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*Thorax* 2010 65: 463

doi: 10.1136/thx.2009.118471

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## LETTER

## Inaccurate clinical nodal staging of non-small cell lung cancer: evidence from the MRC LU22 multicentre randomised trial

The clinical staging of non-small cell lung cancer (NSCLC) is of paramount importance. It determines prognosis and therapy, and inaccurate staging may result in inappropriate treatment. In particular, clinical staging that misses mediastinal metastases may result in the patient undergoing a futile thoracotomy. Conversely, accurately detecting mediastinal metastases preoperatively would allow consideration of concurrent chemoradiotherapy or neoadjuvant treatment.

Although sensitivity and specificity data of CT scanning, positron emission tomography (PET) and mediastinoscopy for the detection of mediastinal metastases exist, the impact on patient outcomes when combined with other standard staging techniques such as mediastinoscopy is limited. The MRC LU22 trial,<sup>1</sup> which compared surgery alone with neoadjuvant chemotherapy followed by surgery, collected prospective data on clinical and pathological staging and therefore allows a comparison of clinical mediastinal node staging with pathological staging from mediastinal lymph node dissection at surgery.

Of the 519 patients in the MRC LU22 trial, 261 were randomised to undergo surgery alone. Detailed clinical and pathological staging were available for 230 of these patients, and 67 were reported as having had a PET scan. Nineteen of these patients underwent mediastinoscopy or anterior mediastinotomy for PET-positive mediastinal lesions. The 67 patients who had

a PET scan were clinically staged as having no evidence of mediastinal disease preoperatively (cN0–1), but 8 (12%; 95% CI 4% to 20%) were subsequently found at operation to have mediastinal (pN2) metastases. A further 9 patients were also understaged as hilar disease was missed preoperatively (ie, they were considered cN0 but were pN1), but this would not have affected the decision to operate. Overall, 17 patients (25%; 95% CI 15% to 36%) were understaged despite the use of preoperative PET scanning (table 1).

PET and mediastinoscopy are complementary techniques that are currently considered to be the gold standard for the clinical mediastinal staging of NSCLC. However, in this trial, clinical staging with PET and mediastinoscopy for PET-positive mediastinal lesions failed to detect mediastinal metastases in 12% of patients and, overall, the nodal status was understaged in 25%. PET-negative mediastinal nodes may harbour malignant cells and invasive sampling of enlarged nodes has been recommended, regardless of metabolic activity on the PET scan.<sup>2</sup> Mediastinoscopy (or other invasive mediastinal sampling) is required for the clarification of PET-positive mediastinal lesions. However, mediastinoscopy is underused in clinical practice<sup>3</sup> and, when performed, can only access the upper and anterior mediastinum.

In order to improve preoperative mediastinal lymph node staging, current guidelines recommend invasive mediastinal staging for patients with central tumours, fluorodeoxyglucose (FDG)-avid hilar N1 disease, low FDG uptake of the primary tumour and lymph nodes  $\geq 10$  mm on the CT scan regardless of FDG uptake.<sup>2</sup> Newer techniques such as endoscopic ultrasound (EUS) and endobronchial ultrasound (EBUS) for the minimally invasive mediastinal staging of

NSCLC are emerging, and their sensitivities for detecting mediastinal metastases appear to be superior to the standard techniques of CT, PET and mediastinoscopy. Preliminary results from a randomised trial have shown that routine use of EUS improves clinical staging and significantly reduced the rate of futile thoracotomies from 25% to 9%.<sup>4</sup> Further data are required on the impact of EBUS, EUS and their combination on the accuracy of clinical staging and the selection of operative candidates.

Improving the detection of mediastinal disease preoperatively would be an important step forward in optimising the selection of patients for surgery and identifying those who may benefit from neoadjuvant chemotherapy or chemoradiotherapy.

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**Competing interests** None.

**Provenance and peer review** Not commissioned; externally peer reviewed.

Accepted 9 August 2009

*Thorax* 2010;**65**:463. doi:10.1136/thx.2009.118471

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**Table 1** Clinical and pathological staging of patients with non-small cell lung cancer who underwent positron emission tomography and thoracotomy

	pN0	pN1	pN2	Total
cN0	28	9	6	43
cN1	13	9	2	24
Total	41	18	8	67