

Smoking cessation after long-term sick leave due to cancer in comparison with cardiovascular disease: Japan Epidemiology Collaboration on Occupational Health Study

Keisuke KUWAHARA^{1,2*}, Motoki ENDO³, Chihiro NISHIURA⁴, Ai HORI^{4,5}, Takayuki OGASAWARA⁶, Tohru NAKAGAWA⁷, Toru HONDA⁷, Shuichiro YAMAMOTO⁷, Hiroko OKAZAKI⁸, Teppei IMAI^{9,10}, Akiko NISHIHARA⁹, Toshiaki MIYAMOTO¹¹, Naoko SASAKI⁶, Akihiko UEHARA^{12,13}, Makoto YAMAMOTO¹², Taizo MURAKAMI¹⁴, Makiko SHIMIZU¹⁴, Masafumi EGUCHI¹⁵, Takeshi KOCHI¹⁵, Satsue NAGAHAMA¹⁶, Kentaro TOMITA^{17,18}, Maki KONISHI¹, Huanhuan HU¹, Yosuke INOUE¹, Akiko NANRI^{1,19}, Naoki KUNUGITA²⁰, Isamu KABE^{15,21}, Tetsuya MIZOUE¹, Seitaro DOHI⁸,
for the Japan Epidemiology Collaboration on Occupational Health Study Group

¹National Center for Global Health and Medicine, Japan

²Teikyo University Graduate School of Public Health, Japan

³Juntendo University Graduate School of Medicine, Japan

⁴Tokyo Gas Co., Ltd., Japan

⁵University of Tsukuba, Japan

⁶Mitsubishi Fuso Truck and Bus Corporation, Japan

⁷Hitachi, Ltd., Japan

⁸Mitsui Chemicals, Inc., Japan

⁹Azbil Corporation, Japan

¹⁰Occupational Health Support Company for SMEs, Japan

¹¹Nippon Steel Corporation Kimitsu Works, Japan

¹²Yamaha Corporation, Japan

¹³Hidaka Tokushukai Hospital, Japan

¹⁴Mizue Medical Clinic, Keihin Occupational Health Center, Japan

¹⁵Furukawa Electric Co, Ltd., Japan

¹⁶All Japan Labour Welfare Foundation, Japan

¹⁷Mitsubishi Plastics, Inc., Japan

¹⁸Healthplant Co., Ltd., Japan

¹⁹Fukuoka Women's University, Japan

²⁰University of Occupational and Environmental Health, Japan

²¹Kubota Corporation, Japan

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*To whom correspondence should be addressed.

E-mail: kkuwahara@med.teikyo-u.ac.jp

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Abstract: In occupational settings, smokers may take quitting smoking seriously if they experienced long-term sick leave due to cancer or cardiovascular disease (CVD). However, no study has elucidated the smoking cessation rate after long-term sick leave. We examined the smoking cessation rate after long-term sick leave due to cancer and CVD in Japan. We followed 23 survivors who experienced long-term sick leave due to cancer and 39 survivors who experienced long-term sick leave due to CVD who reported smoking at the last health exam before the leave. Their smoking habits before and after the leave were self-reported. Logistic regression was used to calculate adjusted smoking cessation rates. Smoking cessation rate after long-term sick leave due to cancer was approximately 70% and that due to CVD exceeded 80%. The adjusted smoking cessation rate was 67.6% (95% confidence interval [CI]: 47.0, 88.2) for cancer and 80.7% (95% CI: 67.7, 93.8) for CVD. Smoking cessation rate after a longer duration of sick leave (≥ 60 d) tended to increase for both CVD and cancer. Although any definite conclusion cannot be drawn, the data suggest that smoking cessation rate after long-term sick leave due to CVD is slightly higher than that for cancer.

Key words: Long-term sick leave, Cancer, Cardiovascular disease, Smoking cessation, Japan

Introduction

Cancer is the second leading causes of death in the world¹⁾, following cardiovascular disease (CVD)¹⁾. Smoking has been associated with an increased risk of many types of cancer²⁻⁵⁾. Data from cancer patients show that continued smoking is associated with worse outcomes⁶⁾. Data also show that quitting smoking can improve chances of survival even after cancer diagnosis^{7, 8)}. Thus, smoking cessation is critically important to improve the prognosis for cancer patients.

Disease diagnosis and associated events have been considered as unique opportunities for promoting smoking cessation⁹⁾. However, a recent study showed that after diagnosis, physicians provide less smoking cessation support to cancer patients than to patients with CVD¹⁰⁾, resulting in a lower smoking cessation rate among cancer patients (36.7% vs. 44.4%)¹⁰⁾. After receiving a diagnosis or being hospitalized for CVD, approximately 50% of smokers quit smoking according to a systematic review¹¹⁾, whereas nearly 30 to 40% of smokers quit smoking after cancer diagnosis in large-scale studies^{10, 12, 13)}. However, these studies focusing on cancer diagnosis^{10, 12, 13)} may have included participants with an early stage of cancer who might therefore have been less motivated to quit smoking⁹⁾. If cancer treatment takes a longer time, resulting in long-term hospitalization or sick leave, patients may take smoking cessation more seriously and be more motivated to quit smoking. Moreover, in Japan, most of the guidelines relating to CVD recommend smoking cessation¹⁴⁾, whereas those relating to smoking-related cancers do not

recommend it¹⁴⁾. This may lead to a higher smoking cessation rate for CVD than cancer in Japan.

To date, no quantitative data are available on smoking cessation rate after long-term sick leave. Given that approximately 30% of cancer patients are of a working age^{15, 16)} and the number of employed cancer patients is expected to keep increasing^{17, 18)}, a better understanding of smoking cessation after long-term sick leave is necessary to develop effective smoking cessation strategies to realize the successful continuance of or return to work of cancer patients. More importantly, existing studies on this topic used data mainly in 1990s to 2000s¹⁰⁻¹³⁾. Given the rapid advancement in treatment, especially for cancer, smoking cessation rate needs to be estimated from updated data. Therefore, we investigated the smoking cessation rate of Japanese workers after long-term sick leave due to cancer in comparisons with CVD using data in 2010s.

Subjects and Methods

Study settings

This is a cohort study using data from the Japan Epidemiology Collaboration on Occupational Health (J-ECOH) Study, an on-going multi-company study of workers in Japan. As of March 2016, both health checkup data and official records of medically certified sick leave from 12 companies were available for the present analysis. We used annual health examination data from April 2008 to March 2016 and long-term sick leave data from April 2012 to March 2016. Details on the J-ECOH Study¹⁹⁾ and assessment of sick leave²⁰⁾ are given elsewhere. The

objective and procedure of the study was announced in each company by using posters. The participants did not provide explicit verbal or written informed consent to join the study, but they could refuse to participate. This procedure follows the national ethical guidelines in Japan for observational studies using existing data. The study protocol was approved by the Ethics Committee of the National Center for Global Health and Medicine, Japan.

Collection of sick leave data

As described elsewhere²⁰, sick leave data in the J-ECOH Study covered date of birth, gender, start and end dates of sick leave, and the subject's diagnosis. Workers in the participating companies received over two-thirds of their salary for at least 1.5 yr as paid sick leave. When applying for paid sick leave, the medical certificate written by the attending physician must be submitted to the company by the employee. We defined long-term sick-leave as sick-leave lasting 30 d or more.

Classification for cause of sick leave

Details of the classification for the cause for long-term sick leave have been explained previously²⁰. In short, the diagnoses were classified according to the International Classification of Diseases 10th revision (ICD-10). Most certificates completely matched an ICD-10 classification and were encoded automatically by text matching. The remaining unmatched certificates were manually and independently encoded by two occupational physicians of the J-ECOH Study group with reference to the master. Both physicians agreed on the coding for the most certificates unmatched at the initial stage. The disagreement in coding between the two physicians for the remaining unmatched certificates were mainly due to multiple diagnoses. As we could not obtain original clinical record to determine the primary diagnosis, another senior occupational physician of the J-ECOH Study group independently coded and ultimately decided on the ICD-10 code.

Participants

We extracted the data of 183 participants (148 men and 35 women) with long-term sick leave due to cancer and 113 participants (105 men and 8 women) with CVD who started long-term sick leave (defined as sick leave days lasting 30 d or more) between April 1, 2012 and March 31, 2014 and ended it before March 31, 2016. We excluded 8 participants who did not attend a health exam before taking long-term sick leave. Of the remaining 288 participants, we further excluded 183 participants (124

with cancer and 59 with CVD) who were non-smokers at their last health examination prior to the long-term sick leave. Of the remaining 105 smokers, we additionally excluded 43 participants who did not attend a health exam after the leave (30 for cancer and 13 for CVD). Data of the remaining 23 cancer survivor smokers and 39 CVD survivor smokers were used in the main analysis of smoking cessation rate.

Smoking

Smoking status was self-report at health exams²¹; participants were classified as current smoker or non-smoker. Participants were considered new quitters if they had smoked before long-term sick leave but reported no smoking at the first health examination after the end of the sick leave.

Other variables

Body weight and height were measured at annual health examinations. Body mass index (BMI) was calculated as body weight (kg) divided by squared height (m). We also collected data on participants' returning to work, retirement, and death to estimate the effect of selection bias due to loss to follow-up.

Statistical analysis

The data are expressed as mean (standard deviation), median (interquartile range), or number (%). Logistic regression was used to assess the association between cause of long-term sick leave and smoking cessation with treating CVD as a reference. We created a crude model and an age- and sex-adjusted model. Age at the start of long-term sick leave (years, continuous) was used for adjustment. Then, we estimated the age- and sex-adjusted smoking cessation rate (95% confidence interval [CI]) after long-term sick leave due to cancer or CVD from the logistic regression using marginal standardization²². As a subgroup analysis, we repeated the analyses according to the duration of long-term sick leave (<60 and ≥60 d). Sex was not included in the model for the analysis of shorter sick leave due to no women. For longer sick leave, adjusted cessation rate was calculated based on the prediction at the means as 95% CIs exceeded 100%. We examined the effect of the duration of long-term sick leave on the association between cause of sick leave and smoking cessation using a likelihood ratio test, comparing models with and without the interaction terms of sick leave duration and cause of sick leave. Given the high dropout rate due to retirement, we performed a sensitivity analysis to ac-

count for selection bias under the following two scenarios: (a) all smokers who retired had continued to smoke or (b) all of them had quit. Two-sided P values lower than 0.05 were considered statistically significant. All analyses were conducted using Stata 14.2 (Stata Corp, College Station, TX, USA).

Results

Table 1 shows the characteristics of participants who reported smoking at their last health exam before long-term sick leave according to the cause of the sick leave, with and without a follow-up health exam after sick leave. Overall, the durations of long-term sick leave due to cancer were greater than those due to CVD. Participants attended their first health exam after sick leave approximately one year after their last health exam before the sick leave. Of 105 smokers, 43 participants (41.0%) did not attend a health exam after their leave. This proportion was higher for cancer: of 53 smokers with cancer, 30 (56.6%) did not attend, whereas the corresponding value was 25.0% for CVD. Smokers who did not attend a health exam after sick leave due to cancer had a higher mortal-

ity rate (43% for cancer vs. 8% for CVD). The smokers who attended a health exam after sick leave had a shorter duration of sick leave and were younger than those who did not attend. Among the smokers who attended a follow-up exam after sick leave, those with cancer (n=23) were older, included more women, and had a lower BMI than those with CVD (n=39). The participants' characteristics did not differ greatly according to duration of long-term sick leave (Supplementary Table 1). As shown in Supplementary Table 2, overall, non-smokers comprised a higher proportion of women and higher BMI levels than smokers.

Details of the cause for sick leave are shown in Supplementary Table 3 for cancer and Supplementary Table 4 for CVD. Among workers who had follow-up data, major cause of sick leave due to cancer was colorectal cancer (n=6) and stomach cancer (n=5) (Supplementary Table 3). For CVD, cerebrovascular diseases (n=17) and ischemic heart disease (n=8) were the major cause of sick leave (Supplementary Table 4). Table 2 shows smoking cessation rate after long-term sick leave among participants who reported smoking at the last health exam before the sick leave. Smoking cessation rate after long-term sick leave due to cancer was nearly 70%, and smoking cessation rate

Table 1. Characteristics of participants who reported smoking at the last examination before long-term sick leave among participants with and without data on smoking at the first examination after the leave

	Cardiovascular disease		Cancer	
	Complete data (n=39)	Lack of data after the leave (n=13)	Complete data (n=23)	Lack of data after the leave (n=30)
Age at the start date of sick leave (yr)	49.9 (7.9)	58.9 (6.0)	54.0 (7.1)	56.2 (5.9)
Male	39 (100)	13 (100)	20 (87.0)	28 (93.3)
Body mass index* (kg/m ²)	24.0 (4.2)	24.1 (3.0)	23.3 (3.3)	22.0 (3.1)
<18.5	3 (7.7)	0 (0)	3 (13.0)	2 (6.7)
18.5 to <25.0	22 (56.4)	7 (53.9)	13 (56.5)	22 (73.3)
25.0 to <30.0	12 (30.8)	6 (46.2)	6 (26.1)	6 (20.0)
≥30.0	2 (5.1)	0 (0)	1 (4.4)	0 (0)
Outcome at the end of long-term sick leave				
Returned to work	39 (100)	4 (30.8)	23 (100)	11 (36.7)
Retired	0 (0)	8 (61.5)	0 (0)	6 (20.0)
Died	0 (0)	1 (7.7)	0 (0)	13 (43.3)
Duration (d)				
From the last health exam before long-term sick leave to the first exam after the leave	370 (358, 693)	NA	376 (364, 737)	NA
From the last health exam before long-term sick leave to the start date of the leave	207 (106, 315)	228 (82, 280)	133 (67, 452)	187 (88, 362)
Long-term sick leave	53 (37, 82)	72 (48, 141)	84 (55, 141)	133 (84, 247)
From the end of long-term sick leave to the first health exam after the leave	155 (90, 233)	NA	147 (59, 240)	NA

Data are shown as mean (standard deviation), number (%), or median (interquartile range). NA: not applicable.

*At the last health exam before long-term sick leave.

Table 2. Rate of smoking cessation after long-term sick leave by cause of sick leave

	Cause of long-term sick leave	
	Cardiovascular disease	Cancer
All (n)	39	23
Quit (n)	32	15
Crude model	82.1 (66.1, 91.4)	65.2 (42.6, 82.6)
		<i>p</i> =0.14*
Age- and sex-adjusted model†	80.7 (67.7, 93.8)	67.6 (47.0, 88.2)
		<i>p</i> =0.30
Duration of sick leave		
<60 d (n=29)		
No.	21	8
No. of quitters (%)	16 (76.2)	4 (50.0)
Age-adjusted model‡	72.7 (52.8, 92.7)	60.7 (26.2, 95.2)
		<i>p</i> =0.55
≥60 d (n=33)		
No.	18	15
No. of quitters (%)	16 (88.9)	11 (73.3)
Age- and sex-adjusted model	92.2 (63.1, 98.8)	76.8 (44.0, 93.3)
		<i>p</i> =0.34

Data are shown as the rate of smoking cessation (95% confidence interval).

**p*-values are derived from logistic regression for the association between cause of long-term sick leave and smoking cessation with treating CVD as reference category.

†Adjusted for age at the start date of sick leave (continuous, years) and sex.

‡Sex was not adjusted for due to a lack of women.

after sick leave due to CVD tended to be approximately 10% higher than that due to cancer, although the difference in smoking cessation rate was not statistically significant. A total of 65.2% (95% CI: 42.6, 82.6) of smokers quit after sick leave due to cancer and 82.1% (95% CI: 66.1, 91.4) of smokers quit smoking after long-term sick leave due to CVD (*p*=0.14). These smoking cessation rates did not change after adjustment for age and sex: the adjusted smoking cessation rate (95% CI) was 67.6% (47.0, 88.2) for cancer and 80.7% (67.7, 93.8) for CVD (*p*=0.30). Smokers with a longer duration of sick leave (≥60 d) were more likely to quit smoking than those with shorter duration of sick leave (<60 d), and the effect modification by the duration of long-term sick leave on the association between cause of sick leave with smoking cessation was not statistically significant (*p* for interaction=0.70 in the age- and sex-adjusted model). The adjusted smoking cessation rate for cancer was 60.7% (26.2, 95.2) for shorter duration of sick leave and 73.6% (51.5, 95.7) for longer duration of sick leave. The corresponding values for CVD were 77.8% (44.0, 93.3) and 92.2% (63.1, 98.8), respectively.

Sensitivity analyses showed that, if all smokers who retired had continued smoking, smoking cessation rate decreased to approximately 60% for both cancer and CVD

(Supplementary Table 5). If all smokers who retired had quit smoking, smoking cessation rate would be higher for CVD (84.7% for CVD and 72.7% for cancer).

Discussion

In this working population-based cohort study, owing to the low incidence rate of long-term sick leave due to cancer and CVD, the eligible participants were limited. Nonetheless, in this first attempt to clarify the smoking cessation rate after long-term sick leave, nearly 70% of smokers quit smoking after long-term sick leave due to cancer. This figure for CVD was approximately 10% higher than cancer, although the observed differences in smoking cessation rate were not statistically significant.

We observed that 68% of smokers quit smoking after long-term sick leave due to cancer and 81% of smokers quit smoking after long-term sick leave due to CVD. Existing studies on smoking cessation rate after diagnosis have shown that the cessation rate was approximately 50% for CVD¹¹ and 30 to 40% for cancer^{10, 12, 13}. Therefore, even after consideration of wide CIs of smoking cessation rate in the present study, the cessation rate after long-term sick leave might be higher than those after diagnosis. The

mechanisms of high smoking cessation rate after long-term sick leave is unclear as this is a little researched area. Psychological factors such as fear of death²³⁾ or recurrence²⁴⁾ might contribute to higher smoking cessation rate compared with those after diagnosis. Our data showing a higher smoking cessation rate among patients with a longer duration of sick leave may support this view, as severity of cancer or CVD might have progressed during long-term sick leave. Alternatively, as the present participants were workers from large-scale companies, its high socioeconomic status may explain high smoking cessation rate^{25, 26)}. Additional information on nicotine replacement therapy, smoking cessation counseling, motivation to quit smoking, and other factors at the patient-provider and health system levels would help uncover the underlying mechanisms.

Owing to the small sample size, we cannot draw any definite conclusion regarding the differences in smoking cessation rate after long-term sick leave due to cancer and CVD. Nonetheless, our results of approximately 10% higher smoking cessation rate after long-term sick leave due to CVD than cancer support a finding from UK showing that smoking cessation rate after CVD diagnosis is higher than cancer diagnosis¹⁰⁾. The reason for a higher smoking cessation rate after long-term sick leave due to CVD in the present study might be related to the differences in the recommendation of smoking cessation in the Japanese clinical guidelines between CVD and cancer as noted above¹⁴⁾. The inclusion of advice on smoking cessation in the clinical guidelines for cancer in Japan as with US²⁷⁾ may help contribute to complete smoking cessation for working adults with cancer in Japan.

The strengths of the present study include the repeated measures of smoking status and the use of medically certified data of long-term sick leave in a well-defined working population. The present study had several limitations. First, although the large population size of the J-ECOH Study enabled us to quantify the association between cause of long-term sick leave and smoking cessation, low incidence rate of long-term sick leave led to wider 95% CIs of smoking cessation rate, making it difficult to draw any definite conclusion. Second, some smokers, especially those with long-term sick leave due to CVD, were excluded as they had no follow-up data due to retirement. If the smokers who retired had continued to smoke, the observed smoking cessation rate would be higher, as shown by our sensitivity analysis. Also, if not attending a health exam after long-term sick leave was due to a high recurrence rate of sick leave, the smoking cessation rate

would be underestimated. However, among the smokers who did not attend a health exam after sick leave, although recurrence rate of sick leave for cancer was higher than that for CVD, the absolute number of cases was small (of 30 participants, 4 experienced recurrence of long-term sick leave due to cancer, while none did for CVD). Therefore, the possibility of this affecting an underestimation is low. Third, smoking status was self-reported, so underreporting of smoking²⁸⁾ may have diluted the association. Fourth, there are no data on the timing of smoking cessation after the last examination before long-term sick leave. If the smokers quit smoking before the leave, the cessation is not elicited by experience of long-term sick leave. Fifth, if the smokers had quit smoking between diagnosis and the date of the last health exam before sick leave, this would reduce the smoking cessation rate after long-term sick leave. Although we confirmed that nearly all smokers who had quit smoking before the last health exam prior to long-term sick leave had no history of cancer or CVD before the leave, we cannot deny this possibility due to underreporting of medical history^{29, 30)}. Sixth, smokers might have reported no smoking if they started to use heat-not-burn tobacco products instead of traditional tobacco. However, during the study period, the prevalence of heat-not-burn tobacco products was very low³¹⁾. Seventh, there are no data on cancer stage or CVD severity which might affect smoking cessation¹¹⁾, although a recent study reported that cancer stage did not change the association between cancer diagnosis and smoking cessation¹²⁾. Moreover, we could not elucidate the smoking cessation rate according to type of cancer or CVD as the number of participants was small when divided by cancer or CVD type (Supplementary Tables 3 and 4). Eighth, we cannot deny a possibility that occupational conditions such industry, occupation, or exposure to physical and/or psychological factors at work may have affected the present findings. Finally, the participants in this study were workers at large-scale companies in Japan, and the majority was men. Therefore, caution should be exercised when generalizing the present findings to workers with different backgrounds, especially those at small- to medium-sized enterprises or women.

In summary, owing to the small number of incident cases of long-term sick, it is difficult to draw any definite conclusion on smoking cessation rate after long-term sick leave. Nonetheless, we cannot deny a possibility that smoking cessation rate was high after long-term sick leave, and the smoking cessation rate after long-term sick leave due to CVD was slightly higher than that for cancer. Given that available evidence is scarce, further

studies with larger sample sizes are warranted for planning evidence-based strategies on smoking cessation among workers with diseases.

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Conflict of Interest

The authors declare no conflict of interest. Chihiro Nishiura, Ai Hori, Takayuki Ogasawara, Tooru Nakagawa, Toru Honda, Shuichiro Yamamoto, Hiroko Okazaki, Teppei Imai, Akiko Nishihara, Toshiaki Miyamoto, Naoko Sasaki, Akihiko Uehara, Makoto Yamamoto, Taizo Murakami, Makiko Shimizu, Masafumi Eguchi, Takeshi Kochi, Satsue Nagahama, Kentaro Tomita, Isamu Kabe, and Seitaro Dohi are/were occupational physicians in the participating companies.

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