Hyperinflation in Asthma and Emphysema*
Assessment by Pulmonary Function Testing and Computed Tomography

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To assess the role of emphysema on the hyperinflation in chronic asthma, we studied 20 subjects with irreversible airflow limitation. Ten of the subjects had asthma and had never smoked; the other ten were cigarette smokers. Pulmonary function testing and chest computed tomography (CT) scans were performed on all subjects. Emphysema was graded using a score based on the percentage of lung involved on CT scan. There was good inter- and intraobserver agreement for the emphysema scores. The median emphysema score was 0 percent in the nonsmoking group and 10 percent in the smoking group. All smokers with a total lung capacity (TLC) of greater than 120 percent predicted had evidence of emphysema on the CT scan. None of the asthmatic subjects with a TLC greater than 120 percent predicted had emphysema identifiable on CT scan. We conclude that chronic asthma with severe hyperinflation does not result in emphysema.

It is widely accepted that subjects with chronic asthma develop some degree of overinflation,1-6 which may persist during remissions. The evidence for the occurrence of emphysema in asthma is controversial. Some researchers believe it to be common;7 others believe that it is uncommon,8 while still others believe it to be almost nonexistent.1,4,9 Thuribeck2 concluded that asthma does not commonly produce emphysema.

The most common etiologic agent producing emphysema is cigarette smoking.9 Many patients with emphysema also have some degree of hyperinflation. The best way to diagnose emphysema is by pathologic assessment of the lung.10-12 The chest radiograph is not very sensitive in detecting emphysema.13,14 Recently, several studies have shown that chest computed tomography (CT) is useful in detecting emphysema in life.14-16 Using state of the art scanners, it is possible to detect even mild emphysema on CT.17,18

In order to examine the occurrence of emphysema in nonsmoking asthmatic subjects and to determine whether hyperinflation in chronic asthmatic subjects is associated with emphysema, we performed pulmonary function tests and CT scans on ten nonsmoking chronic asthmatic subjects and compared the results with ten chronic cigarette smokers.

Materials and Methods

Subjects
Ten patients with asthma who were life-long nonsmokers were studied. The diagnosis of asthma was based on a history of wheezing and/or shortness of breath and presence of variability of air flow obstruction, ie, 20 percent improvement in forced expiratory volume in one second (FEV1) after bronchodilation. They were included in the study if they had asthma for a minimum period of ten years and were more than 45 years of age in an effort to age match them with the chronic smokers. The other ten subjects were chronic cigarette smokers. They were selected randomly from the list of patients who had CT chest scans performed for suspected bronchogenic carcinoma. All the subjects included in this study had some degree of irreversible air flow obstruction; their FEV1/FVC (forced vital capacity) ratio was less than 70 percent. Nine of the subjects in each group were men and one was a woman. All of the subjects were studied during remission on maximal bronchodilator therapy.

The characteristics of the two groups of patients are shown in Table 1.

Computed Tomography
The CT scans were performed on the GE 9800 scanner at 1-cm intervals using 10-mm collimation from the apex of the lung to the base of the diaphragm during breath-holding after deep inspiration. Scans were reviewed at window levels appropriate for pulmonary parenchyma (window level, -650 to -700; window width, 1,000 to 2,000 Hounsfield units).

The CT scans were scored independently on two occasions each

<table>
<thead>
<tr>
<th>Table 1—Patient Characteristics</th>
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<tr>
<td>Asthmatic Subjects</td>
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<tr>
<td>Age (yr)</td>
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<tr>
<td>No. years of symptoms</td>
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<td>No. of cigarettes smoked (pack years)</td>
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Hyperinflation in Asthma and Emphysema (Kinsella et al)
Results by two observers for the extent of emphysema using a visual scoring system based on the criteria described by Goddard et al. Areas of abnormally low attenuation as determined visually, vascular disruption, or obvious bullae were considered to indicate the presence of emphysema. All images were assessed and graded based on the percentage of the overall area that demonstrated emphysematous changes. The CTs were graded as having 0 percent, 1 to 5 percent, 6 to 10 percent, 11 to 20 percent and in 10 percent increments up to 100 percent of the lung parenchyma showing emphysematous changes. The mean of the four observations for each subject was ranked and these ranks were used in the statistical analysis.

Pulmonary Function Testing

All subjects performed tests of spirometry, diffusing capacity and lung volumes. Spirometry was done using a rolling seal spirometer. Maximum FVC maneuvers were performed as recommended by the American Thoracic Society, with the best FEV1 and FVC of three acceptable curves being used for the analysis. Single-breath carbon monoxide diffusing capacity (Dsb) and steady state helium dilution lung volumes were also measured using equipment and techniques recommended by the Inter-Mountain Thoracic Society. The maximum of two Dsb was used if the Dsb divided by single breath helium dilution lung volume was reproducible within 10 percent. Reference equations of Crapo et al. were used to define percentage of predicted value for the spirometry and lung volumes and those of Miller et al. were used for the diffusing capacity.

Statistical Analysis

Standard statistical methods were used. The inter- and intra-observer variability of readings of the CT scan was assessed using the kappa statistic. The emphysema grade between the smokers and the nonsmoking asthmatic subjects was compared using the Wilcoxon rank sum test. The difference in the level of pulmonary function tests between the two groups of subjects was assessed using a two-sample t test.

Results

The pulmonary function data in the two groups of subjects are summarized in Table 2. There was no statistically significant difference in the level of pulmonary function between the two groups of subjects. The range of total lung capacity (TLC) in the patients with asthma was from 80 percent to 136 percent of predicted. Four of these subjects had a TLC greater than 120 percent of predicted. The range of TLC in the smokers was from 75 percent to 141 percent of predicted. Three of them had a TLC greater than 120 percent of predicted.

There was good inter- and intra-observer agreement for the emphysema scores by CT scanning. Kappa for inter-observer agreement was 0.68 (p<0.01) and 0.57 (p<0.01) for the first reading (Fig 1) and second reading, respectively. The intra-observer agreement (observer 1 and observer 2) was 0.57 (p<0.01).

The median emphysema score for the nonsmoking asthmatic subjects was 0 percent with a range of 0 to 4 percent (Fig 2). The median emphysema score for the smokers was 10 percent, with a range of 1 to 60 percent. There was a statistically significant difference in the emphysema score between the two groups (p<0.001). All smoking subjects with a TLC greater than 120 percent of predicted had emphysema on their CT scans, with a median score of 12 percent. None of the four asthmatic subjects with a TLC greater than 120 percent of predicted had emphysema identifiable on CT.

Discussion

Patients with severe asthma often have persistent hyperinflation between attacks and it is not possible clinically or functionally to separate this group of patients or to rule out associated emphysema. In patients with chronic bronchitis and hyperinflation, the presence of coexisting emphysema is a poor prognostic sign; therefore it is important clinically to assess how much the emphysema contributes to the hyperinflation.

Auerbach et al. showed that the prevalence of emphysema was much higher in smokers than in nonsmokers and that this prevalence rose with age. He also showed that the severity of emphysema increased with age, both in smokers and nonsmokers.
However, nonsmokers did not develop severe emphysema. Our own data on the detection of emphysema in vivo are in keeping with his data although the number of patients studied is small. None of our nonsmoking asthmatic subjects had emphysema more severe than 5 percent on CT, which is in keeping with the severity of emphysema among nonsmokers in the general population.8

We used the helium dilution method to measure TLC. This can give falsely low values in patients with obstructive lung disease, irrespective of the cause of the obstruction.28 Because the degree of obstruction in the asthmatic subjects and the smokers is similar, we feel that the degree of underestimation of TLC is similar in both groups of subjects. When only the asthmatic subjects and smokers with a TLC of greater than 120 percent predicted are considered, there is no difference in the degree of obstruction between the two groups. We therefore feel that the estimation of TLC by the helium dilution technique is valid for comparing the two groups of subjects.

Pathologic studies have shown that patients who have chronic asthma and hyperinflation do not necessarily have emphysema.1,4-8 Others have shown the prevalence of emphysema in asthmatic subjects to be high but did not take cigarette smoking into account.7

Computed tomography is more sensitive than the chest x-ray film in the diagnosis of emphysema; even mild emphysema can be detected by CT scanning.17,18 The chest radiograph may detect severe emphysema but is frequently insensitive in detecting mild and moderate parenchymal destruction.12,13 Computed tomography offers several advantages over the chest radiograph in assessing the pulmonary parenchyma. The lungs are viewed in the transaxial plane which decreases superimposition of parenchymal markings and of the chest wall. Spatial resolution is better on the chest radiograph, but with CT superior contrast resolution permits better distinction between normally aerated lung and disrupted alveoli.28 Several studies have shown that CT is sensitive in detecting emphysema in life.14,16

Recent reports have correlated the CT emphysema findings with pathologic assessment of emphysema.17,18 These studies found good correlation between the extent of emphysema by CT scanning and the pathologic assessment of emphysema. It was concluded that CT was useful in both the quantitative and qualitative assessment of emphysema.17 Many reports have looked at the diagnosis of emphysema by conventional chest roentgenogram.29 However, conventional chest roentgenography has not been used for the quantitative assessment of emphysema. For this reason, we used CT scanning to assess the degree of emphysema in our subjects.

Our study demonstrates in vivo that asthmatic subjects with severe hyperinflation have no evidence of emphysema on CT scan regardless of the severity of hyperinflation. In conclusion, irrespective of the extent of the hyperinflation in nonsmoking asthmatic subjects, this is not caused by associated emphysema.

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