Heliyon 10 (2024) e29054

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Incidence, risk factors, and outcomes of chylothorax after cardiac procedure in the United States

Yue Xiao [a], Yanfei Chen [a], Ruijian Huang [a], Feng Jiang [a], Cunhua Su [b,1], Jifang Zhou [c,*,1]

[a] School of International Business, China Pharmaceutical University, Jiangsu, China
[b] Cardiothoracic and Vascular Surgery, Nanjing First Hospital, Jiangsu, China
[c] School of International Pharmaceutical Business, China Pharmaceutical University, Nanjing, Jiangsu, China

ARTICLE INFO

Keywords:
Chylothorax
Cardiac procedure
Retrospective databases
Postoperative complications

ABSTRACT

Background: To examine the epidemiology and risk factors of chylothorax after cardiac procedure in the United States using a contemporary nationally representative database.
Methods: We identified postoperative chylothorax events through National Inpatient Sample database (2016–2019) and compared baseline demographics, comorbidities, and in-hospital outcomes between hospitalizations with and without postoperative chylothorax. The Cochrane-Armitage test was used to analyze trends in incidence rates. Multivariable Poisson regression models were used to identify potential risk factors for postoperative chylothorax after cardiac procedure.
Results: A total of 819 (0.24%) admissions were associated with postoperative chylothorax. The crude and standardized incidence rates of chylothorax were 23.7 (95%CI, 22.1–25.4) and 61.5 per 10,000 cardiac procedure-related admissions, respectively, with no significant temporal change in incidence rate over the study period ($P_{trend} = 0.5249$). Infants [adjusted rate ratio (aRR), 117.3, 95% confidence interval (CI), 94.5–145.5] and children (aRR, 60.2, 95%CI, 48.0–75.5) were more likely to develop chylothorax compared to adults. Heart and great vessel procedures (aRR, 4.36, 95%CI, 3.61–5.26), septal repair (aRR, 1.91, 95%CI, 1.58–2.29), heart transplant (aRR, 5.68, 95%CI, 4.55–7.10) and pericardial procedures (aRR, 4.04, 95%CI, 3.32–4.91) were associated with elevated risk for chylothorax. Admissions with chylothorax were associated with higher inpatient mortality (4.9% vs. 3.0%, $p < 0.0001$), longer inpatient stay, higher costs and greater perioperative complication burden.
Conclusions: Following cardiac procedures, chylothorax is an uncommon but serious complication that affects the prognosis. The analysis reveals varying incidence rates across age groups and specific surgical procedures, with infants at elevated risk.

1. Introduction

Chylothorax, also known as chyle pleural effusion, is a rare but significant complication that can occur after cardiac surgery. It can

* Corresponding author.
E-mail address: 1020202613@cpu.edu.cn (J. Zhou).
[1] These authors share last authorship.

https://doi.org/10.1016/j.heliyon.2024.e29054
Received 9 July 2023; Received in revised form 4 March 2024; Accepted 28 March 2024
Available online 7 April 2024

lead to longer hospital stays and increased healthcare costs [1–4]. Postoperative chyle leakage and accumulation can cause various complications, including systemic infections, atelectasis and acute respiratory failure [5].

The incidence of chylothorax following cardiac procedures varies considerably across published literatures. For example, a multicenter study conducted in 2014 reported an incidence ranging from approximately 2.8%–3.2% [6]. In contrast, a decade-long retrospective analysis spanning two tertiary clinics documented a lower prevalence of adult chylothorax of 0.6% following cardiovascular surgery [7]. Most studies have focused on chylothorax after congenital cardiac interventions in pediatric patients. Therefore, there is a lack of comprehensive data on the national epidemiology of chylothorax across different age groups and types of cardiac procedures, especially in adults undergoing complex cardiac procedures [8].

A national investigation is necessary to examine the incidence of chylothorax following cardiac procedures across different age groups and procedural classifications due to the current lack of literature. The study aims to clarify the epidemiological characteristics and risk factors of chylothorax, as well as assess concurrent perioperative complications. Additionally, it aims to evaluate the potential association between chylothorax and adverse inpatient outcomes, such as prolonged hospitalization and increased healthcare expenses.

2. Material and methods

Disclosure statement

This study adheres to the Strengthening the Reporting of Observational Studies in Epidemiology statement (STROBE) [9] checklist. The Institutional Review Board (IRB) of the China Pharmaceutical University and Nanjing First Hospital approved the study. Informed consent was waived by both IRBs due to the de-identified nature of the National Inpatient Sample (NIS) dataset.

2.1. Data source

The NIS is a prominent database compiled and maintained by the Healthcare Cost and Utilization Project (HCUP), which receives funding from the Agency for Healthcare Research and Quality (AHRQ). It is a publicly available all-payer healthcare database in the United States, with an annual sample of approximately 7 million weighted hospital admissions, representing over 35 million unweighted admissions.

2.2. Inclusion and exclusion criteria

The study used discharge data from the NIS between 2015 and 2019. Diagnoses and procedures were coded using the International Classification of Diseases (ICD) codes. To ensure consistency in case identification and outcome ascertainment, our analyses were

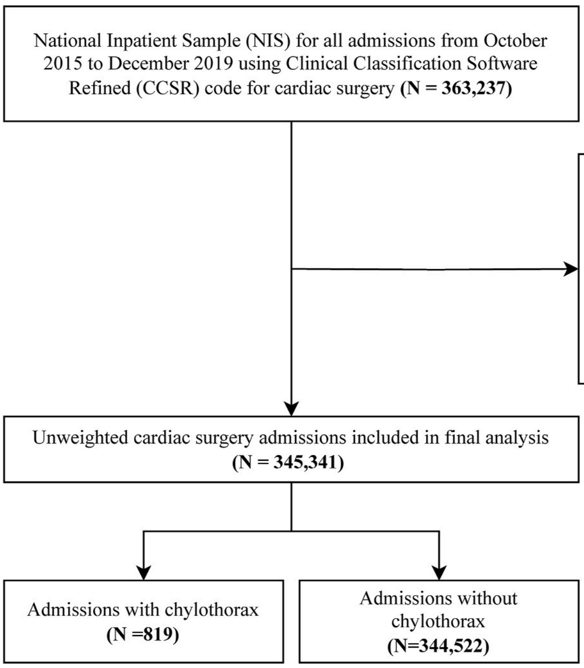

Fig. 1. Flow sheet of the admission selection process from the NIS database Footnotes: Disease predisposing to chylothorax Included Kaposi's sarcoma, multiple myeloma, mediastinitis, yellow nail syndrome, sarcoidosis, tuberculosis, filariasis, malignancy and metastatic solid tumor.

limited to discharge data from October 1st, 2015 onwards, coinciding with the adoption of ICD-10 codes.

Individuals who were admitted with a diagnostic code for chylothorax (ICD-10-CM: J94.0, I89.8) or underwent any cardiac procedures defined by International Classification of Diseases, Tenth Revision, Procedure Coding System (ICD-10-PCS) (Supplemental Table 1) were identified as experiencing postoperative chylothorax due to cardiac procedures. Procedures were classified into seven groups based on the Clinical Classification Software Refined (CCSR) version 2021, maintained by AHRQ [10]. The CCSR for ICD-10-PCS procedures classifies a wide range of more than 80,000 ICD-10-PCS procedure codes into 320+ clinical categories that cover 31 clinical domains. This study focuses on the Cardiovascular Procedures domain (CAR), which includes eight specific clinical categories (CAR003, CAR009, CAR013, CAR017, CAR018, CAR019, CAR022, CAR023). These categories include various cardiovascular interventions, such as coronary artery bypass grafts (CABG), heart valve replacement and other valve procedures (HV), left atrial appendage procedures (LAAP), heart and great vessel bypass procedures (HGVBP), pericardial procedures (PP), heart transplants (HT), septal repairs (SR), and other therapeutic heart procedures (Other) [11–13]. Details and descriptions regarding the conversion between CCSR codes and ICD codes can be found in additional files.

Excluded from the analysis were records that lacked age and death information, referral records, and malignancy records such as lymphoma, leukemia, or metastatic solid tumors. In addition, admissions with coexisting conditions that are known to cause chylothorax [5] were excluded. These conditions include Kaposi's sarcoma (C46), multiple myeloma (C90.0), mediastinitis (J98.51), yellow nail syndrome (L60.5), sarcoidosis (D86), tuberculosis (A15), and filariasis (B74). Further details about the admission process are shown in Fig. 1. Finally, the study included a dataset of 345,341 representative instances of cardiac procedures across 3991 hospitals in the United States. The total patient cohort was 1,726,705 individuals, accounting for the application of sampling weights.

2.3. Outcomes

The investigation primarily focused on the incidence rates of chylothorax following cardiac procedures. Overall incidence rates of chylothorax were evaluated using an indirect standardization method, while accounting for variations in age and sex distribution. The 2010 United States census was used as a reference standard population.

The study's secondary outcomes included various metrics such as inpatient mortality, prevalence of perioperative complications, length of hospital stay, and total costs. To determine the incidence of complications, a comprehensive list was compiled through a thorough review of existing literature [14,15] and expert interviews (Supplemental Table 2).

2.4. Covariates

Our analysis examined a range of baseline characteristics and hospital-related factors as covariates. These included age, sex, Charlson Comorbidity Index (CCI) Score, genetic syndromes, primary payer type, race/ethnicity, income level. Additionally, hospital-related variables comprised bed size and geographic region.

Furthermore, cardiac procedure-related variables constituted a significant aspect of our investigation. These encompassed the type of procedure performed, the surgical approach employed (open, minimally invasive or combined), and the utilization of robotic assistance during surgery.

2.5. Statistical analysis

The chi-square (χ^2) test and Kruskal-Wallis test were employed for comparing categorical variables and continuous variables, respectively. National estimates were derived using hospital and admission-level weights based on survey-specific statements. The SAS PROC GENMOD [16] was used to implement the analytical framework, with adjustments made for age, race, CCI, hospital region, hospital location, teaching status, surgical type, number of procedures, and robotic-assisted surgery status.

The dependent variable was chylothorax when examining it as the primary outcome. In evaluating the impact of chylothorax on other complications, we included chylothorax and additional confounding variables as covariates, as previously delineated.

To account for the divergent occurrence patterns of chylothorax between adults and pediatrics, we conducted a stratified analysis. The cohort was divided into six age categories: infants (0–1 years), children (2–9 years), adolescents (10–17 years), youth (18–39 years), middle-aged (40–59 years), and elderly (60+ years). This division allowed for the evaluation of procedural proportions and chylothorax incidence rates in each subgroup.

Survey regression models were used to determine differences in length of stay and total hospitalization costs between the chylothorax and non-chylothorax groups. The incidence of chylothorax over time was examined, stratified by surgical type or age group, using the Cochran-Armitage trend test.

All statistical analyses were conducted using SAS 9.4.0 (Cary NC, USA), with statistical significance defined as a two-sided p-value <0.05.

3. Results

3.1. Baseline characteristics

As shown in Fig. 1, a total of 345,341 inpatient hospital discharge summaries from the fourth quarter of 2015 to the fourth quarter of 2019 that met the inclusion/exclusion criteria were identified from the HCUP-NIS database. Table 1 summarizes the baseline

Table 1
Baseline demographic and clinical characteristics of inpatient stays for cardiac procedure, stratified by postoperative chylothorax status.

	Total (N = 345,341)	Admissions with chylothorax (N = 819)	Admissions without chylothorax (N = 344,522)	*P*-value
	N (%)	**N (%)**	**N (%)**	
Demographics				
Age at admission, years				
Mean (SE)	64 (0.03)	13 (0.72)	64 (0.03)	<0.001
Median (IQR)	67 (57,75)	0 (0,6)	67 (57,75)	
0-1	9953 (2.9)	528 (64.5)	9425 (2.7)	
2-9	3915 (1.1)	103 (12.6)	3812 (1.1)	
10-17	2535 (0.7)	17 (2.1)	2518 (0.7)	
18-39	12359 (3.6)	27 (3.3)	12332 (3.6)	
40-59	70651 (20.5)	58 (7.1)	70593 (20.5)	
60+	245928 (71.2)	86 (10.5)	245842 (71.4)	
Gender				
Male	225978 (65.4)	458 (55.9)	225520 (65.5)	<0.001
Female	119363 (34.6)	361 (44.1)	119002 (34.5)	
Race/ethnicity				
Non-Hispanic white	256589 (74.3)	398 (48.6)	256191 (74.4)	<0.001
African American	26215 (7.6)	93 (11.4)	26122 (7.6)	
Hispanic	26629 (7.7)	142 (17.3)	26487 (7.7)	
Asian, Pacific Islander	9324 (2.7)	19 (2.3)	9305 (2.7)	
Other/unknown[a]	26584 (7.7)	167 (20.4)	26417 (7.7)	
Charlson Comorbidity score				
0	16419 (4.8)	380 (46.4)	16039 (4.7)	<0.001
1-2	30049 (8.7)	291 (35.5)	29758 (8.6)	
3-4	86591 (25.1)	62 (7.6)	86529 (25.1)	
>4	212282 (61.5)	86 (10.5)	212196 (61.6)	
Genetic syndromes				
Down syndrome	1666 (0.5)	123 (15.0)	1543 (0.5)	<0.001
Noonan syndrome	138 (0.04)	4 (0.5)	134 (0.04)	<0.001
Turner syndrome	7 (0.002)	0 (0)	7 (0.002)	0.90
Insurance type				
Medicare	197392 (57.2)	75 (9.2)	197317 (57.3)	<0.001
Medicaid	32586 (9.4)	328 (40.1)	32258 (9.4)	
Private Insurance	96563 (28.0)	341 (41.6)	96222 (27.9)	
Self-pay	7915 (2.3)	18 (2.2)	7897 (2.3)	
Other/Unknown[b]	10885 (3.1)	57 (6.9)	10828 (3.1)	
Income quartile by ZIP code				
Quartile 1 (lowest)	87780 (25.4)	210 (25.6)	87570 (25.4)	0.91
Quartile 2	88958 (25.8)	213 (26.0)	88745 (25.8)	
Quartile 3	86646 (25.1)	210 (25.6)	86436 (25.1)	
Quartile 4 (highest)	76001 (22.0)	170 (20.8)	75831 (22.0)	
Year of admission				
2015Q4	19143 (5.5)	40 (4.9)	19103 (5.5)	0.56
2016	78579 (22.8)	204 (24.9)	78375 (22.8)	
2017	79169 (22.9)	187 (22.8)	78982 (22.9)	
2018	81966 (23.7)	183 (22.3)	81783 (23.7)	
2019	86484 (25.0)	205 (25.0)	86279 (25.0)	
Admission Outcomes				
Length of stay, days				
Mean (SE)	10 (0.02)	41 (1.62)	9 (0.02)	<0.001
Median (IQR)	6 (4, 10)	23 (11, 53)	6 (4, 10)	<0.001
Prolonged length of stay[c]				
Yes	12015 (3.5)	329 (40.2)	11686 (3.4)	<0.001
No	333326 (96.5)	490 (59.8)	332836 (96.6)	
Inpatient mortality	10267 (3.0)	40 (4.9)	10227 (3.0)	0.001
Cardiac procedure related characteristics				
Procedure type[d]				
Coronary artery bypass grafts	126826 (36.7)	48 (5.9)	126778 (36.8)	<0.001
Left atrial appendage procedures	14275 (4.1)	3 (0.4)	14272 (4.1)	
Heart and great vessel bypass procedures	2574 (0.8)	152 (18.6)	2422 (0.7)	
Pericardial procedures	20821 (6.0)	56 (6.8)	20765 (6.0)	
Heart transplant	2034 (0.6)	29 (3.5)	2005 (0.6)	
Septal repair and other therapeutic heart procedures	15248 (4.4)	157 (19.2)	15091 (4.4)	
Heart valve replacement and other valve procedures	94242 (27.3)	47 (5.7)	94195 (27.3)	
CABG + HV	18575 (5.4)	7 (0.9)	18568 (5.4)	
CABG + LAAP	10531 (3.1)	6 (0.7)	10525 (3.1)	
SR-including complex surgery	19075 (5.5)	283 (34.6)	18792 (5.5)	

(*continued on next page*)

Table 1 (*continued*)

	Total	Admissions with chylothorax	Admissions without chylothorax	*P*-value
	(N = 345,341)	(N = 819)	(N = 344,522)	
	N (%)	**N (%)**	**N (%)**	
Other	21140 (6.1)	31 (3.8)	21109 (6.1)	
Procedure approach[e]				
Open	193214 (70.0)	450 (91.3)	192764 (70.0)	<0.001
Minimal invasive	82806 (30.0)	42 (8.7)	82764 (30.0)	
Robotic-assisted				
Yes	2805 (0.8)	5 (0.6)	2800 (0.8)	0.52
No	342536 (99.2)	814 (99.4)	341722 (99.2)	
Hospital Characteristics				
Hospital bed size				
Small	35423 (10.3)	106 (12.9)	35317 (10.3)	0.02
Medium	82670 (23.9)	205 (25.0)	82465 (23.9)	
Large	227248 (65.8)	508 (62.0)	226740 (65.8)	
Hospital region				
Northeast	63969 (18.5)	144 (17.6)	63825 (18.5)	0.01
Midwest	80209 (23.2)	186 (22.7)	80023 (23.2)	
South	136498 (39.5)	300 (36.6)	136198 (39.5)	
West	64665 (18.7)	189 (23.1)	64476 (18.7)	

Abbreviations: CABG: Coronary artery bypass grafts; HV: Heart valve replacement and other valve procedures; LAAP: Left atrial appendage procedures; SR: Septal repair and other therapeutic heart procedures.

[a] Other/unknown category included admission of unknown racial/ethnicity status, Native American (NA), and others.

[b] Other/unknown category included admission of unknown insurance status, no charge, and others.

[c] Prolonged length of stay was defined as admissions with length of stay equal or above 30 days. About 1.7% missing.

[d] Single procedure category was divided by Clinical Classifications Software Refined (CCSR); CABG + HV and CABG + LAAP were the most frequently combination of multiple procedures; SR-including complex surgery category included multiple procedures with Septal repair and other therapeutic heart procedures.

[e] Combined procedures were excluded; Minimal invasive category included percutaneous and endoscopic approach.

characteristics of eligible admissions undergoing cardiac procedures stratified by the chylothorax status. There were significant differences between the two groups in terms of age, gender, ethnicity, CCI, expected primary payer and hospital location/teaching status. The study cohort exhibited a mean (SE) age of 64 (0.03) years, with males comprising 65.4% and non-Hispanic whites accounting for 74.3%. CABG represented the majority of the entire cohort at 36.7%, followed by HV at 27.3%. Chylothorax was detected in 819 (0.24%) admissions. The mean (SE) age of admissions with chylothorax was 13 (0.72) years, with infants (0–1 years) being disproportionately affected, around 80% of chylothorax cases were found in this age group. Among cases where chylothorax occurred, the predominant procedure was associated with the SR at 19.2%, followed by HGVBP at 18.6%. Supplemental Table 3 summarizes the baseline characteristics and admission outcomes of eligible admissions undergoing cardiac procedures in pediatric groups.

3.2. *Temporal trend of chylothorax incidence rates*

The standardized incidence rate of chylothorax was 61.5 per 10,000 admissions. The incidence rates of chylothorax were inversely associated with increasing age at admission. Infants (0–1 years) had the highest incidence rate of 530.4 (95%CI 488.2–576.4) per 10,000 admissions, followed by children (2–9 years) with 263.1 (95%CI 217.4–318.3), adolescents (10–17 years) with 67.1 (95%CI 41.8–107.7), youth (18–39 years) with 21.8 (95%CI 15.0–31.8), middle-aged (40–59 years) with 8.2 (95%CI 6.3–10.6) and elderly (60 years and older) with 3.5 (95%CI 2.8–4.3) per 10,000 admissions.

The incidence rates of postoperative chylothorax varied among the different types of cardiac procedures groups. The highest rate of chylothorax was observed in the HGVBP group 590.5 95% CI, 506.1–689.0), while the CABG group had the lowest rate 3.8 (95% CI, 2.9–5.0). The rates of chylothorax were highest for SR-combined 148.4 (95%CI, 132.2–166.6), HT 142.6 (95%CI, 99.3–204.6), SR 103.0 (95%CI, 88.1–120.3), and PP 26.9 (95%CI, 20.7–34.9) among other types of cardiac procedures. The lowest rate of perioperative chylothorax was associated with LAAP 2.1 (95%CI, 0.7–6.5).

Fig. 2a and **b** shows the temporal trends in chylothorax incidence over time, stratified by surgical type or age, respectively. The Cochrane-Armitage test indicates a declining trend in HGVBP ($P = 0.01$) and an increasing trend in SR ($P < 0.01$). No significant trends were observed across different age groups.

3.3. *Factors associated with postoperative chylothorax*

The association between hospital-related factors, such as location, surgical volume, and teaching status, with the development of postoperative chylothorax was also described. Of all admissions, 85.1% took place at urban-teaching hospitals, which had a greater likelihood of providing surgical interventions compared to non-teaching or rural hospitals. This trend was consistent across all levels of surgical complexity, as shown in Supplemental Table 4.

According to the Poisson regression model for chylothorax, males and females exhibited a similar incidence rate (aRR, 0.99, 95%CI,

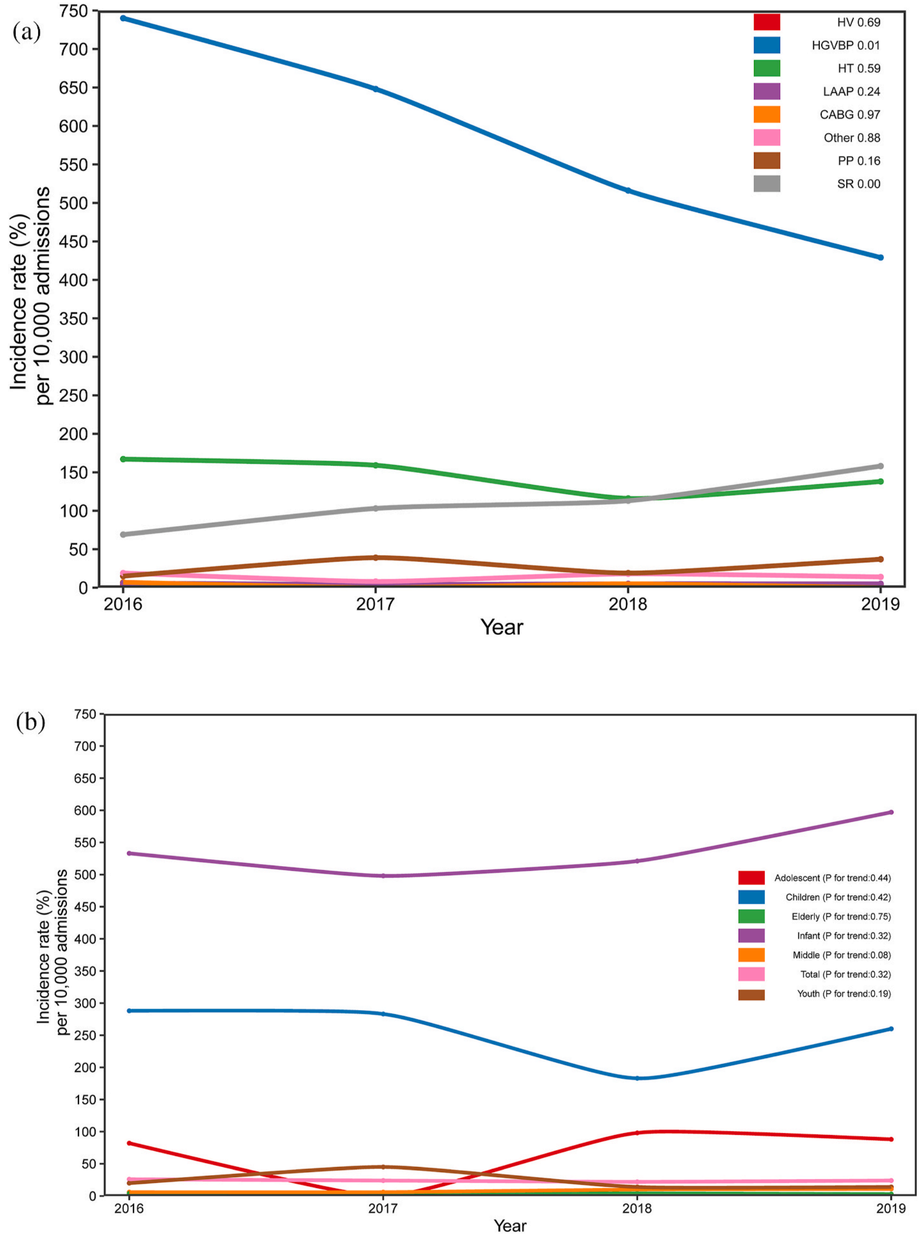

Fig. 2. Incidence rates of chylothorax after cardiac procedure, stratified by procedure type and age Footnotes: Infant: 0–1 years old; Children: 2–9 years old; Adolescent: 10–17 years old; Youth: 18–39 years old; Middle: 40–59 years old; Elderly: 60+ years old Abbreviations: CABG: Coronary artery bypass grafts; HV: Heart valve replacement and other valve procedures; LAAP: Left atrial appendage procedures; SR: Septal repair and other therapeutic heart procedures; HGVBP: Heart and great vessel bypass procedures; HT: Heart transplant; PP: Pericardial procedures.

0.96–1.02). The rate ratio and 95% confidence interval for chylothorax occurrence were 117.3 (94.5–145.5) for infants, 60.2 (48.0–75.5) for children, and 15.9 (11.9–21.4) for adolescents, 5.6 (4.4–7.2) for youth, 2.3 (2.0–2.7) for middle-aged compared to elderly. The rate ratio remained statistically significant for HGVBP, SR-combined or SR, HT, and PP, especially for HT (aRR, 5.68, 95% CI, 4.55–7.10), taking CABG as reference after adjustment for covariates. As to the procedure method, taking open procedure as reference, the rate ratio was comparable for combined procedures at 1.6 (0.9–3.0), but significantly lower for interventional procedures at 0.4 (0.3–0.5). Additional details were presented in Supplemental Tables 5 and 6

3.4. Association of chylothorax with other perioperative conditions

Chylothorax was associated with higher burdens of postoperative complications. Admissions with chylothorax were more likely to develop multiple perioperative complications (78.3% vs. 67.6%, $p < 0.001$) such as acute respiratory failure (78.3% vs. 67.6%, $p =$

0.0006), atelectasis (18.7% vs. 13.9%, $p = 0.002$), pneumonia (12.7% vs. 7.1%, $p < 0.001$), prolonged mechanical ventilation (41.0% vs. 11.9%, $p < 0.001$), pleural effusion (13.3% vs. 9.0%, $p < 0.001$), plasma transfusion (12.7% vs. 5.4%, $p < 0.001$), non-plasma transfusion (22.2% vs. 16.0%, $p < 0.001$), wound complications (7.1% vs. 1.0%, $p < 0.001$), intraoperative bleeding (5.7% vs. 2.5%, $p < 0.001$), as shown in Fig. 3. After stratification by age into infant and adult groups, the Poisson regression model, adjusted for covariates, indicates that wound complication and prolonged mechanical ventilation remain statistically significant.

3.5. *Management of chylothorax and clinical outcomes*

Only 23 (2.8%) admissions with chylothorax underwent thoracic duct ligation and 23 (2.8%) had pleurodesis, with both procedures almost exclusively observed in admissions with chylothorax (Supplemental Table 7). Additionally, the development of chylothorax was consistently associated with prolonged hospital length of stay and higher in-hospital cost throughout the adult and non-adult age groups. The adjusted mean difference in length of stay (LOS) between infants and adults with chylothorax was significantly different, with infants staying longer for an average of 21.3 days compared to 10.3 days for adults. Overall, the adjusted mean difference of LOS was 23.1 days (95%CI, 20.0–26.3). Additionally, admission expenditures were higher for children and adolescents compared to adults, with a total cost difference of 162K (95%CI, 137K– 187K) US dollars. Supplemental Table 8 provides further details.

4. Comments

This study presents the first comprehensive analysis of current incidence rates of postoperative chylothorax following cardiac procedures across all age groups at a national level. Previous data indicate an annual incidence of 500,000 cardiac surgeries in the United States, with 40,000 cases specifically attributed to congenital heart surgeries in non-adults [17,18]. After analyzing discharge data from the NIS database, we identified 345,341 instances of cardiac procedures, with pediatric procedures accounting for 4.8% of the total. The adjusted mean annual surgical volume is estimated to be approximately 400,000 cases, which is slightly lower than the overall estimate. This difference is likely attributable to temporal variations and differing emphases within the database.

The study supports previous research that shows higher incidence rates of chylothorax in pediatric patients compared to adults [19]. Additionally, infants had a higher incidence of chylothorax than children and adolescents. It is important to note that chylothorax

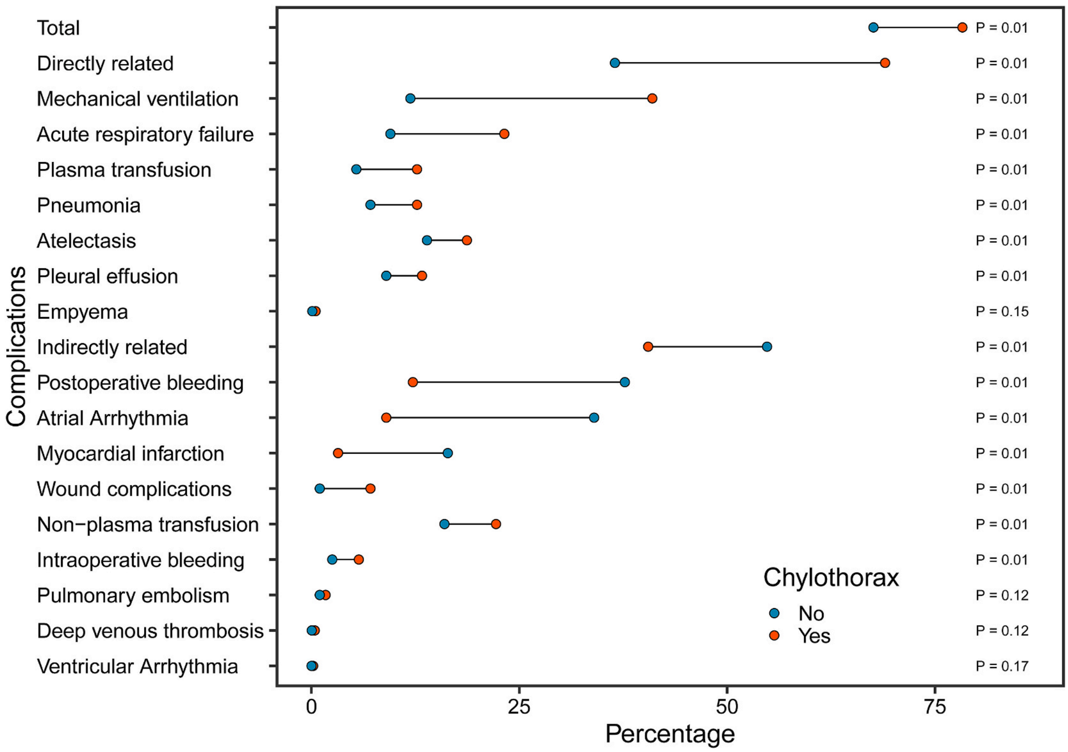

Fig. 3. The association between complications and chylothorax after cardiac procedure Complications were defined through literature review and ICD-10 code references, and further validated by consultation with physicians from the Cardiothoracic Surgery Department at Nanjing First Hospital. The determined complications were categorized as directly related or indirectly related to chylothorax. The "Total" term indicates that the patient is classified as 1 in the binary variable if any complications occur; otherwise, it is considered 0, applying to both directly and indirectly related complications.

was associated with prolonged hospital stays, increased costs, and heightened perioperative complications. Patients undergoing HT, HGVBP, and SR have a higher risk of postoperative chylothorax compared to those undergoing CABG. Temporal trends show a decrease in chylothorax incidence in HGVBP and an increase in SR.

Understanding the multifactorial mechanism of postoperative chylothorax is crucial for effective treatment and prognosis. Based on DeMeester's classification [20], the causes of postoperative chylothorax can be categorized as congenital or surgical. Congenital causes mainly involve lymphatic abnormalities [6,21], which are often associated with syndromes such as Down syndrome [1]. Previous studies have suggested that trauma to the thoracic duct or lymphatic vessels, as well as increased central venous pressure, may be surgical risk factors for chylothorax [22–24]. However, these studies did not differentiate between specific types of cardiac procedures. The aim of our study is to investigate whether chylothorax is significantly associated with different surgical procedures, procedure approach, or the number of procedures performed. Of the various cardiac procedures analyzed, CABG was found to be the most frequently performed, with a relatively low incidence of postoperative chylothorax. This may be due to the absence of cardiac incisions associated with CABG procedures [11]. It is worth noting that HT remained the primary risk factor for chylothorax, even after adjusting for covariates. The presence of adhesions and alterations in the location of the thoracic duct [25] was found to be the cause of this. For more information on surgery volume and chylothorax incidence, please refer to Supplemental Fig. 2.

Stratified analyses by age group revealed distinct patterns in chylothorax incidence rates. Among adults, chylothorax incidence decreased with age, with HT presenting the highest occurrence rate. In contrast, among pediatrics, HGVBP was associated with the highest incidence rate. These findings align with previous reports indicating higher chylothorax incidence in patients undergoing Cavo pulmonary anastomoses (Glenn and Fontan surgeries) and repair of transposition of the great arteries [6].

Chylothorax often occurs alongside other postoperative complications, which can worsen patient prognosis. Previous studies have shown links between chylothorax and several other conditions, including deep vein thrombosis, arrhythmia, prolonged mechanical ventilation, and pulmonary embolism [26,27]. Although our study was limited by sample size, prior literature has established associations between ventricular arrhythmia and deep venous thrombosis, highlighting the importance of careful postoperative care and complication management. To mitigate these risks, it has been identified that enhanced preprocedural planning and surgeon experience are critical factors [28].

Chylothorax poses a unique management challenge, with differing approaches between pediatric and adult populations. Although dietary therapy may lead to self-resolution in pediatric patients, there is no consensus on the optimal management strategies for adults. Medication treatment, particularly with somatostatin, is generally well-tolerated. However, surgical interventions may be necessary if conservative measures are ineffective [29]. Some experts argue that surgical treatment is more effective and cost-efficient than medical management [22]. However, due to limitations of the NIS database, we were unable to access patient medication information. Despite this, our analysis of hospital admissions showed that only a small minority (2.8%) of chylothorax cases underwent surgical intervention. This finding may indicate that physicians in the United States tended to favor conservative management during the cardiac surgery period.

5. Limitations

This study has several limitations. Firstly, there is potential for misclassification due to reliance on ICD-10 codes within discharge records. To mitigate this concern, a rigorous approach was adopted, excluding conditions known to be associated with chylothorax, such as filariasis, and validating the CCSR classification with input from clinical experts.

Furthermore, the depth of our analysis and interpretation may be limited due to the lack of comprehensive pharmacy data and laboratory findings in the NIS database.

Additionally, the presence of unmeasured confounding factors could potentially introduce bias when assessing the impacts of chylothorax on patient outcomes. Although we made efforts to adjust for known covariates, the influence of unidentified variables remains a possibility and could impact the accuracy of our findings.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data source availability statement

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request. The NIS dataset is publicly available and administered by the HCUP under AHQR.

CRediT authorship contribution statement

Yue Xiao: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Investigation, Formal analysis, Data curation, Conceptualization, Methodology. **Yanfei Chen:** Validation, Data curation. **Ruijian Huang:** Software, Methodology. **Feng Jiang:** Visualization. **Cunhua Su:** Funding acquisition, Project administration, Supervision. **Jifang Zhou:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors thank all surgeons of the cardiac surgery centers from Nanjing First Hospital for their hard work and help in providing clinical information. We also thank our colleagues from China Pharmaceutical University for providing consolidated help in accomplishing this study.

All authors were involved in the design of the study, FJ and RH cleaned data and constructed the cohort; YC was involved in conceptualizing the study; YX and JZ were responsible for the analysis of the data and interpretation of the results.; YX, JZ and CS contributed to the drafting of the manuscript. All authors read and approved the final manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e29054.

References

[1] A. Raatz, M. Schober, R. Zant, et al., Risk factors for chylothorax and persistent serous effusions after congenital heart surgery, Eur. J. Cardio. Thorac. Surg. 56 (6) (2019) 1162–1169.
[2] R.D. Shah, J.D. Luketich, M.J. Schuchert, et al., Postesophagectomy chylothorax: incidence, risk factors, and outcomes, Ann. Thorac. Surg. 93 (3) (2012) 897–903. ; discussion 903-4.
[3] V.K. Varshney, S. Suman, P.K. Garg, et al., Management options for post-esophagectomy chylothorax, Surg. Today 51 (5) (2021) 678–685.
[4] M.T. Zuluaga, Chylothorax after surgery for congenital heart disease, Curr. Opin. Pediatr. 24 (3) (2012) 291–294.
[5] L.E. Riley, A. Ataya, Clinical approach and review of causes of a chylothorax, Respir. Med. 157 (2019) 7–13.
[6] C.M. Mery, B.S. Moffett, M.S. Khan, et al., Incidence and treatment of chylothorax after cardiac surgery in children: analysis of a large multi-institution database, J. Thorac. Cardiovasc. Surg. 147 (2) (2014) 678–686, e1; discussion 685-6.
[7] D. Kahraman, G. Keskin, K. Khalil, et al., Ten-year clinical experience on chylothorax after cardiovascular surgery 23 (1) (2020) E081–E087.
[8] S.K. Nair, M. Petko, M.P. Hayward, Aetiology and management of chylothorax in adults, Eur. J. Cardio. Thorac. Surg. 32 (2) (2007) 362–369.
[9] A.A. Ghaferi, T.A. Schwartz, T.M. Pawlik, STROBE reporting guidelines for observational studies, JAMA SURGERY 156 (6) (2021) 577–578.
[10] Available at, Healthcare Cost & Utilization Project User Support Website, Published by Agency for Healthcare Research & Quality, 2021, https://hcup-us.ahrq.gov/toolssoftware/ccsr/ccsr_archive.jsp#ccsr-pcs. (Accessed 22 July 2022).
[11] T. Calway, D.S. Rubin, H.E. Moss, et al., Perioperative retinal artery occlusion: risk factors in cardiac surgery from the United States national inpatient sample 1998-2013, Ophthalmology 124 (2) (2017) 189–196.
[12] K.C. Dewan, K.S. Dewan, J.J. Idrees, et al., Trends and outcomes of cardiovascular surgery in patients with opioid use disorders, JAMA SURGERY 154 (3) (2019) 232–240.
[13] M. Zia Khan, S. Zahid, M.U. Khan, et al., Redo surgical mitral valve replacement versus transcatheter mitral valve in valve from the national inpatient sample, J. Am. Heart Assoc. 10 (17) (2021) e020948.
[14] R.M. Reddy, M.L. Gorrepati, D.S. Oh, et al., Robotic-assisted versus thoracoscopic lobectomy outcomes from high-volume thoracic surgeons, Ann. Thorac. Surg. 106 (3) (2018) 902–908.
[15] D.S. Oh, R.M. Reddy, M.L. Gorrepati, et al., Robotic-assisted, video-assisted thoracoscopic and open lobectomy: propensity-matched analysis of recent premier data, Ann. Thorac. Surg. 104 (5) (2017) 1733–1740.
[16] D. Spiegelman, E. Hertzmark, Easy SAS calculations for risk or prevalence ratios and differences, Am. J. Epidemiol. 162 (3) (2005) 199–200.
[17] Statista. Number of cardiovascular surgeries in North America in 2007, 2014 and 2021. Available at https://www.statista.com/statistics/647958/cardiovascular-surgery-north-america-numbers/. Accessed July 22, 2022..
[18] S.K. Pasquali, D. Thibault, S.M. O'Brien, et al., National variation in congenital heart surgery outcomes, Circulation 142 (14) (2020 Oct 6) 1351–1360.
[19] G. Samanidis, G. Kourelis, S. Bounta, et al., Postoperative chylothorax in neonates and infants after congenital heart disease surgery-current aspects in diagnosis and treatment, Nutrients 14 (9) (2022) 1803.
[20] S.K. Nair, M. Petko, M.P. Hayward, Aetiology and management of chylothorax in adults, Eur. J. Cardio. Thorac. Surg. 32 (2) (2007) 362–369.
[21] T.G. Day, D. Zannino, D. Golshevsky, et al., Chylothorax following paediatric cardiac surgery: a case-control study, Cardiol. Young 28 (2) (2018) 222–228.
[22] M.H. El-Farra, N. Pham, J. Smith, et al., Treatment of chylothorax after coronary artery bypass grafting, Ann. Thorac. Surg. 112 (5) (2021) e349–e352.
[23] V. Agrawal, P. Doelken, S.A. Sahn, Pleural fluid analysis in chylous pleural effusion, Chest 133 (6) (2008) 1436–1441.
[24] S. Romero, C. Martin, L. Hernandez, et al., Chylothorax in cirrhosis of the liver: analysis of its frequency and clinical characteristics, Chest 114 (1) (1998) 154–159.
[25] A. Alam, L. Hou, D. James, et al., A rare case of chylothorax after heart transplantation, Case Rep Cardiol 2019 (2019) 2049704.
[26] J.R. Buckley, E.M. Graham, M. Gaies, et al., Clinical epidemiology and centre variation in chylothorax rates after cardiac surgery in children: a report from the Pediatric Cardiac Critical Care Consortium, Cardiol. Young (2017) 1–8.
[27] S.S. Hoskote, H. Yadav, P. Jagtap, et al., Chylothorax as a risk factor for thrombosis in adults: a proof-of-concept study, Ann. Thorac. Surg. 105 (4) (2018) 1065–1070.
[28] B. Wilkins, M. Fukutomi, O. De Backer, et al., Left atrial appendage closure: prevention and management of periprocedural and postprocedural complications, Card Electrophysiol Clin 12 (1) (2020) 67–75.
[29] E.H. Chan, J. Russell, W.G. Williams, et al., Postoperative chylothorax after cardiothoracic surgery in children, Ann. Thorac. Surg. 80 (5) (2005) 1864–1870.

Appendices 1: Glossary of Abbreviations

LOS: length of stay
PHIS: Pediatric Health Information System

NIS: National Inpatient Sample
STROBE: Strengthening the Reporting of Observational Studies in Epidemiology statement
IRB: Institutional Review Board
HCUP =: Healthcare Cost and Utilization Project
AHRQ: Agency for Healthcare Research and Quality
ICD-CM: International Classification of Diseases Clinical Modification
ICD-PCS: International Classification of Diseases Procedure Coding System
CABG: Coronary artery bypass graft
HV: Heart valve replacement and other valve procedures
LAAP =: Left atrial appendage procedures
HGVBP =: Heart and great vessel bypass procedures
PP =: Pericardial procedures
HT: Heart transplant
SR: Septal repair and other therapeutic heart procedures
CCSR: Clinical Classification Software Refined
CC: Charlson Comorbidity Index
SE: Stand error
CI: Confidence interval
aRR: adjusted rate ratio
CAR: Cardiovascular Procedures domain