Computed Tomography in Differential Diagnosis of Exudative and Transudative Pleural Effusions

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ABSTRACT

Objective: To differentiate between exudative and transudative pleural effusions by using CT attenuation values and CT appearances.

Methods: The retrospective study reviewed 132 patients who were diagnosed of pleural effusions in 2007-2014. All patients were evaluated by chest CT images before or after pleural tapping within 2 days. Pleural effusions were classified as exudates or transudates based on Light's criteria.[1] Pre-contrast and post-contrast CT images were reviewed by measuring the mean attenuation values of pleural effusions and the associated CT findings.

Results: Pleural effusions were 112 exudates and 20 transudates. Exudate group had significant higher mean attenuation values, compared with a transudate, in both pre-contrast (12.8±5.0 HU vs. 9.4±5.2 HU; p<0.001) and post-contrast images (13.8±5.1 HU vs. 10.2±5.7 HU; p=0.006). For differentiation between types of pleural effusions, the CT attenuation cutoff value of 8.5 HU showed highest sensitivity of 84.5% and the cutoff value of 16 HU showed highest specificity of 95%, respectively. The CT findings of pleural nodule, pleural thickening and loculation were more common in exudates, compared with transudates with the statistical significance and specificity of those findings as high as 100%, 90%, and 75%, respectively.

Conclusion: The mean attenuation values of ≥16 HU favor exudates. However, the use of CT attenuation values for differentiating types of pleural effusions alone, showed poor diagnostic performance. Correlation with clinical context and pleural fluid analysis are still essential. We suggest the three helpful CT findings for diagnosis of exudates which are pleural thickening, pleural nodules and loculation.

Keywords: Pleural effusion; attenuation; CT; transudates; exudates (Siriraj Med J 2017;69: 51-56)

INTRODUCTION

Pleural effusion is a common problem in clinical practice which arises from many causes.[1] The types of pleural effusions can be divided into transudates and exudates. Transudative pleural effusion is caused by a loss of balance between hydrostatic and oncotic pressure e.g. congestive heart failure and liver cirrhosis. Whereas, exudative pleural effusion is caused by an inflammatory process e.g. pneumonia, malignancy, and thromboembolism.[2]

In general, the differentiation between exudates and transudates depends on the fluid taken from pleural tapping, being analyzed according to Light's criteria.[2] However, a pleural tapping procedure may cause pneumothorax which leads to a retention of intercostal drainage tube in around 5%.

A computed tomography could evaluate the pathology of lung parenchyma and pleura as well as the appearance of pleural effusions. Nandalur et al,[3] found that mean attenuation values of exudative pleural effusions were higher than those in transudates. Cullu et al,[4] reported CT attenuation values of >15 HU, might be useful to suggest exudates. In contrast, Abramowitz et al,[5] found no significant difference between CT attenuation values of exudates and transudates.

The purpose of this study was to differentiate between exudative and transudative pleural effusions by using CT attenuation values and CT appearances.

MATERIALS AND METHODS
Patient selection

The study protocol was approved by the institutional reviewed board, and the informed consent was waived because of the retrospective study. In total 132 patients, who had pleural effusions and underwent thoracentesis between January 2007 and September 2014, were enrolled in this study. All patients had CT images performed before or after thoracentesis within 2 days. The patients were categorized into transudates and exudates groups according to types of pleural effusion by using Light's criteria. Diagnosis of exudates is given when it meets one or more of the following criteria: (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] Furthermore, exudative pleural effusions were classified into malignant, para-pneumonic effusion and empyema thoracis which were confirmed by the fluid analysis, gram stain, fluid culture, fluid cytology or pathology. Empyema thoracis was diagnosed by a presence of pus or positive pleural fluid culture or very high pleural LDH (>1,000 IU), low pH (<7.1), or low glucose (<40 mg/dL) values.[6]

The patients who underwent insertion of intercostal drainage before CT examination, and who had uncertain final diagnosis, had contrast media allergy, had serum creatinine greater than 1.5 mg/dl, or had pregnancy, were excluded.

Imaging acquisition

All images were obtained using two CT scanners (Light speed, GE Medical Systems, Milwaukee, WI, United States and SOMATOM definition, Siemens, Germany), with collimations of 64 x 1.25 mm and 64 x 0.6 mm; pitch of 1; a tube voltage of 120 kVp; and a reference tube current setting of 250 mA. The reconstructed section thickness was 1.25-1.5 mm.

The axial CT study was performed in pre-contrast and post-contrast phases. Intravenous contrast media (non-ionic contrast media of 80 ml) was administered to all patients at an injection rate of 3 ml/sec.

Imaging and data analysis

The demographic data (age, sex, pleural fluid chemical profile, and pathological reports) were collected. The CT images were reviewed by one thoracic radiologist with 5 years of experience, who was blinded to clinical information and imaging results.

To measure the attenuation values of pleural effusions, the radiologist drew the region of interest (ROI) at area of the maximal fluid accumulation on axial plane, and placed the ROI at each three contiguous slices in the same region. The mean attenuation values (Hounsfield Unit, HU) with standard deviation were measured. The average of the three levels was calculated. The image artifact, rib, lung parenchyma or pleura were avoided while placing the ROI (Fig 1). The CT attenuation value measurement was performed on pre-contrast and post-contrast CT images.
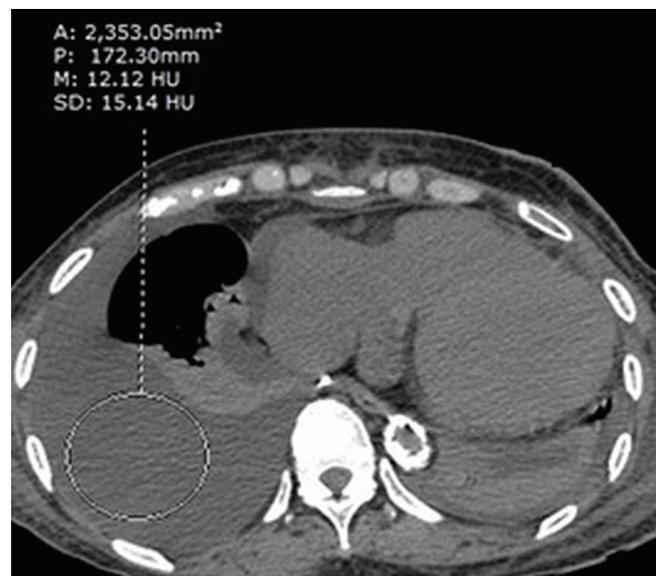

Fig 1. The precontrast image of a 43-year-old woman with acute renal failure and volume overload, shows bilateral pleural effusion. The mean attenuation coefficient of right pleural effusions (circle) 2,353 mm² in size was 12.12 HU. The pleural effusion was classified as a transudate from thoracocentesis.

The CT findings were recorded for pleural nodule (Fig 2), pleural thickening, loculation, and adenopathy. The loculation was defined, when pleural effusion showed compartmentalization, accumulation in a fissure or a nondependent portion of the pleura, septation or convex surface toward the adjacent lung parenchyma (Fig 3). Pleural thickening was diagnosed if a pleural line was visible internally to the ribs or the presence of split pleural sign.

Statistical analysis

Analyses were performed by using statistical software (SPSS v. 18.0; SPSS Inc., Chicago, Illinois, USA). All continuous (quantitative) data, including the patient's age, attenuation value of pleural effusions, were summarized as the mean ± SD. Correlation between types of pleural effusions and mean attenuation values in pre-contrast and post-contrast CT images were reported using 2-tailed T-test. The ability of the CT attenuation values for exudate was assessed using receiver operating characteristic (ROC)

Fig 2. The post-contrast image of a 48-year-old woman with primary lung cancer and pleura metastasis, showed right pleural effusion, enhancing pleural nodule (arrow) and pleural thickening. The mean attenuation coefficient of right pleural effusion (circle) 461 mm^2 in size was 13 HU. The pleural effusion was classified as an exudate from thoracocentesis.

Fig 3. The post-contrast image of a 89-year-old man with empyema thoracis, showed right loculated pleural effusion. The mean attenuation coefficient of right pleural effusion (circle) 464 mm^2 in size was 16 HU. The pleural effusion was classified as an exudate from thoracocentesis.
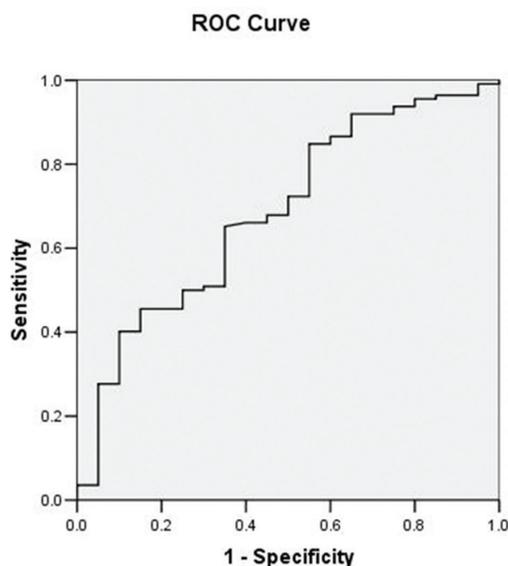

Fig 4. Receiver operating characteristic (ROC) curve showed low accuracy of the mean attenuation values for diagnosis of exudates in precontrast CT images.

curves, and the cut-off point was determined using the ROC curve closest to the point at which the sensitivity and specificity were maximized. Correlation between subgroups of exudate pleural effusion and mean attenuation coefficient were determined using Oneway ANOVA test. Two-sided Chi-square test was used to calculate sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) for the CT findings. The p values <0.05 were considered as statistical significance.

RESULTS

A total of 132 patients in our study included 71 men and 61 women with the mean age of 55.82 years (age range 16-89 years). All patients underwent chest CT scans in pre-contrast and post-contrast phases and underwent thoracocentesis within 2 days at our hospital. There were 20 (15%) patients with transudates and 112 (85%) patients with exudates. The causes of transudates (n=20) were hypoalbuminemia (6, 30%), reactive pleural effusions (5, 25%), congestive heart failure (4, 20%), volume overload (4, 20%) and idiopathic pulmonary arterial hypertension (1, 5%). The causes of exudates (n=112) included malignant effusions (63, 56%), para-pneumonic effusion (33, 30%), empyema thoracis (8, 7%) and other causes e.g. hypereosinophilic syndrome, reactive effusion from adjacent intraabdominal collection and SLE pleuritis (8, 7%).

In pre-contrast CT images, the mean attenuation values of exudates (12.8 HU, SD 5.0) were higher than the transudates (9.44 HU, SD 5.23) with significant differences (p=0.006). The attenuation values of exudates and transudates ranged from 0.44-30.35 HU and 0.92-21.94 HU, respectively. In post-contrast CT images, the mean attenuation values of exudates (13.8 HU, SD 5.1) were also significantly higher than the transudates (10.2HU, SD 5.7) (p=0.006). The attenuation value of exudates and transudates ranged from 1.73-27.76 HU and 1.57-21.99 HU, respectively.

The areas under the mean attenuation values curves for exudates in pre- and post-contrast phases, were similar (Fig 4) ($AUC_{pre-contrast}$ = 0.686; 95% CI, 0.591-0.870 and $AUC_{post-contrast}$ = 0.673; 95% CI, 0.589-0.879). This implied that there was no significant difference between using pre-contrast or post-contrast studies to classify pleural effusions. When the cutoff value of the mean attenuation for exudates in pre-contrast studies was accepted of ≥8.5 HU, the sensitivity, specificity, and accuracy were 84.5%, 45%, and 78%, respectively. There was only one transudate case, showing the CT attenuation value of ≥16 HU in pre-contrast images (Table 1).

TABLE 1. Performance of the mean attenuation values in precontrast CT images for diagnosis of exudates.

HU Cutpoint	Transudate (N=20)	Exudate (N=112)	Sensitivity	Specificity	Accuracy	PPV	NPV
≥8.5	9	95	84.8	45.0	78.7	89.6	34.6
≥10	10	79	70.5	50	67.4	88.8	23.3
≥14	17	46	41.1	85.0	47.7	93.9	20.5
≥15	18	36	32.1	90.0	40.9	94.7	19.1
≥16	19	31	27.7	95.0	37.8	96.9	19.0

Abbreviations: HU=Hounsfield Unit, PPV= positive predictive value, NPV= negative predictive value

To evaluate CT findings, all the findings were more commonly found in exudates than transudates with statistical significance (Table 2). The presence of pleural thickening or pleural nodule was highly specific for exudative pleural effusion. The pleural nodule was found only in the exudate group and only 2 patients with transudates (2/20, 10%) had pleural thickening, but still thin.

In subgroup analysis of types of exudates, the group of empyema thoracis showed the highest mean attenuation values (16.84 HU; SD, 3.85 HU), followed by malignant effusion (12.69 HU; SD, 5.16 HU), and parapneumonic effusion (11.98 HU; SD, 4.61 HU) groups. There were significant differences between mean attenuation values of empyema thoracis and parapneumonic effusions (p=0.04). The CT findings of types of exudates were shown in Table 3.

TABLE 2. Performance of CT findings for diagnosis of exudative pleural effusions.

Findings	Transudate (N=20)	Exudate (N=112)	Sensitivity	Specificity	PPV	NPV	p
Adenopathy	9	78	69.6	55.0	89.7	24.4	0.032
Pleural nodule	0	37	33.0	100.0	100	21.1	0.002
Pleural Thickening	2	62	55.4	90.0	96.9	26.5	0.000
Loculation	5	55	49.1	75.0	91.7	20.8	0.046

Abbreviations: PPV= positive predictive value, NPV= negative predictive value

TABLE 3. Frequency of the CT findings between types of exudative pleural effusions.

Findings	Malignant (N=63)	Parapneumonic (N=31)	Empyema (N=8)	Other (N=10)
Adenopathy	53 (84.1%)	19 (61.3%)	3 (37.5%)	3 (30%)
Pleural nodule	34 (54%)	2 (6.5%)	1 (12.5%)	0 (0%)
Pleural thickening	38 (60.3%)	16 (51.6%)	6 (75%)	2 (20%)
Loculation	26 (41.3%)	18 (58.1%)	5 (62.5%)	6 (60%)
Bilateral	28 (44.4%)	16 (51.6%)	2 (25%)	8 (80%)

TABLE 4. Performance of CT findings for differentiating malignant pleural effusions.

Findings	Non-malignant (N=69)	Malignant (N=63)	Sensitivity	Specificity	PPV	NPV	p
Adenopathy	34	53	84.1	50.7	60.9	77.8	0.000
Pleural nodule	3	34	54.0	95.7	91.9	69.5	0.000
Pleural thickening	26	38	60.3	62.3	59.4	63.2	0.009
Loculation	34	26	41.3	50.7	43.3	48.6	0.356

Abbreviations: PPV= positive predictive value, NPV= negative predictive value

The CT findings for malignant pleural effusion were also evaluated (Table 4). Compared with the non-malignant group (n=69), the malignant effusions (n=63) were significantly associated with the presence of pleural nodule, pleural thickening and adenopathy. The sensitivity and specificity of the CT findings for malignant effusions were also shown in Table 4.

DISCUSSION

A distinction between transudative and exudative pleural effusion is crucial for establishing diagnosis and management of effusions.[7] A diagnosis of types of pleural effusions relies on chemical analysis in the effusion and blood, by using Light criteria.[8] A CT scan is not only a sensitive and specific tool for detecting pleural effusions, but it is also a useful tool for determining causes of effusions as well.[9,10] Moreover, a CT scan can evaluate the associated lung parenchyma and mediastinal disease.

Several studies attempted to find out the clinical use of CT attenuation values in differentiating between exudative and transudative pleural effusions.[3-5] The previous studies[3,4] revealed the significant higher mean CT attenuation value of exudates (13.6-17.1 HU), compared with the transudates (6-12.5 HU). Abramowitz et al,[5] demonstrated the lower mean attenuation values of exudates (7.2±9.4 HU), compared with transudates (10.1±6.9 HU) without statistical significant.

Our results were similar to the prior studies[3,4] which showed significant higher mean attenuation values of exudates (12.8±5.0 HU in pre-contrast images and 13.8±5.1 HU in post-contrast images), compared with the transudates (9.4±3.2 HU in pre-contrast images and 10.2±5.1 HU in post-contrast images). The mean attenuation values in post-contrast CT images were approximately just 1 HU higher than those in pre-contrast images, which represented the small effect of intravenous contrast material to the mean attenuation values.

Cullu et al[4] also reported the benefit of CT attenuation values in differentiating exudates from transudates, by showing good accuracy (AUC 0.912), good sensitivity (85%) and specificity (86.7%) when using the cutoff value of ≥8.5 HU. In our study, the areas under curve of CT attenuation valves for exudates in pre-contrast and post-contrast phases were 0.686 and 0.673, respectively, which were considered as poor diagnostic performance. The difference between results was probably due to a low proportion of high attenuation effusions in our study, in consequence of small number of patients with empyema thoracis (n=8) and more cases of malignant effusions (n=63). However, our result agreed with the study in 2005, which showed the moderate accuracy of the attenuation value for exudates (AUC, 0.775), and did not recommend using the attenuation values alone for separation between types of pleural effusions.[3]

To determine the attenuation cutoff values for exudates, when the cut off values was accepted of ≥8.5 HU, the sensitivity (84.8%) and accuracy (78.7%) were good, but the specificity (45%) was low. When the cutoff value was set at the higher level, of ≥16 HU, the high specificity (95%) was achieved but the sensitivity decreased to 27.7%. According to these results, we may prefer to use the attenuation cutoff value at ≥16 HU, because we concern about the high specificity for diagnosis of exudates.

We found a high degree of overlap in HU values of transudate and exudates, between 0.44-15 HU ranges, in our study. A use of mean attenuation value for determination of types of pleural effusions is sometimes problematic.[3-5] Diagnostic thoracocentesis is still necessary for this situation.

The CT appearances of exudates and transudates were also analyzed by many studies. Arenas-Jimenez et al,[11] observed that loculation, pleural thickening and pleural nodules were considered as the helpful CT findings for

exudates. Meanwhile, Abramowitz et al,[5] reported that these CT findings were unreliable. Several authors[11-14] also reported that pleural thickening, was the only finding found in transudates.

In our study, pleural thickening and pleural nodule demonstrated the high specificity for exudative pleural effusions. The finding of pleural thickening was found in 55.3% of patients with exudates, compared with 10% of patients with transudates, with a specificity of 90% and PPV of 96.9%. The finding of pleural nodule was found only in exudative group (33%) with a specificity of 100% and PPV of 100%. In addition, the sign of loculation had good specificity (75%), but low sensitivity (49.1%).

To differentiate between benign and malignant effusions, Arenas-Jimenez et al,[11] found CT findings of multiple pleural nodules and nodular pleural thickening were seen only in malignant effusions. However, Cullu et al,[4] observed a pleural nodule in only one of 20 cases with malignant effusion and the other author[5] also reported a pleural nodule in non-malignant effusions. In our study, the presence of pleural nodule was suggestive of malignant pleural effusions with high specificity (95.7%) and high PPV (91.9%). Pleural nodule was found in 53.9% of patients with malignant effusions, compared with 4.3% of patients with benign effusions. The benign effusions with pleural nodule were found in one case of empyema thoracis and two cases of parapneumonic effusions. Adenopathy was more frequently found in exudates and malignant effusions, than transudates and non-malignant effusions with statistical significance. However, we found a limitation to apply this result in a clinical practice because of low specificity.

There were limitations in this study. First, this was a retrospective study which could have many uncontrolled factors. Second, this study contained small sample size of transudate effusions and empyema group. Third, we used two different CT scanners with different scanning parameters.

CONCLUSION

The mean attenuation cut off values of ≥16 HU favored exudates. However, a use of CT attenuation values alone showed poor diagnostic performance for differentiating types of pleural effusion. Correlation with clinical context and pleural fluid analysis was still essential. Furthermore, the helpful CT findings for diagnosis of exudative pleural effusion were pleural thickening, pleural nodules and loculation.

Disclosures of Potential Conflicts of Interest: The authors declare that they have no conflict of interest.

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