

# CT scan attenuation value measurement as a diagnostic tool for patients with pleural effusions

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## ABSTRACT

**Background:** Fluid in the pleural cavity is a common clinical problem with many potential causes. Despite the clinical and radiological findings providing important data about the cause(s) of content in the pleural cavity, tube thoracostomy or diagnostic thoracentesis are still required to relieve the pressure and characterize the fluid. These procedures could be avoided by applying a non-invasive method such as measurement of fluid CT attenuation values (CT - AV).

**Aim:** To evaluate CT attenuation values as a diagnostic tool to distinguish between hydrothorax, pyothorax and haemothorax.

**Materials and methods:** For this retrospective observational study we reviewed 89 patient medical records and chest CT scans performed between October 2012 and January 2017. Patients with the diagnosis of either haemothorax, pyothorax or hydrothorax were included. CT - AV were measured in three CT scan slices with the highest amount of pleural effusion. We calculated the mean CT - AV for every study participant and evaluated the accuracy to distinguish pleural contents between haemothorax, pyothorax and hydrothorax groups using Receiver Operating Characteristic (ROC).

**Results:** The mean CT - AV of haemothorax were significantly ( $P < 0.001$ ) higher from those of pyothorax and hydrothorax. The pyothorax mean CT - AV were also significantly higher than hydrothorax values ( $P = 0.042$ ). The diagnostic accuracy of CT - AV to distinguish between haemothorax, pyothorax and hydrothorax was statistically significant ( $P < 0.001$ ).

**Conclusion:** CT attenuation values between hydrothorax, pyothorax, and haemothorax are distinguishable.

**Keywords:** pleural effusions, hemothorax, pyothorax, CT attenuation.

## INTRODUCTION

Pleural fluid is a common clinical problem with many potential causes [1]. The first step in prescribing treatment is to decide whether the pleural fluid is haemothorax, pyothorax (empyema) or hydrothorax (serous pleural effusion) [2,3]. The haemothorax can be classified as either traumatic, originating from blunt or penetrating trauma, or spontaneous, arising from multiple reasons: vascular, connective tissue disorders, haematological disorders, neoplastic and miscellaneous (exostoses, endometriosis) [4,5]. The aetiology of pyothorax is either hospital acquired or community acquired infections [6], including a number of bacterial [7] and fungal [8] infections. Many pathological conditions may attribute to the accumulation of hydrothorax. Malfunction of the heart, liver, pancreas or kidneys; certain medications (amiodarone, methotrexate,

nitrofurantoin, phenytoin); pulmonary embolism and even pneumonia may cause transudate and exudate accumulation within the pleural cavity. [9] Malignant pleural effusions are due to pleural tumours or metastases originating from the lung, breast, ovarian or gastric cancer, lymphoma, etc. [10] Other conditions, such as autoimmune diseases (e. g. Sjögren's syndrome, Lupus, etc.) and even environmental factors, such as asbestos exposure, may cause hydrothorax. [11-13]. Such a wide array of pleural effusion etiological factors is one of the many reasons why it is crucial to optimise the methods for determining the type of fluid in the pleural cavity. Despite the clinical and radiological findings which might provide important evidence about the cause(s) of pleural fluid(s) it might still be necessary to perform tube thoracostomy or diagnostic thoracentesis to relieve the pressure and to characterize the fluid. Even though needle thora-

centesis is less invasive than tube thoracostomy, it still carries small, but significant risks (e. g., the pneumothorax, bleeding (chest wall haematoma and haemothorax), and re - expansion pulmonary oedema) [14]. Pneumothorax occurs in 6% of the procedures and 34.1% of pneumothoraces requires chest tube insertion [15]. These unnecessary complications could be avoided using a non-invasive method such as diagnosing the type of pleural fluid using CT attenuation values (CT - AV). To our knowledge, there are no recent studies addressing this method of differentiating pleural effusions in Lithuania.

The aim of this study is to evaluate CT - AV as a diagnostic tool for distinguishing between hydrothorax, pyothorax or haemothorax.

## METHODS AND MATERIALS

### 2.1. STUDY DESIGN AND SETTING

We performed the retrospective observational study at the largest healthcare institution in Lithuania, annually exceeding 1.3 million outpatient consultations and 95 thousand hospital admissions. Kaunas Regional Biomedical Research Ethics Committee (KRBRE) approved the study protocol and waived an informed consent. In this study, medical health records made between October 2012 and January 2017 are analysed.

### 2.2. PATIENT SELECTION CRITERIA

We reviewed hospital's medical records for patients that underwent chest CT scans for suspected pleural or pulmonary pathology (n = 197) and selected patients with pathological findings in the pleural cavity (n = 113). For this study, patients with pleural effusions (n = 104) were selected and the one's with instances of pneumothorax were excluded. 17 more patients were excluded because they had not undergone any diagnostic studies of the pleural effusions or because the pleural contents were of gastric origin. The 89 enrolled patients were grouped into three categories: haemothorax, pyothorax, and hydrothorax, based on the discharge diagnosis, laboratory results, instrumental tests. The diagnosis of haemothorax was based on pleural fluid appearance or biochemical analysis of the fluid,

determining criteria being haematocrit (Hct) > 50%. The confirmation of pleural content being pus required a visually purulent appearance and/or histological assessment of the pleura. We classified the remaining effusions as hydrothorax.

### 2.3. SCANNING PARAMETERS

All CT scans were performed using GE VCT 64 or GE VCT 16 slice CT scanner, following chest scanning protocols: at a slice thickness of 5 mm; pitch 0.969:1; 120 kV, 100 - 665 mA, rotation speed 0.5 s. When indicated and allowed, the intravenous contrast (80 ml. Sol. Ultravist or Visipaque 300) was injected at the speed of 2.5 ml/s. We reviewed all images using Picture Archiving and Communication System (PACS) server Cedara-I-Reach (TM).

### 2.4. DATA ACQUISITION AND STATISTICAL ANALYSIS

For this study, all CT scans were reviewed independently by two medicine students of Lithuanian University of Health Sciences (LSMU), and experienced radiologists: a doctor resident measured the data, and two doctors radiologists re-measured and described the images. Later the images were also reviewed by the thoracic radiology section chief during multidisciplinary team meetings. In every CT scan (before and after intravenous contrast media administration) we located three slices with the largest pleural effusion volume and measured the attenuation values in Hounsfield Units (HU) using the circular or ellipse region of interest (ROI) tool to mark the area containing only the fluid (Figures 1, 2). We situated the ROI so the measurements would not include bone, fat, lung, thickened pleural tissue or air. For statistical analysis, we recorded and used the mean of three attenuation values.

We analysed all data using IBM SPSS Statistics v. 23.0. Normally distributed data was expressed as the mean value (95% confidence intervals) and non-normally distributed data as the median (minimum - maximum values).

The Scheffe method in the one-way analysis of variances (ANOVA) was used to assess the differences of normally distributed attenuation values between haemothorax, pyothorax, and

hydrothorax groups. Using the Receiver Operating Characteristic (ROC) we determined the sensitivity and specificity of CT attenuation value measurement as a diagnostic tool for all three groups. The Youden's J statistic was applied to determine the cut-off values for all three groups. We evaluated group homogeneity using  $\chi^2$ , one-way ANOVA and Kruskal-Wallis tests. Values of P less than 0.05 were considered significant.

## RESULTS

The study population consisted of 89 patients: 69 (77.5%) were men and 20 (22.5%) women. 12 (13.5%) patients had been hospitalized within 24 hours and 77 (86.5%) within 6 hours after the onset of symptoms.

There were no significant age ( $P = 0.285$ ), gender ( $P = 0.509$ ), hospitalisation length ( $P = 0.503$ ) dif-

ferences between the pleural effusion (haemothorax, pyothorax, or hydrothorax) groups. (Table 1). The mean CT - AV of haemothorax were significantly ( $P < 0.001$ ) different from those of pyothorax, and hydrothorax. The pyothorax mean attenuation values were also significantly higher than hydrothorax values ( $P = 0.042$ ) (Figure 3).

We used the area under the ROC curve (AUC) to determine the accuracy of the mean CT - AV to differentiate between haemothorax, pyothorax, and hydrothorax (Table 2). All results were statistically significant ( $P < 0.001$ ) (Figure 4, 5, 6). The cut-off values were determined as follows: to distinguish haemothorax from pyothorax  $\geq 24.52$  HU (SE: 83.3%; SP: 90.1%); haemothorax from hydrothorax  $\geq 20.17$  HU (SE: 90%; SP: 100%); pyothorax from hydrothorax  $\geq 15.3$  HU (SE: 65.6%; SP: 88.9%).

**Table 1. Demographic and pleural content CT attenuation findings in patients with haemothorax, pyothorax, and hydrothorax.**

	Haemothorax	Pyothorax	Hydrothorax
Count	30 (33.7%)	32 (36.0%)	27 (30.3%)
Age	58.57 (51.82 - 65.31)	52.41 (47.55 - 57.26)	52.81 (45.48 - 60.15)
Gender			
Male	22	27	20
Female	8	5	7
Length of hospitalization (days)	20.5 (2 - 147)	25 (3 - 108)	17 (2 - 73)
CT attenuation value (HU)	33.85 (29.43 - 38.27)	17.29 (15.1 - 19.47)	11.92 (10.54 - 13.3)

**Table 2. ROC curve results, assessing the use of CT attenuation values to distinguish between haemothorax, pyothorax, and hydrothorax.**

	Area under the ROC curve	95% CI
ROC (Haemothorax - Pyothorax)	0.912	0.841 - 0.984
ROC (Haemothorax - Hydrothorax)	0.993	0.981 - 1.000
ROC (Pyothorax - Hydrothorax)	0.774	0.645 - 0.895

Figure 1. 73-year-old patient after thoracic trauma with suspected haemothorax. CT scan shows bilateral dorsal pleural effusion. Ellipse ROI tool shows the mean attenuation value of 34 - 49 HU.

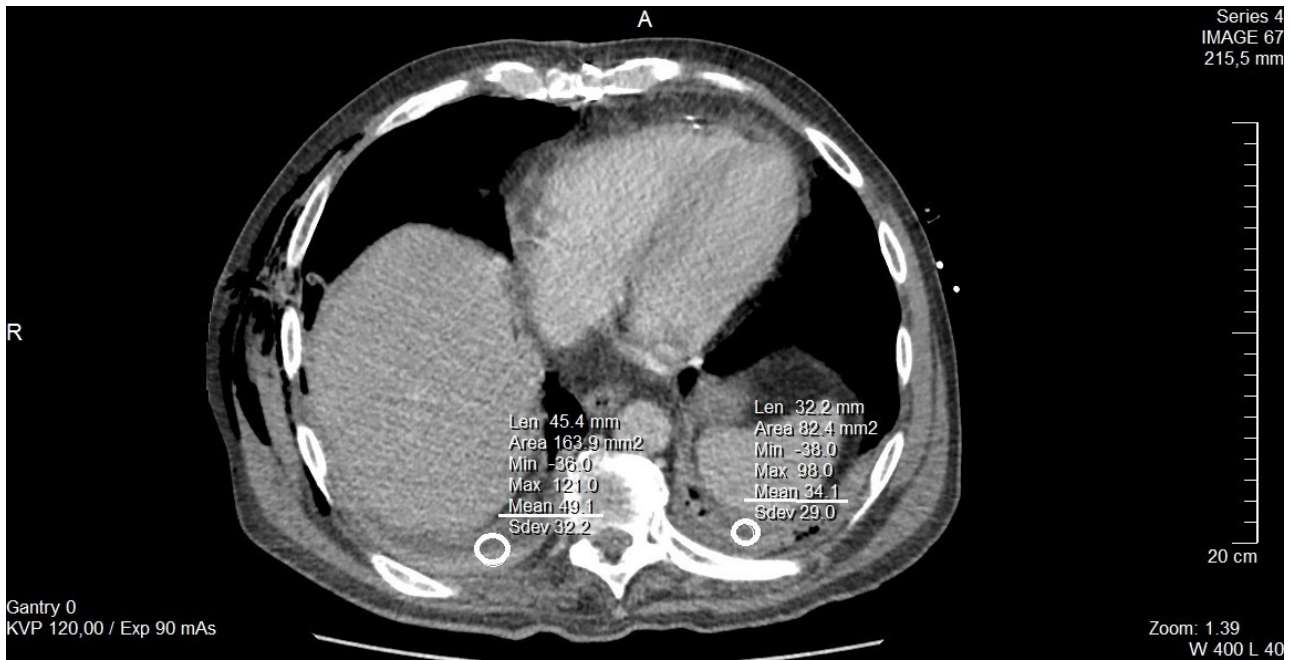


Figure 2. 44 year old patient with fewer, pyothorax and empyema. CT scan shows separated lateral pleural effusions with multiple gaseous bubbles. Ellipse ROI tool shows the mean attenuation value of 19.5 - 20.2 HU.

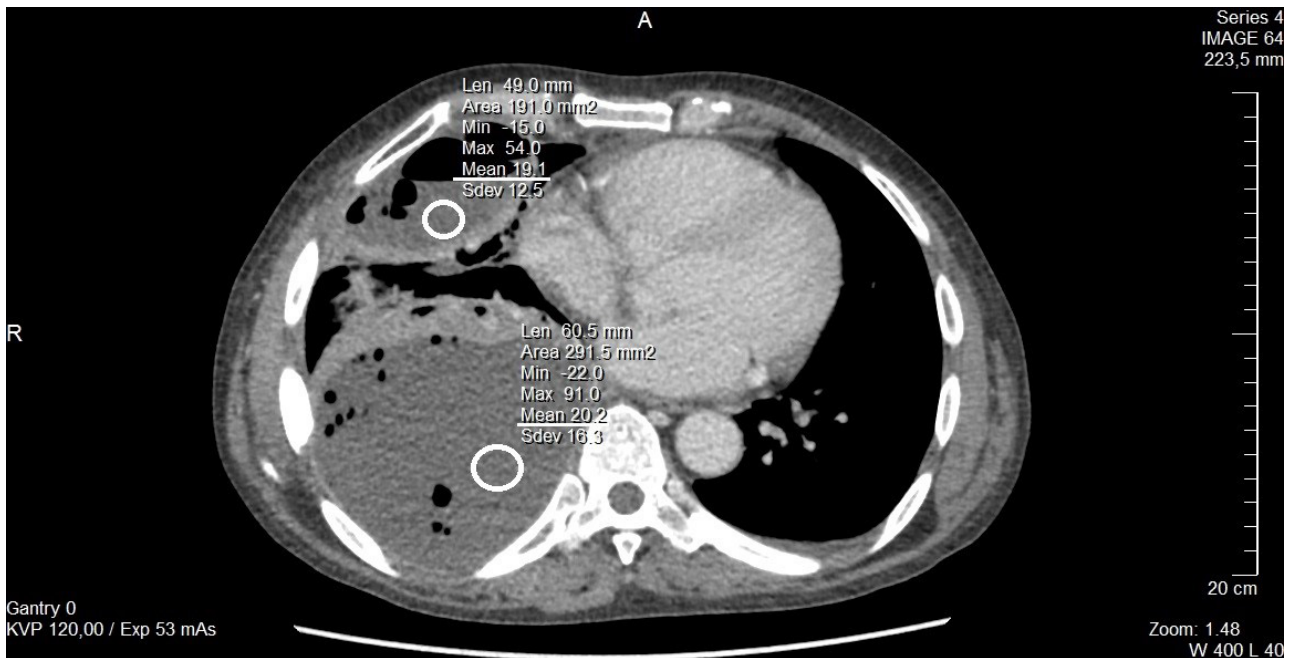


Figure 3. Box and whisker plots demonstrating mean attenuation value in haemothorax, hydrothorax, and pyothorax groups.

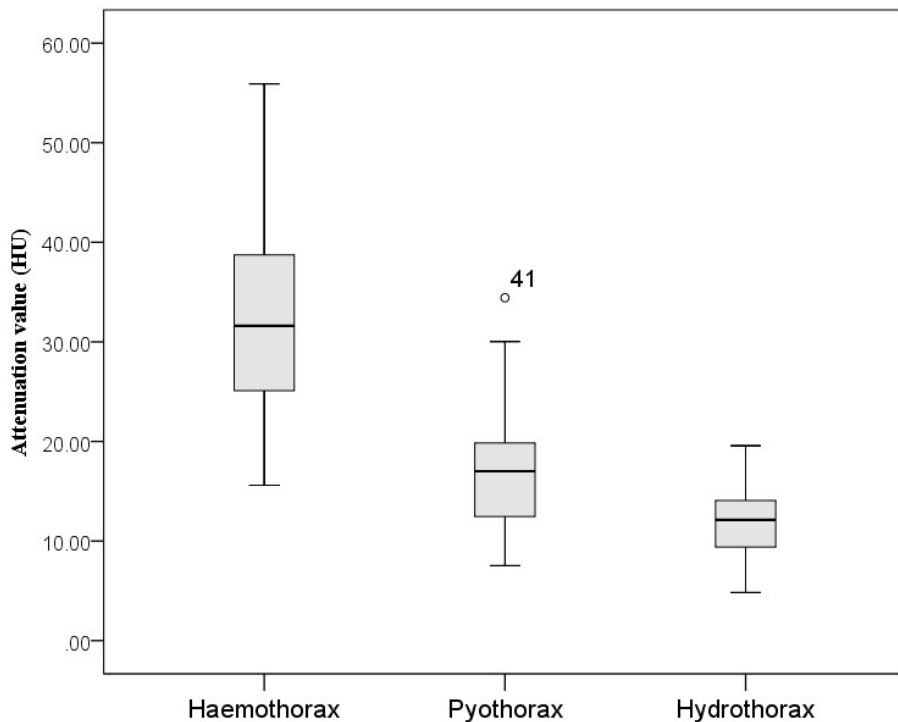


Figure 4. ROC demonstrating excellent diagnostic accuracy differentiating haemothorax from pyothorax using CT attenuation values. ( $P < 0.001$ )

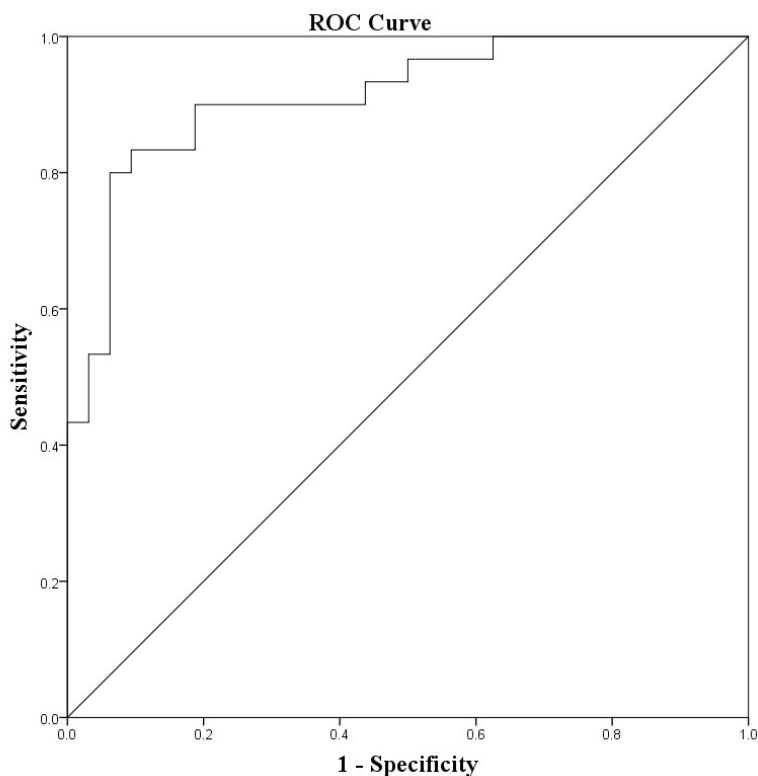


Figure 5. ROC demonstrating excellent diagnostic accuracy differentiating haemothorax from hydrothorax using CT attenuation values. ( $P < 0.001$ )

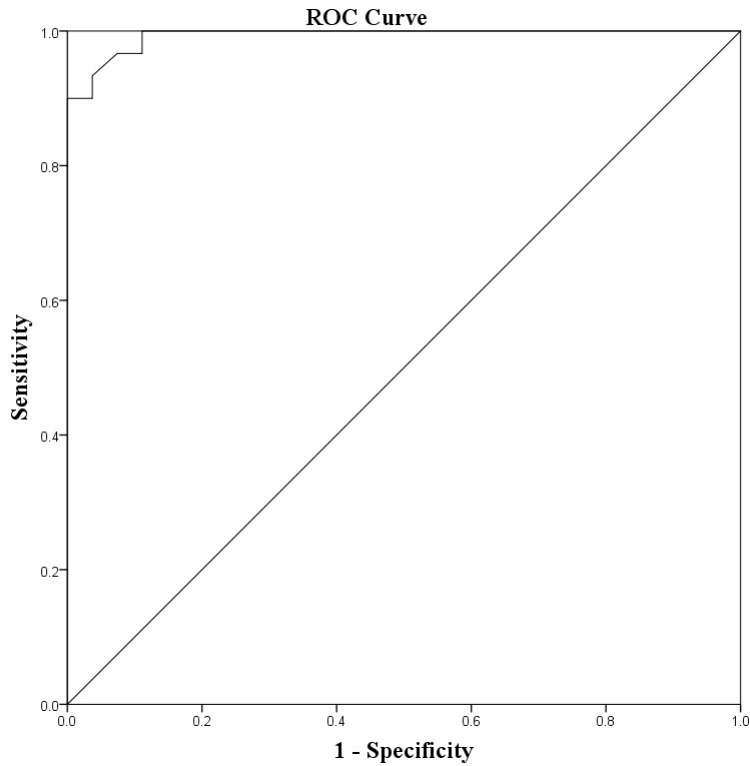
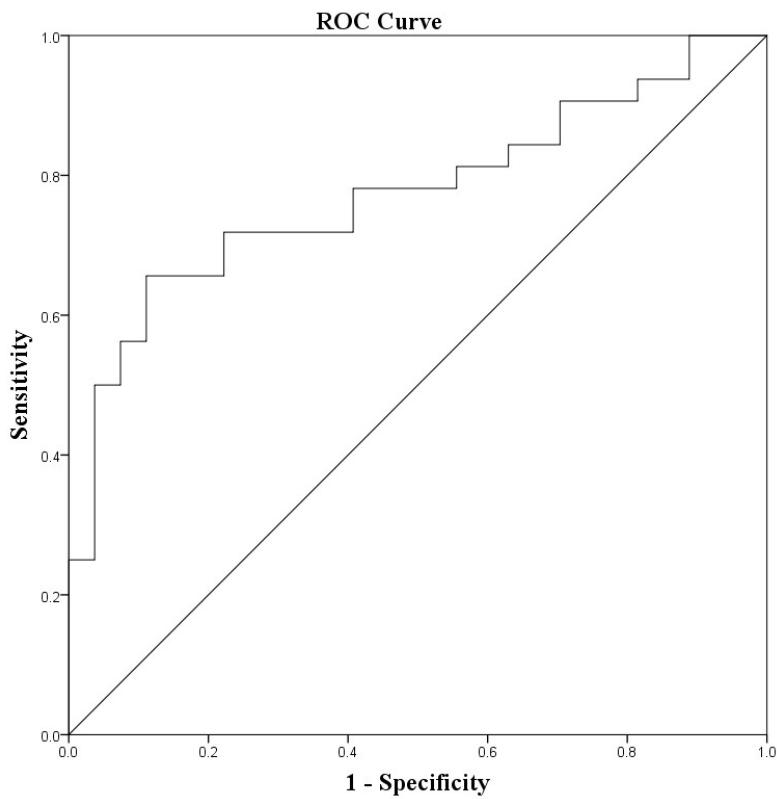


Figure 6. ROC demonstrating fair diagnostic accuracy differentiating hydrothorax from pyothorax using CT attenuation values. ( $P < 0.001$ )



## DISCUSSION

The differential diagnosis to distinguish between haemothorax, pyothorax and hydrothorax in a clinical setting is usually achieved using fluid analysis by means of diagnostic thoracentesis, thoracostomy or pleural biopsy and histological examination [3]. In this study, we found that CT - AV is a relatively accurate measurement to determine the nature of the pleural fluid. In previous studies, researchers have discovered that CT - AV was useful to differentiate even transudates from exudates in patients with pleural effusions [16, 17]. However, more data is required because of the overlapping HU values as they decrease the sensitivity of the diagnostic method.

We predicted that haemothorax would have higher CT - AV than pyothorax and hydrothorax because, in the acute phase, extravasated blood usually has a higher HU value. Iron in the haemoglobin molecule increases tissue density more than protein does in pyothorax and hydrothorax [18]. In most cases, the blood comes from damaged vessels in the ribs, lungs, mediastinum, diaphragm, chest wall, or directly from ruptured great vessels. [19]. Pyothorax should also have higher CT - AV than hydrothorax due to the strands of fibrin, high levels of protein, bilirubin, and LDH contained in the purulent fluid, all of which increase attenuation on a CT scan [14, 20]. To our knowledge, only one study has compared CT - AV between haemothorax, empyema, and pleural effusion. Liu et al. [19] examined 189 patients and found that the cut-off value  $>15,6$  HU to distinguish haemothorax from pleural effusion and a cut-off value of  $\geq 15,9$  HU to distinguish haemothorax from empyema.

In our study we found that the cut-off value of  $\geq 24,52$  HU (SE: 83.3%; SP: 90.6%) and  $\geq 20,17$  HU (SE: 90%; SP: 100%) was excellent to distinguish accordingly haemothorax from pyothorax and hydrothorax, while a cut-off value of  $\geq 15,3$  HU (SE: 65.6%; SP: 88.9%) to differentiate pyothorax from hydrothorax. However, the cut-off values are significantly higher than those, determined in the study performed by Liu et al.[19] This means further studies to establish the optimal cut-off values are necessary.

To sum up, CT - AV could be useful in emergency diagnostics and treatment for patients with contraindications for diagnostic thoracentesis such as hemorrhagic diathesis and cutaneous conditions (e.g., pyoderma or herpes zoster infection) [21]. Although CT is more sensitive than conventional chest sonography and radiography in differentiating between different pleural effusions [20], the value of diagnostic thoracentesis in normal clinical practice remains irreplaceable. The overlapping CT - AV decrease the applicability of this method and should not replace thoracentesis and/or tube thoracostomy as a diagnostic method to distinguish between haemothorax, pyothorax, and hydrothorax, especially when the latter are indicated for decompression or specific diagnostic tests.

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