ORIGINAL ARTICLES

Transit Time Analysis of Forced Expiration in Workers Exposed to Dust: A Cross-sectional Study

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Abstract: Maximal expiratory flow at 25% forced vital capacity ($\dot{V}_{25}$), $\dot{V}_{25}$ divided by height ($\dot{V}_{25}/HT$), and mean transit time (MTT) were calculated from the same forced expiratory maneuver performed in welding workers. The values were compared to determine variations between individuals and changes with age and chest X-ray findings. The results showed that MTT may be a less variable and equally sensitive measurement of the function of peripheral airways as compared with $\dot{V}_{25}$ and $\dot{V}_{25}/HT$. Its usefulness in the detection of the early changes of pneumoconiosis, however, must be further investigated in a prospective cohort study on workers exposed to various kinds of dust.

Key words: Mean transit time — Pneumoconiosis — Spirometry — Flow-volume curve — Peripheral airway.

INTRODUCTION

The detection of mild changes in pneumoconiosis is a matter of interest as exposure to dust has been regulated at low levels in developed countries. Desposition of dust in the peripheral airways and airspaces is considered to be the earliest change in pneumoconiosis.¹⁾ Maximal expiratory flow at 25% of forced vital capacity ($\dot{V}_{25}$) and $\dot{V}_{25}$ divided by height ($\dot{V}_{25}/HT$) are usually taken as indices of peripheral airway function, and the latter has been employed in health examinations in Japan for workers exposed to dust.²⁾ It has been pointed out, however, that $\dot{V}_{25}$ shows considerable interindividual variation.³⁾ One possible source of this variation may be its dependency on lung volume.

Transit time analysis⁴⁾ is a different method of analyzing forced expiration. Parameters obtained from it are theoretically volume independent and are expected

to be good indices of peripheral airway disorder.⁵⁾ This analysis was first employed by Fish *et al.*⁴⁾ in 1974. They analyzed the distribution of time of expiration for fractions of forced vital capacity (FVC), since prolongation of the time of expirations was associated with obstructive disorders of the airways. Since then, transit time parameters have been used in studies on lung growth,⁶⁾ on the effect of smoking,⁷⁾ and on peripheral airway function.^{8,9)}

In this study, we calculated maximal expiratory flow and transit time parameters for the same FVC maneuver in workers exposed to dust to compare the magnitude of variation and to determine their usefulness in health examinations.

METHODS

The data of this study were obtained from workers who had been primarily engaged in welding in a machine manufacturing plant for at least 2 years. In November 1984, 63 male workers selected for this study underwent examinations including chest radiography, pulmonary function, and respiratory symptoms as part of an annual health check-up. Among them, five workers were excluded from analysis because they were suffering from upper respiratory infection on the day of examination. Five other workers were excluded because acceptable results could not be obtained. As a result, satisfactory data were available on 53 workers.

Chest radiographic examination was carried out by a standard health examination for pneumoconiosis used in Japan.²⁾ The reading of all radiograms was performed by one of the authors, who is experienced in radiographic examination of the lung. The findings were described according to the chest X-ray classification of pneumoconiosis used in Japan.²⁾

Spirometry and maximal forced expiration were performed with subjects in a standing position with a dry rolling seal spirometer. The plastic bell of the spirometer was connected to a rotary encoder which released a pulse voltage with each 10-ml change in volume. Time data were sampled when the pulses were generated. Elapsed time and change in volume between pulses provided the magnitude of flow at that time. These data were all digitized and stored in a floppy disk. The beginning of expiration in the FVC maneuvers was determined by the back extrapolation method and expiration was considered to end when flow became negative.

Spirometric measurements were performed at least twice and FVC maneuvers were performed at least three times to obtain acceptable, reproducible results. The value of vital capacity (VC), FVC, percentage rate of FVC expired in the first second (FEV1%), and $\dot{V}_{25}$ were calculated in the standard way.

As a measurement of transit time, mean transit time (MTT) was calculated. When a variable t has probability density function $f(t)$, its r -th moment about the origin can be expressed as

$$\int_{-\infty}^{\infty} f(t) \cdot t^r \cdot dt$$

Because MTT is the first moment of transit time ($r=1$), and $f(t)$ is considered to be $\dot{V}/FVC$, MTT is defined as

$$\begin{aligned} & \int_{-\infty}^{\infty} (\dot{V}/FVC) \cdot t \cdot dt \\ &= \int_0^{FVC} (1/FVC) \cdot t \cdot dV \end{aligned}$$

As stated before, data on time of expiration were obtained at each 10-ml volume change in this study. Accordingly, the value of MTT in this study was calculated as follows:

$$\begin{aligned} \text{MTT} &= \sum_i^N (10 \cdot t_i) / FVC \text{ (ml)} \\ &= \sum_i^N t_i / N \quad (N = \text{number of data}) \end{aligned}$$

No arbitrary truncation of expiration was carried out. The details of calculation of transit times have been reported.^{6,10)}

Student's t -test and χ^2 test were used to compare mean values and variances between groups. Analysis of covariance was also used for between-group comparisons of mean values. Regression analysis was used to estimate variability.

RESULTS

The basic characteristics of subjects are summarized in Table 1. The mean value of %VC (percentage of VC to expected value) was 108%. No subject had a %VC value below 80%. These data suggest that restrictive changes due to pneumoconiosis were not evident in these workers.

The mean, standard deviation, and coefficient of variation (CV) for each index of pulmonary function are listed in Table 2. The variation was largest for $\dot{V}25$ and smallest for FEV1%. Dividing $\dot{V}25$ by height did not improve the variability.

Figure 1 shows the results of regression analysis. Model 1 includes only height, model 2 includes height and FVC, and model 3 includes height, FVC, and age as

Table 1. General characteristics of the subjects (N=53)

Age (yr)	37.1 ± 8.9*
Height (cm)	164.5 ± 6.5
%VC (%)	108.2 ± 9.6
Smoking status	
Non-smoker	25%
Former smoker	15%
Current smoker	60%

* Mean ± 1 standard deviation.

Table 2. Mean, standard deviation, and coefficient of variation of pulmonary function

	Means $\pm$ SD	CV (%)
$\dot{V}_{25}$ (l/sec)	1.66 $\pm$ 0.72	43.5
$\dot{V}_{25}/HT$ (l/sec/cm)	1.00 $\pm$ 0.43	43.5
MTT (sec)	0.60 $\pm$ 0.15	24.6
FEV 1% (%)	85.2 $\pm$ 6.1	7.1

Fig. 1. Regression analysis of pulmonary function.* $p < 0.05$, ** $p < 0.01$

Model 1 includes height, model 2 includes height and FVC, and model 3 includes height, FVC and age as explanatory variables.

explanatory variables. As shown in the figure, the value of the coefficient of determination of $\dot{V}_{25}$ and $\dot{V}_{25}/HT$ in model 2 was significantly greater than that in model 1. In other words, $\dot{V}_{25}$ and $\dot{V}_{25}/HT$ had a statistically significant association with FVC, even if differences in height were taken into consideration. This was not the case for MTT and FEV1%. The difference in the coefficient of determination between models 2 and 3 was statistically significant at almost the same level for every index of pulmonary function.

The relationship between the indices of pulmonary function and chest X-ray findings in the early stages of pneumoconiosis was studied in subjects who had been classified up to stage 1/1 by the chest X-ray examination. The subjects selected were divided into two groups: one consisted of workers in stages 0/0 and 0/1 (stage 0), the other of workers in stages 1/0 and 1/1 (stage 1). Data on pulmonary function were compared between the two groups (Table 3). Each index excluding FVC showed a significant difference between the two groups.

Table 3. Comparison of pulmonary function by findings of chest radiogram

	Stage 0	Stage 1
$\dot{V}25$ (l/sec)	$2.04 \pm 0.65^{**,\dagger}$	$1.15 \pm 0.36^{\ddagger\ddagger}$
$\dot{V}25/HT$ (l/sec/cm)	$1.22 \pm 0.38^{**,\dagger}$	$0.69 \pm 0.21^{\ddagger\ddagger}$
MTT (sec)	$0.54 \pm 0.11^{**}$	$0.71 \pm 0.12^{\ddagger\ddagger}$
FEV1% (%)	$87.9 \pm 5.5^{**}$	$80.6 \pm 4.0^{\ddagger\ddagger}$
FVC (l)	4.34 ± 0.42	4.16 ± 0.42
Age (yr)	$33.3 \pm 9.0^{**}$	42.4 ± 7.7

Values are mean and standard deviation.

** $p < 0.01$ for difference in means by t-test.

$\dagger$ $p < 0.05$ for difference in standard deviation by F-test.

$\ddagger\ddagger$ $p < 0.01$ for difference in means by covariate analysis.

Because the age distribution was differed between the groups, an analysis of covariance was carried out to determine whether or not the difference was independent of age. The result showed that there was still a significant difference in indices between the groups, even after the difference in age had been corrected. In addition, $\dot{V}25$ and $\dot{V}25/HT$ showed a significant difference in variance between the groups on χ^2 test.

DISCUSSION

Flow-volume curve measurement is one of the most widely used tests of pulmonary function in epidemiological studies because of its high practicality. The maximal expiratory flow at 25% FVC obtained from it has been considered to be a good index of obstructive change in peripheral airways. Because the early changes of pneumoconiosis seem to occur in the peripheral airways and airspaces, $\dot{V}25$ is expected to be sensitive to such changes and has been employed in health examinations for pneumoconiosis in Japan. Although the usefulness of $\dot{V}25$ has been confirmed in many studies,^{11,12)} it is sometimes pointed out that $\dot{V}25$ has a large variability.¹³⁾ The large variability makes it difficult to set a normal range or distinguish an abnormal value from normal values. A possible source of variation in $\dot{V}25$ is the variation in FVC. It is clear that those who have a larger FVC tend to have a larger $\dot{V}25$, even when there are no differences in height or the condition of the respiratory system between them.

Transit times, on the other hand, are theoretically independent of FVC. In this sense, transit times have an advantage over $\dot{V}25$. The present results showed that $\dot{V}25$ had a coefficient of variation about two times larger than MTT and was associated with FVC even if height was taken into consideration. The coefficient of variation for $\dot{V}25/HT$ was still as large as that of $\dot{V}25$.

Using regression analysis, the magnitudes of coefficients of determination were compared in several models. Because pulmonary function shows an age-dependent

decline even in normal subjects, the difference in coefficients of determination between models with and without age as an explanatory variable indicates the sensitivity of each index to age-dependent changes in the respiratory system. As shown in Figure 1, the increase in the coefficient of determination caused by adding age as an explanatory variable was almost the same in every index, suggesting that these indices reflect age-dependent changes to a similar extent.

The comparison of pulmonary function by chest X-ray findings showed that there was a significant difference in each index corresponding to the radiographic stage even if age-dependent change was taken into consideration.

These results suggest that MTT may be an index which has similar sensitivity to functional changes in the pulmonary periphery and has lower interindividual variability than $\dot{V}_{25}$ and $\dot{V}_{25}/HT$. Among other indices examined, FEV1% showed good sensitivity and had the least variability. Although it seemed to be the best index in this study, FEV1% has been considered to reflect changes primarily in the central airways.¹⁴⁾ Recent advances in understanding the pathogenesis of pneumoconiosis suggest that the earliest changes in the disease are in peripheral airways and airspaces.^{1,15)} In this sense, pulmonary functional indices of small airways such as MTT and $\dot{V}_{25}$ are better able to detect the early functional changes of pneumoconiosis. Therefore, it is important to determine whether or not these indices of the small airways can detect the early changes of pneumoconiosis in a prospective cohort study on workers exposed to various types of dust.

In conclusion, a cross-sectional analysis suggests that MTT is an equally sensitive and less variable index of function of peripheral airways as compared with $\dot{V}_{25}$ and $\dot{V}_{25}/HT$. The validity of its use in the detection of the early changes of pneumoconiosis, however, must be investigated in longitudinal studies on workers exposed to various types of dust.

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