ORIGINAL ARTICLE

# Efficacy of CT in diagnosis of transudates and exudates in patients with pleural effusion

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PURPOSE
We aimed to evaluate the efficacy of multidetector computed tomography (CT) imaging in diagnosis of pleural exudates and transudates using attenuation values.

MATERIALS AND METHODS
This retrospective study included 106 patients who were diagnosed with pleural effusion between January 2010 and June 2012. After the patients underwent chest CT, thoracentesis was performed in the first week. The attenuation values of the pleural effusions were measured in all patients.

RESULTS
According to Light's criteria, 30 of 106 patients with pleural effusions had transudates, and the remaining patients had exudates. The Hounsfield unit (HU) value of the exudates (median, 12.5; range, 4–33) was significantly higher than that of the transudates (median, 5; range, 2–15) ($P =$ 0.001). Additionally, when evaluated by disease subgroups, congestive heart failure and empyema were predictable in terms of median HU values of the pleural effusions with high and moderate sensitivity and specificity values (84.6% and 81.2%, respectively; 76.9% and 66.7%, respectively). Compared with other patients, the empyema patients had significantly more loculation and pleural thickening.

CONCLUSION
CT attenuation values may be useful in differentiating exudates from transudates. Although there is an overlap in most effusions, exudate can be considered when the CT attenuation values are >15 HU. Because of overlapping HU values, close correlation with clinical findings is essential. Additional signs, such as fluid loculation and pleural thickness, should be considered and may provide further information for the differentiation.

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**P**leural effusion is a common clinical problem; indeed, it can arise from many diseases (1, 2). The first step in assessing a pleural effusion is to decide whether the pleural fluid is a transudate or an exudate (3). Transudate is caused by imbalances in hydrostatic and oncotic forces. It results from diseases such as heart failure, kidney failure, and cirrhosis. However, an exudate occurs when local factors influencing the accumulation of pleural fluid are altered. Exudates can be caused by clinical conditions such as pneumonia, malignancy, and thromboembolism (4).

Although clinical and radiological findings may provide significant evidence about the cause(s) of pleural effusion(s), it may still be necessary to evaluate some cases with diagnostic thoracentesis (4, 5). Clinically, exudative effusion can be successfully separated from transudative effusion using Light's criteria. The nature of the pleural effusion is based on diagnostic thoracentesis (1, 2). However, computed tomography (CT) can be used to evaluate the nature of pleural effusions to avoid the complications of thoracentesis (6, 7). Features such as pleural nodules, pleural thickening, loculation, extrapleural fat tissue thickness, and effusion density can be evaluated by CT to discriminate between exudates and transudates (8). Only two reported studies have examined CT attenuation values in patients with pleural effusions (9, 10); these showed different attenuation values for evaluation of pleural effusions.

The aim of the present study was to evaluate the efficacy of multidetector CT (MDCT) images in diagnosing pleural exudates and transudates using attenuation values.

## Materials and methods
### Study design and patient selection

The study protocol was reviewed and approved by the Harran University Ethics Committee. This retrospective study included 106 patients diagnosed with pleural effusion between January 2010 and June 2012. There were 60 males and 46 females; the median patient age was 68.5 years (range, 4–90 years). This study included patients with pleural effusions on chest CT and who underwent thoracentesis within one week. The classification of pleural effusion was based on Light's criteria, which diagnoses exudate pleural fluid when one or more of the following criteria is met: (a) a pleural fluid total protein/serum total protein ratio >0.5, (b) pleural fluid lactic dehydrogenase (LDH)/serum LDH ratio >0.6, or (c) pleural fluid LDH >two-thirds of the upper limits of the normal serum LDH value (2). The most likely causes of pleural effusion, such as pneumonia, malignancy, empyema, and congestive heart failure (CHF), were determined from the patient history in combination with laboratory data. Malignant pleural effusion was determined via positive pleural cytology or biopsy.

Patients who had pleural tubes prior to chest CT imaging, unclear causes of the pleural effusion, or no sampling in the first week, were excluded.

*CT protocol and imaging analysis*

CT was performed using 16-MDCT scanners (Siemens, Somatom Emotion, Erlangen, Germany) for all patients. Chest CT scanning was obtained at a slice thickness of 5 mm, 1.5 pitch, 110 kV, and 70–90 mAs. Intravenous contrast agent was not administered to patients with renal dysfunction or known allergy to the agent; contrast-enhanced CT was performed in 58 patients. In total, 47 patients underwent standard chest CTs after a standard injection protocol (100 mL of iopamidol-300 [Ultravist, Bayer Schering Pharma, Berlin, Germany]) at an injection rate of 2–2.5 mL/s. An angiographic examination was performed on 11 patients with 100 mL of intravenous contrast agent (iopamidol-300) at a rate of 3.5 mL/s. The attenuation values (Hounsfield units, HU) were measured for all patients using the imaging data. The circular region of interest (ROI) used for the quantitative measurements of the pleural effusion HU values was situated within the maximal amount of fluid in each slice of the three slices used (Figs. 1, 2). To assess pleural fluid attenuation, a circular ROI was situated at the maximum fluid level. The radiologist took care to not include areas in close proximity to the ribs, lung parenchyma, or pleural thickening regions. For each patient, three measurements were taken from the same level. The average of the three HU values was used for the assessment. CT features, such as pleural nodules, pleural thickening, and loculation, were evaluated for discrimination of exudates and transudates. Pleural effusion was considered to be loculated when it was septated, compartmentalized, accumulated in a fissure or a nondependent portion of the pleura, or showed a convex form facing the lung parenchyma. CT images were also assessed for the presence of pleural nodules and thickening. Pleural thickening was diagnosed only if a pleural line was visible. The radiologists were blinded to all clinical information. The HU measurements were performed separately by two experienced radiologists; the measurements were then repeated after three days by the same radiologists to avoid bias. Interobserver disagreement was resolved by consensus.

*Statistical analysis*

All statistical analyses were performed using a computer software (Statistical Package for Social Sciences, Version 20.0, SPSS Inc., Chicago, Illinois, USA). The HU measurements were compared for both intraobserver and interobserver agreement using intraclass correlation analysis. Kolmogorov-Smirnov tests were used to assess the normality of the data distribution. Data are expressed as median (min–max). The Pearson chi-square test was used to compare categorical variables between groups. The Mann-Whitney U test was used to compare continuous variables between groups. Receiver operating curve (ROC) analysis was performed to investigate the efficacy of the attenuation values when diagnosing the exudates and transudates. The sensitivity, specificity, $P$ value, and area under the curve (AUC) were calculated for the attenuation values. The cutoff values were determined to predict the differentiation of exudative and transudative effusions. Statistical significance was defined as $P < 0.05$.

## Results

No significant gender or age difference was seen between the groups ($P = 0.198$ and $P = 0.368$, respectively). We found that the intra/interobserver agreement for the HU measurements was good (intraclass correlation coefficient, 0.94 [95% confidence interval, CI, 0.90–0.98] and 0.88 [95% CI, 0.82–0.94], respectively).

The demographic and CT findings in patients with exudative and transudative effusions are shown in Table 1 and Fig. 3. The median HU values of the exudates were significantly higher than those of the transudates ($P = 0.001$). Intravenous contrast agent was used in 15 of 30 patients with transudative effusions (50%) and 43 of 76 patients with exudative effusions (56%). In patients with exudates, median attenuation was 14.5 HU for those who received a contrast injection (n=43) and 13 HU for those who did not (n=33). In patients with transudates, median attenuation was 6.2 HU for those who received a contrast injection (n=15) and 6.1 HU for those who did not (n=15). No marked distinction
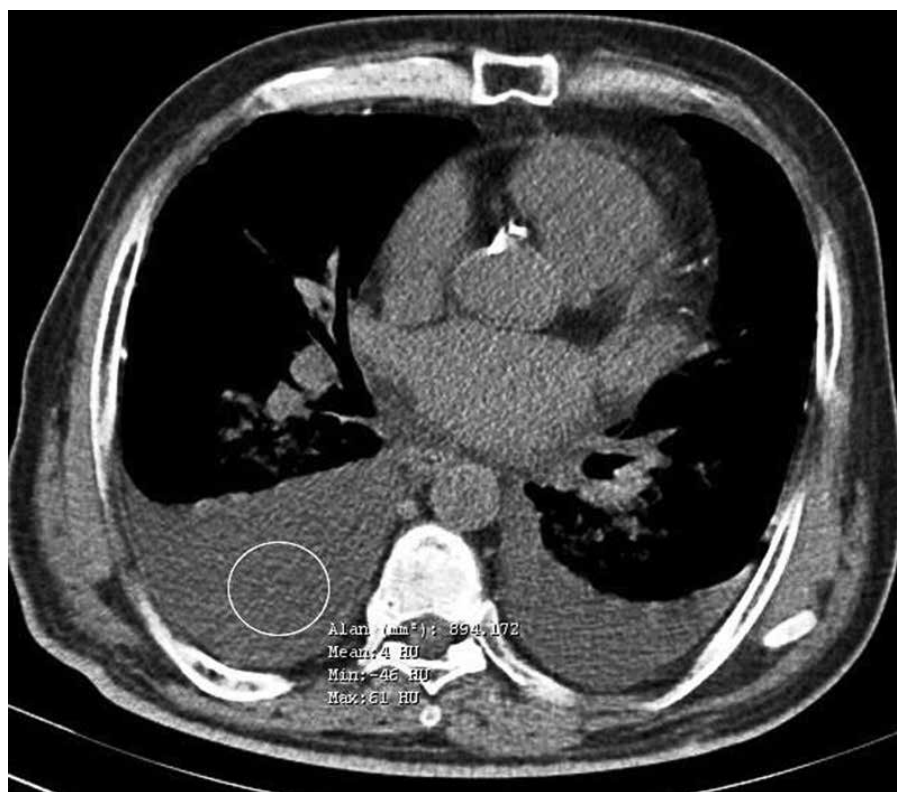


**Figure 1.** Unenhanced axial chest CT image of a 71-year-old male with congestive heart failure showing bilateral pleural effusion. The mean attenuation value of the right pleural effusion (*circle*) was 4 HU. The pleural fluid was defined as transudate at thoracentesis.
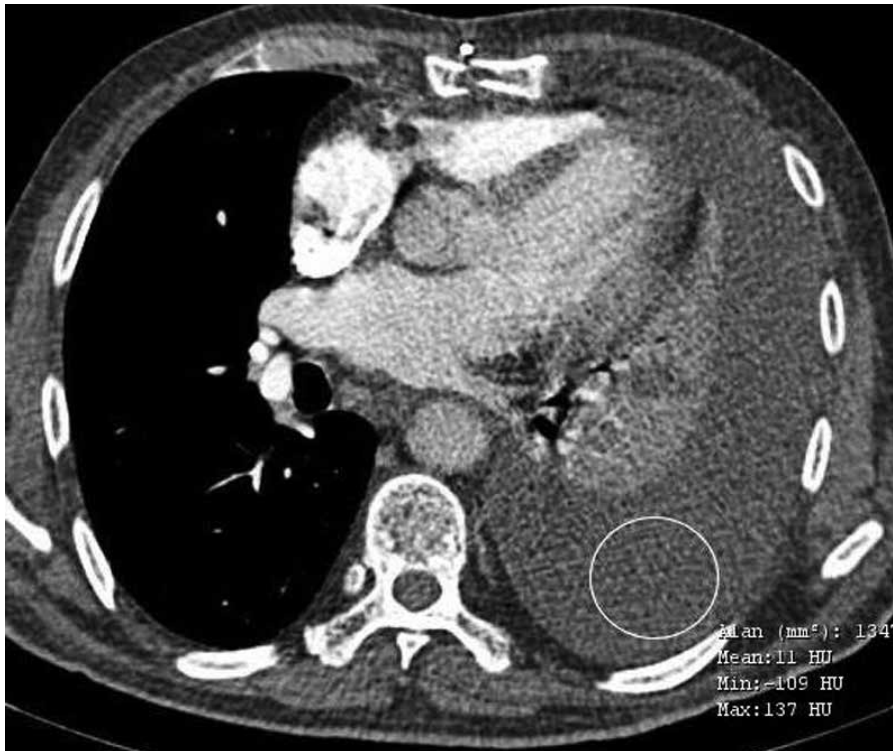
**Figure 2.** Enhanced axial chest CT image of a 74-year-old male with pneumonia showing atelectasis of the lower lobe and left pleural effusion. The mean attenuation value of left pleural effusion (*circle*) was 11 HU. The pleural fluid was defined as exudate at thoracentesis.

**Table 1.** Demographic and CT findings of the patients with exudative and transudative effusions

|  | Patients with transudates (n=30) | Patients with exudates (n=76) | P |
|---|---|---|---|
| Gender (female/male) | 16/14 | 30/46 | 0.198 |
| Age (years) | 75 (27–90) | 65.5 (4–89) | 0.368 |
| CT attenuation (HU) | 5 (2–15) | 12.5 (4–33) | 0.001ᵃ |
| Pleural nodules | 0 | 1 | 0.532 |
| Effusion size (mm) | 29 (8–90) | 32 (6–120) | 0.975 |
| Pleural thickening | 1 (3.3) | 13 (17.1) | 0.072 |
| Loculation | 4 (13.3) | 23 (30.2) | 0.059 |

ᵃ$P < 0.05$ compared with transudates (Mann-Whitney U test).
HU, Hounsfield unit.
Data are given as number of participants (%) or median (range).

had significantly higher loculation ($P$ = 0.006, $P$ = 0.001, and $P$ = 0.033, respectively) and pleural thickening ($P$ = 0.01, $P$ = 0.001, and $P$ = 0.036, respectively).

The diagnostic performance of the HU values in defining exudative and transudative effusions was evaluated by ROC analysis (Table 3). Median HU values were found to be good in differentiating between exudative and transudative effusions (AUC, 0.912; 95% CI, 0.845–0.980). When the cutoff value for exudative effusion was accepted as ≥8.5 HU, and the cutoff value for transudative effusion was accepted as <8.5 HU, the sensitivity and specificity were 85% and 86.7%, respectively.

The diagnostic performance of the HU values in defining the subgroups of patients with pleural effusions was evaluated using ROC analysis. The median HU values were good in differentiating empyema (AUC, 0.805; 95% CI, 0.711–0.900). When the cutoff value for empyema was accepted as ≥12.5 HU, the sensitivity and specificity were 76.9% and 66.7%, respectively. The median HU values were excellent in differentiating CHF (AUC, 0.902; 95% CI, 0.840–0.964). When the cutoff value for CHF was accepted as ≤8.5 HU, the sensitivity and specificity were 84.6% and 81.2%, respectively.

## Discussion

The differential diagnosis of pleural effusions can be conducted by means of thoracentesis, pleural biopsies, and occasionally diagnostic thoracoscopy (11). Thoracoscopy with many biopsy samples has better outcomes (80%–97%) than combined pleural fluid cytological analyses and closed pleural biopsy (73%) in malignant effusion (12). The amount, distribution, accessibility of a pleural effusion, and possible extra intrathoracic pathologies can be evaluated with imaging modalities (13). CT can be useful in determining the causes of pleural effusions (14, 15). CT is commonly used to evaluate patients with pleural abnormalities related to neoplasm, pneumonia, and empyema (16).

Few published studies have evaluated the attenuation values in patients with pleural effusions (9, 10). In the study by Nandalur et al. (9), the mean attenuation values of exudates (17.1±4.4 HU) were significantly higher than those of transudates (12.5±6.3 HU; $P$ = 0.001). The mean HU values were "moderate" in differentiating between

was found in the measurements by the two radiologists, and the analysis revealed that the intravenous contrast agent did not much affect the HU values. Loculation was observed in 15 of 48 patients who did not receive a contrast injection (31%) compared with 12 of 58 patients who did (20%). Pleural nodules were observed in one of 58 patients who received a contrast injection. Pleural thickening was found in six of 48 patients who did not receive

the contrast agent (12.5%), compared with eight of 58 patients who did (13%). Compared with the transudative effusions, the exudative effusions had significantly higher loculation and pleural thickening.

The demographic and CT findings of patients with CHF, pneumonia, malignancy, and empyema are shown in Table 2 and Fig. 4. Compared with the patients with other diseases (CHF, pneumonia, and malignancy), the empyema patients
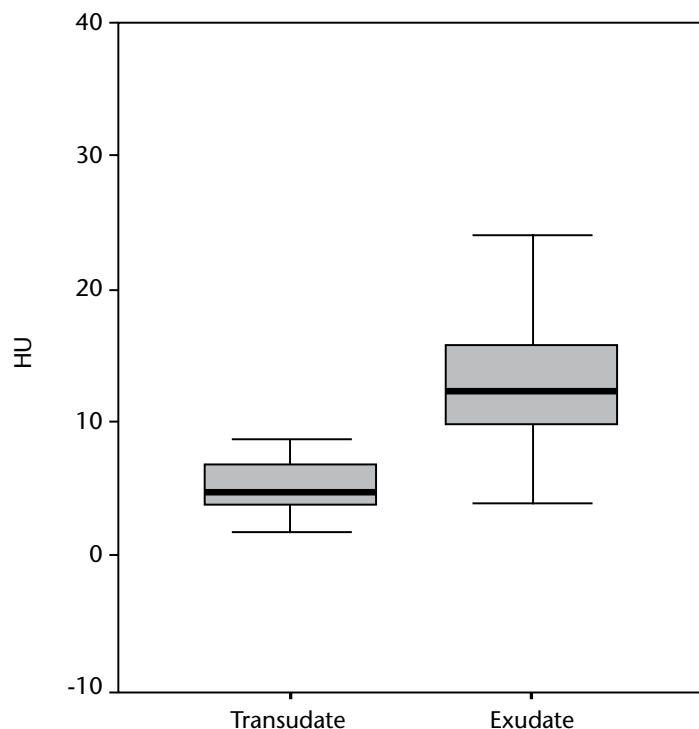
**Figure 3.** Box plots showing the attenuation values for the transudate and exudate groups. The boxes stretch from the 25th to the 75th percentile. The horizontal line across each box is the mean. The vertical lines with whiskers extending below and above the boxes indicate the minimum and maximum values, respectively. HU, Hounsfield unit.

**Table 2.** Demographics and CT findings of the patients with CHF, pneumonia, malignancy, and empyema

| | Patients with CHF (n=26) | Patients with pneumonia (n=47) | Patients with malignancy (n=20) | Patients with empyema (n=13) |
|---|---|---|---|---|
| Gender (female/male) | 13/13 | 21/26 | 5/15 | 7/6 |
| Age (years) | 75 (44–90) | 63 (4–89) | 71.5 (27–87) | 68 (24–76) |
| CT attenuation (HU) | 5 (2–13) | 11 (2–33)[a,b] | 12 (6–20)[b] | 16 (11–27)[b,c] |
| Pleural nodules | 0 | 0 | 1 | 0 |
| Size of effusion (mm) | 39 (8–94) | 39 (8–94) | 20.5 (6–110) | 32 (6–80) |
| Pleural thickening | 1 (3.8) | 4 (8.5) | 2 (10) | 7 (53.8) |
| Loculation | 4 (15.4) | 9 (19.2) | 5 (25) | 9 (69.2) |

[a]P < 0.0125 compared with empyema (Mann-Whitney U test, with Bonferroni adjustment).
[b]P < 0.0125 compared with CHF (Mann-Whitney U test, with Bonferroni adjustment).
[c]P < 0.0125 compared with pneumonia (Mann-Whitney U test, with Bonferroni adjustment).
CHF, congestive heart failure; HU, Hounsfield unit.
Data are given as number of participants (%) or median (range).

exudative and transudative effusions (AUC, 0.775; 95% CI, 0.699–0.851). Although the mean attenuation of exudates was significantly higher than transudates, the clinical use of CT attenuation in describing pleural fluid has not been suggested because of the overlapping HU values. In a study by Abramowitz et al. (10), the mean HU values of exudates (7.2±9.4 HU) were lower than the mean HU values of the transudates (10.1±6.9 HU). However, the difference was not statistically significant (P = 0.24). The clinical use of CT HU values to define pleural fluid was not recommended. In the current study, the median HU values of the exudates (13.6±5.5 HU) were significantly higher than those of the transudates (6±3.2 HU; P = 0.001). The median HU values were

found to be good in the differentiation of exudative and transudative effusions (AUC, 0.912; 95% CI, 0.845–0.980). When the cutoff value for exudative effusion was accepted as ≥8.5 HU, the sensitivity and specificity were 85% and 86.7%, respectively. Additionally, when an evaluation according to disease subgroups was made, CHF and empyema were predictable in terms of the median HU values of the pleural effusions, with high and moderate sensitivity and specificity. When the cutoff value for CHF was accepted as ≤8.5 HU, sensitivity and specificity were 84.6% and 81.2%, respectively. When the cutoff value for empyema was accepted as ≥12.5 HU, sensitivity and specificity were 76.9% and 66.7%, respectively. Nandalur et al. (9) and Abramowitz et al. (10) found a high degree of overlap in HU values in differentiating transudates and exudates. Similarly, we also observed high overlap (59%, 63/106) of the transudates and exudates for a majority of effusions in the 4–15 HU range. Thus, clinical findings and radiological examinations can provide significant evidence regarding the nature of pleural effusions, but, in some cases, it may still be necessary to use diagnostic thoracentesis for the analysis. As reported by Abramowitz et al. (10), the current results showed that the use of an intravenous contrast agent did not affect the HU values.

The roles of ultrasonography (US), CT, and magnetic resonance imaging (MRI) are supplementary when assessing pleural diseases. In some conditions, such as empyemas, hemothorax, and pleural metastasis, the septa are so plentiful that they have a honeycomb appearance. Although these changes may be demonstrated readily using US and MRI, they may not be seen by CT (17).

Arenas-Jiménez et al. (8) demonstrated that the CT findings may be useful in discriminating between exudates and transudates. Pleural nodules and nodular pleural thickening were observed only in malignant pleural effusions. Additionally, mediastinal and circumferential pleural thickening were identified in both malignant effusions and empyemas. Empyemas and pneumonic effusions cannot be discriminated based on CT properties alone; however, loculation and pleural thickening are commonly observed in empyema. Abramowitz et al. (10) observed that CT findings, such as fluid loculation, pleural thickness, and pleural nodules, were
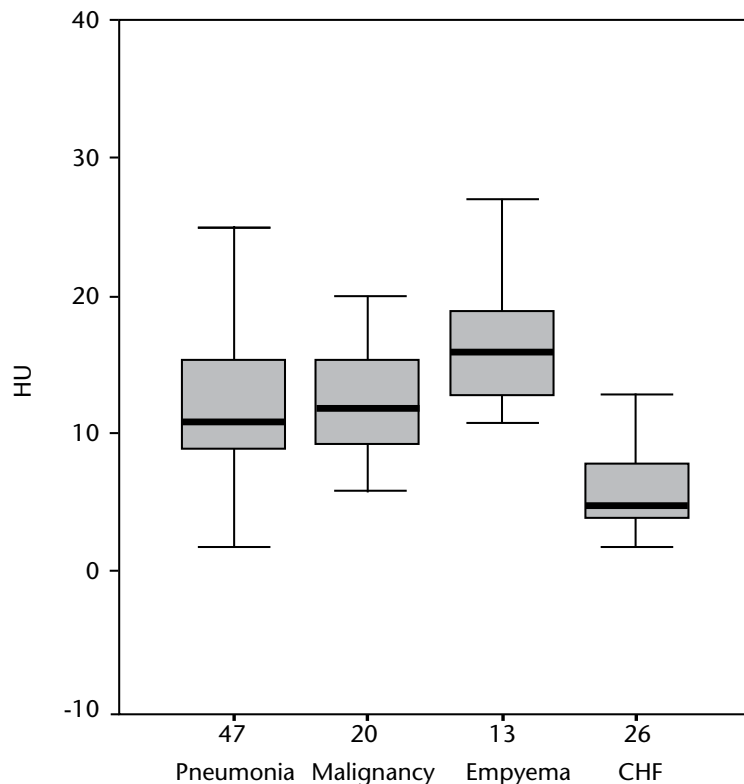
**Figure 4.** Box plots show the attenuation values for the disease groups. The boxes stretch from the 25th to the 75th percentile. The horizontal line across each box is the mean. The vertical lines with whiskers extending below and above the boxes indicate the minimum and maximum values, respectively. CHF, congestive heart failure; HU, Hounsfield unit.

**Table 3.** The AUC, cutoff value, sensitivity, specificity, and *P* values for median HU values of pleural effusions in different diseases at ROC analysis

|  | CHF | Pneumonia | Malignancy | Empyema |
|---|---|---|---|---|
| AUC | 0.902 | 0.602 | 0.607 | 0.805 |
| Cutoff value (HU) | ≤8.5 | ≥9.5 | ≥10.5 | ≥12.5 |
| Sensitivity (%) | 84.6 | 66 | 65 | 76.9 |
| Specificity (%) | 81.2 | 49.2 | 50 | 66.7 |
| *P* | 0.001 | 0.072 | 0.136 | 0.001 |

AUC, area under the curve; CHF, congestive heart failure; HU, Hounsfield unit.

unreliable in distinguishing exudates from transudates. In the current study, the empyema patients had significantly higher loculation and pleural thickening than those with other diseases. Only one malignancy, which was a case with a pleural nodule, was detected in this study population. Compared with transudative effusions, exudative effusions had significantly higher loculation and pleural thickening. The results of the current study showed pleural thickening in one of 30 transudates (3.3%) compared with 13 of 76 exudates (17.1%). However, loculation was found in four of 30 transudates (13.3%) and in 23 of 76 exudates (30.2%).

Certain limitations of the present study should be noted. First, the sample size was relatively small in the malignancy and empyema groups. Another potential limitation was that we did not identify the type of malignancy and agents of pneumonia in each patient. The study has other limitations, such as the long time between the CT and thoracentesis (seven days), CT without administering contrast material, and its retrospective design.

In conclusion, we believe that CT attenuation values may be useful in differentiating exudates from transudates. Although there is an overlap in the majority of effusions, exudate can be considered with CT attenuation values >15 HU.

Because of overlapping HU values, close correlation with clinical findings is essential. Additional signs, such as fluid loculation and pleural thickness, should be considered and may provide further information for the differentiation.

### Conflict of interest disclosure

The authors declared no conflicts of interest.

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