

# Pleural procedural complications: prevention and management

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**Abstract:** Pleural disease is common with a rising case frequency. Many of these patients will be symptomatic and require diagnostic and/or therapeutic procedures. Patients with pleural disease present to a number of different medical specialties, and an equally broad range of clinicians are therefore required to have practical knowledge of these procedures. There is often underestimation of the morbidity and mortality associated with pleural interventions, even those regarded as being relatively straightforward, with potentially significant implications for processes relating to patient safety and informed consent. The advent of thoracic ultrasound (TUS) has had a major influence on patient safety and the number of physicians with the necessary skill set to perform pleural procedures. As the variety and complexity of pleural interventions increases, there is increasing recognition that early specialist input can reduce the risk of complications and number of procedures a patient requires. This review looks at the means by which complications of pleural procedures arise, along with how they can be managed or ideally prevented.

**Keywords:** Pleural disease; pleural intervention; pleural effusion; patient safety; thoracic ultrasound (TUS)

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## Introduction

The incidence of pleural disease in the general adult population is increasing, annually affecting over 3,000 people per million population. The characteristics of this patient group are highly variable, as are the natural history and management of the broad range of conditions included in pleural disease. Primary spontaneous pneumothorax (PSP) is usually seen in an otherwise healthy young adult population, many of whom can be managed conservatively or with simple pleural aspiration; and is associated with minimal long-term morbidity or mortality (1). This contrasts with secondary spontaneous pneumothorax (SSP) which tends to occur in older patients with underlying lung disease, most of whom will be hospitalised as a result with a mortality of between 1-2% (1,2). The incidence of pleural infection has doubled over the past decade (3)—most of these patients will require hospital admission for intercostal drainage whilst one-year mortality is approximately 20 percent (4,5). Malignant pleural effusion

(MPE) is increasing in frequency as the number of patients with new diagnoses of cancer or surviving long-term with improvements in oncological treatment grows. Over 150,000 new cases of MPE are seen annually in the USA alone, and with a median survival of between 3 and 12 months choosing the best treatment option swiftly is crucial to maintaining quality of life (6,7).

The heterogeneity of these conditions means that a patient with pleural disease may present to a number of medical and surgical specialities. There are now a variety of different interventions available and a requirement for clinicians to be capable of selecting the most appropriate one for their patient. Pleural disease is recognised as a subspecialty within respiratory medicine and the early involvement of specialists can benefit care by streamlining diagnostic and therapeutic decision making. Nonetheless, service demands mean that currently physicians of all backgrounds—particularly acute medicine—must maintain an understanding of when, where and how to intervene

for pleural disease. An essential part of training to achieve practical procedural competence is knowledge of risks and complications to allow valid patient consent and maintain safety. A recent patient safety alert and subsequent survey served to highlight the dangers associated with pleural procedures and poor clinical management (8,9). This has in turn prompted updates to national guidelines (1,6,10-12).

The risks of complications from pleural procedures can be greatly reduced with appropriate clinical training and experience. This review will consider broad safety issues that may arise with all pleural interventions; and complications specific to commonly performed procedures, including specialist procedures such as medical or local anaesthetic thoracoscopy (LAT) and indwelling pleural catheter (IPC) management. Issues pertaining to training in pleural interventions will be addressed—however, it should be noted that the suggested approaches to risk reduction are largely based on the authors' experience and expert opinion, with little prospective research specifically addressing patient safety.

### Planning and preparation

The fewer procedures a patient undergoes, the less likely they are to suffer an iatrogenic complication. As such, the clinician responsible for any patient with pleural disease should consider which intervention(s) are necessary for both diagnostic and therapeutic purposes before proceeding. Recent guidelines (12) have noted that the majority of patients presenting with a unilateral pleural effusion do not require an intercostal chest drain (ICD), with the exceptions of haemothorax and pleural infection. Instead, a large volume aspiration of up to 1,500 mL fluid can be performed as a day case for symptom relief whilst further investigations are pursued on an outpatient basis. This simpler initial approach minimises risk and inconvenience to the patient, and also reduces the possibility that an effusion of unknown cause might be drained to dryness—an outcome that can negatively impact on a patient's future diagnostic investigations (12,13). The early involvement of respiratory specialists helps to support this treatment paradigm, and a dedicated, responsive pleural service with access to ambulatory pathways and procedural facilities can be both cost-effective and enhance patient care (14,15).

Maintaining a safe environment for interventions is vital to minimise risk. Procedures performed either outside "normal" daytime working hours or at the bedside (i.e., not in a dedicated procedure suite) should be avoided

except in clinical emergencies, and ideally a designated clean room or theatre stocked with appropriate equipment and monitoring facilities should be available (10). Both medical and nursing staff should have undergone suitable training in pleural procedures as recommended by local and/or national guidelines. Simulation training, both in the procedure itself and the management of severe or life-threatening complications, may improve staff knowledge and confidence (16-18). The use of a universal protocol/checklist and time-out based on the World Health Organisation (WHO) Surgical Safety model (19) should be encouraged for all pleural procedures and can reduce the risk of avoidable complications (20,21), even in pressurised emergency situations (22).

An aseptic technique should be utilised to minimise the chances of causing iatrogenic infection, regardless of the apparent simplicity of a procedure. There is little data to support the use of prophylactic antibiotics except in the situation of penetrating chest trauma (23). Adequate local anaesthesia should be established to ensure any intervention is as painless as possible—poor technique can compromise this (24) and attention should be paid to the entire chest wall including skin, parietal pleura and adjacent periosteum, using generous quantities of local anaesthetic (e.g., 3 mg/kg lidocaine) to create a wide working area.

It is possible that the change with the greatest impact on risk reduction is a restriction on the number of clinicians either required or expected to perform pleural interventions. This has potential implications for service provision, particularly in smaller centres without regular access to specialist input. However, concentrating expertise in the hands of a small cohort of clinicians ensures these individuals maintain knowledge and skills through regular practice. The introduction of this approach to clinical care in one centre resulted in an eight-fold reduction in the rate of iatrogenic pneumothorax following pleural aspiration (16). The advent of thoracic ultrasound (TUS) has started to create this change by default—only a limited number of clinicians are trained in TUS, and the evidence behind its use in reducing complications are well known (8,10).

### Thoracic ultrasound (TUS)

Choosing an appropriate site for intervention is crucial to reducing iatrogenic complications from pleural procedures, given the proximity of vulnerable structures either within (e.g., lung, heart, diaphragm) or adjacent to (e.g., liver, spleen) the thoracic cavity. In the context of a

large pneumothorax or effusion, a traditional landmark approach using the “safe” anatomical triangle limits the risk of visceral injury. This is of little use when a pleural collection is small or loculated, or where plain radiographic opacification is due to something other than fluid (e.g., consolidation, elevated hemidiaphragm, cardiomegaly). The potential for significant harm due to poor site selection has long been recognised (25), and the need for a change in clinical practice was highlighted by a National Patient Safety Agency report in the United Kingdom in 2008 (8).

The increasing use of TUS by physicians (26,27) represents the most significant advance in the management of pleural disease over the past decade. There is growing evidence that TUS reduces risk during pleural procedures (16,28,29). TUS allows accurate identification of relevant anatomy including thoracic and abdominal viscera, and allows precise location of fluid and identification of its characteristics. TUS can reliably distinguish fluid from other causes of opacification on chest X-ray such as consolidation/collapse (unlike clinical examination) and can be used to provide real-time guidance during more complex interventions (30,31). It has the advantages of being portable, non-invasive, non-ionising and low cost. The importance of TUS has been recognised in both guidelines (10) and training documents (32,33) for thoracic and critical care physicians; some commentators have suggested it is no longer medicolegally defensible to perform a pleural intervention for suspected fluid without TUS except in exceptional circumstances (34).

TUS should only be used by practitioners who have completed an approved training syllabus (32,33) under appropriate supervision. It is essential these individuals then maintain a logbook of practice that is subject to internal peer review/audit and can demonstrate continued competence in TUS. Clinicians must be aware of both their own limitations and those of TUS itself. The level of safety TUS provides in defining the thoracic anatomy is only maintained if the planned procedure is performed immediately after marking a safe site, or with real-time guidance throughout (bearing in mind the additional expertise required for the latter technique). A prolonged delay between site marking using TUS and subsequent pleural puncture—for example, departmental radiology marking the chest prior to a later ward-based procedure—is of no more benefit than a “blind” intervention (35,36).

Inappropriate site selection still occurs even with TUS, particularly since pleural fluid is often seen more clearly (and therefore as being more easily accessible) posteriorly. This risks causing injury to the intercostal vessels which are

frequently exposed within the rib space posteriorly, as far as six centimetres laterally from the spine (37). Clinicians should be encouraged to access the pleural space laterally within the “safe” triangle whenever possible, passing needles superiorly to ribs to avoid the neurovascular bundle. There is some evidence suggesting TUS may be capable of identifying the position of intercostal vessels within a chosen rib space (38), although further assessment of this technique is required before wider clinical use given its apparently poor negative predictive value. The practical utility of TUS in identifying pneumothorax for intervention is unclear. There is evidence that TUS can reliably identify pneumothorax, but despite enthusiasm among emergency and critical care physicians (39,40), concerns remain regarding the potential for misdiagnosis with serious consequences (41).

### General complications

There are a number of potentially serious complications associated with any pleural intervention. Awareness of potential complications and knowledge of how to recognise and manage them is a central part of procedural competence.

#### *Pneumothorax formation*

Diagnostic and/or therapeutic aspiration, either for air or fluid, is the most commonly performed pleural procedure. Large case series report pneumothorax formation as being the most frequent iatrogenic complication associated with both this procedure and ICD insertion, with an incidence as high as 18% in non-TUS guided procedures (35). The development of a pneumothorax can be the result of a number of events. Damage to the underlying lung by the aspiration needle has probably been the most common cause in older case series—this can however be almost entirely avoided with the use of TUS for appropriate site selection and/or real-time guidance (26,28). One case series reported a reduction in post-aspiration pneumothorax rate from 8.6% to 1.1% with the introduction of a service comprising physicians with appropriate experience in pleural interventions and the use of TUS (16). The accidental introduction of air into the pleural space may also result in pneumothorax formation, but can be easily prevented with careful technique and the use of a closed aspiration/drainage system. This “complication” has little adverse consequences for ongoing management, and simply

requires accurate recognition.

Other events that can result in pneumothorax formation but may be less predictable and therefore compensated for include the development of transient defects in the visceral pleura during drainage of an effusion. These defects are caused by variation in shear forces across the expanding lung's surface during reexpansion and are probably more common in cases where the underlying lung is already diseased or damaged (42). In the presence of trapped lung—for example, in advanced malignancy with visceral pleural thickening—then drainage will result in hydropneumothorax formation as the lung fails to reexpand to replace the evacuated fluid. Recent research (43) has indicated that advanced TUS techniques including M-mode measurement and speckle tracking imaging of the underlying lung may help predict whether it is trapped prior to the drainage of an effusion. This approach merits further evaluation although the TUS skill set involved means it is likely to remain beyond the usual scope of practice of most physicians for the foreseeable future.

Whilst the authors and published guidelines (10) recognise the evidence base as being equivocal, it is probably appropriate to perform a post-procedural chest X-ray in all patients who have undergone a pleural intervention. Clinicians may wish to use their discretion in cases undergoing straightforward pleural aspiration where TUS guidance has been used throughout. Chest X-ray allows the identification of complications (including pneumothorax formation) and confirmation of correct drain positioning where appropriate. Serial radiography may also be indicated in high-risk procedures where the clinician is concerned about delayed air leak, using a similar approach to that utilised following computed tomography (CT)-guided lung biopsy.

### ***Persistent air leak***

Whether seen in the context of a spontaneous pneumothorax or following pleural intervention, clinicians should recognise the presence of a persistently bubbling chest drain as a sign of continued air leak. There is little consensus as to how to best manage persistent air leak, including the use of thoracic suction and timing of surgical referral. It is universally accepted that a bubbling chest drain must never be clamped due to the risk of causing tension pneumothorax and/or severe subcutaneous emphysema. In those cases where an air leak appears to have resolved clinically (cessation of drain bubbling) and radiologically (reexpansion of underlying lung on chest X-ray), there is

again variation in practice. Some clinicians simply remove the chest drain after an appropriate period of observation to ensure stability—in these circumstances early outpatient follow-up should be arranged and the patient advised to return immediately for assessment in the event that their symptoms (e.g., chest pain, dyspnoea) recur. Other clinicians clamp the chest drain for a period of time prior to removal with interval chest X-ray to exclude a continued slow air leak—this should only be done in observed conditions with experienced staff alert to signs of patient distress. The use of ambulatory devices to manage pneumothorax (44,45) and digital suction devices that can measure and monitor air leak (46) may change the approach to these patients in due course, but both require further prospective evaluation.

The development of subcutaneous emphysema is a specific concern associated with persistent air leak. This occurs most frequently following procedures where the parietal pleura has been breached extensively or on multiple occasions (e.g., LAT, closed pleural biopsy), and/or when the volume of air leak is particularly high (e.g., bronchopleural fistula), and specifically outstripping the drainage capacity of any placed ICD. The identification of subcutaneous emphysema should prompt review of the chest drain for positioning and function, and to consider whether a further drain is needed for adequate treatment. In the majority of cases subcutaneous emphysema will remain confined in proximity to the site of intervention and should simply be documented and observed. Marking out the area of chest wall affected is helpful to ensure consistency of assessment over time. More severe cases, particularly those spreading to involve the upper chest and neck, can rarely result in airway compromise and should prompt urgent intervention. This may include subcutaneous incisions to allow “milking” and release of air from the soft tissues, and in exceptional circumstances endotracheal intubation.

### ***Reexpansion pulmonary oedema (RPO)***

RPO is a rare but potentially life-threatening complication of pleural interventions that can develop in the reexpanding lung following drainage of effusions or pneumothoraces. The reported incidence following pleural drainage is less than 1%, although this is likely to be an underestimate as patients can be asymptomatic and therefore remain undiagnosed (47-49). Early recognition and treatment in symptomatic cases is crucial since mortality from RPO has been described as being up to 20% in one case series (49). Symptoms include dyspnoea, cough, chest pain and hypoxaemia post-drainage with evidence

of diffuse alveolar infiltrates on chest X-ray; these usually develop within 1-2 hours but may be delayed for as long as two days.

Predicting which patients are more likely to develop RPO is difficult, with proposed risk factors including prolonged lung collapse, rapid reexpansion during drainage and underlying cardiac impairment. It is however likely that the greater the volume of pleural fluid drained, the more likely RPO is to occur (50). The physiological mechanisms underlying RPO are poorly understood but may involve one or more of reperfusion injury, increase in alveolar permeability, hypoxic damage or mechanical stress from rapid changes in intrapleural pressure ( $P_{pl}$ ) (48). This has led some clinicians to advocate the routine monitoring of  $P_{pl}$  during drainage (51), with the development of RPO unlikely to occur if the  $P_{pl}$  is kept above—20 cmH<sub>2</sub>O (47,52,53). Whilst continuous pleural manometry during drainage is feasible (54), it is not a technique familiar to most clinicians. The development of symptoms such as coughing or chest pain is a valuable surrogate marker that should prompt termination of drainage (53). Consensus guidelines (10) recommend limiting the volume of pleural fluid drained at any one time to 1.5 L as a further pragmatic method of risk reduction.

In those cases where RPO does occur, treatment is based on an individual patient's symptoms and physiological status. Asymptomatic cases require careful observation; whilst those with symptoms should be managed supportively with measures including diuresis, supplementary oxygen and (in severe cases) critical care admission for positive pressure ventilation and/or haemodynamic support.

### ***Intrapleural haemorrhage***

Iatrogenic intrapleural haemorrhage may be the most feared complication associated with pleural intervention, either through damage to the underlying viscera (heart, great vessels and lung) or more commonly the intercostal vessels. Bleeding in this scenario may be life-threatening given the low-pressure, high-volume nature of the pleural space. Appropriate site selection using TUS and correct procedural technique are the most important preventative measures to reduce the chances of causing intrapleural haemorrhage. All patients undergoing pleural intervention should have regular physiological monitoring (including heart rate, blood pressure, respiratory rate and oxygen saturations as a minimum standard) before, during and after their procedure. Clinical staff should have a clear

departmental protocol to follow in the event an intrapleural bleed is suspected and/or confirmed.

Intrapleural haemorrhage may be recognised through haemodynamic decompensation, drainage of newly blood-stained pleural fluid or an increasing pleural collection post-intervention. Point-of-care bedside TUS may also be of diagnostic benefit through the identification of rapidly accumulating echogenic pleural fluid (55). All cases of intrapleural haemorrhage require urgent escalation of care with initial resuscitation to include restoration of circulating blood volume. There is disagreement about whether or not to immediately drain the accumulating haemothorax. Any decision should be made at a senior level on a case-by-case basis taking into account the patient's current status, likely source of blood loss, medical background and proximity to definitive therapeutic facilities.

Temporising measures can be utilised including the application of external pressure at the site of intervention; local instillation of adrenaline; and/or (in cases of intrapleural haemorrhage during LAT) internal diathermy or other directly coagulating device. However, in many cases definitive treatment will require emergency input from either interventional radiology (angiography and embolization) or thoracic surgery (video-assisted thoracoscopic surgery/open thoracotomy and ligation under direct visualisation) depending on local resource availability.

### ***Malignant metastatic seeding***

The seeding of metastatic malignancy at sites of previous pleural intervention is a rare but widely recognised concern. It is more common following larger procedures (e.g., LAT) and with certain types of cancer, in particular malignant pleural mesothelioma. The role of prophylactic radiotherapy is controversial with wide variation in clinical practice (56,57), although most clinicians appear to err on the side of treatment as opposed to conservative observation. A randomised controlled trial (58) that has recently finished recruiting will provide more guidance in due course.

## **Procedure-specific complications**

### ***ICD insertion***

Temporary ICDs are placed using either a Seldinger or blunt dissection technique, with the former approach becoming increasingly common. The use of a trocar

technique for the insertion of large-bore ICDs is no longer justifiable due to the high risk of complications including damage to underlying structures (59). For similar reasons clinicians should avoid excessive insertion of the dilator provided with Seldinger chest drain kits. Whilst a blunt dissection approach may be safest overall (60) there are no prospective controlled studies in this area of practice, and a number of large case series have shown ICD insertion using a Seldinger technique to have a low complication rate in expert hands (61-64). The TIME1 study (ISRCTN 33288337) comparing efficacy of large (24 Fr) versus small-bore (12 Fr) ICDs in MPE has recently completed recruitment and may provide further information in due course. It is generally accepted that for any indication the smallest size of ICD possible should be utilised in order to minimise the risk of complications (65), bearing in mind that in certain situations (e.g., haemothorax) a larger drain may be of therapeutic benefit. Larger-bore drains (>14 Fr) are associated with increased pain during and post-procedure (66), and all patients with an ICD in-situ should have regular analgesia available. Small-bore (<14 Fr) drains should be sutured in position to prevent them from being dislodged and flushed regularly to avoid blockage (10,64).

### *Indwelling pleural catheters (IPCs)*

IPCs are being used increasingly for the management of symptomatic recurrent malignant and non-MPEs (67-69). Whilst they have a similar spectrum of complications to temporary ICDs, their long-term use is associated with a number of specific issues. Catheter tract metastases may develop in up to 5% of patients with a long-term IPC for management of MPE (70-72), causing significant pain in a minority of cases. These should be treated with palliative radiotherapy if symptomatic, often without requiring the IPC to be removed; there is no role for prophylactic radiotherapy given the continued risk of metastases whilst the IPC remains in place.

IPC-related infection of the chest wall and/or pleural space is a rare occurrence (<5% of patients) with low associated mortality (73), and should be treated with antibiotics according to local guidelines and microbiology results (e.g., pleural fluid culture). It is unusual for IPC removal to be necessary in these circumstances. Ensuring that patients and carers involved in managing the IPC on a day-to-day basis have adequate training and adhere to aseptic technique during use should reduce the risk of infection occurring. It is worth noting there is no significant

increase in risk of IPC-related infection associated with systemic chemotherapy, and the presence of an IPC should therefore not be considered a contraindication to active oncological treatment (74). Of interest is a recent observation that low-grade pleural infection may be associated with improved survival in patients with IPCs for recurrent MPE (75). The reasons for this are unclear and merit further investigation in a larger prospective study.

Symptomatic failure of IPC drainage may be caused by loculation of fluid or catheter blockage. There are no current robust clinical studies in this area, but the use of intrapleural fibrinolytics may be considered with the aim of restoring or improving drainage of fluid. In a small number of cases IPC removal following resolution of fluid and/or auto-pleurodesis may be complicated by adherence of the distal catheter to intrathoracic structures. If this occurs, the IPC is severed at the most distal point accessible to leave a retained portion within the pleural space, rather than pursuing a more aggressive removal strategy (76).

### *Closed pleural biopsy*

Closed pleural biopsy is most frequently used to diagnose pleural malignancy or tuberculosis. Until recently this was most commonly performed using a reverse bevel-type (e.g., Abrams') needle and a "blind" technique. However, clinicians are increasingly using cutting needles under direct radiological guidance (including physician-delivered TUS) due to the improvement in diagnostic yield and lower risk of complications such as pain, visceral damage and pneumothorax (30,77-80). For reasons of safety, clinicians should utilise an in-plane approach under TUS guidance to ensure the biopsy needle is visible at all times and along its entire length. The needle should be passed immediately superior to the rib and (if using an Abrams' needle in particular) the biopsy taken from pleural tissue inferior to the insertion site. Patients may be required to maintain a breath hold whilst the biopsy is taken in order to minimise pleural shearing, particularly in cases with no or little fluid present. Serial interval radiography (e.g., 1 and 4 hours post-procedure) should be performed to exclude a slow or delayed air leak.

### *Local anaesthetic thoracoscopy (LAT)*

LAT (also described as pleuroscopy or medical thoracoscopy) is performed increasingly for the investigation of pleural disease (81). Patients should undergo careful pre-assessment

by the practitioner to ensure they are fit enough for the procedure, with guidelines suggesting a WHO performance status of 2 or above is necessary to proceed (81). A semi-rigid or rigid scope can be employed with the patient under conscious analgo-sedation; allowing assessment of the pleura and both diagnostic and therapeutic procedures including drainage of fluid, pleural biopsy and talc poudrage pleurodesis. The use of TUS prior to LAT allows characterisation of the underlying anatomy, safe site selection and pneumothorax induction in cases without significant pleural fluid present (31,82-84). Practitioners should have access to local guidelines regarding the use of sedative agents during procedures; if there is concern regarding the use of sedation in a high-risk patient (e.g., elevated body mass index, profound dyspnoea, multiple co-morbidities) then a formal anaesthetic opinion should be considered. The most common risks associated with LAT include pain, persistent air leak/pneumothorax and, particularly in cases where pleural biopsies are performed, bleeding (81). Pleural biopsies should be taken from over a rib rather than within an intercostal space to reduce the risk of damaging the intercostal vessels and nerves. If talc poudrage pleurodesis is performed then graded talc is recommended due to an increased risk of respiratory failure and acute respiratory distress syndrome with non-graded talc (81,85-87).

## Conclusions

Pleural procedures are safe with a low complication rate when compared to other invasive medical procedures. However, inexperienced or inappropriate intervention is associated with significant and potentially life-threatening risk to the patient. Adequate training, the use of image guidance, understanding how to recognise and treat potential complications, and limiting the number of clinicians expected to perform these procedures may help enhance patient safety. The growing recognition of pleural disease as a subspecialty within respiratory medicine, alongside the variety of diagnostic and therapeutic procedures available, means that early expert opinion should be sought to ensure patients are treated as swiftly and safely as possible.

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