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ORIGINAL ARTICLE

Relationship between nonrestorative sleep with short sleep duration and diabetes mellitus comorbid among a Japanese occupational population

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Abstract

Objective Nonrestorative sleep (NRS) is one of the symptoms of insomnia and is clearly more associated with objective indices, such as sleep stability, sleep fragmentation, and inflammatory responses, than other insomnia symptoms. However, the link between NRS and diabetes mellitus is poorly understood. Therefore, the prevalence of NRS in workers and the relationships between NRS and diabetes were investigated.

Methods The results of a single year's medical examinations were investigated for 26,144 Japanese active office workers who were 30 to 59 years old. NRS was investigated using a personal computer in a medical interview. Furthermore, the relationships between NRS and diabetes comorbidity in addition to sleep duration were also analyzed.

Results The mean age of the subjects was 47.9 ± 7.3 years old, and the proportion of subjects with NRS was 26%. The presence of NRS together with a sleep duration ≤ 5 h or a sleep duration of 6 h was an independent comorbid factor for diabetes compared with the absence of NRS together with a sleep duration of 7 h (odds ratio [OR] 1.34; 95% confidence interval [CI] 1.14–1.58; $P < 0.001$; and OR 1.25; 95% CI 1.04–1.48; $P = 0.015$).

Conclusion NRS in active workers may contribute to the development of diabetes even if the workers have the same short sleep durations as other workers without NRS.

Keywords Sleep restfulness · Sleep duration · Hyperglycemia · Medical checkup · Office worker

Introduction

Sleep and diabetes mellitus are strongly related [1]. Short and long sleep are well known to cause diabetes mellitus [2–5]. Insomnia increases the risk of developing diabetes [6]. The symptoms of insomnia are defined as difficulty falling asleep, difficulty staying asleep, and early awakening [7]. Although nonrestorative sleep (NRS) is also one of the symptoms of insomnia, NRS is clearly more associated with objective indices, such as sleep stage transitions, sleep stability, sleep efficiency, total sleep duration measured with polysomnography independent of other objective sleep parameters [8–10], and inflammatory responses [11], than other insomnia symptoms. This unrefreshing sleep is considered to reflect the symptomatic physiological lack of rest following sleep.

Therefore, in addition to sleep duration, which is closely related to the onset of diabetes [6, 12], we clarified whether the presence or absence of NRS is related to the comorbidity of diabetes among the current generation of workers. This was a retrospective, single-center, cross-sectional study.

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Materials and methods

Subjects

A medical checkup was conducted for 31,295 company staff members of FUJITSU Limited or affiliated companies between April 1, 2021, and March 31, 2022, at the Health Examination Center, FUJITSU Ltd. Of these staff members, 21,526 Japanese men and 4618 Japanese women who were 30 to 59 years old, had no missing data in this study, were not receiving maintenance hemodialysis, and were free from mental illnesses were included as subjects in the analysis (Fig. 1). Approximately 98% of the final analysis subjects were non-shift office workers. There is a close relationship between mental illness and insomnia [13]. In this study, 1577 subjects who had a history of mental illness, were under treatment for a mental illness, or took hypnotic drugs were excluded from the analysis, because the treatment of mental illnesses has a direct major impact on sleep and subjective symptoms of sleep [14] (Fig. 1).

Information regarding age, gender, height, weight, body mass index (BMI), use of diabetes drugs (including insulin), use or non-use of antihypertensive agents, and use of lipid metabolism disorder drugs was collected at the medical checkup. Blood tests were performed with fasting blood samples collected after a fast lasting ≥ 10 h. Plasma glucose was measured by the enzymatic method (hexokinase-UV method). Glycosylated hemoglobin (HbA1c) was measured by high-performance liquid chromatography. Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG) levels were measured by enzymatic methods. LDL-C was calculated by the Friedewald equation, and a direct LDL-C method was used when TG ≥ 400 mg/dL.

Diabetes mellitus was defined as a glucose level ≥ 126 mg/dL in the fasting state or as HbA1c ≥ 6.5%, in accordance with the National Glycohemoglobin Standardization Program, and/or the current use of diabetes drugs. Hypertension was defined as systolic blood pressure (BP) ≥ 140 mmHg, diastolic BP ≥ 90 mmHg, and/or the current use of antihypertensive medications. Patients with LDL-C ≥ 140 mg/dL, HDL-C < 40 mg/dL, TG ≥ 150 mg/dL, or non-HDL-C (TC—HDL-C) ≥ 170 mg/dL, as well as patients who were receiving treatment for a lipid metabolism disorder, were defined as having dyslipidemia. A medical history of

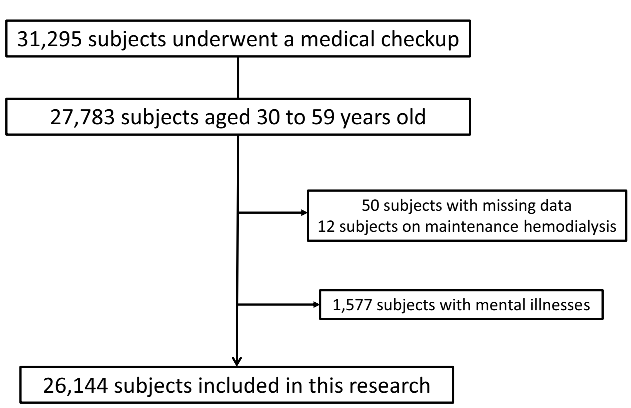

Fig. 1 Flowchart for the inclusion criteria

cerebrocardiovascular disease (CVD) was defined as having an arrhythmia, coronary heart disease, cerebrovascular disorder or non-cardiogenic cerebrovascular disorder, peripheral artery disease, or history of hospitalization for heart failure.

Blood pressure measurement in the waiting area

Each person sat in a backed chair in a waiting area without crossing their legs for a few minutes under supervision by staff. Each of them then measured their BP via the brachial artery on their own with an automatic electronic manometer (HBP-9021, Omron Healthcare Co. Ltd., Kyoto, Japan). BP was measured between 9 and 11 AM after adjusting the height of the measurement table in order to keep the position of the cuff at the heart level; the tourniquet cuff tightened around the upper arm automatically (width, 13 cm). BP was measured once, but a second measurement was performed if the first measurement indicated BP ≥ 140/90 mmHg. If two measurements were recorded, the second one was used in the present analysis.

Questionnaires about sleep and lifestyle

Lifestyle habits in the most recent 2–3 months were investigated using a personal computer at a medical interview before the medical checkup.

The subjects were asked about the time they fall asleep and the time they wake up, and sleep duration was calculated to the closest hour. Subjects who responded with "No" to the following question were defined as having NRS in this study: "Have you been feeling sufficiently rested after sleeping in the most recent two to three months?".

Smoking habit was defined as being a current smoker with a regular smoking habit (including heated cigarettes). The criterion for having a drinking habit was defined as alcohol consumption once a week or more, and the daily average alcohol consumption (g) was calculated. Overdrinking was defined as a daily average alcohol consumption of 20 g or more. Exercise habit was defined as regularly getting 30 min or more of exercise once or more a week.

In Japan, calculation of the time spent outside overtime and regular working hours has revealed that sleep time decreases as overtime work increases [15]. Therefore, the monthly average self-reported duration of overtime work was recorded. A monthly average duration of overtime work ≥ 60 h was defined as the presence of overtime work.

Statistical analyses

The primary endpoint was the odds ratio (ORs) of diabetes comorbidity with or without NRS combined with sleep duration with NRS absent and a sleep duration of 7 h as the reference. The subjects were divided based on the presence or absence of NRS and sleep duration (≤ 5 h, 6 h, 7 h, and ≥ 8 h). Diabetes onset factors (age, BMI, ratio of males, smoking habit, overdrinking, and exercise habit) and overtime work were compared between groups. We also compared the rate of hypertension, dyslipidemia, and CVD, which are comorbidities of diabetes, among the groups. Age, BMI, FPG and HbA1c were subjected to Kolmogorov–Smirnov–Lilliefors test to evaluate the goodness of fit of normal distribution. Age, BMI, FPG, HbA1c were all tested with $P = 0.010$, and the distribution was not normal.

The subjects were classified into the following eight groups: NRS absent and sleep duration ≤ 5 h, NRS present and sleep duration ≤ 5 h, NRS absent and sleep duration of 6 h, NRS present and sleep duration of 6 h, NRS absent and sleep duration of 7 h, NRS present and sleep duration of 7 h, NRS absent and sleep duration ≥ 8 h, and NRS present and sleep duration ≥ 8 h. The Kruskal–Wallis test and Pearson's χ^2 test were used to compare parameters among the eight groups. The data are expressed as mean ± standard deviation values. The associations of each combination of NRS and sleep duration with comorbid diabetes mellitus were analyzed using univariable (unadjusted in model 1) and multivariable logistic regression after adjusting for covariates (age, sex, and BMI in model 2; age, sex, BMI, hypertension comorbidity, CVD comorbidity, smoking habit, overdrinking, exercise habit, and overtime work in model 3) in each group. ORs and 95% confidence intervals (Cis) are presented relative to the subjects with NRS absent and a sleep duration of 7 h (reference). Statistical analyses were conducted using the JMP software for Windows (version 10.0; SAS Institute, Cary, NC, USA). Significant differences were defined at a P value for the hazard ratio of < 0.05.

Ethics

This research was conducted in accordance with the Helsinki Declaration. In conducting the research, we anonymized all information that could identify individuals and conducted the study under strict control with reference to the "Guidelines for Proper Handling of Personal Information by Medical Care/Nursing Care Service Providers" and "Things to Keep in Mind for Proper Handling of Personal Health Information on Employment Management" of the Ministry of Health, Labour and Welfare of Japan. The use of health information so that individuals cannot be identified was clearly stated in each patient's questionnaire, and posters were posted at the Health Examination Center, FUJITSU Ltd. The posters explained that questions about the handling of health information management would be answered and that opting out was allowed. The FUJITSU Clinic Ethics Committee reviewed this study, and we obtained the approval of the Committee before conducting the study (Ethical Committee Approval No. 31).

Results

Background characteristics of the subjects

The average age of the subjects ($n = 26{,}144$) was 47.9 ± 7.3 years old, and the ratio of males was 82% ($n = 21{,}526$). The average BMI of the subjects was 23.9 ± 3.9 kg/m^2. The proportion of subjects with NRS among all subjects was 26%. The proportion of subjects with sleep duration ≤ 5 h, 6 h, 7 h, and ≥ 8 h were 27%, 45%, 24%, and 5%. The rates of diabetes mellitus, hypertension, dyslipidemia, and cerebrovascular disease were 9%, 23%, 53%, and 3%. As for lifestyle habits, the rates of smoking habit, overdrinking, exercise habit, and overtime work in the subjects were 19%, 22%, 59%, and 9%. For sleep duration, the proportion of subjects with NRS showed a stepwise increase as the sleep duration decreased ($P < 0.001$; Table 1).

There were significant differences in age, sex, BMI, diabetes comorbidity, hypertension comorbidity, and the rates of smoking habit, overdrinking, exercise habit, and overtime work among the groups classified by sleep duration. The groups with shorter sleep durations had stepwise higher proportions of subjects with NRS ($P < 0.001$; Table 2).

There were significant differences in age, sex, BMI, diabetes comorbidity, hypertension comorbidity, CVD comorbidity, and the rates of smoking habit, overdrinking, exercise habit, and overtime work among the groups classified by NRS status and sleep duration (Table 3).

Relationships of combinations of nonrestorative sleep and sleep durations with comorbid diabetes mellitus

NRS together with a sleep duration ≤ 5 h and NRS together with a sleep duration of 6 h were independent comorbid factors compared with the reference, even in model 3 (OR 1.34; 95% CI 1.14–1.58; $P < 0.001$; and OR 1.25; 95% CI 1.04–1.48; $P = 0.015$; Table 4).

Discussion

This study was the first cross-sectional study to examine whether NRS with each sleep duration is a risk factor for diabetes comorbidity in office workers. We focused on the comorbidity of NRS and sleep duration, which has already been strongly suggested to be related to diabetes. The findings of this study of 30- to 59-year-old office workers without mental illnesses can be summarized as follows: (i) the

Table 1 Background of the subjects according to absence or presence of NSR

Sleep restfulness	All subjects	NRS -	NRS +	*P* value
Number of subjects, no. (%)	26,144	19,223 (74)	6921 (26)	/
Age, years	47.9 ± 7.3	47.8 ± 7.3	48.0 ± 7.2	0.022[a]
Male, %	82	84	79	< 0.001[b]
BMI, kg/m^2	23.9 ± 3.9	23.9 ± 3.9	24.0 ± 4.1	0.339[a]
FPG, mg/dL	102.1 ± 19.8	102.0 ± 20.0	102.5 ± 19.4	0.273[a]
HbA1c, % (*n* = 25,817)	5.7 ± 0.7	5.7 ± 0.7	5.7 ± 0.7	< 0.001[a]
Diabetes drugs, %	5	5	6	< 0.001[b]
Diabetes mellitus, %	9	9	10	< 0.001[b]
Sleep duration, %				
≤ 5 h	27	20	45	< 0.001[b]
6 h	45	46	42	
7 h	24	28	11	
≥ 8 h	5	6	2	
Comorbidity, %				
Hypertension	23	22	23	0.445[b]
Dyslipidemia	53	54	52	0.051[b]
Cerebrocardiovascular disease	3	3	4	0.003[b]
Lifestyle, %				
Smoking habit	19	19	17	< 0.001[b]
Overdrinking	22	22	20	< 0.001[b]
Exercise habit	59	62	51	< 0.001[b]
Overtime work	9	7	13	< 0.001[b]

Values are mean ± SD values or percentages

NRS nonrestorative sleep, *NRS absent* −; *NRS present* +; *BMI* body mass index, *FPG* fasting plasma glucose, *HbA1c* glycosylated hemoglobin

[a]Kruskal–Wallis test

[b]Pearson's χ^2

proportion of subjects with NRS was 26%. (ii) With the subjects with NRS absent and a sleep duration of 7 h as the reference, the diabetes comorbidity rate was significantly higher in the subjects with NRS present and a sleep duration ≤ 5 h and the subjects with NRS present and a sleep duration of 6 h.

The strengths of this investigation were the performance of the medical checkups under the same conditions, as they were conducted at a single facility, and the large number of subjects. NRS is often noticed at a younger age than the main insomnia symptoms of difficulty falling asleep, difficulty staying asleep, and early awakening [7, 11]. Therefore, investigating the relationships between NRS with sleep duration and health disorders in an occupational population is significant for disease prevention [16, 17].

Nonrestorative sleep

The definition of subjects with NRS has yet to be standardized, making it difficult to draw comparisons between studies [17, 18]. The definition of NRS varies depending on the study, with some studies evaluating it based on only the presence or absence of NRS [19–21], like this study; NRS frequency [11]; severity of feeling that sleep is restless [8]; and the NRS scale [22]. In this study, the subjects were only asked about the presence or absence of NRS in the most recent 2–3 months with a single item. In a study using NRS defined solely by a "yes–no" question about having NRS with no time limit, misperceptions regarding sleep duration were responsible for the perception of NRS [19]. NRS assessed by this simple "yes–no" question was also associated with not only sleep parameters but also depressive mood, mental fatigue, gastroesophageal reflux symptoms, and a lack of habitual exercise [20]. In addition, NRS was significantly and strongly associated with a short sleep duration [20]. It is also known that there are higher proportions of subjects with NRS defined by other methods among short sleepers [9, 23]. However, the diabetic comorbidity OR for the subjects with NRS compared with the subjects without NRS was 1.13 (95% CI 1.02–1.24; $P = 0.016$), even after adjusting for the sleep duration group, and NRS was a diabetic comorbidity factor independent of sleep duration. The results of this study also revealed that the subjects with short sleep durations were often aware of NRS and that even

Table 2 Background of the subjects according to sleep duration

Sleep duration	≤5 h	6 h	7 h	≥8 h	*P* value
Number of subjects, no	6929	11,717	6243	1255	/
Age, years	48.5 ± 6.7	48.0 ± 7.2	47.2 ± 7.7	46.4 ± 8.1	< 0.001[a]
Male, %	84	83	81	74	< 0.001[b]
BMI, kg/m^2	24.5 ± 4.2	23.9 ± 3.9	23.5 ± 3.7	23.5 ± 4.0	< 0.001[a]
NRS, %	45	25	12	10	< 0.001[b]
FPG, mg/dL	103.2 ± 19.8	102.1 ± 20.3	100.9 ± 18.1	101.7 ± 23.1	< 0.001[a]
HbA1c, % (n = 25,817)	5.7 ± 0.7	5.7 ± 0.7	5.6 ± 0.6	5.6 ± 0.7	< 0.001[a]
Diabetes drugs, %	7	5	4	4	< 0.001[b]
Diabetes mellitus, %	11	9	8	8	< 0.001[b]
Comorbidity, %					
Hypertension	24	22	22	23	0.001[b]
Dyslipidemia	54	53	53	53	0.309[b]
Cerebrocardiovascular disease	3	3	3	3	0.135[b]
Lifestyle, %					
Smoking habit	20	19	17	17	< 0.001[b]
Overdrinking	19	22	24	28	< 0.001[b]
Exercise habit	53	60	63	62	< 0.001[b]
Overtime work	16	8	4	2	< 0.001[b]

Values are mean ± SD values or percentages

[a]Kruskal–Wallis test

[b]Pearson's χ^2

Table 3 Background of the subjects according to sleep duration and absence or presence of NRS

Sleep duration	≤5 h		6 h		7 h		≥8 h		*P* value
NRS	–	+	–	+	–	+	–	+	
Number of subjects, no (%)	3783 (14)	3146 (12)	8843 (34)	2874 (11)	5467 (21)	776 (3)	1130 (4)	125 (0)	/
Age, years	48.1 ± 7.4	47.7 ± 7.9	47.1 ± 8.2	46.5 ± 8.8	45.4 ± 9.4	45.0 ± 10.0	43.8 ± 10.3	43.1 ± 10.3	< 0.001[a]
Male, %	88	79	85	77	82	75	75	71	< 0.001[b]
BMI, kg/m^2	24.5 ± 4.1	24.5 ± 4.3	24.0 ± 3.8	23.7 ± 4.0	23.5 ± 3.7	23.4 ± 4.0	23.5 ± 4.0	23.1 ± 3.8	< 0.001[a]
FPG, mg/dL	103.4 ± 20.3	103.1 ± 19.1	102.0 ± 20.4	102.3 ± 19.9	100.9 ± 18.2	101.1 ± 17.7	101.9 ± 23.2	99.9 ± 22.0	< 0.001[a]
HbA1c, % (n = 24,271)	5.7 ± 0.7	5.7 ± 0.7	5.7 ± 0.7	5.7 ± 0.7	5.6 ± 0.6	5.6 ± 0.6	5.6 ± 0.7	5.6 ± 0.5	< 0.001[a]
Diabetes drugs, %	6	7	5	5	4	4	4	4	< 0.001[b]
Diabetes mellitus, %	11	12	9	10	8	9	8	11	< 0.001[b]
Comorbidity, %									
Hypertension	24	24	22	21	21	23	21	23	0.008[b]
Dyslipidemia	55	54	54	53	53	54	55	52	0.067[b]
Cerebrocardiovascular disease	3	4	3	3	3	5	3	6	0.007[b]
Lifestyle, %									
Smoking habit	22	19	20	15	17	15	17	18	< 0.001[b]
Overdrinking	20	18	22	20	24	26	28	29	< 0.001[b]
Exercise habit	57	48	63	54	65	53	64	46	< 0.001[b]
Overtime work	2	3	4	4	7	10	13	19	< 0.001[b]

Values are mean ± SD values or percentages

[a]Kruskal–Wallis test

[b]Pearson's χ^2

Table 4 Results of logistic regression analyses to determine associations with diabetes mellitus

Sleep duration	NRS	Model 1		Model 2		Model 3	
		OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
≤5 h	–	1.50 (1.30–1.73)	< 0.001	1.13 (0.96–1.31)	0.134	1.16 (0.99–1.36)	0.069
	+	1.64 (1.42–1.91)	< 0.001	1.31 (1.11–1.53)	0.001	1.34 (1.14–1.58)	< 0.001
6 h	–	1.14 (1.01–1.30)	0.035	0.98 (0.86–1.12)	0.767	0.99 (0.87–1.14)	0.906
	+	1.30 (1.10–1.52)	0.002	1.23 (1.03–1.46)	0.021	1.25 (1.04–1.48)	0.015
7 h	–	Reference	/	Reference	/	Reference	/
	+	1.14 (0.86–1.49)	0.340	1.11 (0.82–1.48)	0.483	1.08 (0.80–1.45)	0.605
≥8 h	–	1.08 (0.85–1.36)	0.540	1.05 (0.81–1.35)	0.717	1.03 (0.79–1.33)	0.848
	+	1.55 (0.84–2.64)	0.149	1.92 (0.98–3.51)	0.056	1.72 (0.86–3.19)	0.119

OR odds ratio, *CI* confidence interval

Model 1: unadjusted

Model 2: adjusted for age, sex, and body mass index (BMI)

Model 3: adjusted for age, sex, BMI, hypertension, cerebrocardiovascular disease, smoking habit, overdrinking, exercise habit, and overtime work

if they slept the same short duration as other subjects without NRS, the presence of NRS greatly affected their health disorders.

Nonrestorative sleep and diabetes mellitus comorbidity

NRS affected the active generation of the population more frequently and caused greater daytime impairment of physical function, cognitive function, and emotional function than other insomnia symptoms [23]. Since NRS is a symptom that affects not only sleep problems but also causes daytime dysfunction [11], it is highly possible that NRS is related to lifestyle-related diseases and chronic diseases.

It is not known whether NRS is a primary symptom or a secondary symptom due to comorbidities [18]. Patients with insomnia develop diabetes mellitus due to hyperactivity of the sympathetic nervous system and increased secretion of insulin-antagonizing hormones [2]. On the other hand, diabetic patients develop insomnia due to dry mouth and nocturia due to hyperglycemia, deterioration of sleep quality due to deterioration of the neuroendocrine environment [24], and diabetic neuropathy [25]. It is possible that NRS and diabetes were also bidirectionally related.

Impact of combinations of nonrestorative sleep and sleep duration on diabetes mellitus

Based on the results of this study, it was possible to stratify the risk of diabetes comorbidity using the objective index of sleep duration and the subjective index of NRS. Short sleep is known to cause abnormal glucose tolerance due to increased secretion of insulin-antagonizing hormones, impaired glucose utilization mediated by sympathetic nerve activation, impaired insulin secretion in pancreatic β cells, and reduced insulin sensitivity in peripheral tissues [2, 3]. For the subjects with a sleep duration ≤ 6 h and the absence of NRS, diabetes comorbidity disappeared when adjusted for age, sex, and BMI (Table 4 in model 2). In the subjects with a sleep duration ≤ 6 h and NRS absence, age, sex, and BMI strongly influenced diabetes comorbidity [26]. Conversely, NRS in short sleepers was found to be a strong factor for diabetes comorbidity independent of age, sex, and BMI. In other words, the presence of NRS, which may indicate the disruption of sleep homeostasis, increased the risk of diabetes comorbidity in subjects with a short sleep duration even if their sleep duration was the same as that of other subjects without NRS.

Clinical implications of the results of this study

NRS in active workers may contribute to the development of diabetes even if the workers have the same short sleep duration as other workers without NRS. Confirmation of the presence or absence of NRS as a health index and interventions for NRS may lead to health promotion in workers. Active office workers are more likely to be aware of NRS due to short sleep duration, and it is important for workers with NRS to secure sufficient sleep time for good health.

Limitations

Whether or not the results of the present study can be applied to general workers is unclear. This study was also unable to distinguish between cause and effect. The background of the subjects was based on information they provided and diabetes was diagnosed only by the results of a single blood test, so these might have been inaccurate.

NRS symptoms often overlap the main symptoms of insomnia of difficulties in initiating and maintaining sleep and early morning awakening [16]. We were not able to compare these symptoms with NRS in this study. In addition, an evaluation of the comorbidity of sleep disordered breathing, which affects the quality of sleep and causes impaired glucose tolerance [27], was not performed.

Declarations

Conflict of interest The authors declare no conflicts of interest.

Ethical approval This research was conducted in accordance with the Helsinki Declaration. In conducting the research, we anonymized all information that could identify individuals and conducted the study under strict control with reference to the "Guidelines for Proper Handling of Personal Information by Medical Care/Nursing Care Service Providers" and "Things to Keep in Mind for Proper Handling of Personal Health Information on Employment Management" of the Ministry of Health, Labour and Welfare of Japan. The use of health information so that individuals cannot be identified was clearly stated in each patient's questionnaire, and posters were posted at the Health Examination Center, FUJITSU Ltd. The posters explained that questions about the handling of health information management would be answered and that opting out was allowed. The FUJITSU Clinic Ethics Committee reviewed this study, and we obtained the approval of the Committee before conducting the study (Ethical Committee Approval No. 31 and the date of approval was September 16, 2022.).

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