 (110-150)	128 (110-158)	122 (101-161)	133 (101-160)
Fluid Balance (mL/day)	38 (-135-332)	-22 (-104-116)	51 (-98-179)	48 (-106-156)	85 (-11-173)	109 (-0.1-194)	165 (50-229)	117 (48-177)	101 (44-180)	124 (50-200)

	Day 11 (n = 26)	Day 12 (n = 23)	Day 13 (n = 21)	Day 14 (n = 20)	Day 15 (n = 17)	Day 16 (n = 15)	Day 17 (n = 13)	Day 18 (n = 13)	Day 19 (n = 13)	Day 20 (n = 11)
Fluid Intake (mL/kg/day)	145 (112-161)	139 (116-165)	142 (107-170)	135 (122-162)	138 (118-175)	147 (123-175)	148 (115-167)	148 (115-180)	145 (102-171)	153 (123-163)
Fluid Balance (mL/day)	162 (69-210)	160 (113-231)	184 (110-239)	136 (79-209)	119 (67-182)	141 (60-207)	135 (61-152)	168 (120-237)	128 (84-208)	160 (133-257)

	Day 21 (n = 10)	Day 22 (n = 10)	Day 23 (n = 8)	Day 24 (n = 8)	Day 25 (n = 7)	Day 26 (n = 7)	Day 27 (n = 7)	Day 28 (n = 7)
Fluid Intake (mL/kg/day)	133 (121-160)	135 (115-164)	141 (127-150)	156 (138-182)	152 (142-170)	161 (152-166)	153 (117-161)	149 (131-172)
Fluid Balance (mL/day)	117 (-17-165)	86 (44-151)	119 (-19-171)	135 (48-230)	132 (43-178)	149 (108-241)	161 (126-175)	165 (114-232)

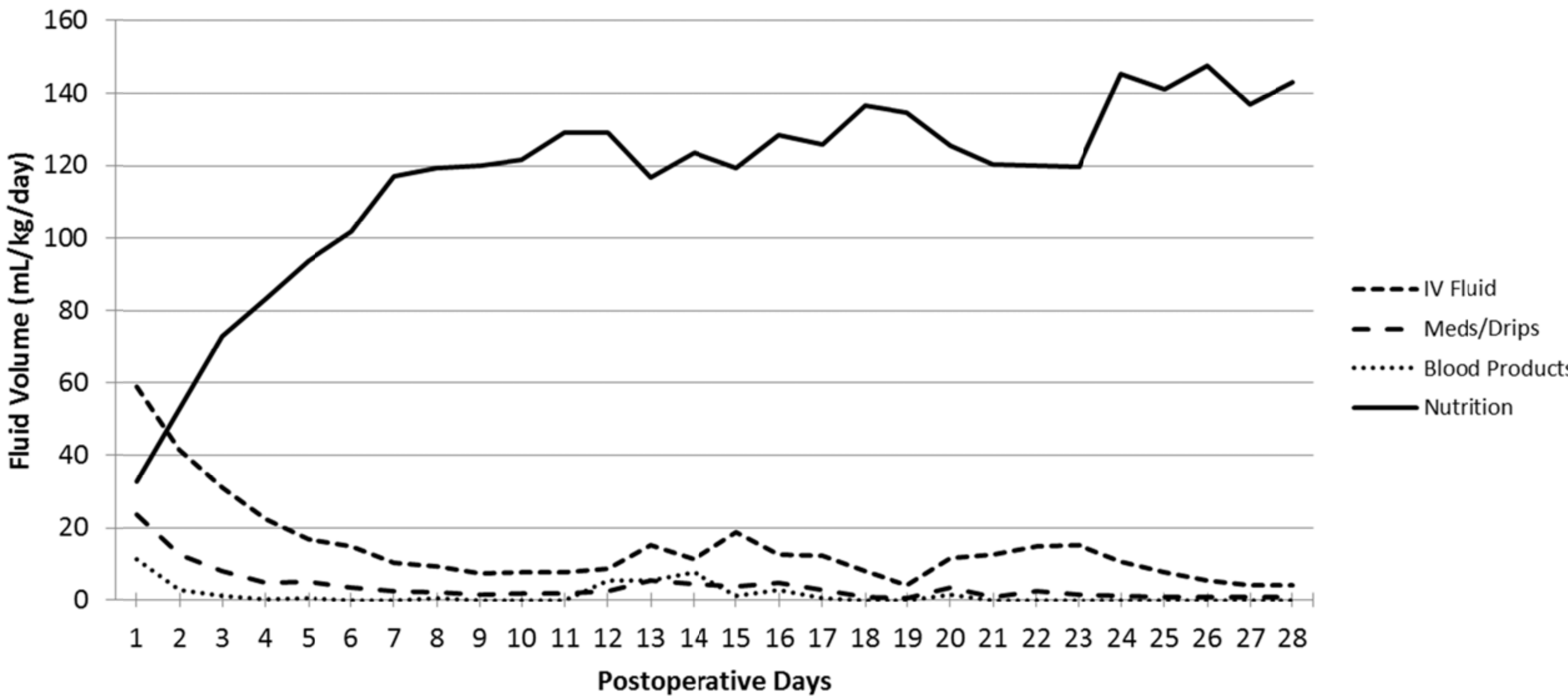
Table 4. Median (IQR) Fluid Intake Based on RACHS-1 Categories on Postoperative Days 1-14

	Day 1 (n = 58)	Day 2 (n = 57)	Day 3 (n = 54)	Day 4 (n = 46)	Day 5 (n = 41)	Day 6 (n = 40)	Day 7 (n = 36)
Category 2 Fluid Intake (mL/kg/day)	125 (99-150)	103 (91-126)	110 (94-129)	116 (99-126)	118 (86-141)	108 (95-127)	110 (102-142)
Category 3 Fluid Intake (mL/kg/day)	103 (96-116)	105 (92-123)	115 (101-131)	107 (90-121)	115 (92-128)	115 (107-144)	128 (109-154)
Category 4 Fluid Intake (mL/kg/day)	110 (96-176)	108 (97-132)	111 (93-141)	115 (102-143)	132 (103-158)	163 (109-179)	150 (136-179)
Category 6 Fluid Intake (mL/kg/day)	105 (92-161)	101 (91-111)	109 (93-120)	110 (103-122)	114 (99-131)	108 (88-128)	120 (115-142)

Table 4. Median (IQR) Fluid Intake Based on RACHS-1 Categories on Postoperative Days 1-14 (continued)

	Day 8 (n = 34)	Day 9 (n = 31)	Day 10 (n = 29)	Day 11 (n = 26)	Day 12 (n = 23)	Day 13 (n = 21)	Day 14 (n = 20)
Category 2 Fluid Intake (mL/kg/day)	111 (94-130)	108 (92-114)	97 (81-127)	111 (93-152)	110 (101-158)	101 (93-149)	110 (97-145)
Category 3 Fluid Intake (mL/kg/day)	129 (116-161)	116 (88-163)	128 (96-152)	142 (114-160)	135 (120-)	106 (105-)	120 (113-)
Category 4 Fluid Intake (mL/kg/day)	168 (123-188)	175 (97-191)	167 (125-193)	165 (135-177)	165 (127-186)	160 (121-186)	156 (132-197)
Category 6 Fluid Intake (mL/kg/day)	131 (115-148)	127 (115-151)	141 (110-162)	148 (120-154)	144 (123-162)	142 (134-166)	138 (133-158)

Figure 2. Mean Fluid Volume According to Method of Distribution for Postoperative Days 1-28



V. EVALUATION OF NUTRITION PRESCRIPTIONS, NUTRITIONAL INTAKE AND GROWTH OUTCOMES IN INFANTS FOLLOWING CARDIAC SURGERY

Abstract

Background: Infants who are recovering from cardiac surgery receive inadequate energy intake during the early postoperative period that may interfere with normal development during a critical period of growth. Studies to date have not fully explored nutritional practice, nutritional intake, and weight concomitantly in this very vulnerable population at high nutritional risk. The aim of this study was to compare the amount of kilocalories and protein prescribed and delivered to infants during the postoperative period following cardiac surgery. Additionally, this study examined the progression of nutritional intake during the postoperative period.

Methods: Infants from birth to 12 months of age who were scheduled for cardiac surgery at Miami Children's Hospital between December 2013 and September 2014 were followed during the postoperative stay. Total fluid intake, subcomponents of total fluid intake, and output were recorded in 24-hour increments for a maximum of 28 days. Patients were divided into two groups: nutrition initiated on postoperative day 1 and nutrition initiated after postoperative day1. Nutrition orders were collected and energy and protein prescibed were calculated and compared to actual intakes.

Results: Patients received significantly less calories (43±17.9 vs. 46±17.9 kcals/kg/day, $P<0.001$) and protein (1.72±0.76 vs. 1.81±0.74 g protein/kg/day, $P=0.001$) than ordered for parenteral nutrition (PN) and significantly less calories

(98±30 vs. 101±28.5 kcals/kg/day, P<0.001) and protein (2.07±0.78 vs. 2.18±0.79 g protein/kg/day, P<0.001) for oral/enteral nutrition (EN) diet orders. The difference in volume received from nutrition, the percent (%) calories and percent (%) protein met, in patients who received nutrition on postoperative day 1, compared to patients who had nutrition initiated after postoperative day 1, were significantly different until postoperative day 6 when volume received was no longer different between groups (p= 0.2). PN orders met less than 50% of the estimated energy requirements (EER) needs. Patients who had specified oral/EN diet orders did not meet 100% of EER until postoperative day 15.

Conclusions: A significant disparity exists between the prescribed diet and the nutrition delivered. Limited fluid volume for nutrition likely contributes to suboptimal nutritional delivery during the postoperative period, however, inadequate nutrition prescription, that meets the patient's needs and special conditions, may also be an important contributing factor. Development of a nutrition protocol for initiation and advancement of nutrition support may reduce the delay in achieving patient's nutritional goals and may attenuate the observed decrease in z-scores during the postoperative period.

Introduction

In the pediatric cardiac patient inadequate energy intake is described during the early postoperative period, and fluid restriction have been suggested as a limiting factor (Lambe et al., 2007; Li et al., 2008; Rogers et al., 2003). A potential confounder or contributing factor can be the philosophy of individual institutions regarding the practice of nutrition support. Unfortunately, current studies in the literature have not fully explored nutritional practice, nutritional intake, and weight concomitantly in the postoperative infant recovering from cardiac surgery. The lack of a comprehensive understanding of fluid restriction and nutritional delivery makes it difficult to determine if the decline in weight-for-age z-scores observed during the postoperative period can be prevented or attenuated (Anderson et al., 2011; Medoff-Cooper et al., 2011; Nicholson et al., 2013; Rogers et al., 2003). The development of evidence-based feeding protocols after surgery require an in-depth study of current practices and its long-term consequences for a group vulnerable to stunting and malnutrition.

The aim of this study was to compare the amount of energy and protein delivered to infants during the postoperative period following cardiac surgery to the amount of Calories and protein prescribed. The hypothesis was that Calories and protein delivered to infants during the postoperative period were less than those intended in the nutritional prescription ordered. Additionally, the extent to which fluid restriction contributes to inadequate intake during the postoperative period was explored to potentially identify other contributing factors.

Methods

Study Design and Subjects

The research design was a prospective cohort study conducted at Miami Children's Hospital. Infants from birth to 12 months of age who were diagnosed with a congenital heart defect and were admitted for surgical intervention between December 2013 and September 2014 were eligible for the study. Infants with a gestational age of less than 36 weeks at the time of surgery or with a diagnosis of renal dysfunction prior to surgery were excluded. The cut-off determined for gestational age was based on the estimated completion time of nephrogenesis (Shaffer & Weismann, 1992). The study was approved by the Institutional Review Boards of Florida International University and Miami Children's Hospital (Western Institutional Review Board). Parental informed consent was obtained prior to enrollment into the study.

Measurements

Nutrition orders and reasons for interruptions in nutritional delivery were documented. Energy and protein intakes were documented as Calories per kilogram body weight per day (kcals/kg/day) and grams of protein per kilogram body weight per day (g protein/kg/day) using the most recent weight available. A Registered Dietitian estimated nutritional needs using the dietary reference intakes (DRIs) for estimated energy requirements (EER) and protein (Food and Nutrition Board, 2005). EER equations are based on healthy infants and were chosen to estimate energy requirements as currently there are no valid equations that predict energy requirements in critically ill children. Standard references for healthy children were selected to estimate energy and protein needs with the understanding that during the postoperative period and in underweight patients requirements may be higher or lower than the estimated value.

Research Electronic Data Capture (REDCap) tools hosted at Florida International University was used to manage the study data (Harris et al., 2009). REDCap is a secure web application designed to capture data for research studies. Forms were designed to calculate Calorie and protein intake based on data inputs.

Data Analysis

Descriptive statistics for continuous variables were reported as percentages, means, and medians with interquartile ranges. Data were tested for normality. Paired t-test was used to compare Calories and grams of protein received compared to ordered for PN orders. Wilcoxon Signed Ranks Test was used for oral/EN diet orders. Patients were divided into two groups: nutrition initiated on postoperative day 1 and nutrition initiated after postoperative day 1. Variances between the groups were determined to be equal as determined by nonparametric Levene's test for the following variables: age, preoperative weight, cardiopulmonary bypass duration, intubation, length of postoperative stay, preoperative weight-for-age z-score and discharge weight-for-age z-score. Mann Whitney U test was used to test for differences between the two groups. Statistical significance was defined as $P<0.05$. The data was analyzed using IBM SPSS Statistics 22 (SPSS Inc, Chicago, IL).

Results

All patients (n = 58) were NPO on postoperative day 0. On postoperative day 1, 52% of patients remained NPO (n = 30) and 48% of patients had nutrition initiated. Patients received nutrition on postoperative day 1 via the following routes: orally (n = 22), EN (n = 1), and PN (n = 5). Of patients who only received IV fluids on postoperative day 1, 15 patients (50%) had nutrition initiated on postoperative day 2, 9 patients on postoperative day 3 (30%), 4 patients on postoperative day 4 (13%) and 2 patients on postoperative day 5 (7%). Two patients were discontinued from the study prior to having nutrition initiated (one patient expired and the other required further surgical intervention). Patients who had nutrition initiated after postoperative day 1 were advanced as follows: 9 patients were advanced to oral feeds, 5 patients had EN initiated, 12 patients had PN initiated, and 2 patients had a combination of PN and EN initiated. One patient who was initially advanced to EN on postoperative day 3 was placed NPO on postoperative day 4 and had PN initiated on postoperative day 5. A schematic of the study cohort's time to initiation of nutrition, routes of nutritional delivery and reason for discontinuation from the study are shown in Figure 1.

Mean energy intake did not exceed 80 kcals/kg/day until postoperative day 7 and did not exceed 100 kcals/kg/day by postoperative day 16 in those patients who remained hospitalized. Mean protein intake did not meet reference intakes for healthy children until postoperative day 4. Median values and interquartile ranges for calorie and protein intake on each postoperative day are presented in Table 1. On average patients met 100% of estimated protein needs by postoperative day 4 but did not meet 90% of estimated energy until postoperative day 11. Median values and interquartile ranges for percent calorie and protein intake met on each postoperative day are presented in Table 2.

Patients who had nutrition initiated on postoperative day 1 were older, had a higher weight at the time of surgery, experienced a shorter postoperative stay, and had a smaller decrease in weight-for-age z-scores compared to patients who had nutrition initiated after postoperative day 1. Characteristics of the two groups are shown in Table 3. The trend in volume for patients who had nutrition initiated on postoperative day 1 and patients who had nutrition initiated after postoperative day 1 is shown in Figure 2A. Patients who had nutrition initiated on postoperative day 1 met 90% of estimated daily calorie needs and 100% of estimated daily protein needs sooner than patient who had nutrition initiated after postoperative day 1 as shown in Figure 2B and 2C. The difference in volume received for nutrition, percent calories met and percent protein met were significantly different between groups until postoperative day 6 when volume received was no longer significantly different between groups ($p = 0.2$). Although the volume of fluid received for nutrition after day 6 was no longer significantly different between the groups, the difference between the percent calorie and protein met between the groups remained significant until day 7, with the group for whom nutrition was initiated on postoperative day 1 meeting a greater percentage of estimated calorie (88±33.5 vs. 77±23.5, $P<0.031$) and protein needs (125±43 vs. 116±48.2, $P<0.045$) than the group that had nutrition initiated after postoperative day 1. A significant difference between groups was no longer observed by postoperative day 7 for all 3 variables. However, neither group met 100% of estimated calorie needs until postoperative day 15, as shown in Figure 2B.

During the study period, 20 patients received PN for a median of 3 days (IQR 2-4.5 days) with a total of 86 PN orders written. There were 2 instances where PN was written but not initiated and 2 instances where PN was delivered, however, the written orders could not be found. Day 2 (IQR 1.75-4) was the median for the initiation of PN. Median calories, protein and fluid ordered for initiation and advancement of PN are shown in Table 4. On average PN orders were written to provide 53 ±15.8 kcals/kg/day and 2.09 ±0.58 g protein/kg/day meeting 47 ±14% estimated calorie needs and 137 ±38% of estimated protein needs. A significant mean difference was observed between PN calories (46±17.9 vs. 43±17.9, $P<0.001$) and protein (1.81±0.74 vs. 1.72±0.76, $P=0.001$) ordered compared to calories received.

Nutrition-related serum markers that may affect nutritional delivery of macronutrients via PN were evaluated. On postoperative days 0, 1, 2, and 3 elevated glucose levels were observed in 64%, 51%, 21%, and 17% of patients, respectively. For patients who met criteria for stage I acute kidney injury (n = 18), serum creatinine peaked on median postoperative day 1.5 (IQR 1-2). Elevated liver function tests (LFTs) were noted in 7% of patients (n = 4).

On average diet orders with specified volumes and frequency of intake met 97±27.5% of estimated calorie needs and 147±55.7% estimated protein needs. Postoperative days with a single diet order (n = 174) were compared to actual intake. The median calories received were 100 kcals/kg/day (IQR 79-120 kcals/kg/day) and median calories ordered were 106 kcals/kg/day (IQR 86-123 kcals/kg/day). The median protein received was 2.1 g protein/kg/day (1.6-2.54 g protein/kg/day) and the median protein ordered was 2.21 g protein/kg/day (IQR 1.65-2.6 g protein/kg/day). Calories and protein received were significantly less than what was ordered (P<0.001 for both calories and protein).

Percent calories met, percent protein met, and volume from nutrition received by patients with specific diet orders was not significantly different than those for patients who had ad libitum orders. The progression of volume received for nutrition is shown in Figure 3A. Patients who were fed ad libitum, however, met 100% of protein needs sooner than patients with specific diet orders as shown in Figure 3C. Patients fed ad libitum did not meet 90% of estimated energy needs until postoperative day 8 while patients with specific diet orders did not meet 90% of estimated energy needs until postoperative day 11 as shown in Figure 3B.

A total of 30 patients were found to have feeding interruptions during the postoperative course with a total of 63 diet downgrades identified. Reasons for interruptions in feeds include preparation for extubation, gastrointestinal intolerance (i.e. abdominal distension, residuals, emesis), and tests/procedures (i.e. cardiac catheterizations, sedated echocardiogram). A list of reasons and the frequency of interruptions are outlined in Table 5.

Discussion

The findings of this study are similar to that of a previous study that looked at nutrition prescription and nutritional delivery in a pediatric intensive care unit setting (de Neef et al., 2008). The authors' interpretation of their findings were that a statistically significant but clinically irrelevant disparity between prescribed and delivered nutrition was observed and inadequate prescription was implicated as the variable responsible for malnutrition (de Neef et al., 2008). We have also found a statistical difference between nutrition ordered and nutrition received. The difference in terms of protein is considered to be clinically irrelevant as the mean difference has little clinical implications. The mean protein intake was greater than 100% of dietary reference intakes for age with patients receiving an average of 1.7±0.76 g pro/kg/day for PN and 1.95±0.83 g pro/kg/day for specific diet orders. The mean difference was only 0.09±0.27 g protein/kg/day for PN orders and 0.12±0.34 g protein/kg/day for specific diet orders. The difference in calories deserves greater attention as a mean difference of 3±6.3 kcals/kg/day for PN orders and a 4.5±15.4 kcals/kg/day for specific diet orders may have some clinical relevance depending on factors surrounding any given patient. To use protein adequately for growth, maintenance and recuperation from critical illness, adequate amount of calories is essential (Finnerty, Mabvuure, Ali, Kozar & Herndon, 2013; Mehta & Duggan, 2009). If calories are inadequate, protein will be used to provide energy, creating wasteful and sometimes toxic nitrogen products (Mehta & Duggan, 2009). Medical status, age, nutritional status, and nutritional intake all influence the clinical relevance of the difference in calories ordered vs calories delivered since these factors influence total energy requirements. In a setting where it is challenging to optimize nutritional intake and adequate growth is a concern, minimizing under delivery of calories is important to either offset the energy deficit during the catabolic state or to promote a positive energy balance during the anabolic state.

Nutritional intake during the postoperative period is inadequate based on reports of poor postoperative growth outcomes (Anderson et al., 2011; Medoff-Cooper et al., 2011; Nicholson et al., 2013; Rogers et al., 2003). Limited fluid volume for nutrition likely contributes to suboptimal nutritional delivery during the postoperative period; however, inadequate nutrition prescription is also a contributing factor. It is suspected that inadequate nutrition prescription may be due to medical complications incurred during surgical recovery, lack of standard guidelines for nutritional expectations in infants recovering from cardiac surgery and the variations between physicians' individual philosophies regarding nutritional delivery. Development and consistent implementation of a nutrition protocol would be prudent to determine if the postoperative progression of nutrition is optimal.

A limitation of the current study is that nutrition prescription vs nutrition delivery was only compared for days with single diet orders. The reason for this was that it was not possible to accurately quantify a gradual progression in oral/EN diet orders throughout the day with the current study design. The time lapse between when orders were written and when diet changes took effect in real time was not accounted for. As a result, an accurate progression of nutrition prescription for specific diet orders could not be evaluated. Another limitation was that volumes were collected in 24 hour increments and we were unable to determine specific time points during the day for which nutritional delivery did not match nutrition orders, and the accompanying reason for the deviation from the diet order.

A prospective study design specifically looking at nutritional intake on hourly increments with documentation of deviations from the diet order, when diet orders are not ordered to be specifically interrupted for certain events, could potentially lead to a narrowing of the gap between nutrition ordered and nutrition delivered. The expectation being that subsequent improvement of nutritional delivery could positively influence the change in weight-for-age z-scores.

Conclusion

A disparity exists between nutrition prescribed and nutrition delivered, contributing to inadequate energy intake during the postoperative period. Our findings suggest that nutrition protocol with early initiation and advancement of nutrition support may reduce the delay in achieving patient’s nutritional goals and may attenuate the observed decrease in z-scores during the postoperative period. Identification and elimination of unnecessary interruptions in feeds may also promote improved nutritional delivery.

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Figure 1. Schematic of Nutrition Initiation and Reason for Discontinuation from the Study

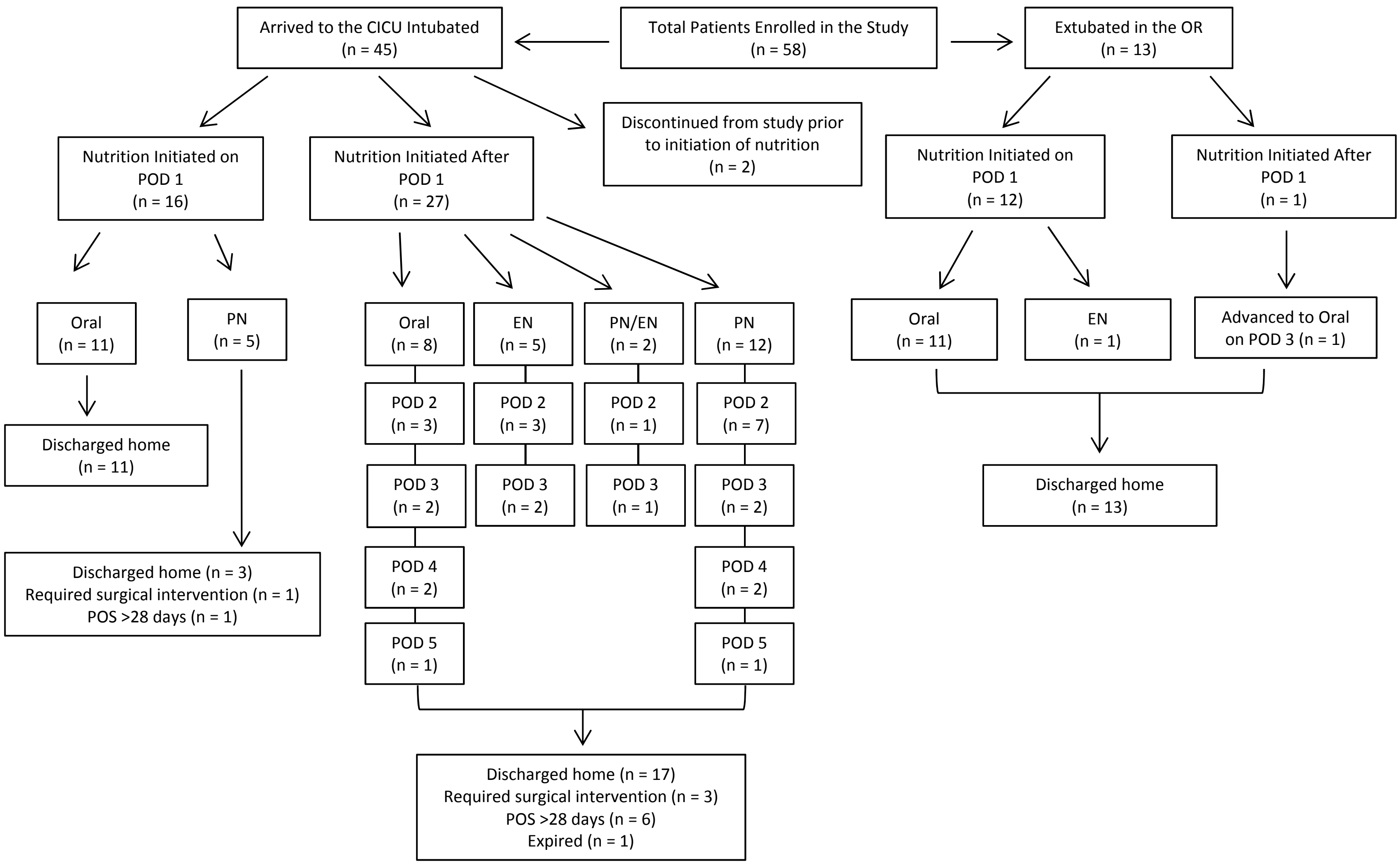


Table 1. Median (IQR) Calorie and Protein Intake on Postoperative Days 1-28

	Day 1 (n = 58)	Day 2 (n = 57)	Day 3 (n = 54)	Day 4 (n = 46)	Day 5 (n = 41)	Day 6 (n = 40)	Day 7 (n = 36)	Day 8 (n = 34)	Day 9 (n = 31)	Day 10 (n = 29)
Calorie Intake (kcal/kg/day)	21 (11-39)	35 (22-60)	50 (33-72)	61 (38-84)	66 (47-94)	72 (53-88)	84 (70-102)	92 (70-106)	91 (71-112)	92 (73-109)
Protein Intake (g/kg/day)	0 (0-0.8)	0.88 (0-1.3)	1.44 (0.7-2)	1.47 (0.7-2)	1.43 (1-2)	1.58 (1.1-2)	1.62 (1.2-2.3)	1.88 (1.4-2.3)	1.85 (1.5-2.3)	1.77 (1.5-2.2)

	Day 11 (n = 26)	Day 12 (n = 23)	Day 13 (n = 21)	Day 14 (n = 20)	Day 15 (n = 17)	Day 16 (n = 15)	Day 17 (n = 13)	Day 18 (n = 13)	Day 19 (n = 13)	Day 20 (n = 11)
Calorie Intake (kcal/kg/day)	95 (78-117)	98 (72-103)	97 (68-118)	89 (74-115)	106 (55-129)	100 (70-135)	100 (76-123)	100 (87-123)	116 (81-134)	118 (73-130)
Protein Intake (g/kg/day)	2.1 (1.6-2.5)	2.2 (1.7-2.7)	2.25 (1.7-2.5)	2.2 (1.6-2.8)	1.99 (1.1-2.6)	2.16 (1.5-2.7)	2.38 (1.7-2.6)	2.47 (2.1-2.9)	2.5 (2.2-3)	2.73 (2.3-3.4)

	Day 21 (n = 10)	Day 22 (n = 10)	Day 23 (n = 8)	Day 24 (n = 8)	Day 25 (n = 7)	Day 26 (n = 7)	Day 27 (n = 7)	Day 28 (n = 7)
Calorie Intake (kcal/kg/day)	114 (80-128)	110 (85-129)	98 (89-119)	115 (92-143)	127 (86-139)	132 (98-138)	127 (81-138)	127 (108-140)
Protein Intake (g/kg/day)	2.47 (2-2.8)	2.37 (1.5-2.9)	2.08 (1.3-2.5)	2.27 (1.5-2.7)	2.5 (1.3-3.3)	2.46 (2-3.6)	2.62 (2.1-3.2)	2.6 (1.8-3.1)

Table 2. Median (IQR) Percent Calories and Protein Met on Postoperative Days 1-28

	Day 1 (n = 58)	Day 2 (n = 57)	Day 3 (n = 54)	Day 4 (n = 46)	Day 5 (n = 41)	Day 6 (n = 40)	Day 7 (n = 36)	Day 8 (n = 34)	Day 9 (n = 31)	Day 10 (n = 29)
Calories met (%)	17 (12-42)	34 (19-69)	47 (29-82)	60 (36-80)	61 (44-86)	68 (48-93)	73 (63-94)	85 (65-99)	88 (66-101)	84 (73-101)
Protein met (%)	0 (0-48)	58 (0-105)	95 (48-136)	100 (59-140)	99 (68-134)	104 (70-136)	106 (84-152)	124 (95-154)	122 (101-148)	116 (99-143)

	Day 11 (n = 26)	Day 12 (n = 23)	Day 13 (n = 21)	Day 14 (n = 20)	Day 15 (n = 17)	Day 16 (n = 15)	Day 17 (n = 13)	Day 18 (n = 13)	Day 19 (n = 13)	Day 20 (n = 11)
Calories met (%)	91 (76-102)	93 (79-117)	93 (61-111)	88 (69-111)	91 (57-111)	92 (83-118)	93 (80-107)	97 (86-107)	108 (85-118)	106 (93-113)
Protein met (%)	138 (108-166)	145 (113-179)	148 (111-170)	152 (103-183)	130 (83-168)	142 (97-186)	161 (111-181)	163 (136-215)	166 (142-206)	193 (174-220)

	Day 21 (n = 10)	Day 22 (n = 10)	Day 23 (n = 8)	Day 24 (n = 8)	Day 25 (n = 7)	Day 26 (n = 7)	Day 27 (n = 7)	Day 28 (n = 7)
Calories met (%)	102 (74-110)	99 (77-110)	88 (81-104)	103 (84-123)	111 (78-126)	113 (89-126)	113 (74-118)	112 (98-123)
Protein met (%)	162 (128-184)	156 (101-189)	137 (89-165)	149 (101-175)	165 (85-214)	162 (132-236)	172 (136-208)	168 (121-205)

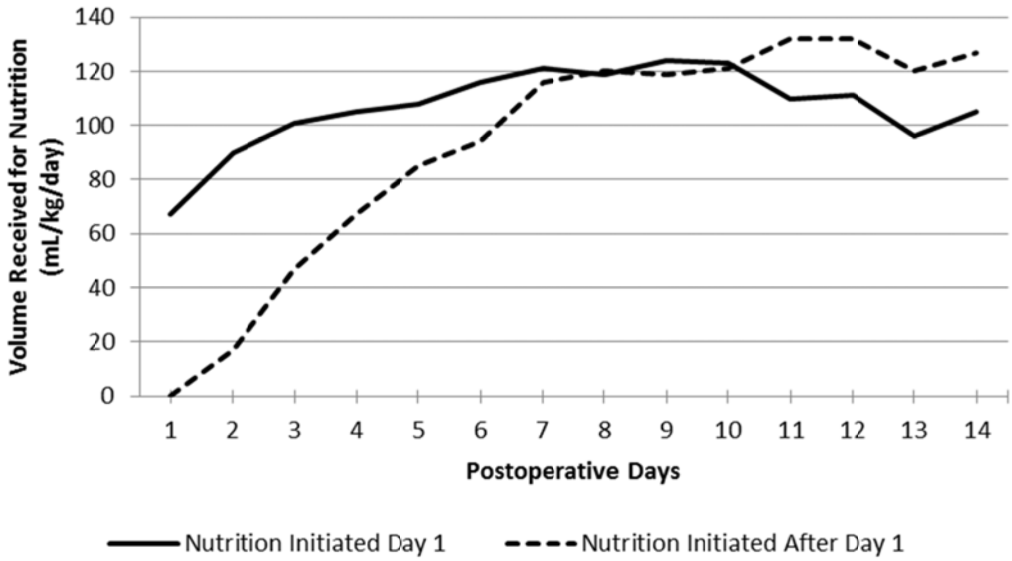
Table 3. Nutrition Initiated on Postoperative Day 1 vs After Postoperative Day 1

	Nutrition Initiated Postoperative day 1 (n = 28)	Nutrition Initiated After Postoperative day 1 (n = 30)	p-value
Median Age (days)	134.5 (IQR 39.3-193.8)	13.5 (IQR 6-51.3)	<0.001
Median Preoperative Weight (kg)	5.26 (IQR 3.64-6.1)	3.37 (IQR 2.85-3.71)	<0.001
Median Cardiopulmonary Bypass Duration (minutes)	102.5 (IQR 82.5-123.3)	166 (IQR 112-230.5)	0.002
Median Duration of Intubation (hours)	22 (IQR 4.5-65.5)	71.2 (IQR 38.4-99.8)	0.002
Median Length of Postoperative Stay (days)	5.8 (IQR 4.8-9.1)	14.1 (IQR 11.1-18)	<0.001
RACHS-1			
Category 2 (n = 20)	13	7	
Category 3 (n = 16)	10	6	
Category 4 (n = 10)	4	6	
Category 6 (n = 12)	1	11	
Mean Preoperative Weight-for-Age z-score	-1.58 ±1.53	-0.96 ±1.27	0.259
Mean Discharge Weight-for-Age z-score	-1.95 ±1.49	-1.81 ±1.19	0.737
Mean Difference in Preoperative vs Discharge Weight-for-Age z-scores	0.37 ±0.34*	0.85 ±0.55*	

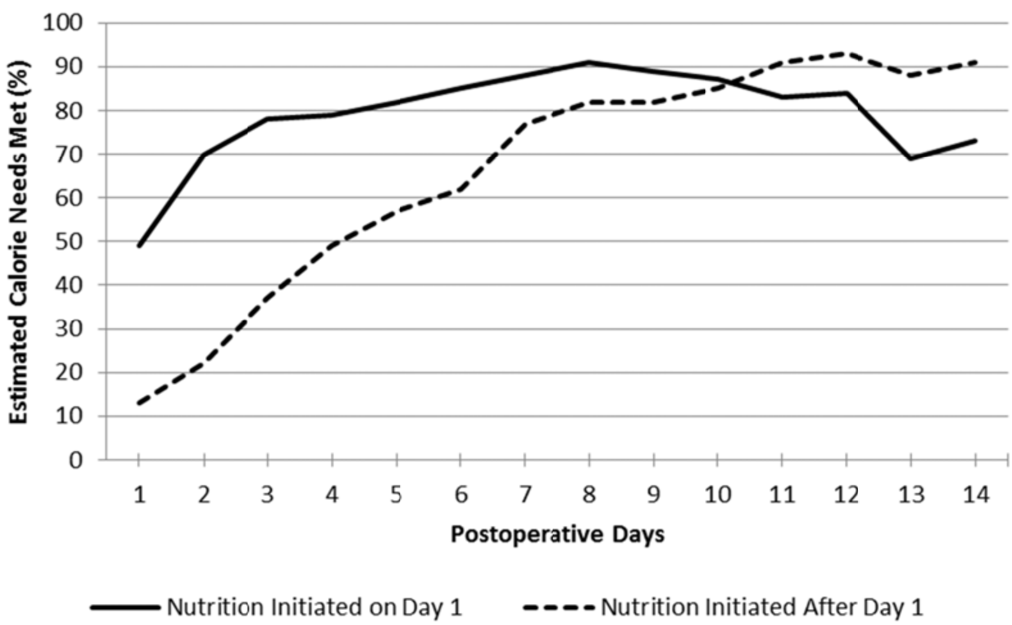
*p<0.001

Figure 2. Volume Received for Nutrition (A), Percent Calories Met (B), and Percent Protein Met (C) for Nutrition Initiated on Postoperative Day 1 vs Nutrition Initiated After Postoperative Day 1

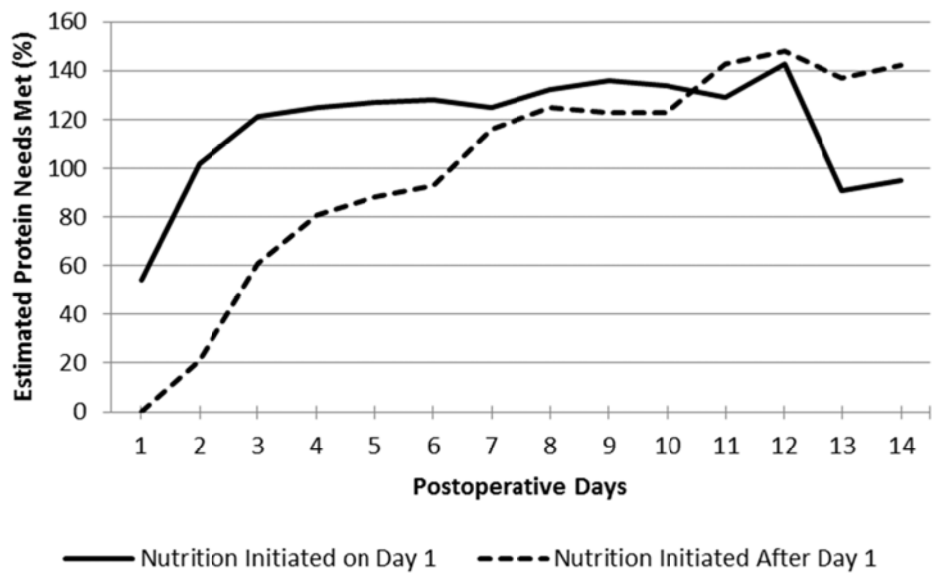
A



B



C



160
140
120
100
80
60
40
20
0
Estimated Protein Needs Met (%)
1 2 3 4 5 6 7 8 9 10 11 12 13 14
Postoperative Days
Nutrition Initiated on Day 1
Nutrition Initiated After Day 1

Table 4. Initiation and Advancement of PN Orders: Median (IQR) for Calories, Protein and Volume

	Day 1 (n = 23)	Day 2 (n = 18)	Day 3 (n = 14)	Day 4 (n = 7)	Day 5 (n = 4)	Day 6 (n = 4)	Day 7 (n = 4)
Calories (kcals/kg/day)	48 (34-60)	52 (42-59)	65 (42-80)	60 (45-71)	55 (45-59)	60 (46-61)	57 (46-64)
Protein (g pro/kg/day)	1.5 (1.47-2)	1.98 (1.79-2.24)	2.48 (1.89-2.77)	2.18 (1.84-3)	2.02 (1.59-2.67)	2.25 (1.67-2.82)	2.65 (2.14-2.93)
Volume (mL/kg/day)	84 (60-99)	77 (63-84)	75 (64-88)	72 (56-76)	63 (60-71)	68 (61-75)	70 (62-76)

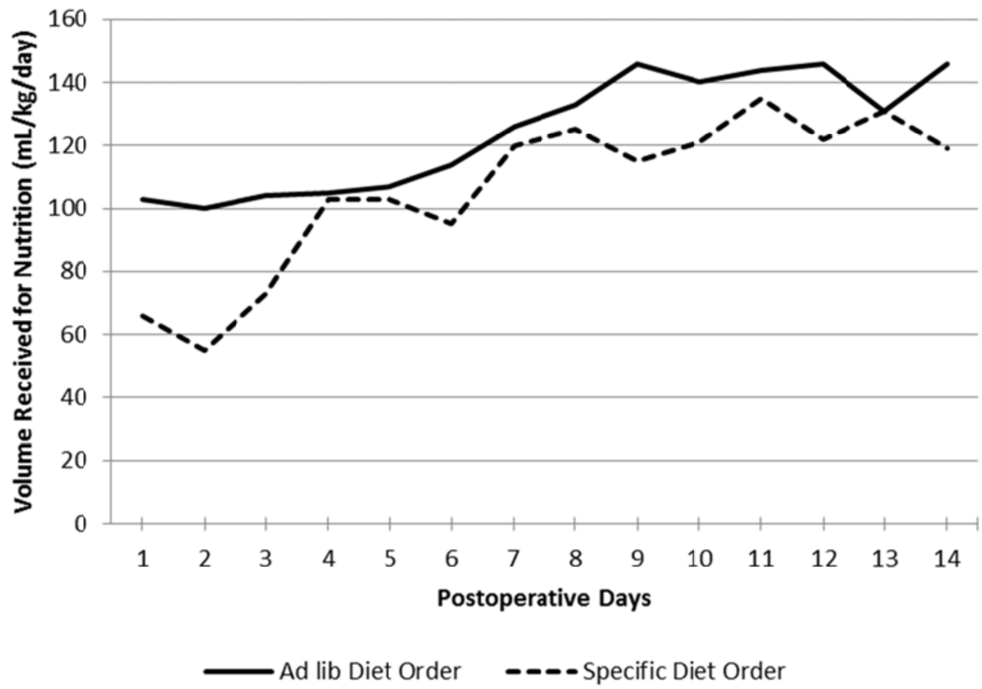
	Day 8 (n = 4)	Day 9 (n = 2)	Day 10 (n = 2)	Day 11 (n = 1)	Day 12 (n = 1)
Calories (kcals/kg/day)	59 (45-64)	50 (35-)	45 (28-)	64	73
Protein (g pro/kg/day)	1.92 (1.59-2.74)	2.42 (1.84-)	2.77 (2.75-)	2.63	3.02
Volume (mL/kg/day)	65 (53-71)	58 (55-)	60 (54-)	65	65

Table 5. Reasons for Oral/EN Feeding Interruptions

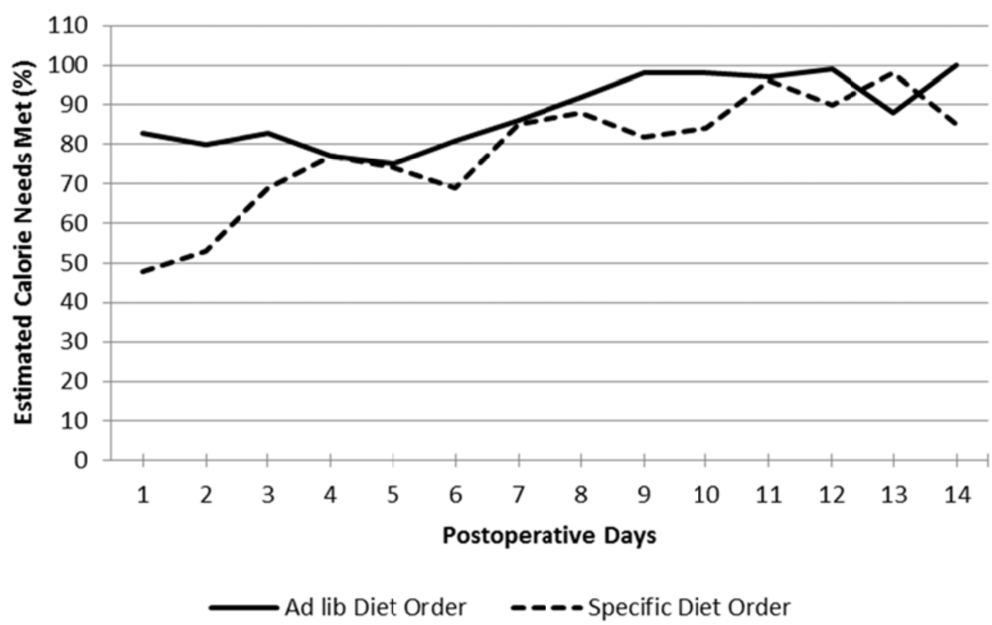
Reason for Feeding Interruption	%
Extubation (n = 12)	19
GI Intolerance (n = 16)	25
Chest tube removal (n = 5)	8
Cardiac Cath (n = 8)	13
Sedated ECHO (n = 4)	6
Heart rate/Respiratory issues (n = 6)	10
Intubation (n = 2)	3
Central line placement/removal (n = 3)	5
Swallowing concerns (n = 3)	5
Other (n = 4)	6

Figure 3. Volume Received for Nutrition (A), Percent Calories Met (B) and Protein Met (C) for Ad libitum diet orders vs Specific Diet orders

A



B



C


200
180
160
140
120
100
80
60
40
20
0
Estimated Protein Needs Met (%)
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Postoperative Days
Ad lib Diet Order
Specific Diet Order

VI. DISCUSSION

The chapters III, IV and V examined the relationship between fluid restriction, nutritional intake and decrease in weight-for-age z-scores from admission to hospital discharge in children undergoing cardiac surgery. The decrease in weight-for-age z-score is clinically relevant and in agreement with previous studies (Anderson et al., 2011; Medoff-Cooper et al., 2011; Nicholson et al., 2013). Although the change observed in our prospective study was smaller, the decrease in weight-for-age z-score was clinically relevant because the nutritional goal is weight maintenance during the critical state and appropriate weight gain during the recovery phase. In theory, a male infant with an age of 37 days and a weight of 3.7 kg would present with a decrease in weight-for-age z-score of 0.56 if weight maintenance was observed for 10 days. A female infant of the same age and weight would theoretically experience a similar change in weight-for-age z-score if weight were maintained for 11 days. Based on these theoretical expected changes in z-scores, it can be inferred that the nutritional support during these critical stages of disease are not meeting the increased energy needs for weight maintenance.

For both genders the time of theoretical weight maintenance is longer than the median length of postoperative stay which means the insufficient weight gain spans both the critical and recovery phases. Based on these theoretical expected changes in z scores, there are two scenarios which may explain the decline is weight-for-age z score. The first scenario is that patients are not sufficiently supported nutritionally during the increased energy needs of the critical phase, resulting in weight loss and subsequent weight gain during the recovery phase, which is not appreciated due to the need to achieve catch-up growth from the accrued deficit. The second scenario is that patients are sufficiently supported during the critical phase; however, nutrition is not adequately progressed during the recovery phase to achieve weight gain. Unfortunately this dilemma is beyond the capabilities of the current study to discern which scenario is more likely to contribute to the observed decline in weight-for-age z-score. It is possible that a combination of both scenarios is contributing to the observed decline in weight-for-age z-scores. Elevated glucose levels observed during the immediate postoperative period may be an indicator of inflammation following cardiac surgery; however, this elevated lab marker may also be influenced by gluconeogenesis causing wasting if energy intake is insufficient. The delay in meeting 90-100% of estimated energy requirements suggests insufficient energy intake during the recovery phase.

In both our preliminary retrospective and the prospective cohort studies, fluid volume during the early postoperative period was higher than the postoperative protocol of 4 mL/kg/hr. Total fluid intake volume was also higher than values reported at other institutions during the early postoperative period (Hazel, 2013; Nicholson, 2014; Rogers, 2003), and this may explain the smaller losses in z-scores found in this study. While we observed a higher volume of intakes during the early postoperative period and the median duration of mechanical ventilation was slightly longer than other studies, median length of hospital stay was shorter than reports at other institutions (Anderson et al., 2011;

Toole et al., 2014). It should be acknowledged that duration of ventilation support and length of hospital stay may be influenced by the complexity of the cardiac defect being addressed. Gillespie et al. (2006) reported a median postoperative mechanical ventilation time of 9.5 hours (range 0-260 hours) in patients who underwent elective surgery and 72 hours (range 0-5304 hours) in patients who underwent non-elective surgery. In infants with univentricular physiology, Medoff-Cooper et al. (2011) reported a median mechanical ventilation time of 72 hours (range 3-624 hours) and a median length of stay of 20 days (range 8-138 days). The variation in mechanical ventilation time and length of postoperative stay was observed within our cohort when the variables were stratified based on RACHS-1 categorization. Duration of mechanical ventilation and postoperative length of stay increased as the risk category increased which coincide with what the risk categories are intended to predict (Jenkins et al., 2002).

In addition to suboptimal growth during the postoperative period, growth is impaired in some patients from birth to surgical intervention. The cardiac condition may cause failure-to-thrive. Weight-for-age, length-for-age, head circumference-for-age and weight-for-length z-scores decreasing below -2 from birth to surgical intervention classifies some infants as underweight, stunted and wasting. Preoperative growth failure is a factor that requires further investigation as minimizing this before elective surgery may improve the postoperative course as adequate nutritional status at baseline is known to be associated with better outcomes (Radman et al., 2014; Toole et al., 2014).

In terms of nutrition prescription and delivery, the findings of this study are similar to that of a previous study that looked at nutrition prescription and nutritional delivery in a pediatric intensive care unit setting (de Neef et al., 2008). The authors' interpretation of their findings was that a statistically significant but clinically irrelevant disparity between prescribed and delivered nutrition was observed and inadequate prescription was implicated as the variable responsible for malnutrition (de Neef et al., 2008). We have also found a statistical difference between nutrition ordered and nutrition received. The difference in terms of protein is considered to be clinically irrelevant as the mean difference has little clinical implications. The mean protein intake was greater than 100% of dietary reference intakes for age with patients receiving an average of 1.7±0.76 g pro/kg/day for PN and 1.95±0.83 g pro/kg/day for specific diet orders. The mean difference was only 0.09±0.27 g protein/kg/day for PN orders and 0.12±0.34 g protein/kg/day for specific diet orders. The difference in calories deserves greater attention as a mean difference of 3±6.3 kcals/kg/day for parenteral nutrition (PN) orders and a 4.5 ±15.4 kcals/kg/day for specific diet orders may have clinical relevance depending on factors surrounding any given patient. Protein utilization is compromised and nitrogen waste products unnecessarily increased when there is inadequate caloric intake. Medical status, age, nutritional status, and nutritional intake all influence the clinical relevance of the difference in calories ordered vs calories delivered since these factors influence total energy requirements. In a setting where it is challenging to optimize nutritional intake and adequate growth is a concern, every calorie that is delivered is important to either offset the energy deficit during the catabolic state or to promote a positive energy balance during the anabolic state.

Based on the studies by Butte and colleagues (1989, 2005) at 1 month of age ~40% of total energy is needed for accretion of tissue in healthy term infants and by 3 months of age ~20% of total energy is needed. Energy requirements for accretion of tissue gradually trends down to 2% of total energy needs by 12 months of age (Butte et al., 2000; Butte, 2005). Estimations of the energy cost of growth are 5-6 kcals to accrue 1 g of tissue (Butte et al., 1989).

Typically PN is prescribed during the critical state at which time point weight maintenance is the goal. If we were to adjust the percentage of estimated energy requirement (EER) downward to exclude energy needed for accretion of tissue, in theory a 1 month old infant would need 60% of EER to maintain weight. However, it is also known that the catabolic state uses a less energy efficient process to synthesize acute phase proteins in the absence of adequate energy intake which likely will increase energy requirements. Given that PN was found to provide a mean of 47±14% of estimated calorie needs, PN prescription was likely inadequate. PN volume ordered is determined based on volume left after subtracting volume used to maintain lines and provide medication drips. As medications are weaned and lines are removed, volume for PN is increased. Conversely, if a medication needs to be started or if a patient is evaluated as not achieving target fluid balance, the PN rate may be adjusted downward. Limited fluid volume allowed for nutrition is likely a limiting factor for providing adequate nutrition; however, it is suspected that inconsistent practice with regards to advancement of PN is also a factor.

When no longer in the critical state, the expectation is appropriate growth for age. Patients who have congenital heart issues are known to have challenges with growth often requiring more calories than the EER. Based on our study findings, infants do not meet 100% of the EER by postoperative day 14. The delay in meeting the EER supports the inference that nutritional intake during the postoperative periods is inadequate to meet estimated energy needs.

Current standards for maintenance fluid volume needs are specifically for parenteral fluid therapy. There is a lack of standardized volume references for feeds received via the oral or enteral route. If fluid volume is limited to maintenance parenteral fluid requirements, oral and enteral feeds will not meet estimated nutritional need. A fluid volume of 100 mL/kg/day will provide only 67 kcals/kg/day from either breast milk or infant formula (standard dilution 20 kcals/oz.) that is not adequate to meet EER. There is a lack of evidenced regarding acceptable volumes of oral and enteral feeds to advance to without incurring complications of fluid overload or feeding intolerance which can explain the slow progression of nutrition during the postoperative period.

Nutritional intake during the postoperative period is inadequate based on poor postoperative growth outcomes and is likely attributed to limited fluid volume available to provide nutrition and inadequate nutrition prescription. Medical complications incurred during surgical recovery, the lack of standard guidelines for nutritional expectations in infants recovering from cardiac surgery and the variations between physicians' individual philosophies regarding nutritional delivery are suspected to influence the adequacy of nutrition prescriptions, and their nutritional outcomes.

VII. STRENGTHS AND LIMITATIONS

Compared to the preliminary retrospective study, the prospective study has a stronger design because its data were collected expressly to test the hypotheses, and because it performed a comprehensive analysis of current nutrition practices and participant's growth parameters. In addition, the prospective study allowed for identification of variables that would improve the understanding of study findings such as, categorization of the complexity of surgical interventions in the cohort and expressing calories and protein ordered and received as a percentage of estimated needs to allow for comparison between groups. Additionally, the use of REDCap improved the accuracy of data entry and minimized the potential for human error in tabulating fluid volumes and calculating calories and protein, providing a strong internal validity to the process of data collection and analysis (Harris et al., 2009).

Limitations of this study included a small sample size and some missing data. The number of eligible patients and the observed enrollment rate was less than anticipated mainly because parents' concerns on the added burden of participation. Although a prospective design was chosen to improve the quality of data collected it was not possible to have all data points collected as some baseline variables were not available at each time point in the electronic medical record. Additionally, some patients required discontinuation from the study due to critical status and need for surgical intervention, limiting the number of observations for certain outcome variables of interest.

It is acknowledged that weight as a primary outcome measure is considered a limitation as it can be influenced by hydration status. Weight is known to fluctuate throughout the day, and diuresis is part of the postoperative management of infants following cardiac surgery. While weights were obtained as available, we selected the two time points (prior to surgery and at hospital discharge) where it was believed that fluid balance was less likely to be an issue. Additionally, weight was the most practical marker for determining adequacy of nutritional intake in a clinical setting.

Another limitation was the challenge of comparing nutrition prescription with nutrition delivery. Single diet orders were only evaluated since it was not possible to accurately quantify a gradual progression in oral/enteral nutrition (EN) diet orders throughout the day based on the current study design, which was based on 24-hour intakes. The time lapse between when orders were written and when diet changes took effect in real time was not accounted for. As a result the progression of nutrition prescription for specific diet orders could not be accurately evaluated. We were able to identify interruptions in nutritional delivery based on documented changes in diet orders, however, communication orders (physician orders to nurses which may be about feeds and are not reflected in the diet order) and/or delays in feeding schedules were not accounted for, which limited our ability to make suggestions as to why nutritional delivery did not match nutrition orders. In our research, we found these conditions to be important enough to warrant a more careful and focused investigation, since findings may be a source for recommendations on how to improve nutrition delivery for our patients.

In summary, the usefulness of our findings for future practice outweighs the field limitations. Every effort was made during the phases of planning, recruitment, data collection and analyses to minimize the effect of these limitations.

VIII. FUTURE RESEARCH

Development and successful implementation of a nutrition protocol is prudent to determine if the postoperative progression of nutrition is optimal. Currently there is lack of uniform standards for implementation and progression of nutrition during the postoperative period in infants recovering from cardiac surgery. Evaluation of the effectiveness of implementing a nutrition protocol will contribute to establishing evidenced based practice to promote favorable outcomes.

Additionally, closer examination of nutrition prescription and nutrition delivery is needed to better understand why nutrition received may be different from nutrition ordered. A prospective study design specifically looking at nutritional intake in hourly increments with documentation of deviations from the nutrition prescribed when diet orders are not ordered to be interrupted could aid in the identification of modifiable variables to improve practice. Improvement in nutritional delivery can potentially lead to improved outcomes by minimizing the change in weight-for-age z-scores during the postoperative period

Another area that warrants investigation is the period from birth to surgical intervention. In comparing birth and preoperative anthropometrics, patients are noted to have marked decreases in weight-for-age and head circumference-for-age z-scores. Length-for-age z-scores were not significantly different; however, the decline in weight-for-length z-scores was significant with z-scores, approaching criteria for classification as wasting per WHO growth standards. Infants who are not scheduled for corrective or palliative surgery until later on in life are expected to thrive, achieve organ maturation and return as a better surgical candidate. Most infants with congenital heart defects are struggling to achieve normal growth expectations of healthy infants. It is suspected that if nutritional status can be improved during the period prior to surgery, improved postoperative outcomes may be observed. Identifying ways to ensure that infants receive adequate nutrition and achieve expected growth rates is necessary for preparation for surgery and for meeting developmental milestones.

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APPENDICES

Appendix 1: Specific Aims and Hypotheses

Aim	Hypothesis	Sample Size	Variables	Methods for Variables	Statistical Analysis	Results
1. Evaluate adequacy of nutritional intake during the postoperative period by comparing preoperative weight status as measured by weight-for-age z-scores to weight status at discharge home or 28 days following surgery (whichever occurs sooner).	Nutritional intake during the postoperative period is less than optimal as reflected by a decrease in weight-for-age z-scores of ≥0.5 from the time of surgery to the time of discharge home or 28 days following surgery.	n = 70 (detect a mean difference as small as 0.22 with a power of 80%)	Preoperative weight-for-age z-score, Postoperative weight-for-age z-score	Obtain documented weights prior to surgery and at hospital discharge from medical chart.	Paired comparison t-test (p value <0.5)	Mean difference of 0.58 ±0.5 (P <0.001)
2. Describe fluid volumes received by infants during the postoperative period following cardiac surgery to identify actual fluid volumes provided in current practice	No hypothesis (descriptive)	Not calculated	Total 24-hour intake volume, current weight	Obtain 24-hour total daily fluid and most current weight from the medical chart and express values as volume in milliliters per kilogram body weight.	Mean, Median (interquartile range)	

Appendix 1: Specific Aims and Hypotheses (continued)

Aim	Hypothesis	Sample Size	Variables	Methods for Variables	Statistical Analysis	Results
3. Describe how fluid volume is utilized and delivered to infants during the postoperative period following cardiac surgery to categorize how fluid volume is distributed in current practice to provide essential products, such as, intravenous fluids, medications, blood products, and nutrition, and identify routes/method of delivery.	No hypothesis (descriptive)	Not calculated	24-hour intake of the following variables: total intake volume, intravenous fluids, medications, blood products, PN, IL, EN, oral and routes/method of delivery	Obtain total 24-hour intake of the variables listed and route/method of nutritional delivery from the medical chart.	Mean values expressed as percentages of total volume	
4. Describe the amount of Calories and protein delivered to infants during the postoperative period following cardiac surgery to identify actual Calories and protein delivered in current practice.	No hypothesis (descriptive)	Not calculated	24-hour intake of total calories and protein, current weight	Registered Dietitian to calculate 24-hour calorie and protein intake from documented volumes and type of product received and use most current weight from the medical chart to express values as Calories per kilogram body weight and grams of protein per kilogram body weight.	Mean, Median (interquartile range)	

Appendix 1: Specific Aims and Hypotheses (continued)

Aim	Hypothesis	Sample Size	Variables	Methods for Variables	Statistical Analysis	Results
5. Compare Calories and protein delivered to infants during the postoperative period following cardiac surgery to Calories and protein prescribed with estimations expressed as a percentage of predefined goals for Calories and protein.	Calories and protein delivered to infants during the postoperative period following cardiac surgery is less than the intended nutrition ordered.	Not calculated (secondary outcome measure)	24-hour intake of total calories and protein, estimated total calorie and protein intake based on physician orders, estimated energy needs per DRI for age, estimated protein needs as per DRI for healthy infants, current weight	Registered Dietitian to calculate actual (documented volumes and type of product received), expected 24-hour calorie and protein intake from the medical chart, estimate energy needs using DRI formula for energy and compare values.	Paired comparison t-test (p value <0.5)	• PN calories ordered vs received (46±17.9 vs. 43±17.9., *P*<0.001) • PN protein ordered vs received (1.81±0.74 vs. 1.72±0.76, *P*=0.001) • For diet orders calories and protein received less than ordered (*P*<0.001)

Appendix 2: Review of Literature Tables

Table 1. Maintenance Fluid Requirements in Infants

Author et al., Year	Study Type	Population	Sample Size	Methods	Results	Limitations
Holliday & Segar, 1957	Narrative Review	n/a	n/a	n/a	• Water requirement for weight 0-10 kg: 100 mL/kg/day • Based on the following assumptions: - 50 mL/100 kcal/day needed to replace insensible water loss - 66.7 mL/100 kcal/day needed to replace average renal loss - Water oxidation supplies 16.7 mL/100 kcal/day	• Based on review of literature • Does not take abnormal fluid loss into consideration

Appendix 2: Review of Literature Tables (continued)

Table 2. Postoperative Fluid Volumes in Clinical Practice

Author et al., Year	Study Type	Population	Sample Size	Methods	Results	Limitations
Nicholson, Clabby, & Mahle, 2014	Retrospective cohort	Neonates who underwent modified systemic-to-pulmonary artery shunt palliation within the first 45 days of life between 1/2009 and 7/2011	n = 65	• Chart review • Documented fluid intake during the postoperative period	<u>Postoperative median fluid intake</u> • Day 1: 43.9 mL/kg/day (IQR 32.9-61 mL/kg/day) • Day 2: 56.7 mL/kg/day (IQR 48-76.1 mL/kg/day) • Day 3: 66.7 mL/kg/day (IQR 56.6-75.5 mL/kg/day)	• Retrospective design • Single institution experience
Nicholson, Clabby, Kanter, & Mahle, 2013	Retrospective cohort	Neonates who underwent modified systemic-to-pulmonary artery shunt palliation within the first 45 days of life at Children's Healthcare of Atlanta between 1/2009 and 7/2011	n = 65	• Chart review • Documented fluid intake during the postoperative period	<u>Median total fluid intake</u>: • While exclusively on TPN: 95 mL/kg/day (IQR 81-103.3) • At time of transfer to CSU: 133.5 mL/kg/day (IQR 121.8-145) • At hospital discharge: 147 mL/kg/day (137.8-155.3)	• Retrospective design • Single institution experience

Appendix 2: Review of Literature Tables (continued)

Table 3. Fluid Intake Volume and Postoperative Outcomes

Author et al., Year	Study Type	Population	Sample Size	Methods	Results	Limitations
Szekely, Sapi, Kiraly, Szatmari, & Dinya, 2006	Prospective cohort	Children admitted to the cardiac ICU following cardiac surgery between 8/15/2001 and 8/14/2002	n = 411	Variables of interest: duration of mechanical ventilation, volume of intake 24 hrs following surgery	• Mean volume intake 24 hrs after surgery of 4.3 mL/kg/hr was associated with mechanical ventilation >61 hrs (adjusted OR 1.73, CI 1.25-2.38; p<0.0007) but not mechanical ventilation >7 days	• Duration of mechanical ventilation groups was arbitrarily determined • Single institution experience
Nicholson, Clabby, & Mahle, 2014	Retrospective cohort	Neonates who underwent modified systemic-to-pulmonary artery shunt palliation within the first 45 days of life at Children's Healthcare of Atlanta between 1/2009 and 7/2011	n = 65	• Chart review • Compared infants who achieved negative fluid balance ≤24 hrs postoperatively to those who achieved negative fluid balance>24 hrs postoperatively • Outcome variables: duration of mechanical ventilation, CICU length of stay, total hospital stay	• Time of achieving negative fluid balance were not associated with outcomes of interest	• Retrospective design • Single institution experience

Appendix 2: Review of Literature Tables (continued)

Table 3. Fluid Intake Volume and Postoperative Outcomes (continued)

Author et al., Year	Study Type	Population	Sample Size	Methods	Results	Limitations
Hazel et al., 2013	Prospective cohort	Infants <6 months old who underwent cardiac surgery with CPB between 7/2009 and 7/2010	n = 49	• Fluid overload expressed as a percentage • Poor outcomes: upper quartile time to extubation, upper quartile length of ICU stay	• Fluid overload expressed as a percentage of daily weight is associated with poor outcomes (OR 1.07; 95% CI 1.01-1.14; p=0.03)	• Small sample size • Single institution experience

Appendix 2: Review of Literature Tables (continued)

Table 4. Perioperative Nutritional Status and Postoperative Outcomes

Author et al., Year	Study Type	Population	Sample Size	Methods	Results	Limitations
Radman et al., 2014	Prospective cohort	Term children <5 yrs of age with RACHS ≤3	n = 71 UCSF (n = 41) UNICAR (n = 30)	• TSF obtained • Outcome variables: 30-day mortality, ICU length of stay, duration of mechanical ventilation, duration of continuous inotropic infusions	• At UCSF median ventilator (hrs): 19 (IQR 11-40) • At UCSF median ICU LOS (days) median: 5 (IQR 3-8) • UCSF TSF z-score median 0.79 (IQR -0.1-1.7) • Increased duration of mechanical vent and ICU LOS were associated with lower preoperative triceps skin-fold z-score ($p<0.05$)	• Small sample size when stratified by center
Toole et al., 2014	Retrospective cohort	Children <24 mos of age with GA >36 wks admitted to CICU >48 hrs	n = 121	• Chart review • Malnutrition categorized by Waterlow Criteria • Outcome variables: duration of mechanical vent, length of CICU LOS	• CICU LOS (days): median 5.7 (IQR 3.7-11.2) • Median length of MV: 2 days • Mild CPEM associated with longer hospital LOS compared to patients without chronic malnutrition ($p<0.005$) • Mean protein and kcal delivery by day 7 was <70% of calculated requirements	• Retrospective design • Single institution experience

Appendix 2: Review of Literature Tables (continued)

Table 5. Adequacy of Postoperative Nutritional Intake

Author et al., Year	Study Type	Population	Sample Size	Methods	Results	Limitations
Li et. al, 2008	Prospective cohort	Infants undergoing Norwood procedure between April and July 2005	n = 17	• VO_2 and VCO_2 were measured and REE was calculated using the modified Weir equation • Daily calorie and protein intake was calculated for each day	• Measured REE - Day 0: 43 kcal/kg/day (±11) - Day 1: 39 kcal/kg/day (±8) - Day 2: 39 kcal/kg/day (±7) - Day 3: 41 kcal/kg/day (±6) • Actual intake was 8%, 34%, 74% and 119% of REE on postoperative days 0, 1, 2, and 3 respectively	• Small sample size • Growth marker not assessed to determine adequacy of nutritional intake
De Wit et. al, 2010	Prospective cohort	Ventilated children admitted to the PICU	n = 21	• Measured REE (30 min steady-state measurement) • Compared measured REE with actual energy intake	• Mean measured REE: 67.8±15.4 kcal/kg/day • Mean intake on the day of measurement: 15.9 kcal/kg/day	• Small sample size • Single institution experience • Time of measurement varied from 0 to 7 days postoperatively • Growth marker not assessed to determine adequacy of nutritional intake

Appendix 2: Review of Literature Tables (continued)

Table 5. Adequacy of Postoperative Nutritional Intake (continued)

Author et al., Year	Study Type	Population	Sample Size	Methods	Results	Limitations
Nicholson et al., 2013	Retrospective cohort	Neonates who underwent modified systemic-to-pulmonary artery shunt palliation within the first 45 days of life at Children's Healthcare of Atlanta between 1/2009 and 7/2011	n = 65	• Chart review • Documented energy intake during the postoperative period • Documented WAZ scores prior to surgery and at discharge home	<u>Median caloric intake</u>: • While exclusively on TPN: 50.4 kcals/kg/day (IQR 41.6-63.6) • At time of transfer to CSU: 94 kcals/kg/day (IQR 85-103) • At hospital discharge: 119 kcals/kg/day (IQR 111-125) • Median WAZ score decreased -1.3 (IQR -1.7 to 0.7) from time of surgery to discharge	• Retrospective design • Single institution experience
Rogers et al., 2003	Prospective cohort	Children admitted to the PICU at least 72 hrs in Melbourne, Australia between 8/2000 and 2/2001	n = 42 (PICU admission after cardiac surgery: n = 18)	• EER and actual energy intake was calculated by a research dietitian • Weight obtained prior to PICU admission, at time of PICU discharge, and at time of hospital discharge	• Median EER intake in the cardiac group was significantly lower than the non-cardiac group (p=0.02) • Median weight-for-age z-score decreased from day prior to PICU admission to PICU discharge in cardiac group (p<0.001) • Decrease in median weight-for-age z-scores from PICU discharge to hospital discharge not significant (p=0.61)	• Small sample size of patients following cardiac surgery • Single institution experience

Appendix 2: Review of Literature Tables (continued)

Table 5. Adequacy of Postoperative Nutritional Intake (continued)

Author et al., Year	Study Type	Population	Sample Size	Methods	Results	Limitations
Medoff-Cooper et al., 2011	Prospective cohort	Neonates with functionally univentricular physiology between March 2003 and May 2007	n = 61	• Growth data collected by daily chart review • Outcome measures: weight-for-age z-score at discharge, change in weight-for-age z-score between surgery and discharge	• Significant difference in change in weight-for-age z-score from surgery to hospital discharge when comparing neonates who were tube fed to those who were exclusively orally fed ($p<0.01$).	• Single institution experience • Nutritional intake was not evaluated
Anderson et al., 2011	Nested Retrospective cohort	Full term infants who underwent cardiac surgery resulting in two-ventricle physiology and who were admitted to the cardiac ICU at The Children's Hospital of Philadelphia between 3/2003 and 5/2007	n = 76	• Weight-for-age z-scores calculated using weight at time of surgery and weight at time of hospital discharge • Type and route of nutrition was documented	• Decrease in median weight-for-age z-scores of -1.0 (range -2.3 to 0.2) from time of surgery to discharge home • Decrease in weight-for-age *z*-scores was associated with failed initial postoperative extubation ($p= 0.001$) and delayed initiation of postoperative nutrition support ($p<0.001$)	• Retrospective design • Nutritional intake was not evaluated • Single institution experience

Appendix 2: Review of Literature Tables (continued)

Table 6. Nutrition Prescription vs. Nutrition Delivery

Author et al., Year	Study Type	Population	Sample Size	Methods	Results	Limitations
de Neef et al., 2008	Retrospective cohort	Mechanically ventilated critically ill children with a PICU length of stay >3 days	n = 84	• Chart review • Prescribed and delivered nutrition were documented and expressed as a percentage of EER as determined by WHO equation which was adjusted using illness and growth factors and an energy absorption coefficient	• Prescribed energy intake was below EER on days 1-4 of PICU admission • Prescribed protein intake was below goal on days 1 through 10. • Calories prescribed vs delivered were significantly different with p≤0.05 on days 1,2,3 and 5. • Protein prescribed vs deliver were significantly different with p≤0.05 on days 1 through 10.	• Study not specific to infants with congenital heart defects • Growth marker not assessed to determine adequacy of nutritional intake

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PUBLICATIONS AND PRESENTATIONS

Li, M., Campa, A., Castellanos, V. H., Rossi, A. F., (February, 2013). *Defining Fluid Restriction in the Management of Infants Following Cardiac Surgery.* American Society for Parenteral and Enteral Nutrition: Clinical Nutrition Week 2013, Phoenix, Arizona.