Cardiology in the Young

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Pre-operative nutritional status and its association with short-term post-operative outcomes in Iranian children with CHD

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Original Article

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Abstract

Background: Nutritional assessment appears to be an essential component of the evaluation of children with CHD undergoing surgery because nutritional status may impact corrective surgery-associated morbidity. *Methods:* A prospective single-centre cohort study with children between 6 and 24 months of age. Patients who had genetic syndromes or those who were premature or low birthweight at birth were excluded. Pre-operative nutritional parameters included anthropometric measurements and serum concentrations of total protein, vitamin D, iron, and ferritin. Outcome measures included ICU length of stay, mechanical ventilation, vasoactive-inotropic score, and duration of inotropes. Linear regression analysis was performed to determine whether pre-operative variables were associated with outcomes. *Results:* Analysis was performed on 120 patients (median age of 8 months), of whom 67 were male. Prior to surgery, 50.8% of patients had reduced ($z \leq -2.0$) weight-for-age z score, 23.3% had reduced length-for-age z score, and 59.2% had reduced mid-upper arm circumference z score. Pre-operative serum total protein levels were 59.36 ± 9.16 g/L. Multiple regression analysis showed that low serum protein was associated with longer ICU length of stay and length of mechanical ventilation, while mid-upper arm circumference z score ≤ -2 was associated with longer ICU length of stay and mechanical ventilation and inotropes duration. *Conclusions:* Pre-operative assessment of nutritional status by performing anthropometric and biochemical measurements including mid-upper arm circumference z score and serum protein concentrations in children undergoing CHD surgery appears to be predictors of some post-operative short-term outcomes and could be used as a guide to highlight patients needing appropriate perioperative nutritional interventions.

CHD is a common congenital defect that occurs in about 1% of live births, with similar prevalence throughout the world.[1] A significant proportion of these children need at least one corrective surgery during their lifetime. Cardiovascular surgery has significantly improved the survival of children with CHD.

Children with CHD often have a normal birthweight but are at risk for malnutrition due to increased metabolic demand and reduced calorie intake and therefore may fail to thrive.[2–7] Malnutrition has been observed in children with CHD in both developed and developing countries.[2,6] Corrective CHD surgery has been shown to have a positive impact on catch-up growth for weight and height.[8,9] However, prior poor nutritional status may impair the outcomes of corrective surgery, leading to increased post-operative morbidity and mortality. The adverse effects of malnutrition on post-operative complications and outcomes have been demonstrated in several studies. Poor nutrition, as defined by low weight-for-age,[4,10,11] low height for age,[4,11,12] or low serum visceral protein levels,[13] was associated with post-operative morbidity including longer hours of mechanical ventilation, a longer length of ICU stay, and a longer duration of inotropic support. Furthermore, micronutrients deficiency, including vitamin D[14] and iron,[15] has been associated with adverse outcomes in CHD children.

Recognition of specific nutritional prognostic factors might lead to interventions that would improve outcomes. Although a complete nutritional assessment includes several aspects, anthropometric measurements and their transformation to relative indices of normal or malnutrition as well as selected laboratory testing could serve as the mainstay of the nutritional assessment of the child with CHD. The purpose of this study was to determine the pre-operative nutritional status of CHD children through anthropometric and biochemical measures and to identify specific parameters that predict poorer short-term post-operative outcomes including ICU length of stay, duration of mechanical ventilation, and duration of continuous inotropic support.

Methods

This was a prospective observational study including patients with CHD who underwent corrective operations between June 2020 and October 2021 at Shahid Rajaei Cardiovascular, Medical, and Research Center, Tehran, Iran. The study was approved by the Ethics Committee of National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran (the ethical committee code was IR.SBMU.nnftri.Rec.1399.017). Families read and signed an informed consent form. Eligibility criteria were age 6–24 months and an indication of surgical intervention. Exclusion criteria were patients with a history of prematurity (born before 37 weeks of pregnancy), low birthweight (birthweight < 2500 g), known genetic malformations (Turner, Down), and intrauterine growth retardation which could lead to malnutrition independent of CHD.

Data collection

Pre-operative demographic and clinical information collected on all patients included gender, age, and anatomic diagnosis. The infants' pre-operative calories and macronutrients intake were estimated with the use of a 24-hour food recall questionnaire from their parents. A digital weighing scale with a length measuring rod was used for weight and length measurement. Mid-upper arm circumference was measured with the measuring tape at the midpoint between the scapula acromion and the ulna olecranon with the relaxed arm and was recorded to the nearest 1 mm. All measurements were done by one individual to minimise the inter-observer variability. Pre-operative anthropometric assessments were entered into the World Health Organization Anthro software (version 3.2.2) to calculate weight-for-age z score, length-for-age z score, or weight-for-length z score, and mid-upper arm circumference z score. In addition to pre-operative laboratory tests as part of the surgical clinical guidelines, serum total protein, vitamin D, iron, ferritin, and B-natriuretic peptide were measured as part of the research protocol. Operative data included cardiopulmonary bypass time, aortic cross-clamp time, and operation time.

The primary outcome variable assessed was the length of ICU stay. Secondary outcome variables included duration of mechanical ventilation, vasoactive-inotropic score in the first 24 hours after cardiac surgery (VIS 24),[16] and duration of inotropes use post-operatively.

Statistics

Data were analysed using SPSS software (version 25.0, SPSS Inc., Chicago, IL, United States of America). Shapiro–Wilk test was used for data normality determination. The normally distributed continuous variable was described as mean and standard deviation, and non-normally distributed continuous variables as the median and interquartile range. The categorical data were shown as frequency and per cent. Initially, based on clinical relevance, and previously reported associations, covariates were identified as potential confounders of the association between nutrition status and outcomes. Univariate regression analysis was used to select parameters associated with outcomes, where variables significant at $p < 0.2$ level in univariate level were entered into the multivariate model. The final model was chosen based on significant variables at $p < 0.05$ level. Due to its non-parametric distribution, outcomes were log-transformed before analysis to satisfy model assumptions. Next, the ICU length of stay has dichotomised into ICU length of stay ≤ 5 days or >5 days, and the differences in perioperative characteristics between the two groups were compared using the t-test or Mann–Whitney U-test for continuous variables and Pearson's chi-squared test for categorical variables.

Results

Study population

Between April 2020 and October 2021, among CHD patients admitted to heart surgery, 120 children with a median age of 8 months were included in this study (Table 1). There were more male than female patients. The most prevalent CHD was ventricular septal defect (30.8%) and tetralogy of Fallot (20.8%) (Table 1). Four (11.8%) of the ventricular septal defect patients, two patients with transposition of the great arteries, one of the patients with tetralogy of Fallot, and one of the patients with single ventricle and transposition of the great vessels, had undergone palliation with a pulmonary artery banding prior to corrective surgery. None of the study patients had documented neurologic injury or abnormalities and did not require tracheostomy or home ventilation prior to surgery.

Pre-operative nutritional variables

The pre-operative caloric intake of infants was about 103 kcal/kg. Pre-operatively, all patients had per oral intake. The mean weight-for-age z score of the enrolled children was −1.97 ± 1.36 (Table 2). Reduced anthropometric-related indices (z score ≤ −2) of the patients were observed by 50.8% (n = 61) by weight-for-age z score, 23.3% (n = 28) by length-for-age z score, 38.3.4% (n = 46) by weight-for-length z score, and 59.2% (n = 71) by mid-upper arm circumference z score. The mean serum total protein and 25 (OH) D levels of the study population were 59.36 ± 9.16 g/L and 29.09 ± 14.83 ng/mL, respectively. The serum total protein level was <60 g/L in 50% of children. The demographics of patients according to serum total protein are presented in Table 3. Serum 25(OH) D level was below 20 ng/mL in 25.0% of children. Low serum iron (<50 μg/dL) concentration was observed by 64.2% of the enrolled children. Pre-operative data of four common CHDs in the study population (ventricular septal defect, tetralogy of Fallot, ventricular septal defect-atrial septal defect, and atrial septal defect) are presented in Table 4.

Post-operative outcomes

The mean length of ICU stay of the enrolled patients was 5.4 days, and the mean length of mechanical ventilation of the study patients was 47.4 hours. The mean duration of inotropes post-operation was 3.3 days.

Effects of age-adjusted anthropometric z scores, serum biochemical values as well as age, sex, cardiopulmonary bypass time, aortic cross-clamp time, and operation time on outcomes were evaluated by linear regression (Table 5). Boys were the reference category for sex, and for anthropometric z scores, the reference category was z score >−2.0. Serum iron and ferritin levels as well as weight-for-age z score were not significant predictors of ICU length of stay in univariate analysis, and these were excluded from multivariate analysis. The multivariable analysis indicated that serum total protein level inversely (p = 0.004) and STAT category 2–4 (p = 0.018), length-for-age z score ≤ −2.0 category (p = 0.028), as well as mid-upper arm circumference z score ≤ −2.0 category

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Table 1. General and clinical characteristics of the study population

Characteristics	Values and frequencies (n = 120)
Age, months	8.0 (7.0, 12.0)
Boys, n (%)	67(55.8%)
Girls, n (%)	53 (44.2%)
STAT category 1, n (%)	40 (33.3%)
STAT category 2, n (%)	77 (64.2%)
STAT category 3, n (%)	2 (1.7%)
STAT category 4, n (%)	1 (0.8%)
Primary cardiac defect, n (%)	
VSD	34 (28.3%)
VSD-ASD	12 (10.0%)
TOF	24 (20.0%)
ASD	10 (8.3%)
ASD-PDA	5 (4.2%)
VSD-PDA	4 (3.3%)
VSD-PS	4 (3.3%)
DORV-VSD	3 (2.5%)
DORV	3 (2.5%)
TGA	2 (1.7%)
ASD-VSAD-PDA	2 (1.7%)
VSD-PA	2 (1.7%)
VSD-PDA-PA	2 (1.7%)
HLHS-VSD	2 (1.7%)
CAVSD	2 (1.7%)
SV-TGA	2 (1.7%)
VSD-COA-MS	1 (0.8%)
TGA-VSD	1 (0.8%)
VSD-PDA-PS	1 (0.8%)
SV	1 (0.8%)
PA	1 (0.8%)
PDA	1 (0.8%)
DORV-ASD	1 (0.8%)
Laboratory	
Hb, g/L	11.30 (10.60, 12.37)
HCT (%)	33.80 (32.00, 37.72)
Neutrophil/lymphocyte	0.64 ± 0.69
PLT, $\times 10^9$/L	292.60 ± 84.75
ESR, mm/hour	5.00 (2.25, 8.00)
Cr, mg/dL	0.40 (0.30, 0.40)
BNP, pg/mL	135.75 (76.62, 379.25)
Operative factors	
Operation time (minute)	301.05 ± 100.63
CPB time (minute)	136.88 ± 73.66
ACC time (minute)	82.47 ± 54.60

Data expressed as median (quartile 1, 3), mean ± standard deviation, or n(%).
ACC=aortic cross-clamping; ASD=atrial septal defect, BNP=B-natriuretic peptide; CAVSD=complete atrioventricular septal defect; CPB=cardiopulmonary bypass; COA=coarctation of the aorta; Cr=creatinine; DORV=double outlet right ventricle; ESR=estimated sedimentation rate; Hb=haemoglobin; HCT=haematocrit; HLHS=hypoplastic left heart syndrome; MS=mitral stenosis; PA=pulmonary atresia; PDA=patent ductus arteriosus; PLT=platelets; PS=pulmonary stenosis; STAT=Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery Congenital Heart Surgery; SV=single ventricle; TGA=transposition of the great arteries; TOF=tetralogy of Fallot; VSD=ventricular septal defect; WBC=white blood cells.

($p = 0.036$) positively were associated with an increased length of ICU stay. The R^2 of the model was 0.299 (regression ANOVA $p < 0.0001$). Regarding the length of mechanical ventilation as the outcome, the multivariable analysis indicated patients with a lower serum protein ($p = 0.004$) or those with mid-upper arm circumference z score ≤ -2.0 ($p = 0.001$) were more likely to have prolonged mechanical ventilation (the R^2 of the model = 0.203, and regression ANOVA $p = 0.001$). The assessment of the relationship between nutritional as well as confounding variables and the VIS 24 (the VIS value at the first 24 hours after surgery) showed that a minor proportion of the variance is explained by the model (the $R^2 = 0.071$ and regression ANOVA $p < 0.036$) indicating that longer surgery time and patients with weight-for-length z score ≤ -2.0 were likely to have higher VIS 24. However, analysis of the relationship between variables and the duration of inotropic infusion (dopamine, milrinone, epinephrine, dopamine, and dobutamine) showed that a larger proportion of the variance of variance was explained by the model (the $R^2 = 0.286$ and regression ANOVA $p < 0.0001$), suggesting that boys, those who were younger, those with higher STAT category, and mid-upper arm circumference z score ≤ -2.0, were likely to receive inotropes for a longer duration.

Patients with ventricular septal defect were the largest number of patients in the study. When these patients were grouped based on serum B-natriuretic peptide level into two groups with high B-natriuretic peptide (B-natriuretic peptide ≥ 100 pg/mL, n = 19) and low B-natriuretic peptide level (B-natriuretic peptide < 100 pg/mL, n = 15) and outcomes, as well as nutritional status indicators (z score categories, serum total protein, 25 [OH] D, calorie, and protein intake), were compared between the two groups, no significant difference was observed in any of the study outcomes or nutritional variables between the two groups which may be due to the small sample size for the analysis.

Table 6 shows the comparisons of anthropometric and laboratory parameters in patients with ICU length of stay ≤ 5 days and >5 days. Patients with ICU length of stay > 5 days were mostly boys and had longer aortic cross-clamp time, cardiopulmonary bypass, and operation time, but serum total protein was lower compared to patients with ICU length of stay ≤ 5 days. Furthermore, in patients with ICU length of stay > 5 days, age, mid-upper arm circumference z score ≤ -2.0 as well as serum 25 (OH) D and B-natriuretic peptide levels tended to differ than those with ICU length of stay ≤ 5.

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Table 2. Patients' pre-operative nutritional status data

Variables	All patients (n = 120)
Weight, kg	6.8 (6.0, 7.9)
WAZ	−2.0 ± 1.4
> −2.0	50.8%
≤ −2.0	49.2%
Length, cm	69.0 (65.0, 73.0)
LAZ	−1.2 ± 1.1
>−2.0	76.7%
≤ −2.0	23.3%
WLZ	−1.8 ± 1.5
> −2.0	61.7%
≤ −2.0	38.3%
Mid-upper arm circumference, cm	12.0 (11.0, 13.0)
MACZ	−2.5 ± 1.3
> −2.0	40.8%
≤ −2.0	59.2%
Energy intake (kcal/day)	735.1 ± 228.9
Energy intake (kcal/kg)	103.2 ± 28.5
Protein intake (g/day)	25.7 ± 14. 6
Carbohydrate intake (g/day)	80.4 ± 26.3
Fat intake (g/day)	33.1 ± 9.1
Serum total protein, g/L	59.4 ± 9.2
Serum 25 (OH) D, ng/mL	29.1 ± 14.8
Serum ferritin, ng/mL	105.5 (55.0, 198.0)
Serum iron, μg/dL	38.0 (27.0, 63.0)

Data expressed as median (quartiles 1, 3), mean ± standard deviation, or n (%).
LAZ=length-for-age z score; MACZ=mid-upper arm circumference for age z score; WAZ=weight-for-age z score; WLZ=weight-for-length z score.

Table 3. Demographics of patients according to serum total protein

Characteristics	Serum protein < 60 g/L (n = 60)	Serum protein ≥ 60 g/L (n = 60)
Age, month	8.0 (7.0, 12.0)	8.50 (7.0, 12.7)
Gender		
Boys, n (%)	32 (53.3%)	35 (58.3%)
Girls, n (%)	28 (46.7%)	25 (41.7%)
STAT category, n (%)		
1	23 (38.3%)	17 (28.3%)
2	36 (60.0%)	41 (68.3%)
3	0	2 (3.3%)
4	1 (1.7%)	0
Primary cardiac defect, n (%)		
VSD	17 (28.3%)	17 (28.3%)
VSD-ASD	4 (6.7%)	8 (13.3%)
TOF	15 (25.0%)	9 (15.0%)
ASD	8 (13.3%)	2 (3.3%)
ASD-PDA	2 (3.3%)	3 (5.0%)
VSD-PDA	2 (3.3%)	2 (3.3%)
VSD-PS	1 (1.7%)	3 (5.0%)
DORV-VSD	0	3 (5.0%)
DORV	1 (1.7%)	2 (3.3%)
TGA	2 (3.3%)	0
ASD-VSAD-PDA	0	2 (3.3%)
VSD-PA	1 (1.7%)	1 (1.7%)
VSD-PDA-PA	1 (1.7%)	1 (1.7%)
HLHS-VSD	1 (1.7%)	1 (1.7%)
CAVSD	0	2 (3.3%)
SV-TGA	2 (3.3%)	0
VSD-COA-MS	0	1 (1.7%)
TGA-VSD	0	1 (1.7%)
VSD-PDA-PS	0	1 (1.7%)
SV	0	1 (1.7%)
PA	1 (1.7%)	0
PDA	1 (1.7%)	0
DORV-ASD	1 (1.7%)	0

Data expressed as median (quartiles 1, 3) or n (%).
ASD=atrial septal defect; CAVSD=complete atrioventricular septal defect; COA=coarctation of the aorta; DORV=double outlet right ventricle; HLHS= hypoplastic left heart syndrome; MS=mitral stenosis; PA=pulmonary atresia; PDA=patent ductus arteriosus; PS=pulmonary stenosis; STAT=Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery Congenital Heart Surgery; SV=single ventricle; TGA=transposition of the great arteries; TOF=tetralogy of Fallot; VSD=ventricular septal defect.

Discussion

The aim of this study was to determine the nutritional status of patients prior to corrective cardiac surgery and examine the impact of nutritional status on the post-operative short-term outcomes. Anthropometric measures were used as indirect measures of nutritional status. Consistent with prior studies, this investigation demonstrates that malnutrition is prevalent in CHD patients. A high incidence of malnutrition according to weight-for-age z score ≤ −2 (50.8%) was observed in children undergoing CHD surgery. However, none of weight-for-age z score, or weight-for-length z score did predict any of the study's post-operative morbidities suggesting that the applied criteria for malnutrition may not be sensitive enough to detect short-term outcomes or were confounded by other factors, including unmeasured ones. The results are consistent with the findings of Lim et al's study in which pre-operative weight-for-age z score was not associated with short-term outcomes, including ICU length of stay and duration of mechanical ventilation, but pre-operative weight-for-age z score was associated with 30-day mortality.[12] In contrast, weight-for-age z score was associated with longer post-operative hospital stays in CHD children undergoing Glenn procedure[10] or Fontan[17] operation or it was associated with duration of mechanical ventilation in Indonesian CHD children.[18] Furthermore, in a retrospective multicentre cohort study using data from the Society of Thoracic Surgeons Congenital Heart Surgery Database, lower values for weight-for-age z score and length-for-age z score were significantly associated with increased infection and longer

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Table 4. Pre-operative data of four common CHDs in the study population

Variables	**VSD** (n = 34)	**TOF** (n = 24)	**VSD-ASD** (n = 12)	**ASD** (n = 10)
Age at the time of surgery, n (%)				
6–8 months	21	11	9	4
9–12 months	10	2	2	5
>12 months	3	11	1	1
STAT category, n (%)				
1	16 (47.1%)	6 (25.0%)	3 (25.0%)	10 (100%)
2	18 (52.9%)	18 (75.0%)	9 (75.0%)	
VSD size, n (%)				
3–5 mm	10 (29.4%)		4 (33.3%)	
6–8 mm	16 (47.1 %)		6 (50.0%)	
9–10 mm	8 (23.5%)		2 (16.7%)	
Serum BNP, pg/mL	129.25 (84.27, 329.30)	241.50 (81.50, 500.05)	159.45 (89.00, 371.25)	106.50 (80.50, 382.50)
Weight, kg	6.4 (5.9, 7.0)	8.2 (7.1, 9.7)	6.3 (5.3, 6.7)	6.4 (5.4, 7.6)
Length, cm	67.5 (65.0, 70.0)	72.0 (66.2, 77.7)	66.5 (64.1, 69.0)	70.0 (64.7, 72.2)
Mid-upper arm circumference, cm	11.0 (11.0, 12.1)	12.7 (11.0, 13.2)	11.0 (10.0, 11.5)	12.0 (10.4, 12,6)
WAZ, n (%)				
> −2.0	10 (29.4%)	17 (70.8%)	3 (25.0%)	4 (40.0%)
≤ −2.0	24 (70.6%)	7 (29.2)	9 (75.0%)	6 (60.0%)
LAZ, n (%)				
> −2.0	24 (70.6)	20 (83.3%)	8 (66.7%)	8 (80.0%)
≤ −2.0	10 (29.4)	4 (16.7%)	4 (33.3%)	2 (20.0%)
WLZ, n (%)				
> −2.0	12 (35.3%)	19 (79.2%)	6 (50.0%)	7 (70.0%)
≤ −2.0	22 (64.7%)	5 (20.8%)	6 (50.0%)	3 (30.0%)
MACZ				
> −2.0	10 (29.4%)	14 (58.3%)	1 (8.3%)	5 (50.0%)
≤ −2.0	24 (70.6%)	10 (41.7%)	11 (91.7%)	5 (50.0%)
Energy intake (kcal/day)	647.8 ± 155.3	865.34 ± 3 ±247.5	687.8 ± 210.5	684.9 ± 185.3
Energy intake (kcal/kg)	102.6 ± 24.6	103.1 ± 19.8	109.8 ± 26.2	107.7 ± 38.9
Protein intake (g/day)	20.6 ± 7.9	34.7 ± 19.5	23.2 ± 8.1	21.5 ± 12.4
Serum total protein, g/L	60.2 ± 11.2	57.5 ± 8.8	60.6 ± 7.7	55.5 ± 8.0
Serum 25 (OH) D, ng/mL	33.9 ± 14.9	24.9 ± 15.1	35.6 ± 18.9	24.4 ± 10.6
Serum ferritin, ng/mL	153.9 ± 92.8	149.9 ± 115.1	112.7 ± 82.6	120.5 ± 73.4
Serum iron, µg/dL	50.3 ± 39.6	67.7 ± 72.8	44.7 ± 36.7	82.5 ± 83.5

Data expressed as median (quartiles 1, 3), mean ± standard deviation, or n (%).
BNP = B-natriuretic peptide; LAZ=length-for-age z score; MACZ=mid-upper arm circumference for age z score; STAT=Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery Congenital Heart Surgery; WAZ=weight-for-age z score; WLZ=weight-for-length *z score*.

hospitalisation after paediatric heart surgery in a diverse population of infants and young children.[11]

The pre-operative caloric intake of infants was about 103 kcal/kg. Since more than half of the studied infants had weight-for-age z score ≤ −2, and regarding the caloric goal of 120–130 kcal or higher in infants with growth retardation,[19] it seems that the amount of pre-operative calories intake by the study patients was inadequate to compensate for elevated energy expenditure in most cases. Thus, in addition to CHD, which itself contributes to malnutrition, it appears that inadequate calorie intake has also contributed to malnutrition of the study patients.

Mid-upper arm circumference z score identified more children in the undernourished category than weight-for-age z score, length-for-age z score, and weight-for-length z score, and patients with mid-upper arm circumference z score ≤ −2 at the time of the corrective operation had a longer ICU length of stay, mechanical ventilation, and duration of inotropic infusion. We could not find any study that used mid-upper arm

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Table 5. Univariate and multivariate linear modelling for predictors of outcomes

	Univariate	Multivariate[a]			
Outcomes/variables	*P*	*B*	95% CI		*P*
ICU length of stay, days					
Age	0.170	−0.003	−0.012	0.007	0.578
Gender					
Girls	0.013	−0.064	−0.144	0.016	0.116
STAT category[b]	0.021	0.087	0.015	0.159	0.018
WAZ category					
≤−2.00	0.901				
LAZ category					
≤ 2.00	0.061	0.107	0.012	0.203	0.028
WLZ category					
≤ −2.00	0.193	−0.067	−0.151	0.017	0.116
MACZ category					
≤−2.00	0.198	0.092	0.006	0.178	0.036
Energy intake (kcal/day)	0.547				
Protein intake (g/day)	0.231				
Carbohydrate intake (g/day)	0.647				
Fat intake (g/day)	0.739				
Serum 25 (OH) D	0.144	−0.001	−0.004	0.001	0.337
Serum total protein	0.001	−0.007	−0.011	−0.002	0.004
Serum iron	0.981				
Serum ferritin	0.939				
Haemoglobin	0.652				
Neutrophil/lymphocyte	0.590				
PLT	0.952				
ESR	0.933				
Cr	0.851				
Serum BNP	0.088	0.00047	−0.00006	0.00016	0.421
Surgery time	0.022	−0.00020	−0.001	0.001	0.608
ACC time	0.061	−0.001	−0.002	0.001	0.408
CBP time	0.006	0.001	−0.00014	.002	0.081
Length of mechanical ventilation, hours					
Age	0.431				
Sex					
Girls	0.305				
STAT category	0.477				
WAZ category					
≤−2.00	0.422				
LAZ category					
≤−2.00	0.677				
WLZ category					
≤−2.00	0.715				

(*Continued*)

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Table 5. (*Continued*)

	Univariate	Multivariate[a]			
Outcomes/variables	*P*	*B*	95% CI		*P*
MACZ category					
≤−2.00	0.041	0.221	0.089	0.353	0.001
Energy intake (kcal/day)	0.297				
Protein intake (g/day)	0.155	0.004	−0.00035	0.009	0.070
Carbohydrate intake (g/day)	0.391				
Fat intake (g/day)	0.387				
Serum 25 (OH) D	0.092	−0.002	−0.007	0.002	0.292
Serum total protein	0.004	−0.011	−0.018	−0.004	0.004
Serum iron	0.451				
Serum ferritin	0.423				
Haemoglobin	0.630				
Neutrophil/lymphocyte	0.436				
PLT	0.642				
ESR	0.932				
Cr	0.546				
Serum BNP	0.071	0.00013	−0.00005	0.00031	0.170
Surgery time	0.134	−0.00026	−0.001	0.001	0.678
ACC time	0.582				
CBP time	0.075	0.001	−0.001	0.003	0.250
VIS 24					
Age	0.773				
Sex					
Girls	0.840				
STAT category	0.537				
WAZ category					
≤−2.00	0.424				
LAZ category					
≤−2.00	0.467				
WLZ category					
≤−2.00	0.113	0.070	0.003	0.138	0.042
MACZ category					
≤−2.00	0.391				
Energy intake (kcal/day)	0.582				
Protein intake (g/day)	0.761				
Carbohydrate intake (g/day)	0.542				
Fat intake (g/day)	0.318				
Serum 25 (OH) D	0.430				
Serum total protein	0.309				
Serum iron	0.295				
Serum ferritin	0.200	0.00026	−0.00005	0.001	0.101
Haemoglobin	0.546				
Neutrophil/lymphocyte	0.323				

(*Continued*)

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Table 5. (*Continued*)

Outcomes/variables	Univariate *P*	Multivariate[a] *B*	95% CI		*P*
PLT	0.256				
ESR	0.736				
Cr	0.991				
Serum BNP	0.857				
Surgery time	0.118	0.00032	0.00000	0.001	0.050
ACC time	0.435				
CBP time	0.326				
Duration of inotropes, days					
Age	0.011	−0.011	−0.021	−0.001	0.038
Sex					
Girls	0.007	−0.097	−0.182	−0.013	0.025
STAT	0.003	0.112	0.037	0.187	0.004
WAZ category					
≤−2.00	0.592				
LAZ category					
≤−2.00	0.423				
WLZ category					
≤−2.00	0.770				
MACZ category					
≤−2.00	0.142	0.103	0.014	0.193	0.023
Energy intake (kcal/day)	0.741				
Protein intake (g/day)	1.00				
Carbohydrate intake (g/day)	0.779				
Fat intake (g/day)	0.782				
Serum 25 (OH) D	0.822				
Serum total protein	0.060	−0.003	−0.008	0.002	0.201
Serum iron	0.624				
Serum ferritin	0.326				
Haemoglobin	0.159	0.019	−0.002	0.039	0.074
Neutrophil/lymphocyte	0.378				
PLT	0.661				
ESR	0.515				
Cr	0.577				
Serum BNP	0.023	0.00011	−0.000001	0.00023	0.053
Surgery time	0.032	0.00040	−0.001	0.001	0.916
ACC time	0.116	−0.00048	−0.002	0.001	0.484
CBP time	0.021	0.00029	−0.001	0.002	0.414

[a]Multivariate linear regression analysis was performed with factors selected from the univariate analysis with $p < 0.2$.
[b]STAT category 1 was set as the reference category.
ACC=aortic cross-clamp; BNP=B-natriuretic peptide; CPB=cardiopulmonary bypass; LAZ=length-for-age z score; MACZ=mid-upper arm circumference for age z score; STAT=Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery Congenital Heart Surgery; WLZ=weight-for-length z score.

circumference z score to diagnose malnutrition and post-operative complications in children with CHD. However, a study comparing the body mass index for age z score with mid-upper arm circumference z score in children with cystic fibrosis reported that mid-upper arm circumference z score identified a larger number of children with malnutrition compared to body

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Table 6. Perioperative data in patients according to the length of ICU stay

Variables	**ICU** length of stay ≤ **5 days (n = 80)**	**ICU** length of stay > **5 days (n = 40)**	p value
Demographics			
Age, month	9.0 (7.0, 12.0)	8.0 (7.0, 11.0)	0.088
Gender			0.0001
Boys, n (%)	35 (43.8)	32 (80.0%)	
Pre-operative food intake and anthropometry			
Energy intake (kcal/day)	737.3 ± 206.2	730.8 ± 271.7	0.88
Protein intake (g/day)	24.8 ± 12.9	27.3 ± 17.5	0.38
Carbohydrate intake (g/day)	80.4 ± 23.8	80.5 ± 30.9	0.98
Fat intake (g/day)	33.6 ± 8.6	32.3 ± 10.1	046
WAZ category, n (%)			0.897
≤−2.00	41 (51.2%)	20 (50.0%)	
LAZ category			0.445
≤−2.00	17 (21.3%)	11 (27.5%)	
WLZ category			0.595
≤−2.00	32 (40.0%)	14 (35.0%)	
MACZ category			0.088
≤ −2.00	43 (53.8%)	28 (70.0%)	
Pre-operative blood values			
Hb, g/dL	11.2 (10.8, 12.3)	11.30 (10.2, 12.5)	0.907
HCT (%)	33.9 (32.0, 37.0)	33.60 (30.6, 41.8)	0.845
Neutrophil/ lymphocyte	0.6 ± 0.8	0.7 ± 0.5	0.793
PLT, $\times 10^9$/L	292.6 ± 85.7	292.5 ± 84.0	0.993
ESR, mm/hour	5.0 (2.0, 8.0)	4.50 (3.0, 7.0)	0.810
Cr, mg/dL	0.4 (0.3, 0.4)	0.4 (0.3, 0.4)	0.765
Total protein, g/L	60.7 ± 9.1	56.7 ± 8.7	0.024
25 (OH) D, ng/mL	30.9 ± 15.7	25.5 ± 12.3	0.062
Iron, μg/dL	38.0 (27.0,63.0)	36.5 (27.2, 56.5)	0.749
Ferritin, ng/mL	102.0 (52.0, 196.7)	130.0 (56.2, 211.5)	0.457
BNP, pg/mL	122.4 (64.2, 363.5)	171.5 (91.8, 464.8)	0.070
Intra-operative data			
Surgery time, minute	286.0 ± 95.6	331.1 ± 104.8	0.020
ACC time, minute	73.4 ± 46.9	100.6 ± 64.2	0.009
CPB, time	119.9 ± 63.5	170.9 ± 81.3	0.0001

Data expressed as the number of patients, median (quartiles 1, 3), or mean ± standard deviation.
ACC=aortic cross-clamp; BNP=B-natriuretic peptide; Cr=creatinine; CPB=cardiopulmonary bypass; ESR=estimated sedimentation rate; Hb=haemoglobin; HCT=haematocrit; LAZ=length-for-age z score; MACZ=mid-upper arm circumference for age z score; PLT=platelets; WAZ=weight-for-age z score; WLZ=weight-for-length z score.

mass index for age z score.[20] Mid-upper arm circumference z score has been listed as an independent indicator for paediatric malnutrition and a more sensitive prognostic indicator for mortality than weight-for-height parameters in malnourished children.[21,22] The observed difference between the prevalence of malnutrition assessed with mid-upper arm circumference z score and other anthropometric indices has already been reported, and it has been proposed that the z score ranges used to define various stages of malnutrition may not be the same for all indicators of malnutrition.[22] This may be due to the fact that each anthropometric parameter reflects the nutritional status differently. Mid-upper arm circumference may have a stronger association with fat mass than fat-free mass.[23,24] Grijalva-Eternod et al examined the associations between mid-upper arm circumference and weight-for-length in infants with fat mass and fat-free mass and found that mid-upper arm circumference was more strongly associated with variability in adiposity relative to variability in fat-free mass. They proposed that mid-upper arm circumference may act more like a composite index of poor growth and wasting, including low adiposity.[24]

Serum total protein level was a better predictor of some type of morbidity, particularly ICU length of stay and mechanical ventilation duration, than many other pre-operative variables. Pre-operative total serum protein level has been a predictor/prognostic factor in adult patients.[25–27] Malnutrition can lead to lower protein reserves, which may affect normal healing, and can hinder the ability to recover after surgical intervention. Serum total protein is an indication of the circulating amount of albumin and globulin. Serum albumin concentration in this study was not available to all patients and therefore was not included in the analysis. However, albumin accounts for more than half of the body's serum total proteins. The presence of hypoalbuminaemia may be a sign of underlying malnutrition, associated inflammatory syndrome, and some other conditions.[28] Serum albumin has been reported to be an independent predictor of clinical outcomes in critically ill children.[29,30] Furthermore, lower serum albumin levels have been associated with increased post-operative morbidity in patients undergoing operative correction of CHD.[13,31]

There are limitations to this investigation that must be acknowledged. Results of the study must be interpreted with caution as only a small proportion of the variance is explained by the models provided. Furthermore, the patients' follow-up was short and the sample size was small. No power calculation was performed to determine sample size since this was an observational study. However, the observed relationship between pre-operative serum total protein and mid-upper arm circumference z score and some of the outcomes warrants further investigation in a larger study. Moreover, patients younger than 6 months were not included in the study. We assumed that in older infants who could not undergo corrective surgery until the time of the study, the effect of congenital heart lesions on anthropometric measurements would be more obvious. Additionally, except for serum total protein, the concentrations of other visceral proteins such as albumin and pre-albumin were not measured. Moreover, the group of patients was heterogeneous, and it might have been preferable to study patients with similar defects in detail. Furthermore, the infant's food intake at the pre-operative time was estimated with the use of food recall questionnaire from their parents and it should be noted that feeding data based on parental survey is vulnerable to a recall bias.

Conclusions

In conclusion, pre-operative identification of malnutrition by performing anthropometric and biochemical measurements including mid-upper arm circumference z score and serum total protein concentrations appears to be the predictors of the post-operative prolonged ICU stay, respiratory support, and the need for any inotropic infusion in children undergoing CHD surgery. These markers could be used as a guide to highlight patients needing appropriate perioperative nutritional interventions to improve nutritional status and potentially reduce post-operative morbidity. Future prospective studies investigating which nutritional interventions could be the most effective, particularly in patients with mid-upper arm circumference z score ≤ -2 and low serum protein, are required.

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Conflicts of interest. None.

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines and with the Helsinki Declaration of 1975, as revised in 2008, and have been approved by the Ethics Committee of National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran (the ethical committee code was IR.SBMU.nnftri.Rec.1399.017).

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