EDITORIAL

NEWER BRONCHOSCOPIC PROCEDURES IN THE DIAGNOSIS OF LUNG CANCER

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Lung cancer kills more men and women in this country than any other malignancy, accounting for nearly one-third of all cancer deaths[1]. The present drive against cigarette smoking in Singapore reflects an international trend to curb this disease. While our local no-smoking campaign and legislation are expected to lower the percentage of adults who smoke cigarettes, the incidence of lung cancer is likely to continue to increase over the next decade because of the extended latent period between commencement of smoking and development of cancer. Ex-smokers and lung cancer patients alike will therefore continue to benefit from early diagnosis and treatment in the coming years.

As in any form of cancer, the only hope for improving lung cancer mortality is to make the diagnosis the moment the disease is suspected while in a limited resectable stage. Interventional Bronchology is a rapidly developing subspecialty of Respiratory Medicine that maximises the use of the flexible fibreoptic bronchoscope (FFB) and rigid bronchoscope in advanced diagnostic and therapeutic techniques. This editorial focuses on newer procedures that improve the use of the FFB in the early diagnosis and staging of lung cancer.

Early lung cancers are difficult to detect with conventional white light bronchoscopy. Woolner et al noted that only 30% of all centrally located squamous cell carcinoma in-situ were visible to an experienced bronchologist[2]. Dysplasias and carcinoma in situ lesions are hard to diagnose even with bronchoscopy because they are only a few millimetres in radius and less than a millimetre in depth. Precancerous lesions and early cancers are also usually asymptomatic. Only 25% of all patients with lung cancer present early enough for curative surgical resection[3]. Survival becomes significantly hampered by the time the patient becomes symptomatic or a lesion appears on the chest X-ray[4]. Thomas et al reported a local recurrence and second primary rate of 3.6% per annum in patients with resected T1N0M0 lung carcinomas[5]. Pastorino et al noted that 17% of completely resected Stage I lung cancers developed a second primary over a 3-year follow-up period[6]. Cortese reported the development of a second primary lung carcinoma at a rate of 5% per annum in patients with radiologically occult, sputum cytology positive tumours who underwent surgical resection[7]. Efforts in the past to diagnose early cancer have been hampered by the need to use photosensitisers such as hematoporphyrin derivative (HpD) or dihematoporphyrin ether (DHE) that are preferentially retained by tumour[8-11]. Hematoporphyrin derivative has an affinity for tumour tissue which emits a fluorescent signal in the red portion of visible light peaking at 630 and 690 nm when excited by a krypton laser or short-arc mercury lamp with a narrow band pass optical interference filter (405 nm) via a thin 400 micron flexible quartz filament. Forty-eight hours following intravenous injection of HpD, FFB is performed and the bronchial tree screened for fluorescence. It is of interest to note that there have been a number of distinct techniques developed to identify the fluorescence induced by the photosensitiser. Tokyo Medical College and the University of California (Santa Barbara) used image intensifiers and Cathode Ray Tube (CRT) displays to locate the green fluorescence from these lesions. The Mayo Clinic system however, used a frequency modulator to produce an audio signal that was directly proportional to the intensity of the fluorescence detected. Using this system, Kato and Cortese studied 11 patients with true occult lung carcinoma who had central airway squamous cell carcinomas which were not visible on chest X-ray[11]. They were able to make the diagnosis in 10 of these patients. Unfortunately, the use of these drugs which required relatively high doses (2-3 mg/kg intravenously), put fluorescence bronchoscopy at a disadvantage because of their dermatological photosensitivity[12]. Recently, Lam et al developed a real time diagnostic imaging system based on natural autofluorescence of early bronchogenic carcinoma and precancerous lesions (Lung Imaging Fluorescence Endoscope or LIFE)[13]. Two image-intensifying CCD (charged couple device) cameras were used to capture the weak, low intensity fluorescence. This system is coupled to the eyepiece of the FFB (Olympus BF20D). The CCD cameras capture simultaneous red (more than 630 nm) and green (480 to 520 nm) images in real time. A helium-cadmium laser which emits blue light at 442nm is delivered through the illumination fibreoptic bundle of the FFB. This blue laser light acts as the excitation light source which induces autofluorescence of the bronchial mucosa without the use of photosensitisers[14]. Precancerous and early carcinomas have an autofluorescent spectrum distinct from normal mucosa when excited by light at 442 nm[15]. A computer controlled image processor creates a real-time colour pseudoimage using the unique fluorescent signals induced by the laser and captured by the CCD camera. Normal mucosa is arbitrarily assigned a green colour while red or brownish red identifies precancerous or early cancer lesions for biopsy on a RGB monitor. The physician is therefore able to determine the area for biopsy more accurately with the diagnosis always based on histopathology. Preliminary work was reported in 94 subjects (mean age 63 years) of whom 41 were volunteers who did not have a history of lung cancer and 53 who had suspected or known carcinoma. Altogether, 328 histology specimens revealed 62 dysplasias (14 mild, 33 moderate, 15 severe), 29 carcinoma in-situ, 64 invasive cancers, and 173 normals. Interestingly, ex-smokers (stopped for more than 10 years) in the volunteer group had 13% carcinoma in-situ and 31% moderate or severe dysplasias. Of 64 patients known to have lung carcinoma, 15% had one or more areas of carcinoma in-situ in addition to the grossly visible invasive cancer. Overall,

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the LIFE diagnostic imaging system had a 72.5% sensitivity and 94% specificity representing a 50% improvement over white light bronchoscopy in detecting carcinoma in-situ or dysplasia[13]. Its main limitation is the range of the FFB which cannot access the outer third of the lung and identify early peripheral lesions. A multicentre trial is presently underway to establish the value and place this procedure has within the context of current accepted practice.

While conventional bronchoscopes are limited by a sizeable outer diameter (OD) of at least 4.9mm, an ultrathin bronchoscope has been developed with an OD of only 1.8mm[16]. Although this FFB has no device controls, it is able to fit through a conventional 2.6mm FFB working channel and access bronchioles down to 1mm in diameter. Transbronchial or open biopsies confirm histological diagnosis of peripheral tumours using this technique. While its clinical application is not clearly defined, wider usage is likely with greater acceptance of laser detection systems like LIFE.

Endobronchial sonography utilises ultrasound to diagnose submucosal and extrabronchial tumours and lymph nodes adjacent to the tracheobronchial tree[17,18]. It has the potential of becoming a valuable adjunct to currently available techniques for diagnosis and staging of bronchogenic carcinoma. This instrument comprises a transbronchoscopic ultrasonic probe, echographic camera, echoenhancement and histogram capability, and a video monitor to view the endobronchial image. Researchers have been able to differentiate echo poor early lung carcinoma and highly echogenic normal bronchial wall and parenchyma[19]. They have also documented tumour invasion of adjacent vessels and extent of endobronchial obstruction. The shortcomings of this technique however, include difficulty in maintaining a bronchial mucosa-fluid interphase making parenchymal lung tumours difficult to diagnose. A large probe head size (6.3mm) also limits examination to the lobar bronchi.

Finally, transbronchial needle aspiration (TBNA) has played a significant role in the staging and diagnosis of both central and peripheral lung carcinomas[20-22]. There are two types of transbronchial needles (TBN) currently available. A 22 gauge retractable cytology needle with a removable stylet has been designed for both central and peripheral lesions, while a 19 gauge dedicated histology needle has been developed for central lesions[23]. The "needle brush" is the latest derivative in this line of retractable transbronchial instruments. Wang et al noted a higher yield than forceps biopsy and brush for malignant nodules[24].

In conclusion, the subspecialty of interventional bronchology has evolved into a major and progressive field in pulmonary medicine. While these newer procedures represent the cutting edge in the early diagnosis and staging of lung cancer, their future role remains to be defined. The challenge we presently face in Singapore is to establish the value and specific indications for these new techniques and integrate it with currently accepted methods of diagnosis in a cost effective fashion that will complement the current no-smoking movement in our national initiative against lung cancer.

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