



Kerman University of Medical Sciences



در روی زمین نیست چو کرمان جایی، کرمان دل عالم است و ما اهل دلیم

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# **OBJECTIVES**

**Define chylothorax and related terms**

**Explain the disease pathophysiology**

**CLINICAL PRESENTATION**

**DIAGNOSTIC EVALUATION OF SUSPECTED  
CHYLOTHORAX**

**Therapies**



## Key Words

- Chyle (lymphatic fluid): Milky white fluid that contains protein, fat, cholesterol, lymphocytes, and electrolytes. Transport of chylomicron.
- Thoracic duct: Paper thin, valved, tubular structure 2-3 mm in diameter. Main conduit of the lymphatic system and transports 60-70% of ingested fat to the blood stream.
- Chylothorax: occurs when chyle collects in the pleural space of the thoracic cavity and cannot drain from the thoracic duct into the subclavian vein

# INTRODUCTION

- . When untreated, chylothorax is associated with high morbidity and mortality**
- . The diagnosis, which is often elusive, should be prompt so that therapy can be quickly initiated.**

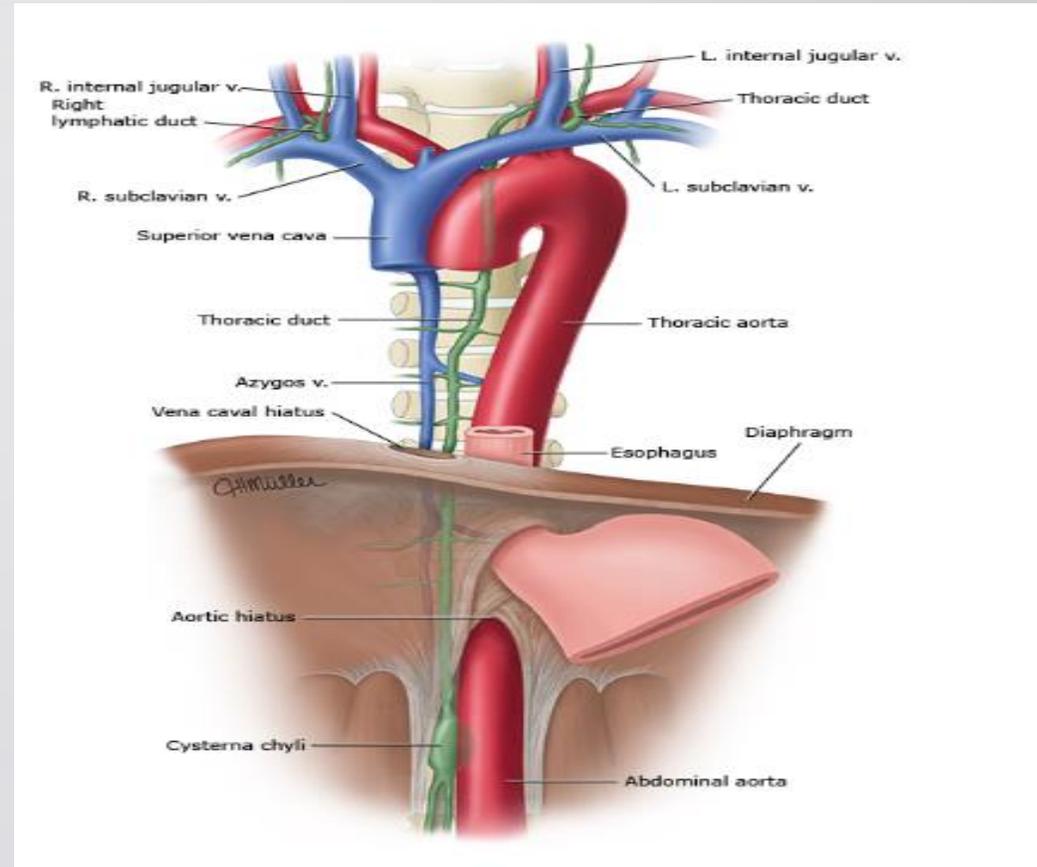
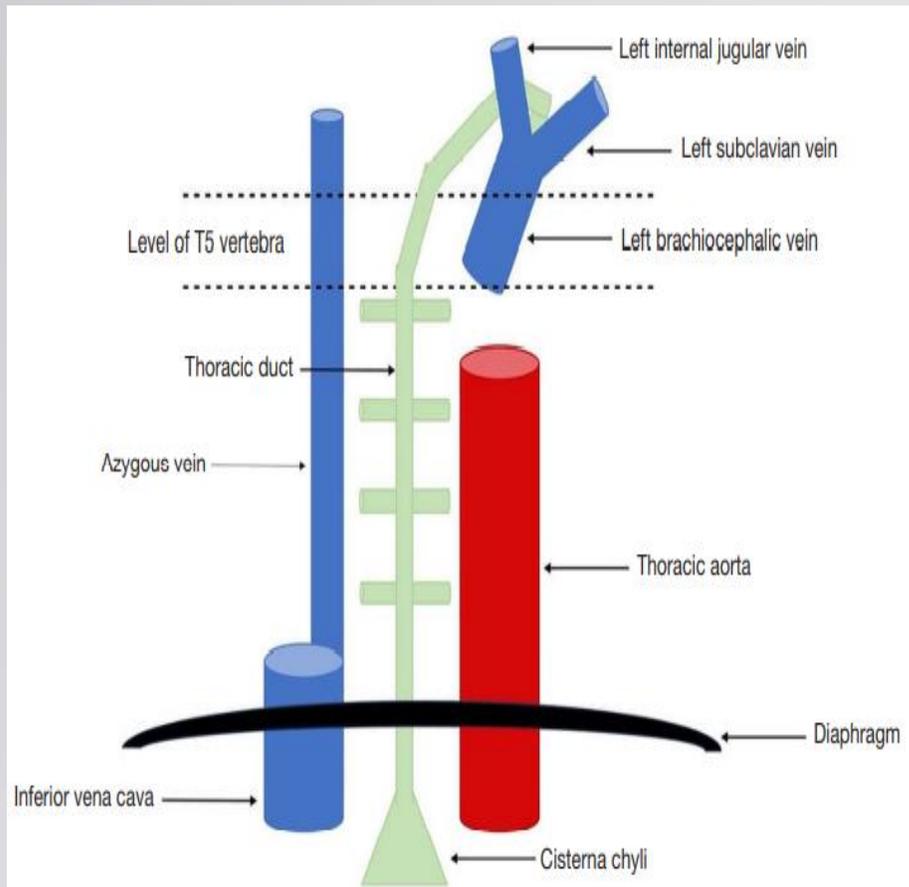
**As approximately 2.4 l of chyle is transported through the lymphatic system every day, damage to, or rupture of the thoracic duct can give rise to a large and rapid accumulation of fluid in the pleural**

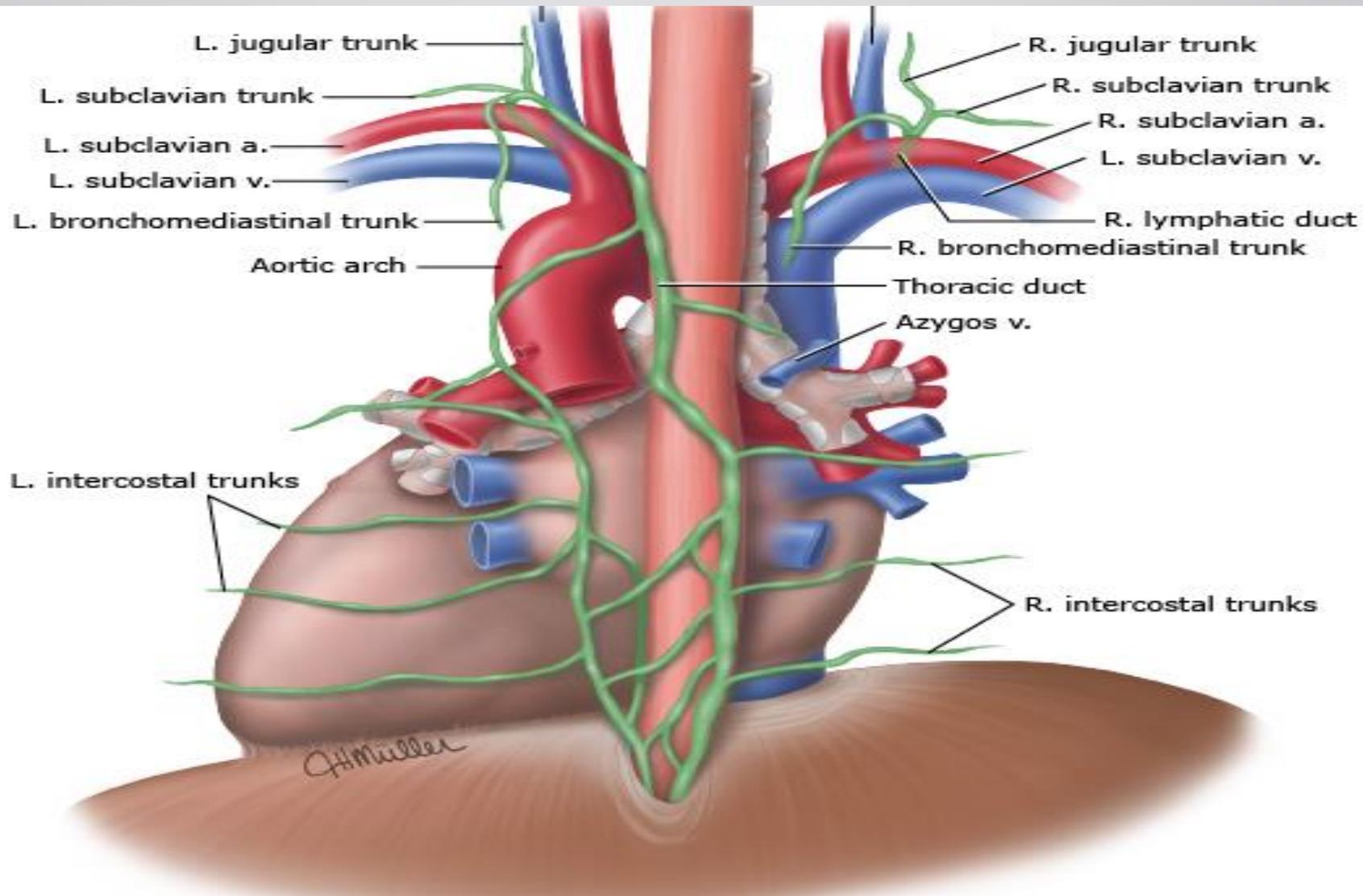
**Although chylothorax is relatively uncommon, accounting for around 3% cases of all pleural effusions , the 90-day mortality rates associated with this condition may be as high as 82%**

**stemming largely from nutritional losses (owing to the high fat content of chyle), immunosuppression (due to its high lymphocyte and immunoglobulin content) and fluctuating intravascular volumes**

# THORACIC DUCT ANATOMY AND PHYSIOLOGY

The thoracic duct carries chyle (which contains triglycerides [TGs] in the form of chylomicrons, T lymphocytes, electrolytes, proteins, immunoglobulins, and fat-soluble vitamins) from the intestine to the bloodstream. It commences at the cisterna chyli which is the convergence of the intra-abdominal lymphatics (hepatic, mesenteric, etc) with the lower extremity and retroperitoneal lymphatics, located in the retroperitoneum anterior to the second lumbar vertebra (T12 to L1) and ends at the junction of the left subclavian and jugular veins .As the thoracic duct passes through the mediastinum, it also receives nonchylous lymph from tributaries that drain regions of the pulmonary parenchyma and parietal pleura





## **PATHOGENESIS AND ETIOLOGY**

Any disruption or dysfunction of the flow of chyle through the thoracic duct can cause chylothorax. Thus, there are several etiologies of chylothorax that can be broadly categorized as nontraumatic or traumatic (iatrogenic or either blunt or penetrating injury)

## Chylothorax (non-traumatic)

3. Increased hydrostatic pressure within lymphatic system

4. Hyperpermeability of lymphatics secondary to lymphatic dysfunction

Pleural space

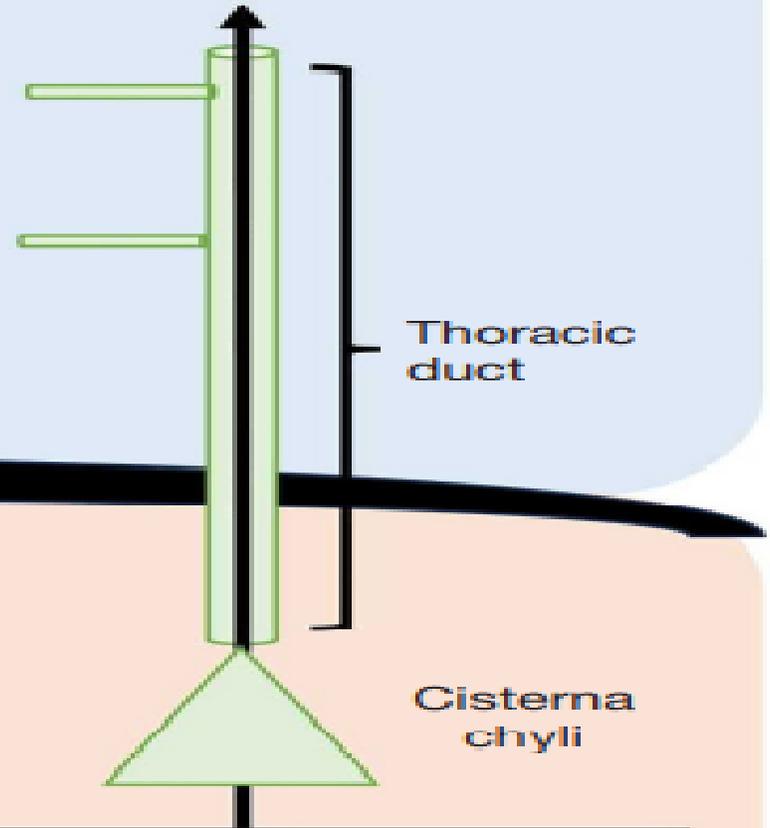
Peritoneal cavity

1. Transdiaphragmatic passage of chylous ascites

2. Direct invasion of thoracic duct by malignant cells

Thoracic duct

Cisterna chyli



# Pathophysiology

- Secondary to injury; thoracic surgery, abdominal surgery, esophagectomy, lymphoma, neck trauma, thyroid lobectomy, lung lobectomy
- Occurs when chyle collects in the thoracic cavity and fills the pleural space
- Dietary fat promotes chyle production.

# Chylothorax

## Traumatic

## Non-traumatic

### *Non-iatrogenic*

### *Iatrogenic*

### *Malignancy*

### *Idiopathic*

### *Diseases*

Knife wound  
Gun shot wound  
Childbirth  
Forceful emesis or cough  
Blunt trauma to chest wall or vertebrae

Radiation  
Thoracic surgery  
Head and neck surgery

Sarcoidosis  
Haemangiomas  
Lymphangiomyomatosis  
Filaria  
Amyloidosis  
Tuberculosis  
Retrosternal goitre  
Superior vena cava obstruction  
Benign tumour  
Cardiac failure  
ascites

## Etiology of chylothorax

Etiology	Number of cases* <sup>[1]</sup> (%)	Number of cases <sup>†</sup> <sup>[2]</sup> (%)
<b>Total nontraumatic PLUS traumatic cases</b>	<b>191 (100)</b>	<b>203 (100)</b>
<b>Nontraumatic</b>		
Malignant neoplasia		
▪ Lymphomatous	70 (37)	23 (11)
▪ Nonlymphomatous (eg, primary lung, esophageal, mediastinal, metastatic extrathoracic malignancies, sarcoma, leukemia)	17 (9)	11 (5)
Total malignant neoplasia cases =	87 (46)	34 (17)
Nonmalignant		
▪ Idiopathic	26 (14)	13 (6)
▪ Miscellaneous (benign tumors, lymphangiomyomatosis, intestinal lymphangiectasis, protein-losing enteropathy, regional ileitis, pleuritis, cirrhosis, thoracic aortic aneurysm, lupus, tuberculosis, sarcoidosis, amyloidosis, venous thrombosis, mitral stenosis, nephrosis, thyroid goiter, tuberous sclerosis, filariasis, heart failure, Down syndrome, Noonan syndrome, other diagnoses* [please refer to UpToDate text for additional causes])	25 (13)	55 (27)
Total nonmalignant cases =	51 (27)	68 (33)
<b>Total nontraumatic cases =</b>	<b>138 (72)</b>	<b>102 (50)</b>

## Etiology of chylothorax

Etiology	Number of cases* <sup>[1]</sup> (%)	Number of cases <sup>¶</sup> <sup>[2]</sup> (%)
<b>Traumatic</b>		
<ul style="list-style-type: none"> <li>▪ Surgical and iatrogenic (cardiovascular and aortic surgery, thoracoplasty, esophageal and gastric surgery, lobectomy, pneumonectomy, mediastinal mass or lymph node resection, Bochdalek herniorrhaphy, transabdominal vagotomy, central venous catheterization, esophageal endoscopic sclerotherapy, neck surgery, spine surgery, embolization for pulmonary arteriovenous malformations, pacemaker insertion, chest wall surgery, sympathectomy, paraganglioma surgery)</li> </ul>	48 (25)	97 (48)
<ul style="list-style-type: none"> <li>▪ Nonsurgical (penetrating or nonpenetrating trauma to the neck, thorax, and upper abdomen, straining, coughing, yawning, vomiting)</li> </ul>	5 (3)	4 (2)
<b>Total traumatic cases =</b>	<b>53 (28)</b>	<b>101 (50)</b>

\* The Valentine et al case series<sup>[1]</sup> did not provide diagnoses for 10 patients so these cases were categorized in the table as "other diagnoses" in the Miscellaneous category.

¶ The lower incidence of chylothorax related to lymphoma in the earlier Doerr series<sup>[2]</sup>, compared with the older Valentine series<sup>[1]</sup>, likely relates to the earlier diagnosis of lymphoma and prompt initiation of effective therapy prior to development of chylothorax.

### References:

1. Valentine VG, Raffin TA. The management of chylothorax. *Chest* 1992; 102:586.
2. Doerr CH, Allen MS, Nichols FC 3rd, Ryu JH. Etiology of chylothorax in 203 patients. *Mayo Clin Proc* 2005; 80:867.

Chylothorax should be suspected in any one or more of the following:

- Pleural effusion in a patient with a known risk factor (eg, malignancy, trauma, lymphangioleiomyomatosis)
- Milky pleural effusion
- Lymphocytic predominant exudative pleural effusion

Measurement of pleural fluid triglycerides and cholesterol\*

Cholesterol level  
<200 mg/dL  
(<5.18 mmol/L)

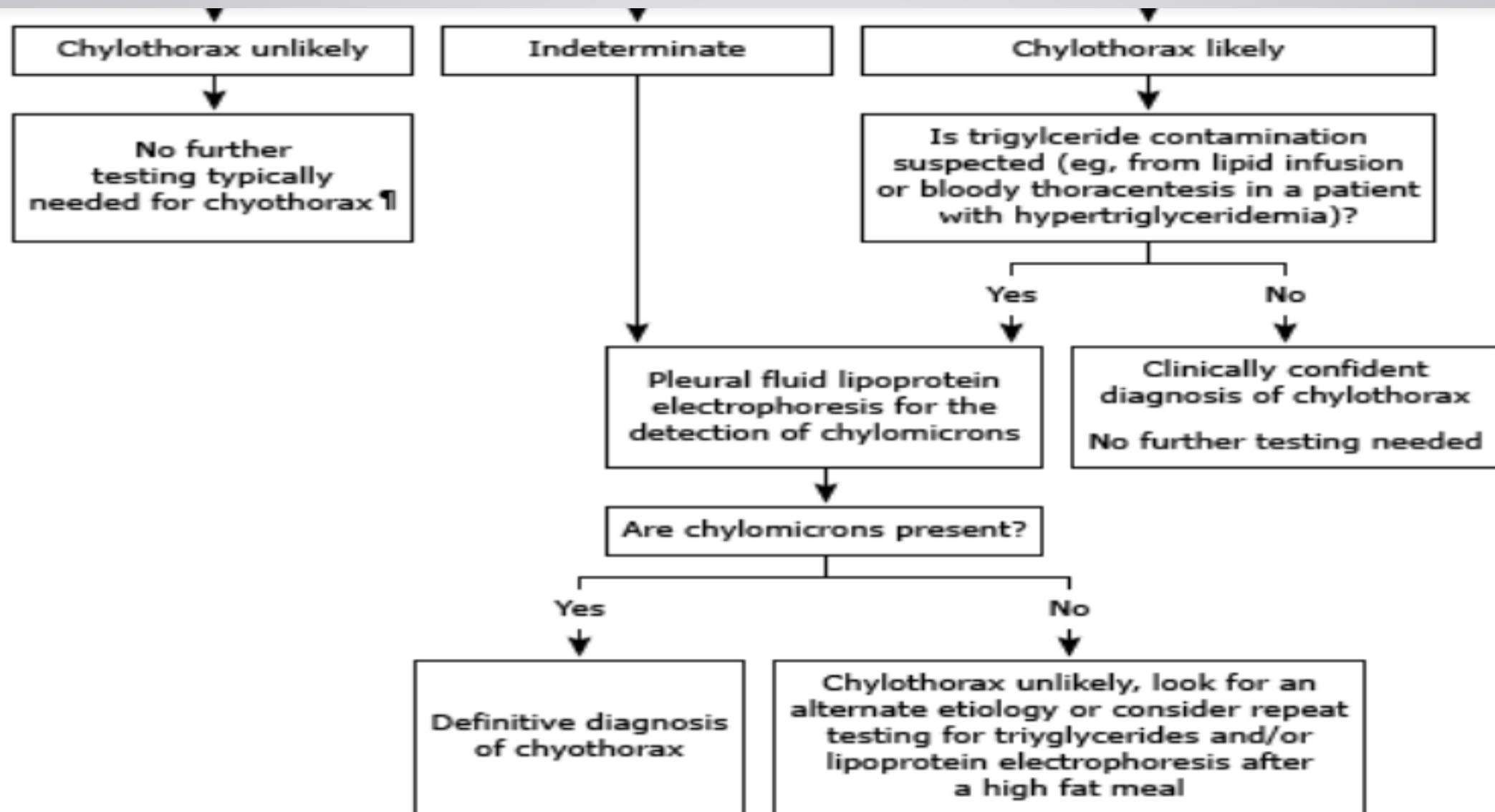
Cholesterol level  
≥200 mg/dL  
(≥5.18 mmol/L)

Triglyceride levels  
<50 mg/dL  
(<0.56 mmol/L)

Triglyceride levels  
50 to 110 mg/dL  
(0.56 to 1.24 mmol/L)

Triglyceride levels  
>110 mg/dL  
(>1.24 mmol/L)

Possible cholesterol pleural effusion  
Refer to UTD content for details



# CLINICAL PRESENTATION

## Signs and symptom

The majority of patients with chylothorax present with dyspnea induced by the mechanical effects of a pleural effusion.

Approximately **83%** of chylothoraces are **unilateral** (50% right-sided, 33% left-sided), while 17% are bilateral

Additional symptoms include a heavy feeling in the chest, fatigue, and weight loss. Fever and chest pain are rare because chyle within the pleural space does not evoke an inflammatory response and rarely becomes infected due to the bacteriostatic effect of immunoglobulins that are contained in chyle .

Chyloptysis (expectorating chylous fluid) is an exceedingly rare manifestation of chylothorax

since chronic loss of chyle is associated with immune suppression from loss of immunoglobulins, these patients may be prone to infection in organs other than the pleural space. On physical examination, findings of decreased breath sounds and stony dullness to percussion may be present depending on the size and location of the effusion.

Some patients may rarely present with uncontrolled atrial fibrillation since [digoxin](#) and [amiodarone](#) and [Ciclosporin](#) are carried through the chyle into the pleural space and may be lost if high volumes of drainage occur

# Laboratory

There are no specific blood laboratory findings associated with chylothorax.

Routine laboratory testing is typically obtained to assess for associated disorders and include a CBC diffcomplete, and BS , total protein, and LDH for comparison with pleural fluid values.

Rarely, when severe, electrolyte loss into the pleural space may result in **hyponatremia, hypocalcemia, and metabolic acidosis**.

Unless the patient is severely malnourished (which is rare), serum triglycerides, total protein, albumin, and immunoglobulin levels are generally normal despite the loss of these molecules into the pleural space.

# DIAGNOSTIC EVALUATION OF SUSPECTED CHYLOTHORAX

## ●Appearance

The appearance of fluid from a chylothorax can be milky, sanguineous, or serous.

The colour of the fluid can be misleading as only **50% of cases** show the classical milky white appearance milky fluid can also be seen in a cholesterol pleural effusion or an empyema

the appearance may be non-milky especially if the patient is malnourished, fasting, or on a low fat diet

Chylothorax can be differentiated from pseudochylothorax by adding 1 to 2 ml of ethylether. The milky appearance disappears in pseudochylothorax.

## ●Cell counts

The white blood cell differential of fluid from chylothoraces typically has a predominance of **lymphocytes**, usually >70 percent of the total nucleated cell count, reflecting the cellular composition of lymph. Lymphocytes are largely a polyclonal population of T cells and concentrations range from 400 to 6800 cells/microL. The predominance of lymphocytes contributes to the **bacteriostatic** nature of chyle, explaining why it rarely becomes infected

## ● **Electrolytes and protein**

Chyle has an electrolyte and protein content similar to that of plasma. Although the protein concentration of chyle within lymphatic channels is usually **between 2 and 3 g/dL** (ie, transudative , **most chylothoraces (up to 85 percent) have a higher protein concentration making them exudates by Light's criteria .**

The mechanisms of the transformation of transudative chyle into exudative chylothorax is unknown.

It may be due to high rates of fluid and solute absorption from the pleural space thereby concentrating intrapleural protein content

Transudative chylothorax has been reported in a small proportion of patients with amyloidosis, cirrhosis, nephrotic syndrome, superior vena cava obstruction, heart failure, and chylous ascites that has crossed the diaphragm into the pleural space (chylothorax due to chylous ascites has biochemical characteristics that match the ascitic fluid from the patient

## ●LDH

The concentration of LDH in chyle is low and, consequently, LDH levels in chylous pleural fluid are also low, being in the range of a transudative pleural effusion by Light's criteria

In some but not all series, elevation of LDH in chylous pleural fluid was associated with an underlying cause of a chylothorax (eg, malignancy) rather than from simple chyle leakage from ruptured lymphatic channels

## ●Glucose .02

The pleural fluid glucose in chylothorax is usually similar to that in plasma. A pleural fluid glucose **below 60 mg/dL** suggests coexisting **empyema or a malignant** pleural effusion. A pleural fluid-to-serum glucose ratio  $>1$  in a patient receiving **total parenteral nutrition** with intravenous lipid solutions indicates the presence of central venous catheter erosion into the mediastinum or pleural space

## pH

Chylous fluid usually has a pH that ranges from 7.40 to 7.80 [[58](#)]. Pleural fluid pH measurement for suspected chylothorax is indicated only for patients who have intrapleural malignancy or infection in the differential diagnosis with chylothorax

**Lipid analysis** — Measurement of TG and cholesterol levels should be the initial lipid tests performed in patients with suspected chylothorax. In a patient on a regular diet, a chylothorax typically contains a high concentration of TGs ( $>110$  mg/dL [ $>1.24$  mmol/L]) and the cholesterol level is generally  $<200$  mg/dL ( $<5.18$  mmol/L). However, 15 percent of chylothoraces have pleural fluid TG concentrations  $\leq 110$  mg/dL ( $\leq 1.24$  mmol/L) and 3 percent have values  $<50$  mg/dL ( $<0.56$  mmol/L).

A cholesterol concentration  $\geq 200$  mg/dL ( $\geq 5.18$  mmol/L) supports a cholesterol effusion and is not typically seen in chylothorax.

**Triglyceride level  $>110$  mg/dL** — A pleural fluid TG concentration  $>110$  mg/dL ( $>1.24$  mmol/L) strongly supports the diagnosis

**Triglyceride level  $<50$  mg/dL** — A pleural fluid TG concentration  $<50$  mg/dL ( $<0.56$  mmol/L) provides strong support that the patient does **not** have a chylothorax and in general no further testing is required.

**Triglyceride level between 50 and 110 mg/dL** — clinicians should perform lipoprotein electrophoresis of the pleural fluid to detect chylomicrons. If lipoprotein electrophoresis is not available, repeat pleural fluid TG measurements after the patient receives a high-fat food challenge is appropriate

**Table 2** Comparison of diagnostic criteria for chylothorax and pseudochylothorax

Condition	Chylothorax	Pseudochylothorax
Diagnostic criteria		
Pleural fluid triglyceride level	>110 mg/dL (>1.24 mmol/L)	<50 mg/dL (<0.56 mmol/L)
Pleural fluid cholesterol level	<200 mg/dL (<5.18 mmol/L)	>200 mg/dL (>5.18 mmol/L)
Pleural fluid to serum triglyceride level	>1	<1
Pleural fluid to serum cholesterol level	<1	>1
Additional confirmatory diagnostic criteria		
Presence of chylomicrons in pleural fluid	Yes	No
Presence of cholesterol crystals in pleural fluid	No	Yes
Classic appearance of pleural fluid	Milky white or opalescent (Note: the absence of this appearance does not exclude chylothorax)	Milky white or opalescent

# DIFFERENTIAL DIAGNOSIS

## Milky fluid

**Cholesterol effusion** — A cholesterol effusion can be easily distinguished from chylothorax by demonstrating an elevated cholesterol level  $\geq 200$  mg/dL ( $\geq 5.18$  mmol/L) and a cholesterol to triglyceride (TG) ratio  $> 1$  in the pleural fluid, neither of which should be present in patients with a chylothorax. In addition, while in chylothorax the TG level is typically  $> 110$  mg/dL (1.24 mmol/L), in a cholesterol effusion, the TG level is typically below 110 mg/dL (1.24 mmol/L); however, **high TG levels can be seen in 25 percent of patients with cholesterol effusions. Chylomicrons, which are characteristic of chylothoraces,** are absent in those with a cholesterol effusion.

## Empyema

## Tube feed or lipid leak

# IDENTIFYING THE CAUSE

## Focused evaluation and testing

### History and physical examination

The clinician should inquire about **recent or distant trauma** (particularly chest trauma), **medical procedures** (eg, central venous catheterization, esophageal/variceal embolectomy), **radiation**, and **surgery**. Clinicians should also inquire about **symptoms** suggestive of **lymphoma** (eg, sweats, weight loss, lymphadenopathy) and metastatic cancer (cough, hemoptysis, change in bowel habits, weight loss, decreased appetite) and look for features of anatomic anomalies of the lymphatic system (eg, lymphedema) as well as subtle features of tuberous sclerosis complex (eg, facial angiomas, subungual fibromas or history of pneumothorax to suggest lymphangiomyomatosis [LAM]), Down syndrome (intellectual disability, frontal bossing, low set ears), or Noonan syndrome (short stature, murmur, deafness, lymphedema, webbed neck). An evaluation of skin and joints for signs of a connective tissue disorder (CTD; eg, systemic lupus erythematosus) and an evaluation of the neck for a goiter (potentially obstructing the thoracic duct), or signs of superior vena cava syndrome (venous distention and raised jugular venous pressure) are also appropriate. A travel history should be obtained (eg, suspected filariasis) and, although rare, a history of intermittent diarrhea and edema (suspected protein-losing enteropathy) should be sought.

**Chest and abdominal CT** — Clinicians should also re-evaluate previous chest imaging . Although conventional chest radiography can identify the side with the effusion, it is usually not helpful in determining the underlying etiology unless a radiograph shows signs of malignancy, nonmalignant masses, or trauma. If not already performed, non-contrast-enhanced CT of the thorax, abdomen, and pelvis should be performed and may identify the following :

- Mediastinal and retroperitoneal lymphadenopathy or masses
- Abdominal or pelvic fluid suggestive of chylous ascites
- Course of the thoracic duct (to identify a potential site for a leak or an obstructing lesion such as mediastinal or retroperitoneal lymphadenopathy)
- Cystic lesions of the thoracic duct suggestive of retroperitoneal or mediastinal lymphangioliomyoma
- Mediastinal (eg, substernal goiter, vascular thrombosis), cardiac (eg, constrictive pericarditis), or pulmonary abnormalities (eg, pulmonary cysts and renal angiomyolipoma as manifestations of LAM)
- Potential iatrogenic complications responsible for a perforated thoracic duct (eg, misplaced central line placement)

CT can also assist in preoperative planning for interventional or surgical procedures for the treatment of chylothorax.

# Laboratory testing

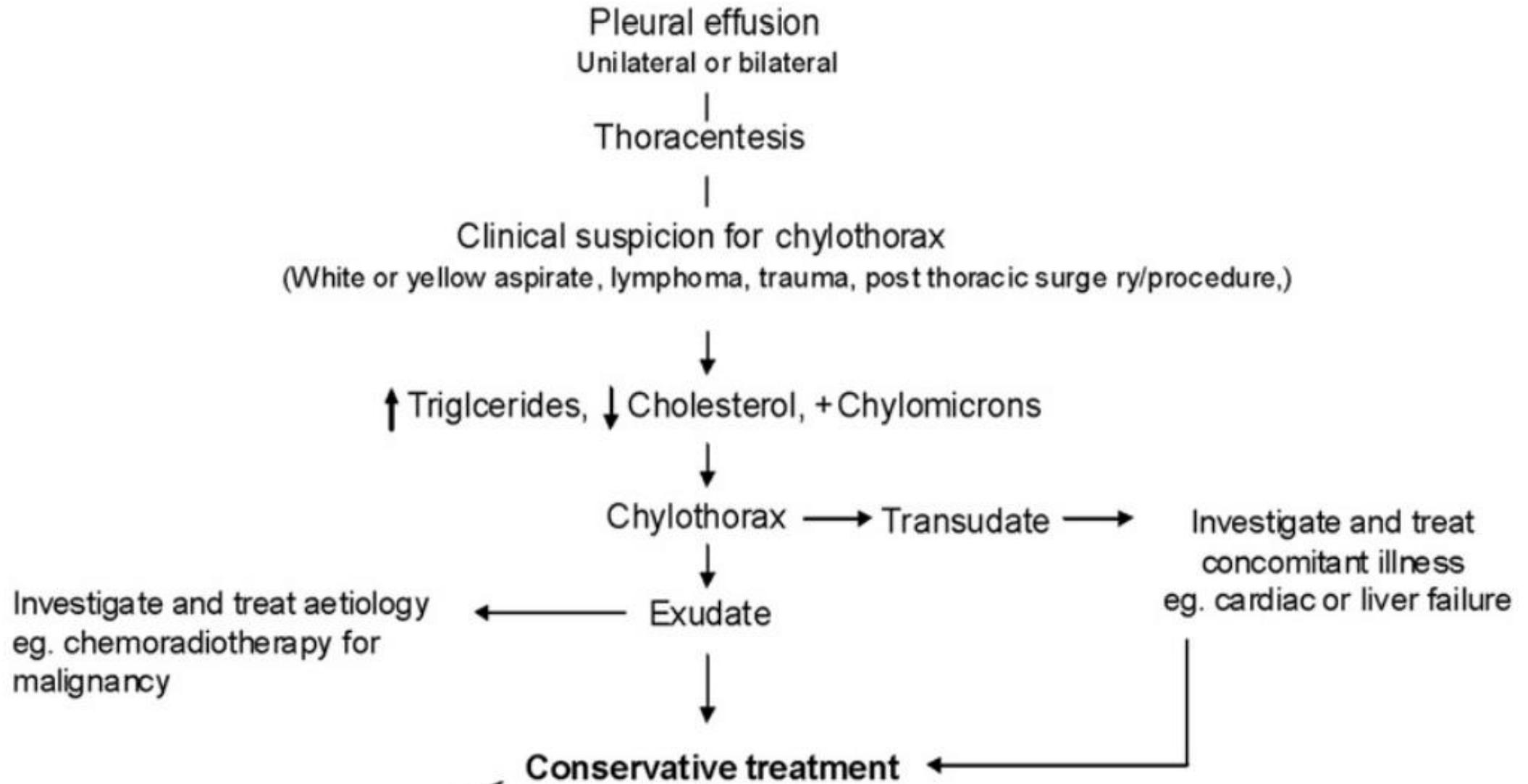
Additional laboratory tests that should be performed routinely include peripheral eosinophil count (eg, suspected filariasis) and liver function tests (eg, suspected cirrhosis) while etiology-specific laboratory tests are only performed when rare specific etiologies are suspected (eg, vascular endothelial growth factor [VEGF]-D level for LAM)

# Other etiology-specific testing

- Echocardiography (suspected constrictive pericarditis)
- VEGF-D or pleural fluid cytology (suspected LAM)
- Angiotensin-converting enzyme level (suspected sarcoidosis)
- CTD screen (suspected CTD; eg, rheumatoid factor, anti-double-stranded DNA, anti-Scl-70)
- Tuberculin skin testing
- Circulating filarial antigen or blood smears (suspected filariasis)

# **Advanced lymphatic imaging**

When the cause of the chylothorax remains unknown after the initial evaluation or when symptomatic patients with a known cause do not respond to disease-specific therapy (eg, therapy for a lymphoma) or conservative management of chylothorax (eg, nutritional therapy), advanced lymphatic imaging can detect the source of chyle leakage and provide a therapeutic intervention, such as lymphatic embolization, to resolve the effusion.



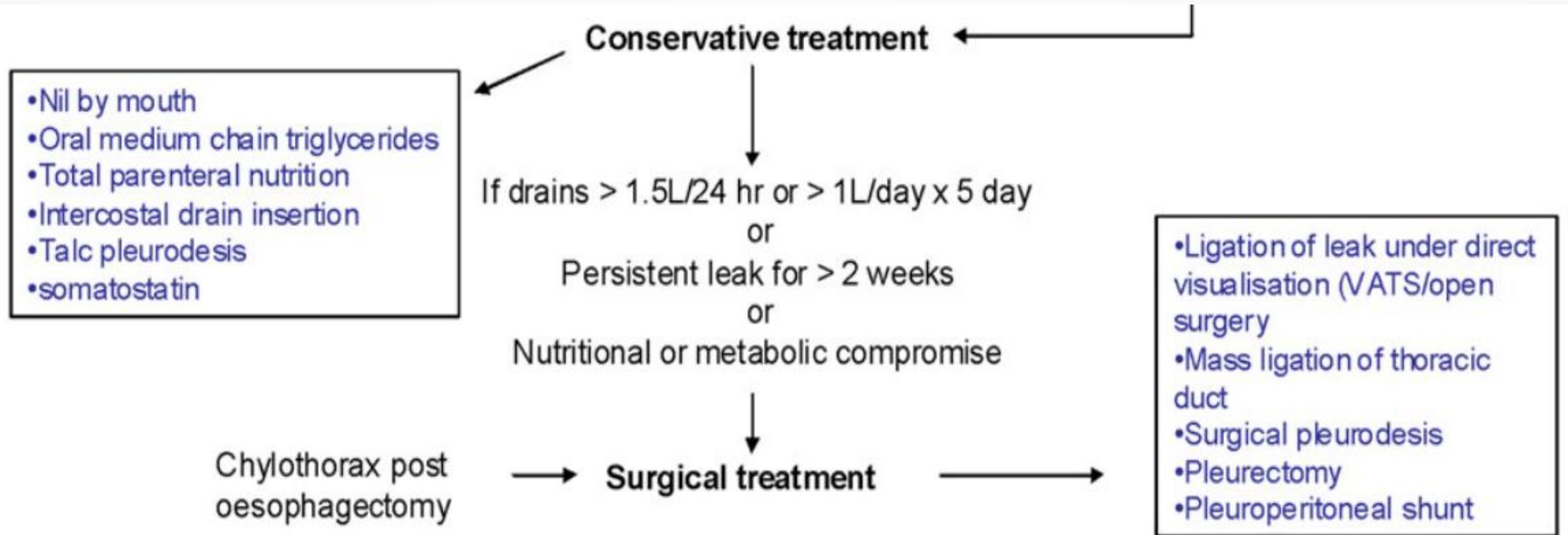
# Treatment

Treatment can be classified under 3 categories

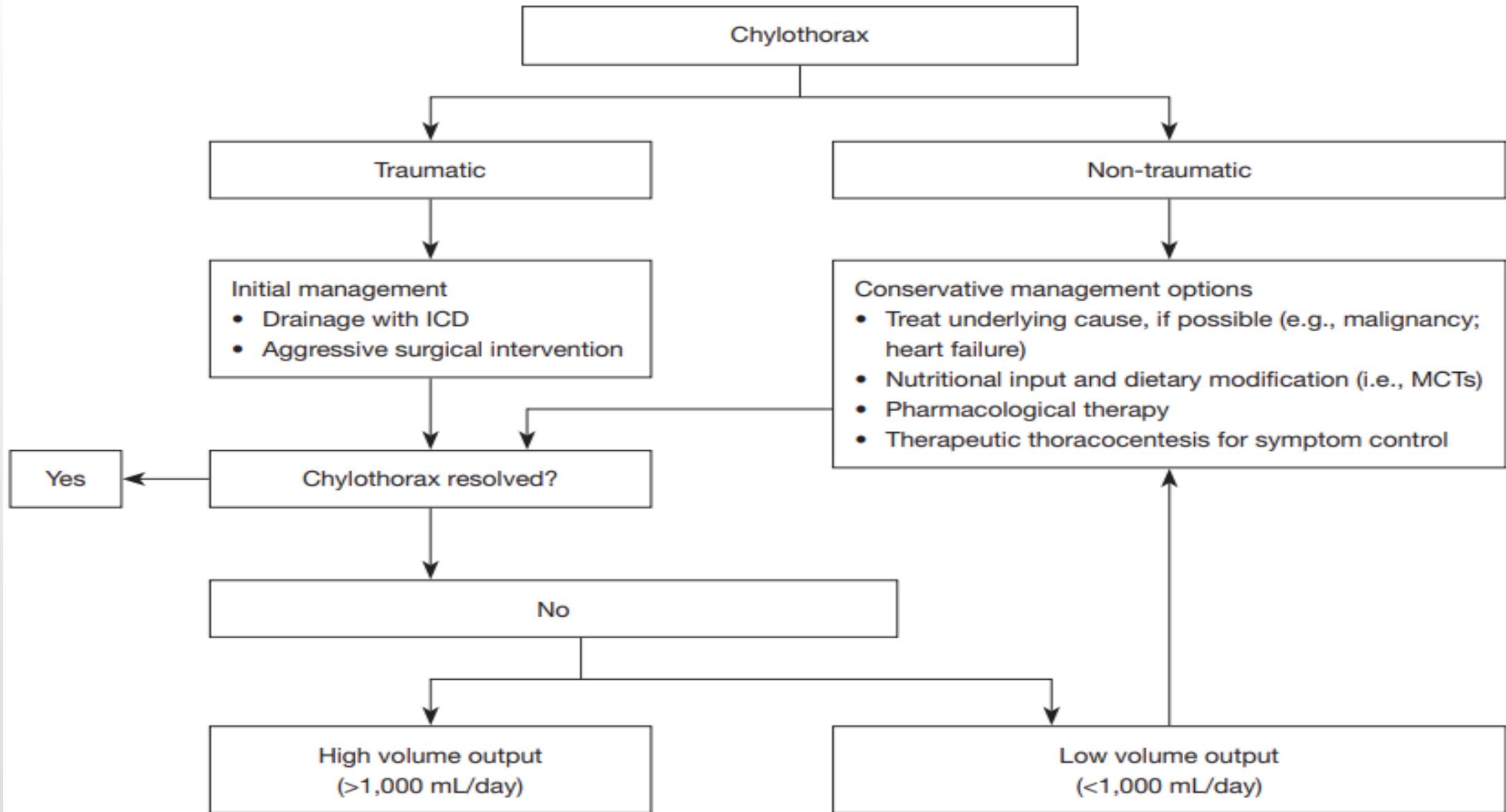
1 treatment of the underlying condition

2 conservative management

3 surgical management



**Figure 4** Recommended treatment pathway for chylothorax.



Multidisciplinary team discussion of appropriate management options  
(including suitability for surgical intervention)

Chemical  
pleurodesis

IPC

Radiological thoracic  
duct embolization

Pleuroperitoneal/  
pleurovenous shunt

Surgical thoracic  
duct ligation

**multi-disciplinary approach is crucial, involving respiratory physicians, thoracic surgeons, oncologists, dieticians, and pharmacists**

**In general, a conservative approach, including drainage of the effusion, nutritional modifications, and pharmacological adjuncts, is adopted first line for a limited period of time, before more invasive interventional measures are considered**

**Conservative approaches Treatment should be directed towards the underlying cause of the chylothorax, if known. For instance, corticosteroids may be utilised in sarcoidosis;**

**Oral or enteral dietary modifications are often adopted first line in low output chylothorax**

**Patients should be assessed by dieticians and instructed to stay on a low or no-fat, high protein diet, ensuring that any fats ingested are MCTs**

**Total parenteral nutrition (TPN) may be adopted preferentially in high output chylothorax, as a major reduction in chyle flow can encourage healing of the leak and avert acute nutritional deficiencies**

# Pharmacological therapies

somatostatin was administered either by intravenous infusion 6 mg/day for 2 weeks or by subcutaneous injection of 50 micrograms every 8 hours.

**midodrine 20 mg three times daily** and etilefrine, in the treatment of refractory, idiopathic and post-operative chylothorax (107-109). The numbers reported are very low, with the largest case series to date including only ten patients

# Pleural interventions

thoracocentesis, placement of an intercostal chest drain (ICD), or use of an indwelling pleural catheter (IPC).

Prolonged chest tube drainage can result in the loss of immunoglobulins, protein, and lymphocytes through chyle, thereby causing malnutrition and immunosuppression

As a general principle, pleural drainage via ICD is limited to less than 2 weeks and may be shortened further in more frail patients

there is no evidence to support preferential use of one size over the other

Chemical pleurodesis through ICD may be considered in patients that fail to improve with conservative management and are not candidates for surgery  
agents such as talc, bleomycin, tetracycline, povidone, elemene, and hypertonic glucose for this purpose

# **Surgical techniques**

**The typical criteria for surgery in patients undergoing initial conservative management include large daily chyle leak of more than 1.5 L in an adult, longer than 2 weeks of chest tube output, and rapidly declining nutritional status (125-127). By contrast, post-traumatic or post-surgical chylothorax requires aggressive early surgical intervention**

**The most commonly described surgical technique is that of thoracic duct ligation.**

**For refractory chylothoraces, pleuroperitoneal shunts (PPS) or pleurovenous shunts (PVS) may be considered**

**Interventional radiology** An alternative to the surgical approaches outlined above is thoracic duct embolization (TDE), which aims to seal the chyle leak at its site of origin.

# **Outcomes in chylothorax**

**The outcome for patients with chylothorax is heavily influenced by the underlying aetiology, and whether this can be successfully reversed.**

**However, the long-term outcomes for patients with non-traumatic chylothorax remain relatively poor**

# Key points for clinical practice

Chylothorax is a rare cause of pleural effusion which carries a high risk of mortality

Clinicians should consider the diagnosis in cases of pleural effusion with ongoing output of uncertain cause

The aetiology is wide ranging, but may be categorised broadly as either 'traumatic' or 'non-traumatic' in nature

In practice, diagnosis is based on demonstrating elevated pleural fluid triglyceride levels and reduced cholesterol levels in the presence of a characteristic milky fluid appearance

Occasionally, direct demonstration of chylomicrons within pleural fluid using lipoprotein electrophoresis is necessary to confirm the diagnosis Various imaging modalities (including CT and MR lymphangiography) may be utilised to support the diagnosis and identify the site of chyle leak Management is often challenging, involving a combination of conservative methods (e.g., dietary modification, medication, intermittent thoracocentesis) and more invasive radiological or surgical intervention (e.g., thoracic duct embolization or ligation)

In cases of persistent chyle leak, treatment decisions should be guided by adopting a multidisciplinary approach to optimise individual patient care



**thank you for your attention**

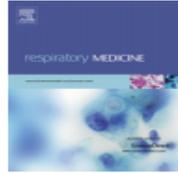
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available at [www.sciencedirect.com](http://www.sciencedirect.com)



journal homepage: [www.elsevier.com/locate/rmed](http://www.elsevier.com/locate/rmed)



REVIEW

## Chylothorax: Aetiology, diagnosis and therapeutic options

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## Non-traumatic chylothorax: diagnostic and therapeutic strategies

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Review Article

## Chylothorax: pathophysiology, diagnosis, and management —a comprehensive review

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