High-Resolution CT Findings in Patients With Near-Fatal Asthma*

Comparison of Patients With Mild-to-Severe Asthma and Normal Control Subjects and Changes in Airway Abnormalities Following Steroid Treatment

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Study objectives: Extensive airway inflammation and excessive mucus production are implicated in deaths from asthma. High-resolution CT (HRCT) can be used to image both large and small airway abnormalities in asthmatics. The aims of this study were to clarify the distinction of HRCT features between near-fatal asthma (NFA) and non-NFA, and to evaluate serial follow-up HRCT scans of patients with NFA.

Patients and design: Abnormalities of the large airway (bronchial wall thickness) and small airways (prominence of centrilobular structures and air trapping) were measured semiquantitatively on HRCT scans of 24 non-NFA, 16 NFA, and 16 control subjects. In addition, these abnormalities were reevaluated after intensive and relatively long-term (>6 months) treatment with inhaled corticosteroids.

Results: Prominence of centrilobular structures was observed in 36% of mild asthma cases, in 70% of moderate-to-severe asthma cases, and in 100% of NFA cases. Prominence of centrilobular structures, but neither bronchial wall thickness nor the area of air trapping, was significantly increased in NFA, as compared with mild or moderate-to-severe asthma (p < 0.05). In the seven non-NFA and five NFA patients who underwent follow-up HRCT scans, only bronchial wall thickness was decreased significantly in the NFA cases (p < 0.05), while bronchial wall thickness and the prominence of centrilobular structures were significantly decreased in the non-NFA cases. These small airway abnormalities were partially reversible in the both groups. Residual prominence of centrilobular structures after long-term inhaled corticosteroid treatment was significantly higher in NFA than non-NFA patients.

Conclusions: The results of our study indicate that extensive small airway abnormalities may be associated with NFA, and that these abnormalities are partially reversible after the successful control of asthma symptoms.

Key words: bronchial wall thickening; CT; near-fatal asthma; small airway

Abbreviations: BWI = bronchial wall index; HRCT = high-resolution CT; HU = Hounsfield unit; NFA = near-fatal asthma

Deaths from asthma continue to occur in spite of our increased understanding of the pathophysiology of asthma, the availability of more effective medications for the control of airway inflammation, and improved asthma education.1,2 To reduce asthma mortality rates, it is important to have a clear definition of the factors that predispose individuals to fatal asthma. A number of fatal asthma-related...
longitudinal study has been undertaken regarding the reversibility of these airway abnormalities by long-term treatments.

The aim of this study was to identify the HRCT findings that could be used to characterize NFA. The parameters of airway wall thickening, prominence of centrilobular structures, air trapping, bronchiectasis, emphysema, and ground-glass opacities were assessed either quantitatively or qualitatively on HRCT scans for NFA and non-NFA patients. In addition, changes in these abnormalities, as assessed on HRCT scans, were observed longitudinally over at least 6-month regimen of inhaled steroids.

**Materials and Methods**

Subjects

We evaluated 40 patients with asthma and 16 normal healthy subjects. All of the asthmatic subjects met the definition of the American Thoracic Society. Each patient showed airway reversibility, as documented by an inhalant bronchodilator-induced improvement of FEV₁ > 15% and/or airway hyperreactivity of < 10 mg/mL (provocative concentration of methacholine causing a 20% fall in FEV₁). The severity of chronic persistent asthma was categorized as mild intermittent to severe persistent, based on the clinical features and the daily medication required for symptomatic control. This study included patients with mild asthma (group 1, n = 14), defined as those asthma patients who were classified into intermittent or mild persistent asthma, and patients with moderate-to-severe asthma (group 2, n = 10), defined as those asthma patients who were classified into moderate-or-severe persistent asthma, according to the guidelines for the diagnosis and management of asthma. NFA (group 3, n = 16) was defined as those asthma patients who were admitted to the ICU with acute respiratory failure, and who matched the following criteria: the presence of hypercapnia (PaCO₂ > 45 mm Hg, 5.9 kPa; normal range, 38 to 42 mm Hg), and signs of hypoxia (cyanosis or PaO₂ < 60 mm Hg, 7.9 kPa; normal range, 80 to 100 mm Hg). Moreover, patients were classified into groups based on the reversibility of their asthma symptoms. Patients in the reversible group showed a 20% improvement of FEV₁ following inhalation of a bronchodilator, while patients in the non-reversible group showed no improvement. The reversibility of asthma symptoms was assessed by methacholine challenge test, which was carried out using the method of Chai and coworkers. The results were expressed as the provocative concentration of methacholine causing a 20% fall in FEV₁, which was measured 6 weeks after the presentation of NFA, except in cases where it had been measured previously. The healthy control subjects included hospital personnel (medical students and staff), who had normal spirometric and chest radiographic findings. Neither the normal control subjects nor the patients with chronic persistent asthma had any history of respiratory infection for at least 4 weeks before the study, and none of the participants smoked. This study was...
performed with the approval of the Ethics Committee of the University Hospital, and informed written consent was obtained from all enrolled subjects.

**HRCT Scanning and Radiologic Evaluation**

All of the subjects underwent HRCT scans of the chest (CT-W2000; Hitachi Medical; Tokyo, Japan) using the thin-section (1-mm collimation at 10-mm increments) technique, 120 kilovolt peak, 200 mA, 1-s scan time, 250- to 350-mm field of view, and a high-spatial-frequency algorithm. Expiratory CT scan was then performed at full exhalation from apices to the diaphragm with 20-mm increments. Instruction was given to the patient to fully exhale before each scan and to hold his/her breath at the end of exhalation. Explanations were given by the technician before the examination and training was performed to check whether full exhalation could be adequately obtained. The images were viewed at two window levels of −450 Hounsfield units (HU) for accurate measurement of bronchial diameters and −700 HU for analysis of other HRCT features. A window width of 1,350 to 1,700 HU was used.

The HRCT scans were evaluated for the presence and/or extent of the following features: (1) bronchial wall index (BWI) for bronchial wall thickening; (2) prominence of centrilobular structures for centrilobular branching linear structure and centrilobular nodule; (3) air trapping on expiratory scan; (4) bronchiectasis; (5) emphysema; and (6) ground-glass opacities (Fig 1). These findings were defined according to the glossary of terms recommended by the Fleischner society. Air trapping was defined as the abnormal retention of gas (<100 HU compared to normal lung parenchyma) within a lung or lung units following exhalation. Bronchiectasis was diagnosed as the cylindrical, varicose, or cystic type. To diagnose bronchiectasis, the observers used not only the classical criterion based on the comparison of the diameters of the bronchial lumen and the homologous pulmonary artery, but also the absence of normal distal tapering of the bronchial lumen, as assessed on successive CT slices, and visualization of bronchi within 1 cm of the pleura. Emphysema was defined as a focal area of very low attenuation, usually without definable wall, that was surrounded by higher-attenuation normal lung parenchyma. Ground-glass opacity was defined as an area of hazy parenchymal opacity that did not obscure underlying vessels and airways.

The BWI (outer diameter − inner diameter/outer diameter) was used to compare bronchial wall thickening between the groups. The outer and inner luminal diameters were measured for all segmental and subsegmental bronchi with a luminal diameter of ≥1.5 mm. Only bronchi seen in cross-section were analyzed. We measured the bronchi that had maximum to minimum outer-diameter ratios of <1.5, because the ratio of the longest to shortest diameter of the airway lumen is the usual way to predict roundness. The photographed CT images were magnified fivefold using an overhead projector, and measurements were made using a caliper. All measurements were done four times on one bronchus by two chest radiologists who had no knowledge of the group to which the subject belonged, and the mean values were recorded.

The lung was divided in six zones—upper, middle, and lower, right and left—by one third and two thirds of the vertical distance between the lung apices and the domes of the diaphragm for each patient. Each of these zones was evaluated and scored separately for the presence and/or extent of the HRCT features. Prominence of centrilobular structures and air trapping were scored according to the cross-sectional area of lung involved in each zone (0 = no involvement, 1 = 1 to 25%, 2 = 26 to 50%, 3 = 51 to 75%, and 4 = 76 to 100% of cross-sectional area). Score sheets were then tabulated. The total scores for centrilobular structures and air trapping ranged from 0 to 24, and the grade was derived by mean score of each lung zones. Grade 1 was defined for a total score of <6. Grades 2, 3, and 4 were defined.

**Figure 1.** A 29-year-old woman with bronchial asthma (group 1). *Left, a:* The full-inspiration HRCT scan shows diffuse bronchial wall thickening (arrows) and prominence of centrilobular structure (arrowheads, score 1) in the right lower lobe. *Right, b:* Expiratory HRCT scan shows geographic air trapping (arrows, score 2) at the same level of the right lower lobe.
for total scores of 6 to 12, 13 to 18, and > 18, respectively. The air trapping in the superior segments of the lower lobes and isolated pulmonary lobules were not scored due to excluding of physiologic air trapping. The remaining HRCT features of emphysema, ground-glass opacities, and bronchiectasis were evaluated in terms of their presence or absence.

Two chest radiologists, who were blinded to the clinical features of the study subjects, interpreted the scans in an independent manner. The final score was obtained from the mean of the scores of the two observers.

Statistical Analysis

All of the statistical analyses were performed using a statistical software package (SPSS/PC WIN 8.0 package; SPSS; Chicago, IL). The results are represented as mean ± SE. Differences between the grades of abnormal CT findings and the clinical parameters were analyzed using analysis of variance. When significant differences were detected between the groups, the Mann-Whitney U test was performed. The Wilcoxon signed-rank test was used for paired samples. A Spearman rank correlation coefficient was calculated to evaluate the relationships between FEV1 and BWI, prominence of centrilobular structures, and air trapping in patients with asthma. Differences were considered to be significant when the p value was < 0.05.

Results

Relationship Between Airway Abnormalities on HRCT and Clinical Parameters and Pulmonary Function Tests

The characteristics of the study subjects are summarized in Table 1. The FEV1 (percentage of predicted) values were lower in groups 2 and 3 than in group 1 (p < 0.05, respectively). The initial arterial blood gas analysis of the patients with NFA was 67.6 ± 11.1 mm Hg (9.1 ± 1.5 kPa) for PaCO2 (range, 45.2 to 84.0 mm Hg; 6.1 to 11.2 kPa) and 47.9 ± 8.4 mm Hg (6.4 ± 1.2 kPa) for PaO2 (range, 34.2 to 55.6 mm Hg; 4.6 to 7.4 kPa) in room air.

The interobserver agreements for the analysis of the HRCT findings were 76% for prominence of centrilobular structures, 71% for air trapping, 84% for bronchiectasis, 76% for emphysema, and 75% for ground-glass opacities. The k values were > 0.75 for prominence of centrilobular structures, bronchiectasis, ground-glass density, and centrilobular emphysema, which represents excellent agreement. The k values for air trapping were between 0.40 and 0.75, which represents fair-to-good agreement.21

No difference was found in the mean number of measured bronchi (20.5 ± 6.3) among the study groups. The mean BWI values were 0.46 ± 0.03 for group 1, 0.53 ± 0.01 for group 2, and 0.55 ± 0.02 for group 3, all of which were significantly higher (p < 0.05) than that of the control subjects (0.40 ± 0.08) [Fig 2, left, A].

A prominence of centrilobular structures was observed in all patients with NFA (100%), but not in the normal control subjects. Prominence of centrilobular structures was observed in 36% of the patients in group 1, and 70% of the patients in group 2. The average grade of prominence of centrilobular structures was significantly higher in group 3 than in groups 1 and 2 (1.81 ± 0.2 in group 3, 0.5 ± 0.3 in group 1, and 1.0 ± 0.3 in group 2, p < 0.05), and was similar in groups 1 and 2 (Fig 2, center, B). The frequency of air trapping was 78.6% (11 of 14 patients) in group 1, 80.6% (8 of 10 patients) in group 2, 81.3% (13 of 16 patients) in group 3, and 0% in the control group. Although the average grade of air trapping increased gradually according to the severity of asthma (1.78 ± 0.4 in group 1, 1.8 ± 0.3 in group 2, and 2.12 ± 0.2 in group 3), there were no differences between the groups (Fig 2, right, C).

Bronchiectasis was present in one case in group 3, and emphysema was present in only one case in group 2 and two cases in group 3. Ground-glass opacities were not found in any of the subjects.

The correlations between airway abnormalities on HRCT scans and the degree of airflow limitation FEV1 (percentage of predicted) in groups 1, 2, and 3

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group 1 (Mild)</th>
<th>Group 2 (Moderate to Severe)</th>
<th>Group 3 (Near Fatal)</th>
<th>Normal Control Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects</td>
<td>14</td>
<td>10</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Age, yr</td>
<td>54.1 ± 3.1</td>
<td>51.1 ± 5.4</td>
<td>59.2 ± 4.6</td>
<td>49.8 ± 2.3</td>
</tr>
<tr>
<td>Male/female</td>
<td>7/7</td>
<td>7/3</td>
<td>5/11</td>
<td>11/5</td>
</tr>
<tr>
<td>Duration of</td>
<td>12.3 ± 5.3</td>
<td>14.0 ± 3.5</td>
<td>10.7 ± 2.5</td>
<td></td>
</tr>
<tr>
<td>Disease, yr</td>
<td>71.9 ± 6.3†</td>
<td>57.6 ± 7.6</td>
<td>56.2 ± 7.5</td>
<td>91.2 ± 3.4</td>
</tr>
<tr>
<td>Initial FEV1, %</td>
<td>97.6 ± 3.1†</td>
<td>85.2 ± 9.8</td>
<td>84.6 ± 5.6</td>
<td>Not done</td>
</tr>
<tr>
<td>Follow-up</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>FEV1, % predicted</td>
<td>257.4 ± 85.3</td>
<td>1342.8 ± 121.2</td>
<td>1300 ± 412.3</td>
<td>Not done</td>
</tr>
</tbody>
</table>

*p < 0.05 vs group 2 or group 3.

Data are presented as No. or mean ± SE.

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†p < 0.05 vs group 2 or group 3.
were also evaluated. Of the parameters of BWI, prominence of centrilobular structures, and air trapping, only BWI was inversely correlated with FEV₁ (percentage of predicted) in groups 1 and 2 ($r = -0.78$, $p < 0.01$). However, no correlation was found between BWI and FEV₁ (percentage of predicted) in group 3. Air trapping and prominence of centrilobular structures were not correlated with FEV₁ (percentage of predicted) in the asthma groups (Table 2).

Changes in Airway Abnormalities Following Long-term Inhaled Steroid Treatment

The HRCT scans were repeated for five patients from group 3, four patients from group 2, and three patients from group 1, after the clinical symptoms of asthma had remained under control for 6 to 12 months. Follow-up HRCT scans were obtained at the same levels as the initial CT scans, and the follow-up interval ranged from 7 to 24 months (mean, 16.8 months) after the initial HRCT scans. At the time of the follow-up HRCT scans, the patients from groups 1, 2, and 3 inhaled $257 \pm 85$ µg/d, $1,342 \pm 121$ µg/d, and $1,300 \pm 412$ µg/d, respectively, of budesonide, or the equivalent dosages of fluticasone. All of the subjects were symptom free, and peak expiratory flow rate variability was <20%.

The BWI ($0.56 \pm 0.03$ vs $0.48 \pm 0.01$) and the level of prominence of centrilobular structures ($1.14 \pm 0.3$ vs $0.43 \pm 0.3$) were decreased significantly after steroid treatment in groups 1 and 2 ($p < 0.05$, respectively; Fig 3, top left, A, and top center, B), although air trapping was not in these groups ($2.0 \pm 0.4$ vs $1.57 \pm 0.3$, $p > 0.05$; Fig 3, top right, C). In group 3, only BWI ($0.6 \pm 0.04$ vs $0.54 \pm 0.02$) was decreased significantly ($p < 0.05$; Fig 3, bottom left, D), the levels of prominence of centrilobular structures ($2.0 \pm 0.3$ vs $1.4 \pm 0.4$) and air trapping ($2.2 \pm 0.2$ vs $1.8 \pm 0.3$) were unchanged ($p > 0.05$, respectively; Fig 3, bottom center, E, and bottom right, F). On follow-up, the BWI scores were still higher in groups 1 and 2 than in the control group ($p < 0.05$). All of the patients in group 3 had higher levels of prominence of centrilobular structures than grade 1 on the follow-up HRCT scans (Fig 3, bottom center, E), while three of seven patients from groups 1 and 2 had grade 1, and the remaining four subjects had grade 0 (Fig 3, top center, B). Despite steroid treatment, the initially

### Table 2—Correlation Coefficients Between the Airway Abnormalities on HRCT and FEV₁ Percentage of Predicted

<table>
<thead>
<tr>
<th>Variables</th>
<th>Groups 1 and 2</th>
<th>Group 3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>24</td>
<td>16</td>
<td>40</td>
</tr>
<tr>
<td>BWI</td>
<td>-0.78*</td>
<td>-0.44</td>
<td>-0.42</td>
</tr>
<tr>
<td>Prominence of centrilobular</td>
<td>-0.04</td>
<td>0.51</td>
<td>0.06</td>
</tr>
<tr>
<td>structure (grade)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Air trapping (grade)</td>
<td>-0.26</td>
<td>0.26</td>
<td>-0.05</td>
</tr>
</tbody>
</table>

*p < 0.01.*
elevated air trapping percentage was not normalized in all of the asthmatic subjects, regardless of the severity of the disease (Fig 3, top right, C, and bottom right, F).

**Discussion**

Our study demonstrates that the abnormalities seen on HRCT scans, such as bronchial wall thickening, air trapping, and prominence of centrilobular structures, are more extensive in all groups of asthma patients than in normal control subjects, regardless of the severity of the disease. One interesting finding is that NFA patients exhibited more severe prominence of centrilobular structures than did patients with moderate-to-severe asthma, with the same FEV₁ values, although there were no significant differences in the BWI and air-trapping parameters. The HRCT finding of prominence of centrilobular structures in asthmatic patients has not received much attention. Lynch et al²² reported that 10% of asthmatic patients had a prominence of centrilobular structures, whereas Grenier et al²³ and Harmanci et al²⁴ reported that at least 20% of asthmatic patients fell into this category. In the present study, 36% of patients with mild asthma and 70% of patients with moderate-to-severe asthma had a prominence of centrilobular structures. The incidence of prominence of centrilobular structures in our study is much higher than that reported previously.²²-²⁴ This may be due to different HRCT scanning methods and analyses. We analyzed quantitatively the HRCT scans for a 10-mm interval of entire lungs, which is a substantially larger overall lung area than those analyzed in the other studies. Prominence of centrilobular structures on HRCT may be due to intrabronchiolar mucoid impaction, peribronchiolar inflammation, and bronchiolar wall remodeling, which includes muscular hypertrophy. In support of this concept, pathologic studies of asthma patients who were dying of status asthmaticus showed severe air trapping and atelectasis, which are related to the

![Figure 3. Changes of BWI, prominence of centrilobular structure, and air trapping on HRCT over a mean interval of 16.8 months (range, 7 to 24 months) of treatment with inhaled steroid in patients with groups 1 and 2 (top left, A; top center, B; and top right, C) and group 3 (bottom left, D; bottom center, E; and bottom right, F). NS indicates p > 0.05.](http://publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/22019/ on 04/28/2017)
plugging of small bronchi and bronchioles with tenacious inflammatory debris. In addition, the inflammatory debris consisted of plasma exudates and inflammatory cells, particularly eosinophils and epithelial cells that were sloughed from the airway surface.25,26 Mucosal biopsies demonstrated the presence of marked eosinophilic inflammation in the small airways of patients with mild asthma.27,28 In addition to airway inflammation, remodeling, and especially collagen deposition, smooth-muscle hypertrophy was also found throughout the peripheral airways.28,29 It is generally believed that the structural airway changes seen in postmortem or surgically resected lungs of patients with severe asthma have more profound physiologic consequences in the distal small airways than in the proximal large airways.30 These pathologic changes are most striking in cases that progress to fatal attacks.9 In the present study, all of the patients with NFA revealed prominence of centrilobular structures on HRCT scans. To our knowledge, the prominence of centrilobular structures on HRCT scans has not been analyzed previously in patients with NFA. The results of this study suggest that extensive small airway changes may be associated with NFA, and that these changes are reflected by prominence of centrilobular structures on HRCT scans.

We also observed increases in air trapping and BWI in patients with moderate-to-severe asthma, and even in those with mild asthma, as compared to the normal control subjects. Air trapping can also be seen in normal subjects, although its extent is limited. Focal areas of relative lucency can be seen in normal subjects on expiratory scans in the superior segments of the lower lobes.31 In a study by Lucidarme et al32 of 10 normal nonsmokers, excluding the superior segments of the lower lobes and isolated pulmonary lobules, no air trapping was visible. It is postulated that the slender segments may be less well ventilated than the adjacent lung, having a tendency to trap air during exhalation.

However, there were no significant differences in BWI between the patients with NFA and those with moderate-to-severe asthma, which corroborates the previous findings of Awadh and coworkers.12 BWI was measured mainly in the large airways, which encompassed the segmental and subsegmental bronchi. Large airway wall thickening is attributed to thickening of the basement membrane, goblet-cell hyperplasia, hypertrophy of the submucosal glands, and bronchial smooth-muscle hyperplasia.33 Dunnill and colleagues6,34 showed a quantitative difference in bronchial wall thickness between patients with status asthmaticus and patients with chronic bronchitis. Enlargement of the mucus gland was observed in both groups, but only in patients with status asthmaticus was there a marked increase in smooth-muscle volume, which accounts for 20% of the bronchial wall in certain cases.35 Airway wall thickening may be a major determinant of airway narrowing, airflow limitation, and symptom severity in asthmatic patients.10,35,36 In our study, derangement of FEV1 correlated strongly with BWI in patients with mild-to-severe persistent asthma, which is in good agreement with the results of previous studies.11,37 However, we could not find any significant difference in the BWI values between the groups of patients with asthma, which indicates that bronchial wall thickening is not a contributory factor to NFA, but is a basic underlying change in all asthma groups, including mild asthmatics. In our study, FEV1 did not correlate with the grade of prominence of centrilobular structures or extent of air trapping in patients with NFA, which suggests that airflow limitation in NFA cases are probably not determined by a single abnormality, such as bronchial wall thickness, but instead appears to be determined by multifactorial abnormalities of the airways.7–9

Paganin et al10,35 considered bronchial wall thickening in asthmatic patients as an irreversible structural abnormality, although bronchial wall thickening has also been described as being reversible.38 The reversibility of bronchial wall thickening depends on the underlying pathologic features. It appears to be reversible when submucosal inflammation or edema predominate, and irreversible when the airways are remodeled extensively. Paganin and colleagues10,35 reported on the evolution of CT abnormalities after antiasthmatic therapy. On follow-up within 1 week or 2 weeks, mucoid impaction, acinar patterns, and lobar collapse were reversible, while bronchial wall thickness, bronchiectasis, and emphysema were unchanged. The reversibility of remodeled airways is supported in part by a pathologic study39 showing that subepithelial collagen deposition, which is one component of bronchial wall thickening, was reduced significantly in asthmatic patients who had undergone intensive anti-inflammatory therapy. However, no study has been undertaken on the changes in airway abnormalities over a relatively long period (6 months) following intensive anti-inflammatory therapy. Our results reveal that bronchial wall thickening is partially reversible in asthmatic patients, regardless of disease severity. However, air trapping was not improved in the non-NFA and NFA patients, which suggests that air trapping is more refractive than bronchial wall thickening to steroid therapy. The different responses of the airway abnormalities to inhaled steroid therapy may be due to differences in the involved sites, ie, bronchus vs bronchiole. The lack of impact of inhaled steroid
treatment on air trapping may not be due to the duration of treatment, but rather appears to be due to a lack of penetration of the inhaled steroid into the peripheral airways. In the present study, the extent of prominence of centrilobular structures decreased during the treatment period, but did not attain the normal level (grade 0) in 43% of the non-NFA patients and in 100% of the patients with NFA. The extent of residual prominence of centrilobular structures was significantly more pronounced in the NFA patients than in the non-NFA patients, which indicates that remodeled small airways are more refractory to intensive and prolonged corticosteroid treatment in NFA patients than in non-NFA patients. The limiting factor of our study should be noted. Since only the bronchi seen in cross-section were analyzed, and only 10% of the lungs were imaged, many bronchi were not analyzed.

In conclusion, among the HRCT findings of airway abnormalities, only the severity of prominence of centrilobular structures differed significantly between the patient groups of NFA, mild, and moderate-to-severe asthma. The small airway abnormalities on HRCT scans may be partially reversible following intensive and relatively long-term treatment. However, these findings are not equally applicable to both NFA and non-NFA patients. NFA patients have lower responses to steroid treatment than non-NFA patients. The exact nature of the small airway abnormalities remains to be elucidated in asthmatic patients, especially in patients with a previous history of NFA.

**References**


34. Dunnill MS, Massarella GR, Anderson JA. A comparison of the quantitative anatomy of the bronchi in normal subjects, in status asthmaticus, in chronic bronchitis and in emphysema. Thorax 1969; 24:176–179


