mediastinoscopy after lymph node staging by EBUS-TBNA. We were also unable to calculate the sensitivity or the positive predictive value of the technique, because positive EBUS-TBNA results are generally not confirmed by surgery.

We conclude that in patients with potentially resectable non-small cell lung cancer, a negative preoperative EBUS-TBNA might not require confirmation by mediastinoscopy in most cases, perhaps with the exception of centrally located tumors.

References


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Incidence and Impact of Upper Airway Symptoms in Patients With Chronic Obstructive Pulmonary Disease

Frecuencia e impacto de los síntomas de las vías respiratorias superiores en pacientes con enfermedad pulmonar obstructiva crónica

To the Editor:

The quality of life (QoL) in patients with chronic obstructive pulmonary disease (COPD), a condition largely caused by smoking, is usually adversely affected. Associated comorbidities contribute to disease severity and lead to poorer QoL. Over the last 15 years, awareness of nasal inflammation in COPD has increased, and the estimated prevalence of upper airway symptoms vary from 40% to 88%. The presence of upper airway symptoms negatively affects the already poor QoL.

The aim of this study is to determine the incidence of upper airway symptoms in patients with COPD and its impact on QoL. Newly referred symptomatic smokers over 35 years of age with COPD according to the Global Initiative for Chronic Obstructive Lung Disease guidelines were included. The incidence of upper airway symptoms was assessed on the basis of the Allergic Rhinitis and its Impact on Asthma (ARIA) workshop report. The study variables were: respiratory symptoms, upper airway symptoms, spirometry with reversibility, peripheral blood eosinophil count, and computed tomography of paranasal sinuses (CT-PNS). CT-PNS was scored in accordance with the Lund-Mackay staging system. QoL in patients with upper airway symptoms was assessed using the St. George’s Respiratory Questionnaire (SGRQ) and Sino Nasal Outcome Test-22 (SNOT-22) questionnaire. Patients were divided into 2 groups: Group 1, COPD with upper airway symptoms; and Group 2, COPD without upper airway symptoms (controls). Radiological sinusitis was defined in accordance with the European Position Paper on Rhinosinusitis and Nasal Polyps 2012 criteria

Table 1
EBUS-TNA False Negatives.

<table>
<thead>
<tr>
<th>Primary Tumor</th>
<th>LN With PET–CT Uptake</th>
<th>LN Diameter (mm)</th>
<th>LNs Analyzed</th>
<th>Malignancy on Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>LUL</td>
<td>4L</td>
<td>8</td>
<td>4L</td>
<td>4L</td>
</tr>
<tr>
<td>RUL</td>
<td>E7, 11L, 10R</td>
<td>11, 8, 5</td>
<td>E7, 11L, 10R</td>
<td>E7</td>
</tr>
<tr>
<td>RUL</td>
<td>None</td>
<td>8</td>
<td>4R</td>
<td>4R</td>
</tr>
</tbody>
</table>

LN: lymph node; LUL: left upper lobe; RUL: right upper lobe.
Table 1
Patient Demographics, Baseline Characteristics and Quality of Life Scores.

<table>
<thead>
<tr>
<th>Descriptor</th>
<th>COPD patients with upper airway symptoms (Group 1)</th>
<th>COPD patients without upper airway symptoms (Group 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years); mean±SD</td>
<td>55.7±10.3</td>
<td>57.8±11.0</td>
</tr>
<tr>
<td>Gender male: n</td>
<td>26 (96.2%)</td>
<td>13 (92.8%)</td>
</tr>
<tr>
<td>Duration of symptoms: mean±SD</td>
<td>7.8±7.7</td>
<td>6.3±6.2</td>
</tr>
<tr>
<td>Current smokers: n</td>
<td>9 (33.3%)</td>
<td>7 (50%)</td>
</tr>
<tr>
<td>Duration of smoking (years): mean±SD</td>
<td>28.2±1.178</td>
<td>31.4±1.63</td>
</tr>
<tr>
<td>Pack years of smoking</td>
<td>29.48±25.47</td>
<td>40.07±32.77 (P=.257)</td>
</tr>
<tr>
<td>Absolute eosinophil count (cells/mm³)</td>
<td>335.03±301.50</td>
<td>149.92±66.17 (P=.02)</td>
</tr>
<tr>
<td>Pre-bronchodilator FEV₁ (L): mean±SD</td>
<td>1.44±0.74</td>
<td>1.96±0.76 (P=.04)</td>
</tr>
<tr>
<td>Post-bronchodilator FEV₁ (L): mean±SD</td>
<td>1.53±0.73</td>
<td>2.07±0.77 (P=.03)</td>
</tr>
<tr>
<td>Pre-bronchodilator FVC (L): mean±SD</td>
<td>2.81±0.89</td>
<td>2.88±0.86 (P=.77)</td>
</tr>
<tr>
<td>Post-bronchodilator FVC (L): mean±SD</td>
<td>2.91±0.87</td>
<td>3.01±0.87 (P=.72)</td>
</tr>
<tr>
<td>Post-bronchodilator FEV₁/FVC ratio: mean±SD</td>
<td>48.8±13.13</td>
<td>50.7±6.7 (P=.64)</td>
</tr>
<tr>
<td>Radiological sinusitis/mucosal thickening on CT-PNS</td>
<td>19/27</td>
<td>3/14 (P=.003)</td>
</tr>
<tr>
<td>CT-PNS (L-M) scores</td>
<td>2.19±2.88</td>
<td>0.29±0.61 (P=.02)</td>
</tr>
<tr>
<td>SNOT-22 score: mean±SD</td>
<td>0.87±0.36</td>
<td>0.38±0.38 (P=.0001)*</td>
</tr>
<tr>
<td>SGRQ symptoms: mean±SD</td>
<td>68.7±16.76</td>
<td>48.46±15.37 (P=.0005)*</td>
</tr>
<tr>
<td>SGRQ activity: mean±SD</td>
<td>76.9±18.2</td>
<td>65.54±20.54 (P=.07)</td>
</tr>
<tr>
<td>SGRQ impact: mean±SD</td>
<td>47.8±22.2</td>
<td>39.8±13.23 (P=.22)</td>
</tr>
<tr>
<td>SGRQ total: mean±SD</td>
<td>64.5±16.7</td>
<td>51.28±14.35 (P=.011)</td>
</tr>
</tbody>
</table>


* Significant difference.

along with CT-PNS findings. All patients gave their informed, written consent. The study was approved by the institutional research ethics committee. Data were analyzed using SPSS (version 11.5, SPSS, Inc., Chicago, IL). Chi-Square, Student’s t-test and Pearson’s correlation test were used for data analysis. A significance level of P<.05 was accepted for all analysis.

Nearly two-thirds (27/41; 65.9%) of patients with COPD had upper airway symptoms (Group 1). These patients presented with higher peripheral blood eosinophilia, more severe lower airway obstruction, and an increased incidence of sinusitis on CT-PNS. They also reported a significantly poorer QoL on the SGRQ and SNOT-22 questionnaires (Table 1).

In Group 1, patients with radiological sinusitis, moderate positive correlation was observed between CT-PNS (Lund-Mackay) and SNOT-22 Qol. scores (r=0.58; P=.009). Furthermore, a positive correlation was observed between nasal symptoms based on SNOT-22 and more general SGRQ scores in these patients (r=0.41; P=.03).

The incidence of upper airway symptoms in different studies ranges from 40% to 88%. Three-quarters of the 61 patients with moderate-to-severe COPD from the East London COPD (ELCOPD) study cohort presented at least 1 nasal symptom. An inverse relationship was established between nasal patency in COPD and severity of airflow obstruction. In our series, patients with upper airway symptoms also presented with more severe lower airway obstruction.

Radiological sinusitis was documented in 19/27 (70.4%) Group 1 patients. Qol. scores were consistent with findings from other studies. The ELCOPD study reported a mean SNOT-20 score of 1.24, showing that nasal symptoms impaired QoL. The higher symptom, total SGRQ and SNOT-22 scores showed significantly poorer QoL in Group 1 patients, highlighting the adverse impact of upper airway symptoms in patients with COPD. A positive correlation was observed between SNOT-22 and total SGRQ scores in Group 1 patients, indicating a negative impact on overall QoL. In the 19 patients with sinusitis on CT-PNS in Group 1, CT-PNS scores showed a moderately strong positive correlation with SNOT-22 scores, which is consistent with a previous study. The small sample size in our study was a limitation.

This study highlights the incidence and significant impact of upper airway symptoms on QoL in patients with COPD. It is therefore imperative to determine upper airway involvement in patients with COPD, as this may lead to suboptimal control of the disease.

Funding

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References

The Influence of Sex on Prognosis of Patients With Idiopathic Pulmonary Fibrosis in a Retrospective Cohort

Influencia del género en el pronóstico de pacientes con fibrosis pulmonar idiopática en una cohorte retrospectiva

To the Editor,

Idiopathic pulmonary fibrosis (IPF) is a disease that occurs more often in men, with a reported male:female ratio of between 1.6:1 and 2:1.1–3 Previous studies indicate that the course of IPF may be more benign in women, an observation which could be based on differences in gene expression.3–5 Given that these studies were conducted prior to the publication of the current diagnostic criteria, and without taking into account the variable of autoantibodies, patients with diagnoses other than IPF might have been included. We believed, then, that a new study comparing the progress of these patients according to gender could provide valuable information.

For this reason, we decided to perform this retrospective cohort study in patients with a diagnosis of IPF (according to the 2011 ATS/ERS/JPS/ALAT)6 seen in a multidisciplinary clinic specializing in interstitial lung diseases (ILD). Patients were recruited between March 2012 and July 2015. The main study exposure variable was time from date of diagnosis to date of all-cause death or lung transplantation. The main study exposure variable was sex. The following variables were analyzed to avoid potential confusion between sex and the outcome variable: age, smoking, time of dyspnea in months, the development of acute exacerbations (defined according to current international recommendations),7 rheumatoid factor (RF) by nephelometry, and antinuclear antibodies (ANA) by indirect immunofluorescence. Other study variables included previous treatment with triple therapy (systemic corticosteroids, azathioprine, and N-acetylcysteine) before attending our clinic, and use of pirfenidone. Results were communicated according to the indications of the STROBE initiative.8

Time of death or transplantation was estimated using Kaplan–Meier methods. The rates of events between the sexes at 18 months were studied using survival estimators and 95% confidence intervals, and compared using the log rank test. A multivariate Cox model was applied, using sex as the first independent variable. Variables that were significant in the univariate analysis and those considered clinically relevant were included. Both crude and adjusted HR and their 95% CI were reported. A P-value of <.05 was considered statistically significant.

The study included 86 patients, of which 21 were women (24.4%). Mean (SD) age was 65.4 (9) years. When characteristics were compared by sex, the prevalence of smoking was higher among men (84.6% vs 59.1%, P<.01). No significant differences in age, baseline forced vital capacity (FVC%), time since onset of dyspnea, or percentage of patients with positive ANA or RF were found at diagnosis. No differences were observed in the time of administration or proportion of patients who received triple therapy prior to attending our clinic, nor in the percentage of patients who received pirfenidone or had an acute exacerbation. In the analysis of time to death or transplantation, overall all-cause mortality was 38.4% (33/86), 35.4% (23/65) in men, and 47.6% (10/21) in women. Median survival was 34.03 months in women and 36.06 months in men. Four patients received a lung transplant (3 men) and the indication for transplantation was established at the time of diagnosis. When survival at 18 months was compared by sex, no statistically significant differences were observed, with rates of 0.75 (95% CI, 0.61–0.85) in men and 0.71 (95% CI, 0.44–0.87) in women (P=.88). In the Cox univariate analysis (Table 1), treatment with pirfenidone was associated with longer survival, but this effect disappeared after adjusting for the remaining variables included. In the Cox multivariate analysis, the only variable that showed statistical significance was baseline FVC% (Table 1).

In our study, we found no significant differences when the survival of patients with IPF was compared by sex. Treatment with pirfenidone was significantly associated with better survival in the univariate analysis, but this effect disappeared in the multivariate analysis, although it maintained a trend toward statistical significance. This may be explained by the fact that patients who received pirfenidone had baseline FVC≥50% predicted value. Our study has some limitations. It is a retrospective study conducted in a single center. Moreover, with the exception of ANA and RF, other antibodies were not routinely analyzed. However, all patients were evaluated by the clinical immunology department, which ruled out the presence of an autoimmune disease by additional tests and determination of specific antibodies (e.g., citrullinated peptide antibodies or myospecific antibodies), when necessary.9 Previous studies indicate that the female sex is associated with better survival in IPF, and was considered a factor for good prognosis in a score proposed by a group of researchers.4,10 However, these studies were performed using the ATS/ERS criteria from the year 2000. A recent study showed that of 60 patients who met diagnostic criteria in the year 2000, only 46 met the current diagnostic criteria,11 suggesting that approximately 25% of patients with IPF according to previous criteria could have had another IPD. This is of interest, given the differences in survival between IPF and other ILD.12 Chronic hypersensitivity pneumonitis may be confused with IPF, which is relevant, since it has a more benign disease course.13 Autoimmune diseases are more common in women13 and may


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