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Bronchoscopy Diagnostic Procedures in Central and Peripheral Lesions: A Narrative Literature Review

Syarlidina Syaf[1]*, Sri Indah Indriani[1]

[1]Department of Pulmonology and Respirology Medicine, Faculty of Medicine, Universitas Riau, Riau, Indonesia

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***Corresponding author:**
Syarlidina Syaf

E-mail address:
syafbocenk84@gmail.com

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A B S T R A C T

Bronchoscopy is a medical procedure that provides tracheobronchial visualization by placing a bronchoscope and is carried out by a competent doctor. Bronchoscopy is the main interventional procedure used in determining the diagnosis and staging of cancer patients and plays a role in interstitial lung disease and infections. The basic principle of bronchoscopy sampling is carried out with a combination of rinsing, brushing, needle aspiration and biopsy. Cryobiopsy has advantages over conventional forceps biopsy and electrocautery because it can produce tissue without artifacts. Navigated bronchoscopy techniques have facilitated peripheral lung tumor biopsies that have better diagnostic yield than conventional transbronchial biopsies. The combination of navigation bronchoscopy with an ultrathin bronchoscope for peripheral lesions is more effective than either modality.

1. Introduction

Bronchoscopy is a medical procedure that provides tracheobronchial visualization by placing optical instruments into the airway. Bronchoscopy comes from the Greek words broncho, which means windpipe, and scopos, which means to see or watch. This procedure is carried out by a competent doctor by examining the bronchi or their branches for diagnostic or therapeutic purposes. The indication for bronchoscopy at the beginning of its development was as a therapeutic procedure that removed foreign bodies and widening strictures caused by tuberculosis and diphtheria infections. Bronchoscopy was first performed in 1897 by a German otolaryngologist named Gustav Killian, who used a rigid endoscope to remove pork bones from the right main bronchus. Killian continues to develop this technique so that the indications for bronchoscopy become wider. Chevalier Jackson, a laryngologist in Philadelphia, began developing endoscope tubes in the early 19th century. Jackson modified the rigid bronchoscope in 1904 by adding a direct ocular, a suction tube, and a distal tip for illumination. Jackson continues to design and refine procedures for safety protocols during the action.[1]

Technology for fiberoptic endoscopy began to develop in 1950. Shigeto Ikeda introduced flexible bronchoscopy with fiberoptic imaging technology in 1966, and it was a revolution in the field of bronchoscopy. Flexible bronchoscopy allows the operator to reach small airways. Flexible bronchoscopy has increased in use, with 500,000 procedures performed in America each year. Bronchoscopy is a relatively safe procedure with a low morbidity rate (0.1 – 2.5%) and a very low mortality rate (<0.05%). Bronchoscopy is the main interventional procedure used in determining the diagnosis and stage of cancer patients and plays a role in interstitial disease and infection. The role of bronchoscopy in cases of lung tumors can help with diagnostic steps in the form of establishing the type and stage of the disease and can be used as a therapeutic measure. The overall sensitivity of the flexible bronchoscope for diagnosing lung cancer in central lesions was 88%. The diagnostic results of bronchoscopy for peripheral lesions with a diameter of less than two centimeters or more than two centimeters show a sensitivity of 34% and 63%.[2-4] This study aims to explore the diagnostic bronchoscopy procedure for central and peripheral lesions and the success rate of the bronchoscopy procedure.

The role of bronchoscopy in the diagnostics of central and peripheral lung lesions

Lesions based on radiography can be divided into endobronchial, central, or peripheral lung lesions. Endobronchial lesions, as presented in Figure 5, are defined as lesions located in the inner third of the hemithorax and adjacent to the bronchial tree based on thoracic CT scan imaging. Meanwhile, peripheral lesions are lesions in the form of nodules or parenchymal masses located on the outside. The bronchoscopy method is adjusted to the patient's case and the type of tissue to be removed. The bronchoscope can be inserted through the nose or mouth, and then the condition of the visible airway is assessed.[5,6]

Results are higher for endobronchial lesions because they can be approached by direct observation through a scope, whereas yields are lower for peripheral lung lesions. Another study using conventional flexible bronchoscopy found 81% central lesions with 40.6% squamous cell carcinoma and 30.1% adenocarcinoma. Squamous cell carcinoma lesions are often central and, therefore, easily diagnosed by bronchoscopy. Adenocarcinoma is a tumor that is most often found in the periphery. In the era of thinner fiber optic coverage, accessibility has improved the diagnosis of even peripheral tumors such as adenocarcinoma. Biopsy is the gold standard in the histopathological diagnosis of lung cancer and should be attempted in all cases with appropriate procedures.[7]

Diagnostic procedures for central lung lesions

Central lesion sampling was performed with a combination of bronchial washing (BW), bronchial brushing (BB), endobronchial biopsy (EBB), endobronchial needle aspiration (EBNA), or Transbronchial needle aspiration (TBNA). Central tumor lesions may appear as exophytic mass lesions, with partial or total occlusion of the bronchial lumen, extrinsic compression of the bronchus, or submucosal tumor infiltration. Bronchial lavage aims to clean the airways from debris and secretions at the location indicated for analysis by spraying 10-20 cc of 0.9% NaCL and then suctioning. The rinse sample is collected in a special sterile container. The sensitivity of BW for diagnosing tuberculosis (TB) microscopically and gene bronchial brushing is performed on abnormal mucosa or mucosa that looks normal but is adjacent to central lesions or peribronchial lesions. The brush is inserted into the working channel using repetitive and rotating movements on the mucosal surface. The brush samples were fixed on a glass slide with 95% alcohol. The diameter or length of the brush does not affect the diagnostic results. Rinse and brush samples are examined for cytopathology, cell-blocked cytology to diagnose malignancy, and microbiology to diagnose infection. The sensitivity of BB in the diagnosis of endobronchial malignancy was 61%. The culture of microorganisms in BB samples has a sensitivity of 89% in diagnosing pneumonia. Complications of the procedure can be minimal bleeding.[8,9]

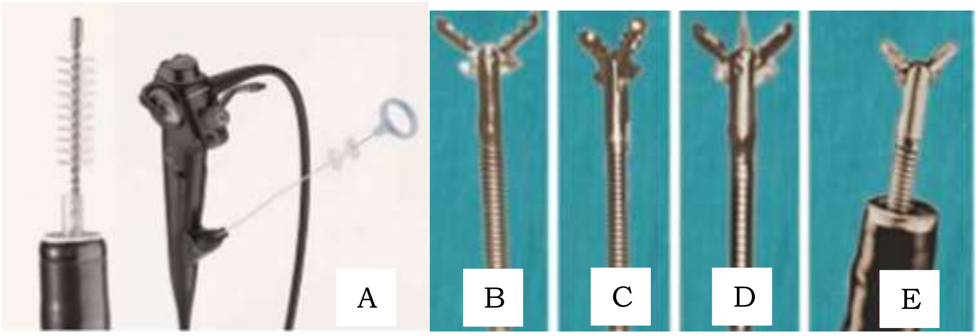

Figure 1. A. Bronchial brush, B and C. Alligator forceps, D. Oval forceps with a needle. E. Oval forceps.

EBB procedure or removal of foreign bodies in central lesions using alligator forceps biopsy or oval forceps with a needle. Forceps are inserted through the working channel bronchoscope, and the biopsy can be repeated 4-6 times. The histopathological diagnostic yield of EBB tumor type is 90% for exophytic lesions. The sensitivity of EBB for the diagnosis of sarcoidosis increases by 10-20% when combined with transbronchial biopsy. Sampling is carried out on abnormal mucosa and carried out on the first and second carina if the mucosa appears normal. The sensitivity of EBB is 84% in detecting endobronchial tuberculoma. The most frequent complication is mild bleeding, which can resolve spontaneously. Stopping bleeding is carried out with cold saline or vasoconstrictors (adrenaline 1: 20,000). EBB sampling should be used with caution in lesions with increased vascularity.[10,11]


Figure 2. EBNA needle.

The recommendation to use endobronchial needle aspiration (EBNA) along with other modalities is beneficial in necrotic and exophytic lesions located in the submucosa. A needle with a size variation of 19-25 G is attached to the distal end of the flexible catheter and then inserted into the working channel of the bronchoscope. The needle is pushed into the lesion, and the catheter is moved repeatedly for several seconds until sufficient sample is obtained. EBNA samples can be treated the same as brush samples. The EBNA procedure has a sensitivity of 56% for malignancy with minimal bleeding complication rates. One study reported that the sensitivity of EBNA for the diagnosis of endobronchial tuberculoma was 19%. The EBNA needle can be seen in Figure 2. The Rapid on-site evaluation (ROSE) technique must be used for all sampling methods to reduce additional procedures and requires good collaboration with an anatomical pathologist.[12,13]

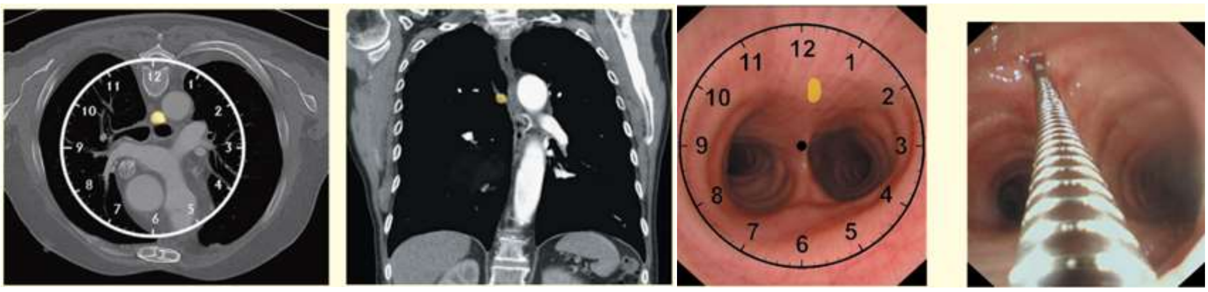

Figure 3. TBNA.

Conventional transbronchial needle aspiration can be performed through the bronchial wall for central lesions that are peribronchial with extrinsic compression and lymph nodes. The needles used are cytology needles (22G) or histology needles (19G). The TBNA technique, as shown in Figure 3, can improve diagnostic yield when EBB or EBNA specimens are inadequate to reach a diagnosis.[13]

Cryobiopsy is a modification of the freezing technique for tissue biopsy. Cryobiopsy provides good-quality tissue. The advantage of this technique compared to conventional forceps biopsy and electrocautery is that it can produce tissue without artifacts due to burning. The hemostatic effect due to freezing also helps reduce artifacts. Comprehensive molecular and immunohistochemical studies can be performed on specimens, which is very important for planning targeted therapy for lung cancer. This cryobiopsy technique uses a flexible bronchoscope. The cryoprobe is inserted through the working channel and attached to the tumor for 20 seconds or until clotting is adequate. The cryoprobe is a therapeutic and diagnostic tool for ablation of endobronchial tumors and airway recanalization by removing blood clots and foreign bodies. The cryobiopsy samples were then examined for histopathology. Another study demonstrated the superiority of cryobiopsy in the diagnosis of endobronchial malignant lesions when compared with conventional forceps without disturbing the morphological structures. Cryobiopsy has a higher diagnostic success value, namely 89-95%, compared to forceps biopsy, namely 66-85%.[14,15]

Diagnostic procedures for peripheral lung lesions

The incidence of finding peripheral lung lesions increases by around 1.5 million new nodules every year, along with the increasing frequency of CT scan use. Peripheral lung lesions with a pretest probability of malignancy and minimally invasive biopsy are often considered based on the American College of Chest Physicians (ACCP) guidelines. Peripheral lung lesions can be biopsied transthoracically under CT guidance or via transbronchial bronchoscopy (TBLB). CT-guided transthoracic biopsy has an excellent diagnostic yield of close to 83% but carries a high rate of complications. The incidence of pneumothorax with transthoracic biopsy is 15%, and the risk of pneumothorax requiring a chest tube is 6.6%. Bronchoscopy with TBLB is much safer, and the risk of pneumothorax is 1%-2%.[16]

Samples from peripheral lesions were taken with a combination of bronchial lavage, bronchoalveolar lavage (BAL), brushing, TBLB, and TBNA. The diagnostic yield of bronchoscopy for peripheral lesions depends on the size of the lesion, the distance of the lesion from the hilum, and the relationship between the lesion and the bronchus. Another study stated that the diagnostic yield of conventional bronchoscopy for peripheral lesions was 46.4% for washing and 37.3% for brushing. Bronchial lavage is superior to brushing. The overall diagnostic yield of rinsing after brushing was 52.4%. Another study on endobronchial cancer with EBB sensitivity of 74%, brushing at 61%, and washing at 47%. Meanwhile, in peripheral lung cancer, TBLB has a sensitivity of 57%, brushing 54%, and rinsing 43%. This study uses navigation with fluoroscopy.[17]

Bronchoalveolar lavage (BAL) is a safe and minimally invasive sampling technique for the peripheral airways. BAL is carried out by spraying 0.9% NaCl through the working channel at 30-60 cc per spray, and the total fluid used is 100-300 cc, depending on the protocol used. Fluid is collected at 5%-30% of the original volume using suction pressure <100 mmHg to avoid airway collapse. The diagnostic yield of BAL is high in diseases other than cancer, such as pulmonary TB, pneumonia, and fungal infections. The diagnosis of BAL on microscopic examination of pulmonary TB has a sensitivity of 58%. Gene Xpert MTB/Rif results with a sensitivity of 83% and specificity of 98%. Opportunistic infection in immunocompromised hosts with a sensitivity of up to 98% for Pneumocystis jiroveci. The sensitivity of BAL in the diagnosis of invasive aspergillosis is 64%, and the galactomannan antigen has a sensitivity of 90% and a specificity of 94%.[18]

BAL examination showed low results in the diagnosis of peripheral lung malignancy, namely 43%. Combined with bronchial washing and sputum cytological examination after bronchoscopy, BAL improves the results by 56%. BAL examination in 162 patients with malignant pulmonary infiltrates showed increased sensitivity in cases of carcinomatous lymphangitis 83% and non-Hodgkin lymphoma 45%. Advances in cell and molecular biology can complement BAL techniques to increase the rate of tumor diagnosis in peripheral lesions and are also useful tools for exploring the molecular mechanisms that regulate lung cancer genesis, discovering the characteristics of immune reactions by analysis of immune cells and mediators as well as molecular characteristics of cancer with free DNA as well as exosome analysis. BAL is primarily contraindicated in patients with cardiopulmonary instability or with severe hemorrhagic diathesis.

Navigation bronchoscopy technique in peripheral lung lesions

The navigation bronchoscopy technique facilitates the method of biopsy sampling of peripheral lesions. These procedures have undergone significant development in the last two decades and consist of fluoroscopy, endobronchial ultrasonography (EBUS), electromagnetic navigation bronchoscopy, ultra-thin bronchoscopy, and virtual bronchoscopy. The latest technology allows us to see beyond the bronchial tree all the way to the mediastinum. The EBUS examination provides an ultrasound image of the tissue outside the airway wall, thereby facilitating TBNA treatment for enlarged lymph nodes. A sampling of peripheral nodules or tumors can use fluoroscopy guidance, electromagnetic navigation bronchoscopy (ENB), virtual bronchoscopy, and ultra-thin bronchoscopy.[15,16]

Fluoroscopy

Fluoroscopy is a type of X-ray imaging that can produce sequel images such as videos. Fluoroscopically guided bronchoscopy is performed when the lesion cannot be assessed directly with a bronchoscope. Biopsy of peripheral lesions called TBLB uses a bronchoscope and smaller forceps. Fluoroscopic guidance can increase sensitivity in cases of peripheral and diffuse cancer lesions. Observational studies have shown the diagnostic yield of conventional fluoroscopy-guided techniques to be 80%. Lesion diameter influences the accuracy of the technique with sensitivity < 30% at nodule sizes < 2 cm. The yield of bronchial brushing in peripheral lesions is 52%.[15]

Fluoroscopically guided transbronchial needle aspiration has been adopted to sample peripheral lung lesions in the form of nodules or masses since 1984. This technique improves the diagnostic yield of transbronchial biopsy of peripheral lung lesions but is time-consuming, requires experience, and is not universally available. Systematic studies and meta-analysis showed a diagnostic yield of 53% in nodules measuring more than 3 cm, the CT bronchus sign was positive, and the use of ROSE was also the most important predictive factor. Comparison between TBNA and TBLB performed simultaneously with TBNA under fluoroscopy guidance showed significant diagnostic advantages of 45% and 65%, respectively.[14]

Ultrasonography endobronchial

The indication for using EBUS is to evaluate endoluminal, intramural tissue, peribronchial structures, lymph nodes, and mediastinum so that early detection in determining tumor staging can be carried out. ACCP guidelines recommend the use of EBUS to diagnose peripheral lung lesions as this approach improves diagnostic yield. A meta-analysis reported that the combined diagnostic yield of bronchoscopy with EBUS for peripheral lung lesions was 70.6%. This tool is an ultrasound transducer integrated into the bronchoscope, which will make contact with the endobronchial mucosa. The tip of the bronchoscope is equipped with a needle to perform a biopsy so that TBNA can be performed. The size of the needle does not affect the diagnostic results.

Another study reported that the accuracy of EBUS-TBNA in diagnosing abnormalities in the mediastinal and hilar lymph nodes was up to 82%. The transesophageal approach can also be used to sample lymph nodes that are within reach of EBUS when the transbronchial method is not possible due to the patient's clinical conditions, such as cough and respiratory failure. Another study reported the results of a randomized controlled trial of conventional bronchoscopy with fluoroscopy (SB-F) compared with thin bronchoscopy with EBUS guidance (TB-EBUS). The diagnostic yield was higher in the TB-EBUS group (43%) than in the SB-F group (37%).[19]

Ultra-thin bronchoscopy

Standard flexible bronchoscopes can penetrate up to the third to fifth-generation bronchi and allow visualization of one to two generations further in adult bronchial patients, whereas the use of ultra-thin bronchoscopes can reach small eighth to twelfth-generation bronchi. Ultrathin bronchoscopes having an outer diameter of 3 mm or smaller are used for peripheral exploration of the airways in adult patients. Ultra-thin bronchoscopes are used only for diagnostic procedures, not for therapeutic procedures. Contraindications for use are the same as for a standard bronchoscope. Ultra-thin flexible bronchoscopes can facilitate endotracheal intubation in difficult situations such as trauma, bleeding or anatomical abnormalities.[20]

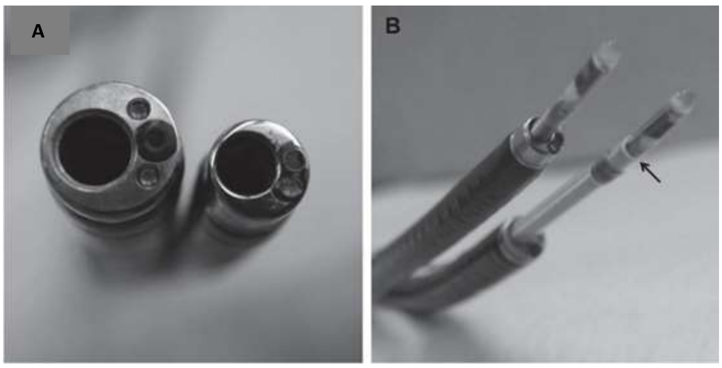

Figure 4. Comparison of bronchoscopes. A. 4.0 mm thin bronchoscope with a working channel of 2.0 mm (left) and 3.0 mm ultra-thin bronchoscope with a working channel of 1.7 mm (right). B. 3.0 mm ultra-thin bronchoscope with 1.4 mm EBUS (left) and 4.0 mm bronchoscope with 1.95 mm EBUS (right).

The ultra-thin flexible bronchoscope having an outer diameter of 1.8 mm with a flexible tip and a channel for biopsy makes it possible to assess bronchioles and perform alveolobronchography as well as study bronchial epithelial cells taken from previously inaccessible airways. Another study conducted a randomized control trial comparing the diagnostic results of EBUS-guided ultrathin bronchoscopy (3 mm), virtual bronchoscopy, and fluoroscopy with conventional thin bronchoscopy (4 mm) with the same navigation in peripheral lesions. The results of this study found ultra-thin bronchoscopy to be superior. The combination of navigation bronchoscopy with an ultrathin bronchoscope is more effective than either modality alone. A fluoroscopy image of a transbronchial biopsy using an ultra-thin bronchoscope is presented in Figure 4.[19]

Electromagnetic navigational bronchoscopy

Electromagnetic navigational bronchoscopy uses an electromagnetic area to track the location of the lesion in real-time, and its position is linked to the results of the CT scan. Guidance is carried out to reach the lesion using a probe that is inserted through the working channel on a flexible bronchoscope. The probe is removed after the bronchoscope reaches the lesion, and then the biopsy instrument is inserted into the working channel. The examination samples are examined for cytopathology or histopathology. The main indication for the use of ENB is to guide the sampling of peripheral lesions that cannot be reached with conventional bronchoscopy. A multicenter prospective study in 2017 showed that ENB successfully guided 910 subjects (94.4%) and 1,036 lesions (91.8%) for biopsy. The incidence of pneumothorax, bronchopulmonary hemorrhage, and respiratory failure was 4.9%, 2.3%, and 0.6%, respectively. Another study compared the effectiveness of EBUS, ENB, and EBUS with ENB in 118 patients with peripheral lung lesions. The positive histopathological results of biopsy with EBUS, ENB, and EBUS with ENB were 59%, 69%, and 88%, respectively. A meta-analysis study of 15 studies involving 1,033 patients with peripheral lung nodules found an accuracy of 73.9% with a sensitivity of 71% but with an incidence of the main complication, namely pneumothorax, of 3.1%. Another study conducted a systematic review and meta-analysis of 40 studies from 2014-2019 with a total of 3,342 research participants. The sensitivity of ENB is 77%, and the specificity is 100% in diagnosing peripheral lung cancer. The use of ENB is also very safe, with a 2% risk of pneumothorax and a <1% risk of bleeding or respiratory failure. The diagnostic efficiency of using ENB shows that lesions in the right upper and middle lobes of the lung are higher than those in the left lobe. This is influenced by heart rate and large blood vessels. The lower lobes of the lung have greater mobility than the upper lobes. These differences can cause ENB navigation and position errors. Biopsy yields for ENB in central and peripheral lesions were 82% and 53%, respectively. The size of the peripheral nodule is a major factor in diagnostic success. Lesions larger than 2 cm have become the consensus for the use of ENB. If ENB positioning technology is combined with percutaneous lung biopsy technology, it can improve the diagnostic performance of lesions with a diameter of less than 2 cm.[20]

Virtual bronchoscopy navigation

Virtual bronchoscopy navigation (VBN) is often used in cases of peripheral lung lesions using a CT scan to form a three-dimensional image of the bronchial tree. The concept used in VBN is similar to that used in ENB, but VBN does not use GPS (Global Positioning System). The VBN images obtained can be viewed simultaneously with direct bronchoscopy. The VBN examination procedure requires CT scan guidance and an ultra-thin bronchoscope with fluoroscopy or EBUS. X-ray radiology modality is required for biopsy instrument placement. The use of VBN is to identify bronchial stenosis, endobronchial malignancy, and corpus alienum in the airways and assess post-operative complications in the bronchi. Another study conducted a randomized multicenter study with the conclusion of bronchoscopy with navigation using a VBN-EBUS guide sheath so that the biopsy instrument could be guided to the lesion without X-ray fluoroscopy. The advantage of VBN is that it can shorten the biopsy time, but it cannot replace the necessary fluoroscopy due to accuracy in sample collection.[21,22]

2. Conclusion

Bronchoscopy is a medical procedure that provides tracheobronchial visualization by placing a bronchoscope and is carried out by a competent doctor. The basic principle of bronchoscopy sampling is carried out with a combination of rinsing, brushing, needle aspiration and biopsy. Navigated bronchoscopy techniques have facilitated peripheral lung tumor biopsies that have better diagnostic yield than conventional transbronchial biopsies. The combination of navigation bronchoscopy with an ultrathin bronchoscope for peripheral lesions is more effective than either modality.

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