Parenchymal Lung Disease Requiring Biopsy

Fredric M. Pieracci, MD MPH

Editorial Review: Clay Cothren Burlew, MD
Eric A. Toschlog, MD
Kimberly A. Davis, MD

Injury/Disease Demographics

- Diffuse parenchymal lung diseases are often referred to collectively as interstitial lung disease (ILD), and represent a heterogeneous group of pathophysiologic conditions that share clinical, radiographic, or pathologic manifestations.
- ILD may be grouped broadly into the following categories: 1) infectious, 2) environmental exposures (e.g., asbestosis, berylliosis), 3) drug induced (e.g., antibiotic or chemotherapeutic), 4) rheumatologic (e.g., rheumatoid arthritis, systemic lupus erythematosis), and 5) idiopathic (e.g., sarcoidosis, cryptogenic or eosinophilic pneumonia).

Clinical Presentation

- The most common clinical presentation of ILD is progressive, hypoxemic respiratory failure.
- The severity of disease ranges from mild dyspnea on exertion to life threatening, ventilator-dependent respiratory failure. The overall respiratory status of the patient influences both the decision to proceed with surgical lung biopsy, and the technique thereof.

Evaluation/Diagnostics/Imaging

- Patients with ILD who are being considered for surgical lung biopsy usually have already undergone an extensive work up, including serologic markers, chest radiograph, chest computed tomography (CT), pulmonary function testing (PFTs), and bronchoscopy. Of these tests, the two most relevant to surgical lung biopsy are chest CT and PFTs.
- Several clinical characteristics are noted from the chest CT:
    - the pattern of ILD (focal vs. diffuse, **Figure 1**)
    - pleural pathology (thickening, effusion, pneumothorax)
    - hilar and mediastinal lymphadenopathy, which may be amenable to biopsy via less invasive modalities such as transbronchial, endobronchial ultrasound (EBUS)-guided or mediastinoscopic biopsy.
- A forced expiratory volume in one second (FEV-1) or diffusing capacity (DLCO) less than 30% of predicted is highly predictive of post-operative morbidity and mortality; this should be considered a relative contraindication to surgical lung biopsy.
- Critically ill patients requiring mechanical ventilation may not be able to undergo PFTs. These patients must be evaluated on a case-by-case basis but are unlikely to tolerate single lung ventilation. Open lung biopsy via “mini thoracotomy” in the supine position may be more appropriate than video-assisted thoracoscopy surgery (VATS) biopsy in these cases.
- Standard ancillary laboratory testing prior to surgery includes electrolytes, complete blood count, and coagulation studies.

Indications for Operative Intervention

- In many cases of ILD, the diagnosis is reached through a combination of history, physical exam, serologic markers, imaging, and bronchoscopic biopsy; surgical lung biopsy is considered in the following scenarios:

- Patients with atypical or progressive symptoms and signs with unclear or discordant serology, radiology, and bronchoalvealoar lavage (BAL) and/or biopsies.
- To exclude malignancy.
- To predict the likelihood of response prior to proceeding with therapies that may have serious side effects.
- To diagnose ILD in a patient with a strong clinical suspicion but a normal chest CT.

- Contra-indications to surgical biopsy include:
  - Chest CT evidence of diffuse end-stage disease (i.e. "honeycombing," **Figure 2**) without areas of milder disease; biopsy of such tissue typically is unrevealing.
  - Severe pulmonary dysfunction (FEV-1 or DLCO less than 30%).
  - Critically ill patients unstable for transport to the operating theater.

Pre-operative Planning

- *Positioning*: All patients should be positioned initially supine in order to facilitate flexible bronchoscopy. Patients who are expected to tolerate single lung ventilation are then positioned lateral decubitus. Patients who are deemed too ill to tolerate either single lung ventilation or lateral decubitus positioning are left supine for open lung biopsy.
- *Choice of airway*: Single lung ventilation, with collapse of the lung that is to be biopsied, is the optimal method under which to perform the surgery. Lung collapse both aids in visualization and facilitates attainment of an adequate biopsy. There are many commercially available tools for achieving lung isolation, ranging from double lumen endotracheal tubes to various bronchial blockers. The advantage of using a bronchial blocker is that it may be passed through a large bore (e.g., greater than 8.0 mm inner diameter) endotracheal tube. A large bore ETT can also accommodate the larger bronchoscopes necessary for optimal visualization of the airways, EBUS, and transbronchial lung biopsies (TBLB, **Figure 3**). A large diameter single lumen endotracheal tube has the additional advantages of improved postoperative pulmonary toilet and the avoidance of airway exchange in critically ill patients.
- *Choice of approach*: The three most common approaches to lung biopsy are TBLB, VATS, and open "mini" thoracotomy.
  - Although TBLB is less invasive than surgical biopsy, it suffers from several limitations. Small tissue purchases render complex diagnoses that require examination of cellular architecture difficult. Furthermore, sampling of lung parenchyma is limited to the hila; this location may be useful in diagnosing diseases that characteristically affect this area (e.g., sarcoidosis); however, it is unlikely to yield a diagnosis in more diffuse disease. Because of these limitations, TBLB is associated with the lowest likelihood of achieving a definitive diagnosis.
  - VATS lung biopsy is currently the preferred approach. Thoracoscopy affords wide viewing of the entire pleural space, making multiple biopsies of each lung lobe relatively straightforward. Smaller incisions also likely minimize post-operative pain and shorten recovery time as compared to a thoracotomy. Finally, a VATS approach allows sampling of both mediastinal and hilar lymph nodes.
  - Open "mini" thoracotomy is reserved for those patients too critically ill to tolerate either single lung ventilation or lateral decubitus positioning.

Operative Techniques/Intraoperative Considerations

- *Flexible Bronchoscopy*: The first step is flexible bronchoscopy with careful examination of the tracheobronchial tree to the level of at the least the segmental bronchi. A BAL is performed routinely, as certain causes of ILD may be diagnosed solely using this method (e.g., acute eosinophilic pneumonia). The BAL should be repeated even if performed previously as it adds little time and risk to the procedure. All endobronchial lesions are biopsied. Evaluation of mediastinal lymph nodes via EBUS with or without biopsies may also be performed at this stage, dependent upon the expertise of the surgeon.
- *Incisions*:
    - For VATS lung biopsy, three 1 cm incisions are typically employed. The first is in the area of the 7th intercostal space, mid axillary line. This incision serves as the camera port. Care must be exercised at this level to avoid injury to the diaphragm; this complication may be avoided by careful direct dissection of the intercostal muscle layers. The axillary incision is often performed first as the intercostal spaces are generally bigger her and facilitate entry into the chest for exploration. Next, a second incision is made, approximately one rib space below the inferior border of the scapula. This port will serve to accommodate the stapler. Finally, an axillary incision is made at approximately the fourth intercostal space, anterior axillary line. This port will serve to accommodate a grasper such as a lung clamp or ring forceps.
    - For an open lung biopsy, a 6-8 cm open "mini" thoracotomy is usually made in the 5th or 6th intercostal space, anterior axillary line.
- *Lung Biopsy*: Considerations include which area to biopsy, how many biopsies to take, what size of biopsy to take, and with what to biopsy the lung. In select cases, the preoperative chest CT may direct the surgeon to a specific area of disease (**Figure 1**). More often, the disease process is diffuse, in which case a biopsy should be obtained from each separate lobe. Recent data suggest an alarmingly high likelihood of discordant pathology from tissue obtained from different lung lobes simultaneously. The most technically straightforward areas to biopsy are the posterior segment of the right upper lobe, the medial segment of the right middle lobe, and the superior segment of the right lower lobe. Furthermore, any grossly diseased area of lung noted at the time of surgery should be biopsied. Biopsies should ideally be 3-5 cm long, and 3-5 cm deep. Typically a post-deployment staple height of 1.0 – 1.5 mm is sufficient to achieve both hemostasis and pneumostasis. Articulating staplers should be used when possible, and tension taken off of the lung prior to stapler deployment; both of these techniques will minimize the chance of a postoperative air leak. Each lung biopsy is bisected and sent for both microbiologic and pathologic analysis. It is imperative to communicate with the referring provider preoperatively, as special tests may be indicated.
- *Closure:* A chest tube is placed through the camera port and terminated at the apex. Locoregional analgesia via either VATS intercostal nerve blocks or insertion of percutaneous analgesic catheters may be employed at this point. The lung is observed to inflate fully prior to removing the camera.

Postoperative Management/Complications

- A chest radiograph is obtained immediately following the procedure.
- The chest tube may be placed to water seal immediately following the operation if there is no air leak and the lung is fully expanded on chest film. Removal of the tube is usually possible within 48 hours of the procedure.
- Routine analgesia, pulmonary toilet, and venous thromboembolism prophylaxis are instituted.

Considerations for Special Populations

- Critically ill patients who will not tolerate either single lung ventilation or lateral decubitus positioning may undergo lung biopsy via an open "mini" thoracotomy in the supine position.
- This procedure may be performed at the bedside in the intensive care unit in patients who are too sick to transport to the operating room, though persistent air leaks will be the norm, and the benefit of the additional information should be weighed carefully against the risk of the operation.

Suggested Readings

1. Ravini M, Ferraro G, Barbieri B, et al. Changing strategies of lung biopsies in diffuse lung diseases: the impact of video-assisted thoracoscopy. Eur Respir J 1998; 11:99.
2. Miller JD, Urschel JD, Cox G, et al. A randomized, controlled trial comparing thoracoscopy and limited thoracotomy for lung biopsy in interstitial lung disease. Ann Thorac Surg 2000; 70:1647.
3. Ayed AK, Raghunathan R. Thoracoscopy versus open lung biopsy in the diagnosis of interstitial lung disease: a randomised controlled trial. J R Coll Surg Edinb 2000; 45:159.
4. Flint A, Martinez FJ, Young ML, et al. Influence of sample number and biopsy site on the histologic diagnosis of diffuse lung disease. Ann Thorac Surg 1995; 60:1605.

Figures

Figure 1: Variations in patterns of interstitial lung disease. Interstitial lung disease may be either diffuse, as may be seen in pneumoconiosis (A), or focal, as may be seen in sarcoidosis (B), which classically affects the bilateral upper lobes. The pattern of lung disease influences the choice of biopsy site.

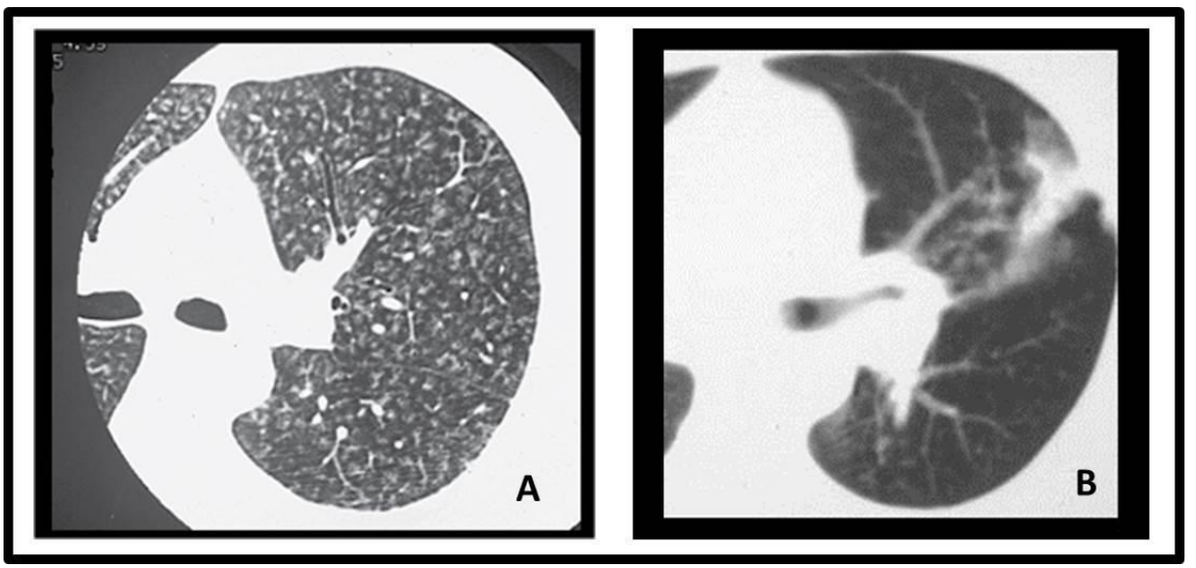

Figure 2: Honeycombing. CT chest depicting diffuse honeycombing, indicative of end stage lung fibrosis, and unlikely to be informative on pathologic analysis.

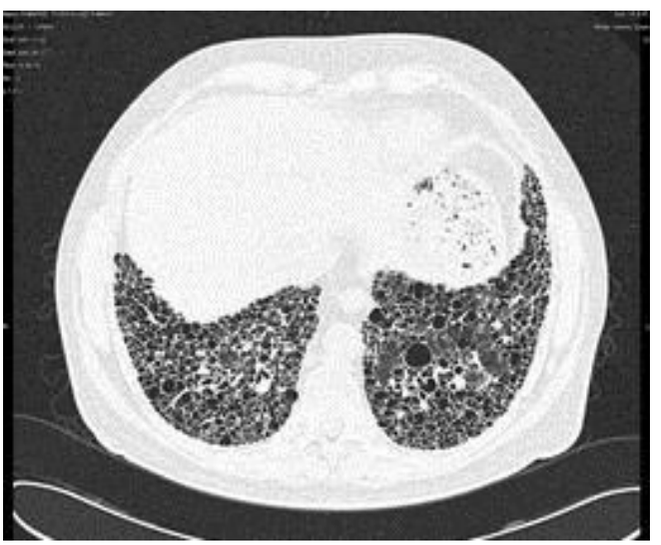

Figure 3: Bifurcated bronchial blocker. A bifurcated bronchial blocker, shown here straddling the carina (C) with the left main stem bronchial balloon inflated, can effectively achieve single lung ventilation while still allowing passage of larger bronchoscopes necessary for both ultrasound and biopsy into the airways.