—Case Reports—

The Relationship Between Premature Ventricular Contractions and Lifestyle-Related Habits among the Japanese Working Population (FUJITSU Cardiovascular and Respiratory Observational Study-1; FACT-1)

Hiromitsu Sekizuka[1,2] and Hitoshi Miyake[2]

[1]Department of Internal Medicine, FUJITSU Clinic, Kanagawa, Japan
[2]FUJITSU LIMITED, Health Promotion Unit, Kanagawa, Japan

Background: Premature ventricular contractions (PVCs) are often found in healthy workers at medical checkups. In this study, we aimed to investigate the frequency of PVCs recorded during medical checkups in Japanese office workers without heart disease or other known contributing factors.

Methods: Participants in this study were 17,641 office workers, who underwent an electrocardiogram examination during a regular medical checkup between April 1 2015 and March 31 2016 and had no known heart disease. The frequency of PVCs was recorded. Participants with PVCs were included in the PVC group and a control group of participants without PVCs was set in a nested case-control study to calculate the rate of complications for lifestyle-related diseases and the risk rate of PVCs for lifestyle-related habits.

Results: Within the participant group, PVCs were observed in 303 individuals (1.7%). When compared with the control group, the occurrence of regularly drinking alcohol (P=0.009) and insomnia (P=0.006) were significantly higher in the PVC group. Factors related to the onset of PVCs were examined using univariate analysis. The odds ratio (OR) was 1.731 in participants who regularly drank alcohol (95% CI: 1.146−2.633, P=0.009) when compared with participants who did not regularly drink alcohol, and 1.569 in participants with insomnia (95% CI: 1.023−2.422, P=0.040) when compared with participants without insomnia.

Conclusion: The frequency of PVCs recorded at regular medical checkups in Japanese office workers without heart disease was 1.7%. Within our group of participants, the factors related to the onset of PVCs were a history of regularly drinking alcohol and sleep disorders.

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Key words: ventricular ectopic beats, medical checkup, office workers, drinking, sleep disorder

Introduction

Premature ventricular contractions (PVCs) are often found at regular medical checkups. The prognosis of patients with PVCs and no history of heart disease is the same as in patients with no PVCs and no history of heart disease[1,2]; however, it is reported that mental and physical stresses and lifestyle-related habits are related to the development of PVCs[3,4]. In this study we aimed to clarify the frequency of PVCs observed during regular medical checkups in Japanese white-collar workers as well as the factors related to the onset of PVCs based on medical checkup data and their reported lifestyle-related habits.

Materials and Methods

Participants

A standard 12-lead electrocardiogram (ECG) examination was performed on 17,721 members of staff of FUJITSU Limited or affiliated companies during a regular

Correspondence to Hiromitsu Sekizuka, MD, PhD, FUJITSU Clinic, 4−1−1 Kamikodanaka, Nakahara-ku, Kawasaki, Kanagawa 211−8588, Japan
E-mail: sekizuka.h@jp.fujitsu.com
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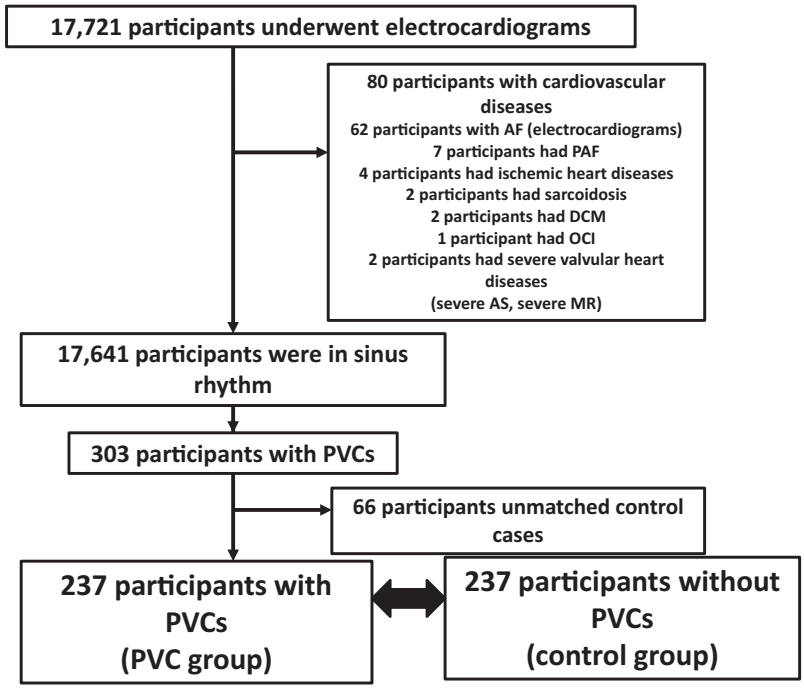

AF, atrial fibrillation; PAF, paroxysmal atrial fibrillation; DCM, dilated cardiomyopathy; OCI, old cerebral infarction; aortic stenosis; MR, mitral regurgitation and PVC, premature ventricular contraction.

Fig. 1 Flowchart for inclusion criteria.

medical checkup between April 1 2015 and March 31 2016 at The Health Examination Center, FUJITSU Ltd. Of these individuals, 17,641 were non-shift workers and white-collar workers (15,052 men and 2,589 women) who had no known heart disease. Retired employees were excluded from the participant group. PVCs were observed in 303 participants. Of these participants, 237 whose matched control case was available (control group 237 participants) were included in the PVC group. A total of 474 participants were included in the final analysis (**Fig. 1**).

Information regarding gender, age, height, weight, body mass index (BMI), abdominal circumference, previous illnesses (including cardiovascular disease), use or non-use of antihypertensive agents, use of anti-diabetic medications (including insulin), and use of lipid metabolism disorder medications was collected at the medical checkup. Obesity was defined as a BMI of $\geq$25 kg/m^2. Hypertension was defined as a systolic blood pressure (BP) $\geq$140 mmHg and/ or diastolic BP $\geq$90 mmHg and/ or current use of antihypertensive medications. Diabetes mellitus was defined as a glucose level of $\geq$126 mg dL^{-1} in the fasting state or as a glycosylated hemoglobin $\geq$ 6.5%, according to the National Glycohemoglobin Standardization Program and/ or current use of anti-diabetic medications. Participants with a low-density lipoprotein-cholesterol $\geq$140 mg dL^{-1}, a high-density lipoprotein-cholesterol <40 mg dL^{-1} or a triglyceride level $\geq$150 mg dL^{-1}, as well as participants who were receiving lipid metabolism disorder treatments, were defined as having dyslipidemia. Participants with neuropsychiatric disorders were defined as individuals who were receiving psychotropic drugs and/or sleeping pills.

Participants with heart disease were defined as persons who responded as having cardiovascular disease (including those who were currently undergoing treatment) in a medical interview at the medical checkup or as persons who were determined to have atrial fibrillation on the electrocardiogram readout during the medical check. Other participants were defined as persons without heart disease.

Questionnaires about Lifestyle

Lifestyle-related habits during the most recent 2–3 months were recorded before the medical checkup. The criterion for a smoking habit was defined as a current smoker with a regular smoking habit at the time of the medical checkup. The criterion for a drinking habit was defined as alcohol consumption once a week or more and a daily average alcohol consumption (g) was calculated. Exercise habit was defined as regular exercise of once a week or more. For sleep, the average sleep duration and the presence of a sleep disorder were recorded. The presence or absence of sleep-onset insomnia, sleep maintenance insomnia, and sleep-offset insomnia were

recorded. The criteria for insomnia were defined as a condition with the occurrence of at least one of the aforementioned signs of a sleep disorder. The monthly average duration of overtime at work was recorded.

Electrocardiogram

An ECG was performed using Cardio Star FCP-7541 (Fukuda Denshi, Tokyo, Japan). Electrocardiograms were measured at a paper speed of 25 mm/s and at a gain of 10 mm/mV. The time of recording was 10 seconds. The electrocardiographic findings were independently evaluated by five trained cardiologists, according to the Minnesota Code. Of the 474 participants who were included in the final analysis, there were no participants with a conduction disturbance in the second- or third-degree atrioventricular block, left bundle branch block, or right bundle block. Furthermore, there were no staff members that indicated they had suffered from ventricular tachycardia with three or more PVC events in succession or polymorphic PVC events in succession. One participant described two monomorphic PVCs in succession.

Case Matching

Participants without PVCs, who were the same sex and age ±3 years as 303 participants with PVCs in the same company and department/office, were selected and included in a control group of 237 participants. Meanwhile, 237 participants with PVCs, whose case-matched control was available, were included in the PVC group (**Fig. 1**). Participants with missing results from the medical interview and/or missing data for blood tests or urine tests, participants with obvious organic renal disease, participants who had an eGFR <50 mL min^{-1} per 1.73 m^2, participants with thyroid disease, quadruple amputees, or participants with muscular conditions were excluded.

Statistical Analysis

The data are expressed as means ± standard deviation. Differences between the two groups were determined by the analysis of variance; Student's t-test was used for multigroup comparisons. Case matching was conducted using a nested case control design. Univariate regression analyses were performed to determine factors related to the onset of PVCs. Statistical analyses were conducted using JMP software for Windows (version 10.0; SAS Institute, Cary, NC, USA). Statistical significance was set at a p value <0.05.

Ethical Approval

This research was conducted in accordance with the Declaration of Helsinki. In conducting research, we made all information that could identify individuals anonymous 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" of the Ministry of Health, Labour and Welfare of Japan. The FUJITSU Clinic Ethics Committee deliberated this study, and we obtained approval from the Committee before conducting this study (Ethical Committee Approval Number 07 and 09).

Results

Participants' Backgrounds

The average age of the participant group (n=17,641) was 47.3±6.9 (19−64) years old. Of these participants, 303 participants (1.7%) indicated the presence of PVCs.

The background of participants included in the final analysis is shown in **Table 1**. The average age of the total 474 participants assigned to the PVC group (237 participants) and the control group (237 participants) was 49.0± 6.2 years old. Men accounted for 89%. There were significant differences in the presence or absence of regularly drinking alcohol (P=0.009) and alcohol consumption on average 0−19 g/day (P=0.010) and the rates of insomnia (P=0.006) and sleep offset insomnia (P=0.006) in the PVC group when compared with the control group (**Table 1**).

Factors Related to PVCs

Factors related to the onset of PVCs recorded with an ECG were examined using a univariate analysis based on factors indicated by a statistical significance noted in **Table 1**. The odds ratios (ORs) were 1.731 and 1.868 in participants who regularly drank alcohol (95% CI: 1.146−2.633, P=0.009) and participants with an alcohol consumption of 0−19 g/day (95% CI: 1.210−2.903, P=0.005) when compared with participants who did not report regularly drinking alcohol respectively. In addition, the OR in participants with insomnia was 1.569 (95 %CI: 1.023−2.422, P=0.040) when compared with participants with no insomnia. In participants with sleep offset insomnia the OR was 3.194 (95% CI: 1.394−8.246, P=0.009) (**Table 2**).

Discussion

This study was conducted based on intra-corporate regular medical checkups excluding retired employees; therefore, it can be considered that there was no difference in health awareness among the participants. Furthermore, comparisons were conducted between staff members in the same workplace in the nested case control design to eliminate differences in the working environment as much as possible.

Table 1 Participant background

	All participants	Control group	PVC group	P-value
Number of participants	474	237	237	/
Men (%)	422 (89)	211 (89)	211 (89)	1.000
Age (years) [27–64 years]	49.0±6.2	49.0±6.3	49.1±6.3	0.895
BMI (kg/m^2)	24.1±3.8	23.9±3.5	24.3±4.0	0.273
Obesity (%)	166 (35)	81 (34)	85 (36)	0.725
Abdominal circumference (cm)	85.3±9.8	84.9±9.6	85.7±10.1	0.362
Current smoker (%)	115 (24)	58 (24)	57 (24)	0.915
Alcohol consumption (%)	349 (74)	162 (68)	187 (79)	0.009
Ethanol 0–19 g/day (%)	246 (52)	109 (46)	137 (58)	0.010
Ethanol 20 g or more (%)	102 (22)	52 (22)	50 (21)	0.823
Exercise habits (%)	187 (39)	88 (37)	99 (42)	0.301
Sleep time (hours)	5.9±1.0	5.8±1.1	5.9±0.9	0.579
<6 hours	158 (33)	84 (35)	74 (31)	0.330
Insomnia (%)	111 (23)	46 (19)	65 (27)	0.039
Sleep onset insomnia (%)	48 (10)	25 (11)	23 (10)	0.761
Sleep maintenance insomonia (%)	64 (14)	26 (11)	38 (14)	0.107
Sleep offset insomnia (%)	28 (6)	7 (3)	21 (9)	0.006
Overtime at work ≥ 40 hours/month (%)	134 (28)	72 (30)	62 (26)	0.308
Hypertension (%)	107 (23)	52 (22)	55 (23)	0.761
Dyslipidemia (%)	247 (52)	125 (53)	122 (51)	0.746
Diabetes mellitus (%)	34 (7)	18 (8)	16 (7)	0.703
Neuropsychiaric disorders (%)	24 (5)	13 (5)	11 (5)	0.675

Abbreviations: BMI, body mass index. The values are presented as the mean±standard deviation.

Table 2 Odds ratios for PVC

(n=474)	Odds ratio	95%CI	P-value
Non drinker	Reference		
Alcohol consumption (+)	1.731	1.146–2.633	0.009
Ethanol 0–19 g/day	1.868	1.210–2.903	0.005
Ethanol 20 g or more	1.442	0.851–2.452	0.174
Insomnia (–)	Reference		
Insomnia (+)	1.569	1.023–2.422	0.040
Sleep onset insomnia	0.911	0.499–1.658	0.761
Sleep maintenance insominia	1.550	0.912–2.670	0.109
Sleep offset insomnia	3.194	1.394–8.246	0.009

Abbreviations: CI, confidence interval.

Clinical Characteristics and Prevalence of Participants with PVCs

PVCs were recorded in 1.7% of the participants (303 participants) using a standard 12-lead ECG. A very small number of studies reported the prevalence of PVCs on a standard 12-lead ECG. Qureshi W et al.[1] reported that PVCs on a standard 12-lead ECG were seen in 1.5% of the participants without heart disease in a study conducted with 7,504 individuals in the United States aged 20 or over. The mean age was 60 years old.

A previous survey was conducted with 11,158 individuals in Japan wherein PVCs on a 12-lead ECG were observed in 1.4% of men and 1.1% of women, excluding persons with cardiovascular disease[5]. In addition, PVCs were recorded in 3–5% of the participants in the United States, and the recording time of the ECG was 40 seconds to 2 minutes in these studies[6,7].

The background of participants and the recording time of the ECG in this study were different from the above reports. It is presumed that an ECG recording time of 10 seconds at medical checkups in Japan is standard practice; therefore, we could not simply compare the fre-

quency of the recorded PVCs. It is known that a longer recording time for ECGs leads to more frequent detection of PVCs[1,5–7].

PVCs in individuals without heart disease is more frequent during the day than it is at night and is transiently suppressed by sinus tachycardia[8]. Therefore, a standard 12-lead ECG recorded during the day and at rest during a medical checkup may be an effective screening test for PVCs.

Relationship between PVCs and Lifestyle

The relationship between participants who regularly drank alcohol or suffered from insomnia and the incidence of PVCs detected at a medical checkup was observed in this study. However, significant differences were not indicated between the two groups for diabetes, hypertension, lipid metabolism disorders, a history of neuropsychiatric disorders, and physical findings such as blood pressure and blood test data (including data related to renal function, liver function and uric acid levels) (Data not shown).

It is known that regularly drinking alcohol is related to the presence of arrhythmias[2,9]. It is considered that excessive alcohol consumption causes cardiac damage, exacerbation of cardiac function, heart failure, and arrhythmias among other things through various actions in a dose-dependent manner[10].

It is unclear how alcohol consumption had an influence on PVCs from the results of this study. Our results indicated that the risk rate of PVCs was high in participants who drank an average of 0–19 g/day of alcohol, but did not indicate that the development of PVCs was high in a dose-dependent manner. It was considered that this result could indicate a statistically significant difference because the percentage of alcohol consumption, on average 0–19 g/day, was high in the group of staff members who drank alcohol regularly. In addition, the study participants who reported drinking might have had several factors, such as tobacco use, caffeine intake, electrolyte imbalances, or stress, that acted synergistically to cause PVCs[3,4,11,12].

There was a relationship between the presence of insomnia and the onset of PVCs in this study, however, there was no relationship between the duration of the participants' sleep and the onset of PVCs. A question asking about diurnal functional disorders due to insomnia, defined in the International Classification of Sleep Disorders, 3rd Edition (ICD-3)[13], was not included in this study. In addition, the duration and frequency of sleep disorders were not included in the investigation. Therefore, the cases that we classified as insomnia might not be clinically defined as insomnia.

There are a number of reports that sleep deprivation can cause PVCs[14,15]; however, there are very few reports describing that insomnia can cause PVCs. However, it is known that depression and mental and physical stresses can cause PVCs[16–18]. Furthermore, insomnia is closely related to depression and mental and physical stresses[19,20]. Therefore, a possibility that insomnia might be linked with development of PVCs was considered. In our study, sleep offset insomnia was linked with the development of PVCs; however, the cause was unclear.

Obstructive sleep apnea (OSA), which is a cause of a sleep disorders, was not included in the results of this study. OSA is also a known causal factor of PVCs[21]; therefore, studies that also include OSA would be needed in the future.

Clinical Implications of the Results of this Study

When a PVC was recorded using an ECG at a medical checkup, regardless of the absence of heart disease, there was a possibility that the individual's lifestyle, such as drinking alcohol or suffering from insomnia, might be reflected in the result[16–20]. In particular, the participants with the highest occurrence of PVCs were found when the amount of alcohol consumption was 0–19 g/day or the participants had sleep offset insomnia.

Follow-up Survey

Of the 303 workers with PVCs in this study, 99 patients underwent complete examinations and at least 9 patients received some kind of therapies. It is still controversial whether a PVC on a standard 12-lead ECG is a significant factor for cardiovascular disease development and mortality. Qureshi W et al.[1] reported that PVCs on a standard 12-lead ECG were not associated with a risk of mortality and cardiovascular disease. On the other hand, Hirose H et al.[4] reported that PVCs on a standard 12-lead ECG were a predictive factor for cardiac death only in healthy men and Watanabe H et al.[22] reported that PVCs on a standard 12-lead ECG were a prognostic factor for the risk of atrial fibrillation. It is vitally important to conduct a follow-up study.

Study Limitations

This was a small, retrospective, single-center, case-controlled study. Therefore, a larger, more comprehensive study is warranted. It is unclear whether the results of the present study would be applicable to general workers. The background of participants was based on the participants' own answers; therefore, they might be inaccurate. Gender differences were not considered in this

study, although there is a report that there are gender differences in the effects of stress at the workplace on the body[23].

The ECGs were recorded for 10 seconds during the medical checkups in this study although a long-duration recording, such as a 24-hour recording, is ordinarily required to make a diagnosis of arrhythmia. In addition, the presence or absence of heart disease was examined based on a medical interview only. Therefore, we could not exclude the possibility that there might be participants with undiagnosed heart disease[24,25]. The morphology and origin of the PVCs were not examined in this study.

Conflict of Interest: The authors declare no conflict of interest.

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