### ◎原 著

Clinical effects of long-term spa therapy on pulmonary emphysema. Evaluation by pulmonary function and pathological changes of terminal airspace of the lung

Fumihiro Mitsunobu, Yasuhiro Hosaki, Kozo Ashida, Naofumi Iwagaki, Takuya Nagata, Makoto Fujii, Shingo Takata, Tadashi Yokoi<sup>1)</sup>, Masanori Hamada<sup>1)</sup>, and Yoshiro Tanizaki

Division of Medicine, <sup>1)</sup>Division of Rehabilitation, Misasa Medical Center, Okayama University Medical and Dental School

Abstract: Clinical effects of long-term spa therapy for 4 years were estimated in 8 patients of pulmonary emphysema (4 with spa therapy and 4 without spa therapy) by pulmonary function and morphological changes of peripheral airspaces of the lung on high-resolution computed tomography (HRCT).

- 1. The values of %FVC, %FEV1.0, and FEV1.0% did not significantly change for 4-year observation both in patients with spa therapy and those without spa therapy.
- 2. The DLco value significantly decreased from 69.9% at the initial level to 48.8% after 4-year observation in patients without spa therapy (p<0.02). However, the DLco value did not significantly decrease in patients with spa therapy. 3. The values of %RV and %LAA of the lung showed a significant increase in patients without spa therapy (%RV:p<0.05, %LAA:p<0.01 after 4-year observation compared with the initial levels), however, a change in %RV and %LAA was not significant in patients with spa therapy. 4. The CT number also significantly decreased in patients without spa therapy, but not in those with spa therapy. The results suggest that spa therapy improves %DLco, %RV and morphological changes of peripheral airspaces, chiefly overinflation, of the lung in patients with pulmonary emphysema.

Key words: spa therapy, pulmonary emphysema, %RV, %DLco, %low attenuation area of the lung

#### Introduction

Bronchial asthma and pulmonary emphysema are diseases showing obstructive ventilatory dysfunction, which causes the morphological changes of terminal airspaces of the lung. It has been shown that the relative area of the lungs with attenuation values less than -950 Hounsfield Units (HU) on high-resolution computed tomography (HRCT) scans obtained at full inspiration is an objective measure of the extent of pulmonary emphysema by comparison with histologic data<sup>1,2)</sup>. The low attenuation area (LAA) of the lungs on HRCT, and a reduction in computed tomographic lung density are also observed in patients with asthma<sup>3,4)</sup>.

Our previous studies have shown that spa therapy is effective for patients with asthma accompanied by emphysematous changes 5-77. The %LAA of the lungs on HRCT decreased in patients with asthma, whose %LAA of the lungs was more than 25%, after spa therapy for 6 to 12 months. The values of forced vital capacity (FVC), forced expiratory volume in one second (FEV1.0), and diffusing capacity for carbon monoxide (DLco) also increased after spa therapy, however, the increase in each parameter was not significant in these patients with asthma<sup>6)</sup>. The efficacy of spa therapy is also observed in patients with pulmonary emphysema8+11). The results obtained from 1-month spa therapy shows that the therapy did not improve the values of ventilatory parameters in patients with advanced emphysema  $(40\% \le \text{mean } \% \text{LAA})$ . However, the values of FVC and peak expiratory flow rate (PEFR) remarkably increased in patients with emphysema at early stage (mean %LAA≤39%) 8).

In the present study, the effects of long-term spa therapy for 4 years on pulmonary emphysema were evaluated in patients with pulmonary emphysema by observing the changes of pulmonary function and morphological changes of the terminal airspaces of the lung.

## Subjects and Methods

The subjects of this study were 8 patients (all males) with pulmonary emphysema. They were all previous and current smokers. Four (their mean age 69.8 years, the average smoking history 34.6 pack-years) of the 8 subjects had complex spa therapy (swimming training in a hot spring pool, inhalation of iodine salt solution, and fango therapy) for more than 4 years. The remaining 4 patients (76.8 years, 45.0 pack-years) had only drug medication without spa therapy, and their clinical course was observed for more than 4 years. The diagnosis of emphysema was performed by a criteria as previously described 91.

Pulmonary function tsets, FVC, FEV1.0, residual volume (RV), and DLco, were carried out in all subjects using a Chestac 33 (Chest Co) linked to a computer.

CT scans were performed on a Toshiba X peed scanner (2.7s, 200 mAs, 120 KVp) without infusion of contrast medium, using 2 mm collimation (high resolution computed tomography, 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<sup>13</sup>. Inspiratory high resolution CT scans were estimated by measuring the percentage of lung area with CT number <-950 HU (low attenuation area; LAA). The mean of %LAA among three anatomical levels was expressed as representative %LAA in each patient with asthma. The LAA could be classified into four types according to morphological findings; 0:no emphysematous change, 1:low attenuation

area < 5 mm in diameter (type 1), 2: circu mscribed 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). The LAA in all patients of this study was type 3 showing diffuse low attenuation area. The mean CT number was calculated from the CT number of the three anatomical levels.

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

#### Results

The %FVC value did not change in patients with spa therapy for 4 years (79.2% at the initial stage before the therapy and 78.5% at the final stage after 4-year spa therapy). The value of %FVC was not significantly different between the values at different two stages, as shown in Fig. 1. The %FEV1.0 tended to increase in

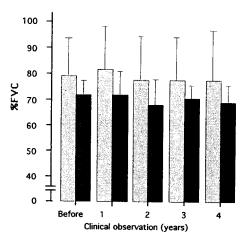


Fig.1. Changes of %FVC in patients with pulmonary emphysema with ( ) and without spa therapy ( )

patients with spa therapy from 52.6% at the initial stage to 58.0% at two years, and 53.5% at 4 years after the starting of spa therapy, however, these differences were not significant. In contrast,

the %FEV1.0 decreased in patients without spa therapy from 48.7% to 42.5% at two years, and 39.9% at 4 years after the beginning of the therapy, but these were not significant (Fig. 2).

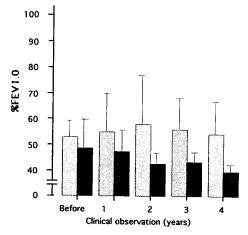


Fig.2. Changes of %FEV1.0 in patients with pulmonary emphysema with ( ) and without spa therapy ( )

The change of FEV1.0% for 4 years was similar to that in %FEV1.0 : the FEV1.0% value tended to increase in patients with spa therapy, and decrease in those without spa therapy, however, these were not significant (Fig. 3).

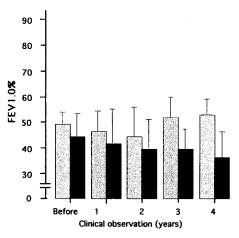


Fig.3. Changes of FEV1.0% in patients with pulmonary emphysema with ( ) and without spa therapy ( )

The DLco value did not significantly change in patients with spa therapy. In contrast, in patients without spa therapy, DLco value significantly decreased from 69.9% at the initial stage to 48.8% at 4 years after the starting of the observation (p<0.02) (Fig. 4).

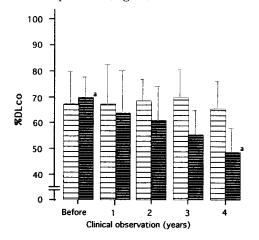


Fig.4. Changes of %DLco in patients of pulmonary emphysema with ( —) and without spa therapy ( ≡). a: p<0.02.

The %residual volume of the lung (%RV) showed a tendency to decrease in patients with spa therapy from 162.0% at the initial stage to 154.3% at the final stage after spa therapy for 4 years, but the difference was not significant (Fig. 5). The %RV value significantly increased in patients without spa therapy from 184.1% to 230.1% at the final stage after 4-year spa therapy (p<0.05) (Fig. 6).

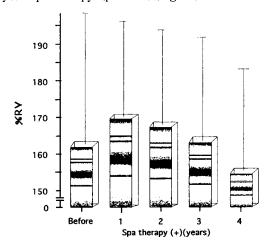


Fig.5. Changes of mean %RV in patients of pulmonary emphysema with spa therapy.

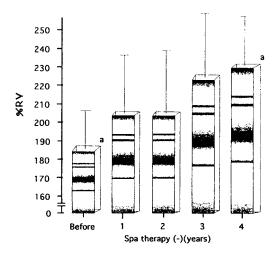


Fig.6. Changes of mean %RV in patients of pulmonary emphysema without spa therapy. a: p<0.05.

The %LAA value did not significantly change in patients with spa therapy, as shown in Fig. 7.

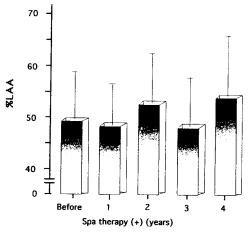


Fig.7. Changes of %LAA in patients of pulmonary emphysema with spa therapy

In contrast, the value of %LAA significantly increased in patients without spa therapy from 50.9% at the initial value to 58.9% at 3 years (p<0.02) and 61.6% at 4 years after the beginning of the observation (p<0.01) (Fig. 8).

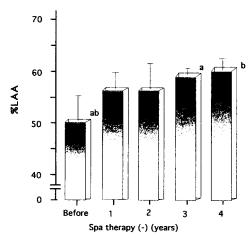


Fig. 8. Changes of %LAA in patients of pulmonary emphysema with spa therapy a: p<0.02, b: p<0.01.

The CT number also significantly decreased in patients without spa therapy from -947 HU to -956 HU at 4 years after the beginning of the observation (p<0.001), however, no significant change was found in patients with spa therapy (Fig. 9).

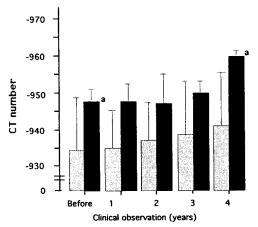


Fig.9. Changes of CT number in patients with pulmonary emphysema with ([ ] ) and without spa therapy ( ] ). a: p<0.001.

#### Discussion

Spa therapy is effective for asthma accompanied by emphysematous changes<sup>5-7)</sup>. Regarding the effects of long-term spa therapy, spa

therapy for 6 to 12 months, and the therapy for 24 months are shown to be effective on LAA of the lungs on HRCT and %RV in patients with asthma<sup>6,7)</sup>. Spa therapy is also effective for patients with emphysema<sup>8-11)</sup>. The values of FVC, %FEV1.0, %PEFR, and %RV were significantly improved after spa therapy for more than 2 months<sup>11)</sup>. In contrast, these values did not significantly change in patients without spa therapy. The value of %MMF did not significantly increase in patients with and without spa therapy. Regarding the effects of long-term spa therapy on pulmonary emphysema for 24 months, it has been shown that spa therapy significantly improved %LAA, %RV and %DLco, but not %FVC and %FEV1.0 in patients with pulmonary emphysema of %LAA less than 50%. However, spa therapy did not improve the values of %LAA, %RV, and DLco, as well as %FVC and %FEV1.0 in patients of pulmonary emphysema with %LAA more than 50%. These results suggest that spa therapy for pulmonary emphysema should start at early stage of the disease.

In the present study, the effects of long-term spa therapy for 4 years were estimated by pulmonary function and morphological changes of terminal airspaces of the lung. Regarding pulmonary function, parameters showing ventilatory function such as %FVC and %FEV1.0 did not significantly change both in patients with and without spa therapy. The %DLco value significantly decreased in patients without spa therapy, but a significant decrease in DLco was not observed in patients with spa therapy. The %RV significantly increased in patients without spa therapy, however, the value tended to decrease in those with spa therapy. The %LAA which is closely related to %RV, significantly increased in patients without spa therapy, but not in those with spa therapy. These results suggest that spa therapy could prevent the progress of pathophysiological changes of the terminal airspaces of the lung in patients with pulmonary emphysema.

### References

- 1. Gevenois PA, de Maertelaer V, de Vuyst P, et al.: Comparison of computed density and macroscopic morphometry in pulmonary emphysema. Am J Respir Crit Care Med 152: 653-657, 1995.
- 2. Gevenois PA, de Vuyst P, de Maertelaer V, et al. : Comparison of computed density and microscopic morphometry in pulmonary emphysema. Am J Respir Crit Care Med 154: 187-192, 1996.
- 3. Gevenois PA, Scillia P, de Maertelaer V, et al.: The effects of age, sex, lung size, and hyperinflation on CT lung densitometry. Am J Roentogenol 167: 1169-1173, 1996.
- 4. Biernacki W, Redpath AT, Best JJ, et al.: Measurement of CT lung density in patients with chronic asthma. Eur Respir J 10: 2455 2459, 1997.
- 5. Ashida K, Mitsunobu F, Mifune T, et al. : Clinical effects of spa therapy on patients with asthma accompanied by emphysematous changes. J Jpn Assoc Phys Med Balneol Climatol 63: 113-119, 2000.
- 6. Ashida K, Mitsunobu F, Mifune T, et al.: 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. J Jpn Assoc Phys Med balneol Climatol 64: 203-209, 2001.
- 7. Ashida K, Mitsunobu F, Hosaki Y, et al.: Decrease in low attenuation area (LAA) of the lung on high resolution computed tomo-

- graphy (HRCT) by long-term spa therapy in patients with asthma. J Jpn Assoc Phys Med Balneol Climotol 66: 115-122, 2003.
- 8. Mitsunobu F, Mifune T, Hosaki Y, et al.: Effects of spa therapy on patients with pulmonary emphysema. Relationship to disease severity evaluated by low attenuation area of the lung on high resolution computed tomography. J Jpn Assoc Phys Med Balneol Climatol 61: 79–86, 1998.
- 9. Mitsunobu F, Mifune T, Hosaki Y, et al.: Improvement of pulmonary function by spa therapy in patients with emphysema, evaluated by residual volume (RV) and low attenuation area (LAA) of high-resolution computed tomography (HRCT). J Jpn Assoc Phys Med Balneol Climatol 62: 121-128, 1999.
- 10. Mitsunobu F, Mifune T, Hosaki Y, et al. : Effects of spa therapy on pulmonary emphysema in relation to IgE-mediated allergy. J Jpn Assoc Phys Med Balneol Climatol 63: 120-126, 2000.
- 11. Mistunobu F, Hosaki Y, Ashida K, et al.:
  Long-term spa therapy prevents the progressive pathological changes of the lung in patients with pulmonary emphysema. J Jpn Assoc Phys Med Balneol Climatol 66: 91-98, 2003.
- 12. Tanizaki Y, Kitani H, Okaki M, et al.: Clinical effects of complex spa therapy on patients with steroid-dependent intractable asthma (SIDA). Jpn J Allergol 42:219-227, 1993.
- 13. Miniati M, Filippi E, Falaschi F, et al. : Radiologic evaluation of emphysema in patients with chronic obstructive pulmonary disease : chest radiography versus high resolution computed tomography. Am J Respir Crit Care Med 151: 1359-1368, 1995.

# 肺気腫に対する長期温泉療法の臨床的効果. 肺機能および末梢肺領域の変化による評価

光延文裕,保崎泰弘,芦田耕三,岩垣尚史, 永田拓也,藤井 誠,高田真吾,横井 正<sup>1)</sup>, 浜田全紀<sup>1)</sup>,谷崎勝朗

岡山大学医学部・歯学部附属病院三朝医療センター 内科、<sup>11</sup>リハビリテーション科

肺気腫に対する 4 年以上にわたる温泉療法の臨床効果を、肺機能の面および末梢肺領域の形態学的変化により評価した。 1. FVC、%FEV1.0、およびFEV1.0%値は、温泉療法を受けた症例と受けなかった症例の間に有意の差は見られなかった。 2. 拡散能 (DLco) は、温泉療法を受けなかった症例では、観察初期の69.9%から 4 年後に

は48.8%と有意の低下を示したが、温泉療法を続けた症例では、有意の低下は見られなかった。

3. %RVおよびHRCT上の-950HU以下の肺のlow attenuation area (LAA)は、いずれも温泉療法を受けなかった症例では有意の増加傾向を示したが、温泉療法を受けた症例では有意の増加傾向は見られなかった。4. CT numberは、温泉療法を受けなかった症例では有意の低下を示したが、温泉療法を続けた症例では有意の変化は見られなかった。これらの結果より、肺気腫に対する温泉療法を続けることにより、%DLcoや%RVは改善する傾向を示し、同時に肺胞の過膨脹の部分(破壊された部分ではなく)が改善されていく可能性が示唆される。

索引用語:温泉療法,肺気腫,%RV, %DLco, %low attenuation area of the lung