Invasive staging of non-small cell lung cancer: a review of the current evidence

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CRD summary
This review concluded that invasive clinical staging of non-small cell lung cancer can be performed effectively by transbronchial needle aspiration, transthoracic needle aspiration, endoscopic ultrasound-guided needle aspiration or mediastinoscopy. The review had a number of methodological and reporting weaknesses and the conclusions may not be reliable.

Authors’ objectives
To investigate the test performance characteristics of transbronchial needle aspiration (TBNA), transthoracic needle aspiration (TTNA), endoscopic ultrasound-guided needle aspiration (EUS-NA), mediastinotomy and mediastinoscopy in staging non-small-cell lung cancer (non-SCLC).

Searching
MEDLINE (from January 1991 to July 2001), HealthSTAR and the Cochrane Library were searched; the search terms were reported. In addition, the reference lists of included studies, textbooks, practice guidelines, systematic reviews, and meta-analyses were scanned for any relevant articles. Studies published between 1980 and 1991 were identified from a previous search of MEDLINE, the table contents of ten medical journals (which were reported), and the reference lists of other articles. The review was limited to studies published in English in peer-reviewed journals.

Study selection
Study designs of evaluations included in the review
The authors did not specify any predetermined inclusion criteria relating to the study design. The included studies were required to have over 20 participants, except for studies of mediastinoscopy, which were required to have over 50 patients. The included studies were prospective or retrospective evaluations.

Specific interventions included in the review
Studies of TBNA, TTNA, EUS-NA, mediastinotomy or mediastinoscopy were included.

Reference standard test against which the new test was compared
Either tissue histologic confirmation or, if that was unavailable, the long-term clinical outcome (i.e. whether the patient survived at least 1 year with no evidence of disease) was considered to be the reference or ‘gold’ standard.

Participants included in the review
Studies of participants with non-SCLC or SCLC were included.

Outcomes assessed in the review
Studies assessing mediastinal nodal biopsy results by histology at the time of resection, or by long-term follow-up of at least one year were included. The original study data had to be available so that the sensitivities, specificities, and positive and negative predictive values (PPVs and NPVs, respectively) could be independently calculated.

How were decisions on the relevance of primary studies made?
At least two independent reviewers assessed the papers for inclusion.

Assessment of study quality
The authors did not state that they assessed validity.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. The sensitivities, specificities and NPVs were calculated from original data.

Methods of synthesis
How were the studies combined?
The summary sensitivity and specificity were calculated along with confidence intervals (CIs). Summary PPVs, NPVs and prevalence were calculated, based on the total number of true-positive, false-negative, false-positive and true-negative results summed across the studies. Studies in which all participants had mediastinal disease were excluded from these calculations. The data were analysed in three ways:

for patients undergoing invasive techniques (regardless of the indication), where a definitive diagnosis of any malignancy was considered positive and a definitive benign diagnosis was considered negative;

for patients suspected of having lung cancer (either non-SCLC or SCLC), where a definitive diagnosis of any lung cancer was considered positive; and

for patients with a confirmed diagnosis of non-SCLC, where a definitive diagnosis of non-SCLC was considered positive, and any other biopsy result was negative.

How were differences between studies investigated?
Differences between the studies do not appear to have been investigated.

Results of the review
A total of 38 studies met the inclusion criteria: 12 of TBNA (n=910), 5 of TTNA (n=215), 5 of EUS-NA (n=215), 14 of standard cervical mediastinoscopy (n=5,687), and 2 assessing extended cervical mediastinoscopy alone or with standard cervical mediastinoscopy (n=206).

Patients suspected of having lung cancer (non-SCLC or SCLC).

For TBNA, the pooled sensitivity was 0.76 (95% CI: 0.72, 0.79), the pooled specificity was 0.96 (95% CI: 0.91, 1.00), and the NPV was 71% (range: 36, 100).

For TTNA, the pooled sensitivity was 0.91 (95% CI: 0.74, 0.97) and the NPV was 78% (range: 42, 100).

For EUS-NA, the pooled sensitivity was 0.88 (95% CI: 0.82, 0.93), the pooled specificity was 0.91 (95% CI: 0.77, 0.97), and the NPV was 77% (range: 68, 100).

For standard cervical mediastinoscopy, the pooled sensitivity was 0.81 (95% CI: 0.76, 0.85) and the NPV was 91% (range: 58, 97). The addition of either extended cervical mediastinoscopy or anterior mediastinotomy to standard cervical mediastinoscopy appeared to improve the sensitivity of any of the procedures alone.

The results for patients undergoing invasive techniques and for patients with a confirmed diagnosis of non-SCLC were reported to be similar to those for patients suspected of having lung cancer (either non-SCLC or SCLC).

Authors' conclusions
Invasive clinical staging of non-SCLC can be performed effectively by TBNA, TTNA, EUS-NA, or mediastinoscopy. Selection of the appropriate test is dependent on the degree of suspicion for metastatic disease, the patient's co-morbid illnesses, and the availability and performance characteristics of procedural options.

CRD commentary
The objective of the review was clear. However, the authors did not specify a priori inclusion criteria for study design.
Only studies published in English were included, so relevant studies may have been missed and the findings might have been influenced by publication and language bias. The validity of the included studies was not assessed; it is therefore unclear whether the results of the studies and the synthesis of them are reliable. In addition, since information relating to the data extraction was not given, it is not possible to determine whether steps were taken to minimise error and bias in this process. There was a lack of information relating to the design of and participants in the included studies. Since differences between the studies do not appear to have been assessed, it is unclear whether statistical pooling was appropriate. The most tentative interpretation of the authors’ conclusions is advisable.

Implications of the review for practice and research
The authors did not state any implications for practice or further research.

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