Diagnosis of small pulmonary lesions by transbronchial lung biopsy with radial endobronchial ultrasound and virtual bronchoscopic navigation versus CT-guided transthoracic needle biopsy: a systematic review and meta-analysis Version 4

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Abstract

Background

Advances in bronchoscopy and CT-guided lung biopsy have improved the evaluation of small pulmonary lesions (PLs), leading to an increase in preoperative histological diagnosis.

We aimed to evaluate the efficacy and safety of transbronchial lung biopsy using radial endobronchial ultrasound and virtual bronchoscopic navigation (TBLB-rEBUS&VBN) with CT-guided transthoracic needle biopsy (CT-TNB).

Method

A systematic search was performed in five electronic databases, including MEDLINE, EMBASE, Cochrane Library Central Register of Controlled Trials, Web of Science, and Scopus, for relevant studies in May 2016; the selected articles were assessed using meta-analysis. The articles were limited to those published after 2000 that studied small PLs ≤ 3 cm in diameter.

Result

From 7345 records, 9 articles on the bronchoscopic (BR) approach and 15 articles on the percutaneous (PC) approach were selected. The pooled diagnostic yield was 75% (95% confidence interval [CI], 69-80) using the BR approach and 93% (95% CI, 90-96) using the PC approach. For PLs ≤ 2 cm, the PC approach was superior to the BR approach. However, for PLs > 2 cm but ≤ 3 cm, the diagnostic yield using the BR approach was increased to 81% (95% CI, 75-85). Complications of pneumothorax and hemorrhage were rare with the BR approach but common with the PC approach.

Conclusion

CT-TNB was superior to TBLB-rEBUS&VBN for the evaluation of small PLs. However, for lesions greater than 2 cm, the BR approach may be considered considering its diagnostic yield of over 80% and the low risk of procedure-related complications.

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Guidelines

Inclusion and exclusion criteria

The following inclusion criteria were used to select studies on TBLB-rEBUS&VBN:

1. rEBUS with a GS was used for the diagnosis of peripheral pulmonary lesions (PPLs).
2. Virtual bronchoscopy was used as a navigational method.

3. A PPL was defined as an endobronchial lesion not detected by bronchoscopy, and the size of these lesions was limited to ≤ 3 cm in diameter.

4. The final diagnosis was confirmed using the biopsy specimen or surgical specimen; in cases of diagnostic ambiguity, the final diagnosis was established at the clinical follow-up.

The following inclusion criteria were used to select studies on CT-TNB:
1. CT-guided transthoracic needle aspiration or biopsy, including conventional CT-guided transthoracic needle biopsy, CT fluoroscopy-guided transthoracic biopsy, and C-arm cone-beam CT-guided transthoracic biopsy, was used for the diagnosis of PL.
2. The biopsy target was a small PL ≤ 3 cm in diameter for which bronchoscopic biopsy was considered unfeasible based on the imaging information. The target lesion was described as a PPL, solitary pulmonary nodule (SPN), pulmonary nodule, ground glass opacity, or PL.

3. The final diagnosis was confirmed using the biopsy specimen or surgical specimen; in cases of diagnostic ambiguity, the final diagnosis was established at the clinical follow-up.

The following exclusion criteria were used when selecting studies on TBLB-rEBUS&VBN or CT-TNB:

1. Studies using non-human subjects, studies analyzing other methods of biopsy, studies written in a language other than English, or studies of an inappropriate type (case report, case series, letter, and review);

2. Central bronchial lesions evaluated by routine bronchoscopy;

3. Electromagnetic navigational bronchoscopy (ENB) procedure in TBLB;

4. Studies devoted to topics other than diagnostic outcomes with or without adverse events.

Before start

When comparing the diagnostic yields of different methods, the lesions should be limited to those ≤ 3 cm in diameter, as established by previous publications. In this analysis, PLs up to 3 cm in diameter were considered.

The purpose of this meta-analysis was to compare the efficacy and safety of TBLB with rEBUS and VBN (TBLB-rEBUS&VBN), a BR approach, with CT-TNB, a PC approach, for tissue diagnosis of small PLs.

Protocol

Literature search

Step 1.

A systematic literature search was performed in May 2016 for all studies describing biopsy of PLs using TBLB with rEBUS, GS and VBN or CT-TNB among five databases: MEDLINE, EMBASE, the Cochrane Library Central Register of Controlled Trials, Web of Science, and Scopus. Articles were identified using combinations of the following key words. The search terms were divided into four categories:

1. Lung lesion type: “lung,” “pulmonary,” “bronchial,” “neoplasms,” “cancer,” “lesion,” “tumor,” or “malignancy”;
2. Biopsy method: “biopsy,” “aspiration,” or “needle”;
3. Biopsy approach: “bronchoscopy,” “endobronchial ultrasound,” “radial EBUS,” “fluoroscopy,” “computed tomography,” or “CT-guided”; and
4. Additional techniques: “sheath” or “navigation.”

Selection of studies

Step 2.

We selected studies for the meta-analysis using the 2009 flow diagram provided by the PRISMA Group. The literature search was limited to papers published after 2000. The screening of each paper’s title and abstract was performed by one investigator (YJH). The full-text article was assessed for eligibility by two independent authors based on the study inclusion criteria. In cases of disagreement, the decisions on paper selection were arbitrated by principal investigator.

Data extraction

Step 3.

From the final selected papers, two authors independently evaluated the characteristics of the selected papers and extracted data according to a standardized protocol. The following general characteristics of the studies were collected: author, countries in which the studies were conducted, year of publication, study design, number of subjects, procedure trial number, gender, age, definition of nodules, mean diameter, guidance methods, diagnostic yields, and the proportion of subjects with malignancy in the study sample. Data on the incidence of complications were also collected. For the criteria of diagnostic yield, the number of enrolled subjects and the number of procedures were

recorded separately. Diagnostic yield was calculated using the following equation: diagnostic yield (%) = 100 x (number of correctly diagnosed cases / total number of biopsy procedures). The final retrieved data were reviewed by one author.

Quality assessment

Step 4.

Two authors independently examined the quality of the included studies using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool. We assessed the risk of bias and the concerns regarding applicability based on four parts of the assessment: patient selection, index test, reference standard, and flow and timing. Inconsistences were resolved by agreement between the authors.

Statistical analysis

Step 5.

Meta-analyses were performed with Comprehensive Meta-Analysis software (version 3.0, Biostat, Englewood NJ, USA). The pooled diagnostic yields of TBLB-rEBUS&VBN and CT-TNB were calculated by the inverse-variance method with the logit-transformed diagnostic yields reported in each article. Pooled estimates of complications from CT-TNB were also extracted. Heterogeneity among study results was assessed by the I^2 statistic, which describes the proportion of the variation across studies that is due to heterogeneity rather than chance. A value of $I^2 \geq 50\%$ was considered to indicate substantial heterogeneity. Heterogeneity was also evaluated with the conventional chi-squared test. When heterogeneity was considered low, the fixed effects model was performed; the random effects model was applied in cases of substantial heterogeneity. Forest plots were used to present the estimated diagnostic yield for each study and the overall pooled diagnostic yields. Publication bias was assessed using a funnel plot and Egger's linear regression test. A P value < 0.05 was considered statistically significant in all analyses. To estimate the diagnostic yields by PL size, the same meta-analysis was conducted separately on PLs $\leq$ 2 cm in diameter and PLs $>$ 2 cm but $\leq$ 3 cm in diameter.