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Complications of thoracentesis: incidence, risk factors, and strategies for prevention

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Abstract

Purpose of review—Although thoracentesis is generally considered safe, procedural complications are associated with increased morbidity, mortality, and healthcare costs. In this article, we review the risk factors and prevention of the most common complications of thoracentesis including pneumothorax, bleeding (chest wall hematoma and hemothorax), and reexpansion pulmonary edema.

Recent findings—Recent data support the importance of operator expertise and the use of ultrasound in reducing the risk of iatrogenic pneumothorax. Although coagulopathy or thrombocytopenia and the use of anticoagulant or antiplatelet medications have traditionally been viewed as contraindications to thoracentesis, new evidence suggests that patients may be able to safely undergo thoracentesis without treating their bleeding risk. Re-expansion pulmonary edema, a rare complication of thoracentesis, is felt to result in part from the generation of excessively negative pleural pressure. When and how to monitor changes in pleural pressure during thoracentesis remains a focus of ongoing study.

Summary—Major complications of thoracentesis are uncommon. Clinician awareness of risk factors for procedural complications and familiarity with strategies that improve outcomes are essential components for safely performing thoracentesis.

Keywords

hemothorax; iatrogenie	c pneumothorax;	re-expansion	pulmonary	edema;	thoracentesis;	ultrasound

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Conflicts of interest

INTRODUCTION

Thoracentesis is a common procedure performed by a wide range of healthcare providers in both the inpatient and outpatient settings [1]. Although generally considered a low-risk intervention, complications of thoracentesis, including pneumothorax, bleeding (puncture site bleeding, chest wall hematoma, and hemothorax), and re-expansion pulmonary edema (REPE), can lead to increased morbidity, mortality, and healthcare cost [2,3]. For example, an iatrogenic pneumothorax can add 4.4 days to hospital length of stay and \$18000 in additional healthcare expenditures [4].

Research into the incidence and risk factors of procedural complications is limited by a lack of randomized trials and publication bias with subsequent underreporting [5,6]. Specifically, this has led to barriers in the study of the true incidence of therapeutic complications, that is complications not present prior to a procedural intervention, in surgical laparoscopy, and in left ventricular assist device placement [7–9]. Nevertheless, in the last several years more evidence has emerged allowing prediction and prevention of thoracentesis complications [6,10].

The goal of this article is to review the latest evidence from the past 3 years, supplemented by historical articles, describing the risk factors and prevention of pneumothorax, bleeding, and REPE (Table 1). Infrequent complications, such as tumor seeding of the catheter tract [15], catheter fracture [16,17], injury to abdominal viscera [17], and vasovagal syncope [18] are out of the scope of this article and will not be discussed.

PNEUMOTHORAX

Pneumothorax is the most common complication of thoracentesis, with historical incidence rates as high as 19% [19]. Iatrogenic pneumothorax significantly impacts patient outcomes. A recent meta-analysis found that up to one-third of cases require chest tube drainage [2]. Furthermore, iatrogenic pneumothorax has been linked to increased healthcare costs and mortality [3,4,20].

It is important to note that the appearance of air within the pleural space on chest radiography following thoracentesis does not necessarily indicate a true procedural complication (injury to the visceral pleura). During drainage of the pleural space, atmospheric air can inadvertently enter the pleural space creating a small pneumothorax that requires no intervention. A unique form of a pneumothorax, termed pneumothorax *ex vacuo*, may also occur when excessively negative pleural pressures are generated in the setting of a lung unable to fully re-expand as seen in endobronchial obstruction, atelectasis, and visceral pleural thickening [21]. The increased intrapleural gradient can entrain air into the pleural space, creating a pneumothorax located in the position of the pleural fluid that was just removed (Fig. 1). A pneumothorax *ex vacuo* rarely requires aggressive treatment, and therefore, we do not believe pneumothorax *ex vacuo* should be viewed as a procedural complication of thoracentesis [22].

Incidence

Although older studies report high rates of procedure-related pneumothorax [19], recent literature, which has emphasized operator experience and the use of ultrasound, has found pneumothorax to be an uncommon complication of thoracentesis.

Ault *et al.* [11], in a review of 9320 thoracenteses performed by an experienced operator, found a pneumothorax rate of 0.6%. Similarly, Heidecker *et al.* [21] identified only one pneumothorax from inadvertent lung puncture in a series of 367 procedures. Although it is important to note that studies over the past 3 years have varied in their use of postprocedural radiography, rates of iatrogenic pneumothorax rates have ranged from 0 to 3% [3,23–25]. Two recent meta-analyses reported an overall pneumothorax rate of 6% [2,5]. We believe the overestimation of pneumothorax rates results from inappropriate chest radiography after thoracentesis identifying clinically insignificant pneumothorax from atmospheric air, not visceral pleural puncture.

Use of ultrasound

The biggest contributor to the reduced incidence of pneumothorax has been the use of ultrasound. Ultrasound allows the operator to visualize the characteristics of a pleural effusion [26], identify the most accessible area of pleural fluid, measure the exact distance a needle must travel to enter the pleural effusion, avoid important surrounding structures, and localize intercostal vessels. There are extensive data supporting the use of preprocedural ultrasound in marking the location of the fluid to decrease the rate of complications from thoracentesis [27,28].

In an observational cohort study of over 61000 thoracentesis (45% of which were performed under ultrasound guidance), Mercaldi and Lanes [3] found that the use of ultrasound reduced the risk of pneumothorax by 19% [odds ratio (OR) 0.81; 95% CI, 0.74–0.90] and reduced healthcare cost and length of stay. Similarly, Cavanna *et al.* [23], in a study of 445 patients undergoing thoracentesis for malignant pleural effusion, showed that the use of ultrasound was associated with a statistically significant decrease in pneumothorax rate (1 vs. 9%, P<0.0001). Numerous other studies have found that the use of ultrasound is associated with a decreased rate of pneumothorax [27,29,30]. In one of the most thorough evaluations to date, Gordon *et al.* [2] performed a systematic review of pneumothorax in thoracentesis. The investigators found that the use of ultrasound significantly reduced the rate of pneumothorax (OR 0.3; 95% CI, 0.2–0.7).

Although not all studies have demonstrated a reduced risk of pneumothorax with the use of ultrasound [5¹¹], the reduced complication rates reported throughout the literature and the minimal risks associated with ultrasound use have led many consensus guidelines and expert reviews to endorse the routine use of ultrasound [31,32].

Whether the use of real-time ultrasound guidance (where the procedure is performed under continuous ultrasound visualization) offers additional benefit beyond that afforded by preprocedural ultrasound use has not been rigorously studied. However, when accessing small or loculated effusions in a challenging anatomic location, we believe clinicians should consider the use of real-time ultrasound guidance.

Additional risk factors

Clinicians should be aware of several patientspecific and procedural factors, which increase the risk of iatrogenic pneumothorax [6]. Ault *et al.* [11¹¹] found that underweight patients (defined as a BMI less than 18kg/m²) were three times more likely to experience a pneumothorax. The authors attributed this risk to several factors: a smaller distance between the lung and chest wall, underestimation of the distance the needle has entered the skin, and the use of underweight patients as a surrogate for poor overall health. Although mechanical ventilation is frequently cited as a risk for pneumothorax, results from several studies failed to show an association [2,11¹¹,33]. Additionally, multiple needle passes through the skin have consistently been associated with higher rates of pneumothorax [2,11¹¹]. The study by Ault *et al.* also showed that sampling a small pleural effusion may raise the risk of pneumothorax [6]. Conversely, multiple studies suggest that the risk of pneumothorax rises with drainage volumes greater than 1.5 liter in contrast to draining less than 1.5 liter [6,11¹¹,34]. However, there are no clear data on the safest amount of fluid drained [35]. There are also no convincing data that the type of needle or catheter used impacts pneumothorax rates [5¹¹].

Finally, operator experience plays a significant role in procedural complication rates including pneumothorax. Gordon *et al.* [2] found a pneumothorax rate of 8.5% in procedures performed by less-experienced operators compared with a rate of 3.9% for experienced providers (P = 0.04). Additionally, Ault *et al.* [11 along also supported this conclusion as they demonstrated a pneumothorax rate of 0.6% when an expert provider performed or directly supervised all procedures. Studies that have examined the impact of simulation and competency-based testing on complication rates further highlight the importance of instituting systems that ensure provider experience and comfort with thoracentesis [36,37].

BLEEDING COMPLICATIONS

A spectrum of bleeding complications, including puncture site bleeding, chest wall hematoma, and hemothorax, can be seen with thoracentesis. Although rare, a hemothorax should be suspected when a patient develops vital sign instability, a drop in hematocrit, or rapid pleural fluid reaccumulation following thoracentesis.

Incidence

The incidence of hemothorax following thoracentesis remains low despite operators increasingly performing procedures on patients with known bleeding risk factors [10]. Ault et al. identified only 17 (0.18%) bleeding complications post-thoracentesis procedures, only five of which were hemothoraces (0.01%). Data from Ault et al. [11] included a number of procedures performed on patients with uncorrected coagulopathy or thrombocytopenia. Similarly, one case series of procedures performed on patients with hematologic malignancies and following stem cell transplant (a majority of which had no evidence of thrombocytopenia or coagulopathy), showed hemothorax rates ranging from 0 to 2% [38,39]. Additionally, a recent systematic review of 48 studies found a similar overall risk of significant hemorrhage of 1% [5].

Correction of bleeding risk

Traditionally, the use of anticoagulant or antiplatelet medications and laboratory markers of abnormal hemostasis, including an elevated international normalized ratio (INR) or partial thromboplastin time (PTT) and low platelet count, were felt to be the best predictors of bleeding complications during thoracentesis. As a result, consensus guidelines, including those from the British Thoracic Society and the Society of Interventional Radiology, recommend not performing a thoracentesis until a patient's INR is less than 1.5, platelet count is greater than 50000/µl, and antiplatelet medications such as clopidogrel have been held for 5 days. This was graded as, 'C level', evidence indicating this was derived from well-conducted case—control or cohort studies by the British Thoracic Society and expert opinion by the Society of Interventional Radiology [31,40].

Several recent studies cast doubt on these recommendations. In a retrospective case—control study, Hibbert *et al.* [12] compared the rate of thoracentesis-related bleeding complications in patients who received blood product transfusions for platelet counts less than 50000/µl and INRs greater than 1.6 to patients with similar abnormal laboratory values who did not receive preprocedural blood products. All four hemorrhagic complications identified in this study occurred in patients who received transfusions prior to their procedure. Puchalski *et al.* [13] prospectively evaluated bleeding complications in 312 patients undergoing thoracentesis, including 130 patients (42%) at increased risk of bleeding (INR>1.5, platelet count <50000/µl, creatinine>1.5mg/dl, use of clopidogrel or use of low molecular weight heparin). No cases of hemothorax were identified in this series of patients and there was no significant difference in the postprocedure hematocrit levels between patient groups. In another prospective cohort study, Mahmood *et al.* [14¹¹] identified only one hemothorax in 25 patients undergoing thoracentesis while on clopidogrel. Similarly, the study by Ault *et al.* [11¹¹] found no association between INR, PTT, or platelet count with the incidence of bleeding complications.

The above studies represent a growing body of evidence that suggests patients can safely undergo thoracentesis procedures while avoiding the risks associated with blood product transfusions or stopping anticoagulant or antiplatelet medications. Randomized trials are needed to better stratify procedural bleeding risk, especially for those patients with multiple risk factors for bleeding. At this time, we do not believe there is enough definitive evidence to guide practice. Therefore, we recommend proceduralists use their clinical judgment and experience in making decisions on bleeding risk and blood product administration before thoracentesis procedures.

Use of ultrasound and defining vascular anatomy

Studies evaluating the use of ultrasound to prevent bleeding complications are confounded by whether abnormal markers of hemostasis were corrected by blood transfusion and an overall low incidence of bleeding events [5¹,10]. This confounding makes it difficult to measure the full effect of ultrasound alone on the reduction of bleeding complications.

Ultrasound allows the operator to clearly identify the structures commonly implicated in hemorrhagic complications of thoracentesis, including the abdominal viscera and posterior

intercostal arteries (ICAs), the latter of which is the most common cause of hemothorax. The ICA is part of the neurovascular bundle, which courses along the subcostal groove below the inferior border of the rib. Although the insertion of a thoracentesis catheter along the superior border of the rib is frequently performed to prevent arterial injury, the degree to which the ICA is exposed within the intercostal space varies significantly [41]. Helm *et al.* [42] described this heterogeneity by measuring the exposure of the ICA within the intercostal space with the use of computed tomography vascular reconstructions of the ICA. Only 17% of ICAs were completely shielded by the superior rib in the subcostal groove 3cm lateral to the spine, while 97% were shielded in the subcostal groove at a distance of 6cm lateral to the spine. ICA exposure also increased in more caudal intercostal spaces and were found to be more tortuous in the elderly.

The above data support performing thoracentesis within the 'triangle of safety', a recommendation supported by guidelines and recent reviews (Fig. 2) [10,31]. However, numerous patient factors including the location of pleural fluid, body habitus, and patient positioning may limit the feasibility of this approach. When performing a thoracentesis close to the spine or along a more caudal rib, clinicians should consider using a vascular ultrasound probe with color flow to identify the ICA and therefore, prevent inadvertent arterial laceration. Limited data suggest that providers can reliably identify the ICA with the use of vascular ultrasound supplemented with color flow, although the impact of this technique on procedural complications has yet to be evaluated [43].

We recommend attempting to localize the ICA with a vascular probe and color flow before thoracentesis procedures, especially for procedures performed in close proximity to the spine and in the elderly.

RE-EXPANSION PULMONARY EDEMA

Symptomatic REPE is an uncommon complication of thoracentesis and is characterized by the development of hypoxemia and new alveolar infiltrates within 24h of pleural fluid drainage (Fig. 3) [44]. Although radiographic evidence of re-expansion edema is most commonly seen in the re-expanded lung, involvement of the contralateral lung has also been reported [45,46].

The exact pathophysiology of REPE remains poorly understood. Nevertheless, evidence from animal models [47,48] and studies of edema fluid [49] in patients with REPE suggest that increased hydrostatic forces in the re-expanding lung and direct injury to the alveolar–capillary barrier may contribute to REPE pathogenesis.

Incidence

Determining the true incidence of symptomatic REPE is challenging as studies have frequently identified cases of REPE based solely on chest imaging without the requirement for concurrent clinical symptoms [27,50]. Asymptomatic REPE has little clinical significance because many patients with radiographic REPE have improved dyspnea following thoracentesis [51]. Numerous studies have also cast doubt on the utility of

obtaining routine chest radiographs following thoracentesis in the absence of clinical symptoms [52–54].

Although REPE rates up to 16% have been reported in the literature, several large prospective case series have confirmed that symptomatic REPE is a rare complication of thoracentesis [5¹¹]. In a review of 185 thoracentesis patients, Feller-Kopman *et al.* [51] identified only one patient (0.5%) who developed symptomatic REPE, whereas the study by Ault *et al.* [11¹¹] found only 10 (0.01%) cases of REPE.

Pleural pressure monitoring

Identifying risk factors for the development of symptomatic REPE is challenging given the low incidence rates in publications with the largest series of patients. Because studies have shown that removal of large volumes of fluid are associated with the risk of REPE, guidelines and reviews frequently advocate for the cessation of fluid removal after drainage of 1–1.5 liters [31,51,55]. However, current evidence suggests REPE is related to intrapleural pressure rather than volume of fluid removed [51,56].

Several strategies are available to assess changes in pleural pressure during a thoracentesis. Pleural pressure can be directly measured during fluid removal with the aid of manometry [57]. Although data linking pleural elastance and drops in measured pleural pressure to procedural complications are limited, many experts advocate direct pleural pressure monitoring and recommend halting further fluid removal if pleural pressure drops below –20 cm H₂O [51,56,58,59]. However, it is unknown if this cutoff is influenced by patient clinical factors (e.g., serum albumin). Data also suggest that operators should avoid rapid drops in pleural pressure, which has led to recommendation of avoidance of vacuum containers for pleural drainage [51,60]. Alternatively, clinicians may choose to use patient symptoms as a surrogate for pleural pressure, as data suggest that the development of chest discomfort correlates with marked drops in pleural pressure [56,61]. In their recent study, Ault *et al.* [11 used *both* symptoms, including chest tightness, cough, and pain referred to the upper chest or neck, and assessment of resistance to fluid aspiration using a 10cm³ syringe as a signal to halt fluid removal and found a 0.01% rate of REPE. This supports the efficacy of monitoring noninvasive surrogates for excessive negative pleural pressure.

CONCLUSION

Although thoracentesis is a well-tolerated procedure, clinicians need to be familiar with potential procedural complications and strategies that reduce the risk of patient harm. Pneumothorax is the most common complication of thoracentesis although the use of ultrasound and an emphasis on operator expertise have significantly lowered complication rates. Bleeding complications such as hemothorax are uncommon and there is increasing evidence that thoracentesis can often be performed without correction of bleeding diatheses. REPE is also a rare complication of thoracentesis. The avoidance of excessively negative pleural pressures either through direct measurement of pleural pressure or attention to patient symptoms may reduce the risk of REPE.

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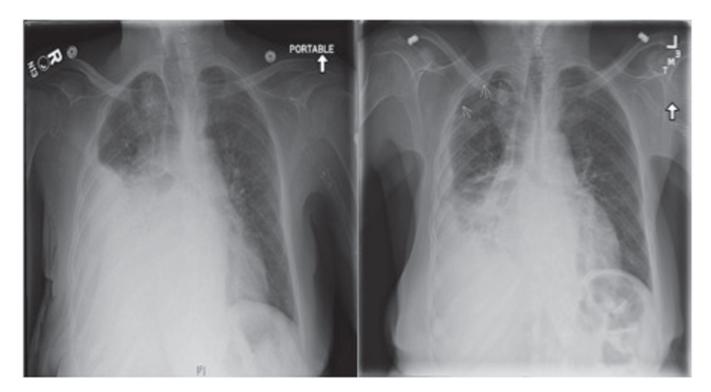
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KEY POINTS

• Thoracentesis is a well-tolerated procedure, although complications can lead to increased morbidity, mortality, and healthcare cost.

- Clinicians must distinguish between pneumothorax *ex vacuo*, which occurs when excessively negative pleural pressures are generated in the setting of a lung unable to fully re-expand, and mechanical puncture of the visceral pleura, a true procedural complication of thoracentesis.
- Pneumothorax is the most common complication of thoracentesis. Operator
 expertise, the use of ultrasound, and recognition of patient-specific and
 procedural risk factors for pneumothorax can reduce this complication.
- Although further randomized trials are needed, current evidence suggests that
 patients may not require correction of abnormal hemostasis before
 thoracentesis.
- Strategies that limit excessively negative pleural pressure may reduce the risk of REPE.



Pneumothorax *ex vacuo*. This anterior-posterior chest radiograph (left) demonstrates a large pleural effusion in a patient with a chronic exudative right-sided effusion. After thoracentesis, repeat posterior-anterior chest radiography (right) showed a partially reexpanded lung with persistent effusion and evidence of apical pneumothorax, as indicated by arrows, consistent with pneumothorax *ex vacuo*.

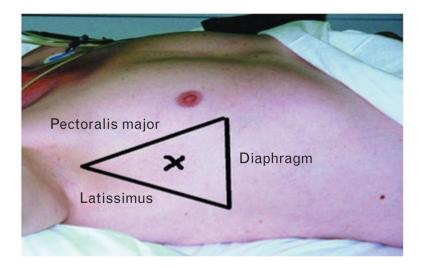


FIGURE 2.

Triangle of safety. The triangle of safety is bordered by the lateral edge of the pectoralis major, the lateral edge of the latissimus dorsi, the fifth intercostal space, and the base of the axilla. The British Thoracic Society recommends that pleural aspiration should occur within the triangle of safety. Reprinted with permission of the British Medical Journal [62].

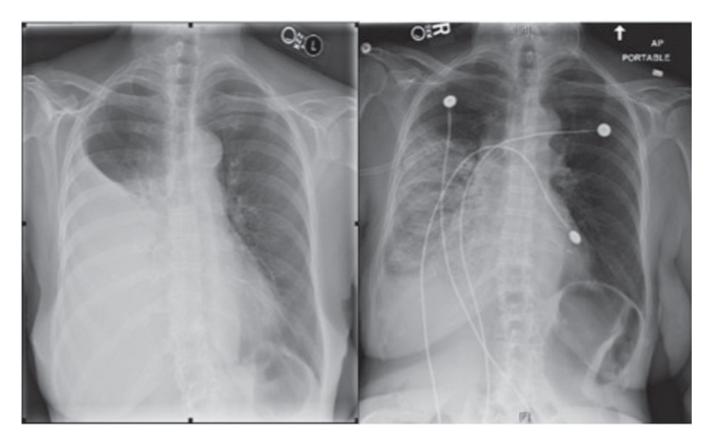


FIGURE 3.

Re-expansion pulmonary edema. The image on the left is an anterior-posterior (AP) chest radiograph showing a large right-sided pleural effusion. Immediately after large volume thoracentesis, the patient developed hypoxemic respiratory failure and post thoracentesis AP chest radiography (right) demonstrated a right-sided alveolar infiltrate consistent with the diagnosis of re-expansion pulmonary edema. Reprinted with permission of the American Thoracic Society. Copyright © 2016 American Thoracic Society [63].

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Table 1.

Summary of studies evaluating the major thoracentesis-related complications over the past 3 years

Author	Study type	Main finding
Pneumothorax (PTX)		
[3]	Retrospective cohort	Decreased risk of PTX with ultrasound guidance (2.26 vs. 3.09%); decreased mortality with ultrasound guidance (7.4 vs. 4.2%); decreased hospital cost (\$2075) and length of stay (1.5 days)
[5■]	Systematic review and meta- analysis	PTX rate 6.0%; no technical aspects of procedure were associated with increased risk of PTX
[11]	Prospective cohort	0.61% PTX rate; PTX associated with greater than 1500 cm ³ removed, unilateral procedure, more than one pass through skin, BMI < 18 kg/m ²
Bleeding complications		
[5••]	Systematic review and meta- analysis	Bleeding complication rate of 1.0%
[11]	Prospective cohort	0.05% rate of hemothorax without correction of bleeding risk; no association of bleeding risk with patient or laboratory parameters
[12]	Case control	No decrease in bleeding complications with correction of coagulopathy and thrombocytopenia
[13]	Prospective cohort	No increased risk of bleeding complications in patients with laboratory evidence of increased bleeding risk (coagulopathy or thrombocytopenia) or on medications that increase bleeding risk (clopidogrel, low molecular weight heparin, heparin)
[14 ⁸]	Prospective cohort	4% (95% confidence interval 0-10%) incidence of bleeding complications when performing thoracentesis in patients on clopidogrel
Re-expansion pulmonary edema (REPE)		
[5••]	Systematic review and meta- analysis	Only two studies included with range of incidence from 0 to 16%
[11=]	Prospective cohort	0.01% incidence of REPE; Association with volume of fluid removed and non-inflammatory conditions