



Multidisciplinary management of adult patients with chylothorax: a consensus statement

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This consensus statement aims to provide multidisciplinary best practice statements to offer guidance in clinical decision making when managing adult patients with chylothorax, while also identifying gaps in knowledge and informing future research. <https://bit.ly/3zkNEgH>

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Abstract

The management of chylothorax remains challenging given the limited evidence and significant heterogeneity in practice. In addition, there are no practical guidelines on the optimal approach to manage this complex condition. We convened an international group of 27 experts from 20 institutions across five countries and four specialties (pulmonary, interventional radiology, thoracic surgery and nutrition) with experience and expertise in managing adult patients with chylothorax. We performed a literature and internet search for reports addressing seven clinically relevant PICO (Patient, Intervention, Comparison and Outcome) questions pertaining to the management of adult patients with chylothorax. This consensus statement, consisting of best practice statements based on expert consensus addressing these seven PICO questions, was formulated by a systematic and rigorous process involving the evaluation of published evidence, augmented with provider experience. Panel members participated in the development of the final best practice statements using the modified Delphi technique. Our consensus statement aims to offer guidance in clinical decision making when managing patients with chylothorax while also identifying gaps in knowledge and informing future research.

Introduction

Chylothorax is defined as the accumulation of chyle in the pleural space, resulting from obstruction or disruption of the thoracic duct or one of its major tributaries. Traumatic chylothorax conventionally

encompasses iatrogenic post-surgical causes such as after cardiothoracic surgeries or trauma that leads to injury to the thoracic duct. Malignancy is the most common cause of non-traumatic chylothorax [1, 2]. Patients with chylothorax, especially those with large-volume accumulation, can present with significant respiratory symptoms, with subacute dyspnoea being the most common symptom [3]. Prolonged high-output chylothorax is associated with high morbidity and mortality due to the consequent nutritional losses, associated immunocompromised state and large intravascular volume fluctuations. Thus, patients with chylothorax require close monitoring as well as aggressive interventions for both symptomatic relief and to prevent further complications. The existing evidence on chylothorax management is largely retrospective, predominantly single centre and skewed toward traumatic chylothorax. There are no guidelines, and consequently, there is significant heterogeneity in practice [1]. This is evidenced by a recent study that evaluated 77 patients with predominantly non-traumatic chylothorax [3]. In this study evaluating real-world practice, dietary measures were infrequently followed (36%), only 3% patients underwent lymphangiography and no patients underwent thoracic duct ligation (TDL) or thoracic duct embolisation (TDE) [3].

Thus, the aims of this multidisciplinary consensus statement are: 1) guidance for the management of patients with chylothorax, 2) address the knowledge gaps and 3) identify areas for future research. The scope of this document is limited to the multidisciplinary management of adult patients with either traumatic or non-traumatic chylothorax. The diagnostic approach, including laboratory tests, pleural fluid and serum studies and imaging modalities, is beyond the scope of this document. In addition, our best practice statements specifically address the management of chylothorax, and may not be extrapolated to that of chylous ascites. Medical management of chylothorax refers to conservative measures such as dietary modification, pharmacological therapy or use of total parenteral nutrition (TPN). Definitive interventions for chylothorax include surgical TDL or image-guided TDE. We refer to leaks as high or low output if >500 or <500 mL·day⁻¹, respectively. Leaks that persevere for >2 weeks are considered as persistent in this document. These empiric cut-offs cannot be extrapolated to every clinical scenario, and management pathways are best determined by physicians at the bedside evaluating trends in daily output.

Methods

This consensus statement on managing adult patients with chylothorax was developed using a comprehensive and systematic approach, involving global experts. The methodology utilised the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist to search and synthesise the evidence. The core writing group (A. Agrawal, U. Chaddha, S. Shojaei, G. Nadolski, M. Liberman and F. Maldonado) formulated seven clinically pertinent PICO (Patient, Intervention, Comparison and Outcome) questions relevant to the management of chylothorax in adults. These questions were designed to guide the literature review and evidence synthesis. An exhaustive literature search was conducted using PubMed. The search strategy included a combination of MeSH (Medical Subject Headings) terms, and selected studies are presented in the supplementary material. The PRISMA flow diagram (figure 1) illustrates the process of study selection, including the number of records identified, screened, included and excluded, along with reasons for exclusion at each stage. The search covered the time period from 1 January 1980 to 29 August 2023.

We included studies that involved the management of adult patients with chylothorax, as our research questions specifically pertained to this demographic. Paediatric cases were excluded to maintain relevance to the adult population. We included primary research studies that provided empirical data relevant to our PICO framework. This ensured that the evidence directly addressed our research questions. We excluded reviews and commentaries to ensure that our analysis was based on original research findings rather than secondary interpretations. Non-human studies were excluded as our focus was on human clinical outcomes. Studies that did not align with specific populations, interventions or outcomes as defined by our PICO framework were excluded. We excluded case reports and series of fewer than 10 patients if studies with better evidence were available to minimise potential biases associated with smaller sample sizes. If further robust prospective and retrospective data were available for the PICO question, we excluded smaller series and case reports. If no robust prospective or retrospective data were available, then smaller series and reports were evaluated to guide best practice statements. Statistical analysis was not performed due to the heterogeneity of study designs, interventions and outcomes, and lack of sufficient data.

Once the records were identified, the core group formulated summary of evidence tables based upon the studies. These were then used to formulate the best practice statements based upon the available evidence along with the rationale for the same. Summary of evidence tables for each PICO question, outcomes evaluated and risk of bias evaluations (using the Newcastle–Ottawa Scale) are provided in the supplementary material.

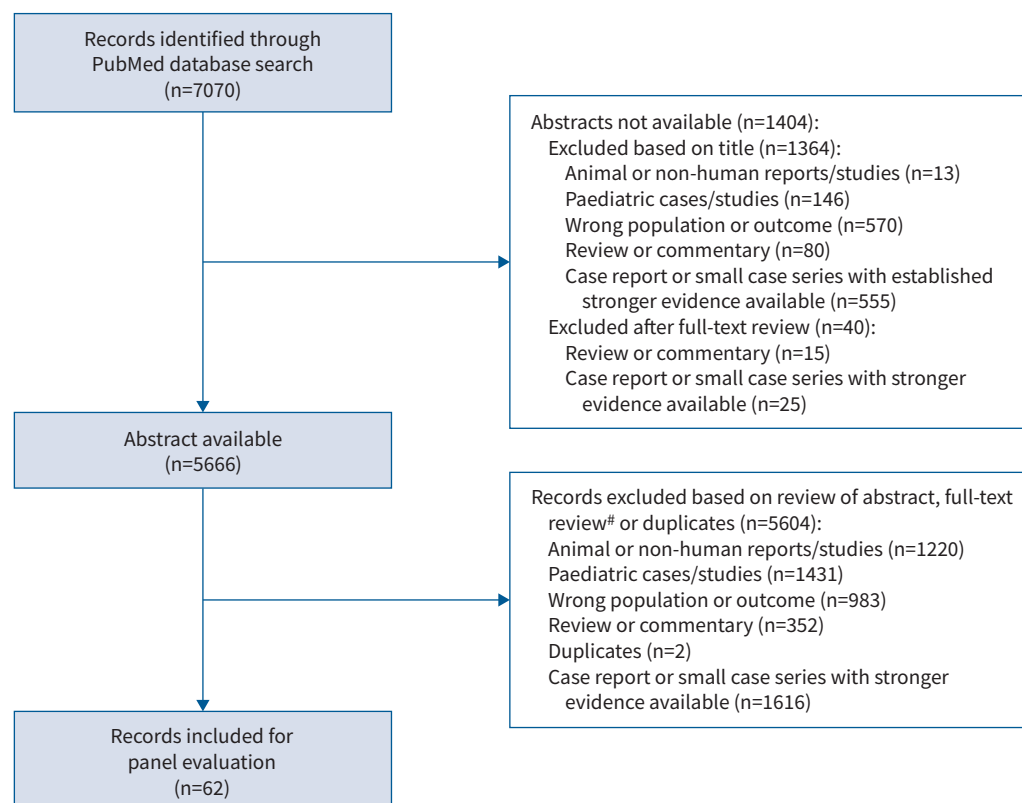


FIGURE 1 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram for management of adult patients with chylothorax. Search Strategy (PubMed): (("Chylothorax" OR "Chylothoraces" OR "Chylothoraxes" OR "Chyle" OR "Chylous" OR "Thoracic Duct Injury" OR "Thoracic Duct Ligation" OR "Thoracic Duct Embolization" OR "Thoracic Duct Disruption")). Search time period: 1 January 1980 to 29 August 2023. #: wherever adequate information was not available from the abstract, a full-text review was performed.

Consensus methodology

A multidisciplinary core writing group first drafted distinct statements as part of this position paper which was circulated among all panel members, inviting opinion as well as any additional suggestions. The multidisciplinary panel of 27 experts included 12 pulmonologists, seven interventional radiologists, seven thoracic surgeons and one nutritionist from 20 hospitals across five countries (USA, Canada, England, Australia and India), all of whom have experience managing chylothorax. The document was revised based on comments from all 27 members and subsequently discussed during a conference call, with 56% participation (15 members). During the conference call, individual suggestions were reviewed and incorporated in real time. The modified Delphi technique, a widely accepted method for developing consensus among experts, was used [4–6]. A survey that incorporated the questions and revised statements was sent to all panel members. The panel anonymously and independently rated the appropriateness of the statements on a 5-point Likert scale. Consensus was defined *a priori* as $\geq 70\%$ agreement (4 or 5 on the Likert scale), with a minimal response rate of 80%. The results of the survey were tallied and reported to the group. There was 100% survey participation and consensus was achieved on all best practice statements (tables 1 and 2).

PICO Question 1: In patients with chylothorax, should dietary modifications be implemented?

Best practice statements based on expert consensus

- In patients with traumatic chylothorax, we suggest that dietary modifications be implemented in all patients to reduce volume of chyle leak
- In patients with non-traumatic chylothorax, we suggest that dietary modifications be considered in all patients to reduce volume of chyle leak
- When dietary modifications are implemented, we suggest that a high-protein and low-fat diet incorporating medium-chain triglycerides (MCTs) be used

TABLE 1 Survey data assessing agreement with best practice statements based on expert consensus[#]

Best practice statements based on expert consensus	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
PICO Question 1 <ul style="list-style-type: none"> In patients with traumatic chylothorax, we suggest that dietary modifications be implemented in all patients to reduce volume of chyle leak In patients with non-traumatic chylothorax, we suggest that dietary modifications be considered in all patients to reduce volume of chyle leak When dietary modifications are implemented, we suggest that a high-protein and low-fat diet incorporating medium-chain triglycerides be used In patients with high-volume traumatic chylothorax refractory to medical management and definitive surgical or percutaneous lymphatic interventions, we suggest that total parenteral nutrition with strict <i>nil per os</i> be considered 				10 (37%)	17 (63%)
PICO Question 2 <ul style="list-style-type: none"> We suggest that pharmacological agents not be routinely used in the management of chylothorax We suggest that use of somatostatin analogues such as octreotide be considered in selected patients with chylothorax that is refractory to optimal dietary modifications and tube thoracostomy, in whom definitive surgical or percutaneous lymphatic interventions are not feasible or have failed 			1 (3.8%)	12 (46.2%)	13 (50%)
PICO Question 3 <ul style="list-style-type: none"> In hospitalised patients with recurrent, symptomatic chylothorax, we suggest that tube thoracostomy be considered for effusion management We suggest that symptom-guided thoracentesis be considered for the outpatient management of recurrent low-volume chylothorax 				14 (53.8%)	12 (46.2%)
PICO Question 4 <ul style="list-style-type: none"> In patients with high-volume post-operative chylothorax, we suggest that TDL be pursued as the first-line definitive intervention In patients with persistent, low-volume post-operative chylothorax despite optimal medical management, we suggest that either TDL or TDE be pursued based on local expertise In patients with a high-volume or persistent chylothorax after a blunt or penetrating trauma, we suggest that either TDL or TDE be pursued based on local expertise In patients with traumatic chylothorax who are not surgical (or re-operative) candidates or in whom TDL is unsuccessful, we suggest that TDE be pursued 	1 (3.8%)		2 (7.7%)	14 (53.8%)	9 (34.6%)
PICO Question 5 <ul style="list-style-type: none"> In patients with high-volume non-traumatic chylothorax that is persistent despite optimal medical management, we suggest that a diagnostic lymphangiogram plus TDE be pursued as the first-line definitive intervention 			1 (3.8%)	12 (46.2%)	13 (50%)
PICO Question 6 <ul style="list-style-type: none"> In patients undergoing TDL, we suggest that concurrent pleurodesis not be routinely performed In patients undergoing surgery, if the site of chyle leak cannot be convincingly identified, we suggest that concurrent mechanical or chemical pleurodesis be considered 	1 (3.8%)		2 (7.7%)	15 (57.7%)	8 (30.8%)

Continued

TABLE 1 Continued					
Best practice statements based on expert consensus	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
PICO Question 7 <ul style="list-style-type: none">In patients with high-volume chylothorax that is refractory to medical, surgical and percutaneous lymphatic interventions, we suggest that interventions aimed at symptom control such as pleuro-peritoneal or pleuro-venous shunt or IPC be consideredIn patients with persistent, low-volume non-traumatic chylothorax that is likely to respond to disease-directed treatment, we suggest that interim symptom control with an IPC be considered		1 (3.8%)		16 (61.5%)	9 (34.6%)
PICO: Patient, Intervention, Comparison and Outcome; TDL: thoracic duct ligation; TDE: thoracic duct embolisation; IPC: indwelling pleural catheter. #: there was 100% survey participation (27 members) and consensus was achieved on all questions (table 2). 26 members participated in answering all questions, while input from the nutritionist member of the group was included for PICO Question 1.					

- In patients with high-volume traumatic chylothorax refractory to medical management and definitive surgical or percutaneous lymphatic interventions, we suggest that total parenteral nutrition (TPN) with strict *nil per os* (NPO) be considered

Remark: All patients should have a nutrition consultation, if available, to help develop a nutrition plan.

Literature review

Dietary modifications can reduce the volume of chyle production, which in turn allows for any present lymphatic injury site to heal, potentially avoiding additional invasive interventions. NPO should lead to near-complete cessation of chyle flow. A MCT diet can be used to provide essential fatty acids as they bypass the lymphatic system and can be absorbed directly through the portal vein. A high-protein diet is recommended due to losses of protein from the chyle, as well as to assist with meeting overall caloric needs.

In small studies of chylothorax post-lung resection, about two-thirds of patients responded to either complete cessation of oral intake and TPN [7] or low-fat diet (<10 g·day⁻¹) [8]. In a more recent study of 37 patients who developed post-operative chylothorax, chyle output dropped to <500 mL·day⁻¹ in 76% (28 out of 37) of patients 24 h after institution of a low-fat diet [9].

Cessation of the fat-containing enteral diet and institution of TPN prevented surgical intervention in 36% (28 out of 77) of patients in a relatively large series of post-operative (all-comers) chylothorax [10], similar to other small, retrospective post-operative chylothorax series using TPN with NPO [11, 12]. A systematic review that assessed various nutritional management strategies in patients with chylous ascites and/or chylothorax revealed that while 72% of patients responded to conservative measures, there was no significant difference between the type of dietary intervention and the rate of resolution [13]. This study did not evaluate outcomes based on the aetiology of the chylothorax. In addition, some patients also received non-nutritional interventions such as chemical pleurodesis, diuretics and somatostatin which likely confounded the outcomes.

Rationale

Medical management remains the first-line approach for patients with traumatic and non-traumatic chylothorax, with dietary modifications forming the cornerstone of this approach in most scenarios. Dietary modifications should be considered when the chyle leak may spontaneously resolve (*e.g.* iatrogenic). Retrospective studies have suggested that dietary modifications play a significant role in patients with traumatic chylothorax and may reduce the need for surgical intervention. While data are limited for non-traumatic chylothorax, these suggestions may be extrapolated to this group. However, caution must be exercised in malnourished patients. Fat-soluble vitamin supplementation and essential fatty acid supplementation equal to 2–4% of daily caloric intake are recommended in patients with prolonged restricted diets, as deficiencies can occur in as little as after 5 days of treatment.

A low-fat diet with MCTs is associated with better tolerance and lower risk of complications compared to TPN. In patients who do not respond to dietary modifications, TPN may be considered on a case-by-case basis, especially in patients with traumatic chylothorax.

TABLE 2 PICO (Patient, Intervention, Comparison and Outcome) questions and best practice statements based on expert consensus

PICO Question	Best practice statements
PICO Question 1: In patients with chylothorax, should dietary modifications be implemented?	<ul style="list-style-type: none"> In patients with traumatic chylothorax, we suggest that dietary modifications be implemented in all patients to reduce volume of chyle leak In patients with non-traumatic chylothorax, we suggest that dietary modifications be considered in all patients to reduce volume of chyle leak When dietary modifications are implemented, we suggest that a high-protein and low-fat diet incorporating medium-chain triglycerides be used In patients with high-volume traumatic chylothorax refractory to medical management and definitive surgical or percutaneous lymphatic interventions, we suggest that total parenteral nutrition with strict <i>nil per os</i> be considered <p><i>Remark: All patients should have a nutrition consultation, if available, to help develop a nutrition plan.</i></p>
PICO Question 2: In patients with chylothorax, should pharmacological therapy to reduce chyle flow be initiated?	<ul style="list-style-type: none"> We suggest that pharmacological agents not be routinely used in the management of chylothorax We suggest that use of somatostatin analogues such as octreotide be considered in selected patients with chylothorax that is refractory to optimal dietary modifications and tube thoracostomy, in whom definitive surgical or percutaneous lymphatic interventions are not feasible or have failed
PICO Question 3: In patients with chylothorax, what is the optimal pleural drainage strategy?	<ul style="list-style-type: none"> In hospitalised patients with recurrent, symptomatic chylothorax, we suggest that tube thoracostomy be considered for effusion management <p><i>Remark: When chest tube placement is being considered, we suggest using a small-bore tube (≤ 14 F).</i></p> <ul style="list-style-type: none"> We suggest that symptom-guided thoracentesis be considered for the outpatient management of recurrent low-volume chylothorax <p><i>Remark: In selected patients, indwelling pleural catheters (IPCs) may be considered as highlighted in PICO Question 7.</i></p>
PICO Question 4: In patients with traumatic chylothorax, should thoracic duct ligation (TDL) or thoracic duct embolisation (TDE) be pursued as the first-line definitive intervention?	<ul style="list-style-type: none"> In patients with high-volume post-operative chylothorax, we suggest that TDL be pursued as the first-line definitive intervention <p><i>Remark: TDE is a safe and effective alternative to TDL even in post-operative cases and may be considered as a first-line approach on a case-by-case basis after multidisciplinary discussion based upon local expertise.</i></p> <ul style="list-style-type: none"> In patients with a high-volume or persistent chylothorax after a blunt or penetrating trauma, we suggest that either TDL or TDE be pursued based on local expertise <p><i>Remark: We suggest a multidisciplinary approach to treatment.</i></p> <ul style="list-style-type: none"> In patients with persistent, low-volume post-operative chylothorax despite optimal medical management, we suggest that either TDL or TDE be pursued based on local expertise In patients with traumatic chylothorax who are not surgical (or re-operative) candidates or in whom TDL is unsuccessful, we suggest that TDE be pursued <p><i>Remark: Traumatic chylothorax encompasses both post-operative (or iatrogenic) cases and those secondary to blunt or penetrating trauma.</i></p>
PICO Question 5: In patients with non-traumatic chylothorax, should TDL or TDE be pursued as the first-line definitive intervention?	<ul style="list-style-type: none"> In patients with high-volume non-traumatic chylothorax that is persistent despite optimal medical management, we suggest that a diagnostic lymphangiogram plus TDE be pursued as the first-line definitive intervention <p><i>Remark: In non-traumatic chylothorax that is being considered for a definitive intervention, the priority must be to localise the chyle leak to guide interventions. The choice of intervention depends upon identification of the site(s) of chyle leak on lymphatic studies, local expertise and the patient's surgical candidacy. We suggest a multidisciplinary approach to these cases. Early referral to centres of expertise should be considered.</i></p>

Continued

TABLE 2 Continued	
PICO Question	Best practice statements
PICO Question 6: In patients being considered for surgical management of chylothorax, should mechanical or chemical pleurodesis be performed in addition to TDL?	<ul style="list-style-type: none">In patients undergoing TDL, we suggest that concurrent pleurodesis not be routinely performedIn patients undergoing surgery, if the site of chyle leak cannot be convincingly identified, we suggest that concurrent mechanical or chemical pleurodesis be considered <p><i>Remark: In patients with chylothorax being managed with tube thoracostomy who are not (re-)operative candidates and in whom percutaneous lymphatic interventions are not feasible or unsuccessful, talc slurry for pleurodesis can be considered on a case-by-case basis after multidisciplinary discussion.</i></p>
PICO Question 7: In symptomatic patients with chylothorax that is refractory to optimal medical management, is there a role of pleuro-peritoneal or pleuro-venous shunt or indwelling pleural catheter (IPC) placement?	<ul style="list-style-type: none">In patients with high-volume chylothorax that is refractory to medical, surgical and percutaneous lymphatic interventions, we suggest that interventions aimed at symptom control such as pleuro-peritoneal or pleuro-venous shunt or IPC be consideredIn patients with persistent, low-volume non-traumatic chylothorax that is likely to respond to disease-directed treatment, we suggest that interim symptom control with an IPC be considered <p><i>Remark: The choice between shunt and IPC placement depends upon patient preference and local expertise. If expertise in percutaneous lymphatic or surgical interventions is not available, consider transfer to a tertiary care centre that can provide multidisciplinary care. IPC placement can be considered as a temporising measure for symptomatic relief.</i></p> <p><i>Remark: The drainage frequency of IPCs in these patients should be “symptom-guided”. In patients in whom the re-accumulation rate is slow, serial thoracentesis may be a better option, depending upon patient preference.</i></p>

Because diet should be individualised and adequate nutritional supplementation provided, a nutrition consultation is suggested for all patients. Dietary modifications may be difficult to adhere to, and compliance with the intervention is hard to assess in the published retrospective data.

PICO Question 2: In patients with chylothorax, should pharmacological therapy to reduce chyle flow be initiated?

Best practice statements based on expert consensus

- We suggest that pharmacological agents not be routinely used in the management of chylothorax
- We suggest that use of somatostatin analogues such as octreotide be considered in selected patients with chylothorax that is refractory to optimal dietary modifications and tube thoracostomy, in whom definitive surgical or percutaneous lymphatic interventions are not feasible or have failed

Literature review

Somatostatin analogues reduce gastric, biliary and pancreatic secretions and constrict smooth muscles in the splanchnic and lymphatic vessels, thereby decreasing lymph production and flow. Other drugs such as orlistat, etilefrine and midodrine have also been used in the management of chylothorax. Orlistat inhibits gastric and pancreatic lipase in the gastrointestinal tract to reduce absorption of fats. Midodrine and etilefrine cause vasoconstriction of the lymphatic system, which can help reduce drainage in patients with high-output chylothorax. The data supporting the use of midodrine, etilefrine and orlistat are limited to case reports and small retrospective series [14–17].

A 2015 systematic review of 19 studies that assessed the use of octreotide in patients with post-operative chylothorax concluded that it is effective in the management of moderate to large chylothorax [18]. A study of 41 patients with chylothorax following pulmonary resections and lymphadenectomy reported a success rate of 90% (37 out of 41) in reducing chyle production with octreotide [19]. It is unclear whether the chylothorax was high or low volume in these cases. In another retrospective study of 20 patients with post-oesophagectomy-related chylothorax, the success rate was higher in those who received octreotide compared to those who did not (87% versus 40%; p=0.03) [20]. Other than these two studies, the systematic review included mainly case reports and animal studies [18–20].

Rationale

Routine use of pharmacological therapy cannot be recommended based on current evidence. The limited data for pharmacological therapy come from the use of octreotide in post-operative chylothorax, with a majority of the benefit seen early in the course. In patients with traumatic chylothorax, it is reasonable to consider somatostatin analogues as adjunct therapy as a last resort for refractory cases, although the evidence for their use remains largely anecdotal. Among all the agents tried, use of somatostatin analogues is the most described. Local availability and cost considerations must be factored into such decision making on a case-by-case basis. Further studies are needed to clarify the role, if any, of these agents. Somatostatin analogue use is not a part of routine clinical practice of the majority of authors on this document.

PICO Question 3: In patients with chylothorax, what is the optimal pleural drainage strategy?

Best practice statements based on expert consensus

- In hospitalised patients with recurrent, symptomatic chylothorax, we suggest that tube thoracostomy be considered for effusion management

Remark: When chest tube placement is being considered, we suggest using a small-bore tube (≤ 14 F).

- We suggest that symptom-guided thoracentesis be considered for the outpatient management of recurrent low-volume chylothorax

Remark: In selected patients, indwelling pleural catheters (IPCs) may be considered as highlighted in PICO Question 7.

Literature review

Post-operative chylothorax is usually high output and benefits from tube thoracostomy for symptom relief (and to avoid frequent thoracenteses) [10, 11, 21, 22]. The rate of chyle accumulation in patients with a non-traumatic effusion is more variable, and serial thoracenteses may be preferred in some cases. In a study of 34 patients with non-traumatic chylothorax, periodic thoracentesis was used in 62% (21 out of 34) of patients [23]. While pleural drainage alone may be reasonable as a first step in these patients, surgical or percutaneous lymphatic interventions are often needed.

Rationale

In this statement, “recurrent” indicates those effusions that recur after the initial complete removal of fluid via a thoracentesis that confirms a chylothorax. Our suggestions on chest tube placement are for those in whom there is no already existing tube *in situ* (e.g. post-operative patients). Chest tubes not only obviate the need for repeated thoracenteses, but also allow the clinician to accurately monitor the rate of fluid re-accumulation. Prolonged high-output chyle evacuation via a chest tube can, however, have the potential downside of leading to nutritional deficiencies and immune suppression. Serial thoracenteses may be considered for slowly accumulating effusions and based on patient and provider preferences [1]. “Slow” is loosely defined and best assessed at the bedside as a function of output and patient symptoms.

There are no studies evaluating the optimal chest tube size in patients with chylothorax, although the use of small-bore chest tubes (≤ 14 Fr) has been described in case series [24–26]. Experience with chest tube size in other pleural effusions and extrapolating data from studies with other aetiologies of non-malignant pleural effusions suggests that a well-positioned, small-bore chest tube should suffice [27–29].

PICO Question 4: In patients with traumatic chylothorax, should thoracic duct ligation (TDL) or thoracic duct embolisation (TDE) be pursued as the first-line definitive intervention?

Best practice statements based on expert consensus

- In patients with high-volume post-operative chylothorax, we suggest that TDL be pursued as the first-line definitive intervention

Remark: TDE is a safe and effective alternative to TDL even in post-operative cases and may be considered as a first-line approach on a case-by-case basis after multidisciplinary discussion based upon local expertise.

- In patients with a high-volume or persistent chylothorax after a blunt or penetrating trauma, we suggest that either TDL or TDE be pursued based on local expertise

Remark: We suggest a multidisciplinary approach to treatment.

- In patients with persistent, low-volume post-operative chylothorax despite optimal medical management, we suggest that either TDL or TDE be pursued based on local expertise

- In patients with traumatic chylothorax who are not surgical (or re-operative) candidates or in whom TDL is unsuccessful, we suggest that TDE be pursued

Remark: Traumatic chylothorax encompasses both post-operative (or iatrogenic) cases and those secondary to blunt or penetrating trauma.

Literature review

Surgical management of chylothorax usually involves ligating the thoracic duct or one of its culprit tributaries, using a minimally invasive approach (video-assisted or robotic-assisted thoracic surgery). Identification of the site of leak can be facilitated by giving the patient cream/fat prior to the surgery, or subcutaneously injecting a lipophilic dye such as Sudan black, indocyanine green or methylene blue [30–32]. Duct ligation can be supplemented with pleurodesis at the end of the surgery.

In one of the first large reports of post-operative chylothorax, 72% (34 out of 47) of patients failed medical management and needed a re-operation, which was successful in 91% [11]. An initial oesophageal surgery (89% (24 out of 27)) and chylous output of $>1000 \text{ mL} \cdot \text{day}^{-1}$ for 7 days predicted the need for re-operation. The need for re-operation for chylothorax after pulmonary resection is reportedly lower (19–57%) than after oesophageal surgery [12, 33]. Small case series have suggested that early surgery may reduce the high mortality rate in patients who have a chylothorax after oesophageal surgery [34–36]. Complications with re-operation, such as prolonged air leak, atrial fibrillation or prolonged ventilation, were noted in up to a third of patients in an older series; however, mortality remains low [11]. The development of chylous ascites after TDL has rarely been reported [37].

In a more recent 2018 report of 97 patients with post-operative chylothorax, TDL was successful in 85% (44 out of 52) [10]. Interestingly, the duct could be clearly identified in only 63% (33 out of 52), with mass ligation being performed in the remaining 37% (19 out of 52). Four percent of the surgical cohort (two out of 52) required TDE as a salvage procedure. Among those who underwent a diagnostic lymphangiogram, a leak could be identified in 85% (34 out of 40). However, the cisterna chyli could be cannulated in only 48% (19 out of 40), and TDE was successful in 79% (15 out of 19). Eight percent (three out of 40) needed TDL as a salvage procedure. Prior to the publication of this study, a 2017 meta-analysis of 407 patients undergoing lymphatic interventions (using pedal lymphangiography) for chylothorax reported that total occlusion of the lymphatic system could be achieved in 63%, and cessation of the chyle leak was achieved in 79% of these (with higher success in traumatic cases) [38]. Thoracic duct disruption (TDD) was attempted in 25% (77 out of 310) of patients who failed TDE and was successful in 61% (47 out of 77). TDD involves causing mechanical disruption of an adequately sized retroperitoneal lymphatic collateral(s) when the thoracic duct/cisterna chyli cannot be adequately identified or accessed. In a single-centre series, TDE was shown to successfully treat patients with persistent chylothorax after TDL with a reported clinical success rate of 90% (45 out of 50) [39]. The use of intranodal lymphangiography augmented by the use of pneumatic compression devices on the calves has resulted in improved rates of thoracic duct cannulation [40].

TDE, in general, is a safer alternative to TDL, with complications such as embolisation of the embolic agent to the lung being only rarely reported. Delayed complications of TDE such as chronic abdominal pain, diarrhoea and lower extremity oedema have been reported, but most patients do not describe these as disabling [41].

Rationale

Chylothorax remains an uncommon complication after thoracic surgery and trauma, with an incidence of $<3\%$ in both [42]. In post-operative cases, TDL is successful in $\sim 90\%$ and therefore may be considered over TDE in re-operative candidates [8, 10, 11, 22, 43]. However, reports of TDL for blunt or penetrating trauma are limited to case reports or series, and an extrapolation of the success of surgery to these cases cannot be made. There are no comparative data on TDL *versus* TDE. While an initial surgical approach is usually considered, the window to re-operate may be narrow and TDE has been shown to be successful even after failed TDL. Therefore, a multidisciplinary discussion on the best intervention remains key.

Patients post-oesophagectomy are likely to have injury to the main thoracic duct and not a tributary, and are therefore likely to have higher volumes of chyle leak. Thus, these patients are less likely to respond to medical management alone [10, 11, 21]. In cases with a high volume of chyle leak, an early (within 5 days) re-operation, before complications such as malnutrition and immune suppression ensue, may reduce operative complications [36, 44]. In addition, early in the post-operative period the pleural space may be free of adhesions, thereby allowing easier identification of the site of chyle leak [1]. Even for patients undergoing TDL, medical management should be continued in the peri-operative period. For patients managed without a re-operation [10], if the output persists, TDL or TDE should be pursued,

before complications of prolonged chyle leak ensue. TDE is a safe alternative to TDL in patients who fail TDL or are not (re-)operative candidates, and depending on local expertise may be considered before TDL on a case-by-case basis after multidisciplinary discussion [41]. Only when TDE is attempted but is technically unsuccessful can TDD be considered in as a salvage intervention during the same procedure; however, evidence for the same is limited.

PICO Question 5: In patients with non-traumatic chylothorax, should TDL or TDE be pursued as the first-line definitive intervention?

Best practice statement based on expert consensus

- In patients with high-volume non-traumatic chylothorax that is persistent despite optimal medical management, we suggest that a diagnostic lymphangiogram plus TDE be pursued as the first-line definitive intervention

Remark: In non-traumatic chylothorax that is being considered for a definitive intervention, the priority must be to localise the chyle leak to guide interventions. The choice of intervention depends upon identification of the site(s) of chyle leak on lymphatic studies, local expertise and the patient's surgical candidacy. We suggest a multidisciplinary approach to these cases. Early referral to centres of expertise should be considered.

Literature review

Published literature on definitive interventions for non-traumatic chylothorax is scarce. Based on subgroup analysis of small published series, definitive interventions such as TDL or TDE were needed in 25–50% of cases of non-traumatic chylothorax that fail conservative management [23, 45–48]. Surgical correction was needed in 56% (19 out of 34) of patients in one of the larger series in 2010; however, 50% (17 out of 34) of patients had re-accumulation or persistence of chylothorax at the end of the study period [23]. In a more recent 2023 study that evaluated practice patterns of primarily non-traumatic chylothorax, only 3% of the patients underwent a lymphangiogram and none of the patients underwent a TDE or TDL [3].

Lymphangiogram with viscous oil-based contrast agents is often performed to identify the site of chyle leak prior to definitive interventions. Interestingly, this alone may be sufficient to resolve the chyle leak in 30–70% of cases (including traumatic and non-traumatic patients) [49, 50]. In a large meta-analysis, technical success of TDE translated into clinical success in only 50% of patients [38]. Dynamic magnetic resonance (MR) imaging of the lymphatic system can characterise the location and source of lymphatic leaks prior to intervention. In a case series utilising MR lymphangiography to evaluate non-traumatic chylothorax, TDE was clinically successful in 93% (38 out of 41) of patients in whom the imaging revealed abnormal lymphatic flow [51].

Rationale

The most common causes of non-traumatic chylothorax are malignancy and primary lymphatic disorders creating malformed and/or aberrant lymphatic vessels in the chest, and many of these patients are poor surgical candidates due to either comorbidities or the diffuse nature of the leak. Furthermore, non-traumatic cases likely often involve thoracic duct tributaries, which may explain the lower success rates of TDL and TDE in these patients.

In patients with low chylous output, without complications, the need for any intervention over medical management should be based on the likelihood of response to aetiology-directed treatment. When response to disease-directed therapy or systemic anticancer therapy is expected (e.g. chylothorax secondary to lymphoma), symptom-guided effusion management should be pursued. Definitive management should be considered when the low output is persistent (>2 weeks) in a patient where limited treatment response is expected, or when high-volume chylous output continues for a prolonged period (>7 days), before complications ensue. Early referral to centres of expertise should be considered.

PICO Question 6: In patients being considered for surgical management of chylothorax, should mechanical or chemical pleurodesis be performed in addition to TDL?

Best practice statements based on expert consensus

- In patients undergoing TDL, we suggest that concurrent pleurodesis not be routinely performed
- In patients undergoing surgery, if the site of chyle leak cannot be convincingly identified, we suggest that concurrent mechanical or chemical pleurodesis be considered

Remark: In patients with chylothorax being managed with tube thoracostomy who are not (re-)operative candidates and in whom percutaneous lymphatic interventions are not feasible or unsuccessful, talc slurry for pleurodesis can be considered on a case-by-case basis after multidisciplinary discussion.

Literature review

Surgical [22, 23] or medical thorascopic [52] pleurodesis for chylothorax has scarcely been described in the published literature. Studies commenting on the use of pleurodesis for either post-surgical or non-traumatic chylothorax report success rates of 80–100% [8, 12, 23, 52], with talc or OK-432 being the most common pleurodesis agent used. However, even the largest study reports the use of pleurodesis in only 27 patients [21]. TDL has been performed in combination with pleurodesis, with one recent study reporting using this in 65% (35 out of 54) of post-operative cases [10]. There are only few published reports of attempting chemical pleurodesis through a chest tube [53, 54].

Rationale

While TDL and pleurodesis have been used in combination [10, 11], the additive benefit of this approach over TDL alone remains questionable, especially considering the high success rate of TDL, at least in post-operative cases. However, once satisfactory cessation of the leak is achieved with TDL, surgeons may use a sealant, fibrin glue or pleurodesis agent to enhance scarring and duct closure [1]. Extrapolating from the malignant pleural effusion literature [55, 56], pleurodesis using talc slurry can also be considered as an alternative to thorascopic instillation of a sclerosing agent, especially in borderline surgical candidates and those in whom percutaneous lymphatic interventions are not feasible or unsuccessful, considering that these patients are all already likely to have a chest tube. A multidisciplinary discussion prior to any definitive step is essential.

PICO Question 7: In symptomatic patients with chylothorax that is refractory to optimal medical management, is there a role of pleuro-peritoneal or pleuro-venous shunt or indwelling pleural catheter (IPC) placement?

Best practice statements based on expert consensus

- In patients with high-volume chylothorax that is refractory to medical, surgical and percutaneous lymphatic interventions, we suggest that interventions aimed at symptom control such as pleuro-peritoneal or pleuro-venous shunt or IPC be considered

Remark: The choice between shunt and IPC placement depends upon patient preference and local expertise. If expertise in percutaneous lymphatic or surgical interventions is not available, consider transfer to a tertiary care centre that can provide multidisciplinary care. IPC placement can be considered as a temporising measure for symptomatic relief.

- In patients with persistent, low-volume non-traumatic chylothorax that is likely to respond to disease-directed treatment, we suggest that interim symptom control with an IPC be considered

Remark: The drainage frequency of IPCs in these patients should be “symptom-guided”. In patients in whom the re-accumulation rate is slow, serial thoracentesis may be a better option, depending upon patient preference.

Literature review

In patients with chylothorax refractory to medical, surgical and percutaneous lymphatic management, reports detail the successful use of a pleuro-peritoneal shunt to manage the effusion in both children and adults [12, 22, 57, 58]. This allows chyle to be diverted into the peritoneum from where it is absorbed systemically. These shunts cannot be considered in patients with concomitant chylous ascites, as their abdominal lymphatics are already overwhelmed by the chyle in their peritoneal cavity. The use of pleuro-venous shunt has also been described for patients with non-traumatic chylothorax [59–61]. Although less invasive alternatives than TDL, these shunts can be associated with complications including infection, skin erosion, migration, shunt failure, pneumoperitoneum, air embolism and ongoing dietary and immune complications [58, 59, 62].

Despite the contraindication per device instruction use [63, 64], the off-label use of tunnelled IPCs for non-malignant chylothorax has recently gained popularity largely due to the ease of placement and low rate of major complications of the intervention (minor complications are not uncommon). In a small study (n=14), no significant adverse nutritional, haemodynamic or immunological outcomes were reported during follow-up. The use of IPCs has been described for chylothorax related to malignancies such as lymphoma, while awaiting systemic anticancer therapy to take effect or for those with poor response to treatment [65, 66].

Rationale

The use of pleuro-peritoneal or pleuro-venous shunts or IPCs can be considered as a palliative intervention in patients with high-volume chylothorax that have failed all other interventions. These decisions should be

pursued after a multidisciplinary discussion that evaluates both surgical and percutaneous lymphatic intervention candidacy, relevant expertise and patient preference. In patients with low-volume chylothorax, especially in those with underlying malignancy, wherein conventional treatment options are unavailable or unsuccessful, or while patients are waiting for response to treatment, IPCs can be considered as a well-tolerated alternative to periodic thoracenteses. The drainage frequency of IPCs in these patients should be symptom-guided as it remains unclear if more frequent drainage will enhance auto-pleurodesis rates in these patients; frequent drainage may increase the risk of malnutrition and infections.

Conclusions

This consensus statement intends to offer guidance on the multidisciplinary management of chylothorax. The strength of this statement is that it summarises all current evidence on this topic and is the first document that provides guidance on the multidisciplinary management of chylothorax, representing the evidence and perspectives of experts from 20 institutions across the world. The limitations of this document arise from the poor quality of the existing evidence. Therefore, most of our best practice statements are either supported by evidence of low quality or purely based on expert consensus. Besides, clinical success rates of definitive interventions for single-site chyle leak aetiologies (e.g. iatrogenic) may not be extrapolated to diffuse chyle leak syndromes; the management of each of these is beyond the scope of this document. Multicentre prospective data, comparative studies and randomised controlled trials are needed to generate higher quality evidence to better guide the management of chylothorax. We anticipate that as further evidence is generated, there will be a need to reassess our practice periodically, building on the suggestions presented in this consensus statement.

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