**REVIEW ARTICLE**

# PLEURAL EFFUSIONS IN THE CRITICALLY ILL PATIENT

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**ABSTRACT:**

Pleural effusions are a frequently encountered problem affecting critically ill patients. They represent a diagnostic dilemma for treating physicians and can have detrimental physiologic effects on oxygenation and hemodynamics. Routine imaging studies and sampling techniques are often limited by the critical nature of the patient's illness. Computerized tomography is more sensitive than plain radiographs in detecting pleural effusions and provides the clinician with additional information which may help in patient care. Diagnostic sampling of undiagnosed pleural effusions can be safely performed aided by bedside ultrasonography and plays a crucial role in determining the appropriate medical management. The appropriate therapeutic drainage method depends on the underlying etiology of the effusion, such as empyema and hemothorax, which often require large bore chest tube placement. Here we review some of the diagnostic and management considerations in the diagnosis and treatment of patients with pleural effusions in the intensive care unit.

**Key Words:** Pleural effusion, intensive care unit, respiratory failure

## INTRODUCTION:

Pleural effusions are commonly present in critically ill patients. The published incidence rate of 8% to 62% varies widely and is highly dependent upon patient populations[1,2]. A wide spectrum of underlying etiologies can lead to the development of transudative and exudative pleural effusions. Many of these effusions are the result of underlying systemic diseases such as pneumonia, heart failure, or malignancy. Alternatively, effusions may result from co-morbid conditions worsened by acute illness. In addition, mechanical ventilation may predispose to the development of a pleural effusion due to positive pressure-related reductions in lymphatic drainage[3,4]. The majority of effusions are small and incidentally discovered[2,5]. However, large effusions can cause significant physiologic impairment which further complicates the care of patients in the intensive care unit (ICU). Diagnostic and therapeutic drainage of pleural effusions is frequently required in the evaluation and management of critically ill patients.

### Identification of Pleural Effusions:

Chest radiographs are commonly used to identify the presence of pleural effusions. Good quality upright posteroanterior (PA) and lateral chest x-rays are quite sensitive and can detect as little as 25 mL of pleural fluid[6]. Critically ill patients, however, are typically unable to undergo traditional upright PA and lateral radiographs.

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Published criteria used to determine the presence of pleural fluid on anteroposterior (AP) supine radiographs include increased homogenous density superimposed over the lung in which visibility of normal bronchovascular markings is maintained but without evidence of consolidation or collapse, loss of the normal silhouette of the hemidiaphragm, blunting of the lateral costophrenic angle (meniscus sign), apical capping, apparent elevation of the hemidiaphragm, decreased visibility of the lower-lobe vasculature below the level of the hemidiaphragm, and thickening of the right minor fissure[7-11]. Supine x-rays require more fluid in order to demonstrate radiographic signs suggestive of a pleural effusion. Supine radiographs only have a sensitivity of 67% and specificity of 70% compared to lateral decubitus films[12]. Blunting of the costophrenic angle is the most prevalent but least specific radiographic finding. Supine x-rays are also less sensitive than other diagnostic imaging methods such as ultrasonography, which is becoming more readily available in many ICU's[13].

Modern modalities of assessing pleural effusions include computerized tomography (CT) and ultrasonography. Chest CT gives the clinician a detailed view of the thoracic cavity and provides insight into the patient's underlying disease processes. Pleural fluid attenuation and characteristics on CT can be used to help differentiate exudative effusions and hemothorax. Radiographic identification of underlying parenchymal consolidation or lung masses, abnormalities in mediastinal vasculature or structures, and cardiac features are helpful in evaluating the cause of the pleural effusion and the management of critical illness. Bedside ultrasonography is a tool commonly at the disposal of the ICU physician and provides rapid real-time clinical information. It is safe, convenient, and has the additional benefit of being available in the ICU and does not require the critically ill patient to be transported for diagnostic studies. Details of performing thoracic ultrasonography have been very well described in the literature[14,15]. Pleural fluid volume can be estimated with ultrasonography with multiple published correlates to intrapleural measurements[13, 16-18].

Identification and localization of complicated pleural effusions is also important for the clinician, as it may affect the site of planned diagnostic or therapeutic procedures such as thoracentesis or chest tube placement. Computerized tomography (CT) is only moderately sensitive in detecting the presence of pleural adhesions with a sensitivity of 71% and specificity of 72% in excluding them[19]. Sensitivity for identifying specific adhesions by CT was significantly worse, however, with only 38% sensitivity and 27% false positive rate. On the contrary, ultrasonography is better suited to localizing individual adhesions by evaluating for pleural sliding with a sensitivity of 81% to 88% and specificity of 83% to 96% [20-21]. Sensitivity of ultrasonography and the pleural sliding sign may be complicated by concurrent pneumothorax, in patients with chronic obstructive lung disease (COPD), and at the lung apices[20-21].

**Complications of Draining Pleural Effusions:**

Drainage of pleural effusions is typically performed via thoracentesis or chest tube thoracostomy. Development of pneumothorax from inadvertent puncture of the underlying lung is of particular concern in critically ill patients who often already have hemodynamic and respiratory compromise. Positioning of ICU patients is also

complicated by their medical condition which can compromise effectiveness of drainage and procedural safety. In addition, positive pressure from mechanical ventilation increases the risk of developing of a tension pneumothorax. Risks of bleeding and development of hemothorax are also accentuated in critically ill populations who frequently have concurrent thrombocytopenia or coagulopathy. A number of observational studies have described thoracentesis in mechanically ventilated patients, with meta-analysis demonstrating a pooled risk of 3.4% for pneumothorax and 1.6% for hemothorax[22]. There is a trend towards increased pneumothorax risk when performed on mechanically ventilated patients[22-23] and with therapeutic thoracentesis[23]. The improved safety profile has led many to support the routine use of ultrasound guidance whenever available[14, 23].

Other risks include infection, subcutaneous hematoma, damage to the neurovascular bundle, damage to abdominal structures from subdiaphragmatic needle insertion, and puncture of mediastinal structures. Furthermore, re-expansion pulmonary edema is a risk with large volume pleural drainage. Re-expansion pulmonary edema is a relatively rare complication, and the volume of pleural fluid that can be safely removed is not entirely clear[24-26]. It is generally recommended not to remove more than 1.5 L at a time and to avoid excessive negative pressure during fluid aspiration such as is generated with the use of a vacuum bottle[27,28]. As such, drainage through a chest tube can be performed with the drainage canister below the level of the patient so that drainage occurs through gravity rather than via negative pressure suction. The drainage system can also be clamped periodically to prevent excessive volumes of transudative effusion from being removed in a short period of time. However, larger volumes have been safely removed without the development of re-expansion pulmonary edema as long as the patient remains asymptomatic during the procedure and manometry pressures remain less than -20 cm $H_2O$ throughout the procedure[24].

**Physiologic Effects of Pleural Effusions and Drainage:**

Under normal circumstances, only a few milliliters of pleural fluid are present between the visceral and parietal pleura within the potential pleural space. The presence of large amounts of pleural fluid results in significant impacts on physiologic parameters including gas exchange, respiratory mechanics, and hemodynamics. Excessive pleural fluid will result in either atelectasis or distension of the chest wall[29]. Studies show that the increase in pleural volume and associated pleural pressures are primarily compensated by expansion of the chest wall with lesser effects on lung volumes[30,31]. Drainage of pleural effusions is associated with improvements in dynamic compliance [32-34]

Therapeutic pleural drainage has been shown to improve oxygenation and the ratio of the partial pressure of oxygen ($P_aO_2$) to the fraction of inspired oxygen ($F_iO_2$) in a number of studies[17, 32-33, 35-37]. Improvements in oxygenation have been correlated with the volume drained[17, 32], pleural elastance[36], and initial severity of oxygenation impairment[35]. Improved oxygenation is not consistently achieved with large volume drainage, however, and may be affected by differences in patient characteristics and the amount of positive end-expiratory pressure (PEEP) used[17, 34-38].

Therapeutic large volume pleural drainage is often performed in patients with impending respiratory failure to prevent potential intubation and to liberate patients from mechanical ventilation. Unfortunately, clinical outcomes of routine, empiric therapeutic drainage of pleural effusions in patients on mechanical ventilation are not well correlated and randomized studies are required.

**Etiologies with Specific Management Strategies:**

Diagnostic thoracentesis is generally recommended for pleural effusions in critically ill populations, especially if the etiology is unknown. Pleural fluid evaluation has been shown to change the diagnosis in 45% of patients undergoing thoracentesis with 33% requiring a change in therapeutic management[1]. Findings that may significantly change therapy include culture results dictating alteration in antibiotic regimens, discovery of empyema or hemothorax necessitating drainage or use of a larger bore chest tube, and the diagnosis of malignancy which impacts global goals of care.

***Complicated Parapneumonic Effusion and Empyema:***

Infectious exudates are a common cause of pleural effusions in the medical ICU, with a reported prevalence as high as 42% to 62%[1, 39]. Antibiotic therapy directed by culture results and possible near-complete drainage with thoracentesis is usually sufficient therapy for most simple, free-flowing parapneumonic effusions[40-41]. More complicated parapneumonic effusions, however, require chest tube placement or other advanced drainage interventions. Larger bore chest tubes are traditionally used as the tube diameter must be of sufficient size to remove infected material from the pleural space without becoming occluded. Smaller bore chest tubes, however, are becoming increasingly popular as they can be placed within loculations using real-time ultrasound guidance and are associated with less patient discomfort[42-43]. Furthermore, the Multi-center Intrapleural Sepsis Trial (MIST1) did not demonstrate any affect of chest tube diameter on mortality, need for surgical intervention, or length of hospitalization[43]. However, it is important to note that selection of tube diameter in this trial was not randomized and was left to the discretion of the treating physician. This introduces the potential for bias based on the physician assessment of the clinical situation and fluid characteristics. Nevertheless, when draining parapneumonic effusions, it is imperative to continuously assess the effectiveness of drainage and consider alternative tube placement or larger bore tube diameter if necessary.

Complicated parapneumonic effusions can result in the development of loculations which complicate the drainage and management of the pleural space. Administration of intrapleural fibrinolytics has mixed outcomes in the prevention and treatment of infection-related pleural loculations. The MIST1 trial is the largest randomized study of this kind which showed no difference in mortality, radiographic outcomes, need for surgical intervention, or hospital length-of-stay in patients randomized to three days of intrapleural streptokinase versus placebo[44]. Numerous other studies have examined single agent intrapleural fibrinolytic use with varying results. However, meta-analysis of these studies does not support their routine use and this sentiment is echoed in current major societal guidelines[43, 45]. It has been theorized that bacterial debris and free

deoxyribonucleic acid (DNA) may limit the utility of intrapleural fibrinolytics. More recently, the MIST2 compared intrapleural tissue plasminogen activator (t-PA) and DNase used independently versus combination therapy versus placebo. Combination therapy resulted in favorable reduction in radiographic opacity, need for surgical referral, and hospital length of stay compared to placebo without significant benefit from either t-PA or DNase alone[46].

*Hemothorax*

Because small amounts of blood can give pleural fluid a bloody appearance, pleural fluid hematocrit more than 50% of the serum hematocrit is used to make the diagnosis of a hemothorax. Hemothoraces are usually the result of trauma or procedure-related injury, but spontaneous hemothorax has been described with endometriosis, exostoses, rupture of pulmonary vascular malformations (Osler-Weber-Rendu syndrome) and rupture of thoracic artery aneuryms (Ehlers Danlos syndrome and neurofibromatosis)[47].

Chest radiography can be used for the detection of fluid in the thoracic cavity but has decreased sensitivity when performed in the supine position, as is common with critically ill patients. Chest CT has several distinct advantages over chest-radiography in evaluating patients suspected of having a hemothorax. In addition to improved image resolution, measurement of Hounsfield units can help distinguish the presence of a hemothorax from pleural fluid, and an arterial blush of contrast into the pleural space can indicate active bleeding requiring immediate intervention. Bedside ultrasonography is another readily available diagnostic tool with higher sensitivity for hemothorax than chest radiography[48].

Initial management of a hemothorax includes the placement of a large bore chest tube for removal of blood and blood clots to prevent the development of infection and trapped lung. Prospective analysis has not demonstrated outcome differences for 28 F to 32 F tubes compared to larger 36 F to 40 F tubes with regards to volume of blood drained, duration of tube placement, or complications such as development of pneumonia, empyema, or retained hemothorax[49]. Eastern Association for Trauma guidelines recommend prophylactic use of first generation cephalosporins for reducing infectious complications in hemothoraces that require chest tube drainage, though these recommendations were generated based on limited data from 9 small studies[50]. A subsequent prospective, randomized, double-blind trial comparing intravenous cefazolin over the duration that a chest tube was in place versus 24 hours of cefazolin therapy versus placebo in 224 patients showed no benefit with prophylactic antibiotics[51]. Prophylactic antibiotics are therefore not routinely used for spontaneous cases of hemothorax but are warranted when secondary to blunt or penetrating chest trauma[52].

Ultimately, surgical exploration may be required to identify and repair damaged vascular structures and evacuate the hemothorax. Video-assisted thoracoscopic surgery (VATS) is commonly the initial procedure used. However, one study demonstrated that 26.5% of patients required two procedures, 5.4% required three procedures, and 20.4% ultimately required a thoracotomy to fully evacuate the pleural space or treat subsequent infection[53]. Timing of surgical procedures must be weighed carefully in critically ill patients who may not tolerate surgical interventions. Surgical repair of damaged

vascular structures are often urgently required to stabilize the patient, but subsequent interventions for retained hemothorax are usually performed once the patient is clinically improved.

***Malignant Pleural Effusion:***

New discovery of malignant cells on pleural fluid cytology is usually a paradigm-changing finding. Aside from the physiologic effects of the effusion, malignant effusions also represent late stage disease and poor overall prognosis. If the patient can overcome their acute illness, the goals of therapy will often switch towards a palliative focus. There are a variety of therapeutic options available for malignant pleural effusions ranging from large volume thoracentesis to chemical pleurodesis[54]. However, most critically ill patients are not good candidates to undergo the stress of chemical pleurodesis. And for rapidly recurring malignant pleural effusions, repeat therapeutic thoracentesis places the patient at unnecessary procedural-related risk and discomfort. Therefore, consideration should be given towards placement of an indwelling pleural catheter for therapeutic relief, unless there is concurrent pleural infection due to the risk of placing a long-term catheter in an infected pleural space. In this case, periodic large volume drainage can be performed for symptom relief and does not preclude the future potential for pleurodesis. Moreover, spontaneous pleurodesis may occur with use of an indwelling pleural catheter[55].

**Conclusion:**

Pleural effusions are a frequent occurance in the critically ill patient. Diagnostic sampling is complicated by risks of pneumothorax and bleeding, but can be safely performed with the use of real-time ultrasonography. Diagnosis of pleural effusions is crucial in guiding medical care. In addition, therapeutic drainage may improve oxygenation, though the impact on other physiologic parameters is not as well established.

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