Decrease in Low Attenuation Area (LAA) of the Lungs on High Resolution Computed Tomography (HRCT) by Long-term Spa Therapy in Patients with Asthma

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抄 録
気管支喘息132例を対象に、High-resolution computed tomography (HRCT) 上の肺のLow attenuation area (LAA) 950HUの臨床的意義づけ、および平均% LAAが30%以上の症例5例を対象に、長期温泉療法のLAAに対する効果について検討した。

1. 気管支喘息で見られるHRCT上の肺のLAAは、肺気腫におけるLAAとは形態的に異なっていることが示唆された。2. 気管支喘息におけるLAAの程度は、残気率(%)と有意の相関を示した。3. 喘息5例の平均% LAAは、温泉療法前33.5%であったが、24ヶ月にわたる長期温泉療法により24.5%へと有意の減少傾向を示した。同時に関数も長期温泉療法により有意の増加傾向を示した。4. % FEV1.0値は、温泉療法前の平均52.1%から温泉療法24ヶ月後には72.1%へと有意の改善しが見られた。% RV値は温泉療法により減少する傾向は見られず有意の差ではなかった。

以上の結果より、喘息における肺の% LAAは、肺の過膨張と関連していること、そしてこのLAAは長期温泉療法により有意の減少を示すことが示唆された。

Key words : asthma, spa therapy, LAA of lungs, FEV1.0, RV
I INTRODUCTION

Asthma is a disease characterized by chronic airway inflammation. Airway and lung parenchymal changes in asthma are considered to be responsible for the irreversibility of airway obstruction that is often observed in patients with severe asthma. Features of airway reconstruction such as bronchial wall thickening, bronchiectasis, emphysema, and mosaic patterns of lung attenuation, have been observed by high resolution computed tomography (HRCT) in patients with asthma. However, evidence for the presence of emphysema in patients with asthma is controversial.

The relative area of the lungs with attenuation values less than -950 Hounsfield Units (HU) on HRCT scans obtained at full inspiration is an objective measure of the extent of pulmonary emphysema by comparison with histologic data. Paganin et al. found that patients with asthma did develop emphysema and that the extent of permanent abnormalities increased as a function of the severity and duration of both allergic and nonallergic asthma. In contrast, Mochizuki et al. found no patients with emphysema among smokers, including those with severe asthma or asthma of long duration, suggesting that asthma alone does not lead to emphysema. Despite these findings, low-attenuation areas of the lungs on HRCT, and a reduction in computed tomographic lung density were observed in patients with asthma. In our previous studies, we evaluated the presence and the severity of low attenuation areas and the mean density of the lung in patients with asthma and chronic obstructive pulmonary disease (COPD) using HRCT, and compared these findings to clinical features and pulmonary function tests to determine whether low attenuation indicate hyperinflation and nonemphysematous expiratory airflow limitation or emphysematous lesions. The results suggested that LAA in asthma is more closely related to hyperinflation or nonemphysematous expiratory airflow limitation than to emphysematous changes.

Our previous studies have shown that spa therapy improves subjective and objective symptoms, and ventilatory function and suppresses bronchial hyperresponsiveness, and normalizes suppressed function of adrenocortical glands in patients with asthma. Furthermore, low attenuation area <-950 HU of the lungs on HRCT tended to decrease after spa therapy. In the present study, characteristics of low attenuation area (LAA) of the lungs on HRCT in asthma and effects of long-term spa therapy on the LAA were examined in patients with asthma.

II SUBJECTS AND METHODS

The subjects of this study were 132 patients (105 females and 47 males) with asthma. Their mean age was 60.0 years, and all subjects were nonsmokers. The subjects were divided into four groups according to their age: <49, 50-59, 60-69, and 70+ years, to clarify the characteristics of %LAA of the lung on HRCT in asthma. The values of %LAA of the lung on HRCT and %residual volume (%RV) were compared among four age groups. Five of these patients were selected to examine effects of spa therapy on %LAA of the lung on HRCT because their mean %LAA was more than 30%, and they had spa therapy for more than 2 years.
CT scans were performed on a Toshiba X peed scanner (2.7s, 200 mAs, 120KVp) without infusion of contrast medium, using 2 mm collimation (HRCT) in patients breathholding at full inspiration. The lungs were scanned as preselected three anatomic levels; (1) top of the aortic arch, (2) origin of the lower lobe bronchus, (3) three cm above the top of the diaphragm, as reported by Miniati et al.\textsuperscript{20}. Inspiratory HRCT scans were evaluated by measuring the percentage of lung area with CT number $<-950$ HU ($\%\text{LAA}$) (Fig. 1). The mean of $\%\text{LAA}$ among three anatomical levels was expressed as representative $\%\text{LAA}$ in each patient with asthma. The mean CT number was calculated from the CT numbers of the three anatomical levels.

Ventilatory function tests, $\%\text{FVC}$ and $\%\text{FEV1.0}$, were performed in all subjects using a Chestac 33 (Chest Co) linked to a computer, when they were attack-free. Residual volume (RV) was measured by body plethysmography (Autobox 2800, Chest Co). The FVC, FEV1.0, and RV measurements for each patient were expressed as a percent of the predicted values.

Statistically significant differences of the mean were estimated using the unpaired Student’s test. A value of $<0.05$ was regarded as significant.

III RESULTS

II. Characteristics of $\%\text{LAA}$ of the lungs on HRCT

Characteristics of LAA of the lungs on HRCT were estimated in 132 patients with asthma. The LAA was divided into four types according to morphological findings; 0: no emphysematous changes, 1: low attenuation area $<5$ mm in diameter (type 1), 2: circumscribed low attenuation area $>5$ mm in diameter with intervening normal lung (type 2), and 3: diffuse low attenuation area $>5$ mm in diameter without intervening normal lung (type 3) (Fig.2). However, only type 1 pattern of LAA can be observed in patients with asthma. In contrast, patients with typical emphysema show often type 3 pattern of LAA, and sometimes type 2 pattern. In this study, all of patients with asthma showed type 1 pattern of LAA of...
The %LAA of the lungs on HRCT more increased as their age was higher. The mean %LAA of the lungs in patients over the age of 70 years was significantly larger than the mean %LAA in those between the ages of 50 and 59 (p<0.001) and in those under age 49 (p<0.02) (Fig.3). The value of %residual volume (RV) tended to increase as patient age was higher. The mean of %RV in patients over the age of 70 was significantly larger in those under the age of 49 (p<0.05) and between the ages of 50 and 59 (p<0.05) (Fig.4).

A significant correlation between %RV and %LAA of the lungs on HRCT was found in patients with asthma studied, suggesting that %LAA of the lungs in asthma is closely associated with hyperinflation, as shown in Fig.5.
12. Effects of spa therapy on %LAA of the lung on HRCT in asthma

Effects of long-term spa therapy on LAA of the lungs on HRCT were observed in 5 patients with asthma, who were selected for this study because their mean %LAA was more than 30%. The mean %LAA showed a tendency to decrease by spa therapy. The value of mean %LAA before spa therapy (33.5%) significantly decreased to 28.7% at 12 months (p<0.02) and 24.5% at 24 months (p<0.001) after the starting of spa therapy (Fig. 6). The mean CT number tended to increase by long-term spa therapy. The value of mean CT number increased from -923.88 HU before spa therapy to -921.4 HU at 6 months, -917.2 HU at 12 months (p<0.01), and -913.6 HU at 24 months (p<0.001) after the starting of spa therapy (Fig. 7).

The %RV also decreased after long-term spa therapy. The mean value of %RV before spa therapy (173.4%) decreased to 170.1% at 6 months, 162.0% at 12 months, and 153.5% at 24 months after the beginning of spa therapy, however, no significant differences were found among the values before and after spa therapy (Fig. 8). The %FEV1.0 value improved after spa therapy. The mean value of %FEV1.0 (72.1%) at 24 months after spa therapy was significantly larger than the value before the therapy (52.1%) (P<0.05) (Fig. 9).

Fig. 7 Increase in CT number on HRCT by spa therapy in patients with asthma. a: p<0.01, b: p<0.001.

Fig. 8 Decrease in residual volume (RV) by spa therapy in patients with asthma.

Fig. 9 Increase in %FEV1.0 by spa therapy in patients with asthma. a: p<0.05.
IV DISCUSSION

Computed tomography (CT) is a sensitive technique of detecting emphysematous lesions in patients with chronic obstructive pulmonary disease (COPD). Regarding pulmonary emphysema, it is generally agreed that the relative lung area with low attenuation values < -950 HU on high resolution computed tomography (HRCT) scan at full inspiration is a sensitive imaging method to measure the extent of emphysema5,6).

However, whether emphysema occurs in patients with asthma is controversial. It has been reported that asthmatic patients with a TLC greater than 120% predicted showed no macroscopic evidence of emphysema by CT scanning22). No patients with emphysema were found in asthmatics among nonsmokers, even those with severe asthma or asthma of long duration7). Lynch et al.23) found mild emphysema in some patients, but most were smokers. Paganin et al.1) showed the presence of emphysema in CT scans of nonsmoking patients with severe asthma, and the same group observed that the irreversible changes, including bronchiectasis, emphysema, and bronchial wall thickening were found more frequently in patients with nonallergic than allergic asthma4).

In this study, characteristics of low attenuation area (LAA) of the lungs on HRCT in asthma were examined to clarify whether the LAA in asthma shows emphysematous change or hyperinflation of the lungs, and then effects of long-term spa therapy on the LAA of the lungs on HRCT in asthma were studied. The results obtained here demonstrate that LAA of the lungs on HRCT in asthma is different from that in pulmonary emphysema, the LAA is associated with RV, and both LAA and RV are affected by aging. These results suggest that LAA in asthma is closely related to hyperinflation, but not to emphysematous changes. It is speculated that the LAA of the lungs usually observed in asthma (type 1 pattern) shows hyperinflation, and appearance of the LAA in asthma is related to aging and severity of asthma. In contrast, if type 2 and type 3 patterns of LAA of the lungs, which is characteristic of pulmonary emphysema, are observed in asthma, appearance of these LAA is closely related to smoking, but not to pathophysiology of asthma.

A significant decrease in %LAA of the lungs on HRCT was observed after long-term spa therapy. At the same time, %FEV1.0 value also significantly increased after spa therapy. The RV value also decreased after spa therapy, however, the decrease was not significant. The result results show that long-term spa therapy is required to improve LAA of the lungs as well as RV in asthma.

References
3.) Park JW, Hong YK, Kim CW, Kim DK, Choe KO, Hong CS: High-resolution computed tomography in patients with bronchial asthma: Correlation with clinical features, pulmonary function and bronchial hyperresponsiveness. J Investig Al-
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Summary

Characteristics of low attenuation area (LAA) of the lungs on HRCT were studied in 132 patients with asthma, and long-term spa therapy on the LAA of the lungs was observed in 5 patients with asthma, whose mean %LAA was more than 30%.
1. The morphology of LAA of the lungs on HRCT observed in asthma was different from that in pulmonary emphysema.
2. The LAA of the lungs in asthma was closely related to residual volume (RV).
3. The mean %LAA value significantly decreased from 33.5% before spa therapy to 24.5% at 24 months after beginning of the therapy. CT number also significantly increased after long-term spa therapy.
4. %FEV1.0 value significantly improved from 52.1% before spa therapy to 72.1% at 24 months after spa therapy. The RV value also decreased by spa therapy, however, the decrease was not significant. These results suggest that LAA of the lungs in asthma is associated with hyperinflation, and the LAA of the lungs decreases after long-term spa therapy.