INPLASY

Balancing Accuracy, Safety, and Cost in Mediastinal Diagnos-tics: A Systematic Review of EBUS and Mediastinoscopy in NSCLC

INPLASY202530117

doi: 10.37766/inplasy2025.3.0117

Received: 27 March 2025

Published: 27 March 2025

Corresponding author:
Ana Adelina Afetelor

afetelorana@gmail.com

Author Affiliation:
"Carol Davila" University of Medicine and Pharmacy.

Matache, SR; Afetelor, AA; Voinea, AM; Cosoveanu, CG; Dumitru, SM; Alexe, M; Dobrea, VC; Orghidan, MG; Smaranda, AM; Serbanoiu, A; Mahler, B; Savu, CF.

ADMINISTRATIVE INFORMATION

Support - This research received no external funding.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202530117

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 March 2025 and was last updated on 27 March 2025.

INTRODUCTION

Review question / Objective Systematical evaluation and comparison between EBUS-TBNA and mediastinoscopy in the mediastinal staging of NSCLC, with particular focus on their diagnostic accuracy, safety profile, procedural costs, and clinical utility, in order to guide evidence-based decision-making in thoracic oncology.

Rationale Given the increasing emphasis on minimally invasive, cost-effective, and personalized approaches in cancer care, it is essential to reassess the roles of EBUS-TBNA and mediastinoscopy in the current diagnostic landscape. This review aims to determine whether EBUS-TBNA can reliably replace mediastinoscopy as the first-line staging procedure and to identify clinical scenarios where a combined or sequential approach may optimize patient outcomes.

Condition being studied Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, accounting for approximately 85% of all cases. Accurate mediastinal staging is critical for determining resectability, guiding treatment decisions, and predicting prognosis. The presence or absence of mediastinal lymph node metastases significantly influences the choice between surgical intervention, chemotherapy, and radiotherapy. As such, reliable and minimally invasive diagnostic tools for staging are essential in optimizing care for patients with NSCLC.

METHODS

Search strategy Systematic searches were conducted in the Medline, Scopus, EMBASE and Cochrane databases, the data ranges being set starting with 01.01.2010. We also performed gray literature searches, which included references in the selected articles. The following search strategy was used for each database: “lung cancer” OR “lung carcinoma” OR “pulmonary cancer” OR “NSCLC” OR “cancer of the lung” OR “lung neoplasm” AND “EBUS” OR “EBUS-TBNA” OR “Endobronchial ultrasound-guided transbronchial

needle aspiration" OR "endobronchial ultrasound" AND "mediastinoscopy".

Participant or population Patients with non-small cell lung cancer (NSCLC) requiring mediastinal staging as part of diagnostic evaluation and treatment planning.

Intervention Use of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) as a minimally invasive diagnostic modality for mediastinal lymph node assessment.
Standard mediastinoscopy, a surgical procedure traditionally used for mediastinal lymph node biopsy and staging.

Comparator The standard for comparing the two methods (EBUS-TBNA, mediastinoscopy) was the result of tumour resection surgery, based on systematic mediastinal lymph node sampling or dissection.

Study designs to be included The studies selected consisted of randomized and nonrandomized clinical trials, com-parative studies, scientific reviews, observational studies, multicentre studies and ret-rospective studies.

Eligibility criteria Studies involving adult patients diagnosed with non-small cell lung cancer (NSCLC) undergoing mediastinal staging.
Studies that directly compare EBUS-TBNA and mediastinoscopy in terms of diagnostic performance, safety, cost-effectiveness, or other clinical outcomes.
Randomized controlled trials (RCTs), prospective and retrospective cohort studies, observational studies, and systematic reviews/meta-analyses published in peer-reviewed journals.
Studies published between 2010 and 2024 to ensure relevance to current clinical practice.
Articles written in English.

Information sources Systematic searches were conducted in the Medline, Scopus, EMBASE and Cochrane databases, the data ranges being set starting with 01.01.2010. We also performed gray literature searches, which included references in the selected articles.

Main outcome(s) The primary outcome of this systematic review was the diagnostic performance of EBUS-TBNA compared to mediastinoscopy in the mediastinal staging of non-small cell lung cancer (NSCLC). This included analysis of sensitivity, specificity and diagnostic yield for detecting mediastinal lymph node metastases.

Additional outcome(s) Safety and Complication Rates: Frequency and severity of adverse events
Sample Adequacy: Proportion of procedures yielding samples sufficient for cytological, histopathological, and molecular analysis.
Cost-Effectiveness: Comparative procedural and hospitalization costs, as well as overall economic impact on healthcare systems.
Feasibility of Repetition: Clinical suitability of repeating the procedure in case of inconclusive results or disease progression.
Anesthesia and Patient Tolerance: Differences in sedation protocols, recovery times, and patient comfort.

Data management All identified records from database searches were imported into the Covidence systematic review management platform, which facilitated the organization, deduplication, screening, and extraction processes. Duplicates were automatically removed, followed by manual verification. Each study was independently screened by at least two reviewers at the title/abstract and full-text levels to ensure consistency. Discrepancies were resolved through discussion or arbitration by a third reviewer. Data extraction was performed using a standardized extraction template within Covidence, capturing key variables such as study design, patient population, diagnostic methods (EBUS-TBNA and mediastinoscopy), outcome measures, and results. The extracted data were exported for synthesis and analysis. Regular backups were maintained, and all review activities were documented to ensure transparency and reproducibility.

Quality assessment / Risk of bias analysis A formal risk of bias analysis using standardized tools (e.g., QUADAS-2 or ROBINS-I) was not performed, as the included studies were heterogeneous in design, encompassing randomized controlled trials, observational studies, and retrospective analyses. Many of the studies did not report all variables required for uniform assessment. Nevertheless, we evaluated methodological quality through critical appraisal of study design, sample size, clarity of inclusion criteria, and transparency in reporting diagnostic outcomes.

Strategy of data synthesis Due to the heterogeneity of study designs, outcome reporting, and patient populations, a narrative synthesis approach was employed. The data extracted from the included studies were organized thematically according to key domains: diagnostic performance (sensitivity, specificity, diagnostic yield), safety and

complication rates, sample adequacy, cost-effectiveness, and feasibility of procedural repetition. Findings were summarized in comparative tables and described narratively to highlight trends, consistencies, and discrepancies across studies.

Subgroup analysis Where feasible, subgroup analyses were performed to explore potential differences in diagnostic performance and clinical utility based on key study characteristics. These included type of study design (randomized vs. observational), geographical setting, year of publication, and sample size. Additional comparisons were made between studies reporting anesthesia protocols, molecular testing feasibility, or combined use of EBUS-TBNA and mediastinoscopy. These subgroup insights helped identify potential context-specific variations in outcomes such as sensitivity, specificity, complication rates, and cost-effectiveness. However, due to heterogeneity and inconsistent reporting across studies, subgroup analyses were primarily descriptive, and statistical testing was not uniformly applicable.

Sensitivity analysis A formal quantitative sensitivity analysis was not conducted due to the methodological heterogeneity of the included studies and the absence of consistent statistical data across all outcomes. However, a qualitative sensitivity approach was applied by assessing the influence of study quality, sample size, and study design on the robustness of the findings. Special attention was given to studies with large cohorts, prospective designs, or those reporting complete outcome data. Studies deemed at higher risk for bias (e.g., small retrospective studies or those lacking clear inclusion criteria) were analyzed separately to evaluate whether their exclusion would significantly alter the overall trends and conclusions.

Language restriction Only articles in English were included in the study.

Country(ies) involved Romania.

Keywords EBUS-TBNA; mediastinoscopy; surgery; flexible bronchoscopy; mediastinal staging; mediastinal imaging; non-small lung cancer.

Dissemination plans The findings of this systematic review will be disseminated through publication in a peer-reviewed journal and presentation at relevant national and international thoracic surgery and oncology conferences. Additionally, the results will be shared with academic institutions and professional societies involved in lung cancer diagnostics to inform clinical guidelines and multidisciplinary decision-making.

Contributions of each author

Author 1 - Serban-Radu Matache - Conceptualization; Supervision; Project administration; Funding acquisition.
Email: radu.matache@gmail.com
Author 2 - Ana Adelina Afetelor - Conceptualization; Methodology; Software; Investigation; Resources; Writing – original draft preparation; Writing – review and editing; Project administration.
Email: afetelorana@gmail.com
Author 3 - Ancuta Mihaela Voinea - Investigation; Resources; Writing – original draft preparation.
Email: anca1502@gmail.com
Author 4 - Codrut George Cosoveanu - Writing – review and editing.
Email: codrut.cosoveanu@gmail.com
Author 5 - Silviu-Mihail Dumitru - Validation; Data curation.
Email: dumitrusm@gmail.com
Author 6 - Mihai Alexe - Validation; Data curation.
Email: alexe.mihai@yahoo.com
Author 7 - Vlad-Cristian Dobrea - Writing – review and editing; Visualization.
Email: dobreavladcristian@gmail.com
Author 8 - Mihnea-George Orghidan - Validation; Visualization; Funding acquisition.
Email: mihnea.org@gmail.com
Author 9 - Alina-Maria Smaranda - Investigation; Resources.
Email: smarandaalina@gmail.com
Author 10 - Alexandru Serbanoiu - Formal analysis.
Author 11 - Beatrice Mahler - Formal analysis; Data curation
Email: beatrice.mahler@umfcd.ro
Author 12 - Cornel Florentin Savu - Methodology; Supervision; Project administration; Funding acquisition.
Email: drsavu25@yahoo.com