

# Short-Term Nutritional Support Improves The Preoperative Nutritional Status of Infants With Non-Restrictive Ventricular Septal Defect: A Prospective Controlled Study

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## ABSTRACT

**Objective:** To investigate the effect of short-term nutritional support on improving preoperative nutritional status of infants with non-restrictive ventricular septal defect.

**Methods:** A prospective randomized controlled study was conducted from June 2021 to December 2021 at a provincial children's hospital in China. The difference of nutritional status between the intervention group and the control group after short-term nutritional support was compared.

**Results:** After one month of nutritional support, the weight, STRONGkids score, albumin, prealbumin, and hemoglobin in the intervention group significantly were higher than those in the control group ( $P < 0.05$ ). The postoperative intensive care time and discharge time of the two groups significantly were lower in the intervention group than those in the control group ( $P < 0.05$ ).

**Conclusion:** The preoperative nutritional support of 1 month for infants with non-restrictive ventricular septal defect can effectively improve their preoperative nutritional status and promote postoperative recovery.

## INTRODUCTION

Congenital heart defect is the most common congenital structural malformations, accounting for about a third of congenital structural malformations, and often is associated with malnutrition [Wong 2015; Toole 2014; Radman 2014; Blasquez 2016]. Malnutrition in children with congenital heart disease is associated with many factors, including cyanosis, congestive heart failure, pulmonary hypertension, feeding difficulties, and so on, among them, congestive heart failure

and pulmonary hypertension are the most common and serious factors [Williams 2011]. Operation is the most important way to treat congenital heart disease. Preoperative nutrition status is beneficial to reducing postoperative mortality and postoperative complications and promoting postoperative recovery [Radman 2014; Mitting 2015]. Most children with congenital heart disease were in a state of malnutrition before surgery, and the more serious the disease is, the more serious the malnutrition is before surgery [Costello 2015]. However, many countries have not established preoperative nutritional support and management plans for children with congenital heart disease, especially in developing countries.

Ventricular septal defect is the most common congenital heart disease, among them the non-restrictive ventricular septal defect. Due to the existence of a large number of left-to-right shunt, there will be serious congestive heart failure and pulmonary hypertension in the early stage, which prone to symptoms such as shortness of breath and difficulty in feeding, resulting in insufficient caloric intake of infants and increased demand for energy, and then malnutrition [Lin 2021]. Therefore, non-restrictive ventricular septal defect often requires surgery in infancy, and severe malnutrition is very common before surgery. To explore the strategies for improving the preoperative nutritional status of infants with congenital heart disease, we selected infants with non-restrictive ventricular septal defect and conducted a prospective randomized controlled study to investigate the effect of short-term preoperative nutritional support on the improvement of preoperative nutritional status.

## METHODS

**Study design:** This study was approved by the ethics committee of our hospital and strictly adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from parents/guardians, and data anonymously were treated following all relevant local regulations. CONSORT guidelines were followed.

A prospective randomized controlled study was conducted at two tertiary hospitals in China, from June 2021 to June 2022. Based on the results of the difference in weight after

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nutritional support from the pre-experiment (the intervention group:  $4.72 \pm 0.71$  kg vs. the control group:  $4.21 \pm 0.80$  kg) and assuming that the alpha value was set at 0.05 with a power of 0.80, the required number of participants was calculated to be 36 in each group. Assuming a 10% expulsion rate, the total sample size was set as 80 (40 per group).

**Eligibility criteria:** Patients who met all the following conditions were enrolled: 1. Infants with unrestricted ventricular septal defect; 2. The condition was relatively stable and the operative treatment was performed within 1-2 months. Patients were excluded if they had: 1, Infants with liver and renal failure; 2, Infants with other serious cardiac structural malformations; 3. In the process of nutritional support, infants undergoing emergency surgery; 4. Parents of infants who refused to participate in this study.

**Randomization:** Patients were randomized and divided into intervention groups and control groups when they fulfilled all eligibility criteria. Simple randomization was done, according to a software-generated random number sequence posted on a dedicated and secure website available on a 24/7 basis. The website generated the randomization, but the sequence was concealed from investigators. Attending doctors in each recruiting assigned patients to the study arm, according to the randomization. Infants randomized to one arm could not cross over to the others during the study.

**Masking:** Due to the nature of the intervention, blinding the caregivers was impossible, and blinding to the patients made no sense. However, the outcome assessors were blinded, as outcome data were recorded by investigators not working in the cardiac department and who reviewed patient files masked for the allocated treatment.

**Primary outcomes:** The primary outcomes were body weight and STRONGkids score of infants after nutritional intervention.

**Secondary outcomes:** The secondary outcomes were albumin, prealbumin, hemoglobin, intensive care time, and discharge time of infants after the nutritional intervention.

**Nutritional support methods:** The infants in the intervention group were admitted to the hospital for nutritional support treatment 1 month before the expected time of operation. We set up a nutritional support team to evaluate the baby's nutritional status and nutritional intake every day, and to develop a nutritional intake plan for the day. To determine the caloric requirements, the Schofield equation was used. We added a growth failure stress factor of 1.5 to the calculated energy requirements, according to Leonberg et al. guidelines with a target caloric intake of 120-150 kcal/kg/day (600KJ/kg/d) to ensure adequate energy intake without refeeding syndrome risk. After admission, all infants were bottle fed, with 120-150kcal/kg/day (600KJ/kg/d) as the target feeding dose. If we couldn't reach the target calorie with breast milk or regular formula, we added a breast milk fortifier or high-calorie milk powder. If the child had feeding difficulties and could not be fed by mouth, nasal feeding would be used. If the goal could not be achieved through enteral nutrition alone, supplement PN would be added to meet the target fluid and energy requirements. Proteins were started with 1- 1.5 g/kg/d and then advanced by 1-1.5 g/kg/

day. Once protein requirement was achieved, safe caloric supplements using carbohydrate and lipid energy sources were added. Carbohydrates were started with 4-6 mg/kg/min then advanced by 2 mg/kg/min, and the goal was 12-14 mg/kg/min (45% of calories). Lipids were started with 1 g/kg/day then advanced by 0.5-1 g/kg/day, and the goal was 3 g/kg/day (40% of calories) [El-Ganzoury 2021].

The infants in the control group did not adopt the nutritional support plan, and the feeding process and feeding method were led by their parents. All infants in the control group were fed on demand without parenteral nutrition support.

Body weight, head circumference, STRONGkids score, albumin, prealbumin, and hemoglobin of all patients were recorded at admission. One month after the nutritional support, body weight, head circumference, STRONGkids score, albumin, prealbumin, and hemoglobin of the intervention group and control group again were recorded.

**Research tool:** The STRONGkids scoring scale was developed by Hulst et al. for nutritional status assessment. The scale accounts for various factors, such as high-risk diseases, subjective clinical assessment, nutritional intake or loss, and a decrease or no increase in body weight [Hulst 2010]. The content of subjective clinical assessment includes the loss of subcutaneous fat or muscle and face thinness. The nutritional intake or loss content includes the following problems: 1. In recent days, defecation occurred more than 4 times/day or vomiting occurred more than 3 times/day; 2. Active feeding decreased in recent days; 3. Lack of adequate intake due to pain. The scoring standard is 2 points for high-risk diseases, 1 point for subjective clinical assessment, 1 point for nutritional intake or loss, and 1 point for decrease or no increase in body weight. The total score ranges from 0 to 5 points. A score of 0 to 1 point indicates low nutritional risk, 2 to 3 points indicates moderate nutritional risk, and 4 to 5 points indicate moderate nutritional risk. (Table 1)

**Statistical analysis:** We use SPSS 25.0 software for statistical analysis. Continuous data were presented as mean  $\pm$  standard deviation and range. Clinical parameters between the two groups were compared with t-test. And the  $\chi^2$  or Fisher's test to categorical variables. A *P*-value of  $<0.05$  was defined as statistical significance.

## RESULTS

During the same period, 83 patients met the eligibility criteria, and three ultimately were excluded, including one patient who underwent emergency surgery and two parents of infants who declined to participate. (Figure 1) The general data of the two groups, including age, weight, head circumference size of the ventricular septal defect, pulmonary artery pressure, STRONGkids score, prealbumin, and hemoglobin at admission time were not statistically significant. (Table 2)

After the nutritional intervention of one month, the weight, STRONGkids score, albumin, prealbumin, and hemoglobin of infants in the intervention group significantly were higher than those in the control group ( $P < 0.05$ ). (Table 3)

Table 1. STRONGkids scoring system

Items	Explanations	Points
Subjective clinical assessment	Is the patient in a poor nutritional status judged with subjective clinical assessment: loss of subcutaneous fat and/or loss of muscle mass and/or hollow face?	1
High-risk disease	Is the patient in a poor nutritional status judged with subjective clinical assessment: loss of subcutaneous fat and/or loss of muscle mass and/or hollow face?	2
Diminished nutritional intake	Is one of the following items present? <ul style="list-style-type: none"> <li>Excessive diarrhea (<math>\geq 5</math> times/day) and/ or vomiting (<math>&gt; 3</math> times/day) during the last 1–3 days</li> <li>Reduced food intake during the last 1–3 days</li> <li>Pre-existing nutritional intervention (e.g., ONS or tube feeding)</li> <li>Inadequate nutritional intake because of pain</li> </ul>	1
Weight loss	Is there a weight loss (all ages) and/or no increase in weight/height (infants $< 1$ year) during the last few week–months?	1

The intensive care time ( $4.8 \pm 1.1$  vs.  $6.2 \pm 1.3$ ,  $P = 0.023$ ) and discharge time ( $13.1 \pm 3.2$  vs.  $16.4 \pm 4.8$ ,  $P = 0.019$ ) of patients in the intervention group significantly were lower than those in the control group.

## DISCUSSION

Congenital heart disease is a fetal malformation caused by the dysplasia of the heart and great blood vessels, which is one of the most common congenital malformations and the leading cause of death of children aged 0–5 years in China [Da 2007]. Malnutrition is very common in children with congenital heart disease, especially for patients with high-risk factors, such as heart failure and pulmonary hypertension; the effect on clinical prognosis is more obvious. On one hand, with the improvement of surgical techniques and level of intensive care, most children with congenital heart disease can be treated in infancy or even newborn stages. The earlier the surgery, the earlier the patients can catch up with same-age children in growth and development. On the other hand, the younger the age of surgery, the higher risk of various risks, including nutritional risks, and the greater the challenge of nutritional support. Malnutrition is very adverse to surgical treatment of children with congenital heart disease. Its adverse effects include slowing postoperative recovery, increasing hospitalization time, increasing complications, increasing mortality, and so on. In recent years, how to provide nutritional support for these children has become a hot research topic worldwide.

Nutritional status potentially is a modifiable risk factor, and optimization of preoperative nutritional status improves short and long-term outcomes [Li 2013]. Kelleher et al. found that nutritional support during hospitalization can improve children's nutritional status before surgery, and they concluded that the strongest association of nutritional status at discharge was with preoperative nutritional status [Kelleher 2006]. Mehta and Duggan described that if the diagnosed cardiac children were left without any targeted nutritional intervention before their planned cardiac surgery, their WAZ

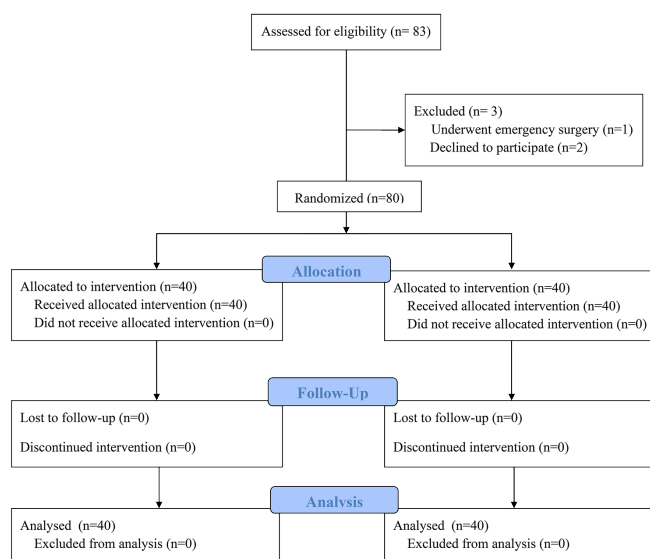


Figure 1.

and weight-for-length Z scores were decreased over time, and half the infants were severely underweight when admitted for major cardiac intervention [Mehta 2009]. El-Koofy et al. performed a nutritional rehabilitation program for 50 infants with left-to-right shunt cardiac disease in 3 months. They recorded a significant reduction in the incidence of moderate malnutrition from 14% to 6% and the incidence of severe malnutrition from 20% to 4% after the implementation of the nutritional rehabilitation program [El-Koofy 2017].

Ventricular septal defect is one of the most common congenital heart diseases, and the non-restrictive ventricular septal defect is the severe type, which easily leads to congestive heart failure and severe pulmonary hypertension at an early time. The obvious malnutrition often exists before surgery, and they often need to accept surgical treatment in infants and even newborns. Preoperative nutritional status has a significant impact on the operative prognosis and

Table 2. Baseline characteristics for included infants

Variable	Intervention group (N = 40)	Control group (N = 40)	P-value
Age (day)	36.7±8.6	35.2±8.8	0.413
Weight (kg)	4.2±0.6	4.1±0.7	0.244
Head circumference (cm)	33.4±1.2	33.3±1.0	0.827
Ventricular septal defect size (mm)	7.2±1.1	7.5±1.0	0.327
Pulmonary artery pressure (mmHg)	61.5±9.2	59.2±10.2	0.283
Albumin (g/L)	32.5±2.0	32.6±2.2	0.744
Prealbumin (mg/L)	133.2±25.1	128.6±20.7	0.350
Hemoglobin (g/L)	98.6±8.5	96.4±7.8	0.216
Score of STRONGkids	3.6±0.6	3.7±0.5	0.416

Table 3. Comparison of the perioperative nutritional status data between the two groups

Variable	Intervention group (N = 40)	Control group (N = 40)	P-value
Weight (kg)	4.7±0.8	4.2±0.7	0.002
Head circumference (cm)	34.1±1.0	33.7±1.1	0.114
Albumin (g/L)	35.4±2.9	32.8±2.3	0.000
Prealbumin (mg/L)	137.0±22.7	126.7±19.5	0.006
Hemoglobin (g/L)	100.3±8.0	96.1±5.8	0.009
Score of STRONGkids	3.2±0.4	3.7±0.6	0.000

postoperative recovery speed. We selected infants with non-restrictive ventricular septal defect as subjects and carried out a randomized controlled study to investigate the effect of preoperative short-term nutrition support on the improvement of preoperative nutritional status. During hospitalization, we conducted nutrition assessment for the infants in the intervention group and guided the nutrition support plan, including setting target calories, using breast milk fortifier or high-calorie milk powder, or even parenteral nutrition, and strictly managing the energy intake. After the nutritional support of one month, the body weight, STRONGkids score, albumin, prealbumin, and hemoglobin in the intervention group were significantly higher than those in the control group, and the infants in the intervention group had better preoperative nutritional status.

Due to a series of complex inflammatory responses, stress responses, and protein catabolism in cardiopulmonary bypass surgery, patients often are in a hypermetabolic state after surgery. In addition, in order to reduce the cardiac load after cardiac surgery, it often is necessary to limit the intake, which makes the poor preoperative nutritional status more serious after surgery [Owens 2009]. Numerous studies have shown that preoperative nutritional status negatively was correlated with intensive care time and hospital stay time, and improving preoperative nutritional status effectively can accelerate postoperative recovery and reduce the intensive care time

and hospital stay time [Anderson 2009; Engelman 1999; Leite 2005]. This study also reached a similar conclusion that short-term preoperative nutritional support effectively can improve the preoperative nutritional status of infants with non-restrictive ventricular septal defect, effectively promote postoperative recovery, and shorten the time of intensive care and hospital stay.

There were some limitations of this study. First, this study was a single-center study. Second, this study looked only at infants with unrestricted ventricular septal defect but did not explore the effect of nutritional support on other congenital heart diseases.

## CONCLUSION

The preoperative nutritional support of one month for infants with the non-restrictive ventricular septal defect effectively can improve their preoperative nutritional status and promote postoperative recovery.

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