



# The Diagnostic Role of Narrow-Band Imaging Bronchoscopy For Early Detection of Lung Adenocarcinoma in a Young Adult

Christina Siuwandy Bu'ulolo<sup>1</sup>, Wayan Wahyu Semara Putra<sup>1</sup>, Novitasari<sup>2</sup>

<sup>1</sup>Department of Pulmonology and Respiratory Medicine, Wangaya Hospital, Denpasar, Indonesia

<sup>2</sup>Department of Pathology Anatomy, Wangaya Hospital, Denpasar, Indonesia

## Abstract

**Background:** Lung adenocarcinoma is a common type of cancer that is typically associated with older individuals who have a history of smoking. However, in some rare cases, this occurs in young adults.

**Case:** This case report discusses the diagnostic challenges and the important role of bronchoscopy in confirming lung adenocarcinoma in a 35-year-old male patient with a history of smoking. The patient had a persistent cough and unexplained weight loss. This raised concerns about various differential diagnoses, such as infectious diseases, abnormalities in the bronchial tree, and rare lung neoplasms. In this case report, we used a combination of White Light Bronchoscopy (WLB) and the Narrow Band Imaging (NBI) technique to identify pre-cancerous lesions and early-stage cancers within the airways.

**Discussion:** This case report highlights the significance of bronchoscopy as a diagnostic tool for lung cancer in unexpected populations like young adults. The successful diagnosis through bronchoscopy led to prompt treatment initiation.

**Conclusion:** This case underscores the importance of a multidisciplinary approach to lung cancer diagnosis and management, adapting to the unique situations of individual patients.

**Keywords:** bronchoscopy, diagnosis, lung adenocarcinoma

## Corresponding Author:

Christina Siuwandy Bu'ulolo |  
Department of Pulmonology and  
Respiratory Medicine, Wangaya  
Hospital, Denpasar, Indonesia |  
[christina.siuwandy@gmail.com](mailto:christina.siuwandy@gmail.com)

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## INTRODUCTION

Lung cancer is the most prevalent malignant tumor found globally and is responsible for the highest number of cancer-related deaths.<sup>1</sup> Of all the various types of lung cancer, 85% belong to the category of non-small cell lung carcinomas (NSCLC), including adenocarcinomas, squamous cell carcinomas, and giant cell undifferentiated carcinomas.<sup>2</sup>

Lung cancer is most commonly diagnosed in individuals between the ages of 65 and 74, while patients under 45 years old represent only about 1.6% of all cases.<sup>3</sup> As it is usually associated with older age, diagnosing the disease in young adults can be challenging. Non-small cell lung cancer (NSCLC) accounts for the majority (85–90%) of lung cancer cases. At the time of diagnosis, 50% of NSCLC patients are aged 70 or older, with 15% being over 80 years old.<sup>4</sup>

The early symptoms of lung cancer are often atypical, resulting in the majority of patients being identified in advanced stages. Consequently, the prompt detection of lung cancer in its initial phases is vital for patient survival, yet remains a demanding task. Therefore, there is an urgent need for advancements in technology to enhance the diagnostic accuracy of early-stage lung cancer.<sup>5</sup>

Low-dose computed tomography (LDCT) for screening has demonstrated a 20% reduction in mortality among individuals at high risk, despite its limited sensitivity in detecting small tumors that develop in the central airway.<sup>6</sup> Computed tomography (CT) can display lung adenocarcinoma in various forms, including a solitary nodule or mass, a thin-walled cyst-like lesion, localized or diffuse parenchymal consolidation, or multiple lesions. When lung adenocarcinoma appears as parenchymal consolidation, it often resembles pneumonia, making accurate diagnosis challenging and frequently delayed.<sup>7</sup> Utilizing imaging techniques

like LDCT may also carry risks associated with the radiation exposure of the CT scan and can pose challenges related to the overdiagnosis and overtreatment of minor lesions.<sup>6,8,9</sup>

Although tissue biopsy is the gold standard for diagnosing malignant and premalignant airway diseases, bronchoscopy is among the safest and most precise methods for assessing both central and distal airway mucosa.<sup>10</sup> To date, the prevailing method for identifying early-stage lung lesions in central airways is conventional white light bronchoscopy (WLB).<sup>11</sup>

However, WLB has limitations in its capacity to identify small intraepithelial, microinvasive, and preinvasive lesions. In comparison, Narrow-band imaging (NBI) is an advanced endoscopic method that enhances the detection of abnormal mucosal and submucosal vascular patterns by utilizing two specific light wavelengths.<sup>12</sup> It uses narrow-band blue (415 nm) and green (540 nm) light waves to generate high-resolution images of the vascular mucosa and submucosa. The visualization of vascular patterns is affected by abnormalities or variations in bronchial epithelium and vascular density. Therefore, narrow-band imaging bronchoscopy is a useful tool for identifying airway cancer lesions in patients suspected of having lung cancer.<sup>13</sup>

As per the research conducted by Elhefny et al, the assessment of the diagnostic accuracy of NBI and WLB for detecting premalignant lung lesions revealed that NBI exhibited a sensitivity of 57.1%. In contrast, WLB showed a sensitivity of only 9.1%. When combined, the sensitivity of both WLB and NBI increased to 76.9%. In terms of diagnosing malignant lung lesions, NBI demonstrated a sensitivity of 26.7%, WLB had a sensitivity of 55.6%, and their combination resulted in a sensitivity of 52.6%. Increased blood content or vessel growth might explain the high false-positive rate associated with NBI, while the specificity remains relatively consistent with WLB.<sup>14</sup>

The combination of both techniques improves the sensitivity in identifying intraepithelial premalignant lesions, even though this advantage does not extend to the detection of invasive lung

cancer. This combination has proven its benefit for airway screening and biopsy selection. NBI can enhance the identification of premalignant and malignant lesions when used alongside WLB. The advantages of this approach are not limited to the targeting of biopsies and treatment planning, but also offer higher specificity and sensitivity compared to WLB on its own. Furthermore, NBI is particularly beneficial in detecting and characterizing the vascular patterns of pre-cancerous and cancerous lesions in the bronchial mucosa.

The purpose of this case is to show the potential of NBI bronchoscopy as a diagnostic tool that can be used for early detection of lung adenocarcinoma, especially in young adults, which is rare and often diagnosed at later stages. Early identification can be useful to improve the treatment outcomes and survival rates.

## CASE

A 35-year-old male with a 10-pack-year smoking history presented to the Hospital with a history of a 4-month-long purulent cough and weight loss of 4 kilos for 4 months. Moreover, he had chest pain and hemoptysis, with neither past medical history nor family medical background. His physical examination was normal.

The patient is suspected of having pulmonary tuberculosis (TB), leading to the performance of Gene X-pert MTB/RIF (Mycobacterium Tuberculosis/Resistance to Rifampicin) - Assay and Human Immunodeficiency Virus (HIV) - Test. MTB was not discovered, and he tested negative for HIV. He had no evident contact with a confirmed TB source. As an outpatient, he received a course of symptomatic medications.

About one month later, he was hospitalized due to a mild, gradually worsening shortness of breath and purulent cough that had developed over the past month. He reported another weight loss of  $\pm 2$  kg in one month but denied any chest pain, fever, or coughing up blood. He mentioned that he had not been smoking for the last 2 months.

On presentation, he was afebrile, his blood pressure was 124/70 mmHg, his heart rate of 82/min, his respiratory rate of 22/min, and his blood oxygen saturation level remained at 95 percent with diminished breath sounds over the left upper and middle lobes. There was a slightly elevated white blood count (WBC) of  $16.52 \times 10^3/\mu\text{L}$ , differential count: neutrophils 68.2%, lymphocytes 9.2%, monocytes 7.3%, eosinophils 14.5%, and basophils 0.8%.

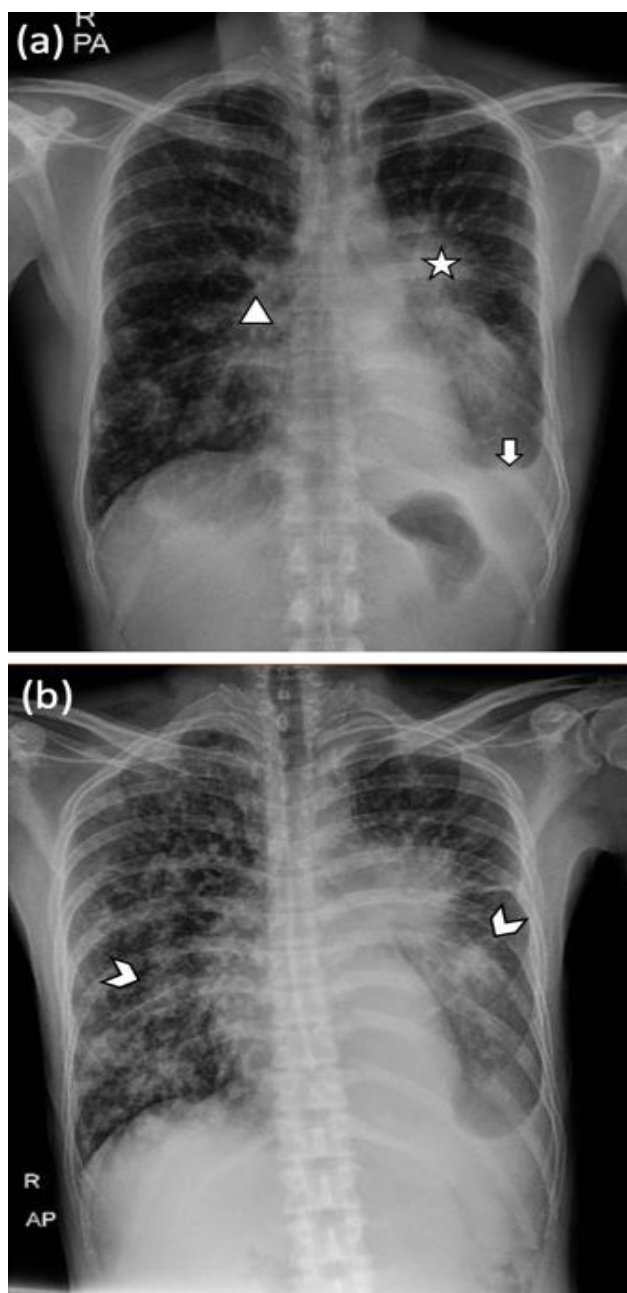


Figure 1. (a) Chest X-ray on first admission showed an area of haziness detected in the left parahilar-paracardial region (star). The right and left supra-para hilar regions, as well as the right paracardial region, show fibrous infiltration (triangle). An adhesion was found in the lower left hemithorax (thick arrow). (b) Chest X-ray one month later. The infiltration in both lung fields has increased (head arrows).

An examination of the chronic unexplained cough in this patient (conducted with the Olympus BF-Q170 scope) was carried out through the oral pathway in the bronchoscopy laboratory. The patient was provided with a written informed consent for the procedure. Local anesthesia was administered via a xylocaine spray, followed by the insertion of a bite block.

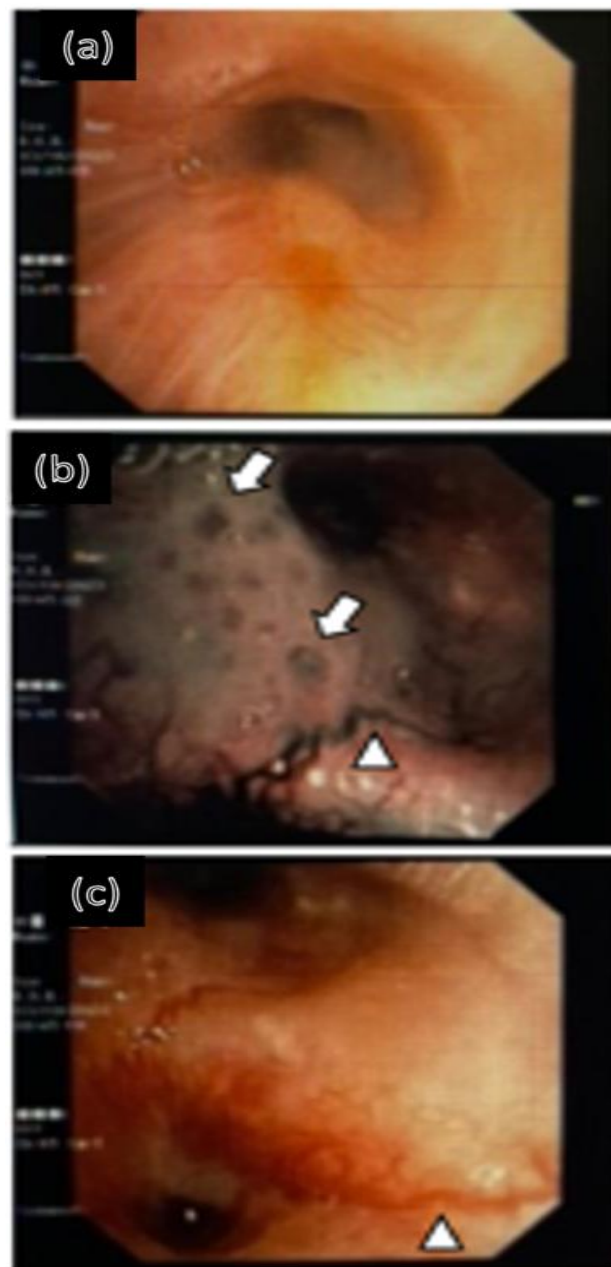


Figure 2. A visual examination of bronchoscopy. (a) The left main bronchus has slight hyperemia, the lumen is partially obstructed due to extraluminal infiltration. The mucosa appears oedematous, the surface is irregular and with hyperemia, very fragile, and prone to bleeding. Small amounts of white gelatinous secretions were observed. By switching from WLB to the NBI technique, (b) atypical dotted vessels (thick arrows) and (c) spiral vascular signs (triangle) were identified, and targeted biopsies were performed to obtain specimens for pathological examination. Bronchial washing and brushing were performed distal to the left main bronchus.

Inspection of the airways was performed starting with the vocal cords, followed by the trachea, and then proceeding to the examination of both the right and left bronchial trees. Initially, the bronchial mucosa was inspected using WLB, which was subsequently followed by NBI (Figure 2(a)-(b)). To further support the bronchoscopy findings, a contrast-enhanced chest MSCT was requested (Figure 3).

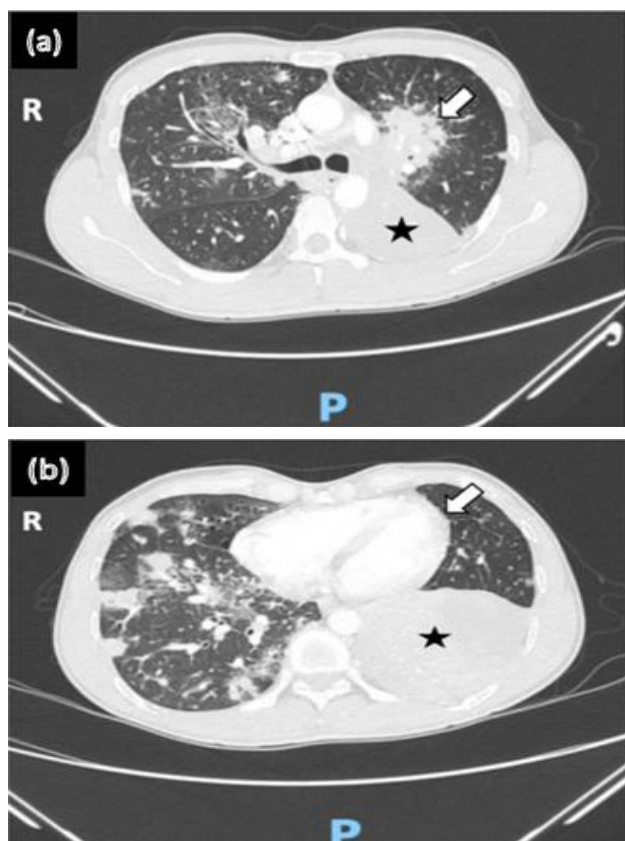


Figure 3. Contrast-Enhanced Chest MSCT – Scan revealed the presence of numerous nodules and infiltrates in both lungs, indicating a rough appearance of the broncho-vascular markings within the lungs. An image shows a mass (thick arrow) with tissue density in the lower left lung lobe. Additionally, enlarged lymph nodes near the para-aortic and subcarinal areas were detected, and a pleural effusion was visible in the left lung (star).

The cytological findings of bronchial washings revealed a smear consisting of sparse clusters of mature squamous epithelial cells (Figure 4). There were also scattered and aggregated lymphocyte inflammatory cells. Meanwhile, bronchial brushing revealed respiratory epithelial cells and neoplastic cells. The respiratory epithelial cells formed sheet-like structures with a morphological appearance of columnar, ciliated cells with oval to round nuclei. Some of these cells had enlarged nuclei (reactive changes). The neoplastic cells appeared to originate

from epithelial cells. They displayed morphological features such as an increased nucleus-to-cytoplasm ratio, pleomorphism, hyperchromatism, prominent nucleoli, some multinucleation, and irregular nuclear membranes. These atypical cells formed sheet-like structures and morula-like arrangements.

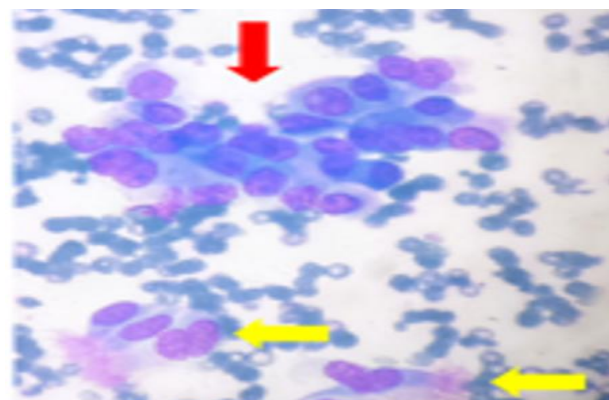


Figure 4. The cytological findings of bronchial brushing –Cluster of malignant cells (red arrow), ciliated respiratory epithelial cells (yellow arrows) (Quik Diff staining, magnification 400x).

This finding is supported by the bronchial tissue biopsy specimen, lined with respiratory epithelium and containing a tumor mass (Figure 5).

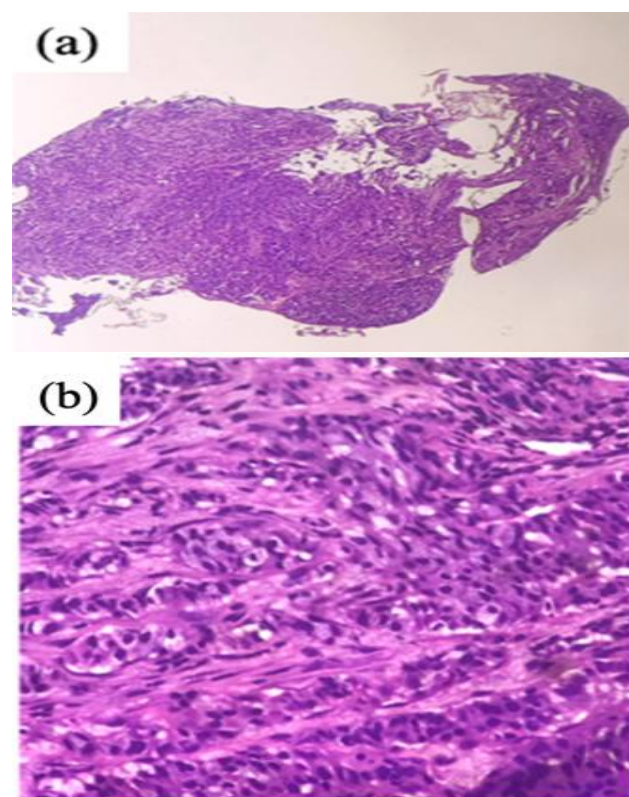


Figure 5. The histopathological findings of Transbronchial Biopsy – (a): The tissue section contains a tumor mass. The typical structure of the bronchial mucosa has become irregular (HE staining, magnification 40x). (b) Malignant cells exhibit an increased nucleus-to-cytoplasm ratio, hyperchromatic nuclei, and clumped chromatin, and some show vacuolated cytoplasm containing mucin material (HE staining, magnification 400x).

The tumor mass consists of a proliferation of neoplastic epithelial cells forming solid, trabecular, and single-file structures. These neoplastic cells display nuclear morphology with an increased nucleus-to-cytoplasm ratio, pleomorphism, hyperchromatism, clumped chromatin, and some cells with vesicular nuclei and prominent nucleoli, along with irregular nuclear membranes. Some cells exhibit vacuolated cytoplasm containing mucinous material. In conclusion, these cytomorphological findings and the conventional morphological features indicate non-small cell lung carcinoma (NSCLC), tending towards the adenocarcinoma subtype.

## DISCUSSION

The 35-year-old male patient reported his condition after experiencing a persistent purulent cough for four months without improvement and an unnoticeable weight loss. These atypical clinical symptoms can potentially lead to a misdiagnosis of lung tuberculosis, especially when his chest X-ray shows an increased infiltration pattern resembling characteristics commonly seen in lung tuberculosis (Figure 1). Bronchoscopy provides valuable insights into the state of the airway, including the detection of hidden pulmonary lesions, potential intraluminal irregularities, obstructions, and the removal of airway secretions as presented above.

The bronchoscopy began with the WLB technique, revealing oedematous mucosa in the right main bronchus. In the left main bronchus, the mucosal surface appears hyperaemic and irregular, and slight obstruction is observed (Figure 2a). This region in the main bronchus is very delicate and prone to bleeding. Switching to NBI mode allowed for the visualization of vascular alterations. To assist our interpretation of the NBI observation, we refer to the classification system used by Elhefny et al. Pathological areas observed under NBI were categorized based on the vascular characteristics of bronchial lesions into four main types: tortuous blood vessels, abruptly ending blood vessels, dotted blood vessels, and polypoid lesions with obstruction of the bronchial orifice.<sup>14</sup>

Based on this reference, we identified dotted blood vessels (Figure 2), which were selected as the location for biopsy as well as for bronchial brushing. Biopsy specimens showed the proliferation of neoplastic epithelial cells leaning towards the adenocarcinoma subtype. This is supported by similar findings in bronchial brushing (Figure 4). To confirm the findings from the patient's bronchoscopy, a contrast-enhanced chest computed tomography was performed. It reveals a mass with tissue density in the lower left lung lobe, multiple nodules in both lungs, and left pleural effusion (Figure 3).

For perspective, a study by Zhu et al. revealed that dotted blood vessels were mostly found in adenocarcinomas.<sup>15</sup> The complications seen with NBI were similar to those encountered during routine bronchoscopy, including post-procedure hemoptysis, in which our patient recovered spontaneously without any further significant issues. By employing this WLB and NBI tandem technique during the examination, misdiagnosis and excessive disease management can be averted, leading to cost savings and preventing this young patient from undergoing unnecessary diagnostic procedures.

## CONCLUSION

Bronchoscopy is a valuable diagnostic tool in the evaluation of lung malignancy, where timely diagnosis and a multidisciplinary treatment approach are essential for confirming the diagnosis. In this case, bronchoscopy in combination with both techniques, WLB and NBI played a crucial role in achieving a precise diagnosis, offering the benefits of both high sensitivity and minimal invasiveness to the patient.

## CONSENT

Written informed consent was obtained from the patient for the publication of their case details and any accompanying images.

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## CONFLICT OF INTEREST

None.

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