Factors associated with the annual change in forced expiratory volume in 1 second of officially acknowledged victims of pollution-related illness in improved environments: a longitudinal study

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Abstract. [Purpose] We examined factors affecting annual change in pulmonary function in residents previously exposed to air pollution in an area where pollution has been reduced and a long time period has elapsed. [Subjects and Methods] Data of 730 officially acknowledged victims of pollution-related illness from an annual survey during 2000 to 2009 were analyzed. The primary outcome was forced expiratory volume in 1 second (FEV_1), along with factors such as age, body composition, smoking habits, respiratory symptoms, and classification of medical management (an index of the need for treatment). Multiple regression analyses were used to identify factors associated with the annual change in FEV_1. [Results] Three significant factors were identified: smoking habit, classification of medical management, and gender. Smoking habits and classification of medical management had stronger effects on the annual change in FEV_1 than gender. [Conclusion] With an improved environment, continuation of smoking accelerates the decline in FEV_1.
Key words: Air pollution-related illness, Longitudinal study, Pulmonary function

INTRODUCTION

In recent years, air pollution has been a serious problem in some Asian countries. An important consequence of air pollution is its effect on health, particularly on the respiratory system[1, 2]. As an assessment of respiratory health, forced expiratory volume in 1 second (FEV_1) is an important measure of the health of older people. The annual decline in FEV_1 is an important predictor of morbidity and mortality related to cardiovascular disease[3]. Usually, FEV_1 reaches a maximum in the third decade of life and then decreases gradually with age[4, 5]. In addition to physiologic factors such as aging, other factors influence the decline in FEV_1. Importantly, cigarette smoking accelerates the age-related decline in FEV_1[6]. Air pollution, as well as respiratory diseases such as asthma and chronic bronchitis, also causes a more rapid

decline in FEV_1[2, 7, 8]. Respiratory symptoms, including dyspnea, wheezing, coughing, and sputum production, occur as a result of air pollution[2], and reflect airway inflammation[9]. However, it is not clear if patients with respiratory symptoms caused by air pollution experience an accelerated decline in FEV_1.

Because of rapid industrialization in the 1960s in Japan, air pollution caused by flue gas emitted from industrial plants became a serious problem[10]. To address the issue of air pollution, the government devised two laws[11]. One of the measures, the Air Pollution Control Law, was intended to improve the environment. This law regulated acceptable levels of air pollutants and implemented measures aimed at preventing pollution. The acceptable level of sodium dioxide (SO_2) was stated to be 40 parts per billion (ppb), that of nitrogen dioxide (NO_2) was 20 ppb (until 1978, when it was changed to 40 ppb), and the acceptable level of suspended particulate matter (SPM) was ≤100 $\mu g/m^3$. Air environmental conditions improved as evidenced by reports from the Air Pollution Office (comprising the General Environmental Air Measurement Office and Motor Exhaust Measurement Office). As an example, Fig. 1 shows the average annual levels of SO_2, NO_2 and SPM recorded in Mizushima district from 1969 to 2009[12, 13]. The level of pollutants decreased to

below the minimum acceptable level from the mid-1970s. The other measure, the Pollution-related Health Damage Compensation Law, protects the cultural lives and health of people. It compensates officially acknowledged victims with pollution-related illnesses for medical fees and other medical services (e.g., medications).

Decades have passed since air pollution was a serious problem in Japan. Environmental conditions have improved over time, as has the help and aid for affected individuals. Many studies on air pollution have focused on the immediate or relatively short-term effects on measures of health[14–16]. There is a lack of studies in settings in which the environment has improved and a long period of time has elapsed. Our research team has reported several longitudinal studies that targeted officially acknowledged victims with pollution-related illness[12, 13, 17]. However, in one of those studies, smokers were excluded to confine observations to the effect of air pollution[12]. In our previous report examining the lung function of officially acknowledged victims with pollution-related illness in two geographical areas within Japan, smokers were excluded for the same reason[13]. Those two studies found that the annual change in FEV_1 in non-smokers who were officially acknowledged victims with pollution-related illness was within the normal range. However, those studies were limited in their application because the effect of smoking was not examined and because factors associated with the annual change of FEV_1 were not clear. If the factor associated with a greater decline in FEV_1 became clear, it could assist in maintaining lung health in countries in which air pollution is present. The aim of the present study, therefore, was to examine the factors, including cigarette smoking, associated with the annual change in FEV_1 of officially acknowledged victims with pollution-related illness in settings in which the environment has improved and a long period of time has elapsed. The present study is unique in that the investigation is a longitudinal study of victims in an area in Japan in which air pollution was once a serious problem but where, over the years, air quality has improved.
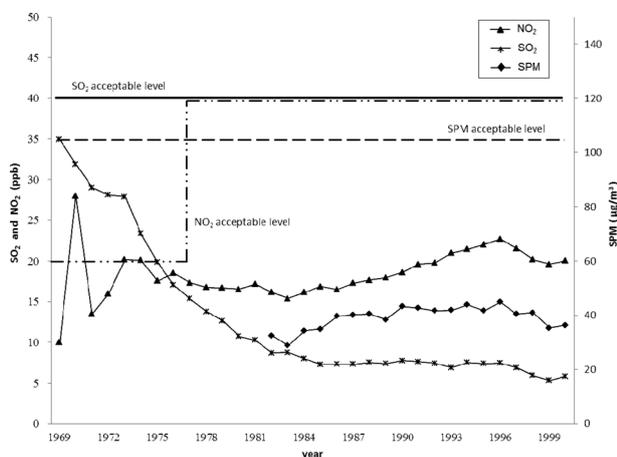

Fig. 1. Concentration of air pollutants in the Mizushima district of Kurashiki from 1969 to 2009[10, 11]

SUBJECTS AND METHODS

The present study was approved by the Ethics Review Committee of Nagasaki University Graduate School of Biomedical Sciences (Nagasaki, Japan). This study was undertaken by analyses of retrospective data obtained from annual health surveys conducted with officially acknowledged victims of air pollution-related illnesses from the Mizushima district of Kurashiki (Okayama Prefecture, Japan) between 2000 and 2009. This area suffered from air pollution during 1960–1970, but the environment improved thereafter.

Officially acknowledged victims of air pollution-related illnesses were registered after fulfilling two main conditions in the Pollution-related Health Damage Special Measures Law (1969) and Pollution-related Health Damage Compensation Law (1973). The first requirement was to register a victim that had been diagnosed to have an air pollution-related illness, such as asthma or chronic bronchitis, by a respiratory physician. Respiratory diseases attributed to air pollution in the Pollution-related Health Damage Compensation Law were categorized into four groups: asthma, chronic bronchitis, a combination of asthma and chronic bronchitis, or another respiratory disease. The diagnosis was made based on the results of medical examinations by certified respiratory physicians and official requirements of the law. Chronic bronchitis was diagnosed by the presence of chronic and copious amounts of sputum and a persistent cough. Asthma was diagnosed by the presence of recurrent episodes of dyspnea and wheezing. The second requirement was that individuals had to reside or spend ≥8 h per day in an area specified as having significant air pollution. Table 1 denotes the time required for certification of exposure to air pollution. They were different for each disease and area in which the subject resided or spent time (including work time).

Figure 2 is a flowchart showing the study's selection process. This was similar to the subjects of a study by Tanaka et al.[12, 13]. In 2009, the number of officially acknowledged victims of air pollution-related illness in Kurashiki was 1392. Of these, 774 (56%) were ≥65 years of age in 2009. Subjects who had health surveys over a 7 year period were selected. However, 44 individuals were subsequently excluded from this analysis because they had not undergone annual spirometry on ≥7 occasions. Therefore, data of 730 subjects were analyzed in the present study.

Table 1. Time required for certification of exposure to air pollution

Category	Chronic bronchitis	Asthma
A (months)	24	12
B (months)	48	30
C (months)	36	18

Category A: subject resided in the designated area before 1973.
Category B: subject did not reside in the designated area but spent ≥8 h/day in the designated area.
Category C: subject resided in the designated area and then relocated, but returned for work in the designated area for ≥8 h/day.

Pulmonary function was measured by spirometry (FU-DAC 70; Fukuda Sangyo Inc., Chiba, Japan). Officially acknowledged victims of air pollution-related illnesses were required to undergo spirometry once a year. Spirometry was undertaken by trained staff at Mizushima Kyodo Hospital (Okayama, Japan). Following standardized instructions, spirometry was repeated until ≥3 reproducible forced expiratory volume-time curve curves had been obtained. A nose-clip was applied to each subject, and subjects were in the sitting position during tests. In our analyses, values of forced vital capacity (FVC) and FEV_1 were used, and these are presented in milliliters or as a percentage of the predicted value (% FVC and % FEV_1) derived from the predicted equations. Percentage FVC was calculated using the equation reported by Baldwin and colleagues[18]. Percentage FEV_1 was calculated using the equation reported by Berglund and colleagues[19].
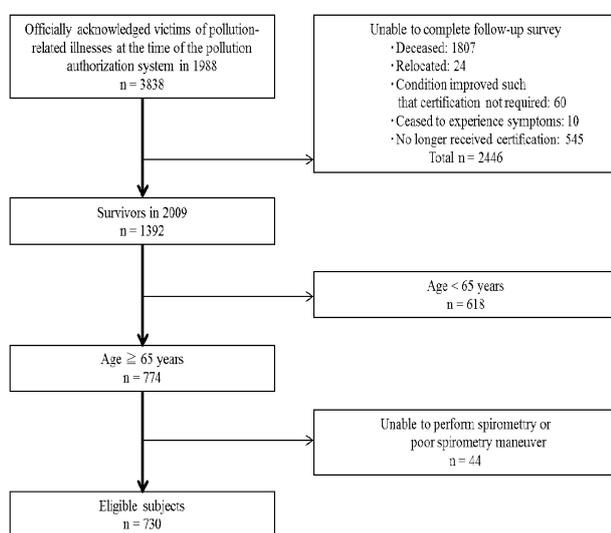

Fig. 2. Flow diagram of the study

Smoking habit was divided into two groups: non-smoker or smoker (including former smokers) as of the year 2000. Respiratory symptoms evaluated comprised "breathlessness", "wheezing" and "cough and sputum production". Respiratory physicians evaluated the presence and severity of symptoms during medical interviews according to a five-grade system. Classification of medical management referred to the extent to which an individual required medical care (e.g., frequency of medical care and necessity for hospitalization). This parameter was also evaluated according to a five-grade system (Table 2).

Statistical analyses were conducted using PASW version 18 (SPSS, Armonk. NY, USA). Values for the mean ± standard deviation were calculated for continuous variables. The regression coefficient for the annual mean change in FEV_1 was calculated using simple linear regression analyses. Further, bivariate analyses were conducted to examine the relationship between the annual change in FEV_1 and other factors. Spearman rank correlation analyses, Mann-Whitney test, and Kruskal-Wallis test were included in bivariate analyses. Factors found to be independent variables associated with the annual change in FEV_1 in bivariate analyses were evaluated stepwise in multiple regression analyses. Significance levels of 10% for bivariate analyses and 5% for multiple regression analyses were adopted. In additional analyses to examine the relationship between annual change in FEV_1 and percentage predicted FEV_1, Pearson correlation analyses were carried out with a significance level set at 5%.

RESULTS

Characteristics of subjects measured in the year 2000 are shown in Table 3. There were more females (63%) than males (37%), and more non-smokers (78%) than smokers (22%). Categories of respiratory symptoms and classifications of medical management were rationalized into two or three groups.

Table 2. Severity of respiratory symptoms and classification of medical management

Grade	Breathlessness	Wheeze	Cough and sputum production	Medical management classification
1	Too breathless to leave the house, or breathless when dressing or undressing	Severe episodes ≥10 days/month during the last year	Daily cough and sputum, with a large amount of sputum or difficulty clearing sputum	Requires hospitalization for exacerbation of symptoms and always requires assistance with activity during daily living
2	Breathless after walking about 50 m or after a few minutes on level ground	Severe episodes ≥5 days/month during the last year, or mild episodes ≥10 days/month during the last year	Daily cough and sputum, with a moderate amount of sputum or difficulty clearing sputum	Always needs medical treatment and hospitalization required for exacerbation of symptoms
3	Breathless when walking on level ground and keeping up with people of the same age, but not breathless when walking at own pace	Severe episodes ≥1 day/month during the last year, or mild episodes ≥5 days/month during the last year	Daily cough and sputum, but not troublesome during daily life	Always needs medical treatment and sometimes needs hospitalization
4	Breathless when walking up a slight hill or the stairs	Mild episodes ≥1 day/month during the last year	Daily cough and sputum for ≤3 months/year	Always needs to consult a doctor and sometimes needs respiratory medication
5	Breathless only during strenuous exercise	No episodes of wheezing	No cough or sputum	No need for medical management

Table 3. Characteristics of the patient cohort as measured in the year 2000

Characteristic	Mean ± SD or n (%)
Age, years	68.8 ± 7.6
Male gender, n	272 (37)
Height, cm	153.2 ± 8.5
Weight, kg	56.3 ± 10.1
BMI, kg/m^2	23.9 ± 3.7
Smoking habit, n	
Non-smoker	567 (78)
Smoker	163 (22)
FEV_1, mL	1546 ± 561
% pred FEV_1	7 ± 11
FVC, mL	2559 ± 750
% pred FVC	9 ± 21
FEV_1 annual change, mL/year	−29 ± 32
Disease, n	
Asthma	218 (30)
CB	411 (56)
Asthma and CB	97 (13)
Others	4 (1)
Respiratory symptoms	
Breathlessness, n	
Grades 1–3	180 (25)
Grade 4	483 (66)
Grade 5	64 (9)
Wheeze,n	
Grades 1–3	207 (28)
Grade 4	276 (38)
Grade 5	247 (34)
Cough and sputum production, n	
Grades 1–3	373 (51)
Grades 4–5	357 (49)
Medical management classification, n	
Grades 1–3	192 (26)
Grades 4–5	538 (74)

BMI: body mass index; FEV_1: forced expiratory volume in one second; % pred FEV_1: percentage of the predicted value of forced expiratory volume in 1 second; FVC: Forced vital capacity; % pred VC: percentage of the predicted value of forced vital capacity; CB: chronic bronchitis; Other: other conditions such as pulmonary emphysema

Table 4. Correlation coefficients (r) and significance levels (p) of annual changes in FEV_1

Factor	r
Age	0.011
Height	−0.100*
Weight	0.034

*p < 0.1

Table 5. Annual change in FEV_1 grouped according to subject characteristics by bivariate analyses

Factor	ΔFEV_1 (mL/year)
Gender*	
Male	−36 ± 40
Female	−25 ± 25
Smoking habit*	
Non-smoker	−25 ± 29
Smoker	−41 ± 38
Respiratory disease*	
Asthma	−23 ± 31
CB	−31 ± 32
Asthma and CB	−32 ± 32
Respiratory symptoms	
Breathlessness*	
Grades 1–3	−20 ± 30
Grade 4	−31 ± 33
Grade 5	−33 ± 25
Wheeze*	
Grades 1–3	−22 ± 31
Grade 4	−29 ± 32
Grade 5	−33 ± 32
Cough and sputum*	
Grades 1–3	−26 ± 31
Grades 4–5	−31 ± 33
Medical management classification*	
Grades 1–3	−20 ± 30
Grades 4–5	−32 ± 32

Mean ± SD; *p<0.1; ΔFEV_1, annual change in FEV_1 (mL); CB: chronic bronchitis

Tables 4 and 5 provide the results of bivariate analyses investigating the relationship between the annual change in FEV_1 and other factors. Results of bivariate analyses showed that sex, height, weight, smoking habit, respiratory disease, all respiratory symptoms, and classification of medical management were significant factors associated with the annual change in FEV_1 (p < 0.1). The annual change in FEV_1 in males significantly exceeded that observed in females (p < 0.05). The annual change in FEV_1 was also accelerated by smoking. People who had more severe symptoms showed a slower decline than people who had mild symptoms. In addition, those who required more medical treatment and assistance with activities of daily living had a slower annual decline in FEV_1 than people who did not require these interventions.

Results of multiple regression analyses are shown in Table 6. The strongest factor related to the annual change in FEV_1 was smoking habit, followed by classification of medical management, and gender. There was no multicollinearity according to the variance inflation factor, which means no correlation between these factors.

Additional analyses revealed a significant weak inverse correlation between the annual change in FEV_1 and percentage predicted FEV_1 (r = −0.26, p < 0.001) (Fig. 3). This finding suggested that subjects with better pulmonary function showed a more rapid decline in FEV_1.

Table 6. Predictors of annual change in FEV$_1$

Factor	ΔFEV$_1$			
	B	β	95% CI	VIF
Smoking habit* (Smoker, 0; Non-smoker, 1)	4.22	0.17	2.08 to 8.88	1.157
Medical management classification* (Grades 1–3, 0; Grades 4–5, 1)	−10.92	−0.15	−14.15 to −3.56	1.007
Gender* (Male, 0; Female, 1)	6.22	0.09	2.62 to 12.86	1.151

*$p < 0.05$ indicates statistical significance. ΔFEV$_1$, annual change in FEV$_1$; B, partial regression coefficient; β, standardized partial regression coefficient; CI: confidence interval; VIF: variance inflation factor
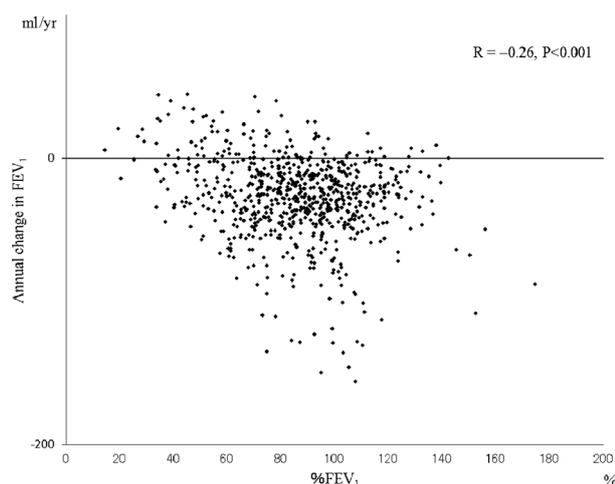

Fig. 3. The relationship between annual change in FEV$_1$ and % predicted FEV$_1$

DISCUSSION

This is the first study to investigate the factors associated with the annual change in FEV$_1$ in residents previously exposed to air pollution after the environmental conditions had improved and a long time period had elapsed.

Multiple regression analyses showed that smoking habit, classification of medical management, and gender were significant factors in order of decreasing effect. The prediction equation for FEV$_1$ is determined mainly by gender[20, 21] but, interestingly, smoking habit exceeded the effects of gender in the present study. This result suggests the significant negative effects of smoking on pulmonary function. Largest decreases in FEV$_1$ occurred in smokers, whereas the smallest decreases occurred in non-smokers. Studies have reported similar results[6, 22]. The annual decline in FEV$_1$ of the non-smokers was −25 mL/year. This value falls in the range that has been reported for healthy Japanese non-smoking males and females aged >65 years (i.e., −31 to −22 mL/year)[23–25]. Even if people had suffered damage from air pollution at one time, those who were non-smokers demonstrated more preserved lung function over time.

All symptoms were identified to be significant in bivariate analyses, but none of these symptoms were found to be significant in multiple regression analyses. Some studies have suggested that males with a chronic cough or sputum production and females with a chronic cough demonstrate a rapid decline in respiratory function[26, 27]. As a result,

respiratory symptoms are usually associated with a decline in FEV$_1$. Conversely, another study found that respiratory symptoms do not necessarily result in a decline in FEV$_1$[28]. The results of our study are consistent with this latter observation.

Classification of medical management was identified as a specific factor associated with the annual change in FEV$_1$. Presence of a single respiratory symptom did not significantly affect the annual change in FEV$_1$, but the classification of medical management might be a comprehensive index and reflect the overall severity of respiratory disease (including all respiratory symptoms). This phenomenon may explain why classification of medical management was a significant factor.

Physical and pulmonary function, in general, decline with aging[29, 30]. Interestingly, as classification of medical management and/or respiratory symptoms became more severe, the decline in FEV$_1$ became less in the present study. In the Understanding Potential Long-term Impacts on Function with Tiotropium (UPLIFT) study, patients with severe chronic obstructive pulmonary disease (COPD) showed smaller declines in FEV$_1$ than those with less severe COPD[31]. Another study reported that the annual change in FEV$_1$ was less in patients with advanced stages of COPD[32]. In general, more treatments (e.g., bronchodilators or other medication) are administered as disease severity increases. As a result, the decline in FEV$_1$ might become smaller. This phenomenon may explain why the annual decline in FEV$_1$ becomes smaller with lower %FEV$_1$ (Fig. 3).

Another factor that could be associated with the annual change in FEV$_1$ is the age of subjects. In the present study, the mean age of subjects was 68.8 years in the year 2000. In contrast, the mean age of subjects in studies that examined longitudinal changes in pulmonary function ranged from 20 years to 60 years[20, 33, 34]. The slope of the prediction equation in those studies was steeper than that in the present study. However, in studies that involved older subjects, the slope of the prediction equation was less pronounced[35, 36]. The annual change in FEV$_1$, in general, declined with age. However, the decline may be slowed at an advanced age and then the impact of aging may be slight. Moreover, height was not selected by multiple regression analyses, and is a factor that may also be influenced by aging. However, the most important factor affecting pulmonary function and the decline of FEV$_1$ was smoking[18, 19]. The impact of the factors affecting FEV$_1$ might, therefore, be affected by disease progression or aging. Further investigations are required for clarification of this question.

The present study was limited by the fact that it was retro-

spective and that some information pertaining to participants was incomplete. For example, details regarding the amount of tobacco smoked by subjects were not available. Furthermore, detailed data pertaining to the medications taken by participants was lacking. The type and dose of medication (e.g., bronchodilators or other treatments) was also not clear.

The findings of our study suggest that smoking is the strongest factor affecting the annual change in FEV_1 in officially acknowledged victims with pollution-related illnesses who now live in environments with improved air conditions. In this population, current smokers showed a more rapid decline in FEV_1 than former smokers or non-smokers. In some Asian countries in which air pollution is a serious problem, interventions are required to improve the environment and to reduce the prevalence of smoking to improve the health of citizens.

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