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Combined endobronchial and endoscopic ultrasound-guided fine needle aspiration for mediastinal lymph node staging of lung cancer: A meta-analysis

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Abstract ***Study objectives:*** This systematic review and meta-analysis was conducted to evaluate the accuracy of the combined endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) techniques and clarify its current role for the mediastinal lymph node staging of lung cancer.

Methods: Medline, Web of Science, Elsevier and Ovid were searched to identify suitable studies up to 15th July 2012. Two investigators independently reviewed articles and extracted data. All EBUS-TBNA plus EUS-FNA studies for the mediastinal node staging of lung cancer were systematically reviewed. Sensitivity, specificity and other accuracy measures were pooled using random-effect models. Summary receiver operating characteristic curves were used to summarise overall test performance.

Results: Eight studies met our inclusion criteria. The estimated summary measures for quantitative analysis of EBUS-TBNA plus EUS-FNA for mediastinal nodal staging of lung cancer were sensitivity, 0.86 (95% confidence interval [CI], 0.82–0.90); specificity, 1.00 (95% CI, 0.99–1.00); positive likelihood ratio, 51.77 (95% CI, 22.53–118.94); negative likelihood ratio, 0.15 (95% CI, 0.09–0.25); diagnostic odds ratio, 416.83 (95% CI, 140.08–1240.31); and area under the curve (AUC), 0.99.

Conclusions: The current evidence suggests that the combined technique is more sensitive than EBUS-TBNA or EUS-FNA alone. The diagnostic power of this combined technique is accurate. As an almost completely minimally-invasive examination, EUS-FNA plus EBUS-TBNA may replace more invasive methods for evaluating mediastinal node staging of lung cancer.

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1. Introduction

Lung cancer is one of the most common cancers in the world and also the most frequent cause of cancer death. Treatment and prognosis depend on both histological type and stage of disease. Surgery is a promising treatment for curing lung cancer, especially in those patients with disease confined to the lung and hilar lymph nodes. However, mediastinal lymph nodes are involved in 28–38% of non-small cell lung cancers at the time of diagnosis.[1] Therefore, accurate staging (including mediastinal node evaluation) is crucial to guide lung cancer treatment. Current scanning modalities, such as computed tomography (CT) and positron emission tomography (PET), although useful, are not sufficiently sensitive or specific to determine mediastinal nodal involvement.[2] Both mediastinoscopy and thoracoscopy have been recommended as diagnostic standards for staging along with tissue confirmation of suspected metastatic mediastinal lymph nodes.[1] However, due to their invasiveness and significant expense, mediastinoscopy and thoracoscopy are not widely used for mediastinal node staging.

Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) and, most recently, endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA)[3–7] are promising invasive imaging tests gaining acceptance as lung cancer staging tools. These methods have been suggested as reasonable alternatives to mediastinoscopy.[3,8–14] Recent studies have found that combining EBUS-TBNA and EUS-FNA into a single procedure has a higher staging accuracy than either procedure alone in patients with confirmed or suspected lung cancer.[3,15–18] Because EBUS-TBNA and EUS-FNA are complementary methods for the diagnosis of mediastinal disease,[6,19–21] they have different accessibilities to the mediastinum.[22–24] This meta-analysis aims to systematically and quantitatively evaluate all published studies assessing the accuracy of the combined approach of EBUS-TBNA and EUS-FNA for the mediastinal node staging of lung cancer.

2. Methods

2.1. Search strategy and study selection

Medline (using PubMed as the search engine), Web of Science, Elsevier and Ovid were searched to identify suitable studies prior to 15th July 2012; no start date limit was applied. The search terms were "EBUS," "TBNA," "EUS," "FNA," "endobronchial ultrasound," "transbronchial needle aspiration," "endoscopic ultrasound," "fine-needle aspiration," "lung cancer," "mediastinal staging," "sensitivity and specificity" and "accuracy." Articles were also identified by use of the related articles' function in PubMed; the references of identified articles were searched manually. If necessary, we contacted the authors for further study details. No language restrictions were imposed. However, conference abstracts to journal editors were excluded because of the limited data they contained.

Studies were included in the meta-analysis if they provided both the sensitivity and specificity of the combined approach of EBUS-TBNA and EUS-FNA for mediastinal node staging of lung cancer. This meta-analysis only selected studies that included at least 10 lung cancer patients, since very small studies may be vulnerable to selection bias. Two reviewers (R.F.Z. and K.J.Y.) independently determined study eligibility, and differing decisions were resolved by consensus. Publications possibly based on the same study (e.g. same authors, institutions, period of study) were discussed by our reviewers (R.F.Z., L.Z. and K.J.Y); only the best-quality study was used.

2.2. Data extraction and quality assessment

The final set of articles was assessed independently by two reviewers (R.F.Z. and L.Z.). The reviewers were blinded to publication details, and disagreements between them were resolved by consensus. Data retrieved from the reports included author, publication year, participant characteristics, test methods, sensitivity and specificity data and methodological quality.

The STARD (Standards for Reporting Diagnostic Accuracy) scoring guidelines[25] assessed the methodological quality of diagnostic study reporting. The QUADAS (Quality Assessment for Studies of Diagnostic Accuracy) scoring guidelines[26] assessed the quality of diagnostic accuracy in primary studies by appraising use of empirical evidence, expert opinion and formal consensus. In addition, the following study design characteristics were retrieved: (1) random sampling of patients; (2) blinded interpretation of determination and reference standard results; (3) prospective data collection; and (4) reference standards.

2.3. Statistical analysis

We used standard methods recommended for meta-analysis of diagnostic test evaluations.[27] Analyses were performed using the following statistical software programs: STATA, version 10.0 (STATA Corporation; College Station, TX, United States) and Meta-DiSc (XI Cochrane Colloquium; Barcelona, Spain). For each study, we computed the following measures of test accuracy: sensitivity; specificity; positive likelihood ratio (PLR); negative likelihood ratio (NLR); and diagnostic odds ratio (DOR). The analysis was based on a summary receiver-operator characteristic (SROC) curve.[27,28] A random-effect model was used to calculate the average