NUTRITIONAL STATUS AND CLINICAL OUTCOME IN POST-TERM NEONATES UNDERGOING SURGERY FOR CONGENITAL HEART DISEASE

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ABSTRACT

Objective

Poor growth is a common complication in infants with congenital heart disease. There has been much focus on low birth weight as having increased risk of adverse outcomes following neonatal heart surgery. In this study we examined whether pre-operative nutritional status, measured by admission weight for age Z (WAZ) score was associated with post-operative clinical outcome.

Design

Retrospective case series

Patients

Neonates undergoing surgery for congenital heart disease. Those undergoing ductus arteriosus ligation alone were excluded. Children with co-existing non cardiac morbidity were excluded. Outcome variables included incidence of post-operative complications (including sepsis, delayed chest closure, renal impairment and necrotizing enterocolitis), duration of ventilation, intensive care stay and post-operative mortality and mortality at 1 year after surgery.

Setting

Paediatric Cardiac Intensive Care Unit at the Royal Brompton Hospital

Measurements and Main Results

248 neonates fulfilled the entry criteria. Median (IQR) age was 7 (2-15) days, median (IQR) weight 3.3 (2.91-3.6) kg and median WAZ score -0.77 (-1.44-0.01). 28 (11%) children had a WAZ score of less than -2. There was no evidence that children with lower WAZ score had less severe surgery as measured by the Risk Adjustment for Congenital Heart Surgery 1 (RACHS-1) score. In multivariable regression analysis, the WAZ on admission had strong correlation with the number of days free of respiratory support (invasive and non-invasive ventilation) at 28 days ($p<0.0001$) and with all-cause mortality at 1 year ($p=0.001$).

Conclusions

Poor nutritional status as measured by WAZ is associated with adverse short and long term outcomes in neonates undergoing surgery for congenital heart disease.

INTRODUCTION

Congenital heart disease (CHD) is a significant health burden, affecting between 0.3 and 1.5% of all pregnancies [1]. Children with congenital heart disease are known to exhibit early and progressive falls in their growth trajectory compared to healthy children, with reductions in weight for age (WAZ) score, head circumference and length for age Z score [2, 3]. It is also known that surgery and bypass, and the burden of cardiac failure and chronic disease results in significant metabolic and nutritional stress. Furthermore inadequate nutritional intake in the post-operative period results in further challenges to restoring normal growth parameters [4, 5].

Early nutritional support is known to be important, particularly in those undergoing surgery in early life, where there is little reserve during a critical time for brain development. As there is an increasing trend towards primary repair of cardiac defects in the early neonatal period [6-10], it is important to identify infants who are at increased risk of poor outcome as a result of their pre-surgical nutritional status. Babies who are growth restricted (birthweight less than 2.5kg) have been shown to have poorer outcomes [11-13]. Whilst intra-uterine growth restriction is an important contributor to low weight at the time of surgery in the first week, inadequate post-natal nutrition may be a significant factor for those babies with more complex cardiac lesions or those operated on later in the neonatal period, and operative weight as well as maturity may affect short and longer term outcomes [13-16]. Finally, it has been shown that necessary calorie and protein intake is often not achieved for up to two weeks after surgery, further impacting on poor nutrition status [17] increasing the risk of later morbidity [18] and prolonged growth restriction.

We wanted to determine whether nutritional status, as measured by WAZ score, had any impact on short and longer term outcomes in neonates undergoing palliative or corrective surgery for congenital heart disease in the first month of life. We hypothesised that children who had lower WAZ score would have poorer clinical outcomes.

METHODS AND MATERIALS

Study design

A retrospective case notes review of 248 post-term neonates less than 28 days of age undergoing corrective or palliative surgery for congenital heart disease at a single tertiary institution. Babies undergoing only ligation of patent ductus arteriosus were excluded from this analysis, as were those with co-existing non-cardiac co-morbidity.

The study was classed as audit and need for Ethics approval was waived by the local Research Ethics Committee.

Data collection

Data were collected from inpatient and outpatient medical records and cardiac surgical databases. Data collected included the cardiac and surgical diagnosis, weight and age at time of Paediatric Intensive Care Unit (PICU) admission, and WAZ score (calculated using the WHO Anthro software v3.2 [19]). Surgical complexity was classified according to the RACHS-1 score[20]. Pre-existing comorbidities were recorded from the medical history on admission to PICU and the timing of surgery in relation to date of birth recorded to assess the relative contribution of intra-uterine growth retardation compared to post-natal malnutrition. Outcomes recorded included length of PICU stay, length of invasive and non-invasive ventilatory support, maximum lactate, use of inotropic support, secondary sepsis, delayed chest closure and survival status in the post-operative period and survival at 1 year after surgery. The incidence of complications including sepsis, delayed sternal closure, low cardiac output state, necrotizing enterocolitis, arrhythmias, renal impairment and neurological morbidity were recorded.

Statistical analysis

Both R –statistical software version 3.0.1 2012 and SPSS version 20 (Chicago, USA) were used to analyse the data. The primary outcome variable was mortality at 1 year. Secondary outcomes included post-operative mortality, days free of invasive and/or non-invasive respiratory support at 28 days, days free of intensive care at 28 days and post-operative complications. The primary predictor variable was WAZ at the time of surgery. Potential covariates included absolute weight, post-operative lactate level, the type of cardiac lesion and surgical approach (Univentricular or biventricular repair, RACHS-1 score).

An initial Spearman rank correlation analysis was undertaken to explore the association of WAZ Score with a range of linear clinical variables. Mann Whitney U Test was used to test the association between Z score and categorical variables. Multivariable logistic regression analysis was performed to adjust for confounders and establish which factors, including WAZ score, impacted on the mortality at 1 year. We also used linear regression analysis to establish the impact of the same factors on length of hospital stay as a continuous variable. Statistical significance was set at p 0.05.Unless specified otherwise values are shown as median and IQR.

RESULTS

Study population:

We reviewed case notes of all neonates undergoing congenital heart surgery (excluding surgical duct ligation) from 2005-2010. 264 neonates underwent surgery in this period. Of these 16 had pre-existing, non cardiac comorbidity and were excluded from the analysis. These included Situs inversus, Tracheal-oesophageal defects, Chromosomal anomalies, Choanal stenosis, Renal dysplasia, Scimitar syndrome and Neonatal Thrombophilia. Of the remaining 248 babies, 156 (62.9%) were male, and 92 (37.1%) were female. 16 (6.5%) died post-operatively. 1 year post surgical mortality was 11.7% (29/248). Further demographic data are shown in Table 1. Three babies underwent 2 surgeries during their first month of life. Each surgical intervention was treated as a separate episode since the patients had been discharged from PICU and readmitted. All three babies survived PICU and were alive at one year after surgery.

Nutritional status:

60.9% (151/248) neonates had a normal WAZ (≥-1). 28.2% (70/248) had a mild degree of malnutrition (WAZ < -1 to ≤ -2), and 10.9% (27/248) had more severe malnutrition (< -2).

Surgical risk factors:

Using the RACHS-1 score as a marker of surgical complexity and classifying whether the cardiac lesion was univentricular or biventricular, we examined whether underweight infants had a different surgical approach. The distribution of WAZ score was the same across the RACHS-1 score groups (p=0.47) and there was no significant difference in WAZ score amongst those having univentricular or biventricular repair (p=0.106).

Children with lower WAZ (less than -2) were more likely to need increased non-invasive respiratory support post-operatively (table 2), although the duration of invasive ventilation and PICU stay were not different between nutrition groups.

Median WAZ scores did not differ significantly for those who had post-operative complications compared to those who had an uncomplicated recovery (overall p=0.26), including sepsis, delayed chest closure, neurological complications and necrotizing enterocolitis.

Regression analysis of the association between admission WAZ score and clinical outcome:

Analysis of risk factors for the length of post-operative intensive care, respiratory support and with mortality (post-operative and at 1 year after surgery) in the entire cohort showed that admission WAZ score had a significant association with days free of respiratory support at 28 days (invasive and/or non-invasive) as shown in Table 3a. We analysed survival in the early post-operative period (hospital mortality) as well as 1 year after operation date. WAZ did not have an association with hospital mortality (p=0.31). However we found a significant impact of a low WAZ score, on mortality at 1 year of age (p=0.002). Odds of death were increased by a factor of 2.36 and 1.1 for every unit decrease in WAZ and age respectively (Table 3b).

DISCUSSION:

In this study we found that low admission WAZ was associated with prolonged respiratory failure and increased late mortality in neonates undergoing surgery for congenital heart disease. We found that admission WAZ score had a significant association with days free of respiratory support at 28 days (invasive and/or non-invasive). We noted in particular an increased use of non-invasive ventilation. Whilst WAZ did not appear to be associated with early post-operative death, there was significantly increased risk of late death (survival status at 1 year after surgery).

Several factors have been implicated in leading to protein-energy malnutrition in children with CHD, including the challenge of delivery, excessive losses and altered resting energy expenditure. Whilst it is recognized that improving nutrition status prior to surgery may be of benefit, the provision of sufficient energy and protein during the post-operative period is particularly challenging as fluid restrictions and the amount of volume required for supportive drug therapy limits the amount of volume available for feed, further exacerbating malnutrition [21]. A number of studies have reported that infants with single-ventricle physiology experience a 1 Z score decrease between neonatal surgery and discharge from hospital [22]. In order to improve the nutritional status decreasing the risk of late mortality more needs to be done to determine novel ways of delivering sufficient nutrition support [23].

We have previously reported an increase in REE in children following cardiac surgery and in particular that children with malnutrition had an increased expenditure, further impacting on the energy deficit often seen in these children[24].

An important consideration on the causes of low WAZ in neonates is the role of Intra-uterine growth retardation, which is likely to have been an important component of the WAZ score in this population – our median age at time of surgery was 7 days after birth. Future studies should examine the changes in WAZ and other markers of nutritional status (including weight-height Z score and anthropometry) serially following surgery for congenital cardiac lesions, to track the association between nutritional intake, growth and clinical, developmental and functional outcomes.

Children with congenital heart disease often have co-morbidities that may affect the ability to swallow or absorb feeds effectively. In addition prolonged intubation and hospitalization is likely to add to swallowing problems and oral aversion. Gastro-esophageal reflux is relatively common in neonates and young infants with congenital heart disease, and may reduce the success or oral feeds at the volumes needed to restore growth patterns[25]. Previous studies have demonstrated that the presence of comorbidities contributes to feeding difficulties and poorer pre and post-operative growth [26] in children with congenital heart disease, but our data suggests that malnutrition affects clinical outcome from surgery even in those neonates without co-existing comorbidity.

Our study is limited by the fact that apart from 1 year mortality, we do not have data on long term outcomes. Subsequent surgery and late complications are likely to have been important contributors to 1 year mortality, and would be an important component of a future prospective study to examine the influence of low neonatal WAZ on long term outcomes, including neurodevelopmental, feeding and growth as well as hospital reattendances and other organ morbidities. There was no association between WAZ and RACHS-1 score suggesting that the severity of the surgical interventions undertaken in the neonatal period were not that different between the malnutrition groups. A prospective study to examine the relationship of neonatal WAZ and the need for further surgeries and long term morbidity is needed to examine this phenomenon.

It would also have been interesting to have more detailed information on the type and route of feeding. A future prospective study could examine whether early enteral nutrition or use of parenteral nutrition might affect clinical outcomes, or whether breast milk has any protective effects. In addition, the impact of prenatal growth restriction is clearly of importance in a neonatal population. It would seem that smaller babies were more likely to have staged corrective repair than a full correction. However, since WAZ did not differ significantly across different RACHS-1 score severities of surgery, it would appear that surgery for severe lesions was undertaken regardless of nutritional status and a longer term study on nutrition and outcomes is needed to examine whether increasing nutrient supply, particularly protein, pre-operatively may be of benefit to counteract the adverse effects of low WAZ in neonates undergoing surgery for congenital heart disease. In addition our study does not have data on length and head circumference, which would have provided data on wasting and stunting and the impact on morbidity and mortality. Follow-up growth measurements would be useful to examine whether neonates exhibit compensatory increases in growth if they had low pre-surgical WAZ.

Since this was an observational study, no power calculation was performed to determine sample size. However the observed strong relationship between WAZ on admission and some of the markers of clinical outcome warrants further investigation in a prospective study.

Our analysis suggests that malnutrition as measured by the simple assessment of WAZ is a reliable predictor of the need for prolonged respiratory support and the risk of late mortality in neonates undergoing congenital heart surgery. As a marker, it could be used as a guide to highlight patients needing dietetic intervention preceding surgery to improve nutritional state and potentially reduce longer term morbidity.

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Table 3 Legend:

Days free of all ventilation refers to days free of invasive and non-invasive modes of ventilation including nasal CPAP and BIPAP.

TABLE 1a:

Patient demographics

Variable	**Median (IQR)**
Weight (kg)	3.3 (3 to 3.6)
Age (days)	7 (3 to 15)
Weight-For-Age z score	-0.77 (-1.41 to 0.01)
PIM2[24] Score	8 (3.5 to 21.1)
Days free of invasive ventilatory support at 28 days	25 (22-26)
Days free of invasive and/or non-invasive respiratory support at 28 days	24 (20-26)
Days free of PICU at 28 days	23.57 (19.36-25.24)

Table 1b: Primary Cardiac Lesion

Primary Cardiac Defect	**n**	**%**
Atrio-ventricular Septal Defect	3	1.2
Coarcation of the aorta	65	26.2
Transposition of the Great Arteries	94	37.9
Hypoplastic Right Heart	1	0.4
Double outlet right ventricle	13	5.2
Ebstein's Anomaly	2	0.8
Hypoplastic Left Heart	9	3.6
Interrupted Aortic arch	11	4.4
Truncus arteriosus	2	0.8
Pulmonary Atresia (intact ventricular septum)	4	1.6
Pulmonary Atresia (ventricular septal defect)	16	6.5
Pulmonary stenosis	5	2
Hemitruncus	1	0.4
Double inlet left ventricle	2	0.8
Tetralogy of Fallot	9	3.6
Total anomalous pulmonary venous drainage	5	2
Tricuspid atresia	5	2
Ventricular septal defect	1	0.4
Total	248	100

Table 2

Table 2: analysis of clinical variables based on malnutrition group (normal, mild or moderate malnutrition) based on admission WAZ score.

		Normal WAZ (+1 to -1)	Mild malnutrition (WAZ less than -1 to -2)	Moderate malnutrition (WAZ less than -2)
Agedays	Count	151.00	70.00	27.00
	Median	7.00	10.00	8.00
	IQR	2 to 12	4 to 17	2 to 21
Weight	Count	151.00	70.00	27.00
	Median	3.60	3.00	2.30
	IQR	3.3 to 3.75	2.8 to 3.1	2.1 to 2.6
Days free of PICU at 28 days	Count	151.00	70.00	27.00
	Median	24.00	23.23	22.87
	IQR	20 to 25	21 to 25.3	1.29 to 24.79
Days free of invasive ventilation at 28 days	Count	151	70	27.00
	Median	25.0	24.5	24.00
	IQR	22 to 26	21 to 26	18 to 26
Days free of all respiratory support at 28 days*	Count	151.00	70.00	27.00
	Median	25.00	23.50	14.00
	IQR	21 to 26	20 to 26	0 to 25

*P=0.006

Table 3

Table 3a: Analysis of independent variables on post-operative morbidity (respiratory support and intensive care stay).

	Days Free of Invasive Ventilation at 28 Days	Days Free of all ventilation at 28 Days	Days free of PICU at 28 Days	Post-operative survival
Weight for age z-score	0.17	0.0005	0.08	0.31
Gender	0.95	0.41	0.41	0.63
Age	0.7	0.39	0.5	0.04
Lactate	<0.0001	<0.0001	< 0.0001	<0.0001
RACH score 3	0.5	0.72	0.17	0.41
RACH score 4	0.003	0.004	0.001	0.77
RACH score 6	<0.0001	< 0.0001	<0.0001	0.005
PIM	0.31	0.35	0.98	0.73

Table 3b: Multivariate analysis of common factors in critically ill children with cardiac disorders on survival status at 1 year of age

	Odds Ratio	95% Confidence Interval		Statistical significance
		Lower	Upper	
Weight-for-age Z score	2.36	1.36	4.28	0.002
Gender	0.77	0.28	2.14	0.61
Age (in days)	1.1	1.03	1.18	0.006
Lactate	0.77	0.69	0.84	<0.0001
RACH score 3	1.13	0.33	3.53	0.82
RACH score 4	1.19	0.21	8.32	0.84
RACH score 6	0.63	0.09	4.55	0.64
PIM score	0.99	0.97	1.01	0.43

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