Diagnostic yield and postoperative mortality associated with surgical lung biopsy for evaluation of interstitial lung diseases: A systematic review and meta-analysis

Qian Han, MD, PhD, Qun Luo, MD, PhD, Jia-Xing Xie, MD, PhD, Lu-Lu Wu, MD, Li-Yue Liao, MD, Xiao-Xian Zhang, MD, and Rong-Chang Chen, MD, PhD

Objectives: Surgical lung biopsy plays an important role in providing pathologic results, thus complementing the diagnostic rationale for suspected interstitial lung diseases. We performed a systematic review and meta-analysis regarding the diagnostic yield and postoperative mortality rate of surgical lung biopsy in patients with suspected interstitial lung diseases because of the wide variation in previously reported effectiveness and safety concerns.

Methods: We systematically searched for published studies between 2000 and 2014 evaluating surgical lung biopsy in the diagnosis of interstitial lung diseases. Subgroup analysis was performed to identify the possible source of study heterogeneity.

Results: Twenty-three studies contributed 2148 patients for the analysis. The median diagnostic yield was 95% (range, 42%-100%), with idiopathic pulmonary fibrosis as the most frequent diagnosis (618, 33.5%). Surgical lung biopsy was mainly guided by high-resolution computed tomography manifestations. Biopsy site, biopsy number, and the surgical lung biopsy method may not be associated with the diagnostic accuracy. The pooled postoperative mortality rate for included studies was 3.6% (95% confidence interval, 2.1-5.5), with significant heterogeneity observed. Subgroup analysis revealed that exclusion criteria based on immunocompromised status, mechanical ventilation, and severe respiratory dysfunction (diffusing capacity of lung for carbon monoxide <35% or forced vital capacity <55% predicted), but not surgical lung biopsy technique or underlying interstitial lung disease subtype, may be possible sources of heterogeneity.

Conclusions: We demonstrated a satisfactory diagnostic performance with a favorable safety profile of surgical lung biopsy in the diagnosis of suspected interstitial lung diseases. Surgical lung biopsy is especially recommended in patients with clinical information indicative but atypical of idiopathic pulmonary fibrosis, whereas the benefit of surgical lung biopsy should be carefully balanced against the risk for patients with immunocompromised status, mechanical ventilation dependence, or severe respiratory dysfunction. (J Thorac Cardiovasc Surg 2015;149:1394-401)

GTS

See related commentary pages 1402-3.

Supplemental material is available online.

From the Division of Respiratory Medicine, Guangzhou Institute of Respiratory Disease, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China.

This work was supported by National Natural Science Foundation of China Young Investigator Funding 2014-2016 (NO. 81300063).

Disclosures: Authors have nothing to disclose with regard to commercial support.

Drs Qian and Qun contributed equally to this article.

Received for publication Oct 10, 2014; revisions received Dec 12, 2014; accepted for publication Dec 25, 2014; available ahead of print Jan 31, 2015.

Address for reprints: Rong-Chang Chen, MD, PhD, Division of Respiratory Medicine, Guangzhou Institute of Respiratory Disease, The First Affiliated Hospital of Guangzhou Medical University, 151 Yanjiang Rd, Guangzhou, China (E-mail: chenrc@vip.163.com).

0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2014.12.057

Interstitial lung diseases (ILDs) comprise a group of lung diseases with a great diversity regarding the cause, pathologic change, treatment, and prognosis. Therefore, the establishment of an accurate diagnosis is essential to determine the therapeutic intervention and prognosis for a given patient. Histologic results may be required to establish a specific diagnosis or complement diagnostic rationale in cases that remain undefined after thorough clinical information combined with thoracic imaging. Bronchoalveolar lavage or transbronchial lung biopsy via bronchoscopy may be useful in selected subtypes, such as sarcoidosis, hypersensitivity pneumonitis (HP), and eosinophilic pneumonia. However, transbronchoscopic sampling may not be representative and indicative because of the amount and size of biopsies.

The current guidelines emphasize the significant role of surgical lung biopsy (SLB) for the definite diagnosis of ILDs,[1,2] whereas it may be associated with a relatively higher morbidity and mortality rate. Therefore, the final decision regarding whether or not to perform a SLB must

Abbreviations and Acronyms

CI = confidence interval
DLCO = diffusing lung capacity for carbon monoxide
FVC = forced vital capacity
HP = hypersensitivity pneumonitis
HRCT = high-resolution computed tomography
ILD = interstitial lung disease
IPF = idiopathic pulmonary fibrosis
MV = mechanical ventilation
NSIP = nonspecific interstitial pneumonia
OLB = open lung biopsy
SLB = surgical lung biopsy
VATS = video-assisted thoracoscopic surgery

be based on the balance between benefits to establish a secure diagnosis and the potential risks. Numerous groups have published their experience with SLB in the diagnosis of ILDs. We conducted a systematic review to evaluate the effectiveness and safety of SLB in the diagnosis of ILDs, and meta-analysis were performed where applicable.

MATERIALS AND METHODS

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement, and the study protocol was approved by the Ethics Committee of Guangzhou Medical University.

Literature Search

A systematic search of 2 databases (PubMed and Embase) for relevant citations (from January 1, 2000 to June 30, 2014) was performed in May 2014, with the following search terms used: "surgical lung biopsy" or "open lung biopsy" or "video-assisted thoracoscopic surgery" or "video-assisted thoracoscopy surgery" in combination with "interstitial lung disease" or "interstitial lung diseases" or "diffuse parenchymal lung disease." The search was restricted to human subjects. Bibliographies from selected articles and major reviews were screened for additional relevant publications that were not identified by the database search.

Outcome Definitions

Two outcomes for this systematic review were diagnostic yield and postoperative mortality. Diagnostic yield indicated the specific diagnosis obtained with SLB samples thus affecting overall patient management. Postoperative mortality was defined as the number of patients who died within 90 days after surgery.

Selection of Studies

Two authors (HQ and LQ) independently reviewed all articles identified by the search strategy for inclusion in this review, sequentially evaluating the title, abstract, and full publication. Discordance was resolved by consensus. Inclusion criteria were as follows: (1) SLB, including both video-assisted thoracoscopic surgery (VATS) and open lung biopsy (OLB) for the diagnosis of suspected ILDs; (2) reported at least 1 of primary outcomes; (3) enrolled at least 30 patients; and (4) published in English. We excluded abstracts, editorials, reviews, and case reports. Studies describing the diagnostic yield of SLB in a specific subset of patients were also excluded. In the event of multiple publications with overlapping study periods, we included only 1 study with the largest number to prevent double counting of the patient cohorts. Authors of studies not reporting sufficient data were contacted to request additional information.

Data Extraction and Quality Assessment

Data were recorded on a standard data extraction form that included the following items: description of study population (number, age, geographic location, and surgery methods); study design (prospective or retrospective); patient enrollment (key inclusion and exclusion criteria); biopsy site; and number. The quality and validity of each article were assessed using the QualSyst tool for quantitative studies.[3] This tool was based on the study design, method of population sampling, strategies of data collection and analysis, and how the conclusions were ascertained. It consists of 14 questions with scores from 0 to 2, with the maximum total score being 28.

Data Synthesis and Statistical Analysis

We conducted a meta-analysis for mortality rate using the variance-stabilization double arc-sine transformation method,[4] because the inverse variance weight in meta-analyses is suboptimum when dealing with binary data with low mortality rates. We applied DerSimonian–Laird weights for the random effects model where heterogeneity between studies was found. The pooled rate can be calculated as the back-transform of the weighted mean of the transformed rates. The impact of statistical heterogeneity on the pooled estimates of individual outcomes was assessed using the I^2 test, which measures the extent of inconsistency among the results of the studies. An I^2 value greater than 50% indicates significant heterogeneity. Subgroup analysis was performed if heterogeneity was demonstrated, according to common methodological/clinical features of the studies. Statsdirect and STATA 12.0 (StatsDirect Ltd, Altrincham, UK) were used to perform all the tests.

RESULTS

Literature Search and Study Selection

The selection of included studies is summarized in Figure 1. Screening of titles and abstracts identified 30 articles for full text review. Of these, 7 articles were excluded: Four articles focused on a special subset of patients, such as those with idiopathic pulmonary fibrosis (IPF) or idiopathic interstitial pneumonia, and those dependent on mechanical ventilation (MV); 2 articles evaluated a certain aspect of SLB in the diagnosis of ILDs; and 1 article recruited only 20 patients. Finally, 23 articles met the eligibility criteria of our systematic review.

Study Description and Quality Assessment

Study characteristics are recorded in Table 1. A total of 2148 patients with suspected ILDs undergoing SLB were included (range, 30-311 patients per study). There were 5 prospective studies and 18 retrospective studies. Three studies were multicenter studies, including 1 retrospective study and 2 prospective studies; others were studies from a single institution.

The quality of studies was generally acceptable, with a median (interquartile) QualSyst score of 21 (range, 17-24) (Table 2). None of the studies were designed as a "double-blind" procedure and could be assessable in "blinding of investigators/subjects" domains. Moreover,