Full Title: Post-thoracentesis Ultrasound vs. Chest X-ray for the Evaluation of Effusion Evacuation and Lung Re-Expansion, A Multicenter Study

Abbreviated Title: Ultrasound vs Xray assessment of post-drainage pleural effusion

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Abstract:

Introduction: Post-thoracentesis chest radiography (CXR) is often used to evaluate the degree of residual fluid post-thoracentesis. Whether post-drainage ultrasound exam is comparable to CXR in the evaluation of pleural space evacuation is unknown.

Research question: How do post-thoracentesis ultrasound and CXR compare in assessing the effectiveness of pleural space evacuation?

Methods: In this prospective, multicenter study, patients with free-flowing pleural effusions with minimal to no septations requiring thoracentesis were recruited. Post-thoracentesis ultrasound was performed immediately post-procedure; CXR was performed within 4-hours post-procedure. The primary outcome was agreement on complete pleural space evacuation between ultrasound and CXR. Complete pleural space evacuation was defined as the absence of pleural fluid on anterior, mid-axillary, and posterior ultrasound views and lack of costophrenic angle blunting on CXR. Interobserver reliability was assessed via independent image reviews by two pulmonologists and two radiologists blinded to patient/procedure data, with disagreements resolved by a third reviewer.

Results: Of the 147 patients enrolled (February/2021 – May/2022), 145 were included in the final analysis. The median age was 64 years (56-75), and malignancy was the most frequent effusion etiology (n=49). The lung was considered trapped in 50% (n=73). A total of 826 ultrasound images were collected for blind review. The Gwet's Agreement Coefficient 1 (AC1) assessing complete pleural evacuation between ultrasound and CXR was 0.93 (95% CI: 0.83-

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1.00). When assessing agreement based on the pre-specified criteria of effusion size (small vs large), a substantial level of agreement was observed between ultrasound and CXR, indicated by a kappa of 0.64 (95% CI: 0.51-0.77). There was a strong agreement (kappa= 0.81 (95% CI: 0.71-0.90)) between proceduralist and blind ultrasound reviewers regarding complete pleural space evacuation.

Conclusion: Post-thoracentesis ultrasound is an equally effective alternative to CXR in evaluating pleural space evacuation in simple pleural effusions.

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Introduction:

In the United States, 1.5 million people are diagnosed with a pleural effusion annually, of whom 175,000 undergo thoracentesis[1–5]. The use of ultrasound-guided thoracentesis has become standard practice, increasing procedural safety and efficiency[6–10]. Thoracentesis is commonly performed after a pre-procedural ultrasound examination of the pleural space, followed by a post-thoracentesis chest radiograph (CXR) to assess the extent of post-drainage lung re-expansion and residual fluid, underlying parenchymal abnormalities, and evaluation for post-procedural complications such as pneumothorax.

After thoracentesis, clinicians typically follow the standard practice of acquiring a post-procedural CXR either in the Radiology Department or with a portable CXR. This additional step in the clinical workflow could lead to extended travel times between different departments, causing delays in discharge and in the recognition of post-procedural complications, as well as, albeit small, increase in radiation exposure. Moreover, CXR may not be the most informative or practical approach for evaluating the ipsilateral lung post-drainage.

Lung apposition at the edges of posterior-anterior (PA) and lateral CXRs has been used as a radiological marker for both successful pleural space evacuation, and predication of success for medical or surgical pleurodesis. Although clinical and non-clinical markers, including chest discomfort and pleural manometry[11], have been investigated to diagnose trapped lung, these indicators are typically used in conjunction with radiographic findings, as no standardized definition currently exists in everyday practice. Accurate recognition of a lung that does not have full apposition with the parietal pleura following thoracentesis is crucial for future treatment planning, such as pleurodesis and intrapleural catheter placement (IPC)[12,13] in patients with or without malignant pleural effusions (MPE).

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The utility of ultrasound in the post-aspiration setting has been poorly characterized. Ultrasound has proven beneficial in diagnosing post-procedural pneumothorax, demonstrating comparable effectiveness to CXR[14,15]. Additionally, ultrasound has the advantage of delivering real-time clinical data without exposing patients to additional radiation[16–18]. Ultrasound can detect a smaller amounts of pleural fluid than CXR, resulting in greater accuracy when assessing for residual effusion[19,20]. Despite these findings, current societal guidelines[12,21] still recommend post-thoracentesis CXR as standard practice, especially for evaluating complications, assessing complete drainage of the pleural space, and determining if the lung is trapped in conjunction with patient symptomatology.

We conducted this multicenter prospective study to investigate the efficacy of post-thoracentesis ultrasound vs CXR examination in determining complete effusion evacuation in patients with non-loculated free-flowing pleural effusion. Additionally, our aim was to elucidate the utility of ultrasound in assessing other clinically significant questions, such as assessment for trapped lung following thoracentesis, in comparison to post-procedural CXR.

Methods:

Study Design

The study was conducted prospectively at six academic centers in the United States. Patient demographics, procedural and imaging data, and data from blinded pulmonologists and thoracic radiologists who reviewed and assessed the ultrasound and CXR images were collected using an electronic collection tool, Research Electronic Data Capture (REDCap)[22,23]. Consent was obtained from participants at each center. The institutional review board of each center approved the study locally.

Patient Population

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This study enrolled individuals undergoing therapeutic thoracentesis for large, free-flowing pleural effusions. Eligible participants were aged >18 and exhibited symptomatic moderate or large free-flowing (non-septated) pleural effusion, confirmed by ultrasound in all patients in addition to CXR or CT scan when available. A moderate − large effusion was defined as: (a) effusion filling ≥1/3 of the hemithorax on CXR or (b) CT scan indicating a maximum anterior-posterior (AP) effusion depth ≥1/3 of the AP dimension; or (c) on ultrasound, an effusion spanning at least three rib spaces with the patient sitting upright. All patients had pre- and post-thoracentesis ultrasound and CXR images available for review. The decision to use a portable vs a PA and lateral CXR was left to each provider for a more pragmatic recruitment process.

Exclusion criteria included 1) the presence of a disease or condition impeding study completion (e.g., coagulopathy or hemodynamic instability); 2) a history of ipsilateral pleurodesis; 3) the presence of more than minimal thin septations (exceeding 3) and/or loculations on bedside pre-procedure ultrasound[24,25]; 4) a pleural effusion smaller than anticipated on pre-procedure ultrasound; and 5) referral solely for diagnostic thoracentesis.

Study Procedures

All patients were positioned in an upright sitting posture with bedside thoracic ultrasound performed by an experienced proceduralist to assess the effusion characteristics and the optimal intervention site. Static ultrasound images collected before and after thoracentesis were obtained at end-expiration from three anatomical perspectives (anterior, mid-axillary, and posterior hemithorax). If an image was not documented or visualized on a specific view due to poor access, patient's inability to remain seated, or proceduralist’s failure to acquire the image, it was classified as missing. All static ultrasound images and chest radiographs were saved in a de-

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identified format. Demographic data, including age, sex, body mass index (BMI), smoking status, laterality of thoracentesis, and suspected etiology of effusion, were recorded.

The ultrasound-captured effusion size was estimated by 2 methods: 1) based on the number of rib interspaces in which you can see fluid and 2) effusion volume using the Goecke 2 formula[26]. Pleural fluid echogenicity (anechoic, echogenic, thin septations, moderate to dense septations) was assessed pre-procedure. The shape and motion of the diaphragm, the presence or absence of lung sliding and B-lines, and parenchymal characteristics were documented pre- and post-procedure. Volume of residual fluid pre- and post-procedure were estimated using the Goecke 2 formula. The reasons for the procedure cessations were documented, which included spontaneous cessation of flow despite catheter repositioning, symptoms suggestive of excessively negative pleural pressure (pain experienced in the front or back of the chest or neck, persistent even after catheter adjustment, intractable cough, increased shortness of breath), or other reasons per proceduralist discretion.

Interobserver reliability

Two blinded pulmonologists reviewed all pre- and post-ultrasound images. The reviewers confirmed the presence/absence of pleural effusion in each anatomical view, assessed fluid echogenicity, the presence and extent of septations, and evaluated overall image quality. Similarly, two blinded radiologists individually assessed all post-procedure CXR images to determine the presence/absence of a pleural effusion. The reviewers also graded effusion size using two distinct validated scales (Supplementary Table 1) and documented any notable parenchymal abnormalities and presence of pneumothorax. Parenchymal abnormalities were classified as atelectasis, pleural thickening, consolidation, ground-glass opacification, re-expansion pulmonary edema (REPE), nodules, or masses. When disparities emerged regarding a

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residual effusion on CXR, a third radiologist was consulted to facilitate consensus. For ultrasound images, the data reported by the primary proceduralist were used as third reviewer data to resolve disparities.

Outcomes

The primary outcome was concordance between ultrasound and CXR in determining complete pleural space evacuation. The absence of fluid was defined *a priori* as no fluid on any ultrasound view (anterior, mid-axillary, and posterior) and no blunting of the costophrenic angle (CPA) on CXR. Post-procedure residual effusions were further classified as "small" or "large". A "small" effusion occupied less than one rib space on all three ultrasound views, while "large" effusions equaled or exceeded one rib interspace on any view. On CXR images, a small effusion was defined as blunting of the CPA only (Grade 2 on Methods 1 and 2, Supplementary Table 1), while any effusion exhibiting more than CPA blunting was considered large.

Exploratory endpoints included the correlation between proceduralists' self-assessment of trapped lung after ultrasound and a second assessment after CXR. Lung was defined as trapped *a priori* based on symptoms suggestive of excessively negative pleural pressure (pain experienced in the front or back of the chest or neck, persistent even after catheter adjustment, intractable cough, increased shortness of breath) and absence of radiographic confirmation of full apposition of the lung with the parietal pleura on ultrasound and CXR. This definition was used to mimic real-world clinical scenarios, where the assessment of trapped lung is based on a combination of patient symptoms, imaging findings and intra-procedural observations. Further we evaluated the concordance of the identification of post-procedural complications by ultrasound and CXR, correlation of observed parenchymal abnormalities across imaging modalities, and the agreement between proceduralist and blinded ultrasound reviewers in

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assessing complete pleural evacuation. Furthermore, we sought to explore any correlation between Body Mass Index (BMI) and the quality of ultrasound images. Finally, we performed an exploratory multivariable logistic regression analysis to identify the pre-procedure ultrasound and patient specific predictors of trapped lung, as judged by the proceduralist at the end of the procedure.

Statistical analysis:

Descriptive statistics were employed, comprising means, standard deviations (SDs), and ranges for continuous parameters and percentages and frequencies for categorical parameters. Spearman's rank correlation was employed to assess the association between BMI, treated as a continuous variable, and the assigned image quality for each view categorized as "Clear," "Suboptimal/Poor," or "Missing" by blind reviewers, both before and after the procedure.

Agreement was measured using Cohen's kappa for all binary data, with interpretation previously described by Landis & Koch[27] . Our analysis revealed a high prevalence of reviews categorizing the outcome as “observed”, resulting in a symmetrically imbalanced contingency table. This resulted in a low or near-zero kappa statistic, falsely indicating poor inter-rater agreement. To address this kappa paradox, we used Gwet's Agreement Coefficient 1 (AC1), which is known for its resistance to such biases and can account for the kappa paradox[28]. Gwet's AC1 ranges from -1 to 1: a coefficient of -1 indicates complete disagreement, less than 0 suggests worse-than-chance agreement, 0 signifies agreement no better than chance, greater than 0 indicates better-than-chance agreement, and 1 reflects high degree of agreement among raters.

An exploratory evaluation was conducted to investigate pre-thoracentesis predictors of trapped lung using a multivariable logistic regression model. Model variables, selected based on clinical relevance, included effusion etiology (MPE or Non-MPE), pleural fluid ultrasound

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image characteristics (anechoic vs echogenic), effusion size, sex, and the number of prior thoracenteses. To account for potential effect modification between cancer and male sex, an interaction term between MPE and sex was developed. Odds ratios are reported with a 95% confidence interval (95% CI). No adjustments were applied to account for missing data. All statistical tests were two-sided with a significance level of 0.05. All statistical analyses were conducted using R version 4.3.0 (R Foundation for Statistical Computing).

Results:

Population Demographics

Between February 2021 and May 2022, a total of 147 patients were enrolled. Two patients were excluded due to missing post-procedure ultrasound images, leaving 145 patients for analysis. The median age of the population was 64 years (IQR 56-75) (Table 1). The median number of prior thoracenteses was 1 (IQR 0-2), and the predominant laterality for the procedure was right-sided in 103 patients (71%). The procedure was terminated due to spontaneous drainage cessation despite catheter repositioning in 65 patients (45%), chest discomfort in 61 patients (42%), and interactable cough in 19 (13%). The median volume of fluid removed was 1300 ml (IQR 850ml-1820ml).

Pre- and Post-Thoracentesis Imaging:

On pre-procedure ultrasound, a posterior view was obtained in all cases, followed by the mid-axillary view in 143 cases (98.6%) and the anterior view in 126 cases (86.9%) (Table 2). Post-procedure, the posterior view was obtained in all cases, followed by the mid-axillary view in 142 (97.9%) and the anterior view in 125 cases (86.2%) (Table 2, Figure 1). On pre-procedure ultrasound, 68 patients (47.1%) had a flattened or inverted diaphragm, which persisted in 14 patients (9.8%) upon procedure completion. Pre-procedure, the pleural space was anechoic in

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112 (77.2%), echogenic in 22 (15.2%), thin septations were noted in 17 (11%), and moderate septations were noted in 6 (4.1%).

Atelectasis was the most frequently observed parenchymal finding on post-procedure ultrasound (32.4%), followed by subpleural consolidations (31%), pleural thickening (18.6%), and less commonly, consolidation with visible air bronchograms, pleural nodularity, and/or lung masses or nodules. A post-procedure pneumothorax was identified in six cases during the post-procedure exam. The proceduralist required a median time of 3 minutes and 8 seconds (s) (IQR 160s-238s) for the pre-thoracentesis ultrasound evaluation and 2 minutes and 41 s (IQR 120s-210s) for the post-procedure evaluation. At the conclusion of the procedure, the proceduralist deemed the lung trapped in 72 cases (49.7%). On CXR, the proceduralist deemed 69 cases (47.6%) as trapped, 72 cases (49.6%) were considered non-trapped, and 4 cases (2.8%) could not be fully assessed.

Ultrasound vs. Radiological Agreement

A total of 826 pleural ultrasound images were collected and available for blind review. Regarding the primary outcome of complete pleural space evacuation, there was a high level of agreement between ultrasound and CXR, with a Gwet's AC1 of 0.93 (95% CI: 0.83-1.00) (Table 3). When assessing agreement based on the pre-specified criteria of effusion size (small vs large), a substantial level of agreement was observed between ultrasound and CXR, indicated by a kappa of 0.64 (95% CI: 0.51-0.77). Ultrasound vs. CXR-guided assessment of trapped lung (per aforementioned *a priori* definition) showed a strong level of agreement with a kappa of 0.89 (95% CI 0.81 to 0.96). When comparing ultrasound vs CXR for parenchymal abnormalities, pleural thickening exhibited the strongest agreement, with a Gwet's AC1 of 0.89 (95% CI: 0.83-0.95).

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When evaluating concordance concerning the presence or absence of pneumothorax between ultrasound and CXR, a slight to moderate agreement (kappa of 0.30, 95% CI: 0.10-0.50) was noted. Thoracic radiologists exhibited limited agreement among themselves in the evaluation of pneumothorax on CXR (kappa of 0.47 (95% CI: 0.23-0.71)). A total of 6 pneumothoraces were reported in the entire population, none of which required an invasive intervention such as chest tube placement. Among these, 3 small pneumothoraces who were considered to have a pneumothorax based on US and by the non-blinded radiologist in the recruiting institution, were discharged without need for additional intervention. The other 3 patients had US evidence of pneumothorax which was not noted on CXR. These patients were discharged after 2-4 hours of observation followed by repeat CXR and clinical evaluation to confirm stability. When assessing the agreement between the proceduralist and the blinded ultrasound reviewers regarding complete pleural evacuation, there was a strong agreement with a kappa of 0.81 (95% CI: 0.71-0.90).

Blind reviewers were more likely to rate the image as suboptimal/poor in individuals with a higher BMI ($\rho = 0.194$, $p = 0.046$) on mid-axillary views, among the 106 participants with available BMI data. 141 patients had available data for analysis in the clinical prediction model. No significant effect modification was noted between effusion etiology and sex (($p = 0.25$). Male sex (OR 2.32; [95% CI: 1.02-5.27]) and an effusion etiology of malignancy (OR 2.61; [95% CI: 1.00-6.81]) were the strongest predictors of trapped lung post-thoracentesis (Figure 2).

Discussion:

In this study, post-thoracentesis thoracic ultrasound and CXR exhibited strong agreement for evaluation of complete pleural space evacuation. This high level of agreement persisted when categorizing ultrasound and CXR images based on residual effusion size (small vs. large).

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Additionally, a substantial agreement was seen between proceduralists' assessment of trapped lung using ultrasound vs CXR based on pre-defined criteria. Pleural thickening exhibited the strongest agreement between ultrasound and CXR regarding post-procedure parenchymal examination. Our study identified male sex and MPE as potential predictors of trapped lung on US.

Post-thoracentesis chest radiography has consistently shown a low utility in the absence of symptoms, in addition to increased healthcare costs and radiation exposure[29–31]. Despite recent societal guidelines[6,32] advocating against the use of CXR for asymptomatic patients following thoracentesis, post-procedure CXR is still included in procedure checklists[33] and prominent medical textbooks[34]. These CXRs are often obtained not only for procedural complication assessment but also to assess the degree of lung apposition, parenchymal abnormalities and remaining fluid.

Ultrasound offers the benefits of being cost-effective, providing real-time, portable imaging, and is widely available. Since the introduction of bedside ultrasound for marking and/or procedural guidance in the early 2000s, the occurrence of common complications, such as pneumothorax, has been significantly reduced[14,35]. However, post-thoracentesis ultrasound has rarely been utilized in clinical practice to evaluate other meaningful questions, such as those highlighted in this study. The strong agreement between ultrasound and CXR on the success of pleural space evacuation in this study extends the role of ultrasound to the post-procedural arena and can impact timely management and follow-up, reduce radiation exposure, and change the current post-procedure care algorithm.

An additional benefit of post-procedural ultrasonography is that clinically important findings, such as the pre and post-procedure motion and shape of the diaphragm, which are

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relevant markers of symptomatic response, can predict post-drainage symptom resolution[36]. We underscore that multiple anatomical views should always be obtained when feasible, as patients with an elevated BMI are more likely to have suboptimal or poor images in the mid-axillary view. With a median time of 161 seconds for post-thoracentesis ultrasound evaluation, proceduralists demonstrate the capability to conduct comprehensive assessments, gathering real-time data on underlying lung/pleural space pathology. Our findings would further mandate the necessity of saving and storage of ultrasound images in the electronic medical record, facilitating providers' access to prior post-thoracentesis ultrasound images, and enhancing clinical continuity.

This study has several notable strengths. To ensure generalizability, we focused on free-flowing pleural effusion, the most common type of effusion, and enrolled patients from six centers. Our study design was crafted to align with real-world clinical workflows, ensuring the practical applicability of our findings. The precision of our measurements was validated through a collaborative, multi-disciplinary approach involving pulmonologists and thoracic radiologists, providing a thorough assessment of inter-observer reliability. Furthermore, the study's investigation of secondary exploratory endpoints, including self-assessment of lung apposition between ultrasound and CXR and concordance of parenchymal abnormalities, provides a more comprehensive perspective on the use of ultrasound in the post-thoracentesis setting, beyond just complication.

However, it's important to acknowledge certain limitations in our study. Firstly, our study exclusively addresses non-loculated free-flowing pleural effusions, restricting the generalizability to patients with more complex pleural spaces. In addition, 50% of our cohort included patients with MPE which may have contributed to a higher number of trapped lung.

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The role of post-procedure ultrasound vs CXR may need to be further explored among populations with higher prevalence of other effusion etiologies. Although ultrasound images were obtained immediately after thoracentesis, CXR images were obtained within 4-hours post-drainage, during which time pleural fluid re-accumulation may have occurred in some patients, which may have contributed to isolated discrepancies Between CXR and ultrasound findings. This, however, represents practice in a real-life setting, as the ultrasound exam at the time of CXR was not considered pragmatic. In this study, proceduralists were interventional pulmonologists from high-volume academic tertiary-care centers; examination quality and speed may not be generalized to all operators. In addition, proceduralists assessment of trapped lung based on CXR, followed their assessment for trapped lung using patient symptoms and post-thoracentesis ultrasound findings, which may have influenced their interpretation of CXR and under or over-estimate trapped lung assessment by CXR. This however represents common clinical practice, as most proceduralists use their clinical bedside information along with CXR to globally assess pleural space physiology.

Finally, while our findings suggest that ultrasound is generally sufficient for post-procedural pleural space assessment, there may be specific scenarios where a CXR remains useful such as in patients with higher BMI where a CXR may provide additional diagnostic clarity. Further research is needed to determine the optimal imaging approach in this patient population. Given the lack of ultrasound image storage in most centers, a CXR could serve as a valuable baseline for comparison in patients at risk for re-accumulation. An important practice limitation is that while ultrasound images are available on a separate database, pre and post-thoracentesis ultrasound images, and, importantly, videos, are not included within the primary image storage database of most hospitals. Our findings suggest that the inclusion of ultrasound

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images and videos in primary image storage systems of hospitals, along with detailed interpretation of ultrasound findings in procedure notes, is a valuable initiative and may impact patient care as well as cost.

Conclusion:

The EVACUTE study presents the first direct comparison of ultrasound and CXR with respect to their clinical utility in post-thoracentesis pleural space evacuation. The results show that CXR offers limited additional benefits over point-of-care post-procedure ultrasound when assessing drainage of the pleural space. These findings show that ultrasound can effectively assess pleural space evacuation in real time and can be a reliable alternative to CXR. Future studies should focus on the cost-effectiveness and feasibility of implementing point-of-care thoracic ultrasonography in standard post-thoracentesis care.

Tables and Figures:

Table 1: Demographics:

Variable	**N = (145)**
Age, y	64 (56-75)
Female	76 (52.8)
BMI (kg/m^2) †	27.4 (23.7-32.4)
Smoking history	
- Never	72 (50)
- Former	58 (40)
- Current	15 (10)
Number of prior thoracenteses	1 (0-2)
Laterality of thoracentesis	
- Right	103 (71)
- Left	42 (29)
Volume of fluid removed (ml)	1300 (850-1820)

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Reason for discontinuation of procedure	
- Spontaneously stopped or tapped dry	65 (45)
- Chest pain	61 (42)
- Cough	19 (13)
Etiology/Diagnosis††	
- Malignant Pleural Effusion	49 (50)
- Hepatic Hydrothorax	22 (22)
- Congestive Heart Failure	11 (11)
- Chronic Kidney Disease	3 (3)
- Chylothorax	2 (2)
- Parapneumonic effusion	2 (2)
- Other	10 (10)
Serum LDH (u/l)	251 (206-305)
Serum protein (g/dl)	6.4 (5.7 – 7.1)
Pleural LDH (u/l)	149 (99 – 342.5)
Pleural protein (g/dl)	3.3 (2.4-4.2)

Table 1: Baseline characteristics with median (IQR) for continuous variables and the number of patients with relative frequencies (%) for categorical variables. The body-mass index is the weight in kilograms divided by the square of the height in meters. †BMI was only recorded in 106. ††A suspected etiology was only recorded in 77 cases.

Table 2: Pre- and Post-Thoractensis Ultrasound Characteristics per Primary Proceduralist

Variable (N = 145)	**Pre-Thoractensis**	**Post-Thoractensis**
Image view obtained n (%)		
- Anterior view	86.9 (126)	86.2 (125)
- Mid-axillary view	98.6 (143)	97.9 (142)
- Posterior view	100 (145)	100 (145)
Size of effusion in rib spaces Median (IQR)		
- Anterior view	3 (2-4)	1 (0-2)
- Mid-axillary view	3.5 (3-5)	1 (0-2)

- Posterior view	4.5 (5-6)	2 (1-3)
Estimated effusion volume on US † Median (IQR)		
- Anterior view	858.9 (614.8-1160.8)	500.5 (302-817.6)
- Mid-axillary view	911.4 (665.4-1212.1)	500.5 (314.3-735.7)
- Posterior view	1026.9 (783.3-1267)	588.4 (362.4-776.7)
Presence of B-lines on US n (%)		
- Anterior view	60 (45.1)	75 (56.4)
- Mid-axillary view	63 (44.4)	80 (55.6)
- Posterior view	76 (53.5)	79 (54.9)
Presence of lung sliding on US n (%)		
- Anterior view	114 (85.1)	118 (86.1)
- Mid-axillary view	120 (85.1)	117 (81.8)
- Posterior view	119 (83.8)	121 (83.5)
Pleural space characteristics pre-procedure n (%)		
- Anechoic	112 (77.2)	X
- Echogenic	22 (15.2)	X
- Thin septations	17 (11.7)	X
- Moderate to dense septations	6 (4.1)	X
Parenchymal abnormalities post procedure† n (%)		
- Atelectasis	X	47 (32.4)
- Subpleural consolidation	X	45 (31)
- Pleural thickening	X	27 (18.6)
- Consolidation with air bronchograms	X	18 (12.4)
- Pleural nodule or mass	X	8 (5.5)
- Lung nodule or mass	X	6 (4.1)
- Other	X	1 (0.7)
Diaphragmic shape n (%)		
- Normal	76 (52.8)	129 (90.2)
- Flattened	45 (31.3)	10 (7)
- Inverted	23 (16)	4 (2.8)
Diaphragmatic movement n (%)		
- Normal	95 (66)	132 (91.7)
- Paradoxical	49 (34)	12 (8.3)
Time to perform US (seconds) Median (IQR)	188 (160-238)	161 (120-210)

Table 2: Pre- and Post Thoractensis and ultrasound characteristics with median (IQR) for continuous variables and the number of patients with relative frequencies (%) for categorical variables. US = Ultrasound. †Quantification of volume was based on the Goecke 2 formula, which is calculated using the chest wall craniocaudal distance on the screen in centimeters (cm) plus the lung's basal distance to the diaphragm's center multiple by the constant 70. X = The variable was deemed not clinically meaningful at this point. † Only obtained on the post-thoracentesis ultrasound examination.

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Table 3: Agreement

Measure	Reader Agreement
Complete pleural space evacuation US – CXR agreement†	0.93 (0.83-1.00)*
Effusion size US - CXR agreement††	0.64 (0.51-0.77)
Complete pleural space evacuation US – blind US reviewers	0.81 (0.71-0.90)
Proceduralist self-assessment of trapped lung between US and CXR*	0.89 (0.81-0.96)
Parenchymal findings between US - CXR	
- Atelectasis	0.21 (0.05-0.38)
- Consolidation	0.13 (-0.05-0.31)*
- Lung Nodules or Masses	0.64 (0.58-0.76)*
- Pleural thickening	0.89 (0.83-0.95)*
Pneumothorax detection US – CXR agreement	
- Proceduralist and radiologist	0.30 (0.11-0.50)
- Radiologists	0.47 (0.23-0.71)

Table 3: Interobserver reliability for key study outcomes. *Agreement is quantified using Gwet's AC1 instead of kappa due to symmetrical imbalances in contingency tables (paradox resistant). †Complete pleural space evacuation is defined as an absence of pleural fluid on ultrasound (US) on all anatomical views and blunting of the costophrenic angle (CPA) or less on CXR. †† Post-procedure residual effusions were classified as "small" or "large" according to pre-defined criteria. A "small" effusion occupied less than one rib space on all three ultrasound views, while "large" effusions equaled or exceeded one rib space on any view. In CXR images, a small effusion was determined by blunting of the CPA (Grade 2 on methods 1 and 2, Supplementary Table 1), while a large effusion was noted to be larger than this. **Trapped lung was determined based on the proceduralists' assessment, considering ultrasound examination results after thoracentesis, the reason for terminating the procedure, and the presence or absence of chest pain.

Figure 1:

Figure 1: Pre- and post-thoracentesis evaluation of pleural effusion using US and CXR. A: Large free-flowing simple pleural effusion visible in the posterior view. B-C: Effusion size measured in the anterior and mid-axillary views. D: Pre-thoracentesis CXR with a pleural effusion (Arrow). E-G: Post-thoracentesis images showing resolution of the effusion and complete pleural evacuation in the mid-axillary, anterior, and posterior views. H: Post-Thoracentesis CXR with complete pleural evacuation.

Figure 2:

Figure 2: Forest plot showing hazard ratios (HR) and 95% confidence intervals (CI) with variables considered in the univariate Cox proportional hazards model with non-trapped lung on ultrasound (US) as the dependent variable. Non-trapped lung was defined radiographically as lung apposition to the parietal pleura. Reference level for Sex='Female', US Image = "Anechoic", Etiology='Non-Malignant'). A P value < 0.05 was considered statistically significant and an independent predictor of increased risk.

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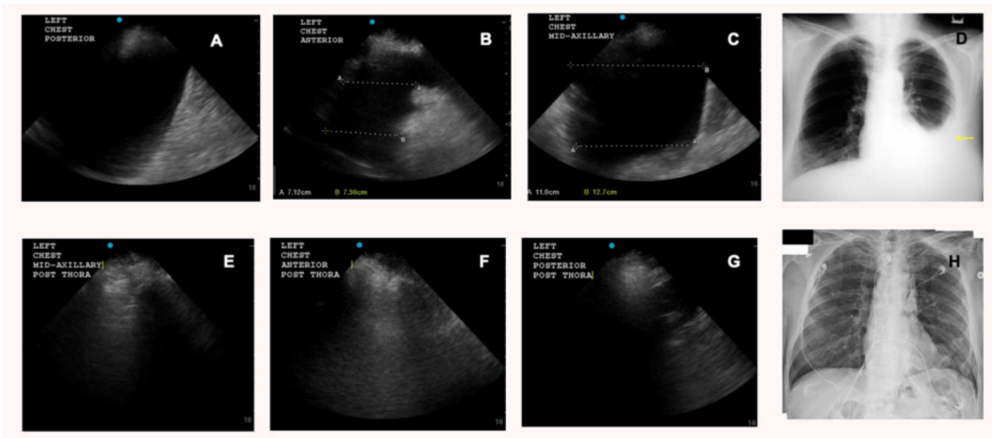

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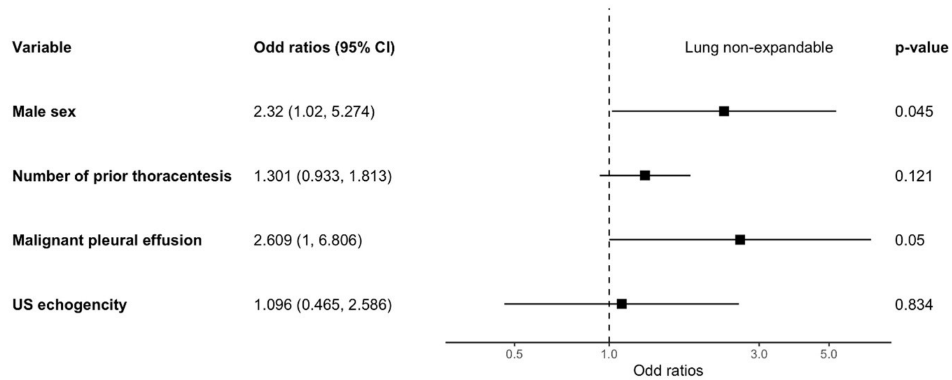

Figure 2: Forest plot showing hazard ratios (HR) and 95% confidence intervals (CI) with variables considered in the univariate Cox proportional hazards model with non-trapped lung on ultrasound (US) as the dependent variable. Non-trapped lung was defined radiographically as lung apposition to the parietal pleura. Reference level for Sex='Female', US Image = "Anechoic", Etiology='Non-Malignant'). A P value < 0.05 was considered statistically significant and an independent predictor of increased risk.

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Post-thoracentesis Ultrasound vs. Chest X-ray for the Evaluation of Effusion Evacuation and Lung Re-Expansion, A Multicenter Study

Data Supplement

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Supplementary Tables

Supplementary Table 1: Radiographic grading of effusion size

Grade	Method 1	Method 2
1	Sharp costophrenic angle, all of hemidiaphragm is visible (no visible effusion)	No pleural fluid present
2	Blunting of the costophrenic angle, but at least part of hemidiaphragm is still visible	Blunting of the costophrenic angle
3	Effusion greater than 1, and up to the inferior border of the vascular pedicle	Fluid occupying up to 25% of the hemithorax
4	Effusion greater than 2, and up to the top of the cardiac silhouette	Fluid occupying between 51-75% of the hemi thorax
5	Effusion greater than 3, above the cardiac silhouette	Fluid occupying between 76-100% of the hemithorax

Supplementary Table 1: Interobserver reliability for key study outcomes stratified by anatomical positioning. *Agreement is quantified using Gwet's AC1 instead of kappa due to symmetrical imbalances in contingency tables (paradox resistant). †Agreement for complete pleural evacuation was determined by comparing the presence or absence of effusion on ultrasound for each view (anterior, mid-axillary, and posterior) immediately after thoracentesis to the radiologist's interpretation on chest X-ray.

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