Early Lung Cancer Detection

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KEYWORDS

• Lung cancer • Carcinoma in situ • Early detection • Sputum cytology
• Autofluorescence bronchoscopy • Narrow band imaging • High magnification bronchovideoscope
• Endocytoscopy

KEY POINTS

- New and innovative bronchoscopic methods have been developed for the early diagnosis of lung cancer.
- High-precision bronchoscopic imaging technology, such as optical biopsy, may potentially replace traditional biopsy techniques.
- During screening, the analysis of gene expression and classifier has a strong potential to improve the diagnostic yield of malignant and benign lesions, and reduce the burden of additional invasive diagnostic procedures.

INTRODUCTION

Lung cancer is the leading cause of cancer death worldwide with an overall 5-year survival rate of 18.1%.[1] Despite investigation of lung cancer genetics and improvements in diagnosis, treatment, and care, the lung cancer death rate rose rapidly over several decades and lung cancer overall survival is quite poor. The reason for the poor survival rate and prognosis is that most cases of lung cancer present at an advanced stage with metastatic disease at the time of presentation. However, early-stage lung cancer, central squamous cell carcinoma in situ,[2–4] and adenocarcinoma in situ have a favorable prognosis.[5–7] Screening for the detection of curative disease has been investigated.[8,9] Indeed, screening and detection of early lung cancer is the key to improve survival.[10] The initial screening method for centrally located early lung cancer is sputum cytology. In the 1970s, several series of lung cancer screening trials with sputum cytology were conducted. However, sputum cytology had limited success with low sensitivity.[11,12] Currently, sputum cytology and chest radiography for early lung cancer screening is not recommended, as it does not improve outcome.[13] White light bronchoscopy (WLB) enables direct visual examination of the central airways[14,15]; however, WLB has been shown to have low sensitivity (approximately 30%) for detecting early-stage lung cancer in the central airways.[16] Autofluorescence bronchoscopy (AFB) has improved the detection of preinvasive and malignant endobronchial lesions.[17,18] High-magnification bronchovideoscope (HMB) is an alternative approach that combines both fiberoptic and videobronchoscope technologies to produce ×100 to ×110 magnification of the bronchial wall compared with standard videobronchoscopes.[14] Narrow band imaging (NBI) is useful for detecting the microvascular network of bronchial mucosa (**Fig. 1**). This system uses an RGB (red/green/blue) sequential videoscope system that was changed from the

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Clin Chest Med 39 (2018) 45–55
https://doi.org/10.1016/j.ccm.2017.10.003

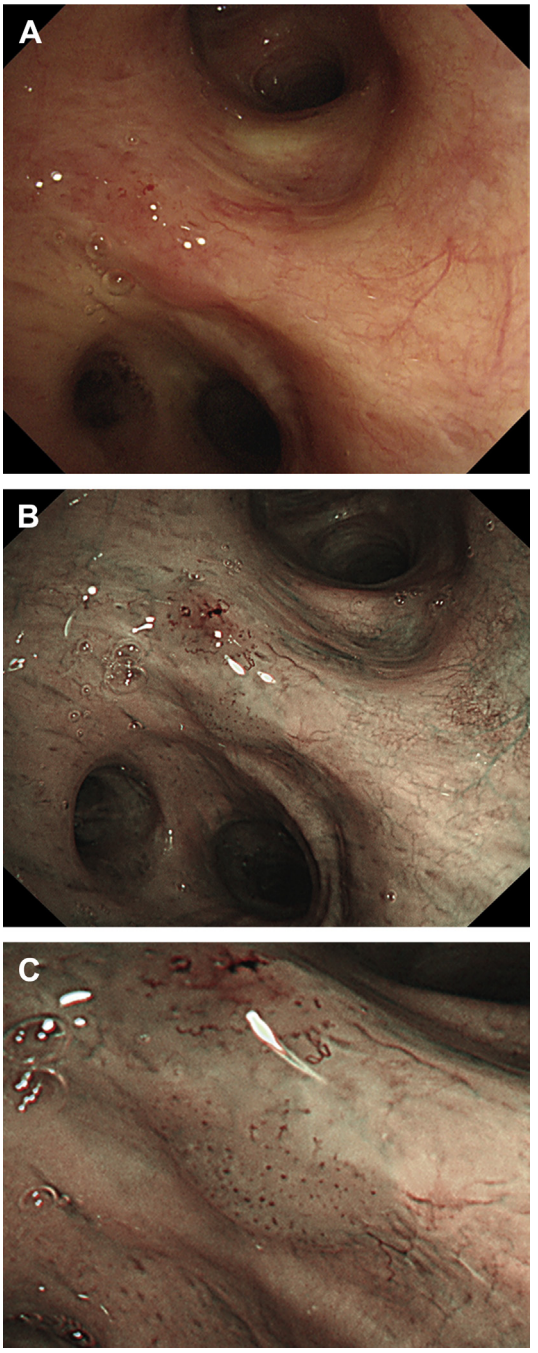

Fig. 1. NBI. Representative case of carcinoma in situ. (*A*) WLB using HD bronchovideoscope. (*B*) NBI of the same area. (*C*) Close view of NBI identified dotted vessel and spiral/screw-type vessels, which was typically observed for carcinoma in situ.

conventional RGB broadband filter to the new NBI filter. The wavelength ranges of the new NBI filter are Blue1: 400 to 430 nm, Blue2: 420 to 470 nm, and Green: 560 to 590 nm. Angiogenic squamous dysplasia tissues have been examined by using a confocal laser scanning microscope equipped with argon-krypton (488 nm) and argon (514 nm) laser sources. NBI enables detection of onset of angiogenesis during multistep carcinogenesis of the lung.[19] These new bronchoscopic modalities have improved screening and detection of early lung cancer of the central airway, especially squamous cell carcinoma in situ. Bronchoscopy is a promising tool not only for detecting early lung cancer visually but also for sampling for tissue diagnosis. In 2015, the new World Health Organization classification of lung adenocarcinoma proposed significant changes with new categories, such as adenocarcinoma in situ (AIS) and minimally invasive adenocarcinoma (MIA).[20] The early lung cancer arising in the peripheral lung fields requires other techniques for early detection. There have been intensive efforts to improve peripheral lung lesion screening, including low-dose helical computed tomography (LDCT). The National Lung Cancer Screening Trial showed a dramatic 20% relative decrease in lung cancer mortality with low-dose CT chest screening in high-risk groups.[21] Screening CT detects smaller peripheral lung lesions, but can cause unexpected anxiety from an incidentally detected nodule.[22] A new bronchoscopic modality using the radial probe endobronchial ultrasound (EBUS) can be used in obtaining a biopsy from early lung cancer arising in the peripheral lung fields.[23] Video-assisted thoracic surgery (VATS)/navigation surgery allows complete resection/diagnosis of nondiagnostic peripheral lung lesions with endobronchial or percutaneous biopsy. Bronchial genomic classifier and exhaled breath condensate are innovative diagnosis techniques with the analysis of gene expression and classifier.

DETECTION OF EARLY SQUAMOUS LUNG CANCER

Sputum Cytology

Sputum cytology is the classic screening method for centrally located early squamous lung cancer.[24] This method is a simple, reliable, cost-effective, and noninvasive procedure for the assessment of benign and malignant pulmonary diseases. However, sputum cytology has had limited success for lung cancer screening with low sensitivity.[11,12] In the 1970s, several series of lung cancer screening trials with sputum cytology were conducted. The National Cancer Institute funded the Cooperative Early Lung Cancer Detection Program designed to assess the screening program of sputum cytology and chest radiographs to reduce lung cancer mortality in male smokers.[25] The program was composed of 3 separate randomized controlled trials. One study