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Original Article

Can Ultrasound Pixel Density Serve as a Non-Invasive Alternative to Thoracentesis in Classifying Pleural Effusions?

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ABSTRACT

Objective: To determine the diagnostic performance of ultrasound pixel density in differentiating exudative from transudative pleural effusions, using Light's criteria as the gold standard.

Methodology: This cross-sectional validation study was conducted at the Pulmonology Department of Pak Emirates Military Hospital, Rawalpindi from January to April 2026, after institutional ethical approval. One hundred and ten patients with pleural effusions confirmed by ultrasound and scheduled for diagnostic thoracentesis were enrolled using a non-probability consecutive sampling technique. Written informed consent was obtained from all patients. A curvilinear ultrasound probe (3-5 MHz) was used with standardized depth (8 cm) and gain (60 dB) settings. Three frozen B-mode images were obtained per patient, and pixel density was quantified within a 1 cm^2 region of interest using ImageJ software. Ultrasonographic pixel density ≥9.5 was classified as exudative. Light's criteria were applied to pleural fluid biochemistry as the gold standard. Data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 27.0.

Results: Among 110 patients (mean age 42.29±9.09 years; 61.8% males), 66(60%) were classified as having exudative and 44(40%) as having transudative pleural effusion according to Light's criteria. At the 9.5 cut-off value, pixel density demonstrated a sensitivity of 25.76%, specificity of 95.45%, positive predictive value (PPV) of 89.47%, negative predictive value (NPV) of 46.15%, and an overall diagnostic accuracy of 53.64%. Receiver operating characteristic (ROC) analysis showed an area under the curve (AUC) of 0.75 (p <0.001). Median pixel density was significantly higher in exudative effusions (3.35) compared with transudative effusions (1.50) (p <0.001).

Conclusion: Pixel density on ultrasound at a cut-off value of 9.5 demonstrated high specificity with low sensitivity for differentiating exudative from transudative pleural effusion. The ROC analysis showed fair diagnostic accuracy of ultrasound pixel density. This technique may serve as a useful adjunct in the evaluation of pleural effusion; however, it cannot be used as the only diagnostic test instead of thoracentesis.

Keywords: *Pleural effusion. Thoracentesis. Sensitivity and specificity.*

INTRODUCTION

Pleural effusion, characterized by excessive fluid in the pleural cavity, is a common clinical condition encountered by pulmonologists, internists, and surgeons alike. It has a wide range of causes, including congestive heart failure, pneumonia, tuberculosis, and cancer.[1] Differentiating between transudative and exudative effusions is the first step in clinical decision-making, which leads to further diagnostic evaluation and specific treatment. The classification is determined through thoracentesis, followed by biochemical analysis using Light's criteria. This is an invasive procedure that can result in complications such as pneumothorax and bleeding, and may be limited by a lack of laboratory support, especially in rural settings.[2]

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Bedside thoracic ultrasound is also frequently used in the detection and evaluation of pleural effusions.[3] Although semi-quantitative sonographic features, such as septations, echogenicity, and pleural thickening, have demonstrated some correlation with exudative effusions, they are subjective and operator-dependent, making them unreliable as independent predictors.[4]

The idea of quantifying pleural fluid echogenicity using pixel density measurements can be more objective and consistent. This quantitative approach minimizes subjective interpretation and reduces inter-observer variability during ultrasound examination.[5] Previous literature revealed that median pixel density was higher in exudative effusions compared to transudative effusions, highlighting the potential of this technique in differentiating pleural fluid types. Therefore, quantitative analysis of pleural fluid echogenicity may serve as a valuable adjunct to conventional thoracic ultrasound and contribute to more accurate clinical decision-making.[6]

The initial studies using ImageJ based platforms for pixel based echogenicity analysis have shown promising results; however, validation across diverse clinical settings remains limited.[5,6] The

rationale of the present study was to address this gap by evaluating the diagnostic utility of ultrasound derived pixel density in a tertiary care hospital in Pakistan, where tuberculosis and infection-related pleural effusions are common. The current study aimed to assess the diagnostic performance of ultrasound-based pixel density in differentiating exudative from transudative pleural effusions, using Light's criteria as the gold standard.

METHODOLOGY

The cross-sectional validation study was carried out from January to April 2026 in the Department of Pulmonology, Pak Emirates Military Hospital, Rawalpindi, following ethical approval from the institutional review committee (Letter No. A/28/ERC/161/25, 30-12-2025). A sample size of 110 was calculated with a 95% confidence level, 10% precision, a prevalence of exudative effusion of 60.2%, and the reported sensitivity and specificity of pixel density (22% and 97%, respectively) using Light's criteria as the gold standard.[6] A non-probability consecutive sampling technique was used to enroll patients after obtaining written informed consent.

Both male and female patients (aged 18 to 60 years) with a pleural effusion of 15 mm or greater on thoracic ultrasound and scheduled for diagnostic thoracentesis as part of their routine care were included. Patients with loculated pleural effusions, history of pleurodesis, hemodynamic instability or respiratory distress, empyema, recent hemothorax or chest trauma, massive pleural effusion requiring urgent drainage, poor ultrasound window (due to subcutaneous emphysema or obesity), and known malignancy with recurrent effusions were excluded.

Chest ultrasound was performed using a curvilinear 3-5 MHz probe with a fixed depth (8 cm) and gain (60 dB). The patient was examined in a seated, or semi-recumbent position, and the probe was positioned longitudinally on the chest wall. The operator captured three frozen ultrasound images in the B (brightness) mode. A 1 cm^2 region of interest within the pleural fluid was used to calculate the pixel density using the image processing software program, ImageJ. Pixel values were initially measured on a scale of 0 to 255 and were then proportionately converted to 0 to 100 for consistency. Any effusion with a mean pixel density of $\geq$9.5 was considered exudative, and <9.5 as transudative. The cut-off value of 9.5 for pixel density was selected based on the findings of Soni et al., who demonstrated that pleural effusions with a pixel density $\geq$9.5 were highly suggestive of exudative effusions.[6] All measurements were made independently by two blinded radiologists (with at least 5 years post-fellowship experience in thoracic imaging) and the average of the two pixel densities was taken.

The lead researcher and clinical team performed thoracentesis within 30 minutes of the ultrasound examination under aseptic conditions. Collected pleural fluid and paired serum samples were analyzed for total protein and lactate dehydrogenase (LDH) concentrations. Effusions were categorized as exudative or transudative based on Light's criteria, which served as the gold standard throughout. An effusion was considered exudative when $\geq$1 of the following criteria was fulfilled: a pleural fluid protein-to-serum protein ratio exceeding 0.5, a pleural fluid LDH-to-serum LDH ratio exceeding 0.6, or a pleural fluid LDH value greater than two-thirds the upper reference limit for serum LDH.[7]

Patients with exudative pleural effusion according to Light's criteria and ultrasound pixel density ≥9.5 were considered true positives (TP)**.** Patients with transudative pleural effusion according to Light's criteria, but a pixel density ≥9.5 were considered false positives (FP**)**. Patients with exudative pleural effusion according to Light's criteria but a pixel density <9.5, were considered false negatives (FN)**.** Patients with transudative pleural effusion according to Light's criteria and a pixel density <9.5 were considered true negatives (TN)**.**

STATISTICAL ANALYSIS

Data were entered and analyzed using the Statistical Package for the Social Sciences (SPSS) version 27.0. Normality of continuous variables was assessed using the Shapiro-Wilk test before analysis. Categorical variables were presented as frequencies and percentages. Normally distributed continuous variables were expressed as mean±standard deviation, while non-normally distributed continuous variables were presented as median and interquartile range (IQR). The Mann-Whitney U test was used to compare non-normally distributed continuous variables.

The diagnostic utility of pixel density was assessed by calculating sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), overall diagnostic accuracy, and ROC curve analysis with estimation of the AUC. An AUC equal to or greater than 0.6 is considered meaningful. Values ≥0.6 and <0.7 indicate poor diagnostic accuracy, ≥0.7 to <0.8 suggest fair accuracy, ≥0.8 to <0.9 reflect good accuracy while values ≥0.9 represent excellent diagnostic accuracy.[8] The

optimal cut-off value was determined using the Youden index. Diagnostic accuracy parameters were reported with 95% confidence intervals (CI). A p-value <0.05 was considered statistically significant.

RESULTS

The Shapiro-Wilk test confirmed normal distribution for all continuous variables (p >0.05) except pixel density (p <0.001). The mean age of patients was 42.29±9.09 years, with 68(61.8%) being males and 42(38.2%) being females. The mean body mass index (BMI) was 23.22±3.05 kg/m². Among BMI categories, 72(65.5%) patients had normal weight, 28(25.5%) were overweight, 8(7.3%) were underweight, and 2(1.8%) were obese. Non-smokers formed the largest group with 58(52.7%) patients followed by smokers 30(27.3%) and ex-smokers 22(20%). The most common co-morbidity was diabetes mellitus [22(20.0%)], hypertension [21(19.1%)], combined hypertension and diabetes [16(14.5%)], and dyslipidemia [13(11.8%)]. The mean duration of symptoms was 3.32±1.53 months.

Based on Light's criteria, 66(60%) patients were classified as having exudative and 44(40%) as having transudative pleural effusions. Using the pixel density cut-off of 9.5, 19(17.3%) patients were classified as having exudative and 91(82.7%) as transudative effusions. The median pixel density was significantly higher in exudative effusions (3.35, IQR:1.45-10.33) compared to transudative effusions (1.50, IQR:0.53-2.41) (p <0.001). The 2x2 contingency table comparing ultrasound pixel density-based classification of pleural effusion with Light's criteria as gold standard is shown in Table 1.

The diagnostic accuracy parameters of ultrasound pixel density at the 9.5 cut-off are presented in Table 2. The ROC curve analysis showed an AUC of 0.75 (p <0.001), indicating fair discriminatory ability (Figure 1). The Youden index suggested an optimal cut-off of 1.65, which offered higher sensitivity (89.4%) but at the cost of reduced specificity (56.8%) and a greater risk of false positives in clinical use.

Stratified analysis demonstrated variation in sensitivity across different subgroups. Sensitivity was higher among females (39.3%) compared to males (15.8%), while specificity remained comparable (92.9% vs 96.7%). In the 46-60 years age group, sensitivity was higher (45%) compared to the 31-45 years group (17.5%). Across BMI categories, normal-weight patients showed higher sensitivity (31.8%) than overweight patients (11.8%). By smoking status, specificity remained consistently above 90% across all subgroups. These findings are descriptive and should be interpreted with caution due to variability in subgroup sample sizes (Table 3).

Table 1: 2×2 Contingency Table of Ultrasound Pixel Density-Based Classification of Pleural Effusion versus Light's Criteria (Gold Standard)

Pixel Density-Based Classification of Pleural Effusion	Light's Criteria on Thoracentesis (Gold Standard)		Total
	Exudative	Transudative	
Exudative (≥9.5)	17(89.5%) (TP)	2(10.5%) (FP)	19(100%)
Transudative (<9.5)	49(53.8%) (FN)	42(46.2%) (TN)	91(100%)
Total	66(60%)	44(40%)	110(100%)

Table 2: Diagnostic Performance of Ultrasound Pixel Density for Classification of Pleural Effusion

Parameters	Value	95% Confidence Interval
Sensitivity	25.76%	16.7% - 37.4%
Specificity	95.45%	84.9% - 98.7%
Positive Predictive Value	89.47%	68.6% - 97.1%
Negative Predictive Value	46.15%	36.3% - 56.3%
Diagnostic Accuracy	53.64%	44.4% - 62.7%

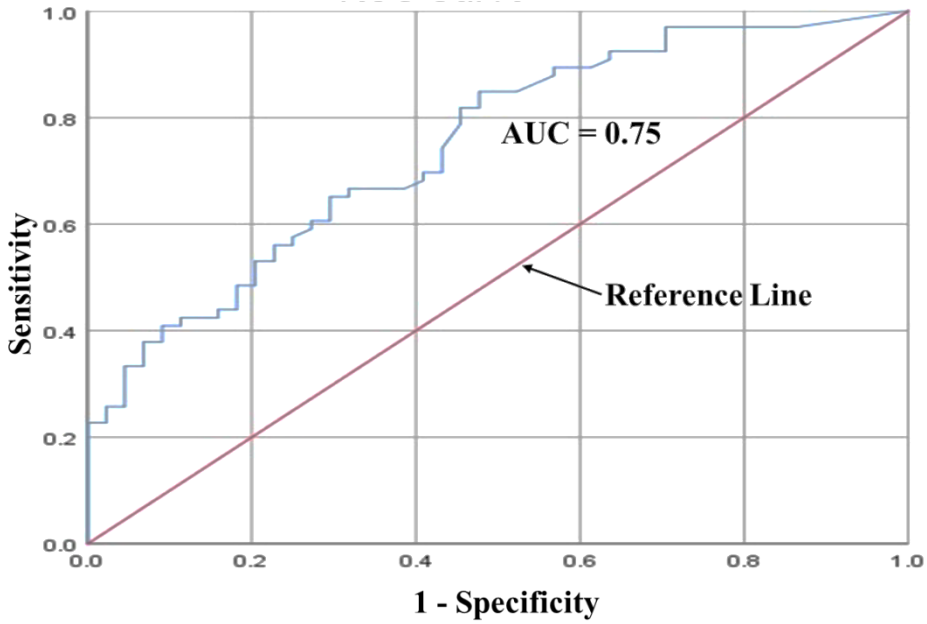

Figure 1: Receiver Operating Characteristic Curve for Ultrasound Pixel Density in Differentiating Exudative and Transudative Pleural Effusion

Table 3: Stratified Diagnostic Performance of Ultrasound Pixel Density by Patient Characteristics

Variables		Total n(%)	Sensitivity	Specificity	Overall Diagnostic Accuracy
Gender	**Male**	68(61.8%)	15.8%	96.7%	51.5%
	Female	42(38.2%)	39.3%	92.9%	57.1%
Age (Years)	**18-30**	9(8.2%)	16.7%	100.0%	44.4%
	31-45	60(54.5%)	17.5%	95.0%	43.3%
	46-60	41(37.3%)	45.0%	95.2%	70.7%
BMI	**Normal BMI**	72(65.5%)	31.8%	92.9%	55.6%
	Overweight	38(34.5%)	11.8%	100.0%	46.4%
Smoking	**Smoker**	30(27.3%)	26.3%	90.9%	50.0%
	Non-smoker	58(52.7%)	25.7%	100.0%	55.2%
	Ex-smoker	22(20.0%)	25.0%	90.0%	54.5%

DISCUSSION

Pleural effusion is a common condition encountered in a variety of benign and malignant diseases. The ability to characterize pleural effusions non-invasively without thoracentesis would be particularly beneficial in low resource settings.[9] This study revealed that, at the 9.5 cut-off value, pixel density yielded a sensitivity of 25.76%, specificity of 95.45%, PPV of 89.47%, NPV of 46.15%, and an overall diagnostic accuracy of 53.64%. Receiver operating characteristic analysis demonstrated an AUC of 0.75, with fair discriminative ability (p <0.001). These findings are comparable to those reported by Soni et al., who observed a specificity of 97% and sensitivity of 22% at the same pixel density cut-off (9.5) in a study of 83 patients.[6] Similarly, El-Dakkak et al. quantified pleural fluid echogenicity using ultrasound-derived pixel density in 140 patients and reported an AUC of 0.77 (p <0.001), with specificity of 90.62%, sensitivity of 47.7%, PPV of 70%, and NPV of 79.1% at a cut-off value of ≤0.2363 for transudative effusions.[10] These findings are broadly comparable with the present study, demonstrating high specificity and fair discriminative ability on ROC analysis. The observed variations in sensitivity and specificity between studies may be attributed to differences in cut-off values, patient populations, ultrasound equipment, and imaging techniques. The Youden index in the present study suggested an alternative

threshold of 1.65, which provided higher sensitivity (89.4%) at the expense of lower specificity (56.8%). Although this cut-off would identify a greater proportion of exudative effusions, it would also increase the number of false-positive results. The trade-off between sensitivity and specificity across different thresholds supports the conclusion that pixel density alone cannot serve as a definitive binary diagnostic test; however, high pixel density values may help rule in exudative pleural effusions.

Kummerfeldt et al. performed a meta-analysis of 5 studies with 1422 effusions, and reported a pooled specificity of 0.92 (95% CI:0.59 to 0.99) and sensitivity of 0.71 (95% CI:0.57 to 0.82) for echogenic ultrasound patterns in detecting exudates, with an overall AUC of 0.81 indicating good discriminatory ability.[11] Although the magnitude of sensitivity in our study was lower, both findings consistently support that ultrasound-based echogenicity or pixel density analysis has better specificity than sensitivity in differentiating exudative from transudative pleural effusion.

Gardiner et al. introduced the score including Diaphragmatic Nodularity, Unilateral Effusion, Echogenicity, Pleural Thickening, and Septations (DUETS). Using a threshold of ≥2, the DUETS score demonstrated a sensitivity of 100%, specificity of 94.6%, PPV of 98.8%, and NPV of 100%. An excellent diagnostic performance was indicated by AUC of 0.999 on ROC curve analysis.[12] This suggests that a combination of ultrasound features may offer superior diagnostic accuracy compared to a single parameter such as pixel density. In contrast, Rampradeep et al. developed the score including Pleural Thickening, Echogenicity, Loculations, and Laterality (TELL) based on multiple ultrasonographic parameters. At a cut-off value of 2, they reported a sensitivity of 98.4% but a lower specificity of 40.0%, with an AUC of 0.79, indicating fair discriminatory ability.[13] Mutlu et al. reported that a sonographic scoring system combining patterns of echogenicity with pleural thickness had a sensitivity of 84.38% and a specificity of 75%, which was better than pixel density alone.[14]

The median pixel density scores were significantly higher in exudative effusions than in transudative effusions (3.35 vs. 1.50; $p < 0.001$) in the present study. A previous study also reported that the median pleural fluid pixel density was significantly higher in exudates compared to transudates (3.53 vs. 2.32; $p=0.038$).[6] These findings are supported by biological evidence that exudates have higher levels of protein, cell debris, and inflammatory factors, all of which contribute to greater echogenicity of pleural fluid.[15] In a study of 582 patients, Wang et al. reported that complex sonographic appearances of pleural effusion were significantly more frequent in exudative than in transudative effusions: 99.7% of transudative effusions appeared anechoic.[16] Ayoubpour et al. also found pleural thickening, nodules and fluid loculation to be significantly associated with exudative effusions in a study of 72 patients.[17]

Bhutta et al. compared computed tomography (CT) scan with ultrasound in classifying pleural effusions, and found that ultrasound was superior in the detection of loculations.[18] Marchi et al. conducted a narrative review of new imaging techniques and noted that although quantitative pixel density analysis is promising, methodological challenges such as inter-operator variability, lack of device standardization, and small sample sizes, continue to limit its use.[19] Another study examined correlations among Light's criteria, pleural fluid procalcitonin levels, and sonographic features in 89 patients. Complex septate patterns and pleural thickening strongly favored exudative effusions, while an anechoic appearance pointed toward transudates.[20] These findings suggest that combining biochemical and ultrasound data may yield better diagnostic results than relying on either approach alone.

Subgroup analysis showed some interesting trends in our study. Sensitivity was higher among females (39.3%) than males (15.8%), and among patients aged 46-60 years (45%) compared with those aged 31-45 years (17.5%). These findings may reflect variations in the inflammatory and proteinaceous composition of pleural effusions across demographic strata. It has been previously reported that ultrasound-derived pixel density is significantly higher in exudative pleural effusions, likely related to increased cellular and protein content.[6] However, unlike the present study, they did not evaluate diagnostic performance across age, gender, or BMI subgroups. The consistently high specificity across all strata in our study suggests that elevated pixel density remains a reliable predictor of exudative effusion irrespective of demographic characteristics. Therefore, the present findings also provided additional insight into potential demographic variations in the diagnostic performance of ultrasound-derived pixel density.

CONCLUSION

Ultrasound derived pixel density demonstrated fair diagnostic performance in differentiating exudative from transudative pleural effusions, with an AUC of

0.75. At the optimal cut-off value of 9.5, the technique showed high specificity but low sensitivity, indicating a greater ability to identify exudative effusions. Stratified analysis revealed variability in sensitivity across demographic and clinical subgroups, whereas specificity remained consistently high. These findings suggest that pixel density may serve as a useful adjunctive tool in the evaluation of pleural effusions; however, it cannot replace thoracentesis or established diagnostic methods.

LIMITATIONS & RECOMMENDATIONS

The cross-sectional, single-centered design of this study may restrict the generalizability of the findings to other healthcare settings. The relatively small sample size, particularly within subgroup analysis, may limit the precision and robustness of the estimates. The use of consecutive sampling may introduce selection bias. The study also did not assess the etiological spectrum of pleural effusions; therefore, diagnostic performance across specific causes such as tuberculosis, malignancy, and heart failure could not be determined. Further large-scale, multi-centered studies with standardized imaging protocols are warranted to validate and extend these findings.

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Authors' Contributions:
A.J: Conceptualization, data collection, analysis, and manuscript writing.
M.Z.H.M: Study supervision, methodology, and critical review.
M.K.A.K: Data interpretation, statistical analysis, and manuscript review.
A.U.K: Patient recruitment, data collection, and manuscript review.
N.A: Ultrasound assessment, data acquisition, and manuscript editing.
M.H: Literature review, data entry, and manuscript formatting.

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