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Original Article

Association of sitting time and cardiorespiratory fitness with cardiovascular disease risk and healthcare costs among office workers

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Abstract: Evidence of the impact of domain-specific sitting time (ST) and cardiorespiratory fitness (CRF) on cardiovascular disease (CVD) risk is currently limited. This study aimed to examine the associations between CRF and domain-specific STs in relation to CVD risk and annual healthcare costs among office workers. This cross-sectional study included 1,749 workers from an insurance company. The Worker's Living Activity-time Questionnaire was used to measure the domain-specific STs, including occupational ST and non-working day ST. Additionally, estimated maximal oxygen uptake as the CRF data was calculated using a validated equation: 59.96 − 0.23 × age + 7.39 × sex − 0.79 × body mass index + 0.33 × physical activity score. The company provided medical checkup results for CVD risk factors and healthcare costs. Multiple logistic regression analyses were used to calculate the odds ratios (ORs) for CVD risk. Significantly lower ORs for CVD risk were seen only with high CRF levels, and it was also associated with low annual healthcare costs. There were no associations between domain-specific STs and annual healthcare costs. Further explorations of domain-specific STs, physical activity, and health risks are warranted, and guidelines should focus on increasing CRF to prevent CVD risk among office workers.

Key words: Sedentary behavior, Cardiorespiratory fitness, Occupational health, Cardiovascular diseases, Domain-specific sitting time

Introduction

There is significant epidemiological evidence demonstrating a strong inverse correlation between cardiorespiratory fitness (CRF) level and cardiovascular disease (CVD) risk[1–3]. Additionally, accumulated sitting time (ST) has a negative association with CVD risk[4–6] and has been recognized as an important health concern[7]. Even though CRF and ST remain significant predictors of CVD risk after controlling for physical activity (PA)[8–11], recent studies have reported that increased ST is directly associated with lower CRF[12, 13]; these results suggest that further studies are needed to determine the impact of low CRF or long ST on CVD risk.

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A few studies[14, 15] have examined the effects of the combination of ST and CRF on CVD risk, demonstrating that a high CRF level may partially offset the health consequences of ST. Although these were noteworthy studies, they focused on fragments of daily life, such as television (TV) viewing or non-working day ST. However, economic advances and industrial innovations have resulted in most working people transferring to sedentary jobs[16], and this is likely to be a greater contributor to overall ST than sitting during leisure-time[17]. Previous accelerometer data from 193 Australian office workers showed significant differences between workdays, mainly working hours, and non-working days in terms of sedentary patterns[18]. ST that accumulated during working hours was the primary basis for the differences observed between working and non-working days. Further, recent evidence suggests contrasting health effects for occupational and leisure-time PA. This is termed the PA health paradox[19]. Moreover, evidence suggests that there are different adverse health effects in different domain-specific STs (that is, occupational and non-working day ST)[20]. From these, the workplace has recently been identified as a key setting in which to improve workers' health. Our understanding of ST across a range of domains in Japanese workers is still limited. It is warranted that we consider whether occupational and non-working day ST occurring over a large proportion of wakeful time (including both during the working and non-working days) has a similar relationship with CVD risk. Given the increasing sedentariness of modern society, combined effects of CRF and various types of ST must be investigated to fully understand how it associates with CVD risk.

Information on the economic burden of health-related behaviors, as such estimates of the healthcare costs associated with CRF and ST, may motivate policymakers to make policy changes. An increasing number of studies have recently focused on the economic consequences of physical inactivity[21] and CRF levels[22, 23]. However, among these studies[21–23], only few have used objectively collected data on healthcare costs, which are further specific among population groups (for example, ≥65 yr-old individuals or veterans). To address this gap, objective data on healthcare costs collected by a company for employees' healthcare can be leveraged. Increased understanding of both the risk and economic burden of CVD can aid in resource prioritization and facilitate efforts to reduce health risks among working individuals. Therefore, this study aimed to examine whether ST (during working and non-working days) and CRF are associated with CVD risk [defined by body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), high-density lipoprotein cholesterol (HDLC), triglycerides (TG), and fasting plasma glucose (FPG)] and healthcare costs among Japanese office workers. A secondary aim was to examine the combined effect of ST and CRF to determine the extent of the impact on CVD risk. We hypothesized that long ST and low CRF would be independently associated with an increased CVD risk and annual healthcare costs, and that high CRF would mitigate the adverse effects related to ST on CVD risk.

Subjects and Methods

Study design and participants

This cross-sectional study was conducted from May to June 2019. The participants were employees in a group companies of an insurance corporation with offices throughout Japan, and the inclusion criteria for this study were as follows: 1) employees in a group companies of an insurance corporation with offices nationwide in Japan; 2) having access to the corporate network system; 3) having membership in the health insurance association of the company. The invitation email included a research explanation (that is, the introduction and purpose of the survey) and content asking for consent to participate and provide medical checkups and healthcare costs. The survey was initiated after the employees provided informed consent; the responses were not incentivized. After the completion of the survey, the health insurance association collated and provided the data on medical checkups and healthcare costs of the employees who agreed to participate in the study. In Japan, employers are obliged by the Industrial Health and Safety Law to provide all employees with medical checkups. The data on employees' health status, medical checkup results, and healthcare costs are managed by the health insurance association, an independent organization of the company. Hence, the data required for this study were obtained from the health insurance association.

An invitation email was received by 9,916 employees. Overall, 25% of the employees opened the informed consent page from the invitation email: 23.6% provided valid responses and 1.4% did not complete the questions and were excluded. Finally, the data of 2,093 respondents were considered; 170 respondents were excluded due to insufficient data, and the data of 1,923 subjects were eventually analyzed. This study was conducted in accordance with the guidelines of the Declaration of Helsinki. The study protocol was reviewed and approved by the Ethics Committee of the National Institute of Occupational Safety and Health, Japan (approval no. 2019N-1-01). All participants provided informed consent.

Assessment of sitting time and cardiorespiratory fitness

The Worker's Living Activity-time Questionnaire (WLAQ) was used to assess ST and CRF. The WLAQ can measure ST separately in three different domains covering a worker's typical weekly life based on the previous month: (a) working time; (b) leisure-time on a working day; and (c) non-working day time. The WLAQ includes questions pertaining to when individuals perform certain activities (for example, going to bed, getting up, leaving the house, as well as arriving at and leaving the workplace). Additionally, WLAQ asks the proportion of time spent sitting or walking/standing during the total work time per day. Once we have this information, we can calculate the number of minutes per day the participant spends sitting or walking/standing for each of the domains (during working hours, leisure-time on working days, and non-working days). For example, "ST during working time" = total working time (min) × reported proportion of ST (%); "ST during leisure-time on a working day" = {(1,440 min (i.e., 24 h) − sleeping time (min) − working time (min) − commuting time (min) × 2) × reported proportion of ST (%)}; "ST on a non-working day" = {1,440 min − sleeping time (min) − working time (min) × reported proportion of ST (%)}. We have previously reported the acceptable reliability (intraclass correlation coefficient, 0.71–0.85) and validity (Spearman's ρ, 0.71–0.85) of the WLAQ[24, 25].

We also used the modified WLAQ to evaluate workers' CRF by adding questions about PA (frequency, duration, and intensity). The PA score (0–44 points) was calculated as the sum of the points scored for the PA data[26]. The modified WLAQ was then used along with age, sex, BMI, and the PA score to develop an equation for estimated maximal oxygen uptake (eVO_{2max}) = 59.96 − 0.23 × age + 7.39 × sex (0: women, 1: men) − 0.79 × BMI + 0.33 × PA score. The results of assessments with the above equation were highly correlated with the treadmill-measured VO_{2max} ($r=0.73$, $p<0.01$)[26].

Cardiovascular disease risk factors

Data on the participants' height, weight, values of specific CVD risk factors (SBP, DBP, HDLC, TG, and FPG), and clinical history were collected from medical checkup records over a 1 yr period. We calculated BMI as the weight in kilograms divided by the square of the participants' height in meters. The presence of CVD risk was derived from the definition of metabolic syndrome[27], which constituted meeting three or more of the following criteria (no criteria met=no CVD risk, and 3≥ criteria met=CVD risk): (1) BMI ≥25 kg/m^2; (2) SBP ≥130 mmHg and DBP ≥85 mmHg or receiving treatment for hypertension; (3) TG level ≥150 mg/dl or HDLC level <40 mg/dl for men and <50 mg/dl for women or receiving treatment for dyslipidemia; and (4) FPG ≥100 mg/dl or the use of glucose-lowering medications (insulin or oral agents).

Lifestyle variables related to CVD risk were self-reported. They included smoking status (current smoker, ex-smoker, or non-smoker); alcohol consumption status (no consumption, once or twice per week, three to five times per week, or every day). In this study, based on the information obtained from the WLAQ, referring to the definition of the Ministry of Health, Labor and Welfare[28], individuals who met the following two criteria were defined as having exercise habits: (1) Exercise frequency of two days or more per week and (2) not less than 30 minutes in duration.

Calculation of annual healthcare costs

The data regarding healthcare costs include hospital discharge, outpatient visits, the type of clinic visited, the diagnoses, and the use of pharmacy services. In this study, annual healthcare costs were calculated as the sum of hospitalization and outpatient visits for all diseases, excluding the costs of dental care and medication, as they cannot be linked to the type of disease. The 2019 medical remuneration points were summed for each individual, and annual healthcare costs were calculated in the Japanese yen.

Statistical analyses

The sample size was calculated using G*Power 3.1.9.4 (Heinrich Heine Universität Düsseldorf, Düsseldorf, Germany) and we determined the minimum to be 1,484 participants to obtain significant odds ratios (ORs) for CVD risk with an alpha risk of 5% and a power of 80%. Continuous data presented as the mean ± standard deviation were used to compare differences between sexes. Categorical data were presented as n (%) and compared using a χ^2 test. The total sample was categorized into tertiles with equal size. ST was categorized into short, middle, and long tertiles for both occupational ST (≤7.8 h, 7.9–9.1 h, ≥9.2 h) and non-working day ST (≤7.5 h, 7.6–10.2 h, ≥10.3 h), respectively. Tertiles of CRF were classified with reference to previous studies[14, 15, 23, 29] to minimize the impact of sex and age. Briefly, we first stratified sex into four age categories: <40 yr, 40–49 yr, 50–59 yr, and

≥60 yr. We then defined tertiles of CRF within each age category according to the eVO_{2max} into low, moderate, and high groups. Finally, we combined the respective tertiles from all age categories, in both sexes, to form the eVO_{2max} categories; CRF-low (mean 33.9 ± 4.4 ml/(kg × min); rage, 16.8–42.0 ml/(kg × min); n=638), CRF-moderate (mean 38.2 ± 3.7 ml/(kg × min); rage, 27.7–45.9 ml/(kg × min); n=644), and CRF-high (mean 42.3 ± 4.0 ml/(kg × min); rage, 34.0–53.9 ml/(kg × min); n=641).

Differences in CVD risk factors within each ST and CRF group were analyzed using covariance analysis (ANCOVA), with age, sex, smoking status, alcohol consumption, and exercise habits as covariates. The Kruskal–Wallis test for nonparametric analysis and the Jonckheere–Terpstra test for trend analysis was used to determine group differences in healthcare costs. Multiple logistic regression analyses were conducted to calculate ORs and 95% confidence intervals (CIs) for the single and combined effects of ST and CRF on CVD risk. The ST and CRF were analyzed using single logistic regressions based on the short/low groups (reference). Combined multiple logistic regression analyses were performed based on nine categories: age and sex-specific tertiles for occupational and non-working day ST (short, moderate, and long), as well as CRF (low, moderate, and high). Short ST with high CRF was used as a reference to examine their combined association with CVD risk. All regression analyses included age, sex, smoking status, alcohol consumption, and exercise habits as confounders. Multiple logistic regression analyses were also performed, followed by propensity scoring matching (for the matched subset) to balance baseline characteristics based on age and sex. After matching, each ST and CRF group was divided into tertiles. We also created a logistic model containing covariates (smoking status, alcohol consumption, and exercise habits) with a significant confounding effect. All statistical analyses were performed using SAS, version 9.4 (SAS Institute Japan, Tokyo, Japan). Results were considered significant at $p<0.05$.

Results

The mean age of the participants was 45.2 ± 8.9 yr, and 52.5% were men. The participants' demographic characteristics are shown in Table 1. The average working hours accounted for 43% of their daily life, and occupational ST accounted for 82.4% of working hours. Non-working day ST accounted for 53.7% of the wakeful time, with significant differences between the sexes ($p<0.01$).

Group differences in CVD risk according to occupational ST, non-working day ST, and CRF are shown in Table

Table 1. Characteristic of the participants

	Total (N=1,923)	Men (n=1,010)	Women (n=913)
Age, yr	45.2 ± 8.9	47.0 ± 8.7	43.1 ± 8.7*
BMI, kg/m^2	22.8 ± 3.6	23.8 ± 3.2	21.7 ± 3.6*
eVO_{2max}, ml/(kg×min)	38.2 ± 5.3	41.1 ± 4.2	34.9 ± 4.4*
Presence of CVD risk, n (%)	206 (10.7)	167 (8.7)	39 (2.0)*
Exercise habit, n (%)	826 (43.0)	536 (27.9)	290 (15.1)*
Current smoker, n (%)	393 (20.4)	301 (15.7)	92 (4.8)*
Alcohol consumers, n (%)	1,343 (69.8)	802 (41.7)	541 (28.1)*
WLAQ			
Working time, h	10.2 ± 1.3	10.8 ± 1.1	9.5 ± 1.2*
ST during the working time, h	8.4 ± 1.8	8.6 ± 2.1	8.2 ± 1.5*
ST on non-working day, h	8.8 ± 3.3	9.2 ± 3.2	7.7 ± 3.4*

Values are presented as n (%) or mean ± standard deviation. *Significant differences between male and female by Student's unpaired *t*-tests and χ^2 ($p<0.05$). The presence of CVD risk was defined as meeting three or more of the following criteria (i.e., not meeting=no CVD risk, and 1 or more criteria=CVD risk): (1) BMI of 25 or more, (2) SBP of 130 mmHg and DBP 85 mmHg or more receiving treatment for hypertension; (3) TG level of 150 mg/dl or more, or HDLC level of 40 mg/dl or more 40 for men and 50 mg/dl or more for women or receiving treatment for dyslipidemia; and (4) FPG of 100 mg/dl or more, or the use of glucose-lowering medications (insulin or oral agents). Exercise habits (0: no exercise; 1: at least 30 min per day, 2 d per week) is defined those who met the following two criteria as having exercise habits: (1) Exercise frequency of 2 days or more per week. (2) not less than 30 min in duration, referring to the definition of the Ministry of Health, Labor and Welfare.
BMI: body mass index; CVD: cardiovascular disease; WLAQ: Worker's Living Activity-time Questionnaire; ST: sitting time.

2. Those with longer occupational and non-working day ST were older (p<0.01), but no significant age differences were observed in the CRF. Moreover, while both occupational and non-working day ST groups showed no significant differences in CVD risk factors and the presence of CVD risk, the CRF groups did. The eVO_{2max} and exercise habits rate were lower in participants with more extended non-working day ST. The frequency of exercise habits also significantly increased as the eVO_{2max} increased. There were no significant differences across working time and occupational ST in the CRF groups. The overall results for the occupational ST, non-workday ST, and CRF groups after propensity score matching were similar to those before matching, although differences were observed in several risk factors, working hours, and non-workday ST among the CRF groups (Supplementary Table 1). Furthermore, even after propensity score matching based on age and sex, a significant difference was observed with respect to sex among the occupational ST, non-working day ST, and CRF groups. Moreover, there was a significant difference in age among the CRF groups (p<0.01).

The adjusted ORs for CVD risk according to occupational ST, non-working day ST, and CRF are shown in Fig. 1. Moreover, all confounders exerted a significant effect on the risk of CVD [regression coefficients (β)] based on analysis using only one of the following covariates: age (β=5.88, p<0.01), sex (β =1.49, p<0.01), smoking status (β =2.18, p<0.01), alcohol consumption (β =2.14, p<0.01), and exercise habits (β =2.04, p<0.01). With the short ST group as the reference, there was no increased risk of CVD for both participants with long occupational ST (OR=0.82, 95% CI: 0.57–1.78) and those with long non-working day ST (OR=0.92, 95% CI: 0.62–1.35). Meanwhile, the moderate (OR=0.19, 95% CI: 0.09–0.39) and the high (OR=0.02, 95% CI: 0.01–0.05) CRF group had significantly lower CVD risk than the low CRF group. These trends remained unchanged after propensity score matching; there was no increase in the risk of CVD for participants with a long occupational ST (OR=0.76, 95% CI: 0.47–1.22) and those with a long non-working day ST (OR=0.70, 95% CI: 0.43–1.12). Meanwhile, the risk of CVD was significantly lower in the moderate (OR=0.34, 95% CI: 0.20–0.56) and high (OR=0.27, 95% CI: 0.16–0.47) CRF groups than that in the low CRF group (Supplementary Fig. 1).

The results of logistic regression analyses examining the combined effect of each ST (occupational and non-working day ST) and CRF on CVD risk are shown in Fig. 2. Using high CRF with short ST as the reference, both occupational and non-working day ST showed no significant difference in CVD risk across combined ST and high CRF. Meanwhile, in occupational ST categories, the CVD risk was increased for low CRF and short ST (OR=28.6, 95% CI: 10.4–79.2), moderate ST (OR=24.0, 95% CI: 8.6–64.0), and long ST (OR=23.8, 95% CI: 8.7–64.5). There was a significant combined effect of low CRF and non-working day ST. The risk of CVD was 52.6 (95% CI: 15.2–182.3), 55.2 (95% CI: 16.1–188.9), and 38.2 (95% CI: 11.2–130.8) times higher among individuals with short, moderate, and long ST, respectively. In addition, a significant combined effect of moderate CRF and non-working day ST was noted: 6.4 (95% CI: 1.7–23.4), 6.3 (95% CI: 1.7–23.0), and 5.3 (95% CI: 1.5–19.2) times higher, respectively. The overall results obtained after propensity score matching were similar to the original results (Supplementary Fig. 2). The combined effects of low CRF with occupational ST [short ST (OR=2.44, 95% CI: 1.01–5.87), moderate ST (OR=2.05, 95% CI: 0.87–4.82), and long ST (OR=2.92, 95% CI: 1.11–7.67)], and non-working day ST [short ST (OR=4.48, 95% CI: 1.87–10.7), moderate ST (OR=4.58, 95% CI: 1.84–11.4), and long ST (OR=2.77, 95% CI:

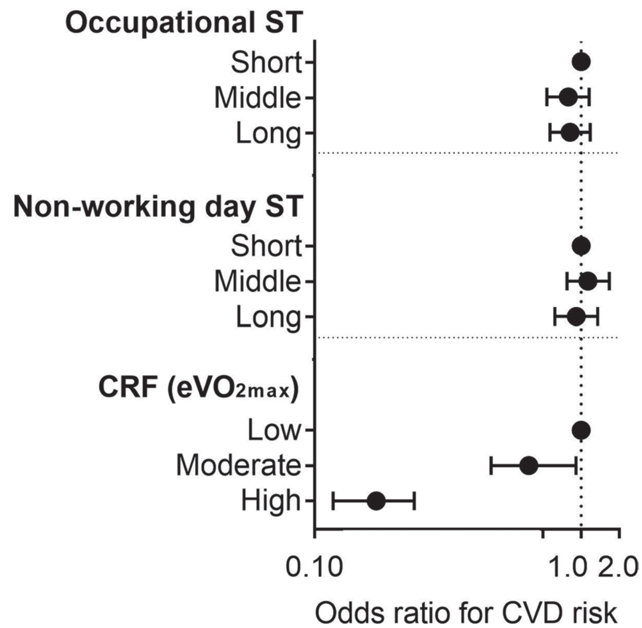

Fig. 1. Odds ratios (ORs) for cardiovascular disease (CVD) risk with respect to occupational sitting time (ST), non-working day ST, and cardiorespiratory fitness (CRF; estimated VO_{2max}). Logistic regression analyses were performed based on each reference group (that is, short occupational ST, short non-working day ST, and low CRF). The analysis is adjusted for age, sex, smoking status (0: ex-smoker and non-smoker, 1: smoker), alcohol consumption (0: no consumption, 1: once or twice per week, 3–5 times per week, and ≥ 6 times per week), and exercise habits (0: non-habit, 1: at least 30 min per day, 2 d per week, over 1 yr or more).

Table 2. The differences of groups acoording to occupational ST, Non-workingdays and CRF (n=1,923)

	Occupational ST			*p* for group differences	Non-workingdays ST			*p* for group differences	CRF			*p* for group differences
	Short	Middle	Long		Short	Middle	Long		Low	Moderate	High	
n (men %)	634 (45.4)	654 (43.9)	635 (68.5)	<0.01[a]	639 (43.5)	643 (54.0)	641 (60.0)	<0.01[a]	638 (52.5)	644 (52.5)	641 (52.6)	0.99[a]
Age, yr	44.4 ± 9.0	45.1 ± 9.1	46.0 ± 8.5	<0.01	44.4 ± 9.1	44.9 ± 8.7	46.1 ± 8.8	<0.01	46.0 ± 8.2	45.2 ± 8.8	44.2 ± 9.5	<0.01
BMI, kg/m^2	22.7 ± 3.4	22.6 ± 3.8	23.1 ± 3.5	0.97	22.4 ± 3.5	22.9 ± 3.6	23.1 ± 3.7	0.31	25.6 ± 3.8	22.0 ± 2.6	20.9 ± 2.2	<0.01
AC, cm	80.2 ± 9.5	80.3 ± 10.3	82.0 ± 9.9	0.84	79.5 ± 9.6	81.0 ± 9.8	82.0 ± 10.3	0.24	87.9 ± 10.3	78.9 ± 8.0	75.7 ± 6.9	<0.01
SBP, mmHg	113.4 ± 14.8	113.2 ± 14.8	114.9 ± 14.4	0.44	112.2 ± 14.7	114.4 ± 15.1	114.9 ± 14.1	0.26	117.6 ± 14.9	112.4 ± 14.2	111.5 ± 14.2	<0.01
DBP, mmHg	71.1 ± 11.9	70.7 ± 11.5	71.9 ± 11.4	0.20	70.1 ± 11.9	71.6 ± 12.0	72.0 ± 10.7	0.51	74.3 ± 11.9	69.9 ± 11.3	69.5 ± 10.9	<0.01
HDLC, mg/dl	64.1 ± 15.7	64.2 ± 15.3	61.6 ± 16.2	0.88	64.8 ± 15.0	62.8 ± 15.8	62.3 ± 16.3	0.74	58.2 ± 15.0	63.9 ± 15.4	67.8 ± 15.4	<0.01
TG, mg/dl	96.5 ± 65.9	96.2 ± 66.9	105.2 ± 71.1	0.90	90.0 ± 59.8	103.8 ± 74.3	104.1 ± 68.5	0.06	118.9 ± 75.5	95.6 ± 67.9	83.5 ± 54.4	<0.01
FPG, mg/dl	94.3 ± 13.2	95.5 ± 16.7	95.3 ± 13.5	0.02	93.7 ± 12.4	95.0 ± 15.0	96.3 ± 15.9	0.80	98.8 ± 17.5	94.2 ± 13.0	92.1 ± 11.7	<0.01
eVO_{2max}, ml/(kg×min)	37.9 ± 5.3	37.6 ± 5.2	39.0 ± 5.3	0.71	38.4 ± 5.3	38.3 ± 5.4	37.8 ± 5.1	<0.01	33.9 ± 4.4	38.2 ± 3.7	42.3 ± 4.0	<0.01
Presence of CVD risk, n (%)	69 (3.6)	60 (3.1)	77 (4.0)	0.23	56 (2.9)	74 (3.9)	76 (4.0)	0.15	157 (8.2)	39 (2.0)	10 (0.5)	<0.01
Exercise habit, n (%)	260 (13.5)	270 (14.0)	296 (15.4)	0.07	306 (15.9)	288 (15.0)	232 (12.1)	<0.01	94 (4.9)	244 (12.7)	488 (25.4)	<0.01
Current smoker, n (%)	139 (7.2)	114 (5.9)	140 (7.3)	0.06	109 (5.7)	138 (7.2)	146 (7.6)	0.03	149 (7.8)	152 (7.9)	92 (4.8)	<0.01
Alcohol consumers, n (%)	430 (22.4)	447 (23.2)	466 (24.2)	0.06	448 (23.3)	453 (23.6)	442 (23.0)	0.83	430 (22.4)	451 (23.5)	462 (24.0)	0.19
WLAQ												
Working time, h	9.5 ± 1.3	9.9 ± 1.0	11.2 ± 1.0	<0.01	10.1 ± 1.4	10.3 ± 1.2	10.3 ± 1.3	0.37	10.2 ± 1.3	10.2 ± 1.4	10.3 ± 1.3	0.38
ST during the working time, h	6.4 ± 1.5	8.6 ± 0.4	10.2 ± 0.9	<0.01	8.0 ± 2.0	8.4 ± 1.8	8.9 ± 1.6	<0.01	8.5 ± 1.8	8.4 ± 1.9	8.4 ± 1.9	0.66
ST on non-working day, h	8.1 ± 3.1	8.9 ± 3.2	9.4 ± 3.4	<0.01	5.2 ± 1.8	8.9 ± 0.8	12.4 ± 1.5	<0.01	9.5 ± 3.3	8.8 ± 3.1	8.1 ± 3.3	<0.01

Values are presented as n (%) or mean ± standard deviation. The differences within groups obtained by χ^2 and ANCOVA adjusted for age, sex, smoking, alcohol and exercise habit.

[a]Significant difference in sex (%)

BMI: body mass index; AC: Abdominal circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDLC: high-density lipoprotein cholesterol; TG: triglycerides; FPG: fasting plasma glucose; CVD: cardiovascular disease; WLAQ: Worker's Living Activity-time Questionnaire; ST: sitting time.

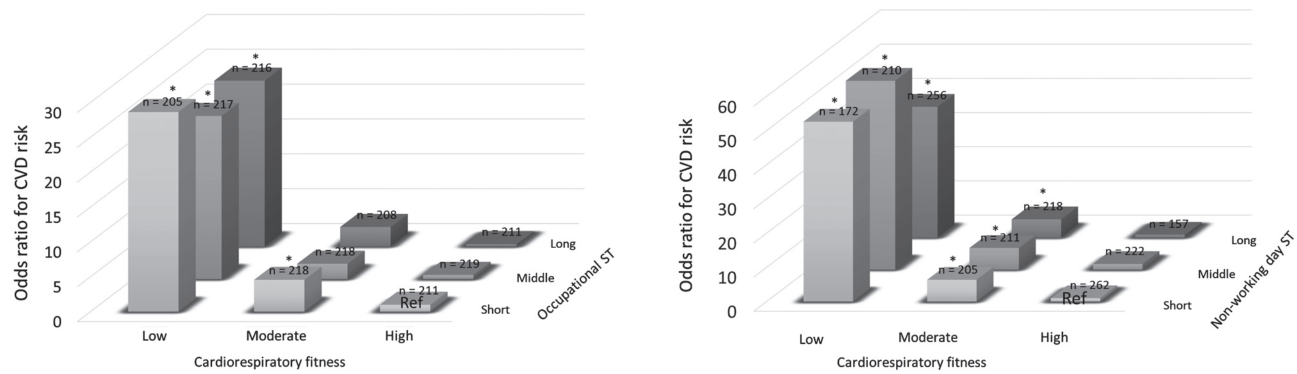

Fig. 2. Full adjusted odds ratios (ORs) for cardiovascular disease (CVD) risk across combined categories of sitting time (ST) ((a) occupational ST and (b) non-working day ST) and cardiorespiratory fitness (CRF; estimated VO_{2max}). Combined multiple logistic regression analyses were performed based on each reference group (that is, short occupational ST combined with low CRF and short non-working day ST combined with low CRF). The analysis is adjusted for age, sex, smoking status (0: ex-smoker and non-smoker, 1: smoker), alcohol consumption (0: no consumption, 1: once or twice per week, 3–5 times per week, and ≥ 6 times per week), and exercise habit (0: no exercise; 1: at least 30 min per day, 2 d per week, over 1 yr or more). *Significant difference from the reference category ($p<0.05$).

1.16–6.58)] on CVD risk were significant.

Figure 3 shows the annual healthcare costs stratified by occupational ST, non-working day ST, and CRF. There were no significant differences in annual healthcare costs associated with occupational and non-working day ST. However, annual healthcare costs were significantly lower with higher CRF ($p=0.01$).

Discussion

The main findings of the present study targeting office workers were that (1) both domain-specific STs (i.e., occupational and non-working day ST) were not independently associated with CVD risk, but a high level of CRF had a marked effect on lowering the CVD risk; and (2) when both domain-specific STs were combined with lower CRF, the CVD risk was significantly higher than that when combined with high CRF. In addition, non-working day ST was associated with a significantly higher CVD risk, even when combined with moderate CRF. Moreover, there are no clear associations between domain-specific STs and annual healthcare costs, but high CRF is clearly associated with low annual healthcare costs.

One of our main findings, that domain-specific STs have no detrimental independent association with CVD risk is inconsistent with the results of previous studies[12, 13, 30], which suggested a positive correlation between ST and CVD risk. Previous studies have focused on ST for common leisure activities such as TV viewing and screen time (i.e., computer use), which may explain the discrepancy in results. However, to fully understand the role of ST as a factor associated with health risk, we need to focus on STs occurring in various domains (e.g., at work, leisure, and on holiday). Contrary to previous studies[12, 13, 30], the present study used the WLAQ, which can measure ST across domains, and found that both occupational and non-working day ST were not associated with CVD risk. These conflicting results may be explained by the possibility that fragments of daily activities, such as TV viewing, do not fully reflect the daily ST[30]. In addition, other large studies using waist-[31] or thigh-worn[32] accelerometers have reported that the correlation between TV viewing and measured ST is very low, ranging from 0.05 to 0.17. As such, TV time may reflect only a small portion of the day and is possibly an incomplete assessment of an individual's ST. Considering these possibilities, future studies must clarify the relationship between CVD risk and domain-specific STs objectively collected by accelerometers and simple self-reporting tools (such as a daily activity time recording app).

On the other hand, this study showed that a high CRF level reduces CVD risk, even with prolonged occupational and non-working day STs. The results of the present study support the findings of many previous studies[13, 14], showing that achieving a higher CRF plays a dominant role in CVD risk. Furthermore, the result of significantly increased CVD risk in non-working day ST, even when combined with moderate CRF, provides interesting insight into the association between domain-specific STs and CRF. These results suggest that non-working day ST affects CVD risk more than occupational ST, which is in accordance with the findings of previous studies, which have reported that occupational ST may have less deleterious

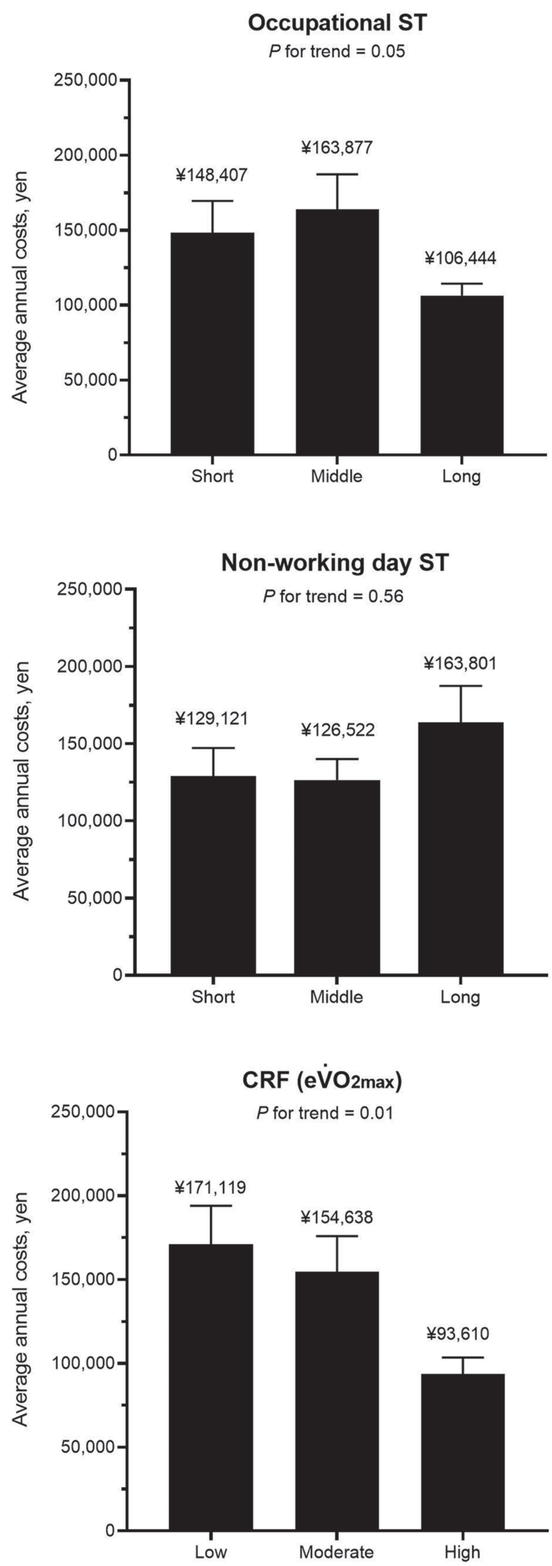

Fig. 3. Group differences in annual healthcare costs according to occupational sitting time (ST), non-working day ST, and cardiorespiratory fitness (CRF; estimated $\dot{V}O_{2max}$). The healthcare cost distribution is strongly skewed; thus, error bars indicate the standard error of the mean.

effects on CVD, cardiometabolic health[33)], and diabetes[34)] than leisure-time ST. However, further research is needed to determine why ST affects CVD risk differently depending on the domain. Holtermann *et al.*[19)] reported that occupational PA, such as moderate to vigorous activities during work, increased the health risk, while non-working day PA, such as exercise, decreased the health risk. These contrasting health effects are termed the PA health paradox and might be explained by differences in various PA characteristics of work and leisure, including the type, duration, and intensity of PA. In addition, Ketels *et al.*[35)] evaluated workers in demanding jobs and suggested that although increased ST can provide a form of rest, the burden caused by occupational ST in sedentary jobs in our study cannot be separated between rest and work. From the outside, the health effects of occupational ST among office workers may differ from those among workers with demanding jobs. Therefore, the relationship between occupational ST and health risk should be interpreted carefully because it can be affected by the study participants' work style (e.g., demanding work vs. sedentary work). Accordingly, these findings prove that domain-specific STs may be important, not just the amount of ST. Therefore, it would be informative if future studies could observe the apparent differences in domain-specific STs.

In the additional analyses, we examined the association between CRF and ST with annual healthcare costs. To the best of our knowledge, this is the first study to investigate the relationship between direct-collected healthcare costs and ST with CRF in Japanese office workers. Our cross-sectional results demonstrated that domain-specific STs were not significantly associated with annual healthcare costs. Meanwhile, there was only a significant downward trend in annual healthcare costs associated with higher CRF. This result is consistent with the findings of recent reports[22, 23)] that focus on the association between economic burden and CRF. Bachmann *et al.* studied 19,571 individuals who underwent a baseline CRF assessment at a mean age of 49 yr and later received Medicare coverage for 10 yr at an average age of 71 yr[22)]. They observed that annual healthcare costs were significantly lower for individuals with a high midlife CRF than for those with a low midlife CRF ($7,559 vs. $12,811 in men; $6,065 vs. $10,029 in women). More recently, Myers *et al.* demonstrated that annual healthcare costs were higher by $14,662 in individuals with low CRF than in those with high CRF[23)]. Nonetheless, healthcare cost estimates should be cautiously compared across studies because variations in methodologies and differences in national healthcare and insurance systems can affect cost calculations.

The main strength of this study is the inclusion of information on domain-specific STs; that is, this study used a validated questionnaire that provided continuous ST during both occupational and non-working day time. As such, more predictive information was included than with categorical variables or daily activity fragments, such as TV viewing. Another strength is that this study included information on direct healthcare costs and CVD risk provided by the health insurance association of the company. Therefore, we used more accurate data than self-reported data that might be associated with recall bias. However, this study also has some limitations. First, among all employees who received an invitation email (n=9,916), only 21.1% (n=2,093) provided valid responses. This may result in a respondent bias, as only a quarter of all recipients opened the invitation email. The possible factors related to obtaining a response are the method of compellation and incentives. When the persons in charge of the company that cooperated with the research called for participation, they urged the employees to participate, saying that responding to the survey could raise individual health awareness, possibly resulting in the participants keen interest in health. In addition, providing no incentive may have led to a low response rate[36]. Accordingly, the results of this study cannot be generalized and are limited to Japanese office workers. Second, causality cannot be determined as the significantly lower ORs for CVD risk were shown with only high CRF and were associated with low annual healthcare costs, because this study used a cross-sectional design. Therefore, longitudinal healthcare cost data are needed, and future research spanning several years would also be helpful. Third, the lack of information on other measures of socioeconomic status and lifestyles, such as education and nutritional information, were limitations of our study, as they may also influence the results. Fourth, although the study was for corporate employees, domain-specific STs and CRF are self-reported assessments; therefore, further studies using objective assessments are needed to clarify these issues. Fourth, this study used information on annual medical checkups and WLAQ conducted in a specific period (i.e., May–June 2019), indicating that the intra-individual validity of measurements may affect their association with disease outcomes[37, 38]. Therefore, the time-varying state of biomarkers needs to be considered in future research.

In conclusion, our results could not confirm that accumulated ST during occupational and non-working days is independently detrimental to CVD risk. However, this study demonstrated that an apparent effect of CRF may mitigate the CVD risk caused by cumulative specific-domain ST, which may be more promising on non-workday ST. Further studies are needed to estimate the healthcare costs associated with ST and CRF. Our results contribute to the evidence that health guidelines for workers should focus on CRF and domain-specific STs, and research in this area will provide information for the prevention of CVD among workers.

Author Contributions

MT and RS conceived and designed the research questions. MF and SW were responsible for data collection operations and data provision. RS and FM analyzed and interpreted the data, and RS wrote the manuscript. MT assisted in the conception and critical review of the intellectual content. All authors read and approved the final manuscript.

Consent for Publication

Not applicable.

Availability of Data and Materials

Data are not deposited in publicly available repositories due to ethical restrictions and participant confidentiality concerns. However, on reasonable request, the derived data supporting the findings of this study are available with approval from the principal investigator (Dr. Tomoaki Matsuo) and the company that provided the data.

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Conflicts of Interest

The authors declare no conflicts of interest.

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