Confirmatory Mediastinoscopy after Negative Endobronchial Ultrasound-guided Transbronchial Needle Aspiration for Mediastinal Staging of Lung Cancer

AABIP JOURNAL CLUB

BACKGROUND & OVERVIEW

THE CLINICAL QUESTION

What is the value of confirmatory video assisted mediastinoscopy (VAM) in patients with a negative EBUS-TBNA for mediastinal staging of NSCLC?

STUDY CONCLUSION

Adding VAM to EBUS-TBNA increases detection of N2/N3 disease by 20%. However, the number needed to treat is 24. This highlights the importance of careful patient selection prior to pursuing VAM after negative EBUS-TBNA.

STUDY BACKGROUND

Mediastinal staging is essential to the work up of non-small cell lung cancer. Invasive staging using EBUS-TBNA is the recommended first line modality. The specificity of EBUS-TBNA approaches 100%, though false negatives have been reported. Prior studies have estimated less than a 10% probably of occult N2/N3 disease in patients with negative EBUS-TBNA, although this number is likely higher in patients with abnormal imaging. The utility of VAM after a negative EBUS-TBNA is unresolved. Given the potential advantages to VAM, including whole lymph node excision, it may be an approach to capturing patients with occult N2/N3 disease.

CURRENT PRACTICE

Prior to diagnostic procedures, patients with suspected lung malignancy often receive cross sectional imaging, either with CT or PET/CT. Following imaging, EBUS-TBNA is the preferred invasive approach to both diagnosis and staging of lung cancers with mediastinal and hilar involvement.

Recommendations vary regarding approach to negative EBUS-TBNA. The National Comprehensive Cancer Network and European Society of Thoracic Surgeons recommends confirmatory VAM in patients with abnormal chest imaging. The American College of Chest Physicians recommends confirmatory VAM without more specifications. This study sought to quantify the added value of VAM after EBUS-TBNA.

METHODS & RESULTS

STUDY DESIGN

Type of trial:
- Systematic review and meta-analysis
- RCT and Observational Studies included

Study groups:
- All studies evaluated patients undergoing EBUS-TBNA for mediastinal staging of NSCLC.
- Studies with or without confirmatory VAM

Settings: Settings of individual studies were not reported.

Enrollment: Studies from 2005-current were considered.

**Follow up:** There was no consistent follow up reported.

Inclusion criteria:
- Studies assessing the performance of EBUS-TBNA for NSCLC mediastinal staging
- Studies must have a surgical reference standard in the case of negative EBUS-TBNA (lung resection with systematic nodal dissection or transcervical lymphadenectomy).

Exclusion criteria:
- Studies evaluating EBUS-TBNA for diagnoses other than NSCLC
- Case series or reports with fewer than 10 patients
- Studies including both EBUS-TBNA and EUS-FNA
- Studies without surgical reference standard

Baseline characteristics:

- 5412 total patients
- 20 Studies without confirmatory VAM
  - 12 retrospective, 8 prospective
  - 2472 patients
- 9Studies with confirmatory VAM
  - 5 retrospective, 4 prospective
  - 2721 patients
- One study included patients with and without VAM. The authors, for practical purposes, considered these populations separately. Thus we report 29 studies, in keeping with the author's decision to split one of the original 28 studies.
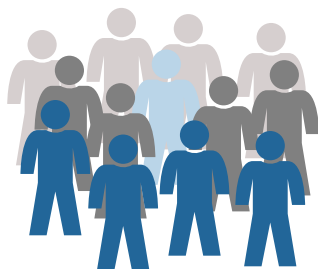
INTERVENTIONS

EBUS-TBNA for mediastinal staging of NSCLC with or without confirmatory VAM.

OUTCOMES

Primary outcome (95% CI)

- Sensitivity of confirmatory VAM for N2/N3 disease after a negative EBUS-TBNA: 66.9 (55.8-77.1)
- Sensitivity of EBUS-TBNA plus VAM: 96.7 (95.1-77.1)
- NPV of EBUS-TBNA plus VAM: 91.8 (87.1-95.5)
- Number needed to treat for confirmatory VAM to diagnosis an additional case of N2/N3 disease: 23.8

Secondary outcomes (95% CI)

- Prevalence of N2/N3 disease in EBUS-TBNA alone versus those with EBUS-TBNA with confirmatory VAM: 40.9% (30.3-51.4) vs. 60.4% (49.5-71.2)
- Sensitivity of EBUS-TBNA alone versus EBUS-TBNA + VAM: 79.3% (73.9-84.7) vs. 91.6% (88.6-94.6)
- Prevalence of N2/N3 disease after negative EBUS-TBNA, in those undergoing VAM: 20% (13.5-27.4)

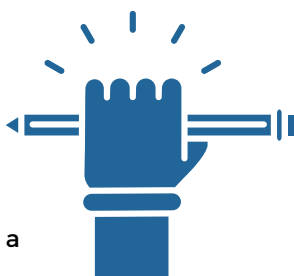**Adverse outcomes:** Not evaluated in this meta-analysis

FUNDING

FUNDING

ARTICLE CRITIQUE

STUDY STRENGTHS

- Meta-Analysis is pooling data for a large number of subjects
- Excluded studies without surgical resection as gold standard
- Authors were able to pool data from a heterogenous group of studies

STUDY LIMITATIONS & POTENTIAL FOR BIAS

- Of the 28 papers included, only 2 were randomized controlled and 12 prospective studies with 1499/5193 subjects studied prospectively
- High heterogeneity of selected studies introduces a high likelihood of bias
- Some missing data were acquired directly (hence, non-peer reviewed) from the authors
- Some of the EBUS-TBNA trials are older or smaller, and have a lower sensitivity than more recent trials
- There was limited description on a patient level basis of preceding imaging findings

TAKE HOME MESSAGE

EBUS TBNA is the procedure of choice for mediastinal staging of NSCLC. Addition of video assisted mediastinoscopy increases the detection of occult N2/N3 disease but with a high number needed to treat of 24. Larger randomized controlled trials are needed to overcome the inherent limitation of inferring from the pooled data provided by a meta-analysis based on the highly heterogeneous studies selected.

REFERENCES

ARTICLE CITATION

Sanz-Santos J, Almagro P, Malik K, Martinez-Camblor P, Caro C, Rami-Porta R. Confirmatory Mediastinoscopy after Negative Endobronchial Ultrasound-guided Transbronchial Needle Aspiration for Mediastinal Staging of Lung Cancer. Ann Am Thorac Soc 2022. 19 (9): 1581-1590. DOI: 10.15.13/AnnalsATS.202111-1302OC

SUGGESTED READING

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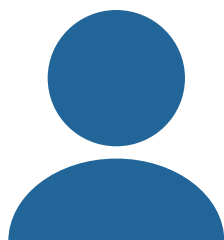
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