

# Bronchogenic carcinoma: incidence of metastases to normal sized lymph nodes

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## Abstract

**Background** – The incidence of metastases to mediastinal lymph nodes was evaluated in patients with normal sized mediastinal nodes on the computed tomographic (CT) scan who underwent thoracotomy. The use of hilar lymph nodes in predicting mediastinal lymph node metastases was also assessed.

**Methods** – Ninety patients with non-small cell lung cancer who later underwent thoracotomy were prospectively examined by CT scanning. Lymph nodes with a short axis diameter of 10 mm or more were considered abnormal.

**Results** – Mediastinal lymph node metastases were present at thoracotomy in 19 patients (21%). In 14 these lymph node metastases were misdiagnosed because the nodes were normal in size on the CT scan. In only one of the 19 patients with N2 nodes was an N1 lymph node enlarged, and four of the 19 patients with N2 nodes had metastases to these mediastinal nodes without N1 disease (“skipping metastases”).

**Conclusions** – Metastases in normal sized nodes seen on the CT scan are a major problem in staging. Hilar lymph nodes did not help to predict reliably the presence or absence of metastases to the mediastinal lymph nodes.

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**Keywords:** computed tomographic (CT) scanning, lung neoplasm, lymph node.

sized mediastinal lymph nodes is a subject of debate that directly affects the sensitivity of CT scanning, although it has been claimed that metastasis to normal sized lymph nodes (incidence 7%) was not a major problem in CT staging of non-small cell lung cancer.<sup>10</sup>

We have further evaluated the incidence of metastases to normal sized nodes in patients with non-small cell lung cancer who underwent thoracotomy. Furthermore, we have assessed the use of hilar lymph nodes in predicting mediastinal lymph node metastases.

## Methods

Between April 1989 and October 1994 243 patients with primary lung cancer were assessed in our department. Of these we prospectively studied by CT scanning 90 patients (66 men) who later underwent thoracotomy for primary lung cancer. Their mean age was 64 years (range 40–79). Selection criteria for thoracotomy in our institution were as follows: (1) no visible direct mediastinal invasion by the tumour on the CT scan; (2) no enlarged contralateral mediastinal nodes on the CT scan; and (3) no known distant metastases.

Patients with stage III B and stage IV disease at preoperative staging did not undergo thoracotomy. CT scans were performed at least three weeks before thoracotomy with a TCT-900S machine (Toshiba, Tokyo, Japan). Contiguous 1 cm thick sections were obtained at 1 cm intervals from the lung apices to at least the adrenal glands. CT scanning was initiated about 30 seconds after start of intravenous power injection of 100 ml contrast material (Iopamidol 300, Bracco Industria Chimica, Milan, Italy) at the rate of 2 ml/s. Standard scanning parameters (120 kVp, 120–250 mA, 512 × 512 matrix, 1 second scanning time) were used, depending on the size of the patient. CT scans were reviewed at levels appropriate for the mediastinum (level, 50 HU; window, 300 HU). The CT scans were independently interpreted by three radiologists (TA, TK, TM). When the analysis was not unanimous a consensus was reached after discussion. Mediastinal lymph nodes were localised according to the lymph node mapping scheme of the Japanese Lung Cancer Society<sup>11,12</sup> derived from the proposition by Naruke *et al*<sup>13</sup> which is used internationally. Lymph nodes were measured along the short axis on the transverse images and were considered abnormal if they were 10 mm or more in diameter.<sup>14</sup> Furthermore, lymph nodes which none of the three radiologists could detect on the CT images were defined as undetectable

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Accurate staging of lung cancer, including the extent of local and distant disease, is essential to determine the resectability and prognosis.<sup>1,2</sup> Preoperative assessment of mediastinal lymph nodes both clinically and radiologically is important, but the value of computed tomographic (CT) staging of bronchogenic carcinoma remains controversial.<sup>3</sup> Although most early studies reported that CT scanning had a high sensitivity for detecting mediastinal lymph node metastases,<sup>4–6</sup> more recent studies suggest that CT scanning has a low sensitivity.<sup>7–9</sup> In a study by McKenna *et al*,<sup>7</sup> in which total nodal sampling was performed, a lower sensitivity (60%) was reported for the detection of mediastinal lymph node metastases with CT scanning than in earlier studies.

In general, the smaller the node size chosen to separate malignant tissue from benign, the higher the sensitivity and the lower the specificity. The frequency of metastases to normal

nodes if found to be metastatic at thoracotomy.

All patients underwent thoracotomy with dissection of the mediastinal lymph nodes. Mediastinoscopy was not performed before thoracotomy in our institution. However, mediastinoscopy was performed to evaluate lymph nodes on the contralateral side of the mediastinum at thoracotomy regardless of staging. If the lymph nodes were accessible, a biopsy specimen was taken. Furthermore, R2b station resection was performed regardless of staging (stage I, II, IIIA).<sup>11</sup> At right thoracotomy all accessible lymph nodes in the superior mediastinum – that is, the superior mediastinal, paratracheal, anterior mediastinal, pretracheal and retrotracheal, and tracheobronchial nodes – and inferior mediastinum – that is, the subcarinal, paraoesophageal, and pulmonary ligament nodes – were resected together with the surrounding fat tissue. At left thoracotomy all accessible lymph nodes in the superior mediastinum – that is, the superior mediastinal, anterior mediastinal, pretracheal and retrotracheal, tracheobronchial, subaortic, and para-aortic nodes – and inferior mediastinum – that is, the subcarinal, paraoesophageal, and pulmonary ligament nodes – were resected. At thoracotomy, hilar (station 10), interlobar (station 11 on the left side, station 11s on the right upper lobectomy, 11i at right lower lobectomy, 11s plus 11i at middle lobectomy) and lobar nodes (station 12) were resected. Specimens from the maximal cut surface of each resected lymph node were routinely stained with haematoxylin and eosin.

## Results

Of the 90 bronchogenic carcinomas 61 were adenocarcinomas, 25 squamous cell, three large cell, and one adenosquamous. Mediastinal lymph node metastases were present in 19 patients (21%) – 14 with adenocarcinoma and five with squamous cell carcinoma. Four hundred and seventy five mediastinal nodal stations (443 at thoracotomy, 32 at mediastinoscopy) and 162 hilar nodal stations (156 at thoracotomy, six at mediastinoscopy) were sampled (mean of 7.1 stations per patient) (table 1). In 40 of the 475 mediastinal nodal stations (8.5%) and in 31 of the 162 hilar nodal stations (19%) metastatic lymph nodes were demonstrated histopathologically (table 1).

A total of 1443 mediastinal lymph nodes and 542 hilar lymph nodes were resected at thoracotomy (mean 22.1 nodes per patient, 3.3 nodes per nodal station). Sixty eight of the resected mediastinal lymph nodes (4.7%) and 63 of the resected hilar lymph nodes (11.6%) contained malignant tissue.

Enlarged N2 lymph nodes were seen on the CT scan in five of 19 patients with mediastinal lymph node metastases (26%). In the remaining 14 patients normal sized N2 nodes or undetectable N2 nodes were seen (table 2). Furthermore, in six of the 19 patients metastatic tumour was present, not in the enlarged nodes, but in nodes that were not identified on the CT scan in different mediastinal nodal stations. In addition, four of the 19 patients

**Table 1** Number of Japanese Lung Cancer Society nodal stations sampled in 90 patients

| Node station | No. of sampled nodal stations | No. of stations with metastases |
|--------------|-------------------------------|---------------------------------|
| 1            | 35                            | 0                               |
| 2R           | 33                            | 1                               |
| 2L           | 23                            | 0                               |
| 3            | 79                            | 9                               |
| 4R           | 46                            | 6                               |
| 4L           | 35                            | 4                               |
| 5            | 33                            | 5                               |
| 6            | 40                            | 1                               |
| 7            | 69                            | 7                               |
| 8            | 41                            | 3                               |
| 9            | 41                            | 4                               |
| Subtotal     | 475                           | 40                              |
| 10R          | 30                            | 4                               |
| 10L          | 30                            | 4                               |
| 11R          | 27                            | 3                               |
| 11L          | 27                            | 6                               |
| 12R          | 25                            | 6                               |
| 12L          | 23                            | 8                               |
| Subtotal     | 162                           | 31                              |
| Total        | 637                           | 71                              |

**Table 2** Analysis of 19 patients and 40 stations with mediastinal lymph node metastases using the size of lymph nodes on the CT scan

| Status of N2 nodes by size | No. of nodal stations | No. of cases |
|----------------------------|-----------------------|--------------|
| Normal sized N2 nodes      | 11 (27.5%)            | 7 (37%)      |
| Undetectable N2 nodes      | 23 (57.5%)            | 7 (37%)      |
| Enlarged N2 nodes          | 6 (15%)               | 5 (26%)      |
| Total                      | 40 (100%)             | 19 (100%)    |

**Table 3** Computed tomographic status of hilar lymph nodes of 19 patients with mediastinal lymph node metastases

| Status of hilar nodes on CT scan      | No. of cases |
|---------------------------------------|--------------|
| Normal sized or undetectable N1 nodes | 14 (74%)     |
| Enlarged N1 nodes                     | 1 (5%)       |
| Without N1 nodes                      | 4 (21%)      |
| Total                                 | 19 (100%)    |

with N2 nodes had metastases to mediastinal lymph nodes without metastases to hilar lymph nodes (“skipping metastases”). In only one of these patients was an enlarged N1 node seen on the CT scan (table 3). In three of the 71 patients without N2 nodes the hilar lymph nodes were enlarged.

Biopsy samples were taken at mediastinoscopy from 38 contralateral stations. Three metastatic stations were found. However, enlarged lymph nodes were not seen in those stations on the CT scan.

The overall sensitivity, specificity, and accuracy of CT scanning in detecting mediastinal lymph node metastases were 58%, 87%, and 81%, respectively.

The presence of mediastinal invasion was seen in four of the 90 patients at thoracotomy. Mediastinal invasion was not evaluated by mediastinoscopy.

## Discussion

We have studied 90 patients with non-small cell lung cancer. Nodes identified as being 10 mm or more in diameter on the CT scan were considered suggestive of malignant involvement. These findings were compared with

results of operative dissection. In 19 of the patients mediastinal lymph node metastases were found, in only one of whom an N1 node was enlarged. Furthermore, in 14 of 19 patients with N2 nodes mediastinal lymph node metastases were misdiagnosed, and four patients had N2 nodes without N1 nodes ("skipping metastases"). The status of hilar lymph nodes was not therefore predictive of N2 involvement, and metastases in normal sized nodes seen on the CT scan were a major problem in staging.

Kerr *et al*<sup>15</sup> reported that malignant mediastinal lymph nodes were not larger than benign nodes and small mediastinal lymph nodes were not infrequently malignant. Their findings support our study in the frequency of metastases to small lymph nodes. Furthermore, they suggested that, in the light of their findings of considerable numbers of "small" lymph nodes containing malignant tissue, small lymph nodes potentially "missed" by the surgeon would clearly be of interest. The higher incidence of patients with metastases to normal sized nodes in our study may be due to the fact that the number of resected nodes was more extensive than that in other studies.<sup>8-10</sup>

The most important findings in our study were that in only one of the patients with N2 disease was an enlarged N1 node seen, and some patients had N2 nodes without N1 nodes ("skipping metastases"). These findings indicate that we are not able to predict the presence or absence of metastases to mediastinal lymph nodes by the size of the hilar lymph nodes, and the absence of metastases to hilar lymph nodes is not always connected with the absence of metastases to mediastinal lymph nodes.

Some limitations of this study must be stressed. Our data are derived from a small and selected group of patients. Furthermore, mediastinoscopy was not performed before thoracotomy so we were not able to evaluate the role of mediastinoscopy in preoperative staging. However, in three of 19 patients with N2 nodes, N3 nodes were seen by mediastinoscopy which

were misdiagnosed because of metastases to normal sized nodes on CT scanning. Mediastinoscopy therefore seems to be more useful than CT scanning in the assessment of N3 nodes.

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