

# **Investigation of a unilateral pleural effusion: What CT scan coverage is optimal?**

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## **ABSTRACT**

The use of thoracic computed tomography (CT) for patients presenting with a unilateral pleural effusion is well established. However, there is no consensus with regards to the inclusion of the entire abdomen and pelvis in the initial imaging protocol. In this prospective UK-based study, 249 patients presenting with a unilateral effusion had a CT thorax/abdomen/pelvis performed. The prevalence of malignancy on thoracic CT was 56% (140/249). Clinically significant findings below the diaphragm were identified in 59 patients (24%). Integrating this approach into standard practice allows more rapid identification of the primary malignancy, upstaging lesions or alternative sites for biopsy.

## **INTRODUCTION**

Undiagnosed unilateral pleural effusions are common and have a wide range of underlying aetiologies, with malignancy high on the differential diagnosis list.[1] The British Thoracic Society (BTS) pleural guidelines recommend the use of computed tomography (CT) which has a sensitivity of 58-68% and specificity of 78-80% for diagnosing pleural malignancy.[2, 3] The use of CT in this situation is well established, however there is no consensus with regards to the inclusion of the entire abdomen and pelvis in the initial imaging protocol. The combined ERS/ESTS[4] recommend a thoracic CT scan; NICE guidelines for lung cancer diagnosis recommend a thoracic CT scan with 'upper abdomen' (to include the liver, adrenals and lower neck)[5]. Whilst the BTS guideline for malignant pleural mesothelioma recognised the clinical equipoise, stating that "a number of centres routinely include the abdomen and pelvis whereas others perform completion scanning according to the results of other diagnostic tests".[6]

This study aimed to ascertain the additional clinically relevant findings yielded by including the abdomen and pelvis in the initial CT scans of undiagnosed unilateral pleural effusions.

## **METHODS**

Consecutive patients presenting to a tertiary pleural service (Bristol, UK) with a unilateral pleural effusion underwent CT examination of their thorax, abdomen and pelvis (as per our standard care). All patients were followed up for a minimum of 12 months. The diagnostic protocol can be found in Appendix 1, the full details of this prospective study have been published previously.[7]

CT scans were reviewed to extract additional findings highlighted below the diaphragm. A consultant thoracic radiologist deemed findings clinically significant if they;

- identified the primary diagnosis,
- upstaged any malignant disease,
- highlighted a favourable site for further investigation such as biopsy, subsequent imaging or otherwise altered management.

Subdiaphragmatic findings were only deemed significant if they gave additional information to what was already known in the superior portions of the scan.

Descriptive statistics were used to quantify the proportion of clinically significant findings and univariate logistic regression was performed to identify any predictive variables. All statistical analysis was undertaken with IBM SPSS statistics 24, and a *p*-value of <0.05 defined statistical significance.

## RESULTS

Between 2012 and 2016, 249 patients were identified as eligible and included in the analysis. Patient demographics are summarised in table 1 and 12-month diagnoses in table 2. Nearly two-thirds (159/249) had a malignant cause underlying their unilateral effusion with lung cancer and mesothelioma the predominant primary malignancies (59 and 53 cases respectively).

**Table 1. Baseline demographics in included patients. (N=249)**

**Table 2. Frequency of underlying cause of pleural effusion determined by 12-month diagnosis.**

When just the thoracic portion of the CT scan was reviewed the diagnostic sensitivity of CT for malignancy was 88% (140/159). Additional clinically significant findings below the diaphragm were identified in 59 of the 249 patients (23.6%), with 29 (11.6%) and 30 (12.0%) located in the abdominal and pelvic portions respectively, see figure 1. Of these findings 17 (6.8%) were of primary tumours, 32 (12.9%) upstaged malignant disease and 5 (2.0%) provided alternative biopsy sites. Full details in Appendix 2.

**Figure 1. Coronal CT scout image depicting anatomical landmarks for abdominal and pelvic portions (abdomen was categorised as between the inferior point of the costophrenic recess to the superior aspect of the iliac crests, whilst the pelvic portion was defined as anything inferior to the iliac crests). With proportion of patients with additional significant CT findings by anatomical region.**

A total of 140 patients had significant findings (including non-cancerous but relevant findings) in the thorax only whilst 31 had significant findings in both the thorax and abdomen (n=19) or pelvis (n=12). Of the 78 patients whose thoracic portion of their CT examination did not show any diagnostic features, 28 (35.9%) had clinically significant findings in either the abdomen (n=10) or

pelvis (n=18). Only patient gender was shown to be a statistically significant indicator of increased yield using logistic regression, see Appendix 3. Female patients were more likely to have additional helpful findings in the pelvic region compared to men ( $p=0.034$ ), with a prevalence of 22.0% in our female population compared to 7.2% in males. Asbestos exposure was negatively associated with additional clinically significant findings in the pelvis ( $p=0.050$ ).

## DISCUSSION

This study demonstrates that nearly one quarter of patients with an undiagnosed unilateral effusion will have clinically significant radiological findings below the diaphragm. This is the first study of its type and was performed given uncertainty amongst international guidelines with regards to the inclusion of the entire abdomen and pelvis in the initial imaging protocol.

The addition of the abdomen and pelvis in initial imaging protocol has advantages for patient care above the increased diagnostic yield. It prevents the need for further 'completion CT' appointments in patients who are being investigated for cancer expediting their diagnostic pathway. It can highlight potential targets for biopsy that may be more accessible and upstage disease.

Disadvantages include the increased dose of ionising radiation. However, given that the median age of this cohort was 72, and the dose of ionising radiation for CT scans continues to fall, this becomes less pertinent. Additionally, including the abdomen and pelvis increases the time taken to scan/report, however, one scanning sequence is likely to be quicker to undertake and report than two separate scans if required. We did not record any additional findings from the CT abdomen or pelvis which were eventually deemed to be clinically insignificant. However, another potential disadvantage is the increased detection of clinically insignificant findings that might lead to unnecessary investigations.

This was a prospectively performed study of consecutive patients presenting (either inpatient or outpatient) to a tertiary pleural referral centre in the United Kingdom. There are several factors that might affect the generalisability of our findings. A high prevalence of malignancy (64%) is likely to have increased the diagnostic yield of CT, however the yield is similar to other diagnostic studies. Hallifax et al performed a retrospective study of 370 patients who had a CT prior to thoracoscopy (a higher risk group).[2] They found that the sensitivity of CT was 68% (95% CI 62% to 75%) with a specificity of 78% (72% to 84%), which is similar to our cohort. The relatively high prevalence of mesothelioma within the malignancy cohort (33%) likely negatively impacts on the perceived benefit

of abdominal/pelvis scanning given mesothelioma has rarely metastasised below the diaphragm at presentation. This may also be reflected in the lower rates of significant pelvic findings in patients exposed to asbestos. The most benefit from scanning the abdomen and pelvis was seen in female patients and those without evidence of thoracic disease on initial CT.

## **Conclusion**

Including the abdomen and pelvis in the initial CT protocol detects clinically significant findings in nearly one quarter of patients presenting with a unilateral pleural effusion. Integrating this approach into standard clinical practice, especially in female patients, may potentially allow more rapid identification of the primary malignancy, alternative sites for biopsy or upstage disease, facilitating a shorter diagnostic pathway for patients with cancer.

**Table 1. Baseline demographics in included patients. (N=249)**

	<b>Frequency (%)</b>
<b>Age (IQR)</b>	72 (66-80)
<b>Sex</b>	
<i>Male</i>	167 (67.1)
<i>Female</i>	82 (32.9)
<b>WHO PS</b>	
0	53 (21.3)
1	102 (41.0)
2	57 (22.9)
3	36 (14.5)
4	1 (0.4)
<b>Admission Type</b>	
<i>Inpatient</i>	59 (23.7)
<i>Outpatient</i>	190 (76.3)
<b>Side of Effusion*</b>	
<i>Left</i>	102 (41.0)
<i>Right</i>	147 (59.0)
<b>Previous Malignancy</b>	
<i>Yes</i>	44 (17.7)
<i>No</i>	205 (82.3)
<b>Asbestos Exposure</b>	
<i>Yes</i>	87 (34.9)
<i>No</i>	162 (65.1)

(WHO PS – World Health Organisation Performance Status, \*as evidenced on ultrasound)

**Table 2. Frequency of underlying cause of pleural effusion determined by 12-month diagnosis**

<b>Diagnosis</b>	<b>Frequency (%)</b>
<b>Malignant</b>	<b>159 (63.9)</b>
<i>Lung</i>	59 (23.7)
<i>Adenocarcinoma</i>	37 (14.9)
<i>Squamous Cell</i>	14 (5.6)
<i>Small Cell</i>	8 (3.2)
<i>Mesothelioma</i>	53 (21.3)
<i>Ovarian</i>	14 (5.6)
<i>Haematological</i>	9 (3.6)
<i>Breast</i>	8 (3.2)
<i>Renal</i>	4 (1.6)
<i>Other</i>	12 (4.8)
<b>Benign</b>	<b>90 (36.1)</b>
<i>CCF</i>	28 (11.2)
<i>Benign Inflammatory Pleuritis</i>	16 (6.4)
<i>Pleural Infection</i>	16 (6.4)
<i>BAPE</i>	8 (3.2)
<i>Tuberculosis</i>	4 (1.6)
<i>Eosinophilic Effusion</i>	4 (1.6)
<i>Other</i>	14 (5.6)

(CCF – Congestive Cardiac Failure, BAPE – Benign Asbestos Related Pleural Effusions)

**Figure 1. Coronal CT scout image depicting anatomical landmarks for abdominal and pelvic portions (abdomen was categorised as between the inferior point of the costophrenic recess to the superior aspect of the iliac crests, whilst the pelvic portion was defined as anything inferior to the iliac crests). With proportion of patients with additional significant CT findings by anatomical region.**

**Appendix 1. Diagnostic criteria for pleural effusions**

**Appendix 2. Details of additional findings on CT of the abdomen and pelvis and their clinical significance**

**Appendix 3. Summary of univariate logistic regression of possible predictive factors for clinically significant findings found in the abdomen and pelvis.**

## References

1. Light RW LY, Sahn SA, Heffner JE. Pleural Fluid Analysis. In: Richard W. Light YCGL, ed. Textbook of pleural diseases. 2 ed2008:209-26.
2. Hallifax RJ, Haris M, Corcoran JP, et al. Role of CT in assessing pleural malignancy prior to thoracoscopy. *Thorax* 2015;70(2):192-3. doi: 10.1136/thoraxjnl-2014-206054 [published Online First: 2014/08/01]
3. Tsim S, Stobo DB, Alexander L, et al. The diagnostic performance of routinely acquired and reported computed tomography imaging in patients presenting with suspected pleural malignancy. *Lung Cancer* 2017;103:38-43. doi: 10.1016/j.lungcan.2016.11.010 [published Online First: 2016/12/28]
4. Scherpereel A, Astoul P, Baas P, et al. Guidelines of the European Respiratory Society and the European Society of Thoracic Surgeons for the management of malignant pleural mesothelioma. *Eur Respir J* 2010;35(3):479-95. doi: 10.1183/09031936.00063109 [published Online First: 2009/09/01]
5. Maconachie R, Mercer T, Navani N, et al. Lung cancer: diagnosis and management: summary of updated NICE guidance. *BMJ* 2019;364:l1049. doi: 10.1136/bmj.l1049 [published Online First: 2019/03/30]
6. Woolhouse I, Bishop L, Darlison L, et al. British Thoracic Society Guideline for the investigation and management of malignant pleural mesothelioma. *Thorax* 2018;73(Suppl 1):i1. doi: 10.1136/thoraxjnl-2017-211321
7. Arnold DT, De Fonseca D, Perry S, et al. Investigating unilateral pleural effusions: the role of cytology. *Eur Respir J* 2018;52(5) doi: 10.1183/13993003.01254-2018 [published Online First: 2018/09/29]