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Original Article

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Sedentary Time is Associated with Cardiometabolic Diseases in A Large Japanese Population: A Cross-Sectional Study

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Aim: Accumulating evidence reveals that sedentary behavior is associated with mortality and cardiometabolic disease; however, there are potential age and sex differences in sedentary behavior and health outcomes that have not been adequately addressed. This study aimed to determine the association of sedentary behavior with cardiometabolic diseases such as hypertension, dyslipidemia, diabetes mellitus, and its risk factors in a large Japanese population according to age and sex.

Methods: Using data from the Japan Multi-Institutional Collaborative Cohort Study obtained from baseline surveys, data of 62,754 participants (27,930 males, 34,824 females) were analyzed. This study uses a cross-sectional design and self-administered questionnaires to evaluate sedentary time and anamnesis. For the logistic regression analysis, sedentary time <5 h/day was used as the reference and then adjusted for age, research areas, leisure-time metabolic equivalents, and alcohol and smoking status. From the analysis of anthropometric and blood examinations, 35,973 participants (17,109 males, 18,864 females) were analyzed.

Results: For hypertension and diabetes, sedentary time was associated with a significantly higher proportion of male participants. Both sexes were associated with a significantly higher proportion of participants with dyslipidemia. Participants who had longer sedentary time tended to have increased levels of blood pressure, triglycerides, and non-high-density lipoprotein cholesterol (HDL-C), and decreased levels of HDL-C, especially in the 60–69 years group.

Conclusions: Independent of leisure-time physical activity, sedentary time was associated with cardiometabolic diseases in a large Japanese population classified by age and sex. Our findings indicate that regularly interrupting and replacing sedentary time may contribute to better physical health-related quality of life.

Key words: Sedentary time, Cardiometabolic diseases, Population approach

Introduction

Accumulating evidence reveals that sedentary (sitting or reclining posture) behavior is associated with negative health connotations[1], including cardiovascular-specific and overall mortality[2]. Similarly, studies have demonstrated a relationship between sedentary behavior and the development of metabolic disease (e.g., obesity, metabolic syndrome, and type 2 diabetes mellitus)[3]. More specifically, these studies report an association between prolonged periods of sedentary behavior and all-cause morbidity and mortality, which cannot be simply explained by differences in engagement in low-, moderate-, or vigorous-intensity physical activity[4]. Sedentary time is associated with an increased risk of mortality and cardiometabolic disease, although there are potential age and sex differences in sedentary behavior and health outcomes that have not been adequately addressed[5].

In Japan, some studies showed an association between sedentary time and erectile dysfunction among patients with type 2 diabetes mellitus[6], kidney function decline[7], chronic obstructive pulmonary disease[8], coronary artery disease[9], and all-cause mortality[10]. However, in Japan, few studies have examined the association between sedentary time and cardiovascular risk according to age and sex.

Aim

This study aimed to determine the association of sedentary behavior with cardiometabolic diseases such as hypertension, dyslipidemia, diabetes mellitus, and its risk factors in a large Japanese population according to age and sex.

Methods

Study Participants

In this study, we evaluated participant data collected during the Japan Multi-Institutional Collaborative Cohort (J-MICC) Study[11] from baseline surveys using cross-sectional data. The cohort study evaluated the general Japanese population using genetic and clinical data to detect and confirm gene–environment interactions related to lifestyle-associated diseases. The study participants were 35–69 years old and were enrolled after responding to study announcements in 13 research areas, attending health check-up examinations that were commissioned by their local governments, visiting local health check-up centers, or visiting a cancer hospital. **Fig. 1** shows the flow chart of the study participants. Of the 13 research sites, two did not collect data on daily life activities, including sitting time from the participants. Excluding the participants in these two research sites, 72,714 participants were initially included in the current study (the dataset is ver. 20190729). Among the 72,714 participants, we excluded a total of 9,960 participants who lacked self-administered questionnaire data as follows: 478 without data on history of hypertension, dyslipidemia, or diabetes; 5,198 without data on smoking and drinking status or daily physical activity times including sitting time; 1,306 without data on medical history of ischemic heart disease and stroke; and 49 without data on drug treatment for hypertension, dyslipidemia, or diabetes. We also excluded 2,929 participants with a medical history of ischemic heart disease and stroke. Data for a total of 62,754 participants (27,930 males, 34,824 females) were analyzed for the associa-

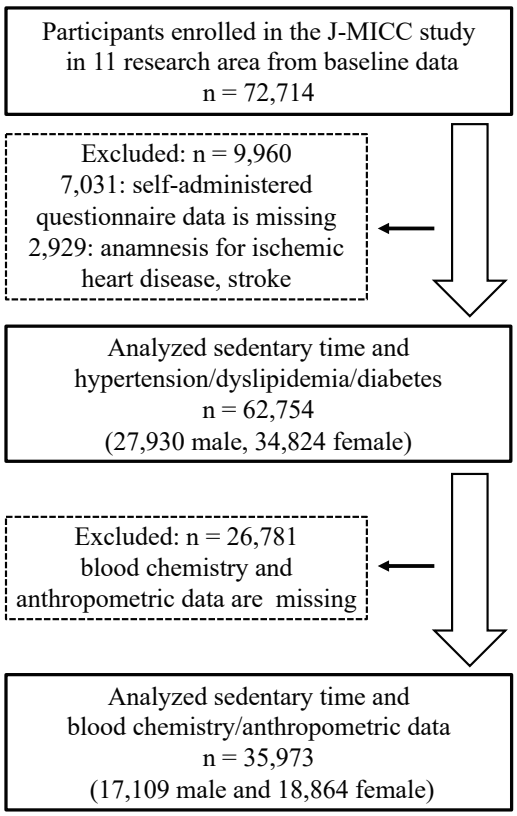

Fig. 1. Flow chart of the study participants

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tion of sedentary time with hypertension, dyslipidemia, and diabetes.

Furthermore, we analyzed participants from seven research sites who underwent anthropometric and blood examinations. We excluded 26,781 participants with missing data for body mass index (BMI), blood pressure (systolic blood pressure [SBP] and diastolic blood pressure [DBP]), and biochemical measurements, including serum triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), non-HDL-C, and glycated hemoglobin (HbA1c). Finally, a total of 35,973 participants (17,109 males and 18,864 females) were included in the analysis of sedentary time.

All study participants gave written informed consent. The study protocol was approved by the Ethics Committees at Aichi Cancer Center, the Nagoya University Graduate School of Medicine (IRB No. 939-13), and other institutions participating in the J-MICC study. This study was conducted according to the principles expressed in the World Medical Association Declaration of Helsinki.

Lifestyle and Blood Biochemistry Data

In this study, we evaluated the lifestyle and medical information obtained through self-administered questionnaires (smoking and drinking status and physical activity, including sitting time). Physical activity was determined using a format similar to a short format of the International Physical Activity Questionnaire (IPAQ)[12]. Leisure-time physical activity was assessed in terms of metabolic equivalents (LT-METs), as previously reported[13, 14]. In brief, METs-hours per day of leisure-time activity was estimated by multiplying the reported daily time that was spent in each activity by the relevant MET intensity. The duration of sitting time was classified into one of the following eight categories: none, <1 h/day, 1 to <3 h/day, 3 to <5 h/day, 5 to <7 h/day, 7 to <9 h/day, 9 to <11 h/day, and ≥ 11 h/day. Sitting time was then categorized based on the quartile value: 5 h/day, 5–<7 h/day, 7–<9 h/day, or ≥ 9 h/day. BMI was calculated as weight (kg) divided by the square of height (m^2). Anamnesis and medication history were assessed using self-administered questionnaires. Hypertension, dyslipidemia, and diabetes were defined as the presence or absence of anamnesis and/or current use of medication. In addition, blood chemistry data (serum levels of TG, total cholesterol, HDL-C, non-HDL-C, and HbA1c) and anthropometric data were obtained from health check-ups performed in the research areas. Laboratories, in each research area, analyzed the serum samples.

Statistical Analyses

Continuous variables are expressed as means, and categorical data are expressed as sums and percentages. We classified sedentary time into four groups according to sitting time (<5 h, 5 to <7 h, 7 to <9 h, and ≥ 9 h) and analyzed each group for sex and age in years (35–49, 50–59, and 60–69 years). Odds ratios (OR) and 95% confidence intervals (CI) were calculated using logistic regression analyses to evaluate the associations of sedentary time with the prevalence of hypertension, dyslipidemia, and diabetes. Sedentary time <5 h was used as a reference. Multiple regression analysis was performed to assess the sitting time (<5 h, 5 to <7 h, 7 to <9 h, and ≥ 9 h) influence on variables of cardiometabolic risk factors. The following factors were considered as independent variables: age, research areas, LT-METs, and drinking and smoking status (never, former, and current). Tests for linear trends (e.g., *P* trend tests) were conducted by including four groups according to sitting time as ordinal variables. This provided a test of significance for the hypothesis that as the amount of sedentary time increases, the risk of cardiometabolic diseases tends to increase. All statistical tests were two-tailed, and differences with a p-value <0.05 were considered statistically significant. JMP 13 software (SAS Institute Inc., Cary, NC) was used for all statistical analyses.

Results

Participant Characteristics

Table 1 presents the participants' characteristics, including drinking and smoking status, anamnesis of hypertension/dyslipidemia/diabetes, and distribution of age and sex differences according to sedentary time. Among the 27,930 participants included in the current analysis for male sex, 9,529 (34.1%), 5,458 (19.5%), 4,491 (16.1%), and 8,452 (30.3%) spent sedentary time <5 h, 5 to <7 h, 7 to <9 h, and ≥ 9 h per day, respectively. Similarly, among the 34,824 participants included in the current analysis for female sex, 14,121 (40.5%), 8,727 (25.1%), 5,715 (16.4%), and 6,261 (18.0%) spent sedentary time <5 h, 5 to <7 h, 7 to <9 h, and ≥ 9 h per day, respectively.

With increasing age, the proportion of sedentary time decreased from 34.5% to 26.0% for males in the 35–49 years old group vs. the 60–69 years old group and decreased from 21.8% to 15.0% for females.

The multivariate-adjusted OR for anamnesis of hypertension, dyslipidemia, and diabetes, according to sedentary time, is shown in **Table 2**. For the logistic regression analysis, sedentary time <5 h/day was used as the reference and then adjusted for age, research areas, LT-METs, and alcohol and smoking status. For

Table 1. Characteristics of participants according to sedentary time

	Male							
	< 5 h *n* = 9,529		5 to < 7 h *n* = 5,458		7 to < 9 h *n* = 4,491		≥ 9 h *n* = 8,452	
	n/mean	(%)/SD	*n*/mean	(%)/SD	*n*/mean	(%)/SD	*n*/mean	(%)/SD
years								
35-49	2,616	31.5%	1,480	17.8%	1,340	16.1%	2,868	34.5%
50-59	2,926	33.9%	1,612	18.7%	1,367	15.8%	2,727	31.6%
60-69	3,987	36.3%	2,366	21.5%	1,784	16.2%	2,857	26.0%
35-49 years								
Drinking status								
Current	1,944	74.3%	1,158	78.2%	1,045	78.0%	2,180	76.0%
Former	46	1.8%	25	1.7%	16	1.2%	48	1.7%
Never	626	23.9%	297	20.1%	279	20.8%	640	22.3%
Smoking status								
Current	1,100	42.0%	522	35.3%	430	32.1%	844	29.4%
Former	751	28.7%	465	31.4%	456	34.0%	934	32.6%
Never	765	29.2%	493	33.3%	454	33.9%	1,090	38.0%
Hypertension	224	8.6%	133	9.0%	129	9.6%	269	9.4%
Dyslipidemia	279	10.7%	178	12.0%	182	13.6%	409	14.3%
Diabetes	78	3.0%	41	2.8%	48	3.6%	85	3.0%
LT-METs (METs • hrs/day)	1.90	3.43	1.83	3.00	1.78	2.73	1.49	2.20
50-59 years								
Drinking status								
Current	2,285	78.1%	1,255	77.9%	1,078	78.9%	2,154	79.0%
Former	62	2.1%	48	3.0%	35	2.6%	74	2.7%
Never	579	19.8%	309	19.2%	254	18.6%	499	18.3%
Smoking status								
Current	1,041	35.6%	547	33.9%	413	30.2%	818	30.0%
Former	1,114	38.1%	683	42.4%	585	42.8%	1,199	44.0%
Never	771	26.3%	382	23.7%	369	27.0%	710	26.0%
Hypertension	640	21.9%	373	23.1%	343	25.1%	631	23.1%
Dyslipidemia	449	15.3%	320	19.9%	331	24.2%	671	24.6%
Diabetes	221	7.6%	134	8.3%	108	7.9%	239	8.8%
LT-METs (METs • hrs/day)	1.76	3.14	1.99	3.11	1.84	2.61	1.66	2.32
60-69 years								
Drinking status								
Current	3,113	78.1%	1,812	76.6%	1,345	75.4%	2,059	72.1%
Former	128	3.2%	111	4.7%	84	4.7%	176	6.2%
Never	746	18.7%	443	18.7%	355	19.9%	622	21.8%
Smoking status								
Current	925	23.2%	530	22.4%	390	21.9%	650	22.8%
Former	1,826	45.8%	1,142	48.3%	922	51.7%	1,504	52.6%
Never	1,236	31.0%	694	29.3%	472	26.5%	703	24.6%
Hypertension	1,328	33.3%	834	35.2%	598	33.5%	1,005	35.2%
Dyslipidemia	712	17.9%	519	21.9%	407	22.8%	678	23.7%
Diabetes	486	12.2%	301	12.7%	245	13.7%	383	13.4%
LT-METs (METs • hrs/day)	3.25	4.67	3.31	3.92	3.02	3.53	2.47	3.25

(Cont. Table 1)

	Female							
	< 5 h *n* = 14,121		5 to < 7 h *n* = 8,727		7 to < 9h *n* = 5,715		≥ 9 h *n* = 6,261	
	n/mean	(%)/SD	*n*/mean	(%)/SD	*n*/mean	(%)/SD	*n*/mean	(%)/SD
years								
35-49	4,952	39.9%	2,750	22.1%	2,007	16.2%	2,709	21.8%
50-59	4,605	42.3%	2,745	25.2%	1,723	15.8%	1,823	16.7%
60-69	4,564	39.7%	3,232	28.1%	1,985	17.2%	1,729	15.0%
35-49 years								
Drinking status								
Current	2,358	47.6%	1,379	50.1%	995	49.6%	1,391	51.3%
Former	118	2.4%	49	1.8%	42	2.1%	80	3.0%
Never	2,476	50.0%	1,322	48.1%	970	48.3%	1,238	45.7%
Smoking status								
Current	516	10.4%	232	8.4%	165	8.2%	292	10.8%
Former	541	10.9%	306	11.1%	211	10.5%	305	11.3%
Never	3,895	78.7%	2,212	80.4%	1,631	81.3%	2,112	78.0%
Hypertension	188	3.8%	93	3.4%	87	4.3%	96	3.5%
Dyslipidemia	223	4.5%	122	4.4%	84	4.2%	153	5.6%
Diabetes	36	0.7%	25	0.9%	18	0.9%	23	0.8%
LT-METs (METs • hrs/day)	1.54	2.74	1.51	2.51	1.33	2.18	1.12	1.86
50-59 years								
Drinking status								
Current	1,836	39.9%	1,093	39.8%	728	42.3%	765	42.0%
Former	64	1.4%	44	1.6%	27	1.6%	33	1.8%
Never	2,705	58.7%	1,608	58.6%	968	56.2%	1,025	56.2%
Smoking status								
Current	410	8.9%	180	6.6%	107	6.2%	150	8.2%
Former	331	7.2%	211	7.7%	129	7.5%	162	8.9%
Never	3,864	83.9%	2,354	85.8%	1,487	86.3%	1,511	82.9%
Hypertension	697	15.1%	421	15.3%	227	13.2%	244	13.4%
Dyslipidemia	753	16.4%	496	18.1%	305	17.7%	352	19.3%
Diabetes	151	3.3%	86	3.1%	45	2.6%	62	3.4%
LT-METs (METs • hrs/day)	1.85	2.88	2.00	2.86	1.65	2.24	1.38	2.11
60-69 years								
Drinking status								
Current	1,372	30.1%	1,071	33.1%	669	33.7%	577	33.4%
Former	51	1.1%	53	1.6%	37	1.9%	44	2.5%
Never	3,141	68.8%	2,108	65.2%	1,279	64.4%	1,108	64.1%
Smoking status								
Current	166	3.6%	99	3.1%	79	4.0%	79	4.6%
Former	194	4.3%	142	4.4%	105	5.3%	108	6.2%
Never	4,204	92.1%	2,991	92.5%	1,801	90.7%	1,542	89.2%
Hypertension	1,155	25.3%	846	26.2%	535	27.0%	470	27.2%
Dyslipidemia	1,279	28.0%	1,056	32.7%	625	31.5%	549	31.8%
Diabetes	255	5.6%	181	5.6%	114	5.7%	100	5.8%
LT-METs (METs • hrs/day)	2.72	3.69	2.84	3.31	2.49	3.18	1.96	2.68

Table 2. Associations between anamnesis and sedentary time

	Male							
	years	<5h	5 to <7h		7 to <9h		≥ 9 h	
			OR	95%CI	OR	95%CI	OR	95%CI
Hypertension	35-49	ref	1.035	0.824-1.301	1.049	0.935-1.178	1.036	0.973-1.104
	50-59	ref	1.071	0.925-1.240	1.096	1.016-1.182	1.024	0.982-1.068
	60-69	ref	1.097	0.984-1.222	1.011	0.952-1.073	1.041	1.006-1.077
Dyslipidemia	35-49	ref	1.135	0.927-1.389	1.031	1.031-1.262	1.122	1.061-1.185
	50-59	ref	1.377	1.175-1.614	1.333	1.231-1.444	1.216	1.163-1.272
	60-69	ref	1.291	1.137-1.465	1.166	1.088-1.249	1.131	1.086-1.177
Diabetes	35-49	ref	0.950	0.646-1.397	1.121	0.932-1.349	1.011	0.910-1.124
	50-59	ref	1.103	0.881-1.380	1.037	0.919-1.169	1.067	1.000-1.137
	60-69	ref	1.047	0.898-1.221	1.071	0.986-1.163	1.042	0.993-1.093
	Female							
	years	<5h	5 to <7h		7 to <9h		≥ 9 h	
			OR	95%CI	OR	95%CI	OR	95%CI
Hypertension	35-49	ref	0.864	0.670-1.114	1.069	0.938-1.218	0.980	0.901-1.067
	50-59	ref	0.999	0.875-1.141	0.914	0.843-0.992	0.951	0.902-1.003
	60-69	ref	1.041	0.938-1.154	1.037	0.977-1.102	1.028	0.986-1.073
Dyslipidemia	35-49	ref	0.968	0.771-1.215	0.965	0.848-1.098	1.103	1.027-1.184
	50-59	ref	1.121	0.988-1.272	1.049	0.974-1.130	1.083	1.033-1.136
	60-69	ref	1.252	1.134-1.381	1.097	1.035-1.162	1.075	1.032-1.119
Diabetes	35-49	ref	1.244	0.745-2.078	1.120	0.842-1.489	1.058	0.887-1.263
	50-59	ref	0.938	0.716-1.230	0.893	0.754-1.059	1.024	0.926-1.134
	60-69	ref	1.007	0.827-1.226	1.015	0.906-1.138	1.019	0.940-1.104

Adjusted for age, research areas, LT-METs, drinking and smoking status

hypertension, a sedentary time of 7 to <9 h/day in the 50–59 years group (OR: 1.096, CI: 1.016–1.182) and in the 60–69 years group (OR: 1.041, CI: 1.006–1.077) were associated with a significantly higher proportion of male participants. In female participants, sedentary time was not associated with a higher proportion of hypertension. For dyslipidemia, both male (excluding 5 to <7 h/day in the 35–49 years group) and female (excluding 5 to <7 h/day and 7 to <9 h/day in the 35–49 years group and the 50–59 years group) sexes were associated with a significantly higher proportion of participants with dyslipidemia. For diabetes, sedentary time ≥ 9 h/day in the 50–59 years group (OR: 1.067, CI: 1.000–1.137) was associated with a significantly higher proportion of male participants. In female participants, sedentary time was not associated with diabetes.

Multiple regression analysis was then performed to identify the variables strongly associated with sedentary time (**Table 3**). The lipid cardiometabolic risk factors were significantly associated with sedentary time. As shown in **Table 3**, sedentary time was significantly associated with TG, HDL-C, and non-HDL-C in males and females. Furthermore, in the 60–69 years group, sedentary time was significantly associated with several variables except HDL-C ($\beta = -0.016$, $p = 0.171$) as follows: BMI ($\beta = 0.058$, $p < 0.001$), SBP ($\beta = 0.042$, $p < 0.001$), DBP ($\beta = 0.047$, $p < 0.001$), TG ($\beta = 0.054$, $p < 0.001$), non-HDL-C ($\beta = 0.039$, $p = 0.001$), and HbA1c ($\beta = 0.024$, $p = 0.044$). Similarly, sedentary time was significantly associated with BMI ($\beta = 0.034$, $p = 0.004$), SBP ($\beta = 0.056$, $p < 0.001$), DBP ($\beta = 0.057$, $p < 0.001$), TG ($\beta = 0.045$, $p < 0.001$), and HDL-C ($\beta = 0.042$, $p = 0.001$) in obese women. **Supplemental Table 1** shows the mean values of BMI, SBP, DBP, TG, HDL-C, non-HDL-C, and HbA1c levels in each group. Compared with participants who spent <5 h/day of sedentary time, those

Table 3. Comparison of the association of cardiometabolic parameter and sedentary time

Male	35-49 years $n=4,800$		50-59 years $n=5,388$		60-69 years $n=6,921$	
	beta	*p*-value	beta	*p*-value	beta	*p*-value
BMI	0.072	0.072	0.015	0.278	0.058	<0.001
SBP	0.006	0.690	0.005	0.693	0.042	<0.001
DBP	0.004	0.808	0.021	0.122	0.047	<0.001
TG	0.029	0.049	0.043	0.002	0.054	<0.001
HDL-C	-0.049	0.001	-0.054	<0.001	-0.016	0.171
non-HDL-C	0.031	0.034	0.038	0.006	0.039	0.001
HbA1c	-0.015	0.309	-0.008	0.572	0.024	0.044
Female	**35-49 years $n=5,929$**		**50-59 years $n=5,986$**		**60-69 years $n=6,949$**	
	beta	*p*-value	beta	*p*-value	beta	*p*-value
BMI	-0.008	0.518	-0.006	0.654	0.034	0.004
SBP	0.034	0.009	0.019	0.139	0.056	<0.001
DBP	0.045	0.001	0.030	0.018	0.057	<0.001
TG	0.038	0.004	0.031	0.017	0.045	<0.001
HDL-C	0.020	0.127	0.007	0.610	0.042	0.001
non-HDL-C	0.046	0.001	0.029	0.027	0.021	0.080
HbA1c	-0.036	0.006	-0.040	0.002	-0.003	0.815

Adjusted for age, research area, LT-METs, drinking and smoking status

who had longer sedentary time tended to have increased levels of BMI, SBP, DBP, TG, and non-HDL-C and decreased levels of HDL-C, especially in the 60–69 years group. Although sedentary time was not associated with a higher proportion of hypertension among female participants, SBP and DBP tended to increase, resulting from increased sedentary time.

Discussion

Considerable evidence suggests that sedentary time affects health outcomes regardless of physical activity4. Especially, many previous studies showed that cardiovascular disease and its risk factors are associated with sedentary time[3, 15-17]. This study was conducted to determine the associations of sedentary behavior with cardiometabolic diseases such as hypertension, dyslipidemia, and diabetes mellitus in a large Japanese population according to age and sex.

Among male participants, sedentary time was associated with cardiometabolic diseases. Although sedentary time was not associated with hypertension in female participants, Sedentary time increased; thus, SBP and DBP tended to increase. These results suggest the association between sedentary time and cardiometabolic diseases in Japanese males and females. In agreement with many previous studies, our study confirmed that sedentary time was associated with cardiometabolic diseases[2, 3, 16, 18-21]. Notably, our results further revealed that sedentary time was strongly associated with dyslipidemia and lipid metabolism, as indicated by the levels of TG, HDL-C, and non-HDL-C. A recent study showed the mechanism of adverse effects of sedentary time; that is, the sedentary time has a potential role in the increased production of reactive oxygen species, low-grade inflammation, and metabolic impairment, which contribute to sitting-induced impaired vascular function[1]. Furthermore, inactivity, such as sitting, quickly engages signals for specific molecular responses contributing to poor lipid metabolism by suppression of skeletal muscle lipoprotein lipase (LPL[22]; a protein important for controlling plasma TG catabolism, HDL-C, and other metabolic risk factors) activity[23]. LPL activity was associated with reduced TG uptake and decreased HDL-C levels[24]. In contrast, the response of lipids and lipoproteins was improved by physical activity, including regular aquatic endurance[25], cardiorespiratory exercise[26], and fitness aerobic exercise[27]. These studies show that sedentary time and physical activity has a significant effect on lipid metabolism, which is consistent with our results. The findings of the present

study partly support these previous results. To the best of our knowledge, this is the first study to show that sedentary time was strongly associated with lipid metabolism in a large Japanese population.

From the analysis of continuous variables, compared with female participants who had < 5 h per day of sedentary time, those who had ≥ 9 h of sedentary time per day in the 60–69 years group had 3.4 mmHg higher SBP. In The Japanese Society of Hypertension Guidelines for the Management of Hypertension, the cardiovascular disease-reducing effects of lowering blood pressure were estimated using the EPOCH-JAPAN database[28]. Briefly, a decrease of only 4 mmHg in the average SBP in the Japanese population is estimated to reduce the age-adjusted mortality from stroke in males and females by 8.9% and 5.8%, respectively (the total number of deaths from stroke will decrease by 10,000 per year) and that for coronary heart disease by 5.4% and 7.2%, respectively (the total number of deaths from coronary heart disease will decrease by 5,000 per year)[28]. This may indicate that reducing sedentary time was an effective strategy to lower the blood pressure of the population. Furthermore, one study indicated that replacing sedentary time with the same amount of moderate- to vigorous-intensity physical activity may contribute to better physical health-related quality of life of Japanese older adults[29]. In summary, regularly interrupting and replacing sedentary time may contribute to better health-related quality of life because of population approach for the prevention of cardiometabolic diseases.

In contrast, HbA1c tended to decrease, in the 35–49 years females group and the 50–59 years both sexes group. The impact of sedentary time on glycaemic biomarkers was limited in a systematic review[30]. It seems difficult to evaluate the relationship between sitting time and HbA1c in the general population[31] or to use HbA1c as an indicator of glucose metabolism[32]. To clarify the relationship between glycemic biomarkers and sedentary time, further study and/or more sensitive measures of insulin resistance are necessary.

Despite our novel findings, this study has some limitations. This study uses a cross-sectional design and self-administered questionnaires to evaluate sedentary time and anamnesis. Although questionnaire evaluation of sitting time is controversial, IPAQ was an acceptable international physical activity surveillance instrument[33]. Most of the studies about sedentary time made use of self-reported sedentary behaviors[19]. Furthermore, a previous study reported that both accelerometer and self-report measurements are similarly associated with cardiometabolic risk factors in the Japanese population[34]. Similarly, a previous study reported that stroke and myocardial infarction appears sensitive enough to be used for baseline evaluation of patient characteristics in Japanese cohort studies[35]. In a follow-up survey, we plan to assess the participants using their actual medical records; therefore, we expect that these additional data will help with further detailed analysis of the direct effect of sedentary time. The strength of the study is that a large number of participants were included, and we implemented a population-based cohort design.

Conclusion

Independent of leisure-time physical activity, sedentary time was associated with cardiometabolic diseases in a large Japanese population classified by age and sex. Our findings indicate that regularly interrupting and replacing sedentary time may contribute to better health-related quality of life because of population approach for the prevention of cardiometabolic diseases.

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Conflict of Interest

The authors declare that they have no conflict of interest.

References

1) Carter S, Hartman Y, Holder S, Thijssen DH and Hopkins ND: Sedentary Behavior and Cardiovascular Disease Risk: Mediating Mechanisms. Exerc Sport Sci Rev, 2017; 45: 80-86
2) Young DR, Hivert MF, Alhassan S, Camhi SM, Ferguson JF, Katzmarzyk PT, Lewis CE, Owen N, Perry CK, Siddique J and Yong CM: Sedentary Behavior and Cardiovascular Morbidity and Mortality: A Science Advisory From the American Heart Association. Circulation, 2016; 134: e262-279

3) Wilmot EG, Edwardson CL, Achana FA, Davies MJ, Gorely T, Gray LJ, Khunti K, Yates T and Biddle SJ: Sedentary time in adults and the association with diabetes, cardiovascular disease and death: systematic review and meta-analysis. Diabetologia, 2012; 55: 2895-2905
4) Biswas A, Oh PI, Faulkner GE, Bajaj RR, Silver MA, Mitchell MS and Alter DA: Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis. Ann Intern Med, 2015; 162: 123-132
5) Copeland JL, Ashe MC, Biddle SJ, Brown WJ, Buman MP, Chastin S, Gardiner PA, Inoue S, Jefferis BJ, Oka K, Owen N, Sardinha LB, Skelton DA, Sugiyama T and Dogra S: Sedentary time in older adults: a critical review of measurement, associations with health, and interventions. Br J Sports Med, 2017; 51: 1539
6) Furukawa S, Sakai T, Niiya T, Miyaoka H, Miyake T, Yamamoto S, Kanzaki S, Maruyama K, Tanaka K, Ueda T, Senba H, Torisu M, Minami H, Tanigawa T, Matsuura B, Hiasa Y and Miyake Y: Self-reported sitting time and prevalence of erectile dysfunction in Japanese patients with type 2 diabetes mellitus: The Dogo Study. J Diabetes Complications, 2017; 31: 53-57
7) Lee S, Shimada H, Lee S, Makizako H, Doi T, Harada K, Bae S, Harada K, Hotta R, Tsutsumimoto K, Yoshida D, Nakakubo S, Anan Y, Park H and Suzuki T: Association between sedentary time and kidney function in community-dwelling elderly Japanese people. Geriatr Gerontol Int, 2017; 17: 730-736
8) Ukawa S, Tamakoshi A, Yatsuya H, Yamagishi K, Ando M and Iso H: Association Between Average Daily Television Viewing Time and Chronic Obstructive Pulmonary Disease-Related Mortality: Findings From the Japan Collaborative Cohort Study. J Epidemiol, 2015; 25: 431-436
9) Ikehara S, Iso H, Wada Y, Tanabe N, Watanabe Y, Kikuchi S and Tamakoshi A: Television viewing time and mortality from stroke and coronary artery disease among Japanese men and women -- the Japan Collaborative Cohort Study. Circ J, 2015; 79: 2389-2395
10) Kikuchi H, Inoue S, Odagiri Y, Inoue M, Sawada N and Tsugane S: Occupational sitting time and risk of all-cause mortality among Japanese workers. Scand J Work Environ Health, 2015; 41: 519-528
11) Hamajima N: The Japan Multi-Institutional Collaborative Cohort Study (J-MICC Study) to detect gene-environment interactions for cancer. Asian Pac J Cancer Prev, 2007; 8: 317-323
12) Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF and Oja P: International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc, 2003; 35: 1381-1395
13) Hara M, Higaki Y, Taguchi N, Shinchi K, Morita E, Naito M, Hamajima N, Takashima N, Suzuki S, Nakamura A, Ohnaka K, Uemura H, Nishida H, Hosono S, Mikami H, Kubo M, Tanaka H and Japan Multi-Institutional Collaborative Cohort Study G: Effect of the PPARG2 Pro12Ala polymorphism and clinical risk factors for diabetes mellitus on HbA1c in the Japanese general population. J Epidemiol, 2012; 22: 523-531
14) Hara M, Hachiya T, Sutoh Y, Matsuo K, Nishida Y, Shimanoe C, Tanaka K, Shimizu A, Ohnaka K, Kawaguchi T, Oze I, Matsuda F, Ito H, Kawai S, Hishida A, Okada R, Sasakabe T, Hirata A, Ibusuki R, Nindita Y, Furusyo N, Ikezaki H, Kuriyama N, Ozaki E, Mikami H, Nakamura Y, Suzuki S, Hosono A, Katsuura-Kamano S, Arisawa K, Kuriki K, Endoh K, Takashima N, Kadota A, Nakatochi M, Momozawa Y, Kubo M, Naito M and Wakai K: Genomewide Association Study of Leisure-Time Exercise Behavior in Japanese Adults. Med Sci Sports Exerc, 2018; 50: 2433-2441
15) Ekelund U, Steene-Johannessen J, Brown WJ, Fagerland MW, Owen N, Powell KE, Bauman A and Lee IM: Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. Lancet, 2016; 388: 1302-1310
16) Patterson R, McNamara E, Tainio M, de Sa TH, Smith AD, Sharp SJ, Edwards P, Woodcock J, Brage S and Wijndaele K: Sedentary behaviour and risk of all-cause, cardiovascular and cancer mortality, and incident type 2 diabetes: a systematic review and dose response meta-analysis. Eur J Epidemiol, 2018; 33: 811-829
17) Powell C, Herring MP, Dowd KP, Donnelly AE and Carson BP: The cross-sectional associations between objectively measured sedentary time and cardiometabolic health markers in adults - a systematic review with meta-analysis component. Obes Rev, 2018; 19: 381-395
18) Lim MS, Park B, Kong IG, Sim S, Kim SY, Kim JH and Choi HG: Leisure sedentary time is differentially associated with hypertension, diabetes mellitus, and hyperlipidemia depending on occupation. BMC Public Health, 2017; 17: 278
19) Lee PH and Wong FK: The association between time spent in sedentary behaviors and blood pressure: a systematic review and meta-analysis. Sports Med, 2015; 45: 867-880
20) Ford ES and Caspersen CJ: Sedentary behaviour and cardiovascular disease: a review of prospective studies. Int J Epidemiol, 2012; 41: 1338-1353
21) Same RV, Feldman DI, Shah N, Martin SS, Al Rifai M, Blaha MJ, Graham G and Ahmed HM: Relationship Between Sedentary Behavior and Cardiovascular Risk. Curr Cardiol Rep, 2016; 18: 6
22) Olivecrona G: Role of lipoprotein lipase in lipid metabolism. Curr Opin Lipidol, 2016; 27: 233-241
23) Hamilton MT, Hamilton DG and Zderic TW: Role of low energy expenditure and sitting in obesity, metabolic syndrome, type 2 diabetes, and cardiovascular disease. Diabetes, 2007; 56: 2655-2667
24) Bey L and Hamilton MT: Suppression of skeletal muscle lipoprotein lipase activity during physical inactivity: a molecular reason to maintain daily low-intensity activity. J Physiol, 2003; 551: 673-682
25) Igarashi Y and Nogami Y: Response of Lipids and Lipoproteins to Regular Aquatic Endurance Exercise: A Meta-Analysis of Randomized Controlled Trials. J Atheroscler Thromb, 2019; 26: 14-30
26) Watanabe N, S SS, Shimada K, Lee IM, Gando Y, Momma H, Kawakami R, Miyachi M, Hagi Y, Kinugawa C, Okamoto T, Tsukamoto K and S NB: Relationship between Cardiorespiratory Fitness and Non-High-Density

Lipoprotein Cholesterol: A Cohort Study. J Atheroscler Thromb, 2018; 25: 1196-1205
27) Igarashi Y, Akazawa N and Maeda S: Effects of Aerobic Exercise Alone on Lipids in Healthy East Asians: A Systematic Review and Meta-Analysis. J Atheroscler Thromb, 2019; 26: 488-503
28) Shimamoto K, Ando K, Fujita T, Hasebe N, Higaki J, Horiuchi M, Imai Y, Imaizumi T, Ishimitsu T, Ito M, Ito S, Itoh H, Iwao H, Kai H, Kario K, Kashihara N, Kawano Y, Kim-Mitsuyama S, Kimura G, Kohara K, Komuro I, Kumagai H, Matsuura H, Miura K, Morishita R, Naruse M, Node K, Ohya Y, Rakugi H, Saito I, Saitoh S, Shimada K, Shimosawa T, Suzuki H, Tamura K, Tanahashi N, Tsuchihashi T, Uchiyama M, Ueda S and Umemura S: The Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH 2014). Hypertens Res, 2014; 37: 253-390
29) Yasunaga A, Shibata A, Ishii K, Inoue S, Sugiyama T, Owen N and Oka K: Replacing sedentary time with physical activity: effects on health-related quality of life in older Japanese adults. Health Qual Life Outcomes, 2018; 16: 240
30) Wirth K, Klenk J, Brefka S, Dallmeier D, Faehling K, Roque IFM, Tully MA, Gine-Garriga M, Caserotti P, Salva A, Rothenbacher D, Denkinger M and Stubbs B: Biomarkers associated with sedentary behaviour in older adults: A systematic review. Ageing Res Rev, 2017; 35: 87-111
31) Bellettiere J, Winkler EAH, Chastin SFM, Kerr J, Owen N, Dunstan DW and Healy GN: Associations of sitting accumulation patterns with cardio-metabolic risk biomarkers in Australian adults. PLoS One, 2017; 12: e0180119
32) Henson J, Yates T, Biddle SJ, Edwardson CL, Khunti K, Wilmot EG, Gray LJ, Gorely T, Nimmo MA and Davies MJ: Associations of objectively measured sedentary behaviour and physical activity with markers of cardiometabolic health. Diabetologia, 2013; 56: 1012-1020
33) Bauman A, Bull F, Chey T, Craig CL, Ainsworth BE, Sallis JF, Bowles HR, Hagstromer M, Sjostrom M and Pratt M: The International Prevalence Study on Physical Activity: results from 20 countries. Int J Behav Nutr Phys Act, 2009; 6: 21
34) Honda T, Chen S, Kishimoto H, Narazaki K and Kumagai S: Identifying associations between sedentary time and cardio-metabolic risk factors in working adults using objective and subjective measures: a cross-sectional analysis. BMC Public Health, 2014; 14: 1307
35) Yamagishi K, Ikeda A, Iso H, Inoue M and Tsugane S: Self-reported stroke and myocardial infarction had adequate sensitivity in a population-based prospective study JPHC (Japan Public Health Center)-based Prospective Study. Journal of clinical epidemiology, 2009; 62: 667-673

Supplemental Table 1. The mean values of BMI, SBP, DBP, TG, HDL-C, nonHDL-C and HbA1c levels in each sedentary time group

Male										
years		<5 h n=6,077		5 to <7 h n=3,440		7 to <9 h n=2,755		≥9 h n=4,837		p trend
		mean	SD	mean	SD	mean	SD	mean	SD	
35-49	BMI (kg/m²)	23.76	3.34	23.66	3.18	23.90	3.38	23.89	3.33	0.176
	SBP (mmHg)	122.8	16.02	122.7	15.89	122.6	15.77	123.9	15.84	0.017
	DBP (mmHg)	77.72	11.81	77.85	11.47	77.68	11.27	78.24	11.18	0.162
	TG (mg/dl)	143.1	124.0	154.7	179.1	150.5	109.1	153.2	113.5	<0.001
	HDL-C (mg/dl)	57.94	15.26	57.14	14.24	56.31	15.41	56.25	14.24	0.002
	non-HDL-C (mg/dl)	145.3	35.35	145.6	37.74	144.7	33.53	148.5	35.18	0.005
	HbA1c (%)	5.47	0.63	5.41	0.55	5.48	0.71	5.41	0.60	<0.001
50-59	BMI (kg/m²)	23.68	2.98	23.87	3.11	23.84	2.92	23.82	2.98	0.151
	SBP (mmHg)	129.3	18.21	128.5	18.20	130.1	18.83	130.0	17.98	0.114
	DBP (mmHg)	81.34	11.60	81.26	11.20	82.43	11.60	82.38	11.56	0.004
	TG (mg/dl)	141.6	98.71	159.1	122.9	160.4	165.6	158.2	111.3	<0.001
	HDL-C (mg/dl)	58.82	15.57	56.76	15.16	56.83	14.91	56.46	14.65	<0.001
	non-HDL-C (mg/dl)	146.1	33.98	150.7	33.73	150.4	35.55	150.0	33.78	0.001
	HbA1c (%)	5.66	0.75	5.71	0.90	5.67	0.75	5.61	0.72	<0.001
60-69	BMI (kg/m²)	23.22	2.71	23.29	2.73	23.42	2.85	23.66	2.93	<0.001
	SBP (mmHg)	133.6	18.71	135.3	19.37	135.6	19.43	135.6	19.40	<0.001
	DBP (mmHg)	80.94	10.74	81.87	10.93	82.22	10.76	82.16	11.04	<0.001
	TG (mg/dl)	127.8	88.90	136.3	97.06	139.5	92.21	142.1	95.58	<0.001
	HDL-C (mg/dl)	59.49	15.98	58.96	15.52	58.13	15.74	58.16	15.66	0.002
	non-HDL-C (mg/dl)	142.8	32.27	144.4	32.49	146.1	33.83	146.1	34.62	0.001
	HbA1c (%)	5.71	0.74	5.71	0.72	5.73	0.69	5.74	0.76	0.370

Female										
years		<5 h n=7,768		5 to <7 h n=4,685		7 to <9 h n=3,067		≥9 h n=3,344		p trend
		mean	SD	mean	SD	mean	SD	mean	SD	
35-49	BMI (kg/m²)	21.71	3.21	21.64	3.13	21.64	3.13	21.60	3.57	0.020
	SBP (mmHg)	115.6	16.51	117.3	16.61	116.2	16.24	117.4	17.08	0.003
	DBP (mmHg)	70.64	11.16	71.60	10.97	71.26	11.06	71.99	11.15	0.001
	TG (mg/dl)	85.18	64.51	88.34	58.70	90.77	67.06	91.08	63.35	<0.001
	HDL-C (mg/dl)	71.15	15.93	69.84	16.11	70.02	16.23	70.90	17.09	0.121
	non-HDL-C (mg/dl)	126.4	32.59	127.8	31.96	129.4	30.46	130.3	32.56	<0.001
	HbA1c (%)	5.34	0.41	5.33	0.41	5.32	0.44	5.28	0.34	<0.001
50-59	BMI (kg/m²)	22.30	3.17	22.35	3.20	22.24	3.15	22.30	3.36	0.735
	SBP (mmHg)	125.2	19.07	127.2	19.91	126.1	20.17	126.6	19.15	0.022
	DBP (mmHg)	75.91	11.49	76.84	11.83	76.25	12.00	77.19	11.58	0.013
	TG (mg/dl)	108.5	66.27	117.2	78.15	113.0	68.94	115.9	75.11	<0.001
	HDL-C (mg/dl)	69.90	17.09	68.05	16.79	69.11	16.00	69.35	17.18	0.170
	non-HDL-C (mg/dl)	151.3	34.76	155.0	34.34	154.0	35.24	154.6	37.01	0.004
	HbA1c (%)	5.58	0.59	5.55	0.63	5.53	0.53	5.50	0.48	<0.001
60-69	BMI (kg/m²)	22.59	3.05	22.61	3.12	22.74	3.27	23.00	3.54	0.023
	SBP (mmHg)	131.6	19.65	133.1	20.19	134.1	20.41	135.0	20.91	<0.001
	DBP (mmHg)	76.88	10.97	77.60	11.16	78.26	11.16	78.63	11.57	<0.001
	TG (mg/dl)	112.3	61.32	122.0	76.42	121.5	77.91	121.8	64.79	<0.001
	HDL-C (mg/dl)	65.97	15.79	65.95	16.91	66.13	16.66	66.94	17.01	0.469
	non-HDL-C (mg/dl)	154.0	33.82	155.9	34.46	155.2	33.35	156.7	33.11	0.017
	HbA1c (%)	5.65	0.57	5.65	0.64	5.62	0.59	5.64	0.67	0.001