



EBUS-TBNA OF THE CONTRALATERAL PET NEGATIVE HILAR N3 LYMPH NODE: IS THE JUICE WORTH THE SQUEEZE?



THE CLINICAL QUESTION

What proportion of patients with hilar N3 nodes showing negative PET-CT scan findings have malignancy by EBUS

STUDY CONCLUSION

Sampling strategies should be individualized based on the clinical context. When using moderate sedation, it is reasonable to start with the mediastinal N3 nodes if the hilar and mediastinal N3 nodes are PET negative. Patients with positive PET scan findings of the mediastinal N3 nodes should probably undergo hilar N3 node sampling.

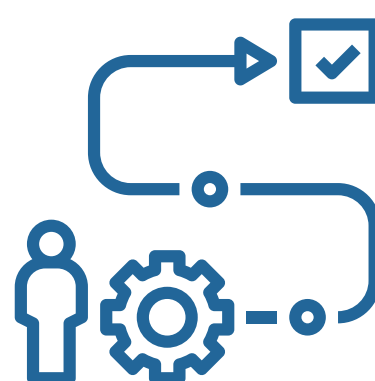


STUDY BACKGROUND

EBUS-TBNA for mediastinal staging can be performed under moderate sedation or general anesthesia (GA) with comparable outcomes in diagnostic yield, complication rates, and patient post procedure satisfaction. Performing EBUS with moderate sedation offers some potential advantages, such as shorter duration and recovery phase with lower costs. However, it is a time-limited procedure because of patient comfort and ability to cooperate. In one trial, 6.7% of all EBUS procedures under moderate sedation could not be completed because of such factors. This raises the question of when starting at the N3 location with EBUS-TBNA under moderate sedation, should we start with the hilar or mediastinal N3 nodes? Knowing the probability of metastatic disease being present in the contralateral hilar lymph nodes when PET negative can help decide this. Thus, the primary objective of the study was to determine the proportion of patients that have malignant hilar N3 lymph node involvement by EBUS when negative on PET-CT.

CURRENT PRACTICE

Systematic EBUS sampling is defined as evaluating the N3 nodes, followed by N2 and then N1 nodes, with biopsy of all lymph nodes that measure ≥ 5 mm by EBUS, regardless of PET-CT scan results.



STUDY DESIGN



Type of trial:

Retrospective, observational, single-center cohort study

Randomization, blinding, controls

N: 739

Study groups:

Patients with NSCLC and clinical-radiographic T1-3, N0-3, M0 disease that underwent first EBUS-TBNA staging, including biopsy of contralateral PET-CT negative hilar N3 nodes

Settings:

Single center, University of Texas MD Anderson

Enrollment:

September 2009 through March 2019

Treatment period: N/A

Follow up: N/A

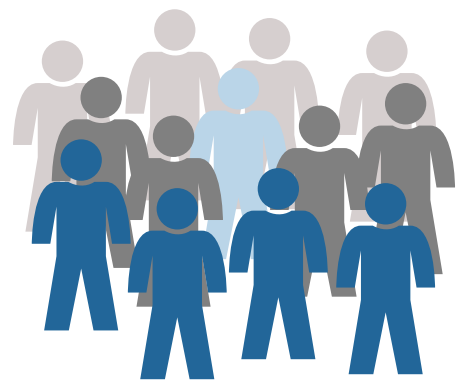
Primary outcome:

proportion of patients with malignant hilar N3 nodes showing negative PET-CT scan findings

POPULATION

Inclusion criteria:

- NSCLC
- Clinical-radiographic T1-3, N0-3, M0 disease
- Underwent first EBUS-TBNA staging from September 2009 through March 2019
- Negative PET-CT scan results for N3 hilar lymph nodes (11L, 11Rs, or 11Ri) who underwent biopsy



Exclusion criteria:

- Small cell carcinoma, synchronous primary malignancies, metastatic disease
- PET or CT evidence of mediastinal invasion
- Positive PET-CT scan results for contralateral hilar N3 nodes
- No PET available before treatment
- Patients who underwent EBUS staging after initial treatment
- Those who did not undergo biopsy of the contralateral hilar N3 nodes.

Baseline characteristics:

739 patients with biopsy of contralateral PET-CT negative hilar N3 nodes measuring ≥ 5 mm by EBUS

Tumor lung location: 302 in the left, 437 in the right

Tumor location: 164 in the central one-third, 575 in the outer two-thirds

Tumor size, cm: 3.62 ± 2.08

Tumor histologic results: 390 adenocarcinoma, 243 squamous cell carcinoma

Lymph node size by EBUS, mm: 7.08 ± 1.84

N stage by PET scan: 391 N0, 116 N1, 186 N2, 46 N3

N stage by CT scan: 328 N0, 108 N1, 240 N2, 63 N3

INTERVENTIONS



All patients underwent systematic EBUS evaluation and sampling, which consisted of evaluating the hilar N3 nodes first, followed by the mediastinal N3 nodes, then the N2 nodes, and finally the N1 nodes.

The nodes evaluated were 11L, 4L, 2L, 7, 4R, 2R, 11Rs, and 11Ri. Any node that was ≥ 5 mm by EBUS was biopsied, regardless of its PET-CT scan status. General anesthesia and rapid onsite cytologic evaluation were used for all patients.

OUTCOMES

Primary outcomes

Five of the 739 patients (0.68%; 95% CI, 0.22%-1.57%) demonstrated occult nodal metastasis in the contralateral hilar N3 nodes.

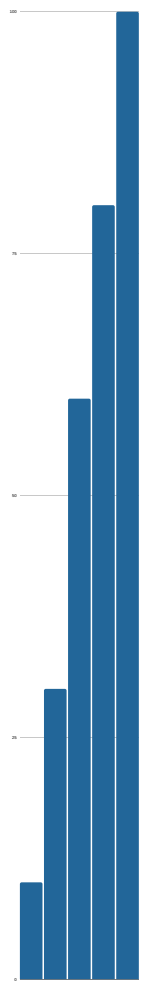
Secondary outcomes

A statistically significant association was found between PET scan N stage and the presence of malignancy in the contralateral hilar N3 nodes showing negative PET-CT scan results ($P = 0.003$).

No association was found between CT scan N stage and the presence of malignancy in the contralateral hilar N3 nodes showing negative PET-CT scan findings ($P = 0.273$).

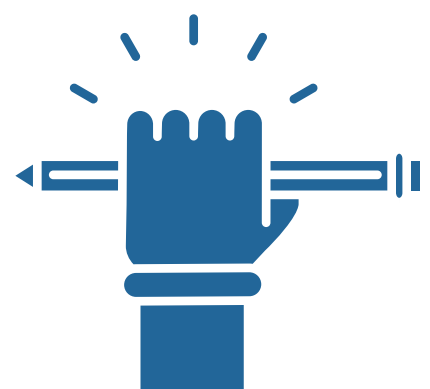
Adverse events

N/A



STUDY STRENGTHS

First retrospective cohort study to quantify the proportion of patients with malignancy in PET-CT negative hilar N3 lymph nodes as determined by EBUS-TBNA.



FUNDING



The authors received no funding for this study.

TAKE HOME MESSAGE

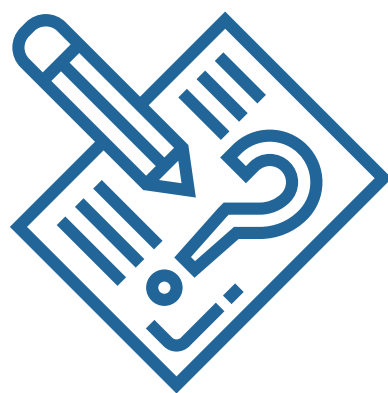
Sampling strategies should be individualized based on the clinical context.

In some instances, such as when N stage by PET scanning is N0, N1 or N2, foregoing sampling of hilar N3 nodes that show negative PET-CT scan results and starting with the mediastinal N3 nodes may be reasonable.



RESEARCH QUESTION

What proportion of patients with hilar N3 nodes showing negative PET-CT scan findings have malignancy by EBUS?



STUDY LIMITATIONS



All cases were done under GA not moderate sedation, so time was not a limiting factor.

Survey of experts drove the sample size calculations: we don't know if 5% threshold value is correct.

The study was performed at a single center with samples analyzed by experienced cytopathologists. Thus, generalizability to other institutions is variable.

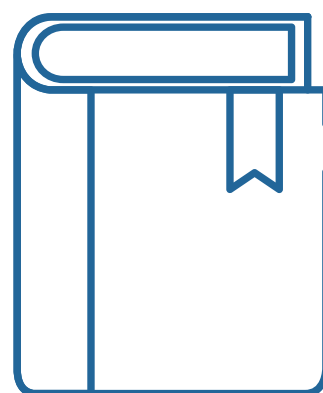
- Stations 10L, 10R, 12L, and 12R are sampled only when PET-CT scan results are positive. The results may not be same if these lymph nodes are always sampled.

The small number of patients with malignancy in the hilar N3 lymph nodes limited the statistical power to test for an association between CT scan N stage and malignancy in the contralateral hilar N3 lymph nodes (chance of false negative).

52.8% of patients with hilar N3 nodes showing negative PET-CT scan results were excluded because the hilar N3 nodes did not undergo biopsy because they measured <5 mm on EBUS.

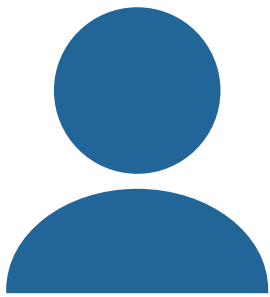
SUGGESTED READING

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2. Long JM. Cutting Corners in the Mediastinum: Should Contralateral Hilar N3 Nodes Be Omitted From Staging?. *Chest*. 2021 Apr 1;159(4):1328-9
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ARTICLE CITATION

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