Emphysematous Change in Chronic Asthma in Relation to Cigarette Smoking*  
Assessment by Computed Tomography  
Yasuhiro Kondoh, M.D.; Hironuki Taniguchi, M.D.; Stigeki Yokoyama, M.D.; Fumio Taki, M.D.; Kenzo Takagi, M.D.; and Tatsuo Satake, M.D., F.C.C.P.

To evaluate the occurrence and the degree of emphysema in chronic asthma in relation to the effect of cigarette smoking, we examined 35 subjects with irreversible airway obstruction (17 nonsmokers and 18 smokers). We performed pulmonary function testing and CT scans on all subjects. The ES was assessed by a visual scoring system on CT scans. Between nonsmokers and smokers, there was a significant difference in the ES (p<0.05), but not in the FEV₁, TLC, and Dsb/V₆ (expressed as percent predicted values). The ES was 2.3±4.7 percent (mean±SD) in nonsmoking subjects and 13.7±16.7 percent in smoking subjects. In all subjects the ES showed significant correlations with Dsb/V₆ (p<0.001) and pack-years of cigarette consumption (p<0.001) but did not show correlations with FEV₁ and with TLC. We concluded that emphysema can occur in smoking asthmatic subjects because of the effect of cigarette smoking, and CT scans are useful for detecting this emphysematous change.  

(CHEST 1990; 97:845-49)

ES = emphysema score (percentage of lung involved as assessed by CT scans); AOD = airway obstructive disease; ITS = Intermountain Thoracic Society

Asthma is a clinical syndrome characterized by its reversibility of airway obstruction, but several studies suggest that chronic asthma may be associated with the development of irreversible airway obstruction. Recently, Burrows et al examined the course and prognosis in subjects who had AOD, and these investigators concluded that asthmatic subjects had a higher survival rate and much lower rate of decline in pulmonary function than emphysematous subjects in an epidemiologic study. Burrows et al emphasized that an effort should be made to distinguish chronic asthma from emphysema; however, it is clinically difficult to distinguish chronic asthma from emphysema because of their similar symptoms of wheezing, cough, and shortness of breath.

It is generally accepted that the most common etiologic agent producing emphysema is cigarette smoking, but the evidence for the occurrence of emphysema in chronic asthma is controversial. Some previous studies have shown the presence of emphysema in chronic asthma to be uncommon, while others have shown it to be common, but these investigators did not take cigarette smoking into account.

Recent reports have correlated the CT findings of emphysema with pathologic assessment of emphysema and concluded that the CT scan was useful in both the quantitative and qualitative assessment of emphysema. In order to evaluate the occurrence and the degree of emphysema in chronic asthma in relation to the effect of cigarette smoking, we performed pulmonary function testing and CT scans on 35 subjects with chronic asthma.

MATERIALS AND METHODS

Subjects

Thirty-five subjects with asthma (17 nonsmokers and 18 smokers) attending outpatient clinics of the Department of Respiratory Medicine at the Tosei Public Hospital were studied. The diagnosis of asthma was based on a history of wheezing or shortness of breath (or both) and the presence of variability of airflow obstruction, i.e., 20 percent improvement in FEV₁ within a period of six months before the study. All of the subjects included in this study had some degree of irreversible airway obstruction during clinical remission from asthma, which was not reversed by intensive treatment including corticosteroids; their FEV₁/FVC ratio was less than 70 percent. The mean duration of asthma in all patients was 24.6±18.1 years. The characteristics of the two groups of subjects are shown in Table 1.

Computed Tomography

The CT scans were performed on a scanner (Toshiba CT 70A) at 15-mm intervals from the apex to the diaphragm at full inspiration using 10-mm collimation. Scans were reviewed at window settings appropriate for lung (window level, −850; window width, 600H). The scoring system for the extent of emphysema was a visual one based on the criteria of Bergin et al. Areas of low attenuation and vascular distention were considered to be suggestive of emphysema. A grade of zero was given if there was no abnormality. If less than 25 percent of the pulmonary parenchyma in a slice was considered to show vascular distention and low attenuation, the score was 1; between 25 and 50 percent, the score was 2; between 50 and 75...
Table 1—Characteristics of Asthmatic Subjects

<table>
<thead>
<tr>
<th>Data</th>
<th>Nonsmokers</th>
<th>Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age; y*</td>
<td>61.8±10.4</td>
<td>61.3±9.7</td>
</tr>
<tr>
<td>Sex</td>
<td>5 M, 12 F</td>
<td>14 M, 4 F</td>
</tr>
<tr>
<td>IgE ≥400 units/ml†</td>
<td>6/17 (35)</td>
<td>4/18 (22)</td>
</tr>
<tr>
<td>Eosinophils ≥5 percent†</td>
<td>10/17 (50)</td>
<td>8/18 (44)</td>
</tr>
<tr>
<td>Cigarette consumption, pack-years*</td>
<td>0</td>
<td>36.7±15.4</td>
</tr>
</tbody>
</table>

*Values are means ± SD.
†Data are numbers of subjects; numbers within parentheses are percents.

percent, the score was 3; and more than 75 percent, the score was 4. The final score for each patient was calculated as a percentage of the maximal possible CT score. The scoring system was independently completed by two observers on two separate occasions, without knowledge of the clinical data or pulmonary function testing. The mean of the four observations for each subject was used in the statistical analysis.

Pulmonary Function Testing

All subjects underwent pulmonary function testing during clinical remission from asthma. Tests of spirometry, Dsb, and lung volumes were all performed (Chestac-25 F system; Chest Co., Tokyo). Spirometry and expiratory flow rates were measured on a rolling-seal spirometer, according to standard techniques. The best values for FEV₁ and FVC of three acceptable curves were used for the analysis. Two reproducible single-breath measurements of Dsb, lung volume (VA), and steady-state helium-dilution lung volume were made in the sitting position using the ITS technique. Spirometric values were expressed as percent predicted using the prediction equations of Crapo et al. Predicted values for the ratio of Dsh/VA were based on the prediction equation of Crapo and Morris. Lung volumes were expressed as percent predicted according to the equation of Goldman and Becklake.

Statistical Analysis

The regression coefficient and the unpaired t-test were used for statistical analysis. All data in this report were expressed as the mean ± SD.

RESULTS

The data from pulmonary function testing of the two groups are shown in Table 2. There was no significant difference in FEV₁, TLC, or Dsb/VA between the two groups of subjects. The FEV₁ of nonsmoking subjects was 68.2±20.7 percent of predicted (mean ± SD), and that of smoking subjects was 67.4±18.5 percent. The TLC of nonsmoking subjects was 110.9±13.8 percent, and that of smoking subjects was 116.0±10.5 percent. The Dsb/VA of nonsmoking subjects was 98.7±20.2 percent, and that of smoking subjects was 83.8±28.5 percent.

Table 2—Data from Pulmonary Function Testing*

<table>
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<tr>
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<th>Nonsmokers</th>
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</tr>
</thead>
<tbody>
<tr>
<td>FEV₁, percent of predicted</td>
<td>68.2±20.7</td>
<td>67.4±18.5</td>
</tr>
<tr>
<td>TLC, percent of predicted</td>
<td>110.9±13.8</td>
<td>116.0±10.5</td>
</tr>
<tr>
<td>Dsb/VA, percent of predicted</td>
<td>98.7±20.2</td>
<td>83.8±28.5</td>
</tr>
</tbody>
</table>

*Values are means ± SD.

There was good intraobserver and interobserver agreement for the ES. The correlation coefficients for ES of intraobserver values were r = 0.98 (p<0.001) and r = 0.89 (p<0.001), respectively, and that of interobserver values was r = 0.93 (p<0.001). There was a

Figure 1. Emphysema score in nonsmokers and smokers.

Emphysematous Change in Chronic Asthma (Kondoh et al)
significant difference in the ES between the two groups (p<0.05) (Fig 1). The mean ES of nonsmoking subjects was 2.3 ± 4.7 percent, while that of smoking subjects was 13.7 ± 16.7 percent. The mean ES of all subjects was 8.2 ± 13.5 percent. Eleven of the nonsmoking subjects and four of the smoking subjects had no emphysematous change (ES = 0).

The relation between the ES and FEV$_1$ in all subjects is shown in Figure 2, and that between the ES and TLC is shown in Figure 3. In all subjects the ES did not correlate with FEV$_1$ and TLC. The relation between the ES and Dsb/VA in all subjects is shown in Figure 4. The ES correlated significantly with Dsb/VA (r = −0.66; p<0.001). The relationship between the ES and the pack-years of cigarette consumption is shown in Figure 5. There was a significant correlation between the ES and the pack-years of cigarette consumption (r = 0.55; p<0.001).

**DISCUSSION**

Emphysema is defined as "a condition of the lung characterized by abnormal permanent enlargement of the airspaces distal to terminal bronchioles, accompanied by destruction of their walls." While several previous studies tried to assess the presence and severity of emphysema during life by clinical examination, pulmonary function testing, and the chest roentgenogram, it seems to be difficult to distinguish patients with moderate emphysema from those with mild or no emphysema by these methods. Recent reports demonstrated that there was a good correlation between the CT findings and pathologic findings of emphysema. The CT scans are considered to be more sensitive than the chest roentgenogram, even in detecting mild emphysematous changes. While recent studies reported more accurate methods using CT density distributions, they are rather time-consuming, so we used the visual scoring system, which is rather simple and convenient.

There has been much confusion in distinguishing chronic asthma from emphysema in patients with AOD because of their similar clinical symptoms and the possibility of their coexistence. Many investigators reported the crucial role of smoking for the pathogenesis of emphysema but there are few reports concerning the evaluation of the emphysematous change in smoking asthmatic subjects up to now. Cockcroft reported that studies of smoking in asthmatic patients are difficult, largely because most asthmatic subjects choose not to smoke; however, the population of smokers in Japan is rather large compared to that in the United States and European countries, and even asthmatic patients tend to continue smoking during clinical remission from asthma. Therefore, the evaluation of emphysematous change in chronic asthma in relation to the effect of cigarette smoking in Japan is clinically important and would provide important clues resolving the complicated
relationship between chronic asthma and emphysema.

In our present study, there are no significant differences in FEV₁ and TLC between nonsmokers and smokers in chronic asthmatic subjects whose FEV₁/FVC ratio was less than 70 percent. The fact that nonsmoking subjects with chronic asthma had decreased FEV₁ (68.2 ± 20.7 percent) may suggest that asthma alone can cause irreversible airway obstruction without the effect of cigarette smoking. Brown et al.² also reported the same conclusion. There is a significant difference in the ES evaluated by CT scans between nonsmokers and smokers in chronic asthmatic subjects. In nonsmoking asthmatic subjects, the mean ES was 2.3 percent, which is in keeping with the severity of emphysema among nonsmokers in the general population.³ On the contrary, in smoking asthmatic subjects, the mean ES was 13.7 percent, which is compatible with the emphysematous change seen in nonasthmatic smokers reported by Kinsella et al.⁴ These results suggest that emphysema can occur in smoking asthmatic subjects, and CT scans are useful in evaluating emphysematous change in chronic asthma.

The ES shows no significant relation to FEV₁ and TLC. West et al.⁵ reported that FEV₁ and TLC significantly correlated with the pathologic emphysema score in AOD, but they excluded asthmatic subjects. We think that it is difficult to evaluate the emphysematous change in chronic asthmatic subjects by the degree of airway obstruction and hyperinflation. On the other hand, there is a significant correlation between the ES and Dsb/Va. In pulmonary function testing, Dsh/Va may be useful in detecting emphysema in asthmatic subjects, and we must carefully evaluate the emphysematous change when the subjects show a decreased diffusing capacity. Several studies emphasized the importance of diffusing capacity in evaluating emphysematous change in COPD.⁶,⁷,⁸

There is a significant correlation between the ES and the pack-years of cigarette consumption. This suggests that the severity of emphysema correlates with the degree of cigarette smoking in subjects with chronic asthma. The most common etiologic agent producing emphysema has been considered to be smoking. Auerbach et al.⁹ reported that cigarette smoking leads to emphysema, and that among subjects who continued to smoke cigarettes, the degree of disease increased with age. This result and our results suggest that smoking is the major cause of emphysematous change in asthmatic subjects, as well as in subjects with COPD.

It is well recognized that the presence of emphysema is a poor prognostic sign in AOD. Burrows et al.¹⁰ demonstrated that asthmatic subjects have shown a very different and more benign clinical course than emphysematous subjects. These investigators¹¹ also pointed out that the clinical course of intermediate-type subjects who seemed to have components of both asthma and emphysema had a rather worse clinical course than purely asthmatic subjects. Recently, Demedics¹² reported that even in subjects with mild emphysema at first observation, the mean ratio of decline in FEV₁ for a further ten-year evaluation was similar to that of classic COPD, and Demedics¹² emphasized that the early recognition of emphysema was quite important from the prognostic standpoint. Taking these findings into consideration, it is possible that asthmatic smokers in our study may have a more severe deline in FEV₁ and a worse prognosis than asthmatic nonsmokers because of the coexisting emphysema. Therefore, the evaluation of ES by CT scans in chronic asthmatic smokers with irreversible airway obstruction is clinically important and would help to clarify much of the current confusion related to patients with AOD.

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