Clinical characteristics of chylothorax: results from the International Collaborative Effusion database

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According to this multinational study, chylothorax is a rare cause of pleural effusion, is mostly caused by malignancies (particularly lymphomas), commonly requires pleural interventions and has a poor prognosis https://bit.ly/3JToven

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Abstract

Background Chylothorax is an uncommon medical condition for which limited data are available regarding the contemporary aetiology, management and outcomes. The goal of this study was to better define these poorly characterised features.

Methods The medical records of adult patients diagnosed with chylothorax at 12 centres across Europe, America and South Africa from 2009–2021 were retrospectively reviewed. Descriptive and inferential statistics were performed.

Results 77 patients (median age 69 years, male to female ratio 1.5) were included. Subacute dyspnoea was the most typical presenting symptom (66%). The commonest cause of chylothorax was malignancy (68.8%), with lymphoma accounting for 62% of these cases. Other aetiologies were trauma (13%), inflammatory/miscellaneous conditions (11.7%) and idiopathic cases (6.5%). At the initial thoracentesis, the pleural fluid appeared milky in 73%, was exudative in 89% and exhibited triglyceride concentrations >100 $mg \cdot dL^{-1}$ in 88%. Lymphangiography/lymphoscintigraphy were rarely ordered (3%), and demonstration of chylomicrons in pleural fluid was never ascertained. 67% of patients required interventional pleural procedures. Dietary measures were infrequently followed (36%). No patient underwent thoracic duct ligation or embolisation. Morbidity included infections (18%), and thrombosis in malignant aetiologies (16%). The 1-year mortality was 47%. Pleural fluid protein >3.5 $mg \cdot dL^{-1}$ (sub-distribution hazard ratio (SHR) 4.346) or lactate dehydrogenase <500 $U \cdot L^{-1}$ (SHR 10.21) increased the likelihood of effusion resolution. Pleural fluid protein ⩽3.5 $mg \cdot dL^{-1}$ (HR 4.047), bilateral effusions (HR 2.749) and a history of respiratory disease (HR 2.428) negatively influenced survival.

Conclusion Chylothoraces have a poor prognosis and most require pleural interventions. Despite the standard recommendations, lymphatic imaging is seldom used, nor are dietary restrictions followed.

Introduction

Chylothorax, formed when the thoracic duct becomes disrupted and chyle enters the pleural space, is infrequently observed in clinical practice [1]. It has not yet been categorised as an orphan disease in Europe, even though other more prevalent pleural conditions, such as empyema or mesothelioma, have been [2]. The exception is congenital chylothorax (ORPHA code number 264688), which is paradoxically the most common cause of pleural effusions in neonates [3]. Truthfully, adult chylothorax should be considered a high-impact orphan disease in that it presents high morbidity. A recently reported diagnostic and therapeutic algorithm for chylothorax was not based on prospective or randomised data due to its unavailability [4]. Rather, current knowledge on the natural history and management of the disease is largely based on individual case reports and very few case series from single centres [5–8].

The International Collaborative Effusion (ICE) database, sponsored by the European Respiratory Society and part of a Clinical Research Collaboration, has enabled the development of several projects on pleural diseases that have been underrepresented in the literature [9]. Data on a specific pleural disease is entered into a centralised research database by different centres (mostly European). Concerning chylothorax, ICE researchers raised five clinically relevant questions [9], which this study attempts to answer: 1) What are the most common causes of chylothorax in adults?; 2) How often does chylothorax present with dyspnoea?; 3) How is chylothorax typically/best investigated?; 4) What treatments are typically required/used for chylothorax?; and 5) What are the negative outcomes associated with chylothorax and factors related to its resolution?

Methods

A total of nine centres from six European countries, and one each from Canada, South Africa and Chile recruited patients for the ICE database of chylothorax using the Research Electronic Data Capture (REDcap) web application. Anonymised information concerning demographics, past medical history, clinical presentation, aetiologies, pleural fluid characteristics, diagnostic imaging, applied therapies and prognosis was entered into the registry, after retrospectively reviewing the medical records of patients who had been diagnosed with chylothorax between July 2009 and April 2021. The identification of chylothoraces was done through the international classification of diseases (ICD) codes and/or pleural fluid databases from research centres. The diagnosis of chylothorax was established by combining the pleural fluid findings (*i.e.* milky appearance and/or triglyceride level >110 $mg \cdot dL^{-1}$ on initial or subsequent thoracentesis with or without a fatty food challenge, or presence of chylomicrons if studied) with the supportive imaging, in the appropriate clinical context. The categorisation of a pleural fluid as exudate or transudate was based on Light's criteria [10]. Where necessary, the study was approved by the local ethics committee from each centre. The need for written informed consent was waived due to study design.

The aims of this study were the description of the clinical features of chylothorax (*i.e.* aetiology, presentation, diagnostic methods and treatments applied) and its outcome, including complications, factors that negatively impact survival and those that predict resolution of the effusion.

Statistics

Continuous variables are expressed as median (25–75th percentiles) and categorical variables as numbers (percentages). Data were compared between different aetiological groups by using the Mann–Whitney U-test and Fisher exact test for continuous and categorical variables, respectively. Those parameters with a $p<0.2$ in the bivariate model were entered into a logistic regression analysis to evaluate predictors of infections and thromboembolic events, the most common complications. Factors related to the resolution of chylothorax were analysed with the Fine and Gray competing risk time-to-event regression model, with death as the competing risk. Patients who did not die or did not achieve resolution of chylothorax were censored. Overall survival was estimated using the Kaplan–Meier method, with proportional hazard regression analysis being used to determine significant variables associated with mortality by Cox models. The statistical significance level was set at 0.05 (two-tailed). All calculations were performed using the SPSS version 24.0 statistical software (SPSS Inc., Chicago, IL, USA).

Results

Participant characteristics

After excluding five patients with critically incomplete data, the study population comprised a total of 77 patients with chylothorax (47 men and 30 women, with a median age of 69 (57–76) years). The

underlying aetiologies of chylothoraces are presented in table 1. The majority of the patients had malignancy (53, 69%), and lymphomas accounted for most malignant chylothoraces (33, 62%).

Table 2 shows some demographic and clinical characteristics of the study population. As expected, a history of current or previously diagnosed malignancy was more common in malignant chylothoraces (70%), while cirrhosis predominated in the inflammatory/miscellaneous group. Chylothorax most commonly presented with dyspnoea (66%), predominantly of >2 weeks duration (89%). However, this symptom was absent in 34% of the cases. On chest radiographs, pleural effusions were indistinctly right-sided (34%), left-sided (41%) or bilateral (25%), occupying >50% of the hemithorax in half the cases.

Pleural fluid characteristics

At the initial thoracentesis, 73% of pleural fluids had a milky appearance, a percentage which rose to 80% when subsequent aspirations were accomplished (table 3). Two (25%) of eight non-milky fluids turned milky on a second thoracentesis; the same occurred in two (67%) of three patients with two previous aspirations of non-milky fluids. A reddish tinge was observed in 10 (14%) patients. The majority of pleural fluids met Light's criteria for exudates (89%) with lymphocyte predominance (64%). The causes of transudative chylothoraces included three malignancies (stomach, pancreas, breast), as well as a cirrhosis, retrosternal goitre and one with an unknown aetiology.

Pleural fluid cholesterol concentrations were within normal range (median 68 $mg \cdot dL^{-1}$). In the initial thoracentesis, triglyceride levels in pleural fluid exceeded 110 $mg \cdot dL^{-1}$ in 58 (88%) of 66 documented cases, ranged between 50 and 110 $mg \cdot dL^{-1}$ in six (9%) and were lower than 50 $mg \cdot dL^{-1}$ in the remaining two (3%). The aetiologies of chylothoraces in the latter two patients were lung cancer and dasatinib therapy. The diagnosis of chylothorax in these eight patients with baseline pleural fluid triglyceride concentrations <110 $mg \cdot dL^{-1}$ was made by the milky appearance or elevation of triglycerides on successive thoracentesis or after a fatty meal.

Imaging and other diagnostic tools

The median time interval from the radiological evidence of pleural effusion to the aetiological diagnosis was 9 (1–63) days. Although chest (86%) and abdominal (69%) computed tomography (CT) scans were commonly performed, magnetic resonance imaging of the chest and abdomen (8%) and, particularly, specific imaging modalities for the lymphatic system were infrequently ordered (3%; only one patient being subjected to conventional lymphangiography and another to lymphoscintigraphy). A high-fat food challenge, usually indicated for doubtful cases, was attempted in 23% of 61 cases.

TABLE 1 Causes of chylothorax

Causes	
Malignancy	53 (68.8)
Lymphoid malignancies	33
Lung cancer	4
Stomach	3
Pancreas	3
Breast	2
Mesothelioma	2
Oesophagus	2
Miscellaneous[#]	4
Trauma	10 (13)
Surgical procedures[¶]	6
Miscellaneous[+]	4
Inflammatory/miscellaneous conditions[§]	9 (11.7)
Idiopathic	5 (6.5)
Total	77

Data are presented as n or n (%). [#]: prostate, colorectal, urothelial and Kaposi sarcoma (one each); [¶]: coronary artery bypass grafting (two patients), aortic valve replacement (one patient), oesophagectomy (one patient), cervical lymphadenectomy (one patient) and urological surgery (one patient); [+]: fall injury, chest tube drainage, central venous catheter placement and sneezing (one each); [§]: cirrhosis (four patients) and one each of heart failure, retrosternal goitre, miliary tuberculosis, autoimmune rheumatic disease and dasatinib treatment.

TABLE 2 Characteristics of patients with chylothorax

Characteristic	Total population	Malignancy	Trauma	Inflammatory/ miscellaneous	Idiopathic	p-value
Patients	77	53	10	9	5	
Age at diagnosis, years	69 (57–76)	68 (58–75)	77 (54–81)	62 (58–75)	57 (31–87)	0.797
Male sex	47 (61)	33 (62)	5 (50)	7 (78)	2 (40)	0.469
Current or former smoker (n=62)	22 (35)	16 (39)	2 (20)	3 (37)	1 (33)	0.731
Exposure to asbestos (n=35)	3 (9)	3 (11)	0 (0)	0 (0)	0 (0)	0.768
Comorbidities						
Underlying respiratory disease	17 (22)	12 (23)	1 (10)	3 (33)	1 (20)	0.675
Underlying cardiovascular diseases	33 (43)	20 (38)	6 (60)	4 (44)	3 (60)	0.498
Underlying kidney diseases	9 (12)	5 (10)	2 (20)	0 (0)	2 (40)	0.117
Cirrhosis	4 (5)	0 (0)	0 (0)	4 (44)	0 (0)	<0.001
Diabetes	5 (7)	5 (9)	0 (0)	0 (0)	0 (0)	0.49
History of malignancy	44 (57)[#]	37 (70)	3 (30)	3 (33)	1 (20)	0.01
Polypharmacy (⩾3 medications)	42 (55)	21 (40)	8 (80)	9 (100)	4 (80)	0.001
Dyspnoea at the time of diagnosis (n=68)	45 (66)	32 (67)	6 (67)	5 (63)	2 (67)	0.997
Dyspnoea duration >2 weeks (n=35)	31 (89)	23 (88)	3 (75)	4 (100)	1 (100)	0.712
Pleural effusion on chest radiograph (n=76)						
Right-sided	26 (34)	21 (40)	1 (10)	3 (33)	1 (25)	0.217
Bilateral	19 (25)	15 (28)	3 (30)	0 (0)	1 (25)	0.217
Size >50% of the hemithorax (n=74)	38 (51)	27 (52)	5 (50)	4 (44)	2 (67)	0.926
Time from presentation to aetiological diagnosis, days (n=71)	9 (1–63)	14 (1–61)	3 (0–26)	3 (0–110)	37 (0–1301)	0.623

Data are expressed as n, median (percentiles) or n (%), unless otherwise indicated. [#]: 35 had active cancer and 13 had a history of malignancy.

Pleural interventions

Conservative management, based on dietary modifications ranging from elimination of dietary fat to fasting, was prescribed in only 36% of the cases (table 4). However, an intervention into the pleural space, other than a diagnostic thoracentesis, was necessary in 67% of the patients. These interventions consisted of, in decreasing order of frequency: repeated thoracenteses (34%), tube thoracostomy (33%), insertion of an indwelling pleural catheter (15%) and pleurodesis (7%). 10 (13%) patients required two of the preceding procedures, and three (4%) patients required three. No patient underwent thoracic duct ligation or embolisation.

TABLE 3 Pleural fluid characteristics of the study population

Pleural fluid characteristics	Total population	Malignancy	Trauma	Inflammatory/ miscellaneous	Idiopathic	p-value
Macroscopic appearance at initial thoracentesis (n=69)						
Milky	50 (73)	34 (72)	7 (70)	7 (78)	2 (67)	0.759
Serous	9 (13)	6 (13)	1 (10)	2 (22)	0 (0)	
Serosanguineous	5 (7)	4 (9)	1 (10)	0 (0)	0 (0)	
Bloody	5 (7)	3 (6)	1 (10)	0 (0)	1 (33)	
Biochemical and cytological analyses						
Exudate by Light's criteria (n=56)	50 (89)	40 (93)	6 (100)	2 (50)	2 (67)	0.024
Protein-discordant exudate[#] (n=47)	11 (23)	9 (26)	2 (33)	0 (0)	0 (0)	0.197
LDH-discordant exudate[¶] (n=47)	4 (9)	3 (9)	1 (17)	0 (0)	0 (0)	0.197
Exudate with lymphocyte predominance (n=56)	36 (64)	31 (72)	3 (50)	2 (50)	0 (0)	0.004
Triglycerides mg·dL^{-1} (n=66)	265 (149–652)	238 (146–475)	513 (216–1061)	266 (138–378)	731 (164–1541)	0.331
Cholesterol mg·dL^{-1} (n=54)	68 (41–94)	69 (50–93)	64 (33–74)	28 (21–127)	110 (48–589)	0.243
Malignant cells (n=66)	11 (17)	10 (21)	1 (17)[+]	0 (0)	0 (0)	0.416

Data are expressed as median (percentiles) or n (%), unless otherwise indicated. LDH: lactate dehydrogenase. [#]: pleural fluid to serum protein ratio >0.5, but pleural fluid LDH concentration ⩽67% of the normal upper limit for serum LDH. [¶]: pleural fluid to serum protein ratio ⩽0.5, but pleural fluid LDH concentration >67% of the upper normal limit for serum LDH. [+]: post-oesophagectomy chylothorax in a patient with oesophageal cancer.

TABLE 4 Treatments and outcomes of the study population

Parameter	Total population	Malignancy	Trauma	Inflammatory/ miscellaneous	Idiopathic	p-value
Therapy						
Nutritional support[#] (n=70)	25 (36)	14 (29)	5 (50)	3 (37)	3 (75)	0.214
Iterative thoracenteses (n=76)	26 (34)	14 (26)	4 (40)	6 (75)	2 (40)	0.056
Chest tube drainage[¶] (n=76)	25 (33)	15 (28)	5 (50)	3 (37)	2 (40)	0.568
Pleurodesis[+] (n=74)	5 (7)	3 (6)	0 (0)	1 (12)	1 (20)	0.458
Indwelling pleural catheter[§] (n=75)	11 (15)	10 (19)	1 (10)	0 (0)	0 (0)	0.351
Any intervention on the pleural space (n=76)	51 (67)	34 (64)	9 (90)	6 (75)	2 (40)	0.215
Drug management[f] (n=75)	5 (8)	1 (2)	3 (30)	1 (8)	0 (0)	0.016
Interventional radiology[##] (n=77)	2 (3)	1 (2)	1 (10)	0 (0)	0 (0)	0.468
Outcomes						
Resolution of chylothorax (n=66)	30 (45)	17 (36)	7 (78)	4 (57)	2 (67)	0.095
Time from diagnosis to resolution, days (n=28)	117 (36–186)	83 (29–224)	125 (35–653)	121 (62–171)	334	0.678
Mortality (n=68)	37 (54)	29 (59)	4 (44)	3 (43)	1 (33)	0.465
Time from diagnosis to death, days (n=34)	74 (32–216)	65 (25–145)	194 (100–328)	272 (10–272)	37	0.259
Overall survival, days (n=76)	286 (0–594)	236 (65–407)	365 (0–734)	NC	NC	0.682

Data are expressed as median (percentiles or, in the case of survival, 95% confidence interval of the median) or n (%), unless otherwise indicated. NC: non-calculable. [#]: low-fat diet, medium-chain triglyceride diet or total parenteral nutrition. [¶]: 77% were treated with a single chest tube, while 23% required additional chest tubes; of the 25 patients who received a tube thoracostomy, nine died with a tube in place (in two talc pleurodesis was attempted, and one was subsequently treated with an indwelling pleural catheter), 11 were eventually resolved (one received a liver transplant), three were lost to follow-up, and two still had the drainage tube in place at the time of data collection. [+]: pleurodesis agents were talc (four patients) and doxycycline (one patient); the procedure failed in one (20%) patient. [§]: at the time of the study closure, autopleurodesis had been achieved in seven (64%) patients after a median time of 2 months (interquartile range, 1–3 months). [f]: somatostatin, octeotride or sirolimus. [##]: one lymphography and one superior vena cava stenting.

The main complications that appeared during the treatment period were infections (12/67, 18%), thromboembolic events in malignant chylothoraces (16%) and electrolyte disturbances (5%). Among the infections, four occurred in the pleural space (one patient with an indwelling pleural catheter, and three with chest tubes), while the rest were extrapleural and unrelated to any pleural procedure (two pneumonias, two urinary tract infections, two sepsis cases of unknown primary source, and one each of spontaneous bacterial peritonitis and diabetic foot infection).

Outcomes

The median follow-up of the study population was 5 (3–12) months. There were 37/68 deaths (54%), of which 32 occurred during the first year of diagnosis (1-year mortality rate 47%). The mortality rate was particularly high among malignant chylothoraces (59% overall and 57% at 1 year; calculated for 49 patients with available data). After entering all the recorded variables, a multivariate logistic regression analysis showed a non-significant trend towards more infections in younger patients (OR 0.969, 95% CI 0.933–1.005; p=0.094) and in those with electrolyte imbalances (OR 0.154, 95% CI 0.018–1.293; p=0.085). The only statistically significant predictor of thromboembolic complications was the insertion of a chest tube (OR 18.5, 95% CI 1.935–176.9; p=0.011). The likelihood of chylothorax resolution was increased in subjects with a pleural fluid lactate dehydrogenase (LDH) $<500\ U{\cdot}L^{-1}$ (sub-distribution hazard ratio (SHR) 10.21, 95% CI 1.58–66.1; p=0.015) or protein $>3.5\ g{\cdot}dL^{-1}$ (SHR 4.346, 95% CI 1.595–11.838; p=0.004). Finally, a Cox regression analysis showed that a history of respiratory disease (HR 2.428, 95% CI 1.11–5.312; p=0.026) and the existence of a bilateral pleural effusion (HR 2.749, 95% CI 1.242–6.083; p=0.013) or pleural fluid protein concentrations $\leqslant 3.5\ g{\cdot}dL^{-1}$ (HR 4.047, 95% CI 1.889–8.668; p<0.001) increased the probability of death.

Discussion

In this study, we evaluated the aetiology, clinico-radiological and pleural fluid characteristics, treatments and outcomes of adult chylothorax in a multicentre series of patients from the ICE database.

Malignancy accounted for nearly 70% of chylothoraces in our study, with lymphoma being the most common tumour type. This agrees with an old compilation of eight separate series in which cancer caused 45.5% of 191 chylothoraces [11]. In contrast, a review of 203 patients of any age spectrum with chylothorax seen at the Mayo Clinic (Rochester, MN, USA) over a 21-year period found surgery to be responsible for half the cases [5]. The predominance of post-operative chylothoraces can be explained by

the fact that this American centre is a referral hospital for cardiothoracic surgical procedures. Post-surgical chyle leakage typically follows oesophagectomy (overall incidence 3.2%) [12], cardiovascular surgery (<5%) [13] and lung cancer surgery (<2%) [14]. However, due to the low incidence of this complication, it would be necessary to include centres with high surgical volumes for post-operative chylothorax to be a predominant aetiology; a circumstance that did not occur in the ICE recruiting centres. On the other hand, it was estimated that ∼89 000 new cases of lymphoma would be diagnosed in the USA in 2022 [15]. Nearly one-third of lymphoma patients may develop pleural effusions [16], and the rate of chylothoraces among tapped effusions is 8% [16, 17].

Two-thirds of chylothorax patients presented with subacute dyspnoea, similar to other descriptions [5], yet subjects may remain asymptomatic when the volume of the pleural effusion is low. Chylothorax had no predilection for any side, though bilateral involvement on chest radiographs was less common (about one-quarter of the cases), as noted elsewhere [7]. Anatomical reasons explain the preferential lateralisation of chylothoraces depending on the level of thoracic duct injury or obstruction. Bilateral effusions result from disruption at the level of the fifth thoracic vertebrae or from the transdiaphragmatic movement of chylous ascites.

The pleural fluid was milky in about three-quarters of our patients, in contrast to only 44% in an early series of 74 patients from the Mayo Clinic [7]. The underlying reason may be the high prevalence of post-surgical chylothoraces in the latter (51%), with the potential lack of milky appearance in the fasting post-operative period. Only around 10% of chylothoraces meet transudative criteria. Notably, the presence of a transudative chylothorax should raise suspicion not only of common causes of transudates (*e.g.* cirrhosis, heart failure), but also of rare causes of transudates such as neoplasms (which, in fact, accounted for half of our transudative chylothoraces). Overall, ∼2% of malignant pleural effusions are categorised as transudates by applying Light's criteria [18]. The current investigation supports the concept that a pleural fluid triglyceride concentration <50 $mg \cdot dL^{-1}$ strongly argues against the diagnosis of chylothorax (unless the patient is fasting or severely malnourished), with this circumstance occurring in only 3%. In cases of diagnostic uncertainty due to a non-milky appearance or low to intermediate triglyceride levels, no patient underwent lipoprotein analysis to assess for the presence of chylomicrons in the pleural fluid, a test that establishes a definitive diagnosis [19] but is not widely available. Instead, clinicians preferred the simple administration of a high-fat meal, which may result in a dramatic change in the aspect and triglyceride content of the pleural fluid.

Imaging studies for chylothorax mainly consisted of CT of the chest and abdomen, since they help to reveal lymphadenopathy. However, lymphatic system imaging techniques were infrequently performed (3%), which may be due to two possible reasons: 1) they are not widely available, and 2) they may not affect clinical management in patients where thoracic duct repair or ligation is not planned, as is the case for most nontraumatic chylothoraces [19].

Pleural space drainage to relieve respiratory symptoms was deemed necessary in two-thirds of the patients, a proportion only slightly higher than that observed for malignant pleural effusions [20]. This partly justifies the consideration of chylothorax as a difficult to manage pleural effusion type. Dietary modifications (*i.e.* no-fat diet, medium-chain triglycerides, total parenteral nutrition) were followed in just over a third of the cases. The reported use of dietary measures among nontraumatic chylothoraces varies widely in the literature, from 15% (five of 34 patients) in one study [8] to 94% (49 of 52 patients) in another [21]. Also, pharmacological therapy as part of the conservative management (*e.g.* somatostatin and its analogues) was prescribed in a minority of patients (8%). It should be noted that half the patients exhibited large effusions, a fact which may limit the efficacy of conservative measures [4]. Physicians may have prioritised symptomatic relief of patients with pleural drainage and relied on treating the underlying disease (*e.g.* lymphoma). Moreover, surgical techniques such as thoracic duct ligation were not performed, likely because they are more successful in post-operative cases [4, 22], which only represented 7.8% of our study population.

Chylothorax has significant morbi-mortality. Infections during the hospitalisation period (18%) exceeded what might be expected. For comparison, the prevalence of nosocomial infections in a respiratory department of a Chinese tertiary hospital during the pre-COVID pandemic (2019) was 2.53% [23]. Multiple factors may have left patients defenceless against infections, including secondary malnutrition, underlying illnesses and their immunosuppressive therapies, use of a diversity of devices (indwelling pleural catheters, tube thoracostomy, central vascular catheters), or prolonged hospitalisations. Specifically, although the number of patients was small, the incidence of indwelling pleural catheter-related infections (one out of 11, 9%) was similar to that reported in large series of pleural effusions (*e.g.* 8% in a series of

336 procedures) [24]. Cancer-associated venous thromboembolism (16%) also represented an important disease burden in chylothoraces of malignant aetiology, and, according to the multivariate analysis, this was possibly influenced by the time of permanence of tube thoracostomy and the lesser mobility that this entails for the patient. Electrolyte abnormalities were infrequently seen.

It is noteworthy that 55% of effusions failed to resolve, a persistence rate very similar to that of a previous series of nontraumatic chylothoraces (50%) [8]. High protein levels and low LDH in pleural fluid, which might reflect a better nutritional state and less tissue injury, predicted a higher probability of recovery. The mortality risk was not negligible (47% at 1 year), but there are no recent mortality data to compare. In part, this elevated mortality rate could be attributed to the high percentage of underlying neoplasms causing chylothorax. Poor prognostic indicators included an underlying respiratory disease, bilateral effusions and low pleural fluid protein concentrations. The association of bilateral effusions, as a possible indication of more advanced disease, with an increased mortality is not novel [25, 26]. In addition, low fluid protein concentrations could be indicative of an advanced emaciation state as suggested for malignant effusions [27].

Limitations of the study

The major limitations of this study were its retrospective design and the relatively small population size. It was not possible to collect some relevant data, including volume output drainage and longer-term follow-up. Also, it cannot be ruled out that some traumatic or surgical chylothorax was omitted in cases of incorrect ICD coding or lack of inclusion in the pleural fluid databases of the participating centres. Importantly, chylothorax cases may have been missed given the diagnostic criteria used, where a patient without clinical suspicion who had a non-milky fluid or intermediate triglyceride levels in pleural fluid (considering that chylomicrons were never ordered) may have mistakenly received other alternative diagnoses. Our results mainly apply to nontraumatic chylothoraces, the predominant aetiology in the series. The algorithmic management of this entity may differ in each centre, based on the availability of diagnostic tools and expert teams. Despite these shortcomings, a notable strength of this multicentre, international and contemporary study is that it supplements the scarce information available on this low-incidence pleural condition.

Conclusion

Neoplasms – specifically lymphomas – are the most common cause of chylothorax. Most pleural fluids have a milky appearance and high triglyceride concentrations. In doubtful cases, clinicians generally indicate a high-fat meal test instead of a lipoprotein electrophoresis of the pleural fluid. Lymphatic imaging is rarely necessary to help guide management. Infections and, in malignant aetiologies, thromboembolic events may complicate the clinical course. Drainage of the pleural space is generally required, but oftentimes the pleural fluid persists or recurs. Physicians usually rely on conservative management of chylothorax rather than surgical or interventional radiology procedures. The exceedingly high mortality of chylothorax should encourage future randomised controlled trials to help a more evidence-based approach to this entity.

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Conflict of interest: J.M. Porcel has received consultancy fees from Becton Dickinson and Suministros Hospitalarios SA (SH Medical Group), and is an associate editor of this journal. The remaining authors declare that they have no relevant conflicts of interest.

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