

◎原 著

Long-term cigarette smoking influences low attenuation area of the lungs on high-resolution CT in elderly patients with asthma, compared with pulmonary emphysema.

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Abstract : The influence of cigarette smoking on the pathophysiology in elderly patients with asthma. Forty asthmatics over the age of 70 years (20 ex-smokers and 20 never-smokers), and 20 patients with pulmonary emphysema over age 70 (all ever-smokers) were studied to determine the influence of cigarette smoke on the low attenuation area (LAA) < -950 HU (RA₉₅₀) of the lungs on high resolution CT (HRCT) scans, and the ratio of expiratory LAA to inspiratory LAA of the lungs in relation to pulmonary function. The LAA value was significantly higher in patients with pulmonary emphysema compared with ever-smokers of asthmatics. The LAA ratio was significantly higher in ever-smokers than in never-smokers of asthmatics, and the ratio was less than 0.5 in all never-smokers, and the ratio was more than 0.5 in 10 of 20 ever-smokers of asthmatics and in all patients with pulmonary emphysema. The %RV (residual volume) was significantly larger and %DLco (diffusing capacity for carbon monoxide) was significantly lower in subjects with the ratio more than 0.5 than in those with the ratio less than 0.5. These results suggest that cigarette smoke influences LAA of the lungs in relation to %RV value and %DLco value.

Key words : cigarette smoking, high resolution CT, %RV, %DLco, elderly asthmatics

Introduction

It has been reported that adult onset of asthma is not associated with ever-smoking, however, current smoking is found to increase

asthma severity¹⁾. Ever-smoking for 3 years is found to increase the risk of asthma two-fold²⁾. Exposure to parental smoking (both parents more than half a pack of cigarette a day) during childhood is significantly associated with physician-reported asthma^{3,4)}. Recent reports have

reinforced previous conclusions that exposure to ETS (environmental tobacco smoke) cause the onset of childhood asthma and exacerbation of symptoms throughout life^{5, 6)}. In contrast, the effects of ETS exposure on adult asthma have not yet been investigated extensively⁷⁾.

The possibility for risk of active smoking for developing adulthood asthma also remains controversial. Several studies have supported higher incidence of asthma in current and former smokers, compared with never-smokers^{8, 9)}.

Our previous studies showed that the high-resolution CT (HRCT) lung densitometry, which correlated with parameters of airflow limitation and lung volume, but not with lung transfer factor, was influenced by aging, disease severity, and cigarette smoking^{10, 11)}. However, influence of long-term cigarette smoking on the pathophysiology of asthma in the elderly is still unclear. In the present study, the influence of cigarette smoke on the low attenuation area (LAA) <-950 HU of the lungs on high resolution CT (HRCT) scans, and the ratio of expiratory LAA to inspiratory LAA in relation to %RV and %DLco was examined in the elderly patients with asthma and in those with pulmonary emphysema.

Subjects and Methods

Forty asthmatic subjects over the age of 70 years (14 women and 26 men), and 20 subjects with pulmonary emphysema (mean age 75.3 years, all men and all smokers) were recruited from Misasa Medical Center. The mean age of elderly subjects with asthma was 74.9 years and age at onset of the disease was 59.2 years. Twenty of them had a history of smoking more than 20 years (50.1 pack-year). All of them were ex-smokers. The remaining 20 elderly subjects were never-smokers. Asthma was diagnosed according to the definition proposed by

the American Thoracic Society¹³⁾. The asthmatic subjects were stable with no changes in asthma symptoms and medication for at least 1 month, except for the use of short acting β_2 agonists. Diagnosis of pulmonary emphysema was made by clinical symptoms, pulmonary function, chest radiography and CT findings¹⁴⁾.

Spirometry was performed by means of a CHESTAC 33 (Chest Co, Tokyo, Japan) linked to a computer when their symptoms were stable. The following measurements were performed on all subjects: forced vital capacity (FVC), FEV₁, and FEV₁/FVC. Residual volume (RV) was measured by body plethysmography (Autobox 2800, Chest Co, Tokyo, Japan). The diffusing capacity for carbon monoxide (DLco) was measured by the single breath technique using a CHESTAC 33. The actual DLco values were corrected for hemoglobin and carbon monoxide levels.

All subjects had a modified HRCT scan of the lungs with a Toshiba Xpeed scanner (Toshiba, Tokyo, Japan) using the thin section (2 mm collimation) technique and a high-resolution reconstruction algorithm. An intravenous contrast medium was not administered. The scanning time was 2.7 seconds, tube current was 200 mA, and voltage was 120 kVp. Maximal inspiratory and maximal expiratory HRCT scans were obtained at the following three selected anatomic levels as described by Miniati et al.¹⁴⁾: (1) top of the aortic arch, (2) origin of the lower lobe bronchus, and (3) 3 cm above the top of the diaphragm. The relative area of the lungs with an attenuation value lower than -950 HU (LAA) from the three anatomic lung levels was obtained both at full inspiration (inspiratory RA₉₅₀) and full expiration (expiratory RA₉₅₀). The LAA value was expressed as the mean of inspiratory RA₉₅₀ at three anatomic lung levels. The ratio of expiratory RA₉₅₀ to inspiratory RA₉₅₀ (RA₉₅₀ ratio) was also calculated. The ratio of expLAA/insLAA

was divided into two degrees : <0.5 and $0.5 <$.

Serum IgE was measured by radioimmunosorbent test (RIST), and IgE antibodies specific to aeroallergens including house dust mite, pollens, moulds, and animal danders were measured using the Pharmacia CAP system (Pharmacia Diagnostics AB, Uppsala, Sweden).

Informed consent was obtained from all subjects and the study protocol was approved by the ethics committee of our institution.

Statistically significant differences of the mean were estimated using the unpaired Student's *t* test. A *p* value of <0.05 was regarded as significant.

Results

The %LAA <950 HU (RA_{950}) of the lungs on HRCT was compared among ever-smokers and never-smokers of asthmatics, and patients with pulmonary emphysema (all ever-smokers). The %LAA value of the lungs in patients with asthma was significantly larger in ever-smokers ($29.4 \pm 11.8\%$, mean \pm SD) than in never-smokers ($10.97.4\%$) ($p < 0.001$). The value was significantly higher in subjects with pulmonary emphysema compared with ever-smokers of asthmatics ($p < 0.001$), as shown in Fig. 1.

The RA_{950} ratio was also significantly higher in ever-smokers of asthmatics (0.48 ± 0.26) compared with never-smokers of them (0.17 ± 0.11) ($p < 0.001$). The RA_{950} ratio was significantly higher in patients with pulmonary emphysema (0.78 ± 0.08) than in ever-smokers of asthmatics ($p < 0.001$) (Fig. 2). The RA_{950} ratio was less than 0.5 in all never-smokers of asthmatics, and the ratio more than 0.5 was observed in 10 of 20 asthmatics with a history of smoking and in all subject with pulmonary emphysema.



Fig. 1. %LAA of the lungs on HRCT in patients with asthma and pulmonary emphysema.

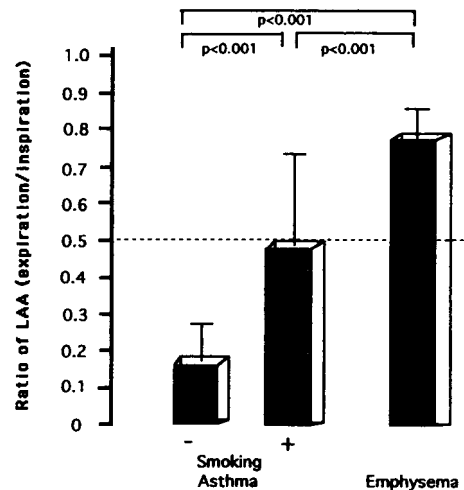


Fig. 2. Ratio of expiratory LAA / inspiratory LAA in patients with asthma and pulmonary emphysema

The %RV and the %DL_{co} were compared among ever-smokers of asthmatics with the ratio <0.5 or >0.5 , and subjects with pulmonary emphysema. The %RV was significantly larger in subjects with the ratio more than 0.5 than in those with the ratio less than 0.5 ($p < 0.05$). However, the %RV was not significantly different between asthmatics with the ratio more than 0.5 and patients with pulmonary emphysema (Fig. 3).

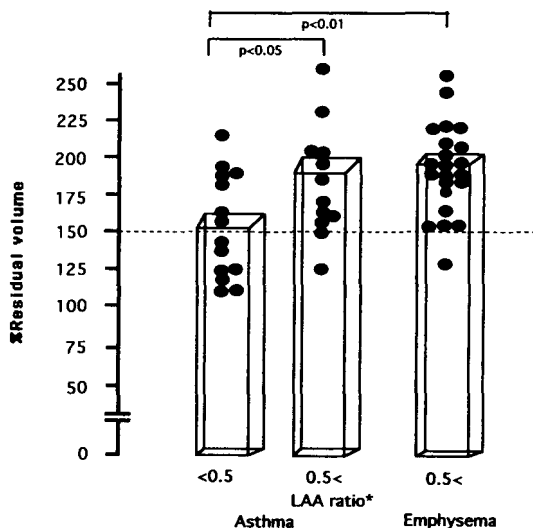


Fig. 3. %Residual volume (RV) in patients with asthma and pulmonary emphysema. *ratio of LAA in expiration/LAA in inspiration

The %DLco was significantly higher in asthmatics with the ratio less than 0.5 compared with asthmatics with the ratio more than 0.5 ($p < 0.05$). However, there was no significant difference between asthmatics with the ratio more than 0.5 and patients with pulmonary emphysema (Fig. 4).

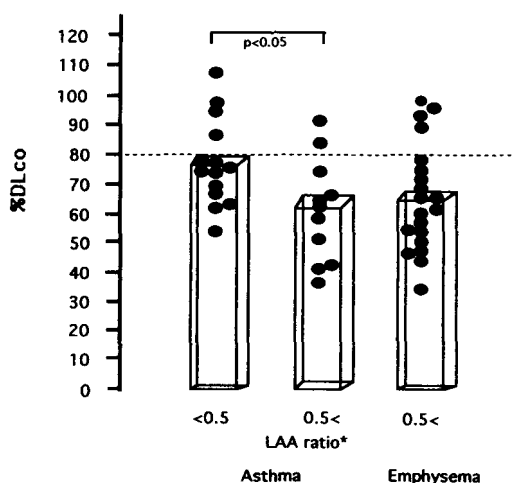


Fig. 4. %DLco in patients with asthma and pulmonary emphysema. *ratio of LAA in expiration/LAA in inspiration

Discussion

It has been reported that incidence of asthma and disease severity were associated with cigarette smoke when these were compared with never-smokers^{9, 10, 15}. In never-smokers with childhood environmental tobacco smoke (ETS) exposure, the prevalence of physician-diagnosed asthma was significantly larger (7.6%) compared with that in nonexposed subjects (5.9%). Childhood exposure to ETS is associated with an increased prevalence of asthma among adult never-smokers, especially in nonatopic subjects¹⁶. The effects of ETS exposure on adult asthma have not yet been investigated extensively, and the available data are limited⁷. However, there are several reports indicate that ETS may induce asthma in adults^{2, 4}.

Our previous studies have demonstrated that aging, disease severity, and cigarette smoke influence low attenuation area (LAA) < -950 HU (RA_{950}) of the lungs on HRCT^{11, 12}. In the present study, to determine the influence of cigarette smoking on the pathophysiology of asthma in the elderly, the LAA of the lungs on HRCT was studied in patients with a history of smoking for more than 20 years. The results were compared with never-smokers of asthmatics and patients with pulmonary function. The results suggest that %LAA of the lungs on HRCT is affected by long-term cigarette smoking. The results also show that an increase in %LAA by cigarette smoke is associated with an increase in %RV and a decrease in %DLco. The %RV in asthmatics with a history of smoking was significantly different between subjects with the %LAA ratio less than 0.5 and those with the ratio more than 0.5. The %DLco value was also significantly different between two groups of asthmatic with a history of smoking.

The relative area of the lungs with attenuation values less than -950 HU (RA_{950}) on HRCT scans obtained at full inspiration is found to be an objective measure of the extent of pulmonary emphysema by comparison with histopathologic data^{17,18}. Our previous studies showed that the RA_{950} of the lungs was significantly larger in asthmatics with a smoking history compared with those without a smoking history¹¹. The RA_{950} is also influenced by aging and disease severity in asthmatics without a smoking history¹². In this study, %RV and %DLco were not significantly different between asthmatics with the LAA ratio more than 0.5 and patients with pulmonary emphysema. The results suggest that airway pathophysiology in asthmatics affected strongly by cigarette smoke become similar to that in patients with pulmonary emphysema.

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高齢者喘息におけるHRCT上の肺のlow attenuation area (LAA) に及ぼす長期間喫煙の影響、肺気腫症例との比較。

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70歳以上の気管支喘息40例(20例喫煙者, 20例非喫煙者)および肺気腫20例を対象に, 長期間喫煙のHRCT上の-950 HU以下の肺のlow attenuation area (LAA) に及ぼす影響について検討した。

HRCT上の肺の%LAAは, 喘息の喫煙例で非喫煙例に比べ有意に高い値を示した。また, この%LAAは, 肺気腫症例で喘息の喫煙例に比べさらに高い値を示した。LAA比(呼気時LAA/吸気時LAA)は, 喘息症例では喫煙例で非喫煙例比べ有意に高い値を示したが, 肺気腫症例ではさらに高い値を示した。LAA比0.5以上を示す症例は, 喘息の非喫煙例では見られず, 喫煙例で20例中10例, 肺気腫症例では全例に見られた。そして, 喘息喫煙例でLAA比が0.5以上を示す症例は, 0.5以下の症例に比べ, %RVは有意に高く, また%DLcoは有意に低い値を示した。しかし, %RV, %DLco値いずれも喘息のLAA比0.5以上の症例と肺気腫の間には有意差は見られず, 喘息における喫煙の影響の高いことが示唆された。