Effect of Spa Therapy on Low Attenuation Area (LAA) of the Lungs on High-resolution Computed Tomography (HRCT) and Pulmonary Function in Patients with Asthma

Kozo ASHIDA, Fumihiro MITSUNOBU, Takashi MIFUNE, Yasuhiro HOSAKI,
Kouzou ASHIDA, Hiroyumi TSUGENO, Makoto OKAMOTO, Norikazu NISHIDA,
Shingo TAKATA, Tadashi YOKOI, Yoshiro TANIZAKI

Department of Medicine, Misasa Medical Branch, Okayama University Medical School

気管支喘息におけるHigh-resolution Computed Tomography (HRCT)上のLow Attenuation Area (LAA)および換気機能に及ぼす温泉療法の効果

芦田耕三，光延文裕，御船尚志，保崎泰弘，
拓野浩史，岡本誠，西田典数，
高田真吾，横井正，谷崎勝朗

岡山大学医学部附属病院三朝分院内科

抄録

High resolution computed tomography (HRCT)上の-950HU以下のlow attenuation area (LAA)は、肺の気腫化傾向を示すと言われている。本論文では、気管支喘息9例を対象に、温泉療法のLAAに及ぼす影響を中心にその臨床効果について若干の検討を加えた。1. HRCT上の肺の第2レベル（下葉気管支の入口部の高さ）および第3レベル（横隔膜上3cmの高さ）における%LAAは、温泉療法前に比べ療法後に有意の減少傾向を示した（p<0.05）。2. CT numberも-924.4HUから-915.5HUへと有意に増加した（p<0.05）。3. %LAAは深呼気時および吸気呼気比では、温泉療法後で有意の差は見られなかった。

4. %FVCや%FEV1.0値は、温泉療法後に増加する傾向が見られたが、これらの症例では、温泉療法前と比べ有意の増加ではなかった。

5. 平均%残気量（%RV）は、温泉療法後に187.7%から142.5%へと有意の減少を示した（p<0.05）。6. %DLco値では、温泉療法前後で有意の変化は見られなかった。

以上の結果より、温泉療法によるHRCT上の%LAAの減少は、%RVの減少とある程度関連していることが示唆された。

Key words: bronchial asthma, %LAA on HRCT, residual volume, DLco, FEV1.0
INTRODUCTION

Asthma is characterized by transient dyspnea with wheezing. The symptoms of asthma are due to such pathophysiological changes in the airways as bronchoconstriction, bronchial wall edema, and mucus hypersecretion. Regarding clinical types of asthma classified by symptoms, the frequency of bronchoconstriction + hypersecretion (type Ib) and bronchiolar obstruction (type II) tends to increase in the elderly patients with asthma \(^1,2\). In addition to pathophysiological features of asthma, emphysematous changes of the lungs are sometimes observed in elderly patients with asthma \(^3\).

The diagnosis of emphysema by pathologic examination has been suggested to be correlated with high resolution computed tomography (HRCT) scan findings \(^4-6\). The low attenuation area (LAA) \(< -950 \text{ Hounsfield Unit (HU)}\) of the lungs on HRCT scans at full inspiration is an objective measure of the extent of pulmonary emphysema \(^7,8\). However, the influences of hyperinflation and of nonemphysematous expiratory airflow limitation on the CT quantification of pulmonary emphysema are still unclear \(^9\).

It has been shown that emphysematous changes of the lung on HRCT are observed in patients with asthma in relation to smoking and severity of asthma \(^10,11\). However, it is unclear whether the %LAA\(<-950\text{HU}\) of the lungs in patients with asthma is associated with hyperinflation.

In this study, the percent of low attenuation area (LAA)\(<-950\text{HU}\) of the lungs on HRCT and pulmonary function including % DLco and % residual volume (RV) were compared before and after spa therapy.

SUBJECTS AND METHODS

The subjects in this study were 9 patients (2 females and 7 males) with asthma. Their mean age was 66.7 years, ranged from 56 to 76 years. Two patients were previous and current smokers with an average smoking history of 29.0±1.4 pack-year. The remaining 7 patients were nonsmokers. Asthma was evaluated according to the criteria of the International Consensus of Diagnosis and Management of Asthma \(^12\). The mean of serum IgE was 427 IU/ml(29-1560 IU/ml). Two of 7 patients showed a positive RAST score against inhalant allergens. All patients revealed reversible airway response with a difference between prebronchodilator and postbronchodilator values of FEV1 exceeding 15%. All subjects had complex spa therapy at our hospital for 6 to 12 months \(^13-15\). An informed consent for study protocol was obtained from all study patients.

CT scans were performed on a TOSHIBA Xpeed scanner (2.7s, 200mAs, 120 kVp) without infusion of contrast medium, using 2-mm collimation (HRCT) in patients breathholding at full inspiration (on three anatomical levels) and full expiration (only on second anatomic level). The lungs were scanned at three preselected anatomic levels; (1) top of the aortic arch, (2) origin of the lowerlobe bronchus, (3) three cm above the top of the diaphragm, as reported by Miniati M, et al \(^16\). Inspiratory HRCT scans were evaluated quantitatively by measuring the percentage of lung area with CT number \(<-950\text{HU}\) (%LAA) (Fig. 1) and the mean CT number in HU. The mean of maximal %LAA between
the second and the third anatomical levels of the lungs was expressed as representative %LAA in each patient with asthma. The CT number was calculated from the CT numbers of the three anatomic levels.

Pulmonary function tests, forced vital capacity (FVC) (%predicted), forced expiratory volume in one second (FEV1)(%predicted), residual volume (RV, %predicted), and DLco value were carried out in all patients using a CHESTAC 33 (Chest Co) liked to a computer, when they were attack-free.

IgE antibodies against house dust mite (HDm), cockroach, and Candida were estimated by radioallergosorbent test (RAST) and serum level of total IgE was measured by radioimmunosorbent test (RIST).

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

RESULTS

The mean of %LAA on second level (origin of the lower lobe bronchus) of the lungs significantly decreased from 36.9 ± 7.2% before spa therapy to 29.0 ± 6.4% after the therapy (p<0.05). The mean %LAA on third level (three cm above the top of the diaphragm) of the lungs also significantly decreased from 40.5 ± 7.3% to 32.1 ± 9.5% after spa therapy (p<0.05). No significant differences were observed between smokers and nonsmokers (Fig. 1).

The mean CT number significantly increased from -924.4 ± 6.6 HU before spa therapy to -915 ± 9.9 HU after the therapy (p<0.05). There was no significant difference between smokers and nonsmokers, as shown in Fig. 2.

The mean %LAA on second level of the lungs at deep expiration was 11.6 ± 5.3% before spa therapy and 8.9 ± 5.8% after the therapy. There was no significant difference before and after spa therapy (Fig. 3). A ratio of %LAAs at inspirationexpiration did not significantly change before and after spa therapy (Fig. 4).

The %FVC value showed a tendency to increase (92.6 ± 8.7%) after spa therapy compared to the initial value (85.3 ± 15.1%) before the therapy. The %FEV 1.0 value also tended to more increase (66.3 ± 16.5%) after spa therapy than the value (59.4 ± 15.6%) before the therapy. However, these increases in %FVC and %FEV1.0 values were not significant (Fig. 5).

A significant decrease in the % residual volume (%RV) of the lung was observed in all patients who had spa therapy, and the mean of %RV significantly decreased from 187.7 ± 52.8% to 142.5 ± 35.1% after spa therapy (p<0.05). There was no significant difference between smokers and nonsmokers (Fig. 6). Regarding DLco value, the mean of this value was not significantly different before and after spa therapy, as shown in Fig. 7. The DLco value in two patients with smoking history was markedly lower compared with the values in those without smoking history (Fig. 7).
Fig. 1 Changes in %LAA on second level (origin of the lower lobe bronchus) and third level (three cm above the top of the diaphragm) of lungs on HRCT before and after spa therapy in patients with asthma. a; p<0.05, b<0.05. ○ smoker

Fig. 2 Changes in CT number before and after spa therapy in patients with asthma. a; p<0.05. ○ smoker

Fig. 3 Changes in %LAA on the second level of the lungs at deep expiration before and after spa therapy in patients with asthma. ○ smoker

Fig. 4 Changes in %LAA at inspiration/expiration before and after spa therapy in patients with asthma. ○ smoker
DISCUSSION

It is generally agreed that CT scanning is a sensitive technique of detecting emphysematous lesions in patients with chronic obstructive pulmonary disease (COPD). It has been shown that the relative lung area with low attenuation values < -950 HU on HRCT scans at full inspiration is a sensitive imaging method to measure the extent of pulmonary emphysema \(^7, 8\). Our previous studies have shown that spa therapy improved the values of %FVC and PEFR in patients with emphysema at early stage, and the increase in PEFR was significant\(^7\). However, spa therapy did not improve the values of ventilatory parameters in patients with advanced emphysema. These results suggest that spa therapy should be performed for patients with emphysema as soon as possible after definite diagnosis. Regarding mean %LAA and mean CT number, a decrease in mean %LAA and an increase in mean CT number were observed after spa therapy, suggesting that spa therapy is beneficial for the treatment of emphysema \(^3\).
The LAA is evaluated by two different aspects: severity and extent.\textsuperscript{16,19)}

The extent of emphysema was on a 4-point scale: 1. <25\% of the lung parenchyma involved, 2. 25 to 50\% lung involved, 3. 50 to 75\% lung involved, and 4. >75\% lung involved. In this study, patients whose %LAA on second level or third level was more than 25\% were selected, and the mean %LAA36.9\% on the second level of the lungs, and 40.5\% on the third level, respectively. In contrast, severity is graded on a 4-point scale: 0. No emphysema, 1. Low attenuation areas <5mm in diameter, 2. Circumscribed low attenuation areas >5mm in diameter with intervening normal lung, and 3. diffuse low attenuation areas without intervening normal lung. Low attenuation areas of the lungs on HRCT can be observed even in patients with asthma\textsuperscript{22)}, however, only type 1 pattern of LAA (LAA<5mm in diameter with intervening normal lung) can be observed in patients with asthma. In contrast, patients with typical emphysema show mainly type 3 pattern of LAA (diffuse low attenuation areas without intervening normal lung).

It is, however, unclear whether the %LAA $<$-950HU of the lungs in patients with asthma (type 1 pattern) is associated with hyperinflation or emphysematous changes.

Regarding the percentage of low attenuation area (%LAA) of the lung, Newman KB, et al. have reported that there was no significant difference between asthmatic patients and control subjects for the inspiratory HRCT scans obtained in the lower lung areas (<-900HU), whereas difference was significant for the upper lung areas \textsuperscript{20}. They concluded that hyperinflation and airflow obstruction without emphysematous lung destruction would not influence densitometric measurements obtained from inspiratory scans.

In this study, effects of spa therapy on %LAA of the lungs on HRCT and pulmonary function (FVC, FEV1.0, RV, and DLco) were examined in patients with asthma showing %LAA more than 25\%. The results obtained here showed that LAA(type 1 pattern, LAA<5mm in diameter with intervening normal lung, observed in patients with asthma) decreased after spa therapy in patients with asthma, and the decrease in LAA of the lungs was accompanied with the decrease in %RV. The results suggest that LAA in patients with asthma is closely related with hyperinflation. The values of FVC, FEV1.0, and DLco also increased after spa therapy, however, the increase in each parameter was not significant in these patients with asthma.

References
LAA and Pulmonary Function in Asthma


