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ORIGINAL ARTICLE

WILEY Congenital Heart Disease

Nutritional outcomes in infants with food allergy after cardiac surgery

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Abstract

Background: Food allergy is a rapidly growing public health concern because of its increasing prevalence, as well as life-threatening potential. There is limited knowledge on the nutritional status for the pediatric congenital heart disease (CHD) patients with food allergy.

Objective: This study investigated both clinical and nutritional outcomes according to the CHD infants with food allergy.

Methods: Forty CHD infants with food allergy and 39 controls were recruited in Shanghai, China. The height and weight for age and weight for height were converted to *z*-scores to evaluate their effects on nutritional status before and after CHD operation.

Results: Cow's milk showed the most frequently sensitized food allergen. The WHZ in the ≥2 allergen group was different before operation and after operation ($P = .040$). The number of sensitized food allergens significantly correlated with the WHZ ($r = -0.431$, $P = .001$), WAZ ($r = -0.465$, $P = .000$), and HAZ ($r = -0.287$, $P = .025$). Infection and NT-BNP showing negative correlation with WHZ and WAZ of infants with food allergy.

Conclusions: The increased number of sensitized food allergens is associated with negative effects on both short-term and long-term nutritional status in infants with CHD. Therefore, the meticulous and continuous evaluation and management of both growth and nutritional status should be considered in CHD patients with a high number of sensitized food allergens.

KEYWORDS
cardiac surgery, infants, food allergy, nutrition

1 | INTRODUCTION

Food allergy has amerged as an unanticipated "second wave" of the allergy epidemic,[1] dramatically increasing the burden of allergic diseases in infants.[1,2] The vast majority of countries reported an increase in food allergy prevalence in the preceding 10 years. A Chinese study showed a doubling of challenge-proven immunoglobin E (IgE)-mediated food allergy from 3.5% in 1999 to 7.7% in 2009.[3]

Food allergy is a rapidly growing public health concern because of its increasing prevalence, as well as life-threatening potential. Early clinical evidence suggested that anaphylaxis was classically mediated by antigen cross-linking of antigen-specific IgE bound to high-affinity IgE receptor (FcεRI) on mast cells. This induced the rapid release of mediators, such as histamine and leukotrienes, which act on responder cells to induce vasodilation, increased vascular permeability and hypotension, and bronchospasm, which commonly manifest as a shock.[4]

Cardiac surgery with cardiopulmonary bypass (CPB) provokes a systemic inflammatory response syndrome. Although there are less studies reported the special clinical manifestation to congenital heart disease (CHD) patients with food allergy, the antigen on the surface of white blood cells from peripheral circulation have already changed before undergoing cardiac surgery. Thus, pediatric patients with food allergy who undergo CPB surgery may be easily occur the complications of CPB technique, including the postoperative effusions and edema ranging from complications as pericardial, pleural, and/or abdominal effusion, liver enlargement, and edema formation to massive

generalized edema[5] and airway hyperresponsiveness, which cause to hypercarbia, hyoxemia, and long usage of mechanical ventilation.[6]

Nutritional management is vital to those with food allergy. Recent studies proved a higher number of sensitized food allergens were associated with negative effects on the growth and nutritional status of infants and young children.[7,8] Additionally, malnutrition owing to food avoidance results in weight loss and damage to the immunomodulatory system, which subsequently exerts a negative effect on the progress, treatment, and prognosis of disease. Pediatric CHD patients are normally at particularly high risk for developing growth retardation and nutritional deficiency. However, there is limited knowledge on the nutritional status for the pediatric CHD patients with food allergy.

Therefore, this study investigated both clinical and nutritional outcomes according to the CHD infants with food allergy.

2 | METHODS

2.1 | Participants

During May 2016 and December 2016, patients who received cardiac surgery in heart center in Shanghai Children's Medical Center were eligible for this study. Forty infants between the ages of 4 and 12 months were identified, with diagnosed food allergy according to the current guidelines for food allergy[9] and all cases were confirmed by at least one positive allergen-specific IgE. Thirty-nine CHD infants with no atopic disorders who were negative in all IgE tests were recruited during the same period as potential controls. All cases and controls had a complete set of allergen-specific IgE testing, and anthropometric measurements. Palliative operation for CHD were excluded in this study. All subjects provided written informed consent to participate in this study. This project was approved by the IRB of Shanghai Children's Medical Center affiliated Shanghai Jiao Tong University, School of Medicine (SCMCIRB-2015003).

2.2 | Measurements

2.2.1 | Anthropometric assessment

The height and weight were measured at admission and discharge from hospital. Child was put in a recumbent position, with the shoes off, and with a light top on, using an automated height and weight measuring instrument. The growth and nutritional status were evaluated using *z*-scores of the World Health Organization.[10] Weight for age, height for age, and weight for height are expressed as *z*-score in standard deviation units (WAZ, WHZ, and HAZ, respectively). *Z*-score of less than −2 represents moderate to severe undernutrition.[11]

2.2.2 | Biochemical tests

Total serum IgE were measured using an immunoCAP assay (Siemens). A total IgE level specific ≥15 IU/mL and a specific IgE level of ≥0.35 IU/mL defined sensitization to egg white, beef, cow milk, shrimp, crab, and peanut. The number of these six sensitized food allergens was calculated for each patient, and the patient were divided into three groups: control groups, 1-allergen group, and ≥2-allergen group.

2.2.3 | Clinical outcomes

A structure questionnaire was conducted to collect data on the clinical outcomes of study participants. The demographic and laboratory examination data were collected before surgery including gender, age, type of cardiac defect, risk adjustment for congenital heart surgery1 (RACHS-1) score,[12] the left ventricular ejection fraction (LVEF) from Echo report, serum biochemical indexes including albumin and prealbumin, and eosinophils and hemoglobin in blood routine index. The clinical data were also recorded after surgery, including duration of CPB and aortic cross-clamp, time of ventilation, duration of hospital stay, nosocomial infection, and plasma aminoterminal brain natriuretic peptide (NT-BNP).[13]

2.3 | Statistical analysis

Continuous variables without normal distribution are expressed as interquartile range. Kruskal Walls test and chi-square test was applied to compare difference in the three groups. The *z*-scores of WAZ, WHZ, and HAZ were used for Kendall's tau-*b* test analysis. All statistical analyses were performed using SPSS version 18.0. A value of $P < .05$ indicated statistical significance.

3 | RESULTS

3.1 | Characteristics of allergen groups and control group

Table 1 shows the characteristics of total food allergy cases and controls. There were no significant differences between cases and controls in the basic demographic characteristics.

3.2 | Distribution of CHD

Table 2 showed the distribution of cardiovascular malformations in cases. Tetralogy of Fallot was the leading cardiac lesion among all cases of CHD (32.5%) and accounted for 81.3% of cases in the cynotic group. Ventricular septal defect (VSD) was the most frequent acyanotic lesion among all cases of CHD (30.3%) among the acyanotic group (50%).

3.3 | Number of sensitized food allergens

Figure 1 shows the most frequently sensitized food allergen was cow's milk, followed by egg white and peanut.

3.4 | Food allergy and nutritional status

The prevalence, distribution, and types of malnutrition observed in the three groups were shown in Tables 3 and 4. The WHZ in the ≥2 allergen group was different before operation and after operation ($P = .040$). Both wasting and underweight were significantly higher in the ≥2 allergen group compared with other groups ($P < .05$).

TABLE 1 Clinical characteristics of infants with food allergy and their controls

	Control group N = 39	1-Allergen group N = 23	≥2-Allergen group N = 17	*P* value
Demographic characteristic				
Age (d)	180 (138–210)	210 (180–240)	180 (136–270)	.076[a]
Gender (M/F)	22/17	13/10	10/7	.985[b]
Type of CHD (acynotic/cyanotic)	17/22	12/11	12/5	.177[b]
Laboratory characteristic				
LVEF (%)	71.10 (66.40–75.90)	68.90 (64.90–75.60)	67.20 (63.15–74.45)	.238[a]
Hemoglobin (g/L)	116.00 (105.00–131.00)	116.00 (107.00–129.00)	117.00 (106.50–127.50)	.914[a]
Albumin (g/L)	41.00 (36.70–43.10)	40.40 (38.70–43.70)	40.85 (39.40–42.57)	.794[a]
Prealbumin (g/L)	0.16 (0.13–0.19)	0.16 (0.14–0.18)	0.16 (0.14–0.20)	.823[a]
Eosinophils (μL)	1.80 (0.64–3.50)	2.40 (1.00–3.94)	3.00 (3.00–3.00)	.754[a]
IgE (IU/mL)	4.63 (4.63–4.63)	35.00 (20.50–57.30)	88.19 (65.00–195.50)	.000[a]
Surgical characteristic				
RACHS-1	2.00 (2.00–2.00)	2.00 (2.00–2.00)	2.00 (2.00–2.50)	.803[a]
Duration of CPB (min)	63.00 (46.00–82.00)	67.00 (48.00–102.00)	66.00 (54.50–90.50)	.581[a]
Duration of aortic cross-clamp (min)	40.00 (28.75–49.75)	45.00 (27.00–67.00)	46.00 (29.00–60.50)	.700[a]

Abbreviations: CPB, cardiopulmonary bypass; LVEF, the left ventricular ejection fraction; RACHS-1, risk adjustment for congenital heart surgery1 score.
[a]*P* by Kruskal Wallis test.
[b]*P* by chi-square test.

3.5 | Correlation between nutritional status and clinical outcomes

The number of sensitized food allergens significantly correlated with the WHZ ($r = -0.431$, $P = .001$), WAZ ($r = -0.465$, $P = .000$), and HAZ ($r = -0.287$, $P = .025$) (see Table 5). In addition, infection and NT-BNP were correlated with WHZ, and NT-BNP was correlated with HAZ as well.

4 | DISCUSSION

According to the WAO reports, the most common food allergens in children less than 5 years of age were relatively similarly across all regions, generally including cow's milk, egg, peanuts, and seafood, with regional variations in the relative frequency of these.[14] Cow's milk is relatively common food allergen and the estimated incidence of cow's milk in infants is relatively high (2%-7.5%).[15] The food allergens distribution in the present study is similar to those global data. Because cow's milk is usually introduced to infants earlier than any other foods, it is the earliest food allergen among others.[16,17]

In this study, the patients with acynotic CHD accounted for 60% in all the allergy groups and VSD was the most frequent acyanotic lesion (30.3%). Previous study found that high pulmonary flow or pulmonary hypertension enhances the manifestation of allergic disease. The high pulmonary flow group was significantly associated with allergic diseases including food allergy, atopic dermatitis, allergic rhinitis, and abnormally high total IgE levels.[18] The present study did not investigate the different level of pulmonary flow and pressure, that may have contributed to the high prevalence of allergy and malnutrition.

As in the present study, the *z* scores of height and weight for age, and weight for height were significantly different among three groups before operation, especially, those delineated the poorest growth and nutritional status in the ≥2 allergen group. It has been reported that the consumed dietary food intake is significantly less in children with two or more food allergies compared to those with a single food allergy.[19] Restricting foods completely that contain the offending allergens maybe effective to avoid the allergy symptoms, however, it limits the energy and protein intake for the increasing metabolic

TABLE 2 Distribution of cardiovascular malformations in infants with allergy

Type of cardiac defect	N (%)
Acynotic group (N = 24)	
Ventricular septal defect (VSD)	12 (30.0%)
ASD+VSD	5 (12.5%)
Coarctation of the aorta	3 (7.5%)
Partial anomalous pulmonary venous connection	2 (5.0%)
Interrupted aortic arch	2 (5.0%)
Cyanotic group (N = 16)	
Tetralogy of Fallot	13 (32.5%)
Transposition of the great arteries +ASD+VSD	2 (5.0%)
Double outlet right ventricle + VSD	1 (2.5%)
Total	40 (100%)

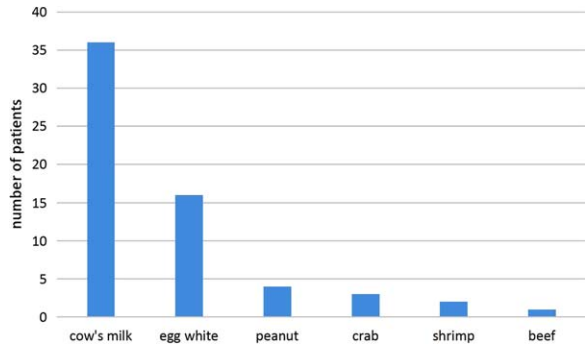

FIGURE 1 Distribution of patients sensitized to food allergens

TABLE 3 The comparison of nutritional status in the three groups

Nutritional status		Control	1-Allergen	≥2-Allergen	*P* value
HAZ	Preoperation	−0.16 (−0.73 to −0.45)	0.41 (−0.53 to 0.97)	−0.76 (−1.93 to 0.83)	.067
	Postoperation	−0.02 (−0.97 to 0.53)	0.49 (−0.53 to 1.33)	−0.88 (−1.78 to −0.45)	.032
	P value	.693	.956	.850	
WAZ	Preoperation	−0.68 (−1.96 to −0.10)	−0.47 (−1.13 to 0.69)	−1.65 (−3.22 to −0.52)	.004
	Postoperation	−0.58 (−1.96 to −0.07)	−0.69 (−1.43 to 0.65)	−2.45 (−3.40 to −1.30)	.000
	P value	.92	.410	.158	
WHZ	Preoperation	−0.86 (−0.12 to −1.94)	0.08 (−1.63 to 0.84)	−1.66 (−3.02 to −0.28)	.008
	Postoperation	−0.95 (−0.23 to −1.97)	−0.36 (−1.65 to 1.24)	−2.63 (−1.19 to −3.59)	.000
	P value	.964	.613	.040	

Abbreviations: HAZ, *z*-score of height for age; WAZ, *z*-score of Weight for age; WHZ, *z*-score of weight for height.

TABLE 4 Pattern of malnutrition among infants with CHD in the three group

Nutritional status	Period	Group N (%)			
		Control	1-Allergen	≥2-Allergen	*P* value
Wasting (WHZ ≤ −2)	Preoperation	8 (20.8%)	6 (26.1%)	8 (47.1%)	.122
	Postoperation	9 (23.1%)	8 (34.8%)	12 (70.6%)	.003
Underweight (WAZ ≤ −2)	Preoperation	9 (23.1%)	3 (13.0%)	8 (47.1%)	.045
	Postoperation	8 (20.5%)	3 (13.0%)	12 (70.6%)	.000
Stunting (HAZ ≤ −2)	Preoperation	4 (10.3%)	3 (13.0%)	5 (29.4%)	.175
	Postoperation	4 (10.3%)	3 (13.0%)	4 (23.5%)	.415

Abbreviations: HAZ, *z*-score of height for age; WAZ, *z*-score of Weight for age; WHZ, *z*-score of weight for height.

requirements of infants with CHD. Additionally, beginning at 6 months after birth, the iron reservoir continues to be depleted, while the iron requirements for rapid growth are increased at this age.[20] Those who have restricted intake of cow's milk and egg, may cause the lack of both protein and iron.[21] Thus, the relative proportions in the more allergens group of wasting, underweight, and stunting before operation were 47.1%, 47.1%, and 29.4%, respectively, which were twice higher than those in the control cases.

It is noteworthy that the number of allergens showed correlation with postoperational WHZ and WAZ, especially, the median of WHZ and WAZ in the ≥2 allergen group postoperationally represented moderate to severe undernutrition. Pediatric patients with more food allergens who undergo CPB surgery more frequently develop the inflammatory reaction, which may contribute to the development of postoperative complications, including myocardial dysfunction, respiratory failure, renal and neurologic dysfunction, bleeding disorders, altered liver function, and ultimately, multiple organ failure.[22] The poor preoperative nutritional state of these allergic infants is often exacerbated postoperatively as the metabolic response is characterized by altered energy demands, a complex inflammatory state, and protein catabolism.[23] Additionally, achieving adequate nutritional intake postoperatively is often difficult and may be affected by a combination of

TABLE 5 Correlation coefficients between *z*-scores of nutritional status and clinical outcomes in the allergy groups

	Correlation with WHZ postoperation		Correlation with WAZ postoperation		Correlation with HAZ postoperation	
Variable	*r*	*P* value	*r*	*P* value	*r*	*P* value
Type of cardiac defect	0.292	.068	0.183	.257	0.153	.347
Time of ventilation	−0.109	.327	−0.149	.180	−0.176	.113
Time of hospital stay	−0.128	.259	−0.159	.162	−0.188	.098
Nosocomial infection	−0.360	.007	−0.332	.012	−0.139	.295
NT-BNP	−0.248	.029	−0.263	.021	−0.218	.055
Number of sensitized food allergens	−0.431	.001	−0.465	.000	−0.287	.025

Abbreviations: HAZ, *z*-score of height for age; NT-BNP, plasma aminoterminal brain natriuretic peptide; WAZ, *z*-score of weight for age; WHZ, *z*-score of weight for height.

genetic factors, increased metabolic demands, inefficient nutrient absorption, postsurgical fluid restriction, oropharyngeal dysfunction, and frequent interruptions of enteral feeding for procedures.[24] Therefore, the weight (a predictor of short-term nutritional status) declined significantly after surgery with the number of sensitized food allergens.

In addition, the declining postoperational WHZ and WAZ contributed to infection. It has reported that the malnutrition is associated with a lowered immune response, atrophy, and an increased permeability of the intestinal epithelial barrier, which facilitates infection and bacterial translocation.[25] Besides, impaired healing of wounds, a higher incidence of pneumonia and sepsis, which lead to increased mortality, prolonged length of intubation and hospital stay, and finally increased health care costs are confounding factors influenced by malnutrition.[26,27]

The increased prevalence of heart failure as a complicating problem in infants with more allergies is a new finding. Currently, the BNP levels are known to be elevated in patients with symptomatic left ventricular dysfunction and may reflect diastolic dysfunction and it has emerged as a sensitive biochemical marker for cardiac dysfunction and heart failure.[28] In this study, the BNP is another variable showing a negative correlation with WHZ and WAZ of infants with food allergy. Malnutrition has proved to impact the physiologic stability of critically ill children, which is of importance in the neonate or child who is often hemodynamically unstable following cardiopulmonary bypass and cardiac surgery.[29] Thus, the infants with more allergens needed stricter caring to promote cardiac function recovery after surgery.

5 | CONCLUSION

In this study, the increased number of sensitized food allergens is associated with negative effects on both short-term and long-term nutritional status and contributed to growth retardation in infants with CHD. The meticulous and continuous evaluation and management of both growth and nutritional status should be considered in CHD patients with a high number of sensitized food allergens.

CONFLICT OF INTEREST

No potential conflict of interest was reported by the authors.

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