

Role of computed tomography and mediastinoscopy in the staging of lung cancer: A Canadian opinion poll

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OBJECTIVES: To address the Canadian Lung Oncology group's recently published results and recommendations suggesting that mediastinoscopy is unnecessary in the staging nonsmall cell lung cancer when computed tomography shows no enlarged mediastinal lymph nodes (larger than 1 cm in short axis); to evaluate the practice of thoracic surgeons across Canada in staging presumably operable lung cancer; and to assess the effect of the Canadian Lung Oncology Group's recommendations on current thoracic surgical practice in Canada.

DESIGN: A survey of Canadian thoracic surgeons (n=38) regarding the roles of computed tomography and mediastinoscopy in evaluating mediastinal disease in patients with operable lung cancer.

RESULTS: There was an 89% response rate. Ninety-one per cent of surgeons used computed tomography routinely, but only 10% of surgeons thought it to be more accurate than mediastinoscopy. Sixty-eight per cent would rely on a negative scan (nodes smaller than 1 cm in shortest diameter) to rule out mediastinal disease.

CONCLUSIONS: There are numerous circumstances where negative computed tomography does not adequately assess nodal status. A guideline for the use of computed tomography and mediastinoscopy in evaluating and staging

lung cancer is presented. Mediastinoscopy should be considered in the staging of patients with negative computed tomography if the patient is at high risk of mediastinal disease, where negative computed tomography is typically unreliable and when the risk associated with an unnecessary thoracotomy is high.

Key Words: *Computed tomography, Guidelines, Lung cancer, Mediastinoscopy, Mediastinum, Staging*

Rôle de la tomodensitométrie et de la médiastinoscopie dans la stadification du cancer du poumon : un sondage d'opinion canadien

RÉSUMÉ: Rôle de la tomodensitométrie et de la médiastinoscopie dans la stadification du cancer du poumon : un sondage d'opinion canadien

OBJECTIFS : Se pencher sur la récente publication des résultats et des recommandations du *Canadian Lung Oncology group* qui laissent croire que la médiastinoscopie n'est pas nécessaire dans la stadification du cancer du poumon non à petites cellules quand la tomodensitométrie ne révèle pas d'adénopathie médiastinale (plus grande que 1 cm dans l'axe court) ; étudier la pratique des chirurgiens thoraciques à travers le Canada en ce qui concerne la stadification du cancer du poumon qu'on estime opérable, et évaluer l'effet des recommandations du *Canadian Lung Oncology group* sur les pratiques courantes de la chirurgie thoracique au Canada.

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MODÈLE : Une enquête menée auprès de tous les chirurgiens thoraciques du Canada (n=38) relativement aux rôles de la tomographie et de la médiastinoscopie dans l'évaluation d'une atteinte médiastinale chez les patients atteints d'un cancer du poumon opérable.

RÉSULTATS : Le taux de réponse était de 89 %. Quatre-vingt onze pour cent des chirurgiens utilisaient systématiquement la tomographie mais seulement 10 % des chirurgiens pensaient qu'elle était plus précise que la médiastinoscopie. Soixante-huit pour cent feraient confiance à une tomographie négative (ganglions plus petits que 1 cm dans l'axe court) pour exclure une

atteinte médiastinale.

CONCLUSIONS : Il est fréquent qu'une tomographie ne soit pas spécifique de l'état ganglionnaire. Une ligne directrice concernant l'utilisation de la tomographie et de la médiastinoscopie pour évaluer et stadifier le cancer du poumon est présentée. On devrait envisager une médiastinoscopie pour la stadification des patients dont la tomographie est négative si le patient est à risque élevé pour développer une affection médiastinale, dans les cas où on ne peut généralement pas se fier à une tomographie négative et quand le risque associé à une thoracotomie inutile est élevé.

The Canadian Lung Oncology Group (1) recently assessed the role of computed tomography (CT) scans and mediastinoscopy in the management of nonsmall cell lung cancer (NSCLC) in a well designed prospective randomized trial. Patients were randomised to either a CT or a mediastinoscopy arm. Patients with a 'positive' CT scan (lymph nodes larger than 1 cm in short axis) had mediastinoscopy. Patients were excluded if the mediastinum was abnormal on chest radiograph or if they had a prior CT scan. The mediastinoscopy group had no CT scan. The impact of CT scan and mediastinoscopy on the primary outcomes of survival and "unnecessary thoracotomy rates" was assessed. An unnecessary thoracotomy was defined as either a thoracotomy for benign disease or thoracotomy without cure (recurrence at three years). There was no difference in the unnecessary thoracotomy rate between the two groups (121 of 342 patients in the mediastinoscopy group had unnecessary thoracotomy compared with 107 of 343 in the CT group). Survival in the two groups was also similar. The sensitivity and specificity of CT scan were reported as 78% and 69%, respectively. The authors concluded that only a select group of patients require both CT scans and mediastinoscopy. They proposed that mediastinoscopy is unnecessary in staging NSCLC when lymph nodes are less than 1 cm in length in their short axis on CT scan. On the basis of these results they recommended that "patients with apparently operable lung cancer should all have CT scan of the chest, and those with nodes greater than 1 cm should undergo mediastinoscopy, whereas the remainder should go directly to thoracotomy".

The purpose of this paper's poll of Canadian thoracic surgeons was to determine current practice regarding the use of CT scan and mediastinoscopy in the preoperative staging of NSCLC. The impact of the Canadian Lung Oncology Group's suggestions on the opinions and practice of surgeons in the evaluation of mediastinal disease in NSCLC was also investigated (1).

PARTICIPANTS AND METHODS

Thoracic surgeons (surgeons with a major interest in thoracic surgery) in Canada were identified from the Canadian medical directory, the General Thoracic Surgery Club directory and personal knowledge. Each surgeon was sent a simple questionnaire via fax consisting of an introductory paragraph followed by five questions each requiring a yes or no answer (Appendix 1). The questions were designed to gain an appreciation of how each surgeon used CT scans and medi-

astinoscopy in the preoperative staging of presumed operable lung cancer.

RESULTS

Thirty-four of 38 questionnaires were returned (89% response). One questionnaire was filled out incorrectly. Thirty-three of 34 (97%) were aware of the study by the Canadian Lung Oncology Group (1). Eleven of 33 (33%) felt that their practice had changed as a result of this publication. Thirty-one of 33 (91%) thoracic surgeons used CT routinely as part of their preoperative assessment. Three of 33 (9%) felt that CT scan had replaced mediastinoscopy as a more accurate measure of mediastinal disease. Ninety-one per cent (91%) felt that mediastinoscopy was more accurate than CT in defining mediastinal disease. Twenty-three of 34 (68%) used CT scans to rule out mediastinal involvement (no nodes larger than 1 cm).

DISCUSSION

Our results indicate that although Canadian thoracic surgeons are aware of the Canadian Lung Oncology Group's recommendations, only two-thirds used CT scans to rule out mediastinal disease and fewer still felt that CT was more accurate than mediastinoscopy in defining mediastinal disease.

Accurate staging of the mediastinal lymph nodes is one of the cornerstones in effective management of lung cancer (2,3). CT and mediastinoscopy are currently used to aid in diagnosis and decision-making in the management of operable NSCLC. The usefulness of these procedures remains controversial. Karmy-Jones et al (4) studied 30 patients with presumed unresectable bronchogenic carcinoma on the basis of radiological results alone and who were referred for palliative radiotherapy. The patients all received further surgical staging, which demonstrated that 10 were candidates for resection. Nine of these patients were alive and disease free at a median follow-up of over two years, demonstrating that chest x-ray and CT may not be specific enough to rule out the possibility of surgical cure.

The Canadian Lung Oncology Group (1) has recommended that mediastinoscopy is not required when the CT is negative (nodes smaller than 1 cm). This current survey was undertaken to determine the current practices of Canadian thoracic surgeons and to determine whether this recent information had affected their clinical practice. We believe that there are instances when mediastinoscopy is appropriate and

necessary even if the CT is negative. Evidence-based recommendations for the use of these procedures in practice will be provided where possible.

The addition of mediastinoscopy to the staging of lung cancer in 1965 improved management by more accurately defining inoperable disease (5). Frequently, the presence or absence of mediastinal lymph node disease (N2 or N3 disease) is pivotal in determining appropriate treatment (6,7). Traditionally, patients with N2 or N3 disease are not candidates for curative surgical resection and, therefore, are offered nonsurgical treatment or are entered into experimental neoadjuvant treatment protocols for their disease (2). Patients with nodal metastases at mediastinoscopy have a worse prognosis than those patients with negative mediastinoscopy and resectable positive mediastinal nodes found at thoracotomy (6).

Pearson and associates (7) reported surgical results of patients with mediastinoscopy positive and mediastinoscopy negative NSCLC. When operative mortality, unresected cases and inoperable resections were included in the survival data, the absolute five-year survival for patients with mediastinoscopy positive lymph nodes (N2 disease) was 9%. For patients with a negative mediastinoscopy in whom the N2 disease was identified at thoracotomy (usually in a site inaccessible by mediastinoscopy), a 24% overall five-year survival was observed. When only patients surviving a complete resection were assessed, the five-year survival was 18% for those with positive mediastinoscopy and 35% for those with negative mediastinoscopy. A review by Shields (8) concluded that less than 20% of patients with N2 disease are surgical candidates, and the overall survival rate for all patients with N2 disease is between 3% and 6% (8). In recent revisions to the TNM staging of NSCLC (9,10) clear differences have been shown in survival curves between N1 and N2 disease when defined clinically or surgically.

The results of the Canadian Lung Oncology Group study centre around the outcome measures used, unnecessary thoracotomy and survival. An unnecessary thoracotomy was defined as not only thoracotomy without resection but also a thoracotomy for benign disease (a comment on failed bronchoscopy or failed needle biopsy more than mediastinoscopy) and thoracotomy with clinical recurrence within three years (a comment on other preoperative staging techniques as much as mediastinoscopy). The authors anticipate mediastinoscopy (a staging tool) might affect the overall survival of lung cancer. Survival end-points appropriately assess the effects of treatment but cannot assess staging protocols.

We are concerned that the recommendation made by the Canadian Lung Oncology Group fails to account for the subsets of patients for whom mediastinoscopy is warranted, even if lymph nodes are less than 1cm on CT scan, specifically patients with adenocarcinoma, patients entering clinical trials, patients with resectable T3 tumours, patients with left upper lobe tumours, and patients with synchronous lung primary and solitary brain metastasis being considered for resection.

The approach to the staging of lung cancer in the late 1980s has been evaluated in the United Kingdom (11) and the United States (12). In the British study, 40% of surgeons did not stage mediastinal disease either by CT scan or mediastinoscopy, resulting in an unacceptably high rate of unnecessary thoracotomies. A similar proportion of British surgeons did not sample mediastinal lymph nodes at thoracotomy, which was felt to lead to "under staging". In the United States, a national survey of lung cancer care reviewed the treatment of 34,000 people with lung cancer and indicated that approximately 6% of all patients had thoracotomy without resection (unnecessary thoracotomy) and 17% had mediastinoscopy – some with enlarged nodes on CT (62%) and others not (38%). In the patients who had positive results on mediastinoscopy, 27% had normal nodes on CT (12) (false negatives).

Izbicki et al (13) prospectively compared the accuracy of CT and surgical assessment for T and N staging of bronchial carcinoma to the final pathology report. The stage of the primary tumour (T stage) was correctly determined by CT and bronchoscopy in 85% of cases. Surgical assessment correctly determined the T stage in 92% compared with the final pathological analysis. On the other hand, CT scan did not accurately predict mediastinal lymph node involvement, having a sensitivity of 29% and a specificity of 93%. When the lymph nodes were grouped according to size criteria, there was a 14% rate of metastatic involvement in nodes smaller than 1 cm on CT scan, and 71% of nodes larger than 1 cm were normal. When CT is used to identify disease in specific nodal stations as defined by the American Thoracic Society (ATS) (14), sensitivities of 44% (15) and 66% (16) have been reported. Furthermore, in CT scans rated positive by size criteria and by mediastinoscopy, tumour was found not in enlarged nodes but in normal-sized nodes from another nodal station (16). In another series 37% of lymph nodes that measured 2 to 4 cm in the short axis were hyperplastic and contained no metastases (15).

Two studies have measured interobserver reliability in describing mediastinal lymph nodes on CT scan. Observer agreement was described as poor to good (17). There was poor agreement between observers with lymph nodes in the left superior mediastinum. The authors concluded that "the disagreement was sufficient that it likely contributes to suboptimal sensitivity and specificity of CT in detecting tumor spread". A study comparing CT scans with mediastinoscopy and thoracotomy findings found large interobserver variability and low sensitivities (40% to 69%), indicating that negative mediastinal lymph nodes do not eliminate the need for mediastinoscopy or exploration of the mediastinum at the time of operation (18).

A prospective study comparing magnetic resonance imaging, CT and mediastinoscopy in bronchogenic carcinoma found CT scan to be frequently misleading in preoperative assessment of mediastinal nodes. These authors found CT scans to have a specificity of 88.7% and a sensitivity of only 71% (19).

Mediastinoscopy remains the most accurate prethorac-

cotomy method of assessing N2 and N3 disease (2,20-22). Metastatic disease in small nodes on a CT scan (nodes smaller than 1 cm) occurs especially in patients with adenocarcinoma (23). Mediastinoscopy may provide the only histological proof of small cell lung cancer and thereby prevent unnecessary thoracotomy. The routine use of preoperative mediastinoscopy has resulted in a resectability rate at thoracotomy of 93% (5).

In experienced hands, cervical mediastinoscopy is safe (24,25) and can be performed on an out-patient basis (26). Mediastinal lymph node location has been defined for the purpose of staging by the ATS (14) with recent modifications by the American Joint Committee on Cancer (9). Mediastinoscopy permits direct visualization and sampling of the paratracheal ATS node station (2 R/L, 4 R/L), tracheal-bronchial (10 R) and anterior subcarinal lymph node (station 7). Anterior mediastinoscopy and extended cervical mediastinoscopy expands the assessment to include the aorta pulmonary window and anterior mediastinal nodes (ATS stations 5 and 6, nodes anterior to the great vessels).

SUMMARY AND RECOMMENDATIONS

In general, a CT scan of the mediastinum appears useful, with comparable results at less cost than mediastinoscopy, when ruling out mediastinal disease in patients undergoing treatment for lung cancer. There are, however, specific circumstances where the presence of small nodes on CT scan does not rule out metastatic disease, and the sensitivity of a CT scan remains the issue when ruling in disease. The best performance is achieved (when ruling in disease) if both size criteria and clinical circumstances are combined, reaching a sensitivity for CT scan of 0.85. To effect a positive outcome in life expectancy, comparing invasive and noninvasive staging strategies, specificity must exceed 0.90. This currently is not possible.

Mediastinoscopy has a sensitivity of 0.87 with a specificity of 1.0. Its accuracy is 0.95. For patients whose mediastinum is positive on a CT scan and in whom the histology (of these nodes) would affect treatment decisions, mediastinoscopy remains the 'gold standard' and is recommended.

When the chest CT scan is negative (nodes smaller than 1 cm) mediastinoscopy can generally be eliminated from the preoperative work-up without affecting survival and unnecessary thoracotomy rates with the following exceptions.

- Mediastinoscopy should be considered in circumstances when small nodes are more likely to contain malignancy (when the tumour is known to be adenocarcinoma; M1 disease if the only known metastasis is a solitary brain metastasis being considered for resection).
- Mediastinoscopy should be considered if the patient will be enrolled in a trial of adjuvant therapy postresection.
- Mediastinoscopy should be considered when the presence or absence of nodal disease will have an extraordinary effect on the risk-benefit ratio in T3 disease.

Sampling of mediastinal nodes at resection is also recommended in those with negative mediastinoscopy. Accurate staging of NSCLC must include mediastinal lymph node sampling intraoperatively when appropriate.

CONCLUSIONS

A recent report by the Canadian Lung Oncology Group suggests the mediastinoscopy should not be used in patients with a negative CT scan (mediastinal lymph nodes less than 1 cm). The present opinion poll of Canadian thoracic surgeons has shown that personal opinions and practices are varied. An overwhelming majority of surgeons does not think that CT scan alone is sufficient to assess accurately mediastinal lymph node involvement. However, two-thirds of Canadian surgeons use CT in isolation to rule out mediastinal disease. The literature supports our belief that the optimum preoperative assessment of mediastinal lymph node status is unclear, but that CT scan and mediastinoscopy have independent and complementary roles in clinical decision-making in both diagnosis and treatment. We recommend that mediastinoscopy be considered in the prethoracotomy staging of patients at high risk of mediastinal disease, where CT is hardest to interpret and when the risks associated with an unnecessary thoracotomy are high.

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Re: Assessing the mediastinum in potentially operable NSCLC.

We are conducting an opinion poll to examine the role of mediastinoscopy and CT scan of the mediastinum in the staging of lung cancer across Canada.

A recent report in the Annals of Thoracic Surgery authored by the Canadian Lung Oncology Group (Ann Thoracic Surg 60: 1382-9; 95) concludes "patients with apparently operable lung cancer should all have CT scan of the chest and those with nodes > 1 cm should undergo mediastinoscopy, whereas the remainder can proceed directly to thoracotomy." In other words; **mediastinoscopy is not needed in the preoperative staging of limited non small cell lung cancer when the CT scan shows no evidence of mediastinal disease (nodes < 1 cm).**

Do you use CT scan routinely ? yes no

Are you aware of the publication referred to above ? yes no

Has your practice changed as a result of this publication ? yes no

Has CT scan of the mediastinum replaced mediastinoscopy as a more accurate measure of mediastinal disease for patients undergoing treatment for a lung cancer ? yes no

In general; Do you use CT scan to rule out significant mediastinal involvement ? If yes are there exceptions to your practice ? (list below , When do you do mediastinoscopy if nodes are < 1 cm?) yes no

Thankyou for your time in responding to these questions.

Appendix 1) Survey/Questionnaire faxed to Canadian thoracic surgeons. CT Computed tomography; NSCLC Non-small cell lung cancer

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