◎原 著

Influence of long-term cigarette smoking on changes of lung density by high-resolution computed tomography in asthmatics —4 years follow-up study—

Fumihiro Mitsunobu, Kozo Ashida, Yasuhiro Hosaki, Hirofumi Tsugeno, Makoto Okamoto, Norikazu Nishida, Takuya Nagata, Shingo Takata, Tadashi Yokoi, Mutsuo Nakai[1], Yoshiro Tanizaki and Mitsune Tanimoto[2]

Department of Medicine, [1]Division of Radiology, Misasa Medical Center, [2]Second Department of Internal Medicine, Okayama University Medical School

Abstract : *Background* - The influence of cigarette smoking on the pathogenesis of asthma in the elderly remains controversial. This study attempts to estimate longitudinal changes in HRCT (high resolution computed tomography) parameters and pulmonary function parameters obtained for ex-smokers and never-smokers in asthmatics during 4-yr follow-up period.

Methods - Fourteen asthmatics (6 ex-smokers and 8 never-smokers) were studied to determine the influence of aging and cigarette smoking on pulmonary function, and mean lung density (MLD) and the relative area of the lung showing attenuation values less than -950 HU (RA_{950}) on HRCT scans.

Results - The values of FVC and FEV_1 were significantly more decreased in asthmatics without a smoking history during 4-yr follow-up period. The values of FVC, FEV_1, FEV_1/FVC and $DLco/V_A$ were significantly decreased and RV/TLC were significantly increased in asthmatics with a smoking history over 4 years, and annual decline in FEV_1 ex-smokers was larger than that in never-smokers. In the upper lung field, inspiratory MLD was observed to shift in a negative direction and inspiratory RA_{950} was found to increase during 4-yr observation period in ex-smokers, but not in never-smokers. In the middle lung field, inspiratory RA_{950} was significantly enhanced in both two groups. Although expiratory MLD, expiratory RA_{950} and exp RA_{950}/ins RA_{950} were observed to change significantly during the observation period in ex-smokers, no changes were observed in never-smokers.

Conclusion - These results suggest that aging augments airspace enlargement predominantly in the middle lung field, while long term cigarette smoking further worsens emphysematous alterations in the upper lung field.

Key words : lung density, high resolution computed tomography, asthma

Introduction

Asthma is considered a chronic inflammatory disease of the airways with participation of complex cellular and chemical mediators (1). It has become evident that the repair of the chronic inflammatory process can lead to various irreversible changes. Airway reconstruction, such as bronchial wall thickening, bronchiectasis, emphysematous changes, and mosaic patterns of lung attenuation has been demonstrated by high-resolution computed tomography (HRCT) in patients with asthma (2, 3).

Smoking is closely related to the onset mechanism of COPD (4, 5). It has been shown that 80-90% of all COPD patients have a history of smoking (6), and patients with mild COPD can reduce their symptoms by stopping smoking (7). With regard to adult asthma, a recent case-control study showed that adult onset of asthma was not associated with a history of smoking (8). In contrast, it has been demonstrated that current smoking increases asthma severity (9), and higher incidences of asthma are found in current and former smokers, compared with never-smokers (10-12). Our previous studies using the relative area of the lungs showing attenuation values less than -950 HU (RA_{950}) on high resolution CT (HRCT) scans revealed that HRCT lung densitometry was influenced by aging and smoking (13, 14). However, to the best of our knowledge, it remains unclear how the long-term cigarette smoking influence on the annual change of HRCT lung density as well as pulmonary function parameters in asthma.

In the present study, we attempted to estimate longitudinal changes in HRCT parameters and pulmonary function parameters obtained for ex-smokers and never-smokers in asthmatics during 4-yr follow-up period.

Methods

SUBJECTS

Fourteen asthmatic subjects were recruited from Misasa Medical Center. Among them, six subjects (all males, mean age=64.5±5.7 years ; age at onset of the disease=51.5±21.0 years) were ex-smokers with a history of smoking>20 years (32.5±11.7 pack-years). The remaining 8 patients (2 males and 6 females, mean age=64.4±7.6 years ; age at onset=55.2±10.4 years) were never-smokers. Asthma was diagnosed according to the definition proposed by the American Thoracic Society (15), as previously described (14). All asthmatic subjects were stable with no changes in asthma symptoms and medication for at least 2 month before pulmonary function tests and HRCT, except for the use of short acting β_2 agonists. Pulmonary function tests and HRCT were annually performed at nearly the same period of time. Transitional variations of all parameters observed for various tests of pulmonary function and HRCT were assessed by estimating the annual change in each parameter. The annual change was calculated on the basis of the linear regression equation constructed using longitudinal data of each parameter obtained for each subjects.

Serum IgE was measured by radioimmunosorbent test (RIST), and IgE antibodies specific to 12 common 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.

PULMONARY FUNCTION TESTS

Pulmonary function tests were performed with

a Chestac 33 (Chest Co., Tokyo, Japan). The following measurements were performed on all subjects : forced vital capacity (FVC), FEV_1, and FEV_1/FVC. Total lung capacity (TLC), functional residual capacity (FRC), residual volume (RV) and RV/TLC were measured using the helium dilution method. The DLco and $DLco/V_A$ (alveolar volume) were measured according to the single-breath technique. The FVC, FEV_1 and FRC measurements for each patient were expressed as a percentage of their predicted values (%FVC, $\%FEV_1$ and %FRC, respectively) according to the prediction equations of the Japanese Society of Chest Diseases (16). $DLco/V_A$ was also expressed as a percentage of the predicted values following the method of Nishida ($\%DLco/V_A$). The ratio of FEV_1 to FVC (FEV_1/FVC) and RV to TLC (RV/TLC) were expressed as percentages.

COMPUTED TOMOGRAPHY

All subjects underwent a non-contrast HRCT scan of the lungs using a Toshiba Xpeed scanner (Toshiba, Tokyo, Japan) with 2 mm collimation, scanning time of 2.7 seconds, voltage of 120 kVp, and current of 200 mA. Maximal inspiratory and maximal expiratory HRCT scans were obtained at the following three selected anatomic levels, as described by Miniati et al. (17) : (1) top of the aortic arch, (2) origin of the lower lobe bronchus, and (3) 3 cm above the top of the diaphragm. The mean lung density (MLD) and the relative area of the lungs with an attenuation value lower than -950 HU (RA_{950}) from each level were obtained both at full inspiration and full expiration. The ratio of expiratory RA_{950} to inspiratory RA_{950} (exp RA_{950} /ins RA_{950}) was also calculated.

STATISTICAL ANALYSIS

Results are expressed as mean±SD. Statistically significant differences of the two values were estimated using the unpaired Student's t test and χ^2 test. The difference in data at entry and those at 4 years later was judged with the paired t test. The significance of annual changes (i.e., changes in values against follow-up time, which were determined with the linear regression) in various parameters of pulmonary function tests and HRCT parameters was estimated on the assumption that the difference in slopes conforms to the t distribution. A p value of <0.05 was regarded as significant.

Results

PATIENT CHARACTERISTICS AT ENTRY

Patient characteristics at entry are shown in Table 1. There were no significant differences between ex-smokers and never-smokers in patient age and asthma duration. Serum IgE levels and frequency of atopy did not differ significantly between ex-smokers and never-smokers in subjects studied. The values of %FVC, $\%FEV_1$ and FEV_1/FVC were significantly larger in never-smokers compared with ex-smokers ($p<0.05$). The RV/TLC value was significantly larger in asthmatics with a history of smoking than in never-smoking asthmatics ($p<0.05$). However the value of %FRC did not differ significantly between the two groups. The $\%DLco/V_A$ was significantly more decreased in ex-smokers than in never-smokers in patients with asthma ($p<0.05$) (Table 1).

Initial inspiratory MLD values in three levels and expiratory MLD values in the middle lung field were significantly more negative in patients with a smoking history than those in the never-smokers. Initial inspiratory RA_{950} values in three levels and expiratory RA_{950} values in the middle lung field were significantly larger in patients with a smoking history than those in the never-smokers (Table 2).

Table 1. Patient characteristics at entry to the study

	Asthmatics		
	Never-smokers (n=8)	Ex-smokers (n=6)	
Male/female, n	2/6	6/0	
Age, years (SD)	64.4 (7.6)	64.5 (5.7)	NS
Age at onset, years (SD)	55.2 (10.4)	51.5 (21.0)	NS
Disease duration, years (SD)	9.2 (8.0)	13.0 (15.9)	NS
Serum IgE, IU/ml (range)*	127 (25-787)	159 (29-1124)	NS
Atopy/nonatopy, n	4/4	3/3	NS
Smoking, pack-years	0	32.5 (11.7)	
FVC,%pred (SD)	104.3 (21.0)	80.1 (25.5)	p<0.05
FEV_1,%pred (SD)	91.1 (29.2)	55.8 (22.8)	p<0.05
FEV_1/FVC, % (SD)	65.1 (9.7)	49.8 (11.1)	p<0.05
FRC,%pred (SD)	110.6 (29.6)	114.9 (7.7)	NS
RV/TLC, % (SD)	65.1 (9.7)	49.8 (11.1)	p<0.05
DLCO/VA, % pred (SD)	137.2 (38.5)	90.2 (17.4)	p<0.05

Values are presented as mean and SD in parenthesis.
+: geometric mean and range in parenthesis.
FVC = forced vital capacity; %pred = percentage of the predicted value
FEV_1 = forced expiratory volume in one second
FRC = functional residual capacity; RV = residual volume; TLC = total lung capacity
DLCO = diffusing capacity of the lung for carbon monoxide; VA = alveolar volume

Table 2. HRCT parameters at entry to the study

	Asthmatics		
	Never-smokers (n=8)	Ex-smokers (n=6)	
Upper lung field (insp)			
MLD (SD)	-889 (14)	-922 (23)	p<0.01
RA_{950} (SD)	6.9 (8.8)	33.3 (20.0)	p<0.01
Middle lung field (insp)			
MLD (SD)	-894 (16)	-921 (12)	p<0.01
RA_{950} (SD)	12.7 (10.2)	33.3 (11.3)	p<0.01
Lower lung field (insp)			
MLD (SD)	-895 (15)	-922 (17)	p<0.01
RA_{950} (SD)	13.2 (8.8)	34.0 (15.0)	p<0.01
Middle lung field (exp)			
MLD (SD)	-856 (24)	-891 (16)	p<0.05
RA_{950} (SD)	2.8 (5.9)	15.7 (9.3)	p<0.05

Values are presented as mean and SD in parenthesis.
MLD = mean lung density
RA950 = the relative area of the lungs with an attenuation value lower than -950 HU

ANNUAL CHANGES IN PULMONARY FUNCTION PARAMETERS

The values of FVC and FEV_1 ($p<0.05$) showed significant annual changes in nonsmoking asthmatics during 4-yr follow-up period (Table 3). In asthmatics with a smoking history, significant differences were observed in FVC, FEV_1, FEV_1/FVC, RV/TLC and DLco/V_A ($p<0.05$). Annual decline in FEV_1 was found to be -0.05L/yr in nonsmoking asthmatics and -0.10L/yr in asthmatics with a smoking history, and the annual decline in ex-smokers was larger than that in never-smokers ($p<0.05$).

Table 3. Pulmonary function parameters at study entry and annual cangeges*

	Never-smokers		Ex-smokers	
	Initial	Change (per year)	Initial	Change (per year)
FVC	2.56 (0.43)	-0.06 (0.03)†	2.63 (0.88)	-0.18 (0.13)†
FEV_1	1.67 (0.44)	-0.05 (0.03)†	1.36 (0.64)	-0.10 (0.05)†,‡
FEV_1/FVC	65.1 (9.7)	-0.46 (0.81)	49.8 (11.1)	-1.30 (1.13)†
FRC	2.69 (0.59)	0.03 (0.30)	3.78 (0.34)	0.01 (0.11)
RV/TLC	38.8 (8.7)	0.89 (1.61)	49.6 (6.4)	1.66 (1.34)†
DLCO/VA	6.71 (2.19)	0.02 (0.10)	4.14 (0.97)	-0.17 (0.14)†

*Values are presented as mean and SD in parenthesis.
FVC = forced vital capacity; FEV_1 = forced expiratory volume in one second
FRC = functional residual capacity; RV = residual volume; TLC = total lung capacity
DLCO = diffusing capacity of the lung for carbon monoxide; VA = alveolar volume
† Differing from zero (i.e., significant annual change, $p < 0.05$)
‡ Differing from values for never-smokers ($p < 0.05$)

ANNUAL CHANGES IN MEAN LUNG DENSITY OF HRCT IMAGES

During the 4-yr follow-up period, inspiratory MLD in three levels did not change significantly in never-smokers (Figure 1). In ex-smokers,

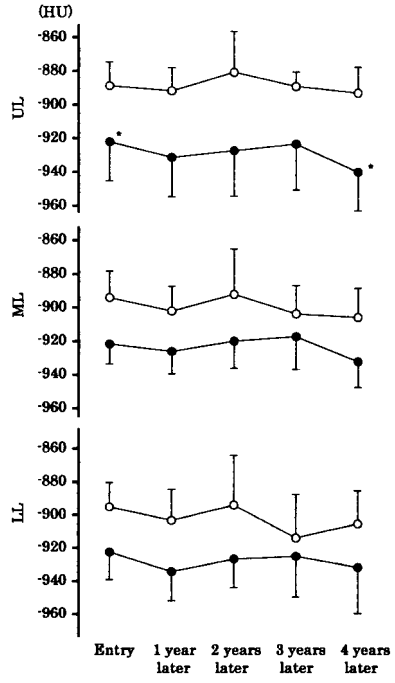

Figure 1.

Fig. 1. Longitudinal changes in inspiratory MLD for upper (UL), middle (ML), and lower (LL) lung fields during 4-yr follow-up period. Open circle=never-smokers with asthma, closed circle=ex-smokers with asthma. Values are means±SD. *Significant increase over 4 yr ($p<0.01$).

inspiratory MLD estimated in the upper lung field shifted significantly negative direction ($p<0.01$), but not in middle and lower lung fields. Expiratory MLD at the middle portion of the lung in ex-smokers was found to shift significantly in a negative direction ($p<0.05$), whereas that in never-smokers did not show any significant change (Figure 2).

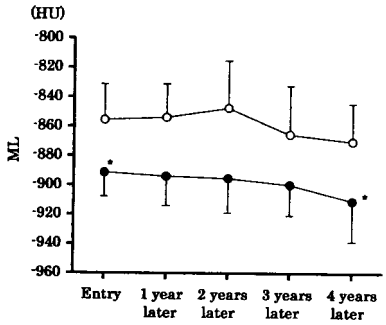

Figure 2.

Fig. 2. Longitudinal changes in expiratory MLD for middle (ML) lung fields during 4-yr follow-up period. Open circle=never-smokers with asthma, closed circle=ex-smokers with asthma. Values are means ±SD. *Significant increase over 4 yr ($p<0.05$).

ANNUAL CHANGES IN RELATIVE AREA WITH LOW ATTENUATION OF HRCT IMAGES

Although significant increase in inspiratory RA_{950} in the upper lung field was investigated for ex-smokers ($p<0.01$), upper lung inspiratory RA_{950} for never-smokers was not altered during follow-up period. (Figure 3). In the middle lung field, inspiratory RA_{950} was significantly enhanced in both two groups ($p<0.05$). Inspiratory RA_{950} at lower lung region did not change over 4 years in never-smokers and ex-smokers. Expiratory RA_{950} in the middle lung field exhibited significant change in ex-smokers ($p<0.05$), whereas that in never-smokers showed no significant change during the observation period (Figure 4).

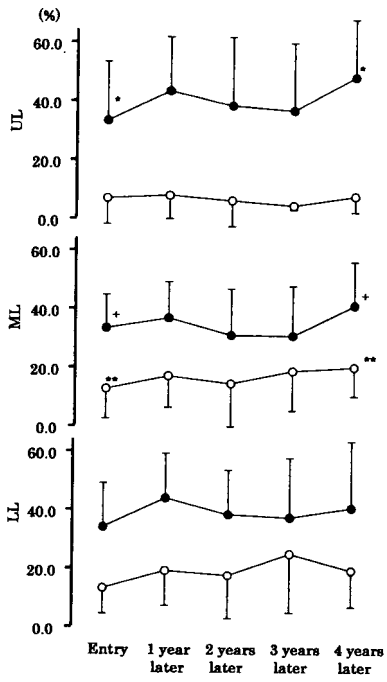

Figure 3.

Fig. 3. Longitudinal changes in inspiratory RA_{950} for upper (UL), middle (ML), and lower (LL) lung fields during 4-yr follow-up period. Open circle=never-smokers with asthma, closed circle=ex-smokers with asthma. Values are means±SD. *Significant increase over 4 yr ($p<0.01$) ; +, **Significant increase over 4 yr ($p<0.05$).

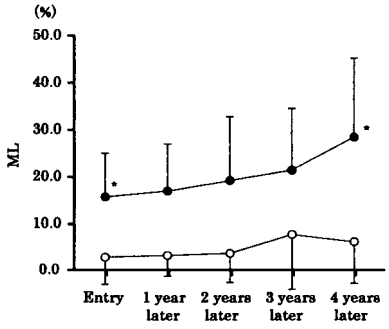

Figure 4.

Fig. 4. Longitudinal changes in expiratory RA_{950} for middle (ML) lung fields during 4-yr follow-up period. Open circle=never-smokers with asthma, closed circle=ex-smokers with asthma. Values are means±SD. *Significant increase over 4 yr ($p<0.05$).

We also found that the value of exp RA_{950}/ins RA_{950} significantly moved to a positive value in ex-smokers over 4 years, but not in never-smokers (Figure 5).

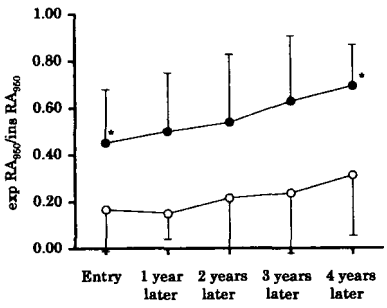

Figure 5.

Fig. 5. Longitudinal changes in exp RA_{950}/ins RA_{950} during 4-yr follow-up period. Open circle=never-smokers with asthma, closed circle=ex-smokers with asthma. Values are means±SD. *Significant increase over 4 yr ($p<0.05$).

Discussion

To investigate the influence of long term cigarette smoking on asthmatics, pulmonary function parameters and HRCT lung densitometry (MLD and RA_{950}) were followed for 4 years in ex-smokers and never-smokers in patients with asthma.

In efforts to minimize radiation exposure, we calculated both MLD and RA_{950} using three cross sections of the lung (upper, middle, and lower). This was considered adequate as Mishima et al described an accurate correlation between the percentage of low attenuation area (LAA) detected from 10 sections (from apex to base of the lung) versus three sections in patients with COPD (18).

We used -950 HU as the cut-off level between the normal lung density area and LAA. Previous studies have used variable levels ranging from -900 to -960 HU (17-24). This discrepancy may be attributed to variations between the CT scanning techniques (equipment & reconstruction of images) as well as CT images (conventional vs. high resolution). In our study, using HRCT of 15 healthy controls, we found the mean MLD minus 1 SD to be -949 HU.

Regarding the relationship between pulmonary function and cigarette smoking, although no significant correlation was found between the frequency of lower respiratory illness (LRI) and decrease in FEV_1 in sustained quitters, the frequency of LRI had an adverse effect on the 5-yr averaged annual rate of decline of FEV_1 in intermittent and continuing smokers of patients with mild COPD (7). In the present study, FVC and FEV_1 were significantly more decreased in asthmatics without a smoking history during 4-yr follow-up period, whereas RV/TLC and %DLco/V_A did not show any significant change. We also observed that FVC, FEV_1, FEV_1/FVC and %DLco/V_A were significantly decreased and RV/TLC were significantly increased in asthmatics with a smoking history over 4 years, and annual decline in FEV_1 ex-smokers was larger than that in never-smokers. The results suggested that cigarette smoking enhances hyperinflation and/or emphysematous change of the lungs expressed by an increase in RA_{950} in patients with asthma.

The relative area of the lungs with attenuation values less than -950 HU (RA_{950}) on HRCT scans obtained at full inspiration has been shown to be an objective measure of the extent of pulmonary emphysema by comparison with histopathologic data (20, 21). Previous studies have demonstrated that RA_{950} was significantly larger in asthmatics with a smoking history compared with those without a smoking history (13). RA_{950} is also influenced by aging and disease severity in asthmatics without a smoking history (14). Here, at the upper portion of the

lung, inspiratory MLD was observed to shift in a negative direction and inspiratory RA_{950} was found to increase during 4-yr observation period in ex-smokers, but not in never-smokers. In contrast, at the middle and lower portion, inspiratory MLD and RA_{950} did not show any significant change. Although expiratory MLD, expiratory RA_{950} and exp RA_{950}/ins RA_{950} significantly were observed to change during the observation period in ex-smokers, no changes were observed in never-smokers. These results demonstrated that the cigarette smoking influenced on HRCT lung densitometry especially in upper lung field and at full expiration.

In this study, we found RA_{950} at the middle portion of the lung was significantly enhanced over 4 years in nonsmoking asthmatics. Our previous study suggested that MLD and RA_{950} are significantly correlated with pulmonary function, patient age and disease severity in nonsmoking asthmatic patients (14). Soejima et al (25) demonstrated that aging influenced airspace enlargement predominantly in the middle and lower lung field. The difference between the findings of their study and ours may be due to the fact that that our subjects are asthmatics but not theirs.

In conclusion, HRCT is superior to pulmonary function measurements in detecting subtle longitudinal changes caused by aging and smoking in asthma. These results suggest that aging augments airspace enlargement predominantly in the middle lung field, while long term cigarette smoking further worsens emphysematous alterations in the upper lung field.

References

1. International Asthma Management Project. International consensus report on the diagnosis and management of asthma. Clin Exp Allergy 22 (suppl 1) : 1-5, 1992.
2. Paganin F, Trussard V, Seenetterre E et al. Chest radiography and high resolution computed tomography of the lung in asthma. Am Rev Respir Dis 146 : 1064-1087, 1992.
3. Angus RM, Davies ML, Cowman MD, McSharry C, Thomson NC. Computed tomographic scanning of the lungs in patients with allergic bronchopulmonary aspergillosis and in asthmatic patients with a positive skin test to Aspergillus fumigatus. Thorax 49 : 586-589, 1994.
4. Siafakas NM, Vermeire P, Pride N, et al. Optimal assessment and management of chronic obstructive pulmonary disease (COPD) : a consensus statement of the European Respiratory Society. Eur Respir J 8 : 1398-420, 1995.
5. British Thoracic Society. BTS Guideline for the management of Chronic obstructive pulmonary disease. Thorax 52 (Suppl 5) : S1-28, 1997.
6. U. S. Department of Health and Human Services. The Health Benefits of Smoking Cessation. A report on the Surgeon General. U. S. Government Printing Office. Washington, DC. 1990.
7. Kanner RE, Anthonisen NR, Connett JE, et al. Lower respiratory illnesses promote FEV_1 decline in current smokers but not ex-smokers with mild chronic obstructive pulmonary disease. Results from the lung health study. Am J Respir Crit Care Med 164 : 258-364, 2001.
8. SirouxV, Pin I, Oryszccsyn MP, et al. Relationship to asthma and asthma severity in EGEA study. Eur Respir J 15 : 470-7, 2000.
9. Troisi RJ, Speizer FE, Rosner B, et al. Cigarette smoking and incidence of chronic bronchitis and asthma in women. Chest 180 : 1557-61, 1995.

10. Larson L. Incidence of asthma in Swedish teenager : relation to sex and smoking-habits. Thorax 50 : 260-4, 1995.
11. Ronmark E, Lundback B, Jonsson E, et al. Incidence of asthma-report from the Obstructive Lung Disease in Northern Sweden Study. Allergy 532 : 1071-8, 1997.
12. Langhammer L, Johnsen R, Holmen J, et al. Cigarette smoking gives more respiratory symptoms among women than among men. J Epidemiol Community Health 54 : 917-22, 2000.
13. Mitsunobu F, Mifune T, Ashida K, et al. Low-attenuation areas of the lungs on high-resolution computed tomography in asthma. J Asthma 38 : 413-22, 2001.
14. Mitsunobu F, Mifune T, Ashida K, et al. Influence of age and disease severity on high resolution CT lung densitometry in asthma. Thorax 56 : 851-6, 2001.
15. American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease (COPD) and asthma. Am Rev Respir Dis 136 : 225-44, 1987.
16. Japanese Society of Chest Diseases. Standards of pulmonary function tests for Japanese. The Japanese Journal of Thoracic Diseases 31 : appendix, 1993.
17. Miniati M, Filippi E, Falaschi F, et al. Radiologic evaluation of emphysema in patients with chronic obstructive pulmonary disease : chest radiology versus high resolution computed tomography. Am J Respir Care Med 151 : 1359-67, 1995.
18. Mishima M, Hirai T, Itoh H, et al. Complexity of terminal airspace geometry assessed by lung computed tomography in normal subjects and patients with chronic obstructive pulmonary disease. Proc Natl Acad Sci USA 96 : 8829-8834, 1999.
19. Muller NL, Staples CA, Miller RR, et al. "Density mask". An objective method to quantitate emphysema using computed tomography. Chest 94 : 782-787, 1988.
20. Gevenois PA, Maertelaer VD, Vuyst PD, et al. Comparison of computed density and macroscopic morphometry in pulmonary emphysema. Am J Respir Crit Care Med 152 : 653-657, 1995.
21. Gevenois PA, Vuyst PD, Maertelaer VD, et al. Comparison of computed density and microscopic morphometry in pulmonary emphysema. Am J Respir Crit Care Med 154 : 187-192, 1996.
22. Sakai N, Mishima M, Nishimura K, et al. An automated method to assess the distribution of low attenuation areas on chest CT scans in chronic pulmonary emphysema patients. Chest 106 : 1319-1325, 1994.
23. Kinsella M, Muller NL, Abboud RT, et al. Quantitation of emphysema by computed tomography using a "density mask" program and correlation with pulmonary function tests. Chest 97 : 315-321, 1990.
24. Bae KT, Slone RM, Gierada DS, et al. Patients with emphysema : quantitative CT analysis before and after lung volume reduction surgery. Work in progress. Radiology 203 : 705-714, 1997.
25. Soejima K, Yamaguchi K, Kohda E, et al. Longitudinal follow-up study of smoking-induced lung density changes by high-resolution computed tomography. Am J Respir Crit Care Med 161 : 1264-1273, 2000.

気管支喘息のlow attenuation are（LAA）に対する長期喫煙の影響－4年間の経過観察－

光延文裕，芦田耕三，保﨑泰弘，柘野浩史，
岡本　誠，西田典数，永田拓也，高田真吾，
中井睦郎[1]，谷崎勝朗，谷本光音[2]

岡山大学医学部三朝医療センター内科，
放射線室[1]，岡山大学医学部第二内科[2]

気管支喘息患者の肺高分解能CT所見に対する長期喫煙の影響を検討することを目的とした。非喫煙喘息患者8名，喫煙歴を有する喘息患者6名を対象として，肺機能，肺平均CT値（MLD），-950 HU以下のlow attenuation area（RA_{950}）について4年間の経過観察を行った。

4年間の観察中，非喫煙喘息患者では努力肺活量，1秒量の低下を認めた。喫煙歴を有する喘息患者では努力肺活量，1秒量，1秒率，肺拡散能の低下および残気率の増加を認めた。喫煙歴を有する喘息患者では吸気において，上肺野MLDの有意の低下，RA_{950}の有意の上昇を認めたが，非喫煙喘息患者では有意の変化は認めなかった。中肺野RA_{950}は喫煙歴を有する喘息患者，非喫煙喘息患者ともに有意の上昇を認めた。また，呼気において，喫煙歴を有する喘息患者でMLDの有意の低下，RA_{950}の有意の上昇を認めたが，非喫煙喘息患者では有意の変化は認めなかった。

喘息患者において，加齢は主に中肺野のlow attenuation area，喫煙は上肺野のlow attenuation areaに影響を及ぼすことが示唆された。