Nutrition-related risk factors for prolonged pleural effusion after congenital heart surgery in Chinese infants

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Qin Deng MSc[1], Zhengxia Pan PhD[2], Lin Kong MPH[1], Min Gong PhD[3], Zhongmin Gao MSc[1], Yongfang Liu MSc[1]

[1]Department of Clinical Nutrition Children's Hospital of Chongqing Medical University, National Clinical Research Center for Child Health and Disorders, Ministry of Education Key Laboratory of Child Development and Disorders, Chongqing Key Laboratory of Pediatric Metabolism and Inflammatory Diseases, Chongqing, China
[2]Department of Cardiovascular Surgery, Children's Hospital of Chongqing Medical University, Chongqing, China
[3]Department of Pediatrics, Richmond University Medical Center, Staten Island, NY, 10310, United States

Authors' email addresses and contributions:
DQ, 18725934442@163.com
Contribution: performed the data analyses and finished the original draft.
PZX, panzhengxia005@sina.com
Contribution: project administration.
KL, 179424871@qq.com
Contribution: data curation.
GM, gongmeiwen@gmail.com
Contribution: writing-review and editing.
GZM, doctorgzm@163.com
Contribution: performed the statistical analysis of the data.
LYF · liuyongfang811@163.com
Contribution: conceptualization and supervision.

Corresponding Author: Dr Yongfang Liu, Department of Clinical Nutrition, Children's Hospital of Chongqing Medical University, 136 Zhongshan 2nd Road, Yuzhong District, Chongqing, 400014, China. Tel: 023-68370241. Email: liuyongfang811@163.com

ABSTRACT

Background and Objectives: Previous studies on the risk factors for prolonged pleural effusion (PPE)have primarily focused on surgical-related risk factors, with little research exploring the influence of postoperative nutritional factors on this delay. This study aimed to identify the nutritional risk factors for PPE in Chinese infants following congenital heart disease (CHD) surgery. **Methods and Study Design:** We retrospectively reviewed the medical records of patients under 3 years old with chylothorax following CHD surgery from 2016 to 2020. PPE was defined as pleural effusion lasting over 14 days. Logistical regression analysis was conducted to identify the risk factors. **Results:** : A total of 136 patients were included in this study, with 42 patients developing PPE (30.9%). The PPE group had significantly lower Height-for-Age Z-scores (HAZ) compared to the non-PPE group, while other demographic factors were not significantly different. Univariate analysis revealed that patients in PPE group exhibited delayed onset of chylothorax, prolonged duration of mechanical ventilation support, increased chest effusion volume on the first postoperative day, and a reduced proportion of energy intake from enteral nutrition (EN) during the stable phase. Variables with *p*-value of <0.1 in univariate logistic regression analysis were included in the multivariate logistic regression analysis. A delayed onset of chylothorax, extended periods of mechanical ventilation, and a lower HAZ were significantly correlated with the development of PPE. **Conclusions:** A delayed onset of chylothorax, extended periods of mechanical ventilation, a lower HAZ, and a reduced proportion of energy intake from EN during the recovery phase predict a higher risk of PPE.

Key Words: congenital heart disease, chylothorax, prolonged pleural effusion, nutrition support, risk factor

INTRODUCTION

Congenital heart disease (CHD) is a common congenital defects in children,[1] and surgery remains a primary treatment for this condition. Despite advancements in surgical techniques and perioperative care, postoperative complications are still unavoidable. Chylothorax, a rare but severe complication following CHD surgery, characterized by the accumulation of lymphatic fluid in the pleural space, presents significant challenges for patient management and recovery. The drainage of chylothorax not only extends hospital stays but also carries risks of malnutrition, immune compromise, and electrolyte imbalances due to the loss of vital nutrients and electrolytes contained within the chyle.[2,3] Furthermore, prolonged pleural

effusion(PPE) elevates the risk of infection,[4,5] and persists as a major cause of postoperative morbidity and mortality.[6-8]

While numerous studies have explored the risk of developing chylothorax or PPE after CHD surgery, they have primarily concentrated on surgical factors, such as the complexity of the surgery, the duration of cardiopulmonary bypass, and the extent of thoracic duct trauma.[9,10] However, there is a paucity of research investigating the impact of nutrition-related factors on these postoperative complications.

This study aims to investigate the risk factors affecting the duration of chylothorax drainage following CHD surgery, with a particular emphasis on the patient's preoperative nutritional status and postoperative nutritional support. To assess the importance of nutritional factors in the management of chylothorax and to provide evidence-based nutritional support strategies for its prevention and treatment.

MATERIALS AND METHODS

Patients

The patients included in study were all aged below three years and had been diagnosed with chylothorax within 30 days following CHD surgery at our institution between 2016 and 2020. Exclusion criteria: patients older than three years, those with congenital chylothorax, lymphatic anomalies, congenital syndromes such as Noonan and Turner syndromes. Furthermore, patients who died within 14 days post-CHD surgery or received a regular low-fat diet postoperatively, or underwent ligation surgery were excluded from the analysis (Figure 1). This study was reviewed and approved by Ethics Committee (2023331).

Diagnosis of chylothorax

Chylothorax was suspected in cases where drainage from a chest tube turned cloudy following the administration of enteral nutrition containing long-chain triglycerides. A definitive diagnosis was established on the basis of a high triglyceride concentration in pleural fluid (≥110 mg/dL or exceeding serum triglycerides) coupled with a lymphocyte predominance (≥80% of cells).[10]

Definition of primary outcome

The primary outcome was determined in cases where patients, having been diagnosed with chylothorax within 30 days after surgery, exhibited a duration of pleural effusion exceeding 14 days, which was subsequently defined as PPE.[11]

Nutritional management protocol

The nutritional support protocol is depicted in Figure 2. The chest tube was removed when the output over a 24-h period was less than 2mL/kg/d.

Data collection and variable definition

Predictive variables were selected based on the clinical judgment and a thorough review of the literature. The baseline data included age at operation, sex, weight, height, weight for age Z-score (WAZ), height for age Z-score (HAZ) and Risk Adjusted Classification for Congenital Heart Surgery (RACHS-1). Perioperative variables encompassed bypass time, cross-clamp time, chest drainage volume on the first postoperative day, timing of chylothorax occurrence, central venous pressure (CVP) on third day after surgery, mechanical ventilation time. Postoperative nutritional variables comprised the proportion of enteral nutrition (EN) energy intake (ratio of actual energy intake to target energy for EN), proportion of parenteral nutrition (PN) energy intake (ratio of actual energy intake to target energy for PN). The postoperative period is divided into three stages: the acute phase (postoperative days 1-2), the stable phase (postoperative days 3-7), and the recovery phase (beyond postoperative day 7). The reference for target energy intake at each stage was based on the recommended energy intake for critical ill children.[12]

Statistical analysis

Continuous variables were presented as the median with the 25th-75th percentile due to their non-normal and non-homogeneous distribution, and comparisons were made using Mann-Whitney U test. Categorical variables were described in numbers and percentages (%), and intergroup differences were analyzed using the chi-squared(χ^2) test. Variables with a p-value of <0.1 in univariate logistic analysis were included in the multivariate logistic regression analysis. A *p*-value of <0.05 was considered statistically significant. All statistical analyses were conducted using SPSS version 25 (SPSS Software, IBM Corp., Armonk, NY, USA).

RESULTS

A total of 136 patients were ultimately included in this study, with 42 patients developing PPE. The baseline characteristics of our study population, categorized by the development of PPE, are presented in Table 1. Patients who experienced PPE had significantly lower HAZ compared to those who did not. However, no significant differences were observed between the two groups in terms of age, sex, weight, height, WAZ and RACHS-1.

The perioperative characteristics of our study cohort revealed that patients who developed PPE had a significantly higher median chest drainage volume (18.2 mL/kg/day) on the first postoperative day than those who did not (11.6 mL/kg/day). Furthermore, the onset of chylothorax was notably delayed in PPE patients, and they required prolonged mechanical ventilation, as detailed in Table 2.

With regards to postoperative nutritional support, during the stable phase, patients in the PPE group exhibited a significantly lower proportion of energy intake derived from EN compared to those in the non-PPE group (Table 3).

Risk factors for prolonged pleural effusion

The drainage time of 14 days in patients with chylothorax was used as the cut-off point for the regression analysis. Variables with a $p \leq 0.1$ in the univariate logistic analysis were included in the multivariate logistic regression model (Table 4). The results revealed that a delayed onset of postoperative chylothorax, prolonged mechanical ventilation, reduced HAZ and diminished EN energy intake during the recovery phase were significant predictors for the progression to PPE (Table 5).

DISCUSSION

In our study, we identified 30.9% of the 136 patients developed PPE following CHD surgery, which is a slightly higher rate compared to previous studies.[9,10] This difference may be attributed to the exclusion criteria used in our study. Notably, we identified several significant factors associated with the development of PPE, including delayed onset of chylothorax, prolonged duration of mechanical ventilation, lower HAZ, and reduced proportion of EN energy intake during the recovery phase.

The mechanism of postoperative chylothorax can generally be categorized as traumatic or non-traumatic. The early emergence of chylothorax after surgery is typically associated with injury of the thoracic duct or its lymphatic branches, which is considered a direct consequence of surgical manipulation where lymphatic vessels may be inadvertently damaged or severed. On the other hand, the delayed onset of chylothorax is usually attributed to cardiac dysfunction or decompensation,[13] compromised hemodynamics, or the formation of deep vein thrombosis.[2,14] These factors contribute to increased hydrostatic pressure, a critical factor in fluid accumulation within the pleural space and the prolongation of the pleural drainage period.[14,15] In this study, patients experiencing later-onset chylothorax postoperatively were more prone to developing PPE, which can be explained by the aforementioned mechanism.

Unfortunately, the central venous pressure of the patients was only documented during the initial phase of the postoperative period, which may have limited our ability to fully assess the relationship between hydrostatic pressure and PPE.

Another independent risk factor highlighted by our analysis is the prolonged duration of mechanical ventilation. A study conducted by Luo et al[9] emphasized that a shorter duration of mechanical ventilation is associated with a lower risk for PPE. This association is likely due to the fact that mechanical ventilation increases intrathoracic and central venous pressures, which subsequently reduce lymphatic drainage and the reabsorption of pleural fluid.[16] Yun et al[17] have also previously demonstrated that a low pulmonary vascular compliance is linked to a higher incidence of PPE. Our findings are consistent with those insights, confirming that prolonged mechanical ventilation is associated with an increased risk of PPE. Furthermore, patients who require extended mechanical ventilation often need additional fluid support, which may exacerbate the condition of PPE.

HAZ, an indicator of growth and development, reflects a child's nutritional status over an extended period. In our study, children with lower HAZ scores were at a higher risk for PPE. This finding suggests that a patient's preoperative nutritional condition and growth trajectory can significantly influence postoperative outcomes, Specifically, those who are malnourished or have growth restrictions may be more prone to postoperative complications, including chylothorax, a condition that has consistently been linked to nutritional vulnerability.[1,18] The underlying mechanism involves a deleterious cycle initiated by lymphatic fluid drainage, which deprives the body of vital nutrients, leading to nutritional deficiencies. These deficiencies, in turn, exacerbate respiratory issues and increase susceptibility to infections, thereby prolonging the duration of chylothorax drainage. Our observation emphasizes the crucial role of adequate nutrition in managing and preventing complications associated with chylothorax.

We further observed that a reduced proportion of EN energy intake during the recovery phase appears to elevate the risk of PPE. Notably, all patients in our study received a formula fortified with medium-chain triglycerides (MCTs), which are absorbed by intestinal cells and transported directly to the liver via the port vein, thereby minimizing chylous leakage into the pleural space.[15,19] The data potentially confirms that MCT-predominant formulas are safe and effective when used in conjunction with medical therapies in the treatment of chylothorax,[20] and suggests that EN support is more favorable during the recovery period. Our findings also underscore the importance of ensuring adequate energy intake throughout the recovery process. Interestingly, the patients in our study cohort either received underfeeding or

appropriate feeding levels.8 It is therefore proposed that increasing caloric intake within the recommended range could potentially have a positive effect on the healing process of chylothorax, leading to a more favorable outcome.

There are several limitations to the present study. Our study population is confined to a single institution, the sample size was relatively small. Secondly, as it was a respective study, we were unable to accurately assess the nutrient intake of patients on a low-fat diet. Lastly, it was not feasible to account for all potential factors that could influence the outcome, so we acknowledge that we may have overlooked certain factors that could potentially influence the occurrence of pleural effusion.

Conclusion

This study suggests that the delayed onset of chylothorax, prolonged mechanical ventilation, a lower HAZ and a reduced proportion of energy intake from EN during the stable phase are potential contributors to PPE in patients with chylothorax after CHD surgery. Developing a preventative strategy that targets these potential risk factors may help to decrease the incidence of PPE and improve in-hospital outcomes.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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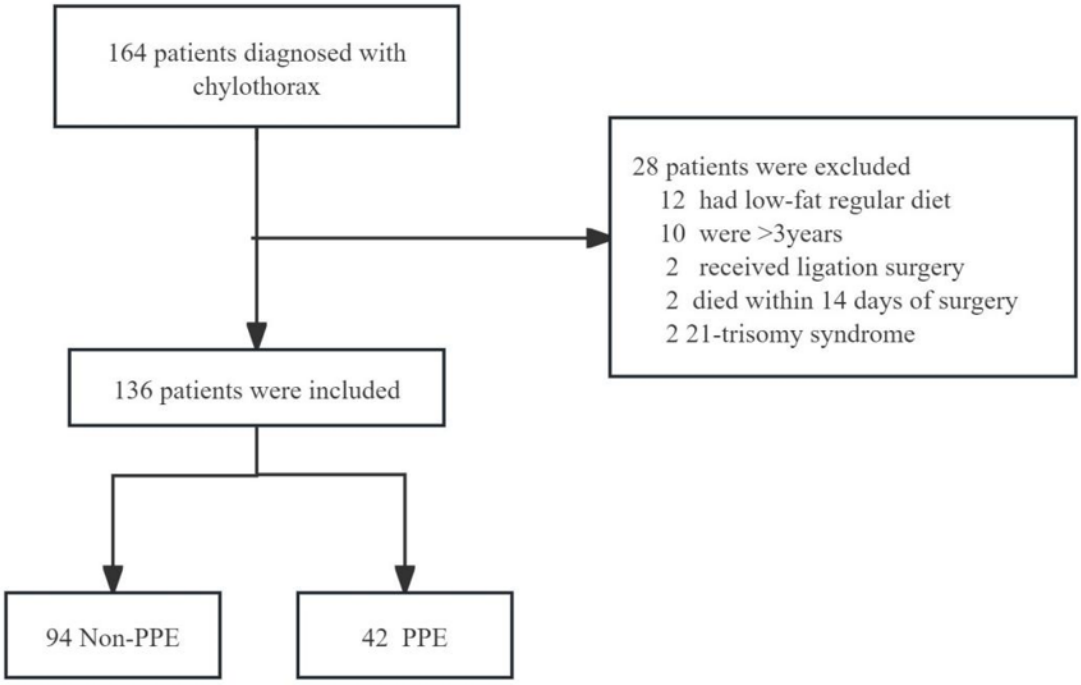

Figure 1. Study profile

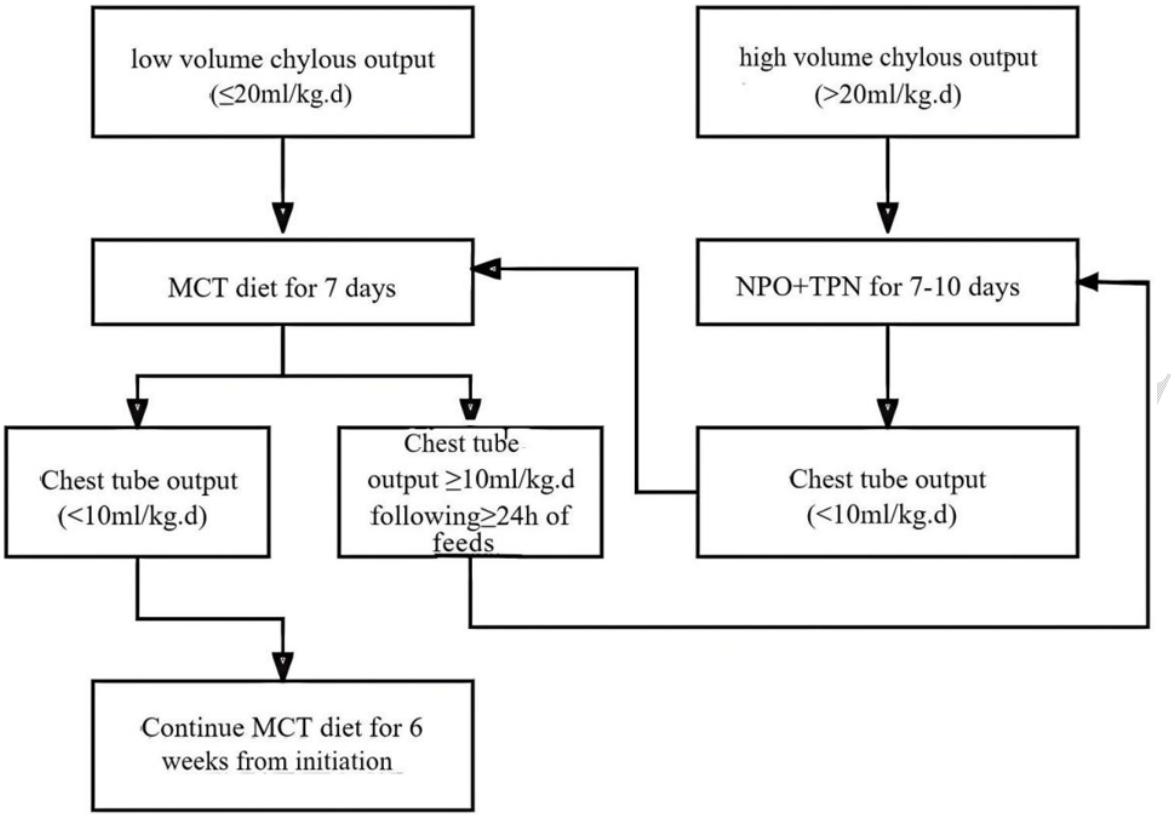

Figure 2. Nutritional management for postoperative chylothorax. MCT: medium-chain triglycerides, NPO: nil per os, TPN: total parenteral nutrition

Table 1. Demographics

Characteristic	Non-PPE	PPE	*p-value*
Age	9.2 (5.4, 15.3)	7.7 (13.0,16.0)	0.120
Sex			0.924
Female	35 (37.2%)	16 (38.1%)	
Male	59 (62.8%)	26 (61.9%)	
Weight	7.50 (5.15, 10.00)	8.00 (6.95, 8.35)	0.721
Height	71.00 (63.50, 78.00)	73.25 (68.00, 75.00)	0.962
WAZ	-1.42 (-2.19, -0.41)	-1.61 (-2.08 ,-1.16)	0.204
HAZ	-0.34 (-1.02, 0.51)	-1.02 (-1.68, -0.55)	<0.001
RACHS-1			
1	15 (16.9%)	3 (7.1%)	0.414
2	46 (48.9%)	24 (57.1%)	
3	23 (24.5%)	12 (28.6%)	
4	10 (10.6%)	3 (7.1%)	

PPE: XXXX; WAZ: XXXX; HAZ: XXX; RACHS-1: XXXX

Table 2. Perioperative characteristics

Variables	Non-PPE	PPE	*p*-value
Bypass time (min)	111.00 (59.50,150.25)	122.00 (101.75,134.00)	0.283
Cross clamp time (min)	60.50 (16.50,86.00)	79.00 (50.25, 89.00)	0.192
Chest drainage volume of the postoperative 1st day (ml)	11.57 (7.18, 20.36)	18.18 (13.68, 27.92)	0.002
Timing of chylothorax occurrence (day)	1 (1, 2)	3 (1, 6)	<0.001
CVP 72h (cmH_2O)	8.65 (7.00, 12.00)	9.00 (7.00, 11.25)	0.998
Mechanical ventilation time (day)	4 (2, 8)	7 (4, 12)	0.005

PPE: XXXX; CVP: XXXX

Table 3. Energy intake during postoperative chylothorax

Variables	Non-PPE	PPE	*p*-value
Acute phase			
EN energy proportion	0.33 (0.09, 0.48)	0.31 (0.17, 0.42)	0.810
PN energy proportion	0 (0, 0)	0 (0, 0)	0.151
Stable phase			
EN energy proportion	0.42 (0.31, 0.59)	0.36 (0.15, 0.61)	0.048
PN energy proportion	0.37 (0.21, 0.48)	0.34 (0, 0.52)	0.523
Recovery phase			
EN energy proportion	0.23 (0, 0.48)	0.17 (0.08, 0.29)	0.384
PN energy proportion	0.26 (0, 0.51)	0.25 (0.11, 0.43)	0.767

PPE: XXXX; EN: XXXX; PN: xXXX

Table 4. Univariate logistic regression analysis of risk factors for PPE

Variables	B	SE	OR (95%CI)	*p*-value
Age	0.02	0.025	1.023(0.974, 1.073)	0.364
WAZ	-0.242	0.160	0.785(0.574, 1.076)	0.132
HAZ	-0.689	0.201	0.502(0.338, 0.745)	0.001
Bypass time	0.004	0.003	1.004(0.998, 1.010)	0.231
Cross clamping	0.007	0.005	1.007(0.998, 1.017)	0.137
Chest drainage volume of the postoperative 1st day (mL)	0.150	0.009	1.015(0.997, 1.033)	0.093
CVP 72h	-0.011	0.052	0.497(0.894, 1.095)	0.835
Timing of chylothorax occurrence (day)	0.361	0.088	1.435(1.207, 1.7.6)	<0.001
Mechanical ventilation time (day)	0.062	0.033	0.297(0.997, 1.136)	0.062
Acute phase				
Proportion of EN energy	-0.023	0.868	0.977(0.178, 5.362)	0.979
Proportion of PN energy	-1.030	1.109	0.357(0.041, 3.139)	0.353
Stable phase				
Proportion of EN energy	-2.143	0.958	0.117(0.018, 0.767)	0.025
Proportion of PN energy	-0.908	0.928	0.404(0.065, 2.486)	0.328
Recovery phase				
Proportion of EN energy	-1.632	0.903	0.196(0.033,1.148)	0.071
Proportion of PN energy	-0.074	0.783	0.928(0.200, 4.310)	0.925

B: xx; SE: xx; WAZ: XXX; HAZ: XXX; CVP: XXXX; EN: XXXX; PN: XXX

Table 5. Multivariate logistic regression analysis of risk factors for PPE

Variables	B	SE	OR (95%CI)	*p*-value
HAZ	-0.782	0.238	0.457 (0.287, 0.729)	0.001
Chest drainage volume on the first day after surgery (mL)	0.011	0.013	1.012 (0.987, 1.037)	0.360
Timing of chylothorax occurrence (day)	0.373	0.103	1.453 (1.187, 1.777)	<0.001
Mechanical ventilation time (day)	0.082	0.036	1.086 (1.011, 1.166)	0.024
Proportion of energy intake from EN during				
Stable phase	-0.652	1.120	0.521 (0.058, 4.677)	0.560
Recovery phase	-2.241	1.153	0.090 (0.009, 0.861)	0.037

B: xx; SE: xx; HAZ: XXX; CVP: XXXX; EN: XXXX