Computed tomography measurements of parapneumonic effusion indicative of thoracentesis

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Running Title: CT measurements deteremining thoracentesis of pleural effusions.

Key words:

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In this manuscript we generate a means of measuring effusions by computed tomography that is comparable to the use of lateral decubitus radiography, which has long been the standard.

What are the clinical implications?
This computed tomography measurement offers an alternative means of assessing clinically significant effusions beyond LDR. Also since chest computed tomography is increasingly used as a first test for hypoxia by emergency room physicians it allows immediate determination of those who might require a thoracentesis from those that do not.
Abstract

Background: Patients with parapneumonic effusions (PPE) that measure <1 cm by lateral decubitus radiograph (LDR) or <5 cm by lateral erect radiograph (LER) do not require thoracentesis. No such data exists for chest computed tomography (CCT). The objective of this study was to identify a PPE measurement by CCT that indicates the need for thoracentesis.

Methods: A secondary data analysis of two pneumonia databases was conducted to identify patients with PPE. Measurements of PPE using LDR, LER, and CCT were correlated by linear regression analysis. The clinical outcome of community acquired pneumonia patients managed with the newly defined CCT measurement was evaluated.

Results: PPE was identified in 419 of 1,460 patients with possible pneumonia. PPE measurements by LDR of 1.00 cm and 5.00 cm by LER correlated with a measurement of 2.5 cm by CCT. Out of 95 patients with CCT measurements <2.50 cm, 31 poor clinical outcomes occurred: 1 outcome was PPE related, 26 were PPE unrelated, and 4 were unevaluable. The single case of a poor outcome also measured <1.00 cm by LDR.

Conclusions: This study indicates that patients with CAP and a PPE measuring <2.50 cm by CCT can be managed without the need for thoracentesis.
Abbreviations:

CAP: Community-acquired pneumonia
CCT: Chest computed tomography
HAP: Hospital-acquired pneumonia
LDR: Lateral decubitus radiograph
LER: Lateral erect radiograph
MRI: Magnetic resonance imaging
PPE: Parapneumonic effusion
US: Ultrasound
VAP: Ventilator-associated pneumonia
**Introduction:**

Parapneumonic effusions (PPE) result from inflammation of the visceral pleura as a consequence of infection of the lung parenchyma from bacterial or viral pathogens.\(^1,2,3,4\) These effusions occur in up to 45% of patients with community acquired pneumonia (CAP) and have a 10% chance of progressing to an empyema with an associated increased morbidity and mortality.\(^2,4,5,6\) An important step in the management of PPE is to ascertain which effusions require further diagnostic evaluation. Aspiration of a PPE is recommended in patients with a lateral decubitus radiograph (LDR) with a PPE measuring >1 cm\(^2\),\(^7\) or in patients with a lateral erect radiograph (LER) with a PPE measuring >5 cm.\(^8\)

Since the 1980’s there has been a nearly 20-fold increase in the utilization of computed tomography.\(^9\) In our clinical experience, there has been an increasing use of computed-tomography-pulmonary angiograms by emergency room physicians for evaluating patients with hypoxemia, many of whom have CAP. Since chest computed tomography (CCT) cannot adequately discern which effusions require thoracentesis by radiographic criteria alone, and no measurement similar to LDR has been established, these patients require subsequent imaging with LDR or LER. This is concerning since a prior study of PPE described a significant delay in time to thoracentesis while awaiting LDR\(^9\) and a delay of successful drainage may result in increased length of stay, cost, complications, and mortality.\(^3,4,10,11\)

We hypothesize that since CCT demonstrates layering effects similar to LDR, it would provide an attractive early alternative in patients who have already received a CCT. Since prior work has established a method of correlating measurements between LDR and ultrasound (US)\(^12\) and
between LDR and LER\textsuperscript{8}, it should be possible to define a correlation between measurements with LDR and CCT. This measurement can be used to define the need for thoracentesis once a PPE is documented by CCT. Therefore, we designed a study, first to determine if a correlation exists between PPE measurements by both LDR and CCT, and LER and CCT, and second, to evaluate if the newly defined PPE CCT measurements can safely be used to define the need for thoracentesis.

**Materials and Methods:**

*Study design:* This was a secondary data analysis of two pneumonia databases with patients hospitalized from December 2005 through March 2009 at the Robley Rex Veterans Administration Medical Center (VAMC) of Louisville, Kentucky. One database contained patients with the diagnosis of CAP enrolled in the Community-Acquired Pneumonia Organization (CAPO) international cohort study. The second database contained patients with diagnosis of hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) enrolled in the Hospital-Acquired Pneumonia Organization (HAPO) study. Only CAPO and HAPO patients enrolled from our VAMC were reviewed due to limitations in film availability of the larger international database. The VAMC Institutional Review Board approved both studies, the IRB approvals are CAPO 350.01 and IMPACT-HAP 519.06.

*Study definitions:* Pneumonia was defined as new radiographic evidence of a pulmonary infiltrate, as well as, one of the following: (1) new or increased cough with or without sputum production; (2) temperature of <$35.6^\circ\text{C}$ or $>37.8^\circ\text{C}$; (3) leukocytosis $>11,000/\text{mm}^3$ or leukopenia $<4,000/\text{mm}^3$, or bandemia of $>5\%$.\textsuperscript{13} Patients were defined as CAP if their infiltrate was present on radiography within 48 hours of admission.
**PPE evaluation:** Films were excluded from measurements if they showed any of the following characteristics: uninterpretable due to under-penetration, inability to visualize the inferior margin of the film, films of the incorrect side (LDR), error in type of image obtained, loculated effusion, hydropneumothorax, bilateral effusions (LER), diaphragmatic elevation (LER), effusion volume too large to determine the fluid level, or patients in the lateral position (CCT). For the purpose of comparing effusions, films were excluded from analysis if they were obtained greater than 72 hours apart.

All effusions were measured in centimeters using a ruler incorporated into the imaging software (CPRS Vista Imaging system, VAMC) in the following fashion: (1) LDR measurement was obtained by measuring from the delineation of the fluid lamella from the air-filled lung to a point parallel to the parietal pleura at the inner reflection of the rib along a path perpendicular to the inferior margin of the film (Fig 1); (2) LER measurement was obtained by measuring from the most inferior visible point of the contralateral sulcus to the fluid lamella using a path perpendicular to the inferior margin of the film (Fig 1); 3) CCT measurement was obtained by measuring from the parietal pleura-fluid junction to the visceral pleura-fluid junction in the middle third of the lung (1.5 cm above to 7.5 cm below the carina) along the mid-scapular line, where the fluid appeared thickest (Fig 1).

**Patient characteristics:** For each CAP patient the following characteristics were evaluated: demographics, radiographic findings, date and results of all thoracenteses including pH, total protein of serum and fluid, LDH of serum and fluid, albumin, glucose, gram-stain and culture, and cytology.

**Study outcomes:** The clinical outcome of CAP patients managed with clinical observation without thoracentesis according to the newly defined CCT measurement was evaluated. Clinical
failure was defined as: (1) death within 30 days of admission; (2) readmission within 30 days of discharge; (3) tube thoracostomy, thoracotomy, or decortication required during hospitalization or within 30 days; or (4) pleural fluid results consistent with complicated parapneumonic effusion or empyema as defined by the ACCP guidelines.\textsuperscript{14,15} Data on patients with clinical failure were reviewed and discussed amongst a panel of six hospitalist, infectious disease, and pulmonary physicians to classify the outcome as PPE related, PPE unrelated, or unevaluable.

**Statistical analysis:** LER, LDR, and CCT measurements were compared using PASW software version 18 to generate a linear regression analysis with best-fit line and $R^2$ analysis. The LDR or LER measurements were defined as independent variables and the CCT measurements were defined as dependent variables. The intersection point of the best fit line with the defined values of the independent variables (1.00 for LDR, and 5.00 cm for LER) was then evaluated for CCT and the two results were compared. The newly defined CCT value was then applied to patients enrolled in the CAPO database to define the clinical outcomes of patients with fluid collections less than 2.50 cm by CCT.

**Results:**

*Correlation of PPE measurements between LDR, LER, and CCT:*

From a total of 1460 patients with possible pneumonia, PPE was identified in 419 patients. The average age of these patients was $70.1 \pm 11.7$ years and 1.2% of patients were female. Of the 419 cases of PPE, 281 (67.1\%) were evaluated by CCT. The imaging modalities available in patients with PPE are summarized in Figure 2. In patients with PPE, a total of 79 pairs of films were available for comparison of LDR and CCT, and 76 pairs of films were available for comparison LER and CCT. LDR values of 1.00 cm and LER values of 5.00 cm correlated with CCT values of 2.50 cm (Figure 3).
Clinical application of CCT measurements to patients with CAP and PPE:

Among the patients with CAP, 41.2% (240 of 582) had PPE. The results of evaluation of the 582 patients with CAP for available films are presented in Figure 4. This analysis showed that 51.9% (302 of 582) of CAP patients underwent a CCT during their hospitalization, with 42.1% (245 of 582) of all CAP patients receiving a CCT within the first 48 hours of hospitalization. Table 1 shows the available films for evaluating parapneumonic effusion in the 240 patients with parapneumonic effusions as well as the limitations of each modality. CCT was the method used to evaluate PPE in 75.4% of cases (181 of 240), while only 23.8% (57 of 240) of patients with PPE were evaluated by LDR, and only 37.5% (90 of 240) were evaluated by LER. Upon applying our new criteria of 2.50 cm to the 181 patients with CAP and PPE, we found that 95 patients had measurements of <2.50 cm on CCT. The outcomes of these 95 patients with effusions measuring <2.50 cm are summarized in Table 2. There were 31 negative outcomes occurring in 29.5% (28 of 95) CAP PPE patients, with all but five of these poor outcomes attributable to causes other than PPE.

Of the five patients with negative outcomes not easily attributable to other causes, 4 outcomes were deaths in which patients were enrolled in hospice and had discontinuation of antibiotics or had inadequate documentation. The 3 remaining poor outcomes were from interventions possibly implying a complicated effusion or empyema (Fig 3). In the 3 outcomes with pleural thoracentesis indicating complicated effusion or empyema, tube thoracostomy, thoracotomy or decortication, two cases were not attributable to the effusion. The first patient had a central line inadvertently placed into the pleural space with infusion of normal saline that required emergent...
thoracotomy. The second patient had a thoracentesis suggesting possible parapneumonic effusion but also had adenocarcinoma invading the pleural space and chest wall with associated postobstructive pneumonia, the effusion was found to be malignant and not related to the pneumonia—the patient received no drainage procedure and suffered no ill outcomes. The remaining patient had a complicated PPE with a pleural fluid pH 6.89, LDH of 7914 md/dL, total protein 4.90 mg/dL, and glucose 21 mg/dL and received chest tube drainage, which was reported to drain purulent material. The LDR measurement in this patient was 0.93 cm, while the CCT measurement was 2.45 cm.

In patients with CAP and PPE, 43 had both LDR and CCT performed. LDR was performed after initial CCT in 62.8% (27 of 43) of these patients. Loculations were found in 10% of CAP patients with PPE (24 of 240) all of whom were detected by CCT during their initial evaluation. Of these 24 patients 8 received both LDR and CCT. Five of these 8 patients with both LDR and CCT had only partial loculations with persistent layering that prevented detection by LDR but still had measurements indicating a need for thoracentesis. One of these missed loculated effusions was less than 1.00 cm and would not have been tapped without CCT. Its aspiration was consistent with complicated parapneumonic effusion or empyema. Lateral decubitus radiography detected only 1 of 9 cases of loculated effusion as determined by CCT. All of these cases were large enough on LDR that despite no loculations being noted aspiration would still have occurred.

**Discussion:**
By correlating measurements between different imaging modalities in patients with PPE we discovered that a value of 2.50 cm by CCT was equivalent to established measurements by LDR and LER. By applying our new measurement to only patients hospitalized with CAP and PPE we found that PPE measuring less than 2.50 cm on CCT could be managed conservatively without thoracentesis. We also found that in our hospitalized CAP patients, CCT was the initial imaging modality in approximately 40% of cases. When PPE was uncovered by CCT, over 60% of these patients received subsequent imaging with LDR. When CCT is already available during the first 24 hours of hospitalization it is likely more efficient to use a measurement of 2.50 cm to determine the need for thoracentesis than to delay intervention while awaiting a LDR, which may be associated with increased morbidity and mortality, and should be avoided.3,4,10,11

The utility of estimating relevant parapneumonic pleural volumes through radiographic measurements was established by Light and colleagues.2 Similar to that seminal paper we found that negative outcomes were common in those with effusions, but that effusion progression was rare when effusions were small—CCT measurements less than 2.50 cm. Unlike the original LDR study we did find a single case of disease progression. However, this failure occurred despite both a measurement of less than 2.50 cm on CCT and less than 1.00 cm on LDR. Given the close approximation of this case’s measurement to both values we feel this represents an unusual occurrence and underscores the importance of clinical judgment and repeat evaluation in borderline cases, regardless of the means of measurement.

Metersky provided evidence that effusions greater than 5.0 cm in height on a LER required thoracentesis8; this also correlated with our CT value of 2.5 cm. Like Metersky we feel that
LDR may lead to delays in patient care when other modalities such as LER or CCT are readily available.\textsuperscript{8,10} In fact, our study found that the majority of patients received a CCT prior to receiving a LDR. Our study benefited from a larger population of patients compared to Metersky and so provides a more reliable linear regression model. As our LDR and LER values provided similar CCT measurements, it supports his assertion that LER measurements of 5.0 cm are an alternative to LDR. Compared to LER, CCT had additional benefits including a successful interpretation rate of 95\% (see Table 1), and allowed better visualization of loculations and septations. In our CAP patients LER failed to demonstrate 88.9\% of loculations visualized by CCT. However, due to the size of their effusions all of these patients received thoracentesis, so this had little clinical significance. In contrast to LER we do report a case of LDR measurements that neither indicated the need for thoracentesis nor detect loculations, but in fact had a complicated parapneumonic effusion.

While several prior studies have attempted to use either CCT or MRI to evaluate pleural effusions, these techniques have only proven efficacious at differentiating transudative from exudative effusions, but cannot discern infected from uninfected exudative effusions.\textsuperscript{16,17,18,19} While US can assess fluid volume similar to LDR and is advantageous because it can both be performed on medically unstable patients and can guide the placement of tubes into loculated effusions,\textsuperscript{20} it is limited by its inaccuracy when assessing small volume effusions\textsuperscript{10} and its failure to recognize purulent collections in a significant portion of patients.\textsuperscript{18,21} Therefore measurements by either LDR or LER and subsequent aspiration is still required in the assessment of PPE; measurements by CCT provide an additional means of evaluating clinically significant effusions, and aiding clinical judgment.
It is important to note that our study has several potential limitations. Foremost, our study was not prospective in nature and some outcomes could not be assessed due to enrollment in hospice or lack of adequate documentation. When measuring radiographic images reviewers were not blinded to the measurements of the other films. While this could introduce some bias into our results we feel this risk is minimized by the application of our generated measurement to clinical outcomes. Our results should also be applied with caution to patients with HAP and VAP, as our outcome measurements were only possible in those with CAP. The chief strengths of our study lie in the number of patients used to generate our linear regression models and the nearly identical values for CCT produced by both LDR and LER regression. Furthermore our study supplies an assessment of clinical outcomes when applying this novel measurement. While our study is limited to an elderly population that is almost exclusively male, we feel that their significant co-morbidities do typify most patients hospitalized with CAP by evaluation of the pneumonia severity index score.\textsuperscript{22} It is possible that due to differences in pleural space volume between men and women that our CCT measurement of 2.5 cm may overestimate the size of an effusion in female patients.

In recent years due to the superiority of this technique there has been an increasing usage of CCT in the evaluation of hypoxic patients to exclude pulmonary embolism.\textsuperscript{23} Although we feel that LDR still has an important role in the evaluation of parapneumonic effusions, it can lead to a delay in care when CCT is already available. It is our belief that patients with CCT measurements of \(>2.50\) cm should receive thoracentesis without additional imaging. We do caution interpretation of any measurements that fall very near cutoff values, and recommend
repeat clinical evaluation and imaging. This study would be best substantiated by a prospectively designed study to see if it does in fact reduce cost and expedite time to thoracentesis.

In conclusion, when CAP patients have a CCT readily available, measurements of <2.50 cm can be conservatively managed without thoracentesis. We feel it is pertinent to conclude with an alteration to Light and Sahn’s famous saying, “The sun should never set on a parapneumonic effusion”\textsuperscript{24}, unless that effusion measures less than 2.50 cm on CCT.

References:


Figure legends:

Figure 1

Three techniques for measuring lateral decubitus radiograph (LDR) (A), lateral erect radiograph (LER) (B), and chest computed tomography (CCT) (C).

Figure 2

Presence of effusion in 1460 patients with possible pneumonia and available radiography for comparison.
Figure 3

Correlation of pleural effusion measurements between 79 patients with both CCT and LDR (A) and 76 patients with both CCT and LER (B).

Figure 4

The distribution of films in patients with community acquired pneumonia (CAP) with regards to timing and number evaluated.
Table 1: Available films for comparison in CAP patients with PPE and their limitations

<table>
<thead>
<tr>
<th></th>
<th>LDR</th>
<th>LER</th>
<th>CT-chest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total films</td>
<td>57</td>
<td>90</td>
<td>181</td>
</tr>
<tr>
<td>Measurable radiographs</td>
<td>50 (87.7%)</td>
<td>64 (71.1%)</td>
<td>148 (81.8%)</td>
</tr>
<tr>
<td>Loculation demonstrated</td>
<td>3</td>
<td>1</td>
<td>24</td>
</tr>
<tr>
<td>Uninterpretable</td>
<td>4 (7.0%)</td>
<td>25 (28.8%)</td>
<td>9 (5.0%)</td>
</tr>
<tr>
<td>Limitation of</td>
<td>2 incorrect side</td>
<td>13 bilateral effusion</td>
<td>4 post thoracentesis</td>
</tr>
<tr>
<td>interpretation</td>
<td>1 incorrect film type</td>
<td>6 inadequate visualization of sulcus</td>
<td>2 contralateral effusion</td>
</tr>
<tr>
<td></td>
<td>1 massive effusion</td>
<td>4 underpenetrated</td>
<td>1 hydropneumothorax</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 post-thoracentesis</td>
<td>1 massive effusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 diaphragm elevation</td>
<td>1 image missed</td>
</tr>
</tbody>
</table>

Table 2: Comparison of clinical outcomes in 95 patients with PPE and CT measuring less than ≤2.5 cm (patients may have more than 1 outcome).

<table>
<thead>
<tr>
<th>Outcome:</th>
<th>Number</th>
<th>Unable to evaluate due to hospice or inadequate information</th>
<th>Negative outcome Attributable to PPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good outcome</td>
<td>67</td>
<td>0</td>
<td>n/a</td>
</tr>
<tr>
<td>Death ≤30 days</td>
<td>16</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Readmission &lt;30 days</td>
<td>12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Thoracentesis indicating complicated effusion or empyema, tube thoracostomy, thoracotomy or</td>
<td>3</td>
<td>0</td>
<td>1*</td>
</tr>
</tbody>
</table>
> Measured 2.45 cm by CCT and 0.93 cm by LDR

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