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Original Article

Can computerized tomography Hounsfield unit values be useful in the differential diagnosis of pleural effusion?

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Abstract

Introduction: We aimed to investigate the efficacy of Hounsfield unit (HU) attenuation measured on computed tomography (CT) as a non-invasive method for pleural effusion characterization.
Methods: Patients with pleural effusion who underwent thoracic CT imaging and thoracentesis within a maximum of three days were included in this retrospective study (15 transudate and 36 exudate). By drawing a circular region of interest (ROI) on the section with the thickest pleural effusion in terms of anteroposterior diameter in the upper-medial-lower zone on axial images, a total of three HU values, one from each level, were averaged. An independent t-test was applied to the CT attenuation (HU) values for the transudate-exudate differentiation. A receiver operating characteristic (ROC) analysis was then made.
Results: The mean attenuation ± standard deviation (minimum-maximum) value for the patients with transudate was 2.17 ± 3.76 ((-7.5)-7.5) HU, whereas the mean HU value for the patients with exudate was 8.38 ± 6.2 ((-6)-22). The independent t test made for the transudate-exudate differentiation revealed a statistically significant difference ($P = 0.001$). In the ROC analysis carried out to determine the cut-off value of the attenuation value of pleural effusion in the transudate-exudate differentiation, the area under the curve was found to be 82.8%. When the cut-off value was taken as 2.75HU for the area under the curve, sensitivity was found to be 84%, and specificity was 60%.
Conclusion: Although CT-HU values are statistically significant in the differential diagnosis of transudate-exudate, there is still a need to establish a correlation with other tomographic findings and clinical laboratory findings.

Introduction

Pleural diseases are estimated to affect 3000 of every 1 million people.[1] Pleural effusion, defined as the accumulation of fluid between the pleural layers, is often seen in daily practice. The pleural cavity normally contains a small amount of fluid, allowing the lungs to move with minimum friction during inspiration and expiration.[2] Any increase in the formation of pleural fluid, any decrease in fluid absorption, or as the most common case, any dysfunction of both at the same time, results in pleural effusion.

Pleural effusion, for differential diagnosis, is classified into transudate and exudate forms.[3] Transudate occurs most frequently as a result of mechanisms such as increased hydrostatic pressure (heart failure), decreased oncotic forces (hypoproteinemia), decreased intrapleural negative pressure, or the movement of abdominal ascitic fluid through the diaphragm (hepatic cirrhosis). Exudate, in turn, is most frequently seen in malignancies and inflammatory conditions that lead to increased capillary permeability and/or impaired lymphatic drainage.[4]

The diagnosis of pleural effusion and the determination of its etiology can be achieved through clinical assessment, imaging, pleural fluid analysis, and pleural biopsy, when necessary. A small amount of effusion is usually asymptomatic, while the most common complaint in a high amount of effusion is dyspnea. The first method of choice in imaging is direct radiography. Pleural fluid may not always be apparent from direct radiography. Therefore computed tomography (CT) and ultrasonography (US) assessment may be required to confirm the direct radiography findings, and to identify any accompanying

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findings. US can easily detect pleural fluid, and can also allow an understanding of the fluid content and reveal whether there is a loculation, and differentiate the fluid from pleural masses.[5] Generally, CT is performed to detect any parenchymal or mediastinal lesions accompanying the pleural fluid.[6]

For a patient diagnosed with pleural effusion, a transudate-exudate differentiation should be made, since the diagnosis and treatment will vary in accordance with the characteristics of the fluid. Transudates have a very limited etiological spectrum, while exudates are associated with multiple diseases and require additional diagnostic tests in order to determine the exact causes, such as culture, pleural biopsy, and diagnostic thoracoscopy, when needed.[7] Transudate-exudate differentiations are made most commonly using Light's criteria, which are established by determining the protein and lactate dehydrogenase (LDH) levels in the blood and pleural fluid.[8] Used to obtain pleural fluid, diagnostic thoracentesis is usually a safe method, although being invasive, it can result in pneumothorax, pain and hemorrhage. The present study aimed to investigate the efficacy of Hounsfield unit (HU) attenuation measured on CT as a non-invasive method for pleural effusion characterization.

Methods

This single-center retrospective study was initiated upon the approval of the Van Yuzuncu Yıl University medicine faculty ethics committee (No: 2020/03-01) and written informed consent was obtained from all the involved patients. The study retrospectively accessed the records of 328 patients through the archives of the clinic, who were identified with pleural effusion on thoracic CT performed for any reason in the radiology clinic between June 2015 and May 2017. Patients who underwent thoracic CT imaging and thoracentesis within a maximum of three days were included in the study. In total 277 patients were excluded from the study as the followings: patients in whom the anteroposterior diameter of pleural effusion was below 1 cm at its thickest point, those with a thoracic tube inserted due to effusion, and patients without thoracentesis. The study was started with 51 patients who were deemed eligible for the study.

CT images were taken using a 16-slice multidetector computed tomography device (Somatom Emotion 16-slice; CT2012E- Siemens AG Berlin and Munich-Germany). For the contrast-enhanced examinations, the patients were administered 100 mL of a non-ionized intravenous contrast agent iohexol (Amersham Health, Ireland) or iopromide (Schering, Germany) through the forearm vein at a rate of 3 ml/sec via an automatic injector (CT 9000 ADV Liebel-Flarsheim). Cross sections were obtained starting from the distal neck to the upper abdomen by having patients hold their breath in the supine position. The axial and multiplanar reformatted images with 3 mm-cross sectional thickness, which were previously uploaded onto the system following image-shooting procedures, were evaluated by a single radiologist with 14 years of experience with high-resolution gray-scale medical monitors used for routine CT examinations. The radiologist was instructed to scan for the presence of pleural effusion and CT-HU measurement, regardless of biochemical analysis results. By drawing a circular region of interest (ROI) on the section with the thickest pleural effusion in terms of anteroposterior diameter in the upper-medial-lower zone on axial images, a total of three HU values, one from each level, were averaged (Figures 1 and 2). Care was taken to take measurements from the central area, as the deepest part, distant from the adjacent lung parenchyma and ribs. Then a transudate-exudate differentiation of pleural effusion was made for each patient considering Light's criteria. Pleural fluid was described as "exudative" when the following criteria were met: (a) fluid protein concentration/serum protein concentration >0.5; (b) pleural fluid LDH/serum LDH

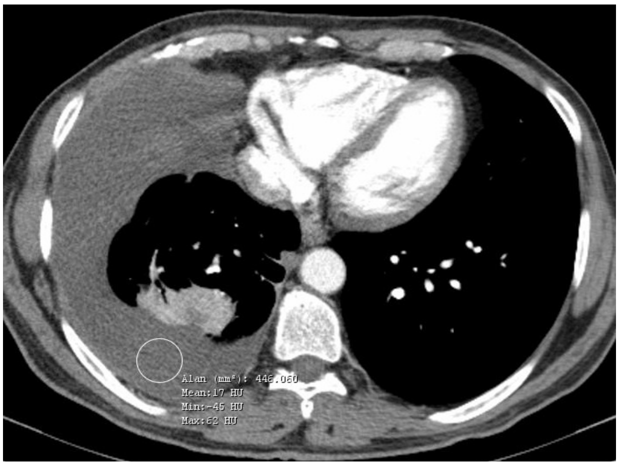

Figure 1. Enhanced axial chest CT scan of a -45year-old male presenting with right side exudative effusion; CT attenuation value is 17 HU.

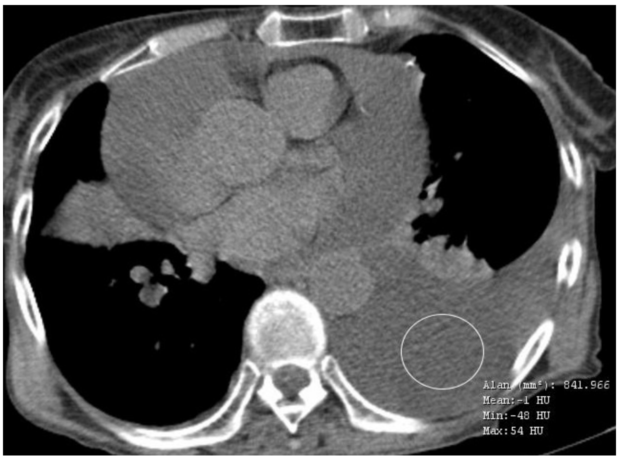

Figure 2. Unenhanced axial chest CT scan of an 80-year-old female diagnosed as congestive cardiac failure presenting with left transudative pleural effusion; CT attenuation value is -1 HU.

concentration >0.6; and (c) pleural fluid LDH >2/3 of the upper limit of normal serum LDH concentration.

The descriptive statistics for continuous variables of the study included mean, standard deviation (SD), minimum and maximum, and categorical variables were expressed as numbers and percentages. An independent sample *t* test was used to compare the mean values of the groups in regard to the continuous variables. The level of statistical significance was set at 5% in the calculations and the SPSS software package was used for the statistical analysis. The sensitivity and specificity values were calculated. Optimum cut-off value for CT-HU value was calculated by receiver operating characteristic (ROC) analysis. The distribution of the data was analyzed with the Kolmogorov-Smirnov test. As the data were normally distributed, arithmetic average and standard deviation values were obtained.

Results

In the biochemical analysis based on Light's criteria, 15 (29.4%) patients were classified as transudative and 36 (70.6%) were classified as exudative. The mean age ± SD of the patients with transudative effusion was 66.5 ± 18.1years (range: 41-90 years), and the mean age ± SD of the patients with exudative pleural effusion (PE) was 61.5 ± 17.3 years (range: 21-81 years). Of the 15 (29.4%) patients with transudative PE, 8 (53.3%) were male and 7 (46.7%) were female. Of the 36 (70.6%) patients with exudative PE, 20 (55.6 %) were male and 16 (44.4%) were female.

The mean attenuation ± standard deviation (minimum-maximum) value for the patients with transudative PE was calculated as 2.17 ± 3.76 ((-7.5)-7.5) HU, whereas the mean HU value for the patients with exudative PE was calculated as 8.38 ± 6.2 ((-6)-22). The independent t-test made for the transudate-exudate differentiation revealed a statistically significant difference ($P = 0.001$, t:4.008 and $t(df)$: 29.687). In the ROC analysis carried out to determine the cut-off value of the attenuation value of pleural effusion in the transudate-exudate differentiation, the area under the curve was found to be 82.8%. When the cut-off value was taken as 2.75 HU for the area under the curve, sensitivity was found to be 84%, and specificity was 60% (Figure 3).

An intravenous contrast agent was used in 30 of the exudative effusions and in four of the transudative effusions. No contrast agent was used in cases with elevated creatinine, with a history of allergy to contrast agent or where the use of a contrast agent was deemed unnecessary. The average HU value was 8.8 ± 6.4 in 30 exudative patients with contrast agent administered, and 6 ± 4.5 in six exudative patients without contrast agent administered. The average HU value was 1.12 ± 6.2 four transudative patients with contrast agent administered, and 2.5 ± 2.7 in 11 transudative patients without contrast agent administered. An independent *t* test was used to determine whether there was a difference in mean HU values between patients with and without contrast agent administration. The findings were not statistically significant, and the use of contrast agent was found to have no significant effect on the HU values ($P > 0.05$).

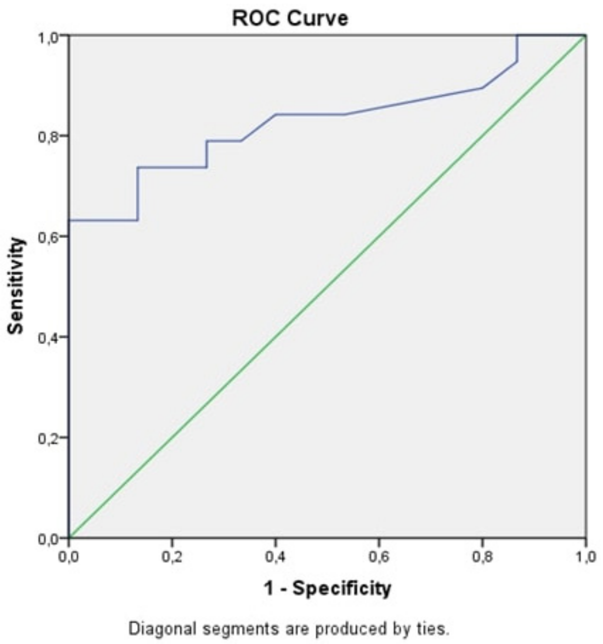

Figure 3. Graph shows receiver operating characteristic (ROC) curve.

Of the patients with transudative PE, six had heart failure, five had renal insufficiency, one had chronic obstructive pulmonary disease, one had a gastric tumor, one had liver cirrhosis, and one had granulomatosis disease.

Of the patients with exudative PE, 10 had pneumonia, six had lung tumors, eight had extrapulmonary malignancies (colon, stomach, esophagus, lymphoma, pleural tumor), three had metastases (breast cancer, renal cell cancer), two had pulmonary embolism, three had tuberculosis, one had pancreatitis, one had pleural fibrosis, one had interstitial lung disease, and one had pleurisy.

Discussion

The pleural cavity, which consists of two thin layers, called the visceral and parietal layers, usually contains around 8 ml of physiological fluid.[9] Differential diagnosis of pleural effusions are made using thoracentesis, pleural biopsy, and diagnostic thoracoscopy, when required. For a patient diagnosed with pleural effusion, a transudate-exudate differentiation should be made, since the diagnosis and treatment will vary in accordance with the characteristic of the fluid. The most common cause of all pleural effusions and transudative effusions is heart failure, while infection and malignancies are the most common cause of exudative effusions. In the present study, the most common cause was heart failure for transudates and infection for exudates. Transudate-exudate differentiations are made based on pleural fluid and blood biochemistry analyses using Light's criteria,[10] as used for all patients in the present study.

Thoracentesis, which is performed to drain pleural fluid, is associated with rare but serious complications, the most common of which is pneumothorax, while minor complications may include hematoma, cough and dyspnea. To the best of our knowledge, based on our clinical archive review, none of the patients in the present study suffered thoracentesis-related complications. A non-invasive method may aid differentiation in cases where thoracentesis is contraindicated, such as with coagulopathy, a non-cooperative patient state and skin lesions at the needle insertion site. CT is a useful imaging method in the diagnosis and treatment of pleural membranes and pulmonary diseases,[11] and can also aid in determination of the etiology of pleural effusion, and in the detection of accompanying lung, mediastinal and heart diseases.[12,13] We also aimed to make a transudate-exudate differentiation through an examination of fluid density on CT.

There have been several studies to date investigating non-invasive transudate-exudate differentiation methods in pleural effusions. In a study conducted using magnetic resonance imaging (MRI),[14] it was demonstrated that the signal intensity values of effusions on T1 and T2A MR images were widely associated with protein content and mostly with blood concentrations in gradient echo imaging. The authors concluded that MRI may be helpful in differentiating between exudate or hemorrhagic effusions and serous effusions. Another study established a distinct contrast enhancement on post-contrast T1WI in exudative effusions.[15] Although significant findings has been reached, MRI is impractical for transudate-exudate differentiation due to cardiac artefacts, a prolonged examination time and being not cost-effective. A study conducted using ultrasound elastography[16] found a statistically significantly higher shear wave elastography value for exudates when compared to transudates, although its stand-alone use was not recommended for transudate-exudate differentiation. The above-mentioned studies were conducted considering intensity and elasticity difference, while the present study has investigated whether CT Hounsfield unit values can be useful in transudate-exudate differentiation. Sharma et al [17] carried out a contrast-enhanced or non-contrast CT study of 26 transudative and 74 exudative patients, using the CT attenuation values to make a transudate-exudate differentiation, and found a statistically significantly higher mean HU value (16.5 ± 1.7) of exudates than the mean HU value (11.6 ± 0.57) of transudates. The authors reported sensitivity and specificity to be 81.08% and 100%, respectively when the cut-off value was taken as ≥15.3 for exudates. We believe that this may be due to the mean values and the number of cases being higher compared to the present study.

In a study conducted by Çullu et al[18] in which 30 transudative and 76 exudative patients were subjected to contrast-enhanced or non-contrast CT, a statistically significantly higher average HU value (12.5) of exudates was reported than the average HU value (5 HU) of transudates. Although the HU values overlapped in most cases, effusion may be considered as exudate when the HU value is >15. The authors reported sensitivity and specificity to be 85% and 86.7%, respectively when the cut-off value was taken as ≥8.5 for exudate and <8.5 for transudates.

In a study by Nandalur et al.[19] including CTs of 101 exudative and 44 transudative patients, the average HU value (17.1) of exudates was found to be statistically and significantly higher than the average HU value (12.5) of transudates, although the authors did not recommend its clinical use in the identification of pleural effusion.

In a similar vein, the present study found the mean HU value of 36 exudative and 15 transudative patients to be 8.38 ± 6.2 ((-6)-22) and 2.17 ± 3.76 ((-7.5)-7.5), respectively, which was statistically significant ($P = 0.001$). In the ROC analysis performed in the present study to determine the cut-off attenuation value of pleural effusion in transudate-exudate differentiation, the area under the curve was found to be 82.8%. When the cut-off value was taken as 2.75 HU for the area under the curve, sensitivity was found to be 84%, and specificity was 60%. The findings of the present study were similar to those of the aforementioned studies.

In the present study, the average HU value was found to be 8.8 in 30 exudative patients with contrast agent administered, and 6 in six exudative patients without contrast agent administered. Furthermore, the average HU value was 1.12 in four transudative patients with contrast agent administered and 2.5 in 11 transudative patients without contrast agent administered. The findings of the present study were not statistically significant, which concurred with the findings of the studies by Çullu et al[18] and Sharma et al.[17] The use of a contrast agent did not have a significant effect on HU value.

Abramowitz et al[20] assessed the findings of contrast-enhanced or non-contrast CT of 22 transudative and 78 exudative patients, but could establish no statistically significant difference in the average HU value between transudates (10.1) and exudates (7.2). Interestingly, the said study found the average HU value of exudates to be lower than that of transudates, which may be attributed to the fact that the 13 patients with a negative HU were all in the exudative group. The present study determined a negative mean HU value in four patients (2 exudative and 2 transudative), in which the two exudative patients had a diagnosis of pneumonia, while one of the two transudative patients had heart failure and the other had gastric cancer.

The retrospective design and the low number of patients assessed with contrast-enhanced and non-contrast CT can be considered as the main limitations of the present study. There was no statistically significant difference in terms of the use of an intravenous contrast agent, which

Study Highlights

What is current knowledge?

- Light's criteria formed by pleural fluid biochemical analysis obtained by thoracentesis are the most commonly used method in the differentiation of transudate-exudate.

What is new here?

- Hounsfield unit (HU) attenuation measured on CT may be useful as a non-invasive method for pleural effusion characterization.

may have affected the findings.

Conclusion

Although CT-HU values are statistically significant in the differential diagnosis of transudate-exudate, there is still a need to establish a correlation with other tomographic findings and clinical laboratory findings.

Conflict of Interest

Authors declare no conflict of interest in this study.

Ethical Approval

The study protocol was approved by the ethical committee of Van Yuzuncu Yil University Faculty of Medicine (2020/03-01).

Authors' contributions

Study design: FD, MÖ. Study conduct: all of the authors. Writing: FD, VA. Analysis: CG. Critic and article search: all of the authors. Data gathering: BC.

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