



Original Article

A 4-Year Follow-up Cohort Study of the Respiratory Functions in Toner-handling Workers



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ABSTRACT

Background: Focusing on the respiratory function for health effect indices, we conducted a cross-sectional study on workers who did and did not handle toner to compare the longitudinal changes.

Methods: Among 116 individuals who worked for a Japanese business equipment manufacturer and participated in the study, the analysis included 69 male workers who we were able to follow up for 4 years. We categorized the 40 workers engaged in toner-handling work as the exposed group and the 29 workers not engaged in these tasks as the referent group, and compared their respiratory function test results: peak expiratory flow rate (PEFR), vital capacity (VC), predicted vital capacity (%VC), forced expiratory volume in 1 second (FEV₁), and forced expiratory volume in 1 second as a percent of forced vital capacity (FEV₁%).

Results: The cross-sectional study of the respiratory function test results at the baseline and at the 5th year showed no statistically significant differences in PEFR, VC, %VC, FEV₁, and FEV₁% between the exposed and referent workers. Also, respiratory function time-course for 4 years was calculated and compared between the groups. No statistically significant differences were shown.

Conclusion: Our study does not suggest any toner exposure effects on respiratory function. However, the number of subjects was small in our study; studies of larger populations will be desired in the future.

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1. Introduction

Toner used in printing with printers and photocopy machines, is an organic powder of approximately 5–10 μm in mean particle diameter containing carbon black as the black colorant. Nanoparticles adhere firmly to the toner surface as an external additive. Since siderosilicosis suspected to be caused by toner was reported in *The Lancet* in 1994 [1], reports on respiratory diseases such as granulomatous pneumonitis among toner-exposed workers have been published [2–5]. The International Agency for Research on Cancer (IARC) has changed the carcinogenicity category of carbon black, a toner constituent, from “group 3: not classifiable as to its carcinogenicity to humans” to “group 2B: possibly carcinogenic to humans [6]” and public attention

concerning toner safety has increased. Toner health effects, however, have been reported only in animal experiments with tremendous artificial exposure [7], or in some human case reports without information about exposure and setting control groups as is required to evaluate the risk. Therefore, epidemiological research considering disease related factors such as latency and exposure periods has been strongly desired. We started a 10-year cohort study to investigate the health effects in toner-handling workers. We were unable to find any longitudinal studies of toner effects on the respiratory function test. Thus, focusing on the respiratory function test as a health effect index, we conducted a cross-sectional study of the respiratory function in groups who did and did not handle toner and compared the longitudinal changes.

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2. Materials and methods

This study commenced in November 2006, with the assistance of a business equipment manufacturer in Japan. The study included annual investigations according to the guidelines prepared by the working group including invited scientific advisors organized in the Japan Business Machine and Information System Industries Association (JBMIA).

2.1. Subjects

The subjects were workers aged <50 years at the start of the study. The workers who were engaged in manufacturing toner cartridges, developing toners, and developing and evaluating laser printers/multifunctional devices were defined as exposed workers, and those who were not engaged in these tasks were defined as referent workers. Referent workers were engaged in desk work in the office.

Workers whose tasks changed during the study period and who were then no longer engaged in toner-handling work were considered as exposed workers. Among the 116 male and female workers who participated in the study, 90 male workers were selected to avoid confounding sex effects in this study. From the 90 workers, 69 subjects who had the respiratory function test at the 1st year (baseline) and 5th year were then included in the longitudinal analysis, excluding the other subjects.

None of the subjects withdrew because of health problems during the study period. Smoking habit has been investigated in three categories: (1) current smoker, (2) former smoker, and (3) never smoker, in a self-administered questionnaire every year. Physicians interviewed the workers based on the questionnaire and confirmed the results.

2.2. Respiratory function test

We used an electronic spirometer HI-801 (Chest M.I. Inc., Tokyo, Japan) with the pneumotachography method recommended by JBMIA guidelines in the respiratory function test. Because the values of the flow volume test depend on the work and training of the examinee, the test was conducted a total of three times under the instruction of certified technicians of the respiratory function test and the average values were used. The test items were (1) peak expiratory flow rate (PEFR), (2) vital capacity (VC), (3) predicted vital capacity (%VC), (4) forced expiratory volume in 1 second (FEV₁), and (5) forced expiratory volume in 1 second as a percent of forced vital capacity (FEV₁%). The %VC was determined by the normal prediction formula for vital capacity proposed by the Japanese Respiratory Society in 2001 based on Japanese data [8]. The normal prediction formula for males proposed by the Japanese Respiratory Society is:

$$0.045 \times \text{height (cm)} - 0.023 \times \text{age} - 2.258 \text{ (L)}.$$

2.3. Measurement of work environment

The institution that measured the work environment in this study had participated in the accuracy management project of the Japan Association for Working Environment Measurement for measuring dust concentration and was approved as a qualified institution. In the workplace of exposed workers, the working environment was examined for respirable dusts. Measurements were taken at three sites (toner laboratory, laser printer evaluation room, and powder testing laboratory) at the level of 1.2 m, which is

the height compatible to the breathing zone, at one point in each workplace for 3 days. The toner laboratory is a workplace used to assemble toner cartridges used for evaluation, to fill toner in the cartridges, and to investigate the filled cartridge quality. The workers wear protective equipment while filling of the toner under operating the local exhaust ventilation. The laser printer evaluation room is a workplace used to activate the laser printer to evaluate the printing and performance of the machine. The workers approach the printer in printing to monitor the operation as many times as needed, and do not wear the protective equipment at that time. The powder testing laboratory is a workplace used to experimentally produce toner by solidly attaching the additive to the core toner particles and to determine its physical properties. The workers wear the personal protective equipment in the laboratory while operating the local exhaust ventilation. The measurements were to be taken during routinely conducted work. For the measurement, a high-volume air sampler equipped with a PM4 size classification system (Shibata Scientific Technology Ltd, Saitama, Japan) and fluorine resin-processed glass fiber filter (Tokyo Dylec Corp, Tokyo, Japan) were used. The aspiration flow rate and sampling time were set as 500 L/minute and 360 minutes.

2.4. Statistical analysis

When the normality of distribution of age, constitution (height, body weight, and body mass index, BMI), and the respiratory function test results were evaluated by the Shapiro-Wilk test, the age at baseline, FEV₁% at the 5th year, and decrease in FEV₁% did not show normal distribution, even after logarithmic transformation. Therefore, the statistical differences in both indices between the referent and exposed workers were tested by *U*-test and Kruskal-Wallis test. Because the other indices showed normal distribution, they were tested by the Student *t* test and Tukey test. Concerning the respiratory function time-course, the annual reduction rate was calculated by subtracting the values of the respiratory function test at the 5th year from that of the baseline and dividing the value obtained by the number of years. All statistical analyses were conducted with PASW Statistics 18 (IBM, Tokyo, Japan).

2.5. Ethical considerations

The following items were considered in advance: guarantee of voluntary participation of subjects in the study, measures for securing subject privacy, methods for obtaining informed consent from subjects, notifying subjects of study results, handling biological samples collected from subjects (methods of storage and disposal, etc.), prohibiting unintended use of biological samples collected from subjects, destruction of the study data after study completion, and possible risks and disadvantages for subjects and measures for handling them when they occurred. We applied for third-party review of the study content, asking the Ethical Review Board of the University of Occupational and Environmental Health, Kitakyushu, Japan, and obtained approval (acceptance number 03-32, December 10, 2003).

3. Results

We analyzed the data of 29 referent workers and 40 exposed workers. The dust concentration at each workplace where exposed workers were working is outlined in Table 1. In the toner laboratory and powder testing laboratory conducting research and development of toner, local exhaust ventilation was operated. The amount of powder handled in these laboratories was very small, and workers wore 1/4 dust respirators. In the powder testing laboratory, there was no toner-handling work on the 1st day and 2nd day.

Table 1
Work environment measurement in each workplace

	Toner laboratory	Laser printer evaluation room	Powder testing laboratory
Size of the room (m ²)	216.0	432.0	18.0
Distance of measurement point from object (m)	2.0–12.0	2.0–11.0	2.8
Environment measurement (mg/m ³)			
Day 1	0.017	0.008	0.011
Day 2	0.019	0.015	0.017
Day 3	0.019	0.026	0.031

On the 3rd day, the measurement was conducted during the toner blending. In the laser printer evaluation room, where printing was evaluated, a local exhaust ventilation was not operated. The workers approached the printer in printing as many times as needed, and did not wear personal protective equipment during that time. The characteristics of age and constitution that could have influenced the baseline respiratory functions of subjects are shown in Table 2. For referent workers, the median age was 36.0 years old [range 24–47, quartile deviation (QD) 6.5], mean height was 170.9 cm [standard deviation (SD) 7.0], mean body weight was 67.7 kg (SD 9.0) and mean BMI was 23.2 kg/m² (SD 2.9). For exposed workers, the median age was 31.5 years old (range 25–44, QD 3.8), mean height was 170.4 cm (SD 5.2), mean body weight was 64.5 kg (SD 8.8), mean BMI was 22.2 kg/m² (SD 2.8), and there were not any statistically significant differences between the groups.

Concerning the baseline smoking status, there were nine current smokers (31.0%), seven former smokers (24.1%), and 13 never smokers (44.8%) in the referent group. In the exposure group, there were 11 current smokers (27.5%), eight former smokers (20.0%), and 21 never smokers (52.5%). The questionnaires showed that, among 20 current smokers at baseline, 10 (3 in the referent group and 7 in the exposure group) stopped smoking by the 5th year. There were seven subjects (4 in the referent group and 3 in the exposure group) who continued smoking in the 5th year without interruption.

The results of the baseline respiratory function test are shown in Table 3. The referent workers showed a mean PEFR for 9.94 L/s (SD 1.41), mean VC for 4.63 L (SD 0.52), mean %VC for 100.80% (SD 11.1), mean FEV₁ for 3.87 L (SD 0.38), and mean FEV₁% for 85.57% (SD 6.78). The exposed workers showed a mean PEFR for 9.84 L/s (SD 1.48), mean VC for 4.59 L (SD 0.62), mean %VC for 98.51% (SD 10.80), mean FEV₁ for 3.88 L (SD 0.53), and mean FEV₁% for 87.08% (SD 6.34). There were not any statistically significant differences between the groups.

The respiratory function test at the 5th year is shown in Table 3. The referent workers showed a mean PEFR for 9.16 L/s (SD 1.45),

Table 2
Baseline characteristics of the participants

	Referent workers (n = 29)	Exposed workers (n = 40)	p
Age [y; median (IQR)]	36.0 (6.5)	31.5 (3.8)	0.07*
Physical indices			
Height (cm)	170.9 (7.0)	170.4 (5.2)	0.74 [†]
Weight (kg)	67.7 (9.0)	64.5 (8.8)	0.14 [†]
Body mass index (kg/m ²)	23.2 (2.9)	22.2 (2.8)	0.16 [†]
Smoking habit			
Current smokers	9 (31.0)	11 (27.5)	
Former smokers	7 (24.1)	8 (20.0)	
Never smokers	13 (44.8)	21 (52.5)	

Data are presented as mean (SD), unless otherwise indicated. IQR, interquartile range.

* Mann-Whitney U test: not significant.

[†] Student t test: not significant.

Table 3
Baseline and fifth respiratory function test results

		Referent workers	Exposed workers	p
Baseline	PEFR (L/s)	9.94 (1.41)	9.84 (1.48)	0.78 [*]
	VC (L)	4.63 (0.52)	4.59 (0.62)	0.78 [*]
	%VC (%)	100.80 (11.1)	98.51 (10.80)	0.39 [*]
	FEV ₁ (L)	3.87 (0.38)	3.88 (0.53)	0.92 [*]
	FEV ₁ % (%)	85.57 (6.78)	87.08 (6.34)	0.35 [*]
5th year	PEFR (L/s)	9.16 (1.45)	9.43 (1.47)	0.46 [†]
	VC (L)	4.54 (0.59)	4.54 (0.59)	0.97 [†]
	%VC (%)	100.93 (10.47)	99.62 (10.56)	0.61 [†]
	FEV ₁ (L)	3.71 (0.39)	3.78 (0.52)	0.54 [†]
	FEV ₁ % [%; median (IQR)]	86.96 (3.48)	87.55 (3.06)	0.77 [†]

Data are presented as mean (SD), unless otherwise indicated.

FEV₁, forced expiratory volume in 1 second; FEV₁%, forced expiratory volume in 1 second as a percent of forced vital capacity; IQR, interquartile range; PEFR, peak expiratory flow rate, VC, vital capacity, %VC, predicted vital capacity.

* Student t test: not significant.

[†] Mann-Whitney U test: not significant.

mean VC for 4.54 L (SD 0.59), mean %VC for 100.93% (SD 10.47), mean FEV₁ for 3.71 L (SD 0.39) and median value for FEV₁% for 86.96% (QD 3.48). The exposed workers showed a mean PEFR for 9.43 L/s (SD 1.47), mean VC for 4.54 L (SD 0.59), mean %VC for 99.62% (SD 10.56), mean FEV₁ for 3.78 L (SD 0.52), and median value for FEV₁% for 87.55% (QD 3.06). There were not any statistically significant differences between the groups.

The amount of decrease in respiratory function per year is shown by smoking habit in Table 4. The group that continued not smoking for 4 years (never smoker) showed a mean PEFR for 0.15 L/(s·y, second times year) (SD 0.28), mean VC for 21.7 mL/year (SD 42.0), mean %VC for -0.02%/year (SD 0.88), mean FEV₁ for 38.4 mL/year (SD 34.2) and median FEV₁% for 0.04%/year (QD 0.39). The group that continued smoking for 4 years (continuous smoker) showed a mean PEFR for -0.06 L/(s·y) (SD 0.16), mean VC for -2.0 mL/year (SD 52.9), mean %VC for -0.52%/year (SD 1.04), mean FEV₁ for 40.3 mL/year (SD 52.0), and median FEV₁% for 0.12%/year (QD 0.11). The group other than continuous smokers for 4 years and never smokers (others) showed a mean PEFR for 0.18 L/(s·y) (SD 0.31), mean VC for 14.1 mL/year (SD 67.8), mean %VC for -0.27%/year (SD 1.47), mean FEV₁ for 19.1 mL/year (SD 39.7), and median FEV₁% for -0.04%/y (QD 0.37). In these three groups, there were no items showing statistically significant differences. The time-course of respiratory function test in all the target subjects and the group that continued not smoking for 4 years is shown for the presence or absence of exposure to toner in Table 5. Among

Table 4
Respiratory function time course by smoking habit[†]

	Never smoker (n = 34)	Continuous smoker (n = 7)	Others (n = 28)	p
PEFR [L/(s·y)]	0.15 (0.28)	-0.06 (0.16)	0.18 (0.31)	0.15 [†]
VC (mL/y)	21.7 (42.0)	-2.0 (52.9)	14.1 (67.8)	0.57 [†]
%VC (%/y)	-0.02 (0.88)	-0.52 (1.04)	-0.27 (1.47)	0.50 [†]
FEV ₁ (mL/y)	38.4 (34.2)	40.3 (52.0)	19.1 (39.7)	0.12 [†]
FEV ₁ % [%/y; median (IQR)]	0.04 (0.39)	0.12 (0.11)	-0.04 (0.37)	0.86 [‡]

Data are presented as mean (SD), unless otherwise indicated.

FEV₁, forced expiratory volume in 1 second; FEV₁%, forced expiratory volume in 1 second as a percent of forced vital capacity; IQR, interquartile range; PEFR, peak expiratory flow rate, VC, vital capacity, %VC, predicted vital capacity.

* The amount of decrease was calculated by subtracting the value at the 5th year from the baseline value and by dividing the obtained value by the number of years (4 years).

[†] Tukey test: not significant.

[‡] Kruskal-Wallis test: not significant.

Table 5
Longitudinal change in respiratory function test*

		Referent workers	Exposed workers	<i>p</i>
All subjects (<i>n</i> = 69)	PEFR [L/(s·y)]	0.19 (0.31)	0.10 (0.27)	0.20 [†]
	VC (mL/y)	22.8 (55.2)	11.4 (54.2)	0.40 [†]
	%VC (%/y)	-0.03 (1.24)	-0.28 (1.11)	0.40 [†]
	FEV ₁ (mL/y)	39.4 (38.5)	24.5 (38.8)	0.12 [†]
	FEV ₁ % (%/y)	0.09 (0.30)	-0.04 (0.35)	0.78 [‡]
Never smoker (<i>n</i> = 34)	PEFR [L/(s·y)]	0.22 (0.30)	0.10 (0.26)	0.21 [†]
	VC (mL/y)	32.3 (42.3)	15.1 (41.4)	0.25 [†]
	%VC (%/y)	0.17 (0.93)	-0.14 (0.86)	0.32 [†]
	FEV ₁ (mL/y)	45.4 (42.8)	34.1 (27.9)	0.36 [†]
	FEV ₁ % [%/y; median (IQR)]	0.15 (0.38)	-0.09 (0.40)	0.87 [‡]

Data are presented as mean (SD), unless otherwise indicated.

FEV₁, forced expiratory volume in 1 second; FEV₁%, forced expiratory volume in 1 second as a percent of forced vital capacity; IQR, interquartile range; PEFR, peak expiratory flow rate, VC, vital capacity, %VC, predicted vital capacity.

* The decrease was calculated by subtracting the value at the fifth year from the baseline value and by dividing the obtained value by the number of years (4 years).

[†] Student *t* test: not significant.

[‡] Mann-Whitney *U* test: not significant.

all the target subjects, the referent workers showed a mean PEFR for 0.19 L/(s·y) (SD 0.31), mean VC for 22.8 mL/year (SD 55.2), mean %VC for -0.03%/year (SD 1.24), mean FEV₁ for 39.4 mL/year (SD 38.5), and median FEV₁% for 0.09%/year (QD 0.30). The exposed workers showed a mean PEFR for 0.10 L/(s·y) (SD 0.27), mean VC for 11.4 mL/year (SD 54.2), mean %VC for -0.28%/year (SD 1.11), mean FEV₁ for 24.5 mL/year (SD 38.8), and median FEV₁% for -0.04%/year (QD 0.35). There were no statistically significant differences between the groups.

Among the subjects who continued not smoking for 4 years, the referent workers showed a mean PEFR for 0.22 L/(s·y) (SD 0.30), mean VC for 32.3 mL/year (SD 42.3), mean %VC for 0.17%/year (SD 0.93), mean FEV₁ for 45.4 mL/year (SD 42.8), and median FEV₁% for 0.15%/year (QD 0.38). The exposed workers showed a mean PEFR for 0.10 L/(s·y) (SD 0.26), mean VC for 15.1 mL/year (SD 41.4), mean %VC for -0.14%/year (SD 0.86), mean FEV₁ for 34.1 mL/year (SD 27.9), and median FEV₁% for -0.09%/year (QD 0.40). There were no statistically significant differences between the groups.

4. Discussion

At the start of the study, there were no significant differences in the indices concerning subject constitution that may affect the respiratory functions between both groups. Some exposed workers used organic solvents, e.g., methyl ethyl ketone and ethyl acetate, in the toner developing process with a local exhaust ventilation system operating in the powder testing laboratory. They, however, used a very small amount of organic solvents; it was difficult to consider the effects on the respiratory functions. When the respiratory function test results of both groups followed up for 4 years were cross-sectionally observed at baseline and 5th year, there were not any statistically significant differences in the PEFR, VC, %VC, FEV₁, and FEV₁% between the groups. The cross-sectional study conducted by Nakadate et al [9] and Kitamura et al [10], which was epidemiological research in which the effects of toner on respiratory functions were investigated, suggested no effect on the respiratory function test. A similar tendency was also observed in this respiratory function test at baseline and 5th year.

Various indices of longitudinal observation for the respiratory function test have been reported [11–14]; the indices of PEFR, VC, %VC, FEV₁, and FEV₁% were used in this study. In order to examine the effects of continuous smoking on respiratory functions, our study compared the time-course of respiratory function among three

groups, including the group that continued smoking for 4 years, the group that continued not smoking for 4 years, and the other group that started smoking again in our study. Among these groups, there were no statistically significant differences. Smoking influences respiratory functions, but this survey did not clarify the effect of smoking on respiratory function because of the short observation period and few subjects. When the time-course according to the presence or absence of exposure to toner was compared between all subjects and the group that continued not smoking for 4 years, there were no statistically significant differences between the groups.

When the working environment was determined for respirable dust at three workplaces, the level of dust was 0.008–0.031 mg/m³. In Japan, the standard for airborne dust in offices is specified as 0.15 mg/m³ or below by the Ordinance on Health Standards in the Office. The current results were well below the standard because the local exhaust system had been installed prior to the study at the target plant as a preventive measure for exposure to toner particles, in compliance with domestic laws related to preventing exposure to dust.

The workers were also instructed to wear personal protective equipment such as dust-protective masks when high exposure was suspected. Therefore, the exposed workers were expected to have little exposure to toner particles, although personal exposure measurement was not conducted this time. As the exposure of the exposed workers to toner particles was suppressed, the effects on respiratory functions were also thought to be suppressed. The effects of emissions including toner related particles from photocopiers on respiratory function have also been reported [15,16], and there is concern about the effects on respiratory functions such as pulmonary inflammation and allergic diseases according to the size and type of particle of toner. Studying the effects of dust on the respiratory functions in the workplace where the exposure of dust to workers is considered low as in this study is therefore necessary, although workplace emissions have not been evaluated in the current study. One limitation in this study is the small sample size. However, verifying the results of the respiratory function test, a health effect index in the workers actually exposed to toner for a long time is useful for studies that will be conducted in larger populations.

In conclusion, protective measures against exposure were taken at the plant prior to the start of the study, and no health effects of toner particles were suggested in the study. The number of subjects was small in our study, however; a report from a larger-sized study is expected in the future.

Conflicts of interest

The business equipment manufacturer where the study took place paid the research costs as a research fee to the University of Occupational and Environmental Health, Kitakyushu, Japan. To avoid bias, the study was conducted based on the JBMA guidelines and approved by the Ethical Review Board of the University of Occupational and Environmental Health, Kitakyushu, Japan. The business equipment manufacturer and the University of Occupational and Environmental Health, Japan ensured the fairness of the study.

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