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Added value of invasive needle techniques in mediastinal and hilar nodal staging of clinical N0-N1 non-small cell lung cancer after positron emission tomography

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ABSTRACT

Previous studies evaluating staging methods of lung cancer have focused on mediastinal disease. We explored the added value of endoscopic techniques after PET scan in the evaluation of N1 nodal stations in 276 patients with a radiologically normal mediastinum demonstrating a potential stage shift in 20% of patients.

1. Introduction

An accurate staging is essential to the optimal treatment of non-small cell lung cancer (NSCLC). Many studies have demonstrated high rates of false-positive and false-negative results using computed tomography (CT) and positron emission tomography (PET) as sole methods for nodal staging [1–3]. The American College of Chest Physicians and the European Society of Thoracic Surgeons elaborated criteria to target patients who are at greater risk of occult mediastinal nodal metastasis and who should undergo invasive mediastinal staging [4,5]. Patients with a tumor larger than 3 cm, a central tumor or enlarged or hypermetabolic N1 lymph nodes should all undergo mediastinal staging prior to curative intent treatment according to these guidelines.

Stereotactic body radiotherapy (SBRT) has demonstrated excellent long term results in the treatment of early stage NSCLC and its use is becoming more widespread [6,7]. Unlike surgical patients, those treated with SBRT will not undergo lymph node dissection to detect imaging occult nodal disease hence confirming nodal status obtained from imaging prior to SBRT is of paramount importance. Endobronchial ultrasound (EBUS) and endosonography (EUS) are minimally invasive methods used to confirm nodal status obtained from imaging which have been mainly studied in the evaluation of mediastinal lymph nodes.

The objective of this study is to explore the potential added value of EBUS and EUS to conventional imaging methods of CT scan and PET CT in NSCLC staging with a particular interest in the performance of EBUS and EUS in detecting N1 disease, given the fact that data regarding this question is scant and of the outmost importance in patients considered for SBRT.

2. Methods

In this retrospective study, we used our local pulmonary investigation clinic database to identify all patients aged 18 years or older with NSCLC staged TxN0-1 M0 after CT and PET who were investigated during the 2013 to 2018 period at our institution. Only patients who underwent surgery with lymph node dissection or patients who were found to have positive N2 or N3 lymph nodes on EBUS or EUS were included. We excluded patients with small cell lung cancer and neuroendocrine tumors, patients with synchronous tumors, patients with history of lung cancer in the past five years and patients with a tumor greater than 5 cm who would not be candidate for SBRT. Lymph nodes were considered positive on CT if they were 1 cm or more in short axis and positive on PET scan if their SUV was equal or greater to 2.5. The clinical stage, obtained by CT and PET was then compared with the gold standard pathologic stage obtained by EBUS, EUS and surgery. Lymph nodes were considered accessible by EBUS if they were in station 2, 4, 7, 10, 11 and accessible by EUS if they were in the stations 5, 8 and 9.

Abbreviations: CT, computed tomography; EBUS-TBNA, endobronchial ultrasound guided transbronchial needle aspiration; NSCLC, non-small cell lung cancer; PET, positron emission tomography; SBRT, stereotactic body radiotherapy.

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We used descriptive statistics to characterize our population and performance of imaging methods to stage appropriately N1 and N2/N3 nodal stations.

This study was approved by the Quebec Heart and Lung Institute Institutional Review Board (2019–3070).

3. Results

After chart review, 276 TxN0-1 M0 patients meeting our inclusion and exclusion criteria who ultimately underwent surgery with lymph node dissection were identified. Two hundred and eighteen (79,0%) patients were classified as cN0 while 58 (20,0%) were classified as cN1 after imaging. Clinical characteristics of patients are presented in Table 1.

Among cN0 patients, 29 (13,3%) and 17 (7,8%) were respectively found on surgery to be N1 and N2/N3. Nine (52,9%) of the 17 patients with N2/N3 involvement were found in EBUS accessible stations while the remaining 8 (47,1%) where in EBUS inaccessible but EUS accessible stations. Thirteen (44,8%) of the 29 pathologic N1 nodes were found in EBUS accessible stations while the remaining 16 (55,2%) where in EBUS inaccessible intralobar stations. Systematic EBUS and EBUS + EUS could have respectively allowed to identify 22 and 30 patients with imaging occult N1 or N2/N3 involvement for a number needed to screen by EBUS and combined EBUS + EUS of 10 and 8 to modify stage in a patient with imaging occult lymph node involvement.

Among cN1 patients, nine (15,5%) patients were found on surgery to be N2/N3, 17 (29,3%) were downstaged to N0 and clinical nodal status was confirmed in 32 (55,2%). Five (55,6%) of the N2/N3 nodes involved were found in EBUS accessible stations while the remaining 4 (44,4%) where in EBUS inaccessible but EUS accessible stations. All of the 17 (100%) cN1 downstaged to N0 were found in EBUS accessible stations. Systematic EBUS and EBUS + EUS could have respectively modified management in 22 and 26 patients for a number needed to screen of 3 and 3.

In the overall N0 and N1 population, EBUS and EBUS + EUS could have respectively modified stage in 44 (15,9%) and 56 (20,3%) patients for a number needed to screen of 7 and 5.

4. Discussion

Our study suggests that incorporating EBUS or combined EBUS and EUS in the staging of patients considered for SBRT can potentially change stage and management in an important proportion of patients. The added value of invasive staging with needle techniques is well documented in surgical NSCLC but very little information is available on its added value prior to curative intent radiation therapy. Peeters et al. [8] have previously demonstrated a 4–5% decrease in geographical miss using an algorithm determining when to include a lymph node in the gross tumor volume when treating N2-3 patients. Demonstrating N1 nodal status prior to surgery will generally not modify decision to proceed to surgery and will only influence post-operative management or type of surgery performed (lobar resection) which may explain why little effort has been put into studying the performance of EBUS to detect false positives and negatives of PET-scan for N1 disease. Pre-treatment knowledge of N1 nodal status has significantly greater importance in patients treated by radiation therapy as there will be no nodal resection allowing to confirm nodal status and as nodal involvement may change radiation treatment plan. In addition to providing information about N1 nodal status, invasive needle techniques can also provide information about mediastinal nodal status as it has already been demonstrated in the surgical population.

Few endoscopic needle techniques studies focusing on hilar nodal status exist. The only previous studies of interest are retrospective which implies procedures may have been performed mainly to examine mediastinal and not hilar nodal status. Vial et al. [9] did demonstrate a stage shift in 19% of potential SABR candidates after EBUS-TBNA while Yasufuku et al. [3] upstaged respectively 7.4 and 4.3% of potential cN0 and cN1 surgical candidates while downstaging 68.1% of cN1 patients.

This study is limited by its monocentric retrospective design. It is also limited by the presumption of EBUS and EUS results. We elected not to analyze EBUS results in the minatory subgroup of patients who underwent the procedure as we do not systematically examine hilar stations unless it is felt of specific clinical interest by the physician performing the procedure. EBUS and EUS are known to be of imperfect sensitivity for mediastinal disease and little is known about their performance in hilar stations. A prospective study examining the added value of EBUS and EUS staging in potential curative intent radiation therapy candidates is warranted.

Table 1
Clinical characteristics of patients.

Characteristic	
Age (years), mean ± SD	65,6 ± 7,8
Sex (female), n (%)	159 (57,6%)
Smoking history (pack-years), mean ± SD	34,2 ± 20,6
COPD, n (%)	100 (36,2%)
Location, n (%)	
RUL	103 (37,3%)
RML	18 (6,5%)
RLL	40 (14,5%)
LUL	76 (27,5%)
LLL	39 (14,1%)
CT tumor size (mm), median ± SD	35,0 ± 18,6
SUV, median ± SD	8,0 ± 6,4
Clinical stage, n (%)	
T1N0M0	79 (28,6%)
T1N1M0	25 (9,1%)
T2N0M0	141 (51,1%)
T2N1M0	31 (11,2%)
Histology, n (%)	
Adenocarcinoma	219 (79,3%)
Squamous cell carcinoma	56 (20,3%)
Other	1 (0,04%)

5. Conclusion

Endoscopic staging can potentially change stage and treatment in a significant proportion of cTxN0-1 M0 who are candidate for SBRT and should be considered in early stage NSCLC prior to curative intent radiation therapy.

6. Consent for publication

Not applicable.

7. Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This project was approved by the Quebec Heart and Lung Institute Institutional Review Board.

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Author contributions

All the authors contributed to the data collection. The data analysis and the redaction of the manuscript were done by MMCC and reviewed by MF and JG.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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