Incidence and treatment of chylothorax after cardiac surgery in children: Analysis of a large multi-institution database

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Objective: There is limited information regarding the true incidence of and risk factors for chylothorax after pediatric cardiac surgery. The objective of this study was to determine, from a large multi-institution database, incidence, associated factors, and treatment strategy in patients undergoing pediatric cardiac surgery.

Methods: All patients younger than 18 years in the Pediatric Health Information System (PHIS) database who underwent congenital heart surgery or heart transplant from 2004 to 2011 were included. Procedure complexity was assessed by Risk Adjustment for Congenital Heart Surgery-1.

Results: In all, 77,777 patients (55% male) of median age 6.7 months were included. Overall incidence of chylothorax was 2.8% (n = 2205), significantly associated with increased procedure complexity, younger age, genetic syndromes, vein thrombosis, and higher annual hospital volume. Patients with multiple congenital procedures had the highest incidence. Incidence increased with time, from 2% in 2004 to 3.7% in 2011 ($P < .0001$). Chylothorax was associated with longer stay ($P < .0001$), increased adjusted risk for in-hospital mortality (odds ratio, 2.13; 95% confidence interval, 1.75-2.61), and higher cost ($P < .0001$), regardless of procedure complexity. Of all patients with chylothorax, 196 (8.9%) underwent thoracic duct ligation or pleurodesis a median of 18 days after surgery. Total parenteral nutrition, medium-chain fatty acid supplementation, and octreotide were used in 56%, 1.7%, and 16% of patients, respectively.

Conclusions: Chylothorax is a significant problem in pediatric cardiac surgery and is associated with increased mortality, cost, and length of stay. Strategies should be developed to improve prevention and treatment. (J Thorac Cardiovasc Surg 2014;147:678-86)

Supplemental material is available online.

The development of chylothorax after pediatric cardiac surgery is a known complication associated with significant respiratory, nutritional, immunologic, hematologic, and metabolic morbidity.¹ It has been associated with longer ventilation dependence,² longer postoperative stay,³ and increased mortality.² According to contemporary single-

institution studies, it is estimated that 4% to 9% of children undergoing cardiac surgery will acquire this complication.³⁻⁵

The mechanisms proposed for the development of chylothorax after cardiac surgery include surgical trauma to the thoracic duct or lymphatic tributaries, increased central venous pressure after procedures such as partial or complete cavopulmonary anastomoses, and the development of central venous thrombosis with consequent impairment of thoracic duct drainage.¹ Accordingly, some of the risk factors that have been found in single-institution studies to be associated with the development of chylothorax after cardiac surgery include type of procedure,^{3,4} secondary chest closure,⁴ low weight,⁴ durations of cardiopulmonary bypass and crossclamping,⁴ and presence of trisomy 21.¹⁰ In particular, patients undergoing a Fontan procedure or heart transplant seem to be at the highest risk.^{3,11}

Despite several small studies reporting the incidence of postoperative chylothorax in pediatric cardiac surgical patients, the actual risk factors for development of this complication, the trends in treatment strategy use, and the effect of this complication on outcomes have not been adequately studied. The goal of this study was to use a large multi-institution database to determine the incidence,

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Abbreviations and Acronyms

CI	= confidence interval
ICD-9-	= <i>International Classification of Diseases,</i>
CM	<i>Ninth Revision, Clinical Modification</i>
IQR	= interquartile range
MCT	= medium-chain triglycerides
OR	= odds ratio
PHIS	= Pediatric Health Information System
RACHS	= Risk Adjustment for Congenital Heart Surgery-1
TPN	= total parenteral nutrition

risk factors, current treatment strategies, and outcomes of children with chylothorax after cardiac surgery.

MATERIALS AND METHODS**Study Population**

All patients younger than 18 years who underwent congenital heart surgery or heart transplant from 2004 to 2011 in the Pediatric Health Information System (PHIS) database were included in this retrospective study.

The PHIS database is an administrative database that contains inpatient, emergency department, ambulatory surgery, and observation data from 43 not-for-profit, tertiary care pediatric hospitals in the United States. These hospitals are affiliated with the Children's Hospital Association (Overland Park, Kan). The data warehouse function for the PHIS database is managed by Truven Health Analytics (Ann Arbor, Mich). For the purposes of external benchmarking, participating hospitals provide discharge and encounter data including demographic characteristics, diagnoses, and procedures. Forty-two of these hospitals also submit resource utilization data (eg, pharmaceutical, imaging, and laboratory resources) into PHIS. Data are electronically collected directly from existing elements located within each PHIS-participating hospital's electronic medical and financial record systems. The health information management office of each PHIS-participating hospital is responsible for data extraction and submission to PHIS. There is no manual data entry. Data are stripped of identifiers at the time of data submission. Data are subjected to a number of reliability and validity checks before being included in the database. Data quality and reliability are ensured through a joint effort between PHIS-participating hospitals and the Children's Hospital Association. Participating hospitals receive data quality reports on submission to the data warehouse and are required to meet predetermined quality thresholds before certification of data submission. The Children's Hospital Association used the PHIS Data Quality Program to audit data at the time of submission, after submission, and after production once in PHIS. For this study, data from 42 hospitals met study criteria.

The PHIS database was queried to include all patients younger than 18 years who had either undergone a procedure with an assigned Risk Adjustment for Congenital Heart Surgery-1 (RACHS) score or a heart transplant (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] procedure code 37.51) during an inpatient admission within the study period.

Measurements

Patients who had an ICD-9-CM diagnosis code of 457.8 assigned to the same admission as the RACHS procedure or the heart transplant were considered to have acquired postoperative chylothorax. Even though the

date of the procedure is captured in the PHIS database, the date of diagnosis of chylothorax is not.

Information on demographic data of sex, age, and race or ethnicity; procedure complexity as assessed by RACHS score; year of surgery; use of total parenteral nutrition (TPN), medium-chain triglycerides (MCT), and octreotide; and total cost for the admission were extracted from the database. Costs in the PHIS database are calculated from hospital charges by means of multiple individual cost-to-charge ratios for each hospital. All costs were adjusted to 2011 US dollars. Information on diagnosis of Down syndrome (ICD-9-CM diagnosis code 758.0), Noonan syndrome (ICD-9-CM diagnosis code 759.89), and Turner syndrome (ICD-9-CM diagnosis code 758.6) was extracted. Similarly, a diagnosis of neck or proximal upper extremity deep vein thrombosis (ICD-9-CM diagnosis codes 453.83-453.87) was noted. The occurrence of a thoracic duct ligation (ICD-9-CM procedure code 40.64) or a pleurodesis (ICD-9-CM procedure codes 34.6 and 34.92) during the same admission but after the cardiac surgical procedure date was included.

Age was classified in several groups according to age at admission: neonates (≤ 30 days), infants (≥ 31 days and < 1 year), young children (≥ 1 year and < 6 years), older children (≥ 6 years and < 12 years) and teenagers (≥ 12 years and < 18 years). Race or ethnicity was classified as white, Hispanic, black, and others.

The data were stratified according to procedure complexity by means of RACHS score as provided by the PHIS database. The PHIS database assigns a single RACHS score to each operation on the basis of a predetermined algorithm. If a patient undergoes multiple procedures as part of the same operation, the operation is assigned the RACHS score for the highest-risk procedure. In our study, patients with RACHS scores of 5 and 6 were included in the same group. Patients with several separate operations during the same admission were assigned to a separate group (multiple procedures). Similarly, patients undergoing only a heart transplant during the admission were assigned to a separate group.

To analyze the data according to hospital volume, the median annual RACHS procedure volume was calculated for each hospital across the years that the particular hospital contributed to the database. All hospitals were then sorted from lowest to highest median volume. The median volumes were cumulatively added, and the hospitals were divided into quartiles according to these cumulative median volumes to ensure that each of the four groups had a relatively equivalent number of patients. The respective hospital volume quartile was then assigned to each entry depending on the hospital where the patient had the procedure performed. A similar analysis was performed to analyze the data according to median surgeon volume.

Data Analysis

The incidence of chylothorax was calculated for the entire group and for each subgroup. To determine the effect of risk factors on the incidence of chylothorax, univariate analyses were performed with χ^2 and Fisher exact tests as appropriate. A logistic multivariate regression model was created to determine the influence of each of the risk factors after adjustment for significant covariates. The results are presented as odds ratios (ORs) with 95% confidence intervals (CIs). The use of different treatment strategies (TPN, MCT, octreotide, and surgical procedures) and changes with time were analyzed with similar univariate methods.

The relationship between diagnosis of chylothorax and hospital stay and cost was determined with the Student *t* test and logarithmic linear regression models to adjust for covariates. The relationship between chylothorax and in-hospital mortality was analyzed with χ^2 testing and logistic regression for univariate and multivariate analyses, respectively.

All analyses were performed with the SAS 9.3 statistical software package (SAS Institute Inc, Cary, NC). Data are expressed as numbers and percentages or medians with interquartile ranges (IQRs) unless otherwise specified.

TABLE 1. Demographic characteristics of the overall cohort

Characteristics	No. (%)
Age group	
Neonates	18,419 (23.7)
Infants	27,514 (35.4)
Young children	19,187 (24.7)
Older children	6376 (8.2)
Teenagers	6281 (8.1)
Male	43,048 (55.4)
Race or ethnicity	
White	40,925 (54.3)
Hispanic	14,316 (18.9)
Black	9747 (12.9)
Other	10,400 (13.8)
Genetic syndromes	
Down syndrome	7343 (9.4)
Noonan syndrome	1820 (2.3)
Turner syndrome	394 (0.5)
Type of procedure	
RACHS	
1	9066 (11.7)
2	27,006 (34.7)
3	27,496 (35.4)
4	8354 (10.7)
5-6	2613 (3.4)
Heart transplant	1329 (1.7)
Multiple procedures	1913 (2.5)
Neck or upper vein thrombosis	175 (0.2)
Year	
2004	7766 (10)
2005	8910 (11.4)
2006	9740 (12.5)
2007	10,378 (13.3)
2008	10,502 (13.5)
2009	10,255 (13.2)
2010	10,074 (12.9)
2011	10,152 (13.1)

RACHS, Risk Adjustment for Congenital Heart Surgery-1.

RESULTS

A total of 77,777 patients in the PHIS database (43,048 [55%] male) with a median age of 6.7 months (IQR, 1.2 months–3.4 years) underwent cardiac surgery or cardiac transplant. The details of the entire cohort can be found in Table 1.

Incidence and Risk Factors for Development of Chylothorax

The overall incidence of chylothorax within this cohort was 2.8% (n = 2205). Table 2 shows the incidence of chylothorax for selected procedures according to ICD-9-CM procedure codes. The procedures associated with the highest incidence of chylothorax were those related to high venous pressures, such as cavopulmonary and atriopulmonary anastomoses (eg, Glenn and Fontan procedures).

TABLE 2. Incidence of chylothorax associated with selected procedures according to International Classification of Diseases, Ninth Revision, Clinical Modification procedure codes

Procedures (ICD-9-CM procedure codes)	Incidence (No. and %)
Atriopulmonary and cavopulmonary anastomoses; Fontan (35.94, 39.21)	430/7589 (5.7)
Total correction of transposition of great vessels (35.84)	125/2887 (4.3)
Heart transplant (37.51)	53/1329 (4.0)
Repair of congenital aortic arch anomalies* (38.34, 38.35, 38.44, 38.45, 38.64, 38.65, 38.84, 38.85)	241/6515 (3.7)
Total repair of total anomalous pulmonary venous connection (35.82)	71/1916 (3.7)
Total repair of tetralogy of Fallot (35.81)	182/5322 (3.4)
Repair of endocardial cushion defect (35.54, 35.63, 35.73)	158/4682 (3.4)
Total repair of truncus arteriosus (35.83)	23/742 (3.1)
Systemic to pulmonary artery shunt† (39.0)	64/3396 (1.9)
Repair of ventricular septal defect (35.53, 35.55, 35.62, 35.72)	150/9299 (1.6)
Patent ductus arteriosus‡ (38.34, 38.45, 38.64, 38.85)	14/1241 (1.1)
Repair of atrial septal defect (35.51, 35.52, 35.61, 35.71)	59/6660 (0.9)

ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification. *Includes patients with ICD-9-CM diagnosis codes 747.10 (coarctation of aorta), 747.11 (interrupted aortic arch), and 747.21 (congenital arch anomalies) as the primary diagnosis. †Includes only patients with a Risk Adjustment for Congenital Heart Surgery-1 score of 3. ‡Includes patients with ICD-9-CM diagnosis code 747.0 (patent ductus arteriosus) as the primary diagnosis.

The relationships between the different risk factors and the incidence of chylothorax are shown in Table 3. Chylothorax was more common in younger age groups, with the incidence being the highest for neonates (4.2%, n = 771) and the lowest for teenagers (0.5%, n = 32; $P < .0001$). After adjustment for significant covariates, neonates were approximately 7 times more likely to acquire chylothorax than teenagers (OR, 7.0; 95% CI 4.6-11).

Patients with genetic syndromes were more likely to acquire chylothorax. In particular, patients with Turner syndrome were more than 4 times more likely to acquire a chylothorax than those without, even after adjustment for other covariates (OR, 4.5; 95% CI, 3.1-6.5). Patients with a diagnosis of neck or upper extremity vein thrombosis were almost 7 times more likely to acquire a chylothorax (OR, 6.7; 95% CI, 4.6-9.7).

The development of chylothorax was also significantly associated with procedure complexity, with the incidence increasing from 1% for class 1 RACHS procedures to 5.2% for classes 5 and 6 ($P < .0001$). The incidence was highest (9.6%) for patients undergoing multiple procedures.

Hospitals in the highest quartile of annual volume had a significantly lower incidence of chylothorax than the rest,

TABLE 3. Risk factors associated with the development of chylothorax

Variable	Incidence of chylothorax (No. and %)	Multivariate analysis (OR and 95% CI)
Sex		
Male (n = 43,048)	1274 (3)	Reference
Female (n = 34,729)	931 (2.7)	0.86 (0.78-0.94)
Race or ethnicity		
White (n = 40,925)	1188 (2.9)	Reference
Hispanic (n = 14,316)	468 (3.3)	1.16 (1.04-1.31)
Black (n = 9747)	185 (1.9)	0.7 (0.59-0.83)
Other (n = 12,789)	364 (2.9)	1.07 (0.93-1.22)
Age group		
Neonates (n = 18,419)	771 (4.2)	7.03 (4.61-10.7)
Infants (n = 27,514)	886 (3.2)	7.44 (4.9-11.3)
Young children (n = 19,187)	456 (2.4)	5.98 (3.93-9.12)
Older children (n = 6376)	60 (0.9)	2.2 (1.35-3.61)
Teenagers (n = 6281)	32 (0.5)	Reference
Down syndrome		
No (n = 70,434)	1877 (2.7)	Reference
Yes (n = 7343)	328 (4.5)	1.66 (1.45-1.9)
Noonan syndrome		
No (n = 75,957)	2136 (2.8)	Reference
Yes (n = 1820)	69 (3.8)	1.42 (1.1-1.83)
Turner syndrome		
No (n = 77,383)	2169 (2.8)	Reference
Yes (n = 394)	36 (9.1)	4.47 (3.1-6.46)
Type of procedure		
RACHS		
1 (n = 9066)	91 (1)	Reference
2 (n = 27,006)	560 (2.1)	1.78 (1.41-2.23)
3 (n = 27,496)	808 (2.9)	2.61 (2.09-3.27)
4 (n = 8354)	374 (4.5)	3.77 (2.96-4.81)
5-6 (n = 2613)	136 (5.2)	4.27 (3.18-5.72)
Heart transplant (n = 1329)	53 (4)	6.29 (2.45-16.14)
Multiple procedures (n = 1913)	183 (9.6)	7.77 (5.92-10.21)
Neck or upper extremity vein thrombosis		
No	2156 (2.8)	Reference
Yes	49 (28.0)	6.68 (4.62-9.66)
Hospital annual volume		
First quartile (n = 19,849)	594 (3)	Reference
Second quartile (n = 20,542)	560 (2.7)	0.86 (0.75-0.98)
Third quartile (n = 17,262)	706 (4.1)	1.26 (1.12-1.42)
Fourth quartile (n = 20,124)	345 (1.7)	0.49 (0.42-0.58)
Surgeon annual volume (n = 72,910)		
First quartile (n = 14,140)	393 (2.8)	Reference
Second quartile (n = 18,437)	482 (2.6)	0.95 (0.83-1.09)
Third quartile (n = 19,373)	699 (3.6)	1.33 (1.16-1.52)
Fourth quartile (n = 20,960)	499 (2.4)	0.93 (0.81-1.07)
Year		
2004 (n = 7766)	152 (2)	Reference
2005 (n = 8910)	185 (2.1)	1.1 (0.87-1.38)
2006 (n = 9740)	243 (2.5)	1.3 (1.05-1.62)
2007 (n = 10,378)	283 (2.7)	1.47 (1.19-1.81)
2008 (n = 10,502)	327 (3.1)	1.66 (1.35-2.03)
2009 (n = 10,255)	321 (3.1)	1.7 (1.38-2.09)
2010 (n = 10,074)	316 (3.1)	1.59 (1.29-1.96)
2011 (n = 10,152)	378 (3.7)	1.95 (1.59-2.39)

OR, Odds ratio; CI, confidence interval; RACHS, Risk Adjustment for Congenital Heart Surgery-1.

even after adjustment for procedure complexity and other covariates (OR, 0.49; 95% CI, 0.42-0.58 vs first-quartile hospitals). [Figure 1](#) shows a plot with the incidence of chylothorax for each hospital stratified by volume and RACHS score. Even though hospitals with higher volume tended to have a lower incidence of chylothorax, there were some low-volume hospitals with similar incidence of chylothorax to the high-volume centers. No significant association was found between surgeon annual median volume and the incidence of chylothorax.

The incidence of chylothorax has increased with time, from 2% (n = 152) in 2004 to 3.7% (n = 378) in 2011 ($P < .0001$), even after adjustment for other covariates.

Treatment Strategies for Chylothorax

Among patients with chylothorax, TPN, MCT, and octreotide were used in 1229 (56%), 38 (1.7%), and 360 (16%) patients, respectively. The median durations of treatment with each medical strategy were 12 days (IQR, 5-25 days), 4 days (IQR, 2-8 days), and 7 days (IQR, 4-13 days), respectively. Surgical treatment (thoracic duct ligation and pleurodesis) was used in 196 (8.9%) patients a median of 18 days (IQR, 7-28 days) after the cardiac procedure. Patients were discharged from the hospital a median of 22 days (IQR, 10-47 days) after surgical treatment of chylothorax. The use of octreotide decreased with time, from 24% in 2004 to 13% in 2011 ($P = .034$). There was no significant change in the use of the other treatment strategies with time ([Figure E1](#)).

Association Between the Development of Chylothorax and Outcomes

The development of chylothorax was consistently associated with a significantly longer hospital stay and greater risk of in-hospital mortality throughout the different subgroups ([Table 4](#)). After adjustment for significant covariates (age, procedure complexity, neck or upper vein thrombosis, and hospital volume), there was still a significant association between the development of chylothorax and the length of the hospital stay ($P < .0001$) and the in-hospital mortality (OR, 2.13; 95% CI, 1.75-2.61). Similarly, chylothorax was associated with a significantly increased cost of hospitalization, even after adjustment for significant covariates ($P < .0001$).

The diagnosis of neck or upper vein thrombosis was associated with significant increases in length of stay ($P < .0001$), in-hospital mortality (OR, 4.08; 95% CI, 2.64-6.31), and cost of hospitalization ($P < .00001$) after adjustment for covariates. These associations were true for patients with chylothorax and those without.

DISCUSSION

Chylothorax is an infrequent complication that carries significant morbidity in patients undergoing pediatric

FIGURE 1. Plots depicting the incidence of chylothorax and total volume for each hospital, stratified by type of procedure. Each individual *bar* represents a different center, with different *colors* indicating different quartiles according to median hospital annual volume. The line represents the total cumulative volume (VOL) for each hospital for that particular type of procedure. *RACHS*, Risk Adjustment for Congenital Heart Surgery-1.

cardiac surgery. In this study, chylothorax was associated with 2.8% of pediatric cardiac surgical procedures. The incidence is slightly lower than contemporary reports from multiple single-institution studies, which have shown that chylothorax complicates 4% to 9% of pediatric cardiac surgical operations.³⁻⁵

Previous small single-institution studies have shown an association between type of procedure and incidence of chylothorax. It has been suggested that procedures that lead to high systemic venous pressure may be more likely to lead to postoperative chylothorax.¹ In a study including 48 patients with postoperative chylothorax, Chan and

TABLE 4. Effects of chylothorax on outcomes

	Hospital stay (d, median and interquartile range)		Mortality (No. and %)		Cost (\$1000 US, median and interquartile range)	
	No chylothorax	Chylothorax	No chylothorax	Chylothorax	No chylothorax	Chylothorax
Age						
Neonates	20 (13-36)	47 (30-74)	849/17,648 (4.8)	87/771 (11.3)	99 (63-165)	210 (132-332)
Infants	7 (5-13)	17 (9-36)	276/26,628 (1)	38/886 (4.3)	42 (30-69)	82 (48-160)
Young children	5 (3-9)	17 (10-30)	98/17,831 (0.5)	5/456 (1.1)	34 (24-53)	74 (47-127)
Older children	4 (3-6)	14 (6-27)	33/6316 (0.5)	1/60 (1.7)	35 (25-53)	59 (26-162)
Teenagers	5 (4-7)	10 (7-41)	28/6249 (0.45)	0/32 (0)	41 (30-62)	50 (32-198)
Type of procedure						
RACHS						
1	4 (3-5)	8 (5-26)	46/8975 (0.5)	7/91 (7.7)	25 (19-35)	36 (25-70)
2	6 (4-10)	17 (9-38)	168/26,446 (0.6)	22/560 (3.9)	39 (29-59)	78 (50-151)
3	9 (5-17)	23 (14-40)	436/26,688 (1.6)	21/808 (2.6)	53 (35-89)	106 (63-187)
4	13 (6-23)	23 (10-47)	233/7980 (2.9)	22/374 (5.9)	70 (36-121)	116 (42-213)
5-6	26 (17-41)	46 (35-62)	179/2477 (7.2)	19/136 (14)	134 (92-200)	223 (151-314)
Heart transplant	36 (17-72)	92 (52-138)	27/1276 (1.2)	4/53 (7.6)	279 (196-449)	450 (347-809)
Multiple procedures	40 (19-87)	66 (42-106)	195/1730 (11)	36/183 (19.7)	196 (101-392)	316 (202-582)
Neck or upper vein thrombosis						
No	16 (4-16)	39 (12-49)	1264 (1.7)	120 (5.6)	82 (30-85)	186 (56-224)
Yes	70 (24-91)	80 (36-101)	20 (15.9)	11 (22.5)	366 (136-498)	447 (175-614)
Hospital volume						
First quartile	7 (4-17)	23 (11-48)	386/19,255 (2)	41/594 (6.9)	47 (31-85)	98 (56-206)
Second quartile	7 (4-16)	28 (13-52)	394/19,982 (2)	33/560 (5.9)	46 (30-87)	126 (66-263)
Third quartile	7 (4-16)	27 (13-49)	231/16,556 (1.4)	37/706 (5.2)	48 (30-94)	129 (62-229)
Fourth quartile	7 (4-15)	23 (12-51)	273/19,779 (1.4)	20/345 (5.8)	42 (28-79)	93 (45-226)

RACHS, Risk Adjustment for Congenital Heart Surgery-1.

colleagues³ showed that patients undergoing cavopulmonary anastomoses (Fontan and Glenn procedures) were more likely to acquire postoperative chylothorax. In another study, in which the incidence of postoperative chylothorax was 9.2%, Biewer and associates⁴ found that complex procedures such as Norwood procedures, repairs of atrioventricular septal defects, procedures for transposition of the great arteries, and truncus arteriosus repairs had an incidence of chylothorax as high as 11% to 33%. These studies were limited by the small numbers of procedures in each category. By using a large multi-institution database, our study showed that the incidence of chylothorax does increase with higher procedure complexity, as measured by RACHS score. Interestingly, the incidence of chylothorax after heart transplant was comparable to that after congenital cardiac procedures of high complexity. By far the highest incidence of postoperative chylothorax was that of patients who underwent several cardiac procedures during the same admission. Similarly, procedures associated with high systemic venous pressure, such as Fontan procedures, carried a very high incidence of chylothorax.

The incidence of chylothorax seems to have increased during the last decade, with the risk of development of chylothorax being 2 times greater in 2011 than in 2004, even after adjustment for significant covariates. Similar

conclusions had been inferred from comparing older series with an incidence of chylothorax of around 0.5% to 2%⁶⁻⁹ with newer series reporting an incidence as high as 4% to 9%.³⁻⁵ The increased incidence had been partly attributed to increased complexity of pediatric cardiac surgical procedures^{1,3}; however, our study does not support that assumption, because the findings remained significant even after adjustment for procedure complexity according to RACHS score. One possible explanation is that RACHS score failed to completely control for procedure complexity and that the higher incidence is indeed due to more complex procedures being performed currently. Another possible explanation for the increased incidence is the recent trend toward earlier enteral feeding in these patients. It is also possible that a heightened awareness of this problem has led to an increase in the diagnosis of chylothorax, rather than a real increase in its incidence.

Another factor that was found to be significantly associated with development of chylothorax was age. Neonates, infants, and younger children had a significantly higher incidence of chylothorax than did older children and teenagers. Although this finding had not been reported previously, the median age in most single-institution series has been younger than 1 year.^{3,4,12} Even though the obvious differences in type of operations performed in the different age groups may play a role in the incidence of chylothorax,

the higher incidence in young children may also be related to a larger number of lymphatics and lymph nodes that could be disrupted in this population. Chylothorax was also more common among patients with Turner syndrome, a finding likely related to the known lymphatic abnormalities that are part of this syndrome.

An interesting and novel finding of the study was that the incidence of chylothorax was lower in the highest volume centers than in the lowest volume ones. As with other diseases, increased volume as a surrogate for experience can be associated with better management protocols and lead to improved outcomes. It is unclear whether the relationship between high-volume centers and lower incidence of chylothorax is related to better preoperative selection, differences in postoperative patient care and feeding protocols, differences in the reporting of chylothorax between centers, or differences in surgical technique. In general, the incidence of chylothorax was uniformly low among high-volume centers; however, there were also some low- and medium-volume centers with similarly low incidences of chylothorax. Thus there may be certain practices, not identified as part of this study, prevalent in high-volume centers and some lower volume centers, that are responsible for the lower incidence of chylothorax.

Interestingly, the incidence did not seem to be related to annual surgeon volume. It is plausible that differences in surgeon's performance and surgical technique as they relate to the development of chylothorax are more related to whether a particular surgeon practices in a high-volume center or not, or to other practices more prevalent among high-volume hospitals, rather than to the actual number of cases the surgeon performs within the center.

There is no overall consensus regarding the best management of postoperative chylothorax. As such, institutions have reported different algorithms that have been based on physician experience and preference.^{3,4,13} The decision among the various therapeutic strategies and the time elapsed before moving to more invasive strategies is variable and depends mainly on physician and institutional preferences. Our analysis showed that the use of TPN was common in these patients. Unfortunately, because of the limitations of the PHIS database, it is impossible to know whether TPN was used after the diagnosis of chylothorax or during the regular recovery of the patient before development of the complication. Even though the PHIS database does not include information on types of diet, MCT supplementation, which is processed by pharmacy, was available. Use of MCT supplementation in this study was extremely low, with only 1.7% of patients receiving it. Whether this low usage rate is real or due to underreporting in the database is unclear. The use of octreotide decreased with time, from 24% in 2004 down to 13% in 2011, probably

related to the recognition of some side effects and the time that it takes for octreotide to be effective.¹³ Surgical options for the treatment of chylothorax, such as pleurodesis and thoracic duct ligation, are usually reserved for patients with failure of conservative management, as evidenced by the infrequent use and the timing of these strategies in our study. Because of the limitations of the database, the actual effectiveness of any of these strategies on the resolution of chylothorax is not available.

The impact of development of chylothorax is considerable, because it leads to increased morbidity.¹ Our analysis showed that the diagnosis of chylothorax not only significantly increased the hospital stay but was also associated with a higher risk of mortality, even after adjustment for age, procedure complexity, and hospital volume. The adjusted mortality of patients with a diagnosis of chylothorax was twice as high as that of patients who did not carry such a diagnosis. These results should be taken with caution, because the nature of this database did not allow further adjustment of other comorbidities. The increased morbidity and mortality from chylothorax may be related to significant loss of protein, lipids, lymphocytes, and electrolytes, which can lead to nutritional, immunologic, hematologic, and metabolic complications.¹ Furthermore, patients with a diagnosis of neck or proximal upper extremity deep vein thrombosis had worse outcomes in this study. In addition to increased morbidity and mortality, the diagnosis of chylothorax was associated with a significant increase in hospital cost. To the best of our knowledge, this is the first study to report an increase in the incremental cost of treatment for patients who acquire postoperative chylothorax.

This study has several limitations, mainly related to its observational and retrospective nature and the fact that it is based on a large national database primarily recording hospital cost data. As such, long-term follow-up and robust clinical information are not available, limiting the ability to elaborate on the clinical risk factors and making it difficult to perform an adequate risk adjustment. The diagnosis of chylothorax is based on reporting from each institution by *ICD-9-CM* diagnosis code rather than on a series of precise diagnostic tests. It is known that the use of *ICD-9-CM* diagnosis codes may underestimate the incidence of diseases.^{14,15} It is therefore possible that the incidence of chylothorax may be higher than the actual rate reported in this study. Another limitation of this study is the lack of information regarding the timing of diagnosis of chylothorax with respect to the cardiac surgical procedure. It was assumed that the chylothorax occurred postoperatively, although it is possible though unlikely that some patients may have had a diagnosis of chylothorax before the surgical procedure.

The procedures in this study were determined from procedure codes reported by the participating institutions.

These codes are mainly used for billing purposes, and therefore the definition of the procedures may not be as reliable. To minimize variations in coding between institutions, we therefore decided to use RACHS scores to create the procedure groups. A limitation of this approach is that cardiac surgical procedures without an assigned RACHS score were not included in the study. It is plausible that some of these procedures may have been associated with a higher or lower incidence of chylothorax. Information on reoperations, which intuitively would seem to be potentially associated with a higher risk of chylothorax, is not available in the PHIS database.

Despite these limitations, the use of a multi-institution national database allows the compilation of multiple and diverse cases to determine risk factors and treatment strategies that would otherwise be impossible to analyze.

In conclusion, acknowledging the limitations of this study, chylothorax is a significant problem in pediatric cardiac surgery and is associated with increased mortality, cost, and hospital stay. Further studies are warranted to develop strategies for prevention and treatment of this disease, especially among the group of patients at highest risk, such as neonates undergoing complex congenital cardiac procedures.

References

1. Zuluaga MT. Chylothorax after surgery for congenital heart disease. *Curr Opin Pediatr*. 2012;24:291-4.
2. McCulloch MA, Conaway MR, Haizlip JA, Buck ML, Bovbjerg VE, Hoke TR. Postoperative chylothorax development is associated with increased incidence and risk profile for central venous thromboses. *Pediatr Cardiol*. 2008;29:556-61.
3. Chan EH, Russell JL, Williams WG, Van Arsdell GS, Coles JG, McCrindle BW. Postoperative chylothorax after cardiothoracic surgery in children. *Ann Thorac Surg*. 2005;80:1864-70.
4. Biewer ES, Zürn C, Arnold R, Glöckler M, Schulte-Mönting J, Schlensak C, et al. Chylothorax after surgery on congenital heart disease in newborns and infants—risk factors and efficacy of MCT-diet. *J Cardiothorac Surg*. 2010;5:127.
5. Cormack BE, Wilson NJ, Finucane K, West TM. Use of Monogen for pediatric postoperative chylothorax. *Ann Thorac Surg*. 2004;77:301-5.
6. Allen EM, van Heeckeren DW, Spector ML, Blumer JL. Management of nutritional and infectious complications of postoperative chylothorax in children. *J Pediatr Surg*. 1991;26:1169-74.
7. Higgins CB, Mulder DG. Chylothorax after surgery for congenital heart disease. *J Thorac Cardiovasc Surg*. 1971;61:411-8.
8. Nguyen DM, Shum-Tim D, Dobell AR, Tchervenkov CI. The management of chylothorax/chylopericardium following pediatric cardiac surgery: a 10-year experience. *J Card Surg*. 1995;10:302-8.
9. Beghetti M, La Scala G, Belli D, Bugmann P, Kalangos A, Le Coultre C. Etiology and management of pediatric chylothorax. *J Pediatr*. 2000;136:653-8.
10. Doell C, Bernet V, Molinari L, Beck I, Balmer C, Latal B. Children with genetic disorders undergoing open-heart surgery: are they at increased risk for postoperative complications? *Pediatr Crit Care Med*. 2011;12:539-44.
11. Chan SY, Lau W, Wong WH, Cheng LC, Chau AK, Cheung YF. Chylothorax in children after congenital heart surgery. *Ann Thorac Surg*. 2006;82:1650-6.
12. Nath DS, Savla J, Khemani RG, Nussbaum DP, Greene CL, Wells WJ. Thoracic duct ligation for persistent chylothorax after pediatric cardiothoracic surgery. *Ann Thorac Surg*. 2009;88:246-51; discussion 251-2.
13. Panthongviriyakul C, Bines JE. Post-operative chylothorax in children: an evidence-based management algorithm. *J Paediatr Child Health*. 2008;44:716-21.
14. Johnson DW, Adair C, Brant R, Holmwood J, Mitchell I. Differences in admission rates of children with bronchiolitis by pediatric and general emergency departments. *Pediatrics*. 2002;110:e49.
15. Hsu VP, Staat MA, Roberts N, Thieman C, Bernstein DI, Bresee J, et al. Use of active surveillance to validate international classification of diseases code estimates of rotavirus hospitalizations in children. *Pediatrics*. 2005;115:78-82.

Discussion

Dr Glen Van Arsdell (Toronto, Ontario, Canada). I have no disclosures that relate to this presentation.

In this report of nearly 80,000 patients undergoing congenital heart surgery, Mery and colleagues have shown that not only is chylothorax frustrating for caregivers, it can also be lethal.

Most of the findings are consistent with what we would expect. Somewhat surprisingly, however, there was a lower incidence than previously identified in single-institution case series, and there was a difference in incidence between institutions. Perhaps there is also an increasing incidence with time. Of course, we would like to know why these findings might be.

Dr Mery, bearing in mind the limitations of an administrative database, and they are substantial, did you look for and were you able to identify clues as to practice patterns that might help explain a different incidence between institutions? The fact that surgeon volume did not impact the incidence of chylothorax, but institution volume did, suggests that institution protocols could be conceivably more important than individual surgical technique. For example, protocol findings might be differing age of treatment between institutions for the same RACHS classification, or, for example, a higher use of low-molecular weight heparin, which might impact the thrombotic risk for chylothorax. Was there an analysis that you performed in this regard that had either positive or negative results?

Dr Mery. Thank you for your very insightful comments. Indeed, some of the findings of this study were somewhat surprising.

One of the problems with using administrative databases that are based on ICD-9-CM codes is that you can actually underestimate the incidence of disease. There are some studies that have compared the incidences of reported diseases such as bronchiolitis and aspergillosis in an administrative database with actual clinical data and have found that the real incidence of disease may be between 10% and 40% higher than that reported in the administrative database. From this, I would say that the chylothorax incidence is at least 2.8% and could actually be higher.

As far as the relationship between the incidence of chylothorax and hospital volume goes, I totally agree with you. Some possible explanations could be due to differences in protocols for enteral feeding, patient selection, and postoperative patient management. I submit that even surgical technique may play a role, even though it may not be related to surgeon volume itself. Surgeons that operate in hospitals that have higher volume may have different techniques than surgeons that do not; obviously something we cannot prove. Part of the explanation may also have to do with the way the data were analyzed. If you actually look at the hospital volume quartiles that we used, the highest hospital volume quartile included only 5 hospitals, compared with 19 hospitals that were included on the first quartile, so the data may be more heterogeneous for the lower volume hospitals.

We did not look at the use of low-molecular weight heparin.

Dr Van Arsdell. I suspect there may be a few broad large categories, such as drug usage or age, that you could see whether

there are any differences between institutions, and it would be an interesting analysis to perform.

In our own database, about 15% of patients did not fit into the RACHS classification. These patients had a similar mortality to RACHS 5 and 6. Were you able to account for all patients who had heart surgery, even if they did not fit into a RACHS classification? And if not, might that be some of the explanation as to why there was a relatively low incidence of chylothorax?

Dr Mery. That is a very good point. By definition, we only took patients who had a RACHS-associated procedure; that is how we identified patients in the database who had cardiac surgery. We could definitely be missing patients with a different incidence of chylothorax. One of the limitations of the PHIS database is that it uses *ICD-9-CM* diagnosis and procedure codes, and these can be unreliable. For example, we do not know which patients had Norwood procedures, because there is no *ICD-9-CM* procedure code for a Norwood. It is instead a combination of procedure codes for an atrial septectomy, an aortic arch reconstruction, and some type of systemic-to-pulmonary shunt. That is why we relied on the RACHS scores that are reported on this database, rather than using particular procedure codes. We did not perform any analyses comparing drug usage or age between institutions, but I agree that it would be an interesting analysis.

Dr Van Arsdell. And my last question, you found this increasing incidence of chylothorax with time. Similar to the first question, did you look for practice pattern changes, such as billable feedings, which you alluded to, that might suggest protocols that would drive this change?

Before you answer that, congratulations on a great presentation and a very nice manuscript as well. And thank you for stimulating this discussion on an important topic.

Dr Mery. Thank you very much. We did not look at difference in practice patterns. It may be true that the increase in incidence that we are seeing might just be an increase in detection and reporting, because there has been increased awareness of this problem during the last few years. It is interesting, though, that single-institution studies have also shown an increasing incidence with time. The incidence in the 1970s and 1980s was reported to be between 0.5% and 1%, and now it is much higher. It is unclear whether that is a result of increased awareness, changes in enteral feeding patterns, or actual increasing incidence.

Dr J. William Gaynor (Philadelphia, Pa). I have no disclosures. I just want to mention a novel therapy that we have been using recently that was developed by Dr Max Itkin, one of our interventional radiologists, that has been very successful in many cases. He uses percutaneous cannulation of the cisterna chyli and then performs a lymphangiogram. He can identify anatomic variations. He can sometimes identify a leaky vessel. And then he embolizes with the thoracic duct or the lead. This has been done in infants as young as 1 month, and it has been very, very successful. We go to it much quicker than we used to sticking with feeds and chest tube drainage and going in. We have all

had the frustration of trying to go in with somebody with a chylothorax, and the lymph seems to be coming from everywhere and you cannot identify a single leak. Obviously, this needs to be replicated. He has published several papers on the technique, and it has been very successful. Thank you, I enjoyed your presentation.

Dr Mery. I agree. Techniques like these may play a role in trying to decrease the amount of time that goes from the diagnosis of chylothorax to successful treatment. Our data do not allow us to know when the diagnosis of chylothorax was made during the admission, but the surgical procedures were performed a median of 18 days after cardiac surgery. So there was good lapse of time where conservative management was used, and these techniques could potentially minimize that time.

Dr Peter Manning (St Louis, Mo). I think this is a good example of a study where you have to be careful about drawing conclusions about cause and effect versus association. You have done a good job of that. As I think you said on your first slide, the etiology of chylothorax can be multifactorial. Most of these cases are not major thoracic duct injuries, but the thrombosis of central veins or high central venous pressures are really important factors, and consideration of these issues must be factored into the evaluation and management of chylothorax.

My question is, do you think chylothorax itself is the morbid entity, or is it a marker of very complex patients who have high central venous pressures and have intravenous lines for a long time that thrombose the superior vena cava?

Dr Mery. I think you are totally correct, and that is the difficult part of database studies like this, because we cannot really assess causation, just association. It is true, the development of chylothorax may just be a proxy for multiple comorbidities that are both increasing the risk of chylothorax in these patients and at the same time increasing the risk of morbidity and mortality.

Dr Pedro J. Del Nido (Boston, Mass). Following up on that, I think the institutional differences argue against an anatomic factor. Presumably, these are the same children who are undergoing surgery in one institution versus another. So I think one would argue more for practice patterns as playing a significant role.

Dr Osama Eltayeb (Tulsa, Okla). In your study, did you look at the incidence of Chylothorax in early repair of tetralogy of Fallot? Most of the centers have moved toward early repair; does that increase the incidence of chylothorax? If not, maybe it is for the panel to comment whether there is any increase of chylothorax incidence after early repair of tetralogy.

Dr Mery. One of the problems with this database is that we rely on very simplified codes, so we cannot really obtain a lot of clinical data. For example, trying to differentiate between Glenn and Fontan procedures is impossible, because they are both coded as cavopulmonary anastomoses unless the Fontan is a lateral tunnel procedure, which would be coded as an atriopulmonary anastomosis. So unfortunately, we do not have details in terms of the particulars of procedures because of the nature of the PHIS database.

FIGURE E1. Use of treatment strategies for chylothorax across time. *TPN*, Total parenteral nutrition; *MCT*, medium-chain triglycerides.