Evaluation of Emphysema in Patients With Reversible Airway Obstruction Using High-Resolution CT*

Toshio Mochizuki, MD; Hiroaki Nakajima, MD; Fumio Kokubu, MD; Tamio Kushihashi, MD; and Mitsuru Adachi, MD

**Objective:** This study was carried out to determine whether asthma affects the development of emphysema.

**Methods:** We studied 62 patients with reversible airway obstruction during remission, and evaluated the presence and severity of emphysema using high-resolution CT. The emphysema score (ES) was evaluated with the visual scoring method on CT scans.

**Results:** Of the 62 patients, 14 were judged to have emphysema. Patients with emphysema were significantly older and more likely to be male than those without emphysema. All patients with emphysema were smokers. There was no significant difference in the duration or severity of asthma between patients with and without emphysema. The 62 patients were divided into three groups according to the ES: 48 patients without emphysema (ES=0%), 8 patients with mild emphysema (0%<ES<15%), and 6 patients with more severe emphysema (ES≥15%). Highly significant differences between patients without emphysema and those with more severe emphysema were found in FEV₁ (p<0.01), FEV₁/FVC (p<0.001), diffusing capacity for carbon monoxide (Dco) (p<0.01), and Dco/alveolar volume (p<0.0001).

**Conclusion:** Neither the duration nor the severity of asthma was correlated with the presence of emphysema, while smoking history, sex, and age were strongly correlated. No patients with emphysema were found among the nonsmokers, including those with severe asthma or asthma of long duration. These results suggest that asthma does not lead to emphysema.

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**Key words:** asthma; computed tomography; emphysema; pulmonary function tests; reversible airway obstruction

**Abbreviations:** Dco=diffusing capacity for carbon monoxide; ES=emphysema score; HU=Hounsfield units; RV=residual volume; TLC=total lung capacity; VA=alveolar volume

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Asthma was previously considered a reversible obstructive disease of the airways. Now, asthma is considered a chronic inflammatory disease of the airways with participation of complex cellular and chemical mediators. It has become evident that the repair of the chronic inflammatory process can lead to various irreversible changes. However, whether asthma leads to emphysema is controversial.

Emphysema is a condition of the lung characterized by abnormal, permanent enlargement of the airspaces distal to the terminal bronchioles, accompanied by destruction of their walls, without obvious fibrosis. The diagnosis of emphysema has been difficult to make during life without examination of lung tissue because of its pathologic basis. Chest radiographs are poor for diagnosing emphysema, their use is limited to patients with severe emphysema in whom secondary signs of hyperinflation or vascular pruning are evident. Recently, radiologic-pathologic correlation has demonstrated that CT, more specifically, high-resolution CT, is superior to chest radiography for the diagnosis of emphysema, even mild or asymptomatic forms, and is useful for the quantitative evaluation of emphysema.

However, it is not always easy to demonstrate chronic inflammation of the airways. Most patients are still given the diagnosis of asthma if airway obstruction is reversible, either spontaneously or as a result of therapy.

We evaluated the presence and severity of emphysema in patients with reversible airway obstruction.
using high-resolution CT and compared these findings with clinical features and results of pulmonary function tests.

**Materials and Methods**

**Subjects**

We studied 62 patients (34 smokers and 28 nonsmokers), ages 21 to 80 years with normal findings, except for emphysematous change, on chest radiographs (Table 1). All patients had received a diagnosis of asthma on the basis of the presence of intermittent symptoms of wheezing, coughing, or chest tightness and reversible airway obstruction. Reversible airway obstruction was characterized by an improvement exceeding 20% in FEV1 with no evidence of respiratory infection or cardiovascular disease in the 6 months before the study. Patients were randomly chosen for the study, but those who were unable to maintain full inspiration to obtain CT scans were excluded. All patients were studied during remission lasting for at least 2 weeks after intensive treatment. The mean duration of asthma was 13.2 years. The severity of asthma was graded according to the classification of the International Consensus Report.1 The study was carried out after obtaining both the informed consent of the subjects and the approval of the ethics committee of the hospital.

**Computed Tomography**

The CT scans were performed with a scanner (ProSpeed Scanner; GE YMS, Ltd; Tokyo) at 15-mm intervals from the apex of the lung to the diaphragm using 1-mm collimation with the high-resolution CT technique. All subjects underwent scanning in the supine position at full inspiration. No IV contrast agent was used. Images were obtained at a window width of 750 Hounsfield units (HU) and a window level of −800 HU.

**Evaluation of Emphysema**

We considered areas of low attenuation and vascular disruption to be suggestive of emphysema.10-19 The severity of emphysema was judged subjectively with the visual scoring method of Goddard et al.19 Each slice was evaluated individually, and the right and left lungs were graded separately according to the percentage area that demonstrated changes suggestive of emphysema. A score of 0 was given if there was no abnormality. If <25% of the pulmonary parenchyma in a slice was considered to show vascular disruption and low attenuation, the score was 1; between 25% and 50%, the score was 2; between 50% and 75%; the score was 3; and >75%, the score was 4. Therefore, the right and left lungs could each receive a maximal score of 4, totaling a maximal score of 8 per slice. All slices above the level of the diaphragm were assessed in each patient. For each subject, an emphysema score (ES), which is the total of scores for each slice as a percentage of the total possible maximal score, was calculated. Each subject was evaluated independently on two separate occasions by two observers (a pulmonologist and a radiologist) without knowledge of the clinical data or results of pulmonary function tests.

**Pulmonary Function Tests**

All subjects underwent pulmonary function testing during remission from asthma. Pulmonary function tests included spirometry and measurement of lung volumes and diffusing capacity for carbon monoxide (DCO) which were performed using computerized equipment (Chestac-33; Chest Co., Tokyo). Spirometry tests were measured with a rolling seal spirometer, according to standard techniques. The lung volume subdivisions of residual volume (RV) and total lung capacity (TLC) were measured with the helium dilution method. The DCO was measured with the single-breath method.

Values for each pulmonary function test, except for FEV1/FVC, were expressed as percentages of predicted with the prediction equations of Crapo et al10-21,22 for spirometry and lung volume and those of Burrows et al20 for DCO and DCO/VA (alveolar volume). Both pulmonary function tests and chest CTs were obtained within a period of 6 h.

**Statistical Analysis**

We used the unpaired t test to compare age, level of cigarette consumption, and duration of asthma; the Mann-Whitney U test to compare severity of asthma; and x2 test to compare sex and smoking history in patients with and without emphysema. Analysis of variance was used to evaluate differences in results of pulmonary function tests among groups divided on the basis of the ES. Reproducibility of the ES was evaluated by assessing intraobserver and interobserver variation using Spearman’s rank correlation. Probability levels <0.05 were considered significant, while levels <0.01 were considered highly significant. Values are expressed as means±SD.

**Results**

Of the 62 patients with reversible airway obstruction, 14 were judged to have emphysema because of areas of low attenuation on high-resolution CT scans. The characteristics of patients with and without emphysema are summarized in Table 2. Patients with emphysema (64.7±10.1 years) were significantly older than those without emphysema (51.5±18.0 years). The ratio of men was significantly higher among the patients with emphysema (11 men and 3 women) than those without emphysema (22 men and 26 women). All patients with emphysema were smokers. There was no significant difference in the duration or severity of asthma between patients with and without emphysema.

Table 1—Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No.</th>
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<tbody>
<tr>
<td>No. of patients</td>
<td>62</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>33/29</td>
</tr>
<tr>
<td>Age, yr, mean±SD</td>
<td>54.5±17.4</td>
</tr>
<tr>
<td>Smoking history, nonsmoker/smoker</td>
<td>28/34</td>
</tr>
<tr>
<td>Duration of asthma, yr, mean±SD</td>
<td>13.2±13.2</td>
</tr>
<tr>
<td>Severity of asthma, mild/moderate/severe</td>
<td>21/21/20</td>
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There was good intraobserver and interobserver reproducibility of the ES. The intraobserver correlation coefficient was r=0.98 (p<0.001) for the pulmonolo...
Table 2—Characteristics of Patients With and Without Emphysema

<table>
<thead>
<tr>
<th></th>
<th>Without Emphysema (n=48)</th>
<th>With Emphysema (n=14)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, male/female</td>
<td>22/26</td>
<td>11/3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Age, yr, mean±SD</td>
<td>51.5±18.0</td>
<td>64.7±10.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Smoking history, nonsmoker/smoker</td>
<td>28/20</td>
<td>0/14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of asthma, yr, mean±SD</td>
<td>13.2±12.6</td>
<td>13.4±15.6</td>
<td>NS*</td>
</tr>
<tr>
<td>Severity of asthma, mild/moderate/severe</td>
<td>14/16/18</td>
<td>7/5/2</td>
<td>NS*</td>
</tr>
</tbody>
</table>

*NS=not significant.

gist and r=0.99 (p<0.001) for the radiologist. The interobservation correlation coefficient was r=0.93 (p<0.001). Then, we used the mean of the four observations for each subject for statistical analysis. The ES ranged from 0 to 58.8% with an average of 4.2%. Sixty-two patients with asthma were divided into three groups according to the ES. There were 48 patients without emphysema (ES=0%), 8 patients with mild emphysema (0%<ES<15%; mean score, 8.8%), and 6 patients with more severe emphysema (ES≥15%; mean score, 31.9%). The difference in the level of cigarette consumption between patients without emphysema (12.9±22.3 pack-years) and those with emphysema (51.4±24.3 pack-years) was highly significant. In particular, all patients with more severe emphysema were heavy smokers whose level of cigarette consumption was more than 45 pack-years.

On pulmonary function testing, FEV₁ (p<0.01), FEV₁/FVC (p<0.001), Dco (p<0.01), and Dco/VA (p<0.0001) (Figs. 1-4) differed highly significantly, and RV/TLC (p<0.05) differed significantly between patients without emphysema and those with more severe emphysema. A significant difference in Dco (p<0.05) and a highly significant difference in Dco/VA (p<0.001) were also detected between patients with mild emphysema and those with more severe emphysema. There was a significant difference in FEV₁/FVC (p<0.05) between patients without emphysema and those with mild emphysema. However, in FEV₁, Dco, Dco/VA, and RV/TLC, patients without emphysema and those with mild emphysema did not differ significantly. Furthermore, neither TLC nor RV differed significantly among the three groups.

**DISCUSSION**

Whether emphysema tends to occur in patients with asthma is controversial. In the present study, of the 62 patients, 14 (22.6%) were judged to have emphysema on the basis of high-resolution CT. A CT study by Lynch et al⁰²³ found that the incidence of emphysema in patients with asthma is 19%. Comparing the incidence of emphysema in patients with and without asthma is difficult because even the reported pathologic incidence of emphysema in the general population has varied greatly, ranging from 12 to 100%.⁰²⁴ However, neither the duration nor the severity of asthma was correlated with the presence of emphysema, while smoking history, sex, and age were strongly correlated. No patients with emphysema were found among the nonsmokers, including those with severe asthma or asthma of long duration. These results lead us to conclude that asthma does not affect the development of emphysema. However, Paganin et al⁰⁶ reported that the severity of asthma was significantly correlated with the presence...
of emphysema. The difference between our results and theirs might be attributed to differences in the criteria for reversibility of airway obstruction. Their criterion for reversibility of airway obstruction was an increase exceeding 12% in FEV₁, whereas ours was 20%. Patients with severe asthma occasionally experience a decrease in reversibility of airway obstruction and may even go on to develop irreversible airway obstruction. Thus, the present study might have been biased against patients with severe asthma. Moreover, patients who were unable to maintain full inspiration necessary to produce CT scans were excluded from the present study. It remains to be determined whether such patients have emphysema. Further investigation will be needed before the relationship between asthma and the development of emphysema is clarified.

Patients with reversible airway obstruction were selected for this study. While reversible airway obstruction is one of the major features of asthma, patients with COPD may also have partially reversible airway obstruction. Although the selection criterion was reversibility of airway obstruction exceeding 20% in FEV₁, patients with COPD but with no component of asthma might have been included in our population, mainly among the smokers. It is prudent and practical to separate asthma from COPD according to the statement of the American Thoracic Society. However, patients with COPD may have airway hyperreactivity in addition to reversible airway obstruction, and distinguishing between asthma and COPD is clinically often impossible. There are some difficulties with the definitions of asthma and COPD. Particularly with asthma, there is a lack of general agreement even as to its definition. In contrast, emphysema is clearly defined in terms of anatomic abnormality and can be detected with CT, as is demonstrated with radiologic-pathologic correlation.

While high-resolution CT is probably not as sensitive as histologic examination for detecting emphysema, it can accurately detect physiologically significant emphysema. This also seems to hold true in patients with reversible airway obstruction. Kondoh et al. report that Dco/VA may be useful for detecting emphysema in patients with asthma. In our study, patients with more severe emphysema had highly significantly lower FEV₁, FEV₁/FVC, Dco, and Dco/VA than those without emphysema. It is suggested that these parameters are useful for detecting severe emphysema in patients with reversible airway obstruction in pulmonary function tests. However, of the parameters in pulmonary function tests, only FEV₁/FVC differed significantly between patients without emphysema and those with mild emphysema. Therefore, pulmonary function tests would not be as useful as high-resolution CT for detecting emphysema and even patients with normal pulmonary function during remission might have mild emphysema.

Chest CT has been reported to be a noninvasive and sensitive technique for evaluating the presence and severity of emphysema. Two main methods to quantify the extent of emphysema on CT have been proposed. One method is visual assessment of the scan and the other is objective assessment of attenuation values. Objective assessment, unlike visual assessment, is not subject to interobserver variability. However, for objective assessment, the threshold level between the density of normal pulmonary parenchyma and emphysematous changes must be determined. The CT number is not an absolute value and the threshold level ranged from −900 to −960 HU in previous studies. Moreover, in asthma, the threshold level might be lower.
than that in previous studies because the mean density of pulmonary parenchyma decreases with hyperinflation. Consequently, determining the optimal threshold level is difficult without correlating CT findings with pathologic observations. Visual assessment was used in the present study. The window setting was more negative in level (−800 HU) and narrower in width (750 HU) than usual, to provide better contrast between areas of low attenuation and normal pulmonary parenchyma.

We conclude that emphysema occurs irrespective of the severity or duration of asthma and that asthma does not lead to emphysema.

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