Original Article

Utilizing thoracic ultrasonography in determining the characteristics of pleural fluid: Development of a novel sonographic scoring system

Sükran Mutlu, Coşkun Doğan[1], Salih Küçük

Department of Pulmonology, Kocaeli City Hospital, [1]Department of Pulmonology, Faculty of Medicine, Istanbul Medeniyet University, Istanbul, Turkey

ABSTRACT

BACKGROUND: To evaluate the utility of thoracic ultrasound imaging (USI) in assessing the nature of pleural fluid (PF) using a scoring system.

METHODS: The files of patients who underwent thoracic USI and thoracentesis due to PF accumulation were retrospectively examined. PF sonographic patterns and pleural thicknesses were retrieved from the USI records. Based on the Light's criteria, PFs were classified into transudative PF (TPF) and exudative PF (EPF). A scoring system was established based on the sonographic patterns and pleural thickness. Sonographic scores and other clinical, radiological, and demographic characteristics of the two groups were comparatively analyzed.

RESULTS: Among the 64 cases analyzed, 32 (50%) were categorized as TPF. The average pleural thickness in the TPF group was 1.4 mm. The hypoechoic sonographic pattern rate in the TPF group (75%) was significantly different from that in the EPF group ($p < 0.001$). A hypoechoic sonographic pattern ($p = 0.002$) and pleural thickness >1.5 mm ($p = 0.031$) were independent predictors of EPF. The scoring system demonstrated a sensitivity of 84.38% and a specificity of 75.00% for predicting EPF when the sonographic score was ≥ 3.

CONCLUSION: Thoracic USI can serve as a noninvasive method to predict the nature of PFs by combining sonographic patterns and pleural thickness.

KEYWORDS

Exudative pleural fluid, pleural fluid, pleural thickening, thoracic ultrasonography, transudative pleural fluid

Background

Thoracic ultrasound imaging (USI) is a reliable and effective method for evaluating pleural fluid (PFs), imaging of peripheral lung lesions and anterior mediastinal mass lesions, and determining parenchymal involvement in pneumonia, pneumothorax, pulmonary embolism, pulmonary edema, and various interstitial lung diseases. Currently, thoracic USI has clinical applications in diagnosing the various pleuropulmonary pathologies. The advantages of thoracic USI include real-time processing, nonexposure of patients and operators to radiation, and bedside applications.[1] The accumulation of PFs, a characteristic presentation of various pulmonary diseases, is majorly caused by congestive heart failure (CHF), infections, and malignancies.[2] In patients with PF, thoracentesis is the initial diagnostic procedure used for etiological investigations. The current guidelines

Corresponding author: Dr. Coşkun Doğan,
Faculty of Medicine, Istanbul Medeniyet University, Istanbul, Turkey.
E-mail: coskund24@hotmail.com

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recommend image-guided thoracentesis at the level of strong evidence to reduce the risk of complications in PF examination/thoracentesis procedures.[3] After the thoracentesis procedure, PFs are classified as transudative PF (TPF) and exudative PF (EPF) according to the gold standard Light's criteria.[4]

As thoracentesis is an invasive procedure, there is a need to develop noninvasive procedures to predict the etiology of PFs. Yang *et al*.[5] were the first to evaluate the value of USI in determining the nature of PFs in 1992. Subsequent studies, although limited, have also evaluated the utility of USI in determining the nature of PFs.[6-8] This study determined the etiology of PFs without performing thoracentesis based on a novel scoring system established by combining pleural thickness and ultrasonographic patterns.

Material and Methods

Patient population

This retrospective study examined the records of patients who visited the Chest Diseases Clinic between May 2023 and June 2024. These patients presented PFs on chest X-ray and/or thorax computed tomography (CT) scans and were scheduled for thoracentesis to investigate the etiology of PF. This study was performed according to the Declaration of Helsinki principles. The exclusion criteria were as follows: Patients who were previously examined and in whom the etiology of PF was known; patients with symmetric PF and clinical and radiological findings of CHF; and patients who responded to diuretic treatment. The detailed inclusion and exclusion criteria are shown in Table 1. This study was approved by the Ethics committee of our hospital (Decision No: 2024-95).

Patients with radiologically suspected PFs were first evaluated with thoracic USI by an experienced pulmonologist in our clinic. The sonographic parameters of the cases were examined and recorded [Table 2]. In cases with no contraindications and those who did provide informed consent, thoracentesis was performed in line with the procedure. The PF collected through thoracentesis was delivered to the biochemistry laboratory under the appropriate conditions and analyzed according to the Light's criteria [Table 3]. The levels of lactate dehydrogenase and total protein in the collected fluid and serum were routinely determined.

Determination of pleural fluid with thoracic ultrasound imaging

Thoracic USI was performed by an experienced chest disease specialist using the General Electric (GE) Logiq 7 device (GE Ultraschall, 2018, Solingen; Germany) with a 3.5 MHz convex probe in the abdominal mode. The probe was moved transversely and longitudinally through the intercostal spaces with the patient in a sitting position. The entire thorax, including the parasternal line, mid and lateral clavicular line, anterior-mid and posterior axillary line, lateral and medial scapular line, and healthy

Table 1: Inclusion and exclusion criteria

Inclusion criteria
1-Age >18 years
2-Cases with an indication for thoracentesis procedure (who were not examined before, had no clinical and radiological findings of CHF, had asymmetric PF, or had no response to diuretic treatment)
3-Cases who accepted thoracentesis procedure
4-No contraindications to thoracentesis (not using anticoagulants, platelet count >30,000, or INR <1.5)
Exclusion criteria
1-Age <18 years
2-Pregnant cases
3-Cases without an indication for thoracentesis (who had been previously examined and in whom the etiology of PF was known, had symmetric PFs with clinical and radiological findings of CHF, or had responded to diuretic treatment)
4-Cases who do not accept the thoracentesis procedure
5-Cases with contraindications for thoracentesis (using anticoagulants, platelet count <30,000 or INR >1.5)

INR=International normalized ratio, CHF=Congestive heart failure, PF=Pleural fluid.

Table 2: Sonographic parameters and related definitions

Parameter	Definitions
1-Hypoechoic pattern	Similar to GB echogenicity and presence of echo-free spaces
3-Complex septa-free pattern	Multiple fibrin strips without small septations in fluid echogenicity. Echogenicity less than that of the LV (hypoechogenic)
4-Complex septate pattern	Presence of dense septations in fluid echogenicity (hyperechogenic). Echogenicity is higher than that of the LV
2-Hyperechogenic pattern	Heterogeneous echogenicity similar to LV echogenicity (isoechogenic)
5-Presence of snowy landscape appearance	Subtle echogenic fluctuation with position or respiratory movement in hyperechogenic fluid (snowy landscape appearance)
6-Presence of fibrin band	Fibrin bands in the fluid
7-Presence of atelectatic lung segment	The presence of an atelectatic lung segment in the fluid
8-Accompanying consolidation presence	The presence of consolidation in the lungs in areas adjacent to the fluid

GB=Gall bladder, LV=Liver.

Table 3: Light's criteria

Light's criteria
Ratio of PF protein to serum protein is >0.5
Ratio of pleural LDH to serum LDH is >0.6
PF LDH level is more than two-thirds the upper limits of laboratory value for serum LDH
Pleural effusion was considered exudative if one or more of the following criteria were met

LDH=Lactate dehydrogenase, PF=Pleural fluid.

areas along the paravertebral line, was scanned until PF was detected. Sonographic parameters, which were evaluated based on the methods of Yang *et al*.[5] were used to classify the sonographic patterns of PFs. The echogenicity of the gallbladder and the liver was used as the reference for the hypoechogenic and hyperechogenic patterns, respectively. The detailed classification of sonographic patterns is shown in Table 2 and Figure 1. The sonographic patterns of all cases were recorded.

Evaluation of the pleura using ultrasonography

After detecting PF using thoracic USI, the hemithorax containing the PF was scanned using a 10 MHz linear probe in the superficial mode with the GE Logiq 7 device (GE Ultraschall, 2018, Solingen; Germany). The visceral pleura was evaluated as a thin, bright, and echogenic line surrounding the lungs just below the PFs. The parietal pleura were just above the PF and closer to the linear probe. The thickness of the parietal pleura was measured and recorded in millimeters (mm) [Figure 2].

Thoracentesis procedure

Written informed consent was obtained from all the participants. The procedure was not performed in the following cases: Patients with platelet counts of <30.000/μL; patients with an international normalized ratio value of >1.5; patients who did not consent to thoracentesis. The area where the procedure was to be performed was sterilized with iodine-alcohol. Thoracentesis was performed with a 21G 50 mL syringe. Aspiration was performed after passing the intercostal space and pleura, which were previously marked based on thoracic USI.

General demographic data, smoking history, chronic diseases, and medications of the study cases were recorded. The radiological findings of the cases were evaluated. PFs were classified as follows based on the chest radiograph findings: Massive, PF extended to the second anterior rib; moderate, PF detected between the second and fourth anterior ribs; minimal, PF was detected below the fourth anterior rib. If available, the area where the fluids were the thickest on the thorax CT scan was recorded in mm. PFs were divided into the TPF and EPF groups based on the serum and PF biochemical examination results and Light's criteria. The data of these two groups were comparatively analyzed.

Ultrasonographic scoring model

This study developed a sonographic scoring system, called the PF Sonographic Scoring (PESS) system, by combining some parameters that can predict EPF or TPF. Each sonographic parameter was scored [Table 4]. Cases with PESS values of ≥3 points were classified into the EPF group, while those with PESS values of <3 points were classified into the TPF group. The findings based on the PESS system were compared with those based on the Light's criteria.

Statistical analysis

Statistical analysis was performed using the SPSS 17.0 (IBM Inc. Released in 2008. SPSS Statistic for Windows Chicago, USA). For descriptive statistics, continuous variables are expressed as mean ± standard deviation, whereas categorical variables are expressed as percentages. Normal distribution of the data was determined using the Kolmogorov–Smirnov test. The data of the groups were compared using the Mann–Whitney U test and the Chi-square test. The sensitivity, specificity, positive predictive value, and negative predictive value were calculated using the MedCalc software. Logistic regression analysis was used to determine the significance of ultrasonographic factors affecting the classification of PFs as EPF. To develop the pleural effusion sonographic scoring system, multivariable models were obtained with binary logistic regression. The results were considered significant at $P < 0.05$ with a confidence interval (CI) of 95%.

Results

Among the 64 patients with PFs, 19 (29.7%) were women and 45 (70.3%) were men. The average age of the patients

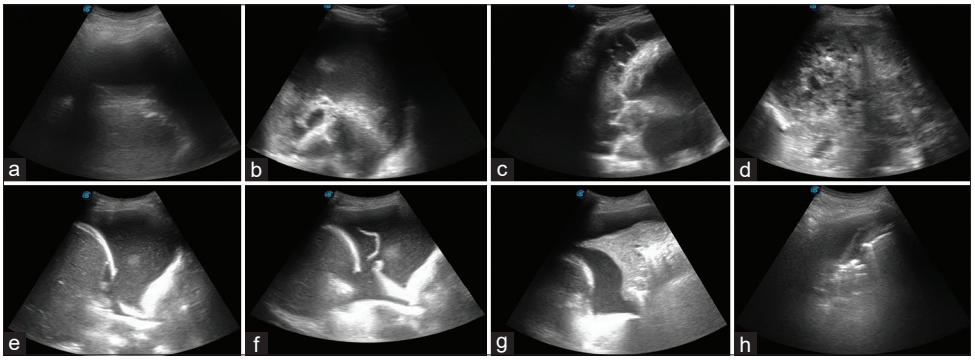

Figure 1: (a) Anechoic sonographic pattern, (b) Hyperechogenic sonographic pattern, (c) Complex septa-free sonographic pattern, (d) Complex septal sonographic pattern, (e) Presence of snowy landscape appearance, (f) Presence of fibrin band in the fluid, (g) Presence of consolidated lung space in the fluid, (h) Presence of atelectatic lung area.

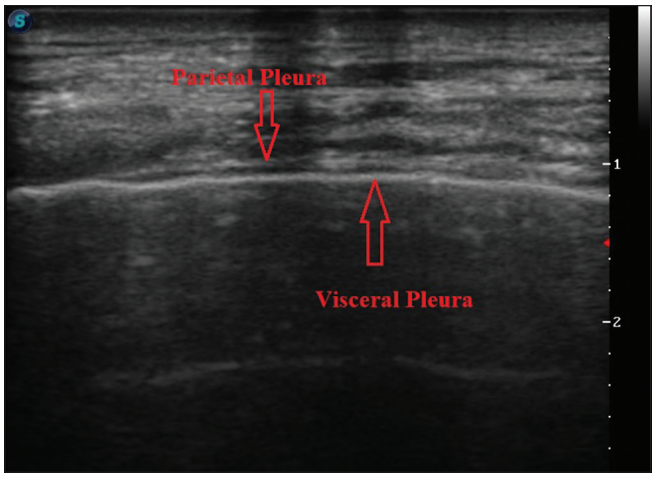

Figure 2: Thoracic ultrasonographic imaging with a 10 MHz linear probe view of the pleura in the superficial mode.

was 67.5 ± 15.2 years. Based on the Light's criteria, 32 (50%) cases had EPF and 32 (50%) cases had TPF. The number of cases with and without comorbidities was 21 (32.8%) and 43 (67.2%), respectively. The most common comorbidity was hypertension (32 [50%] cases) [Table 5]. Analysis of the treatment characteristics revealed that diuretics was used for treating PFs in 14 (21.9%) cases [Table 5]. Meanwhile, analysis of the radiological characteristics revealed unilateral and bilateral fluid accumulation in 36 (56.3%) and 28 (43.8%) cases, respectively. Minimal PFs determined based on chest radiography were observed in 33 (51.6%) cases. The average thickness of the fluid on the thorax CT scan was 58 ± 32.9 mm [Table 5].

Analysis of thoracic USI findings revealed that the most frequently detected sonographic finding was atelectasis (40 [62.5%] cases). The average pleural thickness was 2.53 ± 2.6 mm. The detailed sonographic characteristics are shown in Table 6.

In the logistic regression analysis model established using ultrasonographic factors affecting the classification of PF as EPF, hypoechoic pattern (P = 0.002 and CI: 3–164.5) and pleural thickness of >1.5 mm (P = 0.031 and CI: 0.056–0.867) were the independent factors [Table 7].

The parameters having $P < 0.20$ in the comparison of pleural thickness and sonographic patterns between the EPF and TPF groups were included in the multivariable models. The selected parameters were pleural thickness, anechoic sonographic pattern, complex septa-free pattern, hyperechogenic pattern, snowy landscape appearance, fibrin bands in the fluid, and consolidated lung space. Data sampling methods were applied using 80% of the data for the training set and 20% for the test set. Since high area under the curve, F1, and sensitivity values were obtained, we decided to use these parameters to develop the scoring system.

Table 4: Pleural effusion sonographic scoring system

Parameter	Point
Pleural thickness=0–1.5 mm	0
Pleural thickness=1.5–3 mm	1
Pleural thickness=3–4.5 mm	2
Pleural thickness >4.5 mm	3
Presence of anechoic sonographic pattern	0
Presence of hyperechogenic pattern	1
Presence of complex septa-free pattern	1
Presence of snowy landscape appearance	1
Presence of fibrin bands in the fluid	1
Presence of consolidated lung space	1
Total score 0–2	Low probability of EPF
Total score ≥3	High probability of EPF

EPF=Exudative pleural effusion.

The average PESS value of the cases was 3.9 ± 2.99. Meanwhile, the PESS values of the EPF and TPF groups were 5.5 ± 2.8 and 2.2 ± 2.1, respectively ($P < 0.001$).

The characteristics of 37 cases with a PESS value of ≥3 points determined using the PESS system were compared with those determined based on the Light's criteria. Comparative analysis revealed that 27, 8, 5, and 24 patients were true positive, false positive, false negative, and true negative cases, respectively. The sensitivity, specificity, positive predictive value, and negative predictive value of the PESS system for predicting EPF were 84.38%, 75.00%, 77.14%, and 82.76%, respectively, when the PESS value was ≥3 points.

Discussion

This study measured pleural thickness using USI and established a scoring system. This scoring system based on the combination of sonographic changes, such as anechoic, echogenic, or complex septa-free patterns, fibrin band, snowy landscape appearance of the fluid, and the presence of consolidated lung areas accompanying the fluid. The success of the scoring system in predicting the nature of PFs was examined. The sensitivity and specificity of the PESS system to predict EPF were 84.38% and 75.00%, respectively.

PF, which is caused by more than 60 clinical conditions associated with both benign and malignant etiologies, is among the leading causes of hospital admissions, morbidity, and mortality. In the United States, PF affects 1.5 million patients each year and accounts for approximately 20% of admissions at chest disease clinics.[3,9]

PF accumulates due to excessive filtration resulting from pressure changes (hydrostatic-oncotic pressure balances) when the pleura is intact. The cell content of PF is similar to that of the sera. EPF is caused by pleural damage/inflammation. The cellular content and density

Table 5: Clinical, demographic, laboratory, and treatment characteristics of study cases

	EPF (*n*=32)	TPF (*n*=32)	*P*
Age (years), mean±SD	64.3±17.4	70.7±12.2	0.094
Gender (female/male), *n* (%)	8/24 (25/75)	11/21 (34/66)	0.412
Smoking history	14 (44)	13 (41)	0.800
Smoking history (pack/year), mean±SD	24.9±18.4	23.4±22.2	0.809
Comorbidities, *n* (%)			
Comorbidity (presence)	20 (63)	23 (72)	0.424
HT	15 (47)	17 (53)	0.617
CHD	6 (19)	20 (62)	<0.001
DM	7 (22)	12 (38)	0.171
CRD	9 (28)	5 (16)	0.226
CKD	3 (9)	3 (9)	0.664
CND	3 (9)	2 (7)	0.500
Cancer (lung + extrapulmonary)	9 (39)	2 (7)	0.794
Treatment characteristics, *n* (%)			
Antihypertensive treatment	10 (31)	17 (53)	0.076
Antibiotic treatment	15 (47)	8 (25)	0.068
Diuretic therapy	3 (9)	11 (34)	0.016
Radiological characteristics, *n* (%)			
Unilateral PF	20 (62)	16 (50)	0.313
Bilateral PF	12 (38)	16 (50)	0.313
Solid PF	7 (22)	1 (3)	0.053
Moderate PF	11 (34)	12 (38)	0.794
Minimal PF	14 (44)	19 (59)	0.211
Fluid thickness on thoracic CT scan (mm), mean±SD	60.0±36.9	55.8±28.5	0.645
Laboratory values, mean±SD			
PF LDH (U/L)	365.9±219.6	79.4±25.9	<0.001
PF total protein (g/L)	43.3±9.9	26.5±18.3	<0.001
PF albumin (g/L)	2.6±0.7	1.4±0.7	<0.001
Serum LDH (U/L)	225.0±59.5	230.6±96.5	0.779
Serum total protein (g/L)	66.1±9.4	62.6±6.2	0.088
Serum albumin (g/L)	3.5±0.8	3.6±0.4	0.467

CT=Computed tomography, DM=Diabetes mellitus, PF=Pleural fluid, EPF=Exudative PF, TPF=Transudative PF, SD=Standard deviation, CRD=Chronic respiratory disease, CAD=Coronary artery disease, CHD=Chronic heart disease, CKD=Chronic kidney disease, CND=Chronic neurological disease, HT=Hypertension, LDH=Lactate dehydrogenase.

Table 6: Ultrasonographic characteristics of the cases

Sonographic feature	EPF (*n*=32), *n* (%)	TPF (*n*=32), *n* (%)	*P*
Presence of atelectatic lung segment	20 (63)	20 (63)	1
Echogenic sonographic pattern	26 (81)	8 (25)	<0.001
Anechoic sonographic pattern	6 (19)	24 (75)	<0.001
Snowy landscape appearance	16 (50)	7 (22)	0.019
Consolidation presence	14 (44)	7 (22)	0.062
Presence of fibrin band	14 (44)	5 (16)	0.014
Complex septa-free sonographic pattern	14 (44)	2 (6)	0.001
Complex septate sonographic pattern	1 (3)	0	0.313
Pleural thickness (mm), mean±SD	3.5±2.9	1.4±1.7	0.001

EPF=Exudative pleural effusion, TPF=Transudative pleural effusion, SD=Standard deviation.

of EPF are higher than those of the serum. EPF exhibits distinct sonographic echogenicity and is associated with increased pleural thickness. Meanwhile, TPF is associated with decreased cellular components in the fluid and hypoechogenicity without increased pleural thickness.[5,7,10] Based on these findings, this study hypothesized that EPF is associated with increased pleural thickness. Thus, EPF can be detected based on some sonographic changes resulting from increased density and excess cellular content.

Previous studies have reported that increased pleural thickness can predict EPF.[11,12] These studies measured pleural thickness in patients with EPF resulting from malignancy or infection. Limited studies have investigated pleural thickness in TPF. Yang *et al*.[5] reported that among the 76 cases in whom the pleural thickness was ≥3 mm, only 3 (3.9%) cases were TPFs, while 73 cases (96.1%) were EPFs. Wang *et al*.[13] reported that 98% of 307 cases with TPF had a pleural thickness of ≤3 mm. Sajadieh *et al*.[14] examined the utility of USI in predicting the nature of PF in PF cases as an alternative to thoracentesis and reported that pleural thickening (>3 mm) along with septation and echogenicity could predict EPF at high rates. In this study, the pleural thickness was significantly different between the TPF and EPF groups. The average pleural

Table 7: Multivariate logistic regression model for exudative pleural effusion

Variables	*B*	*P*	OR	95% CI
Hypoechoic pattern	3.116	0.002	22.559	3.093–164.539
Pleural thickness >1.5 mm	−1.516	0.031	0.220	0.056–0.867
Presence of snowy landscape appearance	1.137	0.256	3.119	0.438–22.190
Presence of fibrin band	−0.215	0.798	0.806	0.155–4.205
Presence of atelectatic lung area	0.170	0.820	1.186	0.273–5.153
Presence of consolidated lung space	0.340	0.666	1.405	0.300–6.580

CI=Confidence interval, OR=Odds ratio.

thickness in the TPF group was 1.4 mm. Pleural thickness of >1.5 mm was one of the two independent risk factors for predicting EPF.

Previous studies have reported that sonographic hypoechogenic or hyperechogenic imaging can be employed to determine the nature of PF. A review of these studies revealed that hyperechogenic sonographic appearance analysis is an effective method for predicting EPF. However, some studies reported that TPF can exhibit a hyperechoic appearance in a significant number of cases.[15] Asciak *et al*.[16] reported that sonographic echogenicity had a low specificity (57%) in determining the nature of the exudate. In this study, the hypoechoic sonographic pattern, which was detected in 75% of cases with TPF, was one of the independent risk factors to distinguish TPF from EPF. The hypoechoic pattern was not detected in 8 cases (25%) with TPF.

The specificity of the scoring system developed in this study was 75%. This low specificity may be because some sonographic parameters included in this study differ from those included in previous studies (consolidation, presence of fibrin band, and presence of atelectatic lung segment). The specificity (75%) reported in this study is higher than that reported by Asciak *et al*.[16] However, this specificity is not high enough to consider USI as an alternative for thoracentesis in distinguishing the nature of PFs owing to the heterogeneity of TPF. Acute or chronic TPF, TPF in patients using diuretics, and TPF complicated by infection may be associated with differential sonographic patterns (especially hyperechoic patterns and increased pleural thickening). Evans *et al*.[15] reported similar results and arrived at similar conclusions. The authors examined 166 PF cases and reported that anechoic images are not reliable for distinguishing TPF from EPF.

The contents of protein, blood, and fibrin particles in EPF are higher than those in TPF, rendering the EPF echogenic. In TPF, the fluid in the pleural space, which is the ultrafiltrate of the serum, contains decreased amounts of protein, blood, and fibrin.[17]

The sensitivity and specificity of the Light's criteria-based evaluation were 91.3% and 83.3%, respectively. These values indicate that Light's criteria can sometimes incorrectly classify EPF and TPF. Among the etiological factors of EPF, a limited number of conditions, such as lung cancer and pulmonary embolism can be incorrectly considered to be the etiological origin of TPF. However, the etiology of TPF is complex. In patients with TPF receiving diuretic treatment, Light's criteria may not be effective in determining the nature of PF. This is because PF can cause pleural thickening by promoting a pleural reaction due to the change in the cellular content of fluid or the prolonged accumulation of fluid in the pleural space.[18-20]

The sensitivity of the scoring system developed in this study was close to acceptable limits for a noninvasive method. However, the specificity of the scoring system was low because of the wide range of etiologies of TPF and the lack of understanding of the potential effects of treatment conditions or the duration of fluid accumulation in the pleural space on sonographic patterns and pleural thickness. Future studies must consider these features of TPF.

This study has several limitations that must be considered while interpreting the study results or planning similar studies. The sample size of the study was small. In addition, the ultrasonographic evaluations were performed in a single center. The interpretation of different observers may significantly affect the power of the study. The treatment characteristics of the cases, especially in the TPF group, were unknown. Various conditions, such as the duration of fluid presence in the pleural space before detection, can potentially affect the sonographic pattern and pleural thickness and can consequently affect the interpretation of the results.

Conclusion

This study demonstrates that thoracic USI is an effective noninvasive tool for differentiating EPF from TPF based on sonographic patterns and pleural thickness. The proposed sonographic scoring system exhibits high sensitivity and specificity and could serve as a complementary diagnostic tool in clinical practice. However, further prospective, multicenter studies are needed to validate these findings.

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Authors' contributions
ŞM,CD,SK conceived the research idea; ŞM,CD,SK conducted the research; CD performed the statistical analysis. All authors contributed substantially to the write-up of the article and all take responsibility of the content of the publication.

Ethical statement
This study was approved by the Ethics committee. (Decision No: 2024-95).

Participation consent
Informed consent was obtained from patients and volunteers.

Data availability statement
Data is available.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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