AABIP JOURNAL CLUB

EVIDENCE FOR EXPANDING INVASIVE MEDIASTINAL STAGING FOR PERIPHERAL T1 LUNG TUMORS

CHEST 2020

THE CLINICAL QUESTION

Does the size and location of lung tumor increase the risk of metastasis to hilar and mediastinal lymph nodes?

TAKE HOME MESSAGE

This multi center, retrospective study evaluated the rate of hilar and mediastinal lymph node metastasis based on quantitative assessment of T1 lung tumor location and size. The study showed a high rate of N2 or N3 metastasis even among small tumors. The location of the tumor (i.e. central versus peripheral) did not modify the risk of metastasis. These compelling results suggest that small, peripheral tumors should potentially be staged invasively.

BACKGROUND

Lung cancer is one of the leading causes of death among other cancers. Therapy and prognosis for lung cancer are determined by proper staging. Noninvasive staging with PET-CT has only 65-70% sensitivity for detection of metastases to the hilar and mediastinal lymph nodes. Invasive staging is a superior method, which can be completed via endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TNBA), transesophageal endoscopic ultrasound with fine-needle aspiration (EUS-FNA), or mediastinoscopy.

Major society guidelines recommend invasive mediastinal staging in patients at high risk for metastatic disease, specifically those with large tumors, enlarged hilar lymph nodes, or 'central' tumor location. However, 'central location' is not strictly defined. Some define 'central' as the inner two-thirds of the hemithorax, while others define 'central' as inner one-third, visible during standard video bronchoscopy, or located within 2 cm of any critical structure.

STUDY DESIGN

Type of trial: Retrospective study using quantitative image analysis via the Chest Imaging Platform. In order for the study to be blinded, the image analysis was performed prior to accessing documented final stage.

Image analysis:

- Coordinates based on distance from the main carina to the center of the lesion on three axes (X - the medial-lateral axis, Z - the superior-inferior axis, Y - the anterior-posterior axis)
- Absolute distance from main carina itself (normalized based on the cube root of the patient's lung volume, then converted to idealized lung based on the average lung volume)
- Tumor size

Primary outcome:

- Presence of lymph node metastasis based on documented final stage (adjusted for clinical and epidemiologic variables known to be associated with lymph node metastasis: age, gender, smoking pack-years, lung cancer histopathology, and tumor diameter)

POPULATION

Subset of patients from the National Lung Screening Trial cohort, a multicenter study of 50,000 at-risk patients randomized to annual CT or chest x-ray screening.

Inclusion criteria: Patients from the study with single, screen-detected non-small cell lung cancer between 8 and 30 mm in size without enlarged lymph nodes.

Exclusion criteria: Ground glass lesions (given the low risk of mediastinal and hilar lymph node metastasis)

Baseline characteristics:

Three hundred and thirty-two (332) cases
Average patient age: 63 (54% male)
Tumor type:
68% adenocarcinoma
17% squamous cell
15% large cell or not otherwise specified

OUTCOMES

Out of the 332 patients that met inclusion criteria, 69 had mediastinal lymph node involvement (20.8%), 27 of which were N2 lymph nodes. There was no significant difference in patient or tumor characteristics (including histopathology and distance from carina) between those who did or did not have lymph node metastasis. The mean tumor diameter was 14.1 mm. There was no difference in rate of lymph node metastasis based on tumor size (OR 1.03, P=0.248). The average distance from carina to cancer was 97.5 mm. There was no statistically significant difference in the normalized distance from the carina to the tumor between those with and without metastases (93.6 mm vs 98.5 mm, P = 0.096).

None of the normalized tumor coordinate positions (X, Y, or Z) were associated with an increased risk for metastasis (Figure 1). The study also used a model to predict N2 or N3 (versus N0 or N1) disease. No location parameter (coordinate or carina-to-cancer distance) was significantly associated with the risk of N2 or N3 metastasis. When adjusted using multivariable and univariate logistic regression (for clinical and epidemiologic variables known to be associated with lymph node metastasis: age, gender, smoking pack-years, lung cancer histopathology and tumor diameter), neither the coordinate variables nor the carina-to-cancer distance was significant, confirming the lack of association between the distance/coordinate values and the risk of lymph node metastasis. Additionally, presence of lymph node metastasis was not significantly different when tumors were broken down by 10 mm size groupings. The presence of metastasis was 19.3% for tumors ≤10 mm in diameter, 20.1% for tumors 10-20 mm in diameter, and 26.5% for tumors >20 mm in diameter (p=0.56).

COMMENTARY

This valuable study evaluated the risk of metastasis to mediastinal lymph nodes based on size and location of non-small cell lung cancer tumors. By doing so, the investigators exposed potential deficiencies in the currently recommended selection criteria for invasive mediastinal staging. However, there are limitations, as the study was retrospective. Furthermore, as the authors note, 'the NLST only provides the final clinical stage according to the TNM staging criteria'. Therefore, the N stage is inferred, and the T stage could be increased by other factors such as invasion of the visceral pleura.

FUNDING

NIH HLK23133476

SUGGESTED READING

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ARTICLE CITATION

DuComb EA, Tonelli BA, Tuo Y, et al. Evidence for Expanding Invasive Mediastinal Staging for Peripheral T1 Lung Tumors [published online ahead of print, 2020 Jun 26]. Chest. 2020;S0012-3692(20)31815-8. doi:10.1016/j.chest.2020.05.607

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