Staging and Investigations of Lung Cancer

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Abstract

Lung cancer is a common malignancy. Investigation and staging of lung cancer form an important aspect of managing this disease. The initial assessment usually requires imaging such as a chest radiograph, computed tomography (CT) and Positron Emission Tomography (PET) CT. These imaging techniques aid in the staging of lung cancer and targeting the biopsy sites for histological diagnosis. A CT guided biopsy, radial endobronchial ultrasound (EBUS) or navigational bronchoscopy may be used for sampling more peripheral lesions. Flexible bronchoscopy may be used for endobronchial lesions biopsy. EBUS and endoscopic ultrasound or surgical mediastinoscopy are used for the accurate mediastinal lymph node staging. There are designated pathways, which allow for accurate and timely investigations of lung cancer. Due to the complexity of the investigations of lung cancer, a multidisciplinary approach is required in order to provide the best outcomes for the patients.

Introduction

There are around 1.8 million lung cancer cases diagnosed worldwide each year including around 39,000 cases of lung cancer in the UK [1, 2]. The staging of lung cancer affects significantly the prognosis as well as the initial investigational pathways. In England,

according to the Office for National Statistic, the average 5 year survival for lung cancer is 12.9% and 17.7% for men and women respectively. However patients diagnosed with the advanced disease have a survival at 5 years in the range of 4% [1, 2]. There is data to suggest that the average time from the presentation and the diagnosis of lung cancer is around 3 months but for the patients diagnosed with the early stages of the disease it may be longer at approximately 5 months [3]. There is also evidence to suggest that there is an element of patients' reluctance to seek medical review with studies revealing a median delay of 99 days from the onset of the symptoms and the patients seeking medical opinion [4]. This can be improved by designated awareness campaigns, which showed increase in consultation for new respiratory symptoms [5].

The majority of patients with lung cancer would be referred to a respiratory fast track lung cancer clinic allowing for rapid investigations and diagnosis [6]. The investigational pathway for lung cancer is based on undertaking tests that involve the least risk to the patient and provide information on both the histological diagnosis and the staging [7]. There is evidence that a rapid diagnostic pathway, which results in a decreased time from the referral to the diagnosis can improve survival [7]. The initial investigational tools include imaging such as a chest radiograph followed by a computed tomography (CT) of the thorax. The staging CT scan should include imaging of the liver, the adrenals and the lower neck as this would allow to assess for any distal metastases. Occasionally, other modalities such as an ultrasound or a magnetic resonance imaging (MRI) may be required to assess the chest wall involvement or better visualisation of the superior sulcus neoplasm [8]. The next stage of investigations would involve if appropriate a Positron Emission Tomography (PET) scan, which can provide

additional information with regards to distal metastases and staging of the mediastinal and hilar lymph nodes where it has sensitivity of 77% and specificity of 91% [9]. This is of particular importance for patients considered for radical treatment. Brain imaging in the form of a CT or ideally an MRI may be required in patients with stage I disease who have neurological symptoms or patients with stage II and IIIA disease who are considered for treatment with curative intention. Patients who have neurological symptoms especially those suggestive of a cord compression, which is an oncological emergency, would also require brain and spine MRI.

PET scan allows for a non-invasive imaging of the mediastinal lymph node. Historically, mediastinoscopy has been regarded as the gold standard for histological staging with diagnostic accuracy of up to 96% for mediastinal lymph nodes stations 1, 2, 3, 4, 7 [10]. In the recent years, Endobronchial Ultrasound (EBUS) and Endoscopic Ultrasound (EUS) have become more widely used for the mediastinal lymph nodes staging. Both EBUS and EUS are relatively safe procedures with reported serious complications of 0.05% to 1.43% and morbidity of 0.6% to 1.1% [11, 12]. EBUS has an ultrasound probe usually a 7.5 MHz transducer, which allows the real time visualization and biopsy of the lymph nodes of the ATS stations 2, 3, 4, 7, 10, 11 [1, 2]. The EUS allows for examination of stations 2L, 4L, 7, 8, 9 [12]. A meta-analysis review confirmed a sensitivity of 0.90 (CI 0.84 to 0.96) for EBUS [13]. Combined EBUS and EUS was reported to have 85% sensitivity for detection of cancer, which was similar to that for mediastinoscopy [10]. However, in cases where EBUS and EUS node sampling showed no evidence of cancer the addition of mediastinoscopy increased sensitivity

by 9% [10]. For this reason, the best approach to staging mediastinal lymph nodes would require access to the surgical mediastinoscopy as well as the EBUS and the EUS. EBUS and EUS sampling of mediastinal lymph nodes should follow higher nodal stations first in order to reduce the risk of contamination, which may result in upstaging of the nodal disease. These investigations are of help when assessing for N1, N2 and N3 disease. In addition, the use of ultrasound can guide sampling of the cervical, axillary lymph nodes or liver metastases. The EUS may be able to provide histological diagnosis from adrenal metastases again providing important staging and diagnostic information.

The diagnosis of endobronchial cancer relies on the use of fibreoptic bronchoscopy, which allows for histological analysis. The EBUS can be utilised to sample lung mass lesions which are outside of the, but within proximity to the bronchi and can be visualised using the ultrasound probe. Peripheral lung lesions can be sampled using a trans-thoracic CT guided biopsy which has accuracy sensitivity of over 90% [14]. The recognised complications of CT guided biopsy include pulmonary haemorrhage which can occur in upto 16.9% of procedures and pneumothorax [14]. In cases where CT guided biopsy may not be technically possible, there are other techniques that may be applied such as navigational bronchoscopy or radial EBUS. The diagnostic yield of navigational bronchoscopy was reported at 73% [15]. Many patients at high risk group are offered to be part of lung cancer screening, which was shown to reduce lung cancer mortality [16]. For example, a randomised controlled screening trial revealed a 26% reduction in lung cancer deaths in men and 39% for women [17]. In the screening group, 50% of cancers were at an early stage [17]. Patients diagnosed at an earlier

stage of the disease would require a formal fitness assessment such as lung function before radical treatment including surgery could be offered. The FEV_1 and transfer factor have been shown to be an independent predictive factor for estimating mortality and morbidity [18]. Fitness for surgery in borderline cases would also require a cardio pulmonary exercise testing [18]. If patients with the early stages of lung cancer are found not be fit for surgery an alternative can be considered such as radiotherapy including a stereotactic ablative radiotherapy (SABR), intensity-modulated radiotherapy (IMRT) or image-guided radiotherapy.

In conclusion, timely and accurate investigations of patients with lung cancer allow for a precise staging of the disease and histological sampling. There are now a number of new techniques such as navigational bronchoscopy that allow for sampling peripheral lesions. Similarly, EBUS and EUS as well as the mediastinoscopy allow for an accurate mediastinal lymph nodes staging, which has a significant effect on the therapeutic options. The advances in imaging such as PET CT scanning, provided more accurate non-invasive mediastinal staging and detection of the distal metastases. Therefore, access to the whole range of investigational procedures is paramount in successfully diagnosing and staging of lung cancer. This is best achieved through a multidisciplinary team approach.

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