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Chylothorax following pediatric cardiac surgery

Pediatrik kardiyak cerrahisi sonrası şilotoraks

Okan Yıldız,[1] Erkut Öztürk,[2] Hüsnü Fırat Altın,[1] Pelin Ayyıldız,[2] Taner Kasar,[2] Ahmet İrdem,[2] Yakup Ergül,[2] Sertaç Haydın,[1] Alper Güzeltaş,[2] Mehmet Yeniterzi[1]

Departments of [1]Pediatric Cardiovascular Surgery and [2]Pediatric Cardiology,
İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital, İstanbul, Turkey

ABSTRACT

Background: This study aims to evaluate the incidence, treatment protocols, and impact of chylothorax on early outcomes after pediatric cardiovascular surgery.

Methods: Records of 1,123 pediatric patients who underwent heart operation at our clinic between June 2011 and June 2014 were reviewed retrospectively. Thirty-five patients (19 males, 16 females; median age 240 days; range 5 days to 15 years) who developed postoperative chylothorax were included in the study.

Results: Development of chylothorax was detected most frequently in single ventricle repairs (n=11, 31%). It was followed by aortic arch repairs (n=9, 25%), tetralogy of Fallot (n=4, 1%), atrioventricular septal defect repairs (n=4, 11%), arterial switch operations (n=3, 8%), ventricular septal defect repairs (n=2, 6%), and other operations (n=2, 6%). Median duration of drainage of chylothorax was nine days (range, 2 to 44 days). Nutritional management included low lipid diet, enteral feedings enriched with medium-chain triglycerides, and total parenteral nutrition. Fourteen patients were administered octreotide, four patients were administered thoracic duct ligation, and four patients were administered pleurodesis. Sepsis was observed in nine patients and three patients died.

Conclusion: Chylothorax developing after pediatric cardiac surgery is not a rare complication. It occurs most frequently after single ventricle repair and has a significant impact on postoperative clinical course and morbidity.

Keywords: Cardiac surgery; children; chylothorax.

ÖZ

Amaç: Bu çalışmada şilotoraksın insidansı, tedavi protokolleri ve pediatrik kardiyovasküler cerrahi sonrası erken dönem bulgular üzerindeki etkisi değerlendirildi.

Çalışma planı: Haziran 2011 - Haziran 2014 tarihleri arasında kliniğimizde kalp ameliyatı geçiren 1123 pediatrik hastanın kayıtları retrospektif olarak incelendi. Ameliyat sonrası şilotoraks gelişen 35 hasta (19 erkek, 16 kız; ortanca yaş 240 gün; dağılım 5 gün-15 yıl) çalışmaya dahil edildi.

Bulgular: Şilotoraks gelişimi en sık tek ventrikül tamirlerinde saptandı (n=11, %31). Bunu aortik ark tamiri (n=9, %25), Fallot tetralojisi (n=4, %11) atriyoventriküler septal defekt tamirleri (n=4, %11), arteriyel switch ameliyatları (n=3, %8), ventriküler septal defekt tamirleri (n=2, %6) ve diğer ameliyatlar (n=2, %6) izledi. Ortanca şilotoraks drenaj süresi dokuz gün (dağılım 2-44 gün) idi. Beslenme yönetimi yağdan fakir diyet, orta zincirli yağ asitlerinden zengin enteral beslenme ve total parenteral beslenmeyi içerdi. On dört hastaya oktreotid, dört hastaya duktus torasikus ligasyonu ve dört hastaya plörodezis uygulandı. Dokuz hastada sepsis gözlendi ve üç hasta kaybedildi.

Sonuç: Pediatrik kardiyak cerrahi sonrası gelişen şilotoraks nadir olmayan bir komplikasyondur. En sık tek ventrikül tamiri sonrasında gelişir ve ameliyat sonrası klinik seyir ve morbidite üzerinde anlamlı etkiye sahiptir.

Anahtar sözcükler: Kardiyak cerrahi; çocuklar; şilotoraks.

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Correspondence: Erkut Öztürk, M.D. İstanbul Mehmet Akif Ersoy Göğüs Kalp Damar Cerrahisi Eğitim ve Araştırma Hastanesi, Pediatrik Kardiyoloji Kliniği, 34303 Küçükçekmece, İstanbul, Turkey.
Tel: +90 212 - 692 20 00 e-mail: erkut_ozturk@yahoo.com

Chylothorax, which develops as a result of the deposition of fatty acids along with lymphatic fluid into the pleural cavity, is one of the reasons for postoperative morbidity.[1,2] The primary mechanisms that lead to postoperative chylothorax are direct trauma to the lymphatic vessels or the thoracic duct and secondary to central venous hypertension (HT) after a cavopulmonary connection (Glenn or Fontan). Venous thrombosis has also been reported but is less common. Prolonged chylothorax places patients at risk for malnutrition, poor wound healing, infections, fluid imbalance, electrolyte abnormalities, prolonged mechanical ventilation and device utilization, and longer stays in the hospital and intensive care unit (ICU).[3,4]

The first step in chylothorax treatment is the drainage of the pleural fluid to decrease the flow of the lymphatic fluid from the ductus thoracicus. This is followed by a low-fat or fat-free diet or the replacement of enteral food with liquid intake [nil per os (NPO)] or the use of total parenteral nutrition (TPN) including intravenous lipids.[1-3] Pharmacotherapy with the somatostatin analogue octreotide has also been proposed to decrease the blood flow to the hepatic, portal, and splanchnic circulations, resulting in a decrease in the lymphatic flow through the ductus thoracicus.[5] If medical therapy fails, surgical intervention should be considered, with thoracic duct ligation, pleurodesis, and pleural peritoneal shunting being appropriate options for persistent chylothorax.[6]

The aim of this study was to evaluate the demographics, diagnoses, primary cardiac surgical procedures, and treatment protocols of patients with postoperative chylothorax and assess their effects.

PATIENTS AND METHODS

A total of 1,123 patients underwent cardiac surgery during the study period, and 35 (3.1%) of these had chylothorax in the postoperative period [19 males, 16 females; median weight 8 kgs (range 2-45 kgs); median age 8 months (range 5 days-15 years)] and were included in the study, which took place at our facility over a three-year period beginning in June of 2011. These patients were identified using the hospital medical records database.

After a retrospective review of these records, the demographic data related to age, weight, time of diagnosis, cardiac diagnosis, and primary cardiac surgical procedure as well as the data associated with chest tube output, fluid intake and output, dietary intake, medical and surgical treatments for chylothorax, hospital mortality, length of stay in the ICU and hospital, mechanical ventilation duration, number and duration of chest tube placements, duration of NPO and TPN diets, and bloodstream infections were recorded. In addition, we also noted the Risk Adjustment for Congenital Heart Surgery (RACHS-1) category scores.[7] The diagnosis of postoperative chylothorax was carried out by investigating the characteristics of the pleural fluid, and a triglyceride level of >110 mg/dL or a white cell count (WCC) of >1,000 cell/μL with a significant lymphocyte fraction (80%) confirmed its presence.[4,8] The onset of chylothorax was considered to be the point at which diagnostic fluid was first recovered.

The instutional protocol for the management of postoperative chylothorax was followed during the study period. Chest tube drainage of ≤5 mL/kg/day was classified as low volume while >5 mL/kg/day was considered to be high volume. All of the patients diagnosed with chylothorax were fed with only medium chain triglyceride (MCT) oil-based formulas, and the same food was provided to those who showed persistent low volume drainage. Octreotide treatment was started when the drainage did not diminish to a volume of <2 mL/kg/day after three to five days of NPO followed by TPN administration. For the patients with high volume drainage, oral feeding was stopped, and TPN was given directly. In addition, intravenous octreotide infusion was added to the treatment in cases that were unresponsive to TPN alone. When the drainage decreased to <2 mL/kg/day, the MCT oil-based formulas were added to the diet without the octreotide infusion for another one or two weeks until the chylothorax ceased, and then the chest tubes were removed. Pleurodesis was applied to some of the patients when the amount of drainage was >10 mL/kg/day at the end of 10 days of treatment via 500 mg vancomycin in a 50 mL saline solution. This was given through the chest catheter or tube with the patient positioned toward the left or right lateral decubitus in both the face down and supine positions for 10 minutes each. The chest catheter was kept closed for 24 hours. The patients who did not respond to conservative management after two to three weeks were evaluated for thoracic duct ligation, which was then applied directly to some patients without pleurodesis. Additional recommendations included an echocardiogram to determine whether correctable abnormalities were present, the monitorization of serum albumin and C-reactive protein (CRP) levels, hemocoagulation, a hemogram, a biochemical analysis, and daily chest X-rays. Additionally, 14 or 16 G single-lumen venous catheters were chosen for delayed chylothorax drainage instead of regular chest tubes.

Statistical analyses

The statistical evaluation of the data was performed by using the SPSS for Windows version 15.0 software program (SPSS Inc., Chicago, IL, USA). Categorical variables were presented as absolute and percent frequencies, whereas quantitative variables were given as medians and ranges. The Mann-Whitney U test was used to compare the mean values between the groups while chi-square and Fisher's exact tests were performed to compare the rates between the groups. Statistical significance was set at $p<0.05$.

RESULTS

The primary diagnoses of the the 35 patients with chylothorax included 11 patients with complex lesions (treated with cavapulmonary connection), five with hypoplastic left heart syndrome (HLHS), four with atrioventricular septal defect (ASD), four with tetralogy of Fallot, three with transposition of the great arteries, two with ventricular septal defect (VSD) and six with other simple lesions. The patient characteristics and procedures are listed in Table 1.

Surgery was performed via a median sternotomy in 28 patients and a thoracotomy in the other seven. The median duration of the initial mechanical ventilation was two days and ranged from less than 1 day to 18 days. Six patients required re-intubation, and two died before ever being extubated. Excluding the three patients who died, the median initial ICU length of stay was seven days (range 1-30 days), but four patients required readmission to the ICU. Furthermore, the median total postoperative length of hospital stay for the 32 survivors was 25 days (range 7-64 days), including the subsequent

Table 1. Demographic and clinical characteristics of the patients diagnosed and treated for chylothorax

	n	%	Median	Range
Total number of patients	35			
Gender				
Male	19			
Female	16			
Median age in days			240	5-5400
Median weight (kg)			8	2-45
Index procedure				
Cavapulmonary connection	11			
Glenn*	9			
Fontan**	2			
Arch reconstruction	9			
Norwood	5			
Vascular ring	2			
Coarctation + interruption	2			
Ventricular septal defect	2			
Tetralogy of Fallot	4			
Arterial switch	3			
Atrioventricular canal repair	4			
Others	2			
RACHS-1 classification				
1-3	18			
4-6	15			
Unclassified	2			
Chest tube output (mL/kg/day)				
Low	12	34		
High	23	66		
Average time from surgery to chylothorax diagnosis in days			6	1-28

* Glenn operation [Double inlet left ventricle (DILV)-pulmonary atresia (n=2), hypoplastic left heart syndrome (HLHS) (n=1), tricuspid atresia (n=2), intact ventricular septum-pulmonary atresia (n=1), right atrial isomerism (n=1), left atrial isomerism (n=2), and bilateral bidirectional cavapulmonary connection (n=3)]; ** Fontan operation [DILV-pulmonary atresia (n=1), tricuspid atresia (n=1), and extracardiac Fontan modification (n=2)].

readmission of the four patients for persistent or recurrent chylothorax.

The chylous pleural effusion was in the right chest in 18 patients (51%), the left chest in 17 others (49%), and on both sides in six more (17%). Four patients (11%) also had additional pericardial effusion.

The median time for diagnosing the chylothorax was six days (range 1-28 days) after the surgery, with 20 patients being diagnosed within seven days after the operation and 15 after the postoperative seventh day. Among those with an early diagnosis, five did not have chest tubes at the time of their diagnosis, whereas 15 did. None of the patients who were diagnosed later had chest tubes, and for them, the chylothorax was diagnosed by a clinical examination, a chest X-ray, and the testing of fluid samples by pleurocentesis. The median drainage on the day of diagnosis was 10 mL/kg (range 4-36 mL/kg), and the median drainage time of the chylothorax was nine days (range 2-44 days).

The chylothorax was evident from the laboratory testing of the fluid in 21 patients (60%) because of the presence of a triglyceride concentration of >110 mg/dL. Moreover, 18 patients underwent additional testing of the fluid cell counts, and this showed that nine (50%) had a total white blood cell (WBC) count of over 1,000 cells/mm^3. In addition, the percentage of lymphocytes was more than 80% in 13 of the patients (72%), and two had at least one of the three fluid abnormalities. However, we found no significant differences between the characteristics of chylous drainage after the cavapulmonary connection procedures and those that developed after other surgeries (Table 2).

Nutritional management included the use of MCTs for all 35 patients. Total parenteral nutrition was used for 23 patients, and octreotides were used in 14. In four patients who did not respond to these therapies, pleurodesis was performed, and one of these was also treated with thoracic duct ligation. The medical and surgical treatments for the chylothorax are listed in Figure 1.

In addition, nine patients had sepsis, and five had arrhythmias and a pneumothorax. All of the complications are summarized in Table 3. Three patients died during their initial hospital stay at the postoperative 10th, 30th, and 42nd days because of chronic lung disease and sepsis, without any resolution of their chylothorax. Furthermore, two of the patients who did not survive underwent a Norwood stage 1 operation, and one underwent an arterial switch operation. No surgical intervention was performed for the chylothorax in these patients.

In four patients, chylothorax developed after they were discharged, and it was determined that all of these had a single-ventricle pathology. One of them was treated with ductal ligation, and two received pleurodesis, with both showing improvement with the use of octreotides and TPN. One patient treated with medical therapy.

DISCUSSION

The incidence of chylothorax from various centers in different years has varied. Allen et al.[9] reported an incidence rate of 1% in their study in 1979 and 1987 while the latest reported incidence rates were 3.5% by Chan et al.[3] and 5% by Ismail et al.[10] The higher rates were likely due to the increased complexity of the patients along with the number of single-ventricle repairs and redo surgeries.[3] The incidence of chylothorax in our study population was 3.1%, which

Table 2. Characteristics of the clinical course of the patients who underwent cavopulmonary connections versus all other patients

Characteristic	Cavopulmonary (n=11)				Other (n=24)				
	n	%	Median	Range	n	%	Median	Range	*p*
Average days before diagnosis	14			2-28	10			1-20	0.34
Pleural fluid characteristics at diagnosis			1.56				1.35		0.87
Triglyceride level (mmol/L)			2,000				1,500		0.64
White blood cell count (cells/mm^3)			83				86		0.55
Percentage of lymphocytes	14			4-44	9			2-30	0.46
Average maximum daily drainage (mL/kg)	48			10-115	37			14-672	0.21
Average number of days in the hospital	26			10-64	20			7-61	0.25
Treatment modality									
Octreotide group	6	55			8	33			0.23
Pleurodesis group	3	27			1	4			0.08
Ductus ligation group	3	27			1	4			0.08

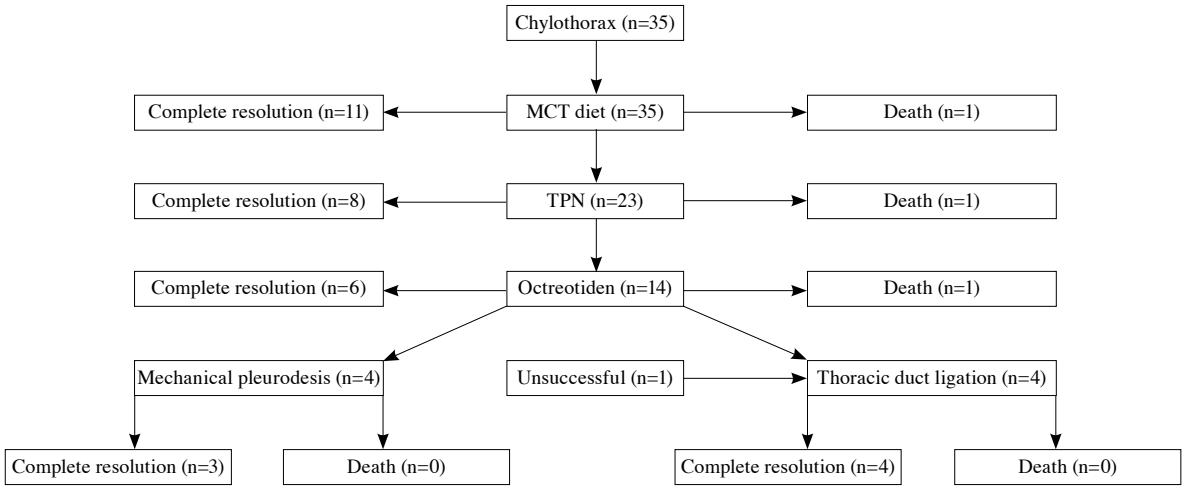

Figure 1. Flowchart showing the management strategies and outcomes for the patients diagnosed with postoperative chylothorax. MCT: medium chain triglyceride; TPN: Total parenteral nutrition.

was in line with the more recent studies. Furthermore, 45% of our cases involved single-ventricle repairs. Five of these patients had HLHS, and four underwent redo surgeries. Chan et al.[3] reported that chylothorax is mostly seen in heart transplantation operations and patients with Fontan circulation. In our study, the single-ventricle surgeries were most frequently complicated by chylothorax (n=11, 31%) followed by arch repairs (n=9, 25%); VSD repairs (n=2, 6%), ASD repairs (n=4, 11%), arterial switch repairs (n=3, 8%), and other types of repair (n=2, 6%). However, heart transplantations are not performed at our center.

The limited number of patients studied in each series precludes having a consensus regarding which protocol is the most effective, and there is limited data related to the treatment of postoperative chylothorax, both of which have led to wide variations in practice. In addition, most of the published pediatric studies are also limited to small case series.[10] The optimal management of chylothorax is unclear because no prospective studies exist to aide in the choice of therapy since different protocols and strategies are followed in each center.[11,12] The primary modes of treatment include pleural space evacuation, the use of MCT oil-based formulas, enteric rest, and parenteral alimentation,[12,13] and these have shown a success rate of 77% within a maximum of 45 days, with an average time of approximately 12 days.[14] Previous studies have suggested that persistent chylous output for more than three weeks and lesions associated with elevated systemic venous pressure were risk factors for the failure of conservative management options.[1,2,13] Conservative treatment was successful in 15 (83.3%) of our patients, and they were hospitalized for an average of 2.3 weeks. Since we knew that cavopulmonary anastomosis procedures have a higher risk for prolonged pleural drainage, a more aggressive therapy with early initiation might be indicated for these patients;[3] hence, the need for a standard treatment protocol for chylothorax is crucial. Yeh et al.[11] formulated a chylothorax algorhythm treatment in 2013 that produced an early diagnosis which reduced the time in the hospital as well as the use of mechanical

Table 3. Comparison of early postoperative complications

Complications	Cavopulmonary		Other		*Total*		
	n	%	n	%	n	%	*p*
Mortality	–	–	3	12.5	3	8.5	0.53
Septicemia	3	27.3	6	25.0	9	25.7	0.98
Arrhythmias	2	18.2	3	12.5	5	14.2	0.64
Re-intubations	2	18.2	4	16.7	6	17.1	0.99
Acute renal failure	1	9.1	1	4.2	2	5.7	0.53
Pneumothoraces	2	18.2	3	12.5	5	14.2	0.64
Thrombosis	2	18.1	1	4.2	3	8.5	0.22

ventilation. Their patients were fed with medium chained fatty acids when the amount of drainage was <20 mL/kg/day, but the oral intake ceased when the amount of drainage was >20 mL/kg/day. Then TPN was started, and octreotide therapy of approximately 3 mcg/kg/h was given for a period of between seven and 10 days. In addition, tube ligation, both with and without pleurodesis, was performed in the patients who did not have a decrease in the amount of drainage. We have been applying this modified protocol at our clinic for almost two months now, and thus far, it appears to be practical and useful. However, further studies should be conducted to evaluate whether earlier intervention can reduce the hospitalization times and improve the prognoses.

If conservative therapy fails to control the leak, surgical intervention is advocated, although there is not yet a consensus regarding the specific, precise criteria needed to abandon the conservative therapy.[12] Nevertheless, it is generally accepted that in spite of the use of conservative therapy, if lymphatic leakage persists beyond a few weeks or if massive fluid and nutritional losses present a danger to the patient, then operative intervention is indicated.[12] Some authors have recommended that the surgery take place within five to seven days to limit the morbidity and mortality associated with the operation,[12] but others believe it is better to wait for approximately two weeks or longer in order to provide an adequate time for medical treatment.[8,12] Two surgical strategies predominate: direct wound ligature and en masse supradiaphragmatic ligature. Particularly for our patients with a single ventricle, we treated the postoperative chylothorax aggressively, believing that we should not wait for pleurodesis and ligation. Pleurodesis has been recommended for refractory chylothorax that does not respond to medical or surgical intervention or the fenestration of the diaphragm, and some have also advocated for the creation of pleura-peritoneal windows to treat this condition.[14-16] However, none of our patients required these procedures. The vast majority responded to the use of conservative management or thoracic duct ligation without the need for further interventions that are often necessary in severe refractory cases.

In recent years, there has also been an increase in the use of the somatostatin analogue known as octreotide. It is not yet known how this analogue results in less chylothorax drainage, but it might be associated with a reduction in splanchnic blood flow as well as hepatic venous pressure which results in the decreased movement of the chylous triglyceride content toward the ductus thoracicus. More importantly, no side effects have been reported with octreotide therapy.[17,18] In our study, this therapy was given to 14 patients, but five of these later required pleurodesis or ligation.

The morbidity associated with chylothorax is potentially severe because the large losses of fluids, proteins, lipids, and WBCs can cause dehydration, nutritional deficiency, and immunological dysfunction.[10] In our study, three patients died (8.5%), which was similar to previous studies that had mortality rates of between 6 and 21%.[1,9,12,13] The cause of death in our patients was likely multifactorial due to the unfavorable hemodynamics, sepsis, and multiple organ dysfunction. The most observed complication in our study was septicemia in nine patients. In addition, six had to be reentubated, five developed arrhythmias and pneumothoraces, and four were rehospitalized because of the chylothorax, with two of these being treated with medical therapy, one with pleurodesis, and the other with successful ligation.

Our study had some limitations. It had relatively small sample size and also contained no control group. Furthermore, the cases were reviewed retrospectively, and there was a lack of hemodynamic and laboratory testing of the fluid, especially in the patients who underwent single-ventricle repair.

Conclusion

Chylothorax after pediatric cardiac surgery is not a rare complication. It occurs more commonly after single-ventricle repair and has a significant impact on the postoperative course and morbidity. An accurate diagnosis and early treatment are important to achieve a favorable outcome; therefore, the development of pleural effusion after a cardiothoracic procedure should always raise the suspicion of chylothorax. Surgical intervention should be reserved for the minority of patients who fail to respond to medical treatment, which may be lengthy but can prevent significant morbidity and mortality. While a period of nutritional modifications may be justified, the earlier implementation of octreotide therapy for those with a risk of prolonged chyle loss, such as those with elevated systemic venous pressure, might be beneficial, but prospective randomized controlled trials are needed to confirm the efficacy of this treatment modality.

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