450. Progress in endoscopy for lung cancer

P4399
Analyzing images of endobronchial ultrasonography (EBUS) using histogram to assist in the diagnosis of lung cancer
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Background: Recently, brushing and biopsy techniques of EBUS using a Guide Sheath (EBUS-GS) is available for the diagnosis of lung cancer. Obstetrics and gynecology fields have previously reported that quantification of sonographic echogenicity with histogram were useful for the diagnoses of tissue.

Aim: To evaluate whether histogram data collected from EBUS-GS images can contribute to the diagnosis of lung cancer or not.

Methods: Fifty clear EBUS images (25 lung cancer and 25 inflammatory disease) were included in this study. The region of interest (ROI), was set within a 5mm radius from the EBUS probe with 400 pixels (20×20). Histograms were created and compared using imageJ software, with a width of the histogram: (maximum – minimum gray scale)/256 (full gray scale)×100 (%), height of the histogram: (maximum pixel counts), and the standard deviation of the histogram.

Results: The diagnosis yield by the width of the histogram were sensitivity of 84%, specificity of 88%, and positive predictive value of 87% when the cut-off level was 22 for lung cancer. Standard deviation of histograms also contribute to diagnosis of lung cancer, sensitivity of 80%, specificity of 88%, and positive predictive value of 87% when the cut-off level was 10.7. Height of the histogram was not useful due to low sensitivity.

Conclusion: The width and standard deviation of EBUS image histograms were useful in differentiating lung cancer from inflammatory lesion.

P4400
Aberrant methylation in lung cancer identified by EBUS-TBNA as a marker of advanced staging
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Introduction: Aberrant methylation of DNA results in gene silencing and is frequently observed in tumours from lung cancer patients. Methylation aberrancies can also be detected in lymph nodes, but it is unknown if the assessment of the nodal methylation status may identify more advanced stages of the disease.

Objective: To determine the relationship between the methylation status of 5 genes in metastatic lymph node and tumours samples obtained by EBUS-TBNA and the presence of an advanced stage of lung cancer.

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Methods: Nodal and tumour samples positive for lung cancer were obtained with EBUS-TBNA. The methylation status of DAPK, p16, RASSF1, APC and CDH13 genes was determined by methylation-sensitive high resolution melting.

Results: 23 samples were analysed, 15 (67.4%) nodal and 8 (32.6%) tumour samples were obtained. If the distinction of the normal tissue and tumour tissue is possible and applies it to an endoscopic diagnosis by measuring lungs tumor, normal lung, IB value of the pathology organization diagnosis and invasive level of the tumor may be enabled by bronchus echo endoscopy examination.

P4403 Diagnostic yield, clinical impact and cost aspect of EBUS-TBNA in mediastinal staging in lung cancer patients

Background: In lung cancer minimally invasive staging of the mediastinum with endobronchial ultrasonography transbronchial needle aspiration (EBUS-TBNA) has become an important alternative to the gold standard of mediastinoscopy.

Aim: First: To determine the diagnostic yield of EBUS-TBNA and calculate the reduction in number of mediastinoscopies that can be achieved when this technique is used as initial modality for mediastinal staging in lung cancer. Second: Calculate the reduction in health care costs when EBUS-TBNA is used in this setting.

Methods: In a retrospective cohort study all patients in our hospital in whom EBUS-TBNA was performed for mediastinal staging in lung cancer from September 2008 until January 2011 were identified and the results of EBUS-TBNA were analysed. If metastatic tumour cells were found there was no indication for additional mediastinoscopy. Diagnostic yield of EBUS-TBNA and the number of mediastinoscopies that were avoided were calculated, as well as the achieved cost reduction.

Results: EBUS-TBNA was performed on 77 patients for mediastinal staging: 47 male and 30 female, average age 62.1 years (extremes 39-81). In 51% of patients (39/77) mediastinal lymph node metastasis were found and mediastinoscopy could be avoided. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were 91%, 100%, 100% and 89% respectively.

The achieved cost reduction was €241 per patient (31%).

Conclusion: Mediastinoscopy can be avoided in more than 50% of lung cancer patients when EBUS-TBNA is used as initial staging modality for mediastinal staging, leading to a significant reduction of health care costs.

P4404 Adequacy of endobronchial ultrasound tranbronchial needle aspiration samples in the sub-typing of non small cell lung cancer

Introduction: The histological sub-typing of non small cell lung cancer (NSCLC) has become increasingly important due to advances in systemic therapy. There are now important differences in the treatment of squamous and non-squamous cancers. Non-squamous cancers (particularly adenocarcinomas) are also suitable for targeted therapy if the epidermal growth factor receptor (EGFR) mutation status is present.

Background: Diagnosis is frequently made by fine needle aspiration from lymph node metastases. The EGFR testing was requested in 36 patients. The sample was sufficient to allow testing in 32 patients (88.8%).

Conclusion: This data shows that EBUS TBNA samples are of adequate size to allow the determination of NSCLC sub-type and EGFR mutation status provided appropriate laboratory techniques are used.

P4405 How do cytology samples compare with histology specimens when used for EGFR testing in patients with NSCLC?

Background: With the evolution of individualized treatment strategies in non small cell lung cancer (NSCLC), it is becoming increasingly important to obtain adequate tissue for accurate pathologic subtyping and molecular testing. In most
cases diagnosis and staging is done using small biopsies or cytology specimens obtained by minimally invasive techniques.

Aim: To compare the adequacy of cytology and histology samples used for epidermal growth factor receptor (EGFR) mutation screening.

Methods: Retrospective study of 135 consecutive samples obtained from NSCLC patients between Jan 2010 and Dec 2011.

Results: Of the 135 samples sent for EGFR testing, 13 were positive, 115 were negative, and 7 were considered inadequate or failed molecular testing. 106 had adenocarcinoma, 11 adenosquamous, 13 NSCLC-NOS (not otherwise specified), 4 squamous, and 1 small cell. Positive EGFR was noted in 4 cytology and 9 histology samples (p=0.27).

Cytology samples include 46 endobronchial ultrasound (EBUS) guided fine needle aspiration (FNA), 8 pleural fluid, 7 ultrasound guided or superficial FNAs from lymph nodes or masses, 1 transbronchial (mini-probe), 2 bronchial washings and 2 brush biopsies. Histology biopsies include 29 endobronchial biopsies, 19 CT guided lung biopsies, 8 thorascopic and 1 ultrasound guided pleural biopsies, 1 renal biopsy, and 11 surgical excision samples (bone, brain, lymph node and groin mass).

Conclusions: Fluoroscopy guided ultrathin bronchoscope obtains specific diagnosis in 43% of the patients, 85% of them with endobronchial abnormality. In 42% of patients with an endobronchial abnormality we were not able to reach a diagnosis. In 37% (11/30) of patients we could not see any endobronchial abnormality. Dedicated needles and more accurate methods to locate and reach the PPL are needed.

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in parenchymal haemorrhage, out of which 9/102 (7.8%) were visually classed as substantial.

None of the patients required insertion of chest drain or transfusion, although 6 patients were kept in the hospital for observation (maximum stay 4 days).

Conclusion: We have shown that CT guided biopsy is a safe procedure and can be carried out without major complications in a DGH. In our sample the complication rate (usually described as 2% patients requiring chest drain insertion) was very low. We are at present in the process of re-writing hospital guidelines regarding post procedure observation and patient guidelines.

P4410

EUS-FNA for mediastinal lesions of unknown aetiology: A 4-year experience from a single centre
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Aim: Endoscopic ultrasound guided fine needle aspiration (EUS-FNA) allows access to the posterior mediastinum and tissue acquisition under real-time ultrasound guidance through the oesophageal wall. The aim of this study was to report the experience of mediastinal EUS-FNA in a large UK tertiary centre.

Methods: The study included all patients who underwent mediastinal EUS-FNA in our institution from January 2008 to December 2011. Patient and procedure related data were collected from endoscopy reports. Cytology and microbiology culture reports were compared to the final clinical diagnoses made during the follow-up. We calculated sensitivity, specificity, positive and negative predictive value (PPV, NPV) of mediastinal EUS-FNA for most common conditions.

Results: 195 patients (n=195, males 65%, mean age 58.6) underwent mediastinal EUS-FNA during the study period. Mean size of the lesions was 15.82mm (range 3.9-43) in short axis and 28.23mm (range 8-60) in long axis. Sub-carinal lymph nodes (n=116) were the common (145/195, 73.8%) target lesion.

Table 1. Overall and condition specific results of mediastinal EUS-FNA

<table>
<thead>
<tr>
<th>Condition</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignancy</td>
<td>82.4 (71.4-89.9)</td>
<td>100 (99-100)</td>
<td>100 (99-100)</td>
<td>90.5 (80-98)</td>
</tr>
<tr>
<td>Metastatic cancer</td>
<td>79.6 (68-91)</td>
<td>87.4 (81-97)</td>
<td>97 (95-99)</td>
<td>94.8 (90-97)</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>82.5 (70-95)</td>
<td>98.8 (95-99.7)</td>
<td>97.5 (95-99)</td>
<td>94.4 (90-97)</td>
</tr>
<tr>
<td>Overall</td>
<td>79.8 (70-90)</td>
<td>82.5 (70-95)</td>
<td>97 (95-99)</td>
<td>94.4 (90-97)</td>
</tr>
</tbody>
</table>

Conclusion: Our large series shows that mediastinal EUS-FNA has high sensitivity and specificity for malignancy and sarcoidosis. With overall high sensitivity & specificity, it should be a useful tool in the assessment of mediastinal pathology.

P4412

Performance of transbronchial needle aspiration (TBNA) of mediastinal lymphadenopathies in the diagnosis of pulmonary neoplasms
Rafael Garcia Montesinos, Nuria Maria Reina Martí, Ezequiel Ortega Sáenz de Tejada, Concepción Mena Escober, Lidia López López, María Victoria Hidalgo Sanjín.

Aim: To know the contribution of TBNA of mediastinal lymphadenopathies in the diagnosis of extension and anatopathologic diagnosis of lung neoplasms.

Methods: During 63 months (October 2006-December 2011) we made 184 fibrobroncoscopies (FB) with TBNA to patients with mediastinal lymphadenopathies suspected of neoplastic origin. We performed a “blind” TBNA of the lymphadenopathies larger than 1cm, using a 19 or 21ga needle, in the presence of the anatopathologist. We took samples from the ganglionic stations 4R, 7, 10R and 11L. We take samples until we got a positive result or we did 3-4 perforations, depending on tolerance of the patient. We considered as positive samples which allowed to make a therapeutic decision and negative samples those reported as “carcinoma” without specifying the type, presence of “malignant” or “atypical cells”.

Results: The TBNA was (+) for neoplasia in 122 (66.3%) patients, giving the diagnosis of extension (N2). The average number of punctures per patient was 1.8; in 58 patients (59.5% of TBNA positives) only one puncture was required. In 41 cases (33.6%) was the only positive sample of FB, and gave the extension and pathological diagnosis. The only complications during FB were small hemorrhages. We did not detect significant clinical or radiological complications following the procedure.

Conclusions: 1. TBNA of mediastinal adenopathies was useful in the extension diagnosis in 122 (66.3%) patients and resulted in diagnosis of lung cancer in 41 (33.6%) patients. 2. TBNA was well tolerated and without significant complications.

P4413

Performance of transbronchial needle aspiration (TBNA) of mediastinal lymphadenopathies in the diagnosis of pulmonary neoplasms
Rafael Garcia Montesinos, Nuria Maria Reina Martí, Ezequiel Ortega Sáenz de Tejada, Concepción Mena Escober, Lidia López López, María Victoria Hidalgo Sanjín.

P4414

Results of endobronchial ultrasound in mediastinal nodal staging of lung cancer
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Aim: To evaluate the sensitivity and predictive negative value (PNV) of endobronchial ultrasound (EBUS) in patients with non small cell lung cancer (NSCLC).

Methods: Descriptive retrospective transversal study of all performed EBUS in a tertiary hospital during a 3 year period, for mediastinal nodal staging of NSCLC with fluorodeoxyglucose positron emission tomography positive nodes. Cases were considered positive (PC) when nodal metastases was demonstrated. If not, were considered as non-positive cases (NPC) and a mediastinoscopy was performed, if the clinical situation of the patient allowed the procedure.

Results: A total number of 41 patients were evaluated, 34 of them male and 7 females. Mean age was 65.39 years old. EBUS results were: 22 PC and 19 NPC. Mediastinoscopy was performed to the NPC supporting the negative result in 14
cases, but showed a positive result in other 3 cases. In 2 cases no additional testing was done. We found 3 false negative cases (17,64%), a VPN of 82% and a sensitivity of 88% for EBUS in our patient series. EBUS was able to stage 20 cases as N2 and 2 cases as N3. In four N2 staged cases a neoadjuvant therapy was applied and then a mediastinoscopy was performed previous to the surgery. Conclusions: In this patient series EBUS allowed us to avoid more than a 50% of prognostic mediastinoscopies in NSCLC, given the high NPV and sensitivity we obtained with this technique. In cases staged as N2 responding to neoadjuvant therapy, a mediastinel reevaluation can be performed through a mediastinoscopy.

P4415 Transthoracic needle biopsy
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Introduction: Transthoracic needle biopsy (TNB) is a safe method used to achieve diagnosis for most thoracic lesions, whether the lesions located in the pleura, the lung parenchyma or mediastinum. TNB are performed on an outpatient basis by using only 1% lidocain local anesthesia.

Methods: TNB was performed in 148 patients, 44 (29.7%) women and 104 (71.3%) men, age 28-82, average 74 years; changes in the thoracic wall, pleura, parenchyma et the lung and mediastinum. Needles that were used in the procedure were BardMagnum 18-19G x 200mm, and sample length was 19 mm. Needles were activated using BardMagnum automatic trigger, under RT control with the C-arm Ziehm-Vision.

Results: In 148 patients the TNB was done:

<table>
<thead>
<tr>
<th>Localization/Size</th>
<th>Parenchyma changes</th>
<th>Anterior mediastinum</th>
<th>Posterior mediastinum</th>
<th>Thoracic wall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20–50 mm</td>
<td>50–100mm</td>
<td>&gt;100mm</td>
<td>Total / Efficiency</td>
</tr>
<tr>
<td>Parenchyma changes</td>
<td>39 (35)</td>
<td>54 (52)</td>
<td>11 (10)</td>
<td>104 (97) – 93.2%</td>
</tr>
<tr>
<td>Anterior mediastinum</td>
<td>6 (5)</td>
<td>13 (11)</td>
<td>1 (1)</td>
<td>20 (17) – 85%</td>
</tr>
<tr>
<td>Posterior mediastinum</td>
<td>2 (2)</td>
<td>7 (6)</td>
<td>3 (3)</td>
<td>12 (11) – 91.6%</td>
</tr>
<tr>
<td>Thoracic wall</td>
<td>1 (1)</td>
<td>9 (9)</td>
<td>2 (2)</td>
<td>12 (12) – 100%</td>
</tr>
<tr>
<td>Total / efficiency</td>
<td>48 (43) – 89.5%</td>
<td>83 (78) – 93.9%</td>
<td>17 (16) – 94.1%</td>
<td>148 (137) – 92.8%</td>
</tr>
</tbody>
</table>

Success of the procedure was greater if the changes were bigger and closer to the thoracic wall. Total diagnostic success is 92.8%. Carcinoma bronchogene was proven in 134 (90.5%) patients: carcinoma squamous-cellulare 62 (46.2%), adenocarcinoma 52 (38.8%), carcinoma macrocelulare 5 (3.7%), SCLC 15 (11.5%). Lymphoma – 5 (3.7%), TB – 2 (1.3%), Thymoma malignum – 1 (0.6%), Carcinoma metastaticum – 4 (2.7%), Mesotheloma – 2 (1.3%). Complications: pneumothorax – 4 (2.7%), hemoptysis – 8 (5.4%).

Conclusion: TNB is safe and cheap diagnostic procedure for histological and/or cytological confirmation of changes in the lung and mediastinum. Sensitivity of TNB is 92.8% and specificity 100%.

P4416 Negative predictive value of EBUS in lung cancer staging
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Introduction: EBUS (endobronchial ultrasound) is a technique developed for mediastinum diagnosis and staging. A negative puncture in lung cancer staging remains uncertain in current guidelines.

Objective: To evaluate the negative predictive value of EBUS in the lung cancer algorithm when adequate lymph node sampling is achieved.

Method: Patients with a definitive pathological diagnosis of lung cancer nodal staging after EBUS were analyzed. Clinical characteristics, final diagnosis and treatment of patients with negative EBUS were investigated.

Results: A total of 100 definitive diagnostic EBUS were analyzed. A definitive pathologic diagnosis of malignant disease was obtained in 56 (56%), whereas 44 procedures were representative of lymph node with no evidence of malignant disease. 20 patients with negative diagnosis underwent surgery, 8 were treated with quimio and/or radiotheraphy, and 16 were not treated or had a final diagnosis of benign disease. Two out of the 20 patients that underwent surgery showed a final diagnosis of malignant disease in a N2 lymph node station (adenocarcinoma and non-small undifferentiated cell lung cancer), which gives a predictive negative value of 90% for EBUS (that reaches 95.45% considering the final outcomes in all the patients with negative samples). Positron emission tomography scan was positive for N2 in one of the two false negative cases. The diagnostic accuracy of EBUS if an adequate sample is achieved is 98%.

Conclusion: EBUS is a reliable and accurate diagnostic tool for the staging of lung cancer. Considering that an appropriate lymph node sample is obtained, a negative result has a negative predict value of at least 90%, which can reassure a change in the lung cancer algorithm.