

Developments in Diagnostic and Interventional Procedures in Lung Cancer



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Short Communication

Worldwide around 1.8 million cases of lung cancer are diagnosed each year [1]. The overall 5year survival is poor at around 4% mainly due to the fact that only approximately 15% of the cases are diagnosed with the early stages of lung cancer [1]. The investigational procedures form an important part of staging and diagnosing lung cancer with timely investigations resulting in better outcomes [2]. For example, the Lung-BOOST trial showed that rapid diagnostic pathway shortened time from the referral to diagnosis by 15 days, which resulted in an increase by 191 days of the median survival [3]. The initial imaging tests such as a Computed Tomography (CT) of the thorax and a Positron Emission Tomography (PET) scan allow to determine staging and to guide diagnostic tests. The most important aspect of these tests is to determine the nodal staging and the presence of distant metastases. The PET scan has been shown to have sensitivity of 77.4% and specificity of 90.1% for detecting mediastinal lymph nodes involvement [4]. Nevertheless, usually further evaluation and biopsy of the mediastinal lymph nodes is of importance in managing patients with lung cancer, which nowadays is undertaken using Endobronchial Ultrasound (EBUS) or Endoscopic Ultrasound (EUS) [5]. EBUS similarly to the flexible fiberoptic bronchoscopy are composed of glass fibers, which transmit the light and the images and a working channel allowing for the suctioning, and introduction of the biopsy instruments but have 35° rather than direct visualization angle. An EBUS has an ultrasound probe, which allows real time visualization and biopsy of the lymph nodes using a 21 or 22-gauge needle with recommendation that each lymph node should be sampled 1 to 3 times and on each occasion 10 to 15 needle passes should be undertaken [6]. The current guidelines suggest that 40 to 50 procedures are

required to be undertaken before proficiency in EBUS can be achieved with simulation-based training similarly to learning bronchoscopy showing to speed up learning [7-9]. Combining EBUS, which can access and sample the ATS stations 2, 3, 4, 7, 10, 11 with the EUS which examines stations 2L, 4L, 7, 8, 9 allows for more comprehensive assessment of the mediastinal lymph nodes with reported sensitivity of 85% for detection of cancer which was similar to that of mediastinoscopy [10,11]. Mediastinoscopy, however is still perceived as the gold standard and in cases where mediastinal lymph node sampling with EBUS and EUS was negative for cancer, mediastinoscopy was reported to increase the sensitivity by 9% [11]. Therefore, in patients with suspicion for mediastinal lymph nodes involvement and who are candidates for radical treatment in the context of negative EBUS and EUS sampling mediastinoscopy should be considered as it may provide additional sensitivity and diagnostic yield.

Bronchoscopy remains an important procedure when assessing patients with lung cancer with over 500,000 procedures being undertaken yearly in the USA [8-12]. Bronchoscopy provides a very good tool for histological confirmation of endobronchial lung cancer. Many units now combine EBUS, EUS and bronchoscopy within one setting as this allows for the best flexibility and diagnostic strategies. In addition to the white light bronchoscopy, technology allows for an auto-fluorescence bronchoscopy that uses differential fluorescence emission, which distinguishes between the normal and abnormal mucosa, which may be of relevance in detecting very early neoplastic lesions. In the context of diagnosing peripheral lung cancer, which is not visible endo-bronchially when using fiberoptic bronchoscopy there are other diagnostic options such as a CT guided biopsy and some newer bronchoscopic techniques. One

of them is the radial EBUS, which is a flexible bronchoscope that has an ultrasound probe allowing for a 360° ultrasound visualisation of peripheral solid lung lesions and biopsy [13]. The diagnostic yield from the radial EBUS was reported at 78% for the lesions greater than 20mm and that of 56% for the lesions less than 2cm [14,15]. Another newer technique that allows to sample peripheral lesions is the navigational bronchoscopy [16]. The virtual bronchoscopy is a type of navigational bronchoscopy where the CT images are reconstructed to form a detailed bronchial tree in order to use simulation bronchoscopy as a guide and when combined with the radial EBUS this technique was shown to provide a 94.4% diagnostic yield [16-18]. Another technique namely electromagnetic navigational bronchoscopy uses a flexible bronchoscope and a guide wire with a sensor, with the electromagnetic field being used to track it into the lung lesion applying processed CT images and subsequently allowing for the sampling of the lesion [16-18]. A recent large prospective study reported diagnostic yield of the electromagnetic navigational bronchoscopy at 73% [19]. In addition, as a result of technological developments there are some newer techniques that have been introduced such as the hybrid EBUS or the thin convex probe EBUS, which have improved angle of view and the scope flexibility with resulting benefits of endo-bronchial manoeuvrability and potentially higher diagnostic yields [9].

A proportion of patients with lung cancer develop pleural effusion, which would require formal assessment and if causing symptoms therapeutic interventions. Thoracic ultrasound has become an important technique for imaging and guiding of the pleural procedures as it has shown to improve their outcomes and to reduce their complications such as pneumothorax by around 19% [20-22]. When diagnostic pleural biopsy is required a local anaesthetic thoracoscopy forms an important procedural option with relatively low levels of complications [23,24]. The procedure involves an introduction of most commonly a rigid thoracoscope, although semi-rigid scopes are also available, into the pleural cavity and examination and sampling of the pleura [25,26]. The diagnostic sensitivity of the rigid thoracoscopy was reported at 94.1% with slightly lower figures for the semi-rigid thoracoscopy [27]. In addition, thoracoscopy allows for the pleural fluid drainage and talc pleurodesis. A newer technique auto-fluorescence thoracoscopy has been shown to have 100% sensitivity for detecting abnormal pleural lesions [28]. In some patients thoracoscopy may not be appropriate and alternative options such as CT guided biopsy of the pleura have been shown to have overall sensitivity of 87.5% [25-27].

Many patients may require diagnostic or therapeutic procedures such as ultrasound guided thoracentesis, chest drain or indwelling pleural catheter insertion [29,30]. The decision on which procedures to undertake will depend on the patients' symptoms, prognosis and preference with studies suggesting cost benefits and symptom improvement in 95% of cases for indwelling pleural catheter and perhaps better effectiveness of thoracoscopy when managing malignant pleural

effusion [30,31]. An insertion of indwelling pleural catheter was shown to have better pleural effusion control of 82% at 30 days compared to that of 52% for chest drain and pleurodesis but no difference in controlling breathless [32-34]. However, patients who had indwelling pleural catheter compared to those who had chest drain insertion and pleurodesis were reported to have a shorter hospital stay and needed fewer number of subsequent pleural procedures [35]. In addition, in a proportion of patients with indwelling pleural catheter a spontaneous pleurodesis may occur. Moreover, there is increasing evidence that talc pleurodesis through the indwelling pleural catheter may result in a higher pleurodesis rates of 43% compared to that of 23% observed in patients who had indwelling pleural catheter drainage of the fluid alone [35]. Similarly, there are reports to suggest that the insertion of an indwelling pleural catheter at the end of the thoracoscopy procedure is safe and may reduce the hospital length of stay [36].

There is a range of possible interventional bronchoscopic techniques including Nd-YAG laser, plasma argon coagulator, cryotherapy, brachytherapy or photodynamic therapy, which could be applied mainly to manage neoplastic bronchial obstruction [37]. Similarly, bronchoscopy can be used for the insertion of stents, which main function is to maintain bronchial patency. These therapeutic techniques are of relevance in the context of the symptomatic bronchial lumen obstructing or occluding lung cancer. A recent report revealed that therapeutic bronchoscopy improved health related quality of life by around 5.8% per day of life representing most likely the aggregate of multimodality treatments [38]. An earlier study reported that laser resection of central obstructing lesion improved survival by showing 40% mortality at 7 months and 72% at 1 year compared to historical data of 76% mortality at 4 months and 100% at 7 months [39]. Another study reported better survival following Nd-Yag laser and radiotherapy of 267 days compared to historical survival of 150 days for the radiotherapy alone [40]. From the diagnostic aspects, it is therefore important to be aware that for the patients presenting with dyspnoea as a result of central airway obstruction interventional bronchoscopy if performed earlier has better effects on the health-related quality of life and improvement in breathlessness.

In conclusion, over the recent years there have been technological improvements resulting in new diagnostic and interventional procedures. These novel techniques together with the already well-established modalities are becoming important part of diagnostic and therapeutic options for patients with lung cancer. Therefore, patients with lung cancer should have access to these bronchoscopic and pleural techniques. Moreover, physicians should be aware of their indications and applications.

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