Endobronchial ultrasound in diagnosis of lung cancer

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There are around 39,000 cases of lung cancer in the UK with the average 5 year survival for lung cancer is 12.9% and 17.7% for men and women respectively[1]. The investigations of patients with a suspected lung cancer have become more complex. The assessment of patients with a suspected lung cancer should aim to deliver histological confirmation and staging in a timely manner[2]. The initial investigational imaging approach usually includes a chest radiograph and a computed tomography (CT) of the thorax. A Positron Emission Tomography (PET) scan has an important role as it provides more accurate staging information. The PET scan is of a particular importance for staging of the mediastinal and hilar lymph nodes where it has sensitivity of 77% and specificity of 91%[3]. Nevertheless, there is still a requirement for sampling of the mediastinal and hilar nodes as this allows to provide histological information as well as more accurate staging of lung cancer. This in turn assists in making decisions regarding the most appropriate treatment options. Historically, sampling of the mediastinal lymph nodes required a surgical mediastinoscopy[4]. However, since the development of an endobronchial ultrasound (EBUS) a minimally invasive approach is possible for sampling of the mediastinal lymph nodes. For this reason, EBUS has become an important investigational tool for diagnosing and staging of lung cancer[5]. In addition, EBUS can provide histological sampling of mediastinal lymph nodes for other than cancer

conditions such as sarcoid, haematological disorders as well as providing microbiology sampling. This report describes experience of the usage of endobronchial ultrasound in sampling of the mediastinal lymph nodes including the range of diagnostic conditions and the diagnostic yield.

Methods

A retrospective analysis of the EBUS procedures performed between January 2019 and January 2025 were undertaken. The data reviewed included the patients' demographics, size of the mediastinal lymph nodes, stations of the mediastinal lymph nodes sampled, diagnostic yield as well as correlation with the radiological CT or PET scan findings.

The EBUS procedures were undertaken in the endoscopy department. The procedures were undertaken using the Olympus (Olympus Japan) system. The biopsy procedures were undertaken using 21G Olympus needle, or 21G Vizishot2 Olympus needle. The procedures were undertaken using local anaesthetic 1% lidocaine to the vocal cords and the bronchial tree. All patients received sedation using Fentanyl (dose ranging from 25mcg to 100 mcg) and Midazolam (dose ranging from 1 mg to 5 mg). The EBUS scope was introduced through the mouth and the mouth guard. The local anaesthetic lidocaine 1% was applied to the vocal cords and the bronchial tree. The mediastinal lymph nodes were localised with the endobronchial ultrasound. Transbronchial needle biopsies of the mediastinal lymph nodes were undertaken. Each node was sampled between 2 to 4 times. During each sampling a minimum of 15 needle passes were undertaken. The procedure was undertaken by two

experienced operators. One of the operators was driving the scope and locating the mediastinal lymph nodes. The second operator was undertaking sampling ('needling') of the lymph node. The procedure was undertaken with the assistance of two nurses. One nurse was manging the patients' observations, airway protection, suctioning and communication. The second nurse was handling the needles, preparing and processing the histological samples. The samples were processed through histopathology and if appropriate microbiology laboratories

Results

Between January 2019 and January 2025, 401 EBUS procedures were undertaken. The mean age of the patients was 68.5 years (range 28 years to 88 years) of which 169 were female. In 192 patients, lymph nodes were size was less than 2 cm and marked as small lymph nodes with the smallest sampled lymph node having size of 6 mm. In the rest of the patients, the sampled lymph nodes were size 2 cm or above with the largest being 6 cm.

The diagnostic distribution of the EBUS findings included 107 cases of adenocarcinoma of the lung origin, 61 cases of squamous cell lung cancer, 51 cases of sarcoidosis, 36 cases of small cell lung cancer, 28 cases of non-small cell lung cancer, 25 cases of other types of cancer, 7 cases of neuroendocrine cancer, 5 cases of large cell cancer, 4 cases of adenocarcinoma other than lung, 4 cases of inflammation and 3 cases of infection. In 27 cases sampling revealed a normal lymph node tissue. In 5 cases a scanty sample were obtained and in 11 cases no biopsies were undertaken. There were 20 confirmed true negative lymph node

biopsies in patients with cancer and 7 false negative cases were cancer was not detected during the EBUS lymph node sampling in patients with subsequently confirmed cancer in mediastinal or hilar lymph nodes.

Amongst the 25 cases with other types of cancer; 3 had breast cancer, 5 cases had poorly differentiated cancer, 5 cases had lymphoproliferative disorders including lymphoma, 1 case had malignant mesothelioma, 2 cases had cancer of unknown primary, 1 case had prostate cancer, 1 case had adenoid cystic cancer, 1 case had transitional cell cancer, 1 case melanoma, 1 case urothelial cancer, 1 case had sarcomatoid cancer and 1 case of pancreatic cancer. In this group also were included 1 case of fibrous tissue and 1 case of duplication cyst.

Malignancy was the most common diagnosis observed in 300 cases. Of those 7 cases were false negative where the lymph node biopsy did not reveal cancer in the presence of confirmed cancer. This gives a false negative rate at 2.3%. Therefore, the sensitivity of EBUS for diagnosis of malignant lymph nodes was 97.7%. In 11 cases biopsy was not undertaken. The reason for this were related to the lack of accessibility to the lymph nodes due to the surrounding structures or blood vessels. In 5 cases, the samples collected were scanty and did not allow for diagnosis. In 27 cases the samples were representative of a lymph node with no evidence of any other pathology i.e. the lymph nodes were not pathological.

The lymph node station sampled were: subcarinal (station 7) lymph node in 147 cases, right paratracheal (4 R) station in 142 cases, right hilar nodes (11 R) station in 71 cases, left

paratracheal (4 L) station in 50 cases, left hilar (11 L) in 50 cases, 10 R station in 43 cases, 10 L station in 9 cases. In 18 cases a pulmonary mass was biopsied.

PET scan was available in 247 patients with the standardised uptake value (SUV max) measurements varying between 2.6 and 27.7.

Discussion

In this report we describe our retrospective data on the outcomes of the endobronchial procedures. The majority of patients undergoing endobronchial ultrasound procedure were diagnosed with lung cancer. The most common histological findings were adenocarcinoma of lung origin, squamous small cell cancer of the lungs, small cell lung cancer and non small cell lung cancer. Lymphoma was diagnosed in a small proportion of patients. This is related to the technical issues in relation of diagnosing of haematological malignancies, which require larger size of the lymphoid tissue or ideally the whole of the lymph node. A small proportion of patients had other conditions diagnosed such as sarcoidosis or reactive lymph nodes. In a small number of patients mediastinal sampling was perform for a microbiological analysis and diagnosis of infective conditions. In a few patients EBUS transbronchial fine needle aspiration was undertaken to sample a lung mass. Overall, the diagnostic yield from the EBUS sampling of the mediastinal lymph nodes was 97.7%, which is similar to that reported in the literature[9].

Historically, surgical mediastinoscopy has been used to sample and stage of the American Thoracic Society mediastinal lymph node stations 1, 2, 3, 4, 7[4,5]. Mediastinal lymph nodes can

be blindly sampled, without the use of an endobronchial ultrasound, using a flexible bronchoscopy scope and a trans bronchial fine needle. However, this approach has a relatively low diagnostic yield between 40 to 75%[4,5]. In contrast, EBUS allows for examination and sampling under the ultrasound visualisation of the American Thoracic Society mediastinal lymph node stations 2, 3, 4, 7, 10, 11[4,5]. In this series the most commonly sampled lymph nodes were from the stations 4 and 7 as well as the hilar nodes. In a small proportion of patients, the sampling of a lung mass was undertaken. EBUS can be performed under the general anaesthesia or undertaken under an awake sedation and local anaesthesia. In fact, all our EBUS procedures were undertaken under local anaesthesia and sedation. EBUS is a safe procedure which has mainly self-limiting complications such as sore throat, mild hypoxia, tachycardia, cough and pyrexia and relatively uncommon serious complications such as pneumothorax reported in 0.05% to 1.43%[6]. In our series the commonest complications were mild hypoxia during the procedure, which was corrected with inhaled oxygen supplementation, transient tachycardia, sore throat post procedure, minimal self-limiting endobronchial bleeding related to trans bronchial fine needle aspiration of the lymph nodes and occasional minor respiratory tract infection.

Computed Tomography (CT) of the thorax and a Positron Emission Tomography (PET) scanning are very helpful for imaging of the mediastinal nodes. They both allow for a non-invasive staging of the mediastinal lymph node, with the PET scan providing a more accurate information. PET scan compared to the CT is more accurate in assessing the mediastinal lymph nodes involvement with sensitivity and specificity of 77.4% and 90.1% respectively[7]. The PET scan may also be helpful in diagnosing distal metastases. However, there are

limitation of the PET scan as it may not necessarily distinguish between neoplastic, inflammatory or infective pathology. Therefore, EBUS has acquired an important role in staging and sampling of the mediastinal lymph nodes. Surgical mediastinoscopy is still regarded as the gold standard for histological staging, with reported diagnostic yield of around 96%[8,9]. It requires a general anaesthetic and is undertaken by a thoracic surgeon. The less invasive, or minimally invasive sampling of the mediastinal lymph nodes can be undertaken using an endobronchial ultrasound (EBUS) and/or endoscopic ultrasound (EUS). EBUS and EUS are safe procedures with recognised low rates of serious complications of 0.05% to 1.43% and morbidity rates between 0.6% to 1.1%[10]. 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[11,12]. The EUS allows for examination of stations 2L, 4L, 7, 8, 9[10]. A meta-analysis review confirmed EBUS sensitivity of 90%[13]. In another study diagnostic accuracy of EBUS was reported at 98% compared to that of 60.8% for the CT and 72.5% for the PET scan[14]. This is similar to our findings of EBUS sensitivity of 97.7%.

In conclusion, our report showed that sampling of mediastinal and hilar lymph nodes using EBUS provides a high diagnostic yield. The most common diagnosis obtained was metastatic lung cancer. It is therefore recognised that EBUS should form an important part of investigation and staging of lung cancer. EBUS allows to sample a wide range of different lymph node samples and when performed by an experienced operators provides high diagnostic yields.

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