

ORIGINAL ARTICLE

Overtime work, insufficient sleep, and risk of non-fatal acute myocardial infarction in Japanese men

Y Liu, H Tanaka, The Fukuoka Heart Study Group

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See end of article for authors' affiliations

Correspondence to: Ying Liu, Cancer Information and Epidemiology Division, Research Institute, National Cancer Center, Tokyo 104-0045, Japan; yliu@gan2.res.ncc.go.jp

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Objectives: To examine the relation between working hours and hours of sleep and the risk of acute myocardial infarction (AMI), with special reference to the joint effect of these two factors.**Method:** Case-control study in Japan. Cases were 260 men aged 40–79 admitted to hospitals with AMI during 1996–8. Controls were 445 men free from AMI matched for age and residence who were recruited from the resident registers. Odds ratios of AMI relative to mean weekly working hours and daily hours of sleep in the past year or in the recent past were calculated.**Results:** Weekly working hours were related to progressively increased odds ratios of AMI in the past year as well as in the past month, with a twofold increased risk for overtime work (weekly working hours ≥ 61) compared with working hours ≤ 40 . Short time sleep (daily hours of sleep ≤ 5) and frequent lack of sleep (2 or more days/week with < 5 hours of sleep) were also associated with a two to three-fold increased risk. Frequent lack of sleep and few days off in the recent past showed greater odds ratios than those in the past year.**Conclusions:** Overtime work and insufficient sleep may be related to increased risk of AMI.

As early as 1977, Joseph Eyer found that mortality from ischaemic heart disease rose during periods of economic prosperity and fell during periods of depression according to the analysis of mortality data for 26 years in the United States.^{1,2} He suggested that overtime work peaked with the boom of production and reached the lowest level at the peak of unemployment and that overwork was the most prominent source of stress. In Japan, deaths were repeatedly reported to have occurred after extremely long work times and deprivation of sleep, and this was broadly recognised by the specific name “karoshi” in the 1980s when Japan reached its climax in economic development³; working time then was much longer than in most of the other developed countries.⁴ It was reported that most cases of karoshi were the result of acute cardiovascular events.⁵ These facts suggested that overtime work might be an important risk factor for acute myocardial infarction (AMI).

A prospective study in the United States showed that standardised mortality ratio of coronary heart disease (CHD) was highest among those who worked 67 hours or more a week.⁶ Case-control studies in The Netherlands,⁷ Denmark,⁸ and Sweden⁹ also reported that prolonged working time was associated with an increased risk of AMI. Another case-control study in Japan found significantly increased odds ratios (ORs) of AMI for those who worked more than 11 hours a day and for those who had prolonged their working time by more than 3 hours a day in the recent past.¹⁰

Overtime work results in short sleeping time, which may exert a specific effect on the onset of AMI. The American Cancer Society study found that men sleeping 4 hours or less had higher mortality from CHD than those sleeping 7.0–7.9 hours.¹¹ Another American study and a Finnish study also noted that men who slept less than 6 hours as well as those who slept 9 hours or more had a higher risk of CHD than men sleeping 7–8 hours.^{12,13}

The present study examined the relation between working hours and hours of sleep and the risk of AMI in Japanese men, with special reference to the joint effect of these two factors.

METHODS

Subjects

Eligible cases were patients aged 40–79 who were admitted to 22 collaborating hospitals for a first AMI occurring during the period from September 1996 to September 1998 who survived to receive rehabilitation and who were within a month after the onset of AMI. Thirteen hospitals were selected to cover the patients in Fukuoka City at the time when the study was started, and nine hospitals subsequently joined the study from June 1997 to recruit the patients in adjacent municipalities. These collaborating hospitals had one or more expert cardiologists and the facilities for treating AMI.

Research nurses checked all admissions with a diagnosis of AMI or suspected AMI, and asked eligible patients to participate in the study. Collaborator cardiologists were responsible for the diagnosis of AMI, which was based on an electrocardiogram, ischaemic cardiac pain lasting at least 30 minutes, and enzyme change. A total of 756 potentially eligible patients were identified, and 660 patients (87%) participated in the study; participation rates in men and women were both 87%.

At most two controls for each case, matched by sex, age (within 2 years), and residence, were recruited from the resident registers, which list residents in order of house numbers; eligible residents listed subsequently to the case were selected. Two potential control subjects who lived nearest to a case were firstly invited to participate in the study. If one or two refused, then a third one was chosen and so on till at least one control was recruited. From September 1996 to March 1999, a total of 2613 control candidates were first approached by post. Two further letters were sent to non-respondents, then they were contacted by telephone if telephone numbers were available. Finally, 1277 participated in the study. The information about non-participants was as follows: non-resident or emigration 26, history of myocardial infarction 79, refusal 889, death 22, undelivered mail 53, no response to mail 267. Thus the net participation rate was estimated to be 52% (1277/2433);

Abbreviations: AMI, acute myocardial infarction; CHD, coronary heart disease

participation rates in men and women were 56% and 45%, respectively. No control was recruited for one case, only one control was recruited for 41 cases each, and two controls were recruited for each of the remaining cases.

Because working women were few, the present study included working men only. After exclusion of all women (181 cases and 346 controls) and men without a job (171 cases and 293 controls), 308 cases and 638 controls remained. Also, men with incomplete information on working hours (nine cases and 16 controls) were deleted. We further excluded cases without a matched control and controls without a matched case (39 and 177, respectively). Finally, 260 cases and 445 individually matched controls remained in the analysis.

Risk factors

A questionnaire based interview elicited details of work related factors, lifestyle factors, and medical and family history before AMI in cases and before interview in controls.

The subjects were asked about their mean working hours each week, number of days off a year, hours of sleep a day on working days and on days off separately, and days each week with less than 5 hours sleep in the past year. Weekly working hours and number of days off in the past month and days of sleeping less than 5 hours in the past week were also recorded. We then grouped weekly working hours, monthly days off, and daily hours of sleep into three arbitrary categories (≤ 40 , 41–60, and ≥ 61 ; <2, 2–7, and ≥ 8 ; and ≤ 5 , 6–8, and ≥ 9 respectively). Weekly working hours ≥ 61 , monthly days off <2, daily hours of sleep ≤ 5 , and 2 or more days a week with less than 5 hours sleep were defined as overtime work, few days off, short sleep time, and frequent lack of sleep, respectively.

Exposure to cigarette smoking was expressed by cigarette-years, the number of cigarettes smoked a day multiplied by years of smoking, which was categorised into 0, 1–399, 400–799, and ≥ 800 cigarette-years. The average amount of alcohol consumed a day was calculated for current alcohol drinkers, and alcohol use was categorised into never, past, and current use with a consumption of <50 or ≥ 50 ml of alcohol a day. History of diseases related to AMI (hypertension, hyperlipidaemia, and diabetes mellitus) was defined as positive if subjects had ever been prescribed medication, special diet, or exercise for these conditions. Height and body weight were also recorded, and a body mass index (kg/m^2) of 25 or greater was defined as overweight. Job titles were coded according to the classification used in the national census. They were grouped into white collar jobs (professional, managerial, clerical, and sales work) and blue collar jobs (craft, labouring, and

service work). Shift work was defined if subjects had rotating work. Subjects self rated their occupational physical activity as mostly sedentary, moderately active, quite active, or having a job related to sport. The last three categories were combined as non-sedentary. Job strain was assessed in accordance with the Karasek model.¹⁴ The detailed procedures have been described elsewhere.¹⁵ In brief, job demand and control scores were determined on the basis of two and five questions, respectively. These scores were dichotomised at the median values, and high job strain was defined as a combination of low control and high demand.

To examine the characteristics of control candidates who did not participate in the present study, we posted an abbreviated questionnaire containing 13 questions to 456 such people until December 1997. Of these, 217 responded to the questionnaire, and unanswered questions were completed by telephone interview. Subjects who reported a history of myocardial infarction ($n=4$) were excluded from participating as control subjects. Among the remaining 213 subjects, 72 men with a job were used in the analysis. In this survey, questions about mean weekly working hours, monthly days off, and daily hours of sleep on work days in the past year were included.

Statistical analysis

Analysis of variance (ANOVA) and analysis of covariance (ANCOVA) were used to compare the means of working hours, days off, and hours of sleep among groups. Conditional logistic regression analysis was used to obtain ORs of AMI relative to working hours, numbers of days off, and hours of sleep; 95% confidence intervals (95% CIs) were calculated with standard errors of the logistic regression coefficients. The interaction was assessed by the likelihood ratio test. Covariates included in the multivariate models were hypertension, diabetes mellitus, hyperlipidaemia, overweight, cigarette smoking, alcohol intake, parental CHD (angina pectoris and myocardial infarction), job type (blue collar job and white collar job), and sedentary job. They were treated as categorical variables with indicator variables representing the categories. All computations were performed with the SAS software package version 6.04 (SAS Institute, Cary, NC, USA)

RESULTS

There was no material difference between the surveyed controls and non-participant control candidates for weekly working hours (44.1 versus 45.7) and monthly numbers of days off (1.8 versus 1.7) in the past year, but participants took slightly shorter sleep than non-participants (7.0 versus 7.3 hours).

Table 1 Coronary risk factors and work related factors according to categories of weekly working hours in the past year in cases and controls

Risk factor	Case (working h/week)			p Value	Control (working h/week)			p Value
	<40 n=86	41–60 n=131	≥ 61 n=43		<40 n=174	41–60 n=231	≥ 61 n=40	
Age (y, mean)	60.3	56.1	54.0	0.0001*	59.2	55.0	55.8	0.0001*
Current smoking	59.3	70.2	76.6	0.09	42.5	47.6	60.0	0.13
Current weekly alcohol use	50.0	53.4	44.2	0.57	69.5	73.2	72.5	0.72
Parental CHD	19.3	22.6	18.6	0.79	11.7	16.1	22.5	0.18
Hypertension	24.4	38.2	18.6	0.02	22.0	12.1	22.5	0.02
Hyperlipidemia	20.9	16.0	16.3	0.63	9.8	5.2	7.5	0.21
Diabetes mellitus	15.1	9.9	14.0	0.49	8.1	5.6	10.0	0.47
Overweight†	22.4	35.1	32.6	0.13	23.0	27.3	22.5	0.57
Days off/month*	11.7	8.2	5.9	0.0001	10.9	8.3	6.4	0.0001
Workday sleeping hours*	6.8	6.9	6.4	0.05	7.0	6.9	6.6	0.10
Days/week of <5 h sleep*	0.7	0.8	1.4	0.006	0.5	0.5	0.9	0.13
Shift work	9.3	9.9	18.6	0.23	11.5	7.8	17.5	0.13
Sedentary job‡	70.9	62.6	60.5	0.36	72.4	54.1	60.0	0.001
Blue collar job	22.4	45.8	44.2	0.002	30.6	38.1	41.0	0.22
Job strain	23.2	36.8	31.0	0.12	15.7	23.7	52.8	0.0001

CHD: coronary heart disease; numbers are percentages unless otherwise specified; p values are based on a χ^2 test; *p values are based on ANOVA; †body mass index ≥ 25 ; ‡one out of four categories regarding occupational physical activities.

Table 2 Means (SE) of working time, sleeping time, and numbers of days off of cases and controls

Variable	Reference period*	Crude			Adjusted		
		Case	Control	p Value†	Case	Control	p Value‡
Working h/week	Past year	48.8 (1.0)	45.1 (0.7)	0.003	49.2 (1.0)	45.2 (0.8)	0.002
	Past month	47.7 (1.0)	44.6 (0.8)	0.02	48.0 (1.1)	44.6 (0.8)	0.02
Days off/month	Past year	9.0 (0.3)	9.1 (0.2)	0.71	9.0 (0.3)	9.2 (0.2)	0.61
	Past month	8.2 (0.3)	8.4 (0.3)	0.56	8.2 (0.4)	8.4 (0.3)	0.56
Workday sleeping (h)	Past year	6.8 (0.1)	6.9 (0.1)	0.05	6.8 (0.1)	6.9 (0.1)	0.13
Days off sleeping (h)	Past year	7.6 (0.1)	7.7 (0.1)	0.19	7.6 (0.1)	7.7 (0.1)	0.23
Days/week of <5 h sleep	Past year	0.84 (0.1)	0.55 (0.1)	0.001	0.81 (0.1)	0.56 (0.1)	0.01
	Past week	0.95 (0.1)	0.52 (0.1)	0.0001	0.95 (0.1)	0.52 (0.1)	0.0001

*Period before the onset of acute myocardial infarction in cases and before the interview in controls; †p values are based on ANOVA; ‡p values are based on ANCOVA adjusting for cigarette-year, alcohol drinking, overweight, hypertension, diabetes mellitus, hyperlipidaemia, parental coronary heart disease, job type, and sedentary job.

Table 1 shows coronary risk factors according to categories of working time in the past year in cases and controls separately. Those who worked shortest were oldest, were more likely to have a sedentary job, and tended to be white collar workers in both cases and controls. Those controls who worked longest were more likely to have high job strain. In cases, the prevalence of hypertension was highest among those who worked 41–60 hours a week, whereas in controls, hypertension was lowest among those who worked 41–60 hours a week. Longer working hours was related to fewer days off, shorter hours of sleep, and more days a week with less than 5 hours of sleep in both cases and controls.

Table 2 gives means of working hours and numbers of days off in the past year as well as in the past month and hours of sleep in cases and controls. Cases worked longer and slept less. Mean working hours and hours of sleep on working days were significantly longer, and the number of days with less than 5 hours sleep was significantly greater among cases than among controls. Numbers of days a month off and hours of sleep on days off were slightly less in cases, but the differences were not significant. Adjustment for several known risk factors did not change the results.

Weekly working hours in the past year (table 3) as well as in the past month (table 4) were related to progressively

increased ORs of AMI. Although the number of days off in the past year was unrelated to the risk of infarction (table 3), a moderate increase in the OR was found among men with less than 2 days off in the past month (table 4). Men who had slept for 5 hours or less each working day on average in the past year had a twofold increased risk. Men with short sleep time on days off also had an increased risk, but the increase did not reach significance (table 3). The number of days with less than 5 hours sleep was also positively associated with the risk of AMI; the frequent lack of sleep in the past week was more noticeably associated with an increased risk. Adjustment for the coronary risk factors did not change the results much except for a significantly increased OR associated with few days off in the past month.

Tables 5 and 6 show the interaction between working hours and sleep or number of days off relative to the risk of AMI in the past year and in the recent past, respectively. For ease of presentation, each intermediate level was combined as the referent category because ORs for the intermediate levels were not much greater than unity. The categories of longer work and less days off or short sleep time generally showed the greatest increase in the OR, none of the tests for the interaction were significant.

DISCUSSION

The present study showed that working long hours was associated positively with the risk of AMI, independent of the other coronary risk factors. Short sleep time or frequent lack of sleep, especially very recently, was also related to an

Table 3 The ORs (95% CIs) of acute myocardial infarction relative to working time, numbers of days off, and sleeping time in the past year

Variable	OR (95% CI)	
	Crude	Adjusted*
Working h/week:		
≤40	1.0 (referent)	1.0 (referent)
41–60	1.3 (0.9 to 1.8)	1.3 (0.9 to 2.0)
≥61	2.1 (1.3 to 3.6)	1.8 (1.0 to 3.3)
Days off/month:		
≥8	1.0 (referent)	1.0 (referent)
2–7	1.0 (0.8 to 1.4)	1.0 (0.7 to 1.4)
<2	1.0 (0.8 to 1.2)	1.0 (0.8 to 1.3)
Workday sleeping hours:		
≥9	1.3 (0.6 to 2.6)	1.5 (0.6 to 3.8)
6–8	1.0 (referent)	1.0 (referent)
≤5	2.3 (1.3 to 3.4)	2.5 (1.1 to 5.3)
Days off sleeping hours:		
≥9	1.0 (0.7 to 1.5)	1.1 (0.7 to 1.7)
6–8	1.0 (referent)	1.0 (referent)
≤5	1.6 (0.8 to 3.6)	1.8 (0.7 to 4.7)
Days/week of <5h sleep:		
0	1.0 (referent)	1.0 (referent)
1	1.2 (0.9 to 1.7)	1.1 (0.7 to 1.7)
≥2	2.3 (1.2 to 4.4)	2.1 (0.9 to 4.6)

Matched odds ratios are based on conditional logistic regression analysis; *adjusted for cigarette-year, alcohol drinking, overweight, hypertension, diabetes mellitus, hyperlipidaemia, parental coronary heart disease, job type, and sedentary job.

Table 4 The ORs (95% CIs) of acute myocardial infarction relative to working time, and numbers of days off in the past month and sleep time in the past week

Variable	OR (95% CI)	
	Crude	Adjusted*
Working h/week:		
≤40	1.0 (referent)	1.0 (referent)
41–60	1.3 (0.9 to 1.9)	1.2 (0.8 to 1.9)
≥61	2.2 (1.4 to 3.7)	1.9 (1.1 to 3.5)
Days off/month:		
≥8	1.0 (referent)	1.0 (referent)
2–7	1.3 (0.9 to 1.8)	1.3 (0.9 to 1.9)
<2	1.6 (0.9 to 3.1)	2.9 (1.3 to 6.5)
Days/week of <5 h sleep:		
0	1.0 (referent)	1.0 (referent)
1	1.3 (0.9 to 1.8)	1.3 (0.8 to 2.0)
≥2	3.3 (1.9 to 5.6)	3.6 (1.9 to 6.9)

Matched ORs are based on conditional logistic regression analysis; *adjusted for cigarette-year, alcohol drinking, overweight, hypertension, diabetes mellitus, hyperlipidaemia, parental coronary heart disease, job type, and sedentary job.

Table 5 The ORs (95% CI) of acute myocardial infarction relative to few days off, short sleep, and insufficient sleep according to weekly working hours in the past year

Days off or sleep	≤60 OR (95%CI)	≥61 OR (95%CI)	p Value for interaction
Days off/month:			
≥2	1.0 (referent)	1.3 (0.8 to 2.4)	0.70
<2	1.5 (0.3 to 7.1)	3.6 (0.7 to 19.0)	
Working day sleep (h):			
≥6	1.0 (referent)	1.4 (0.8 to 2.5)	0.66
≤5	2.2 (0.9 to 5.2)	4.8 (0.9 to 26.4)	
Day off sleep (h):			
≥6	1.0 (referent)	1.5 (0.9 to 2.6)	0.81
≤5	1.6 (0.5 to 4.8)	3.3 (0.3 to 35.6)	
Days/week of <5 h sleep:			
≤1	1.0 (referent)	1.5 (0.9 to 2.8)	0.40
≥2	2.5 (0.9 to 6.4)	1.5 (0.4 to 5.9)	

Adjusted for cigarette-year, alcohol drinking, overweight, hypertension, diabetes mellitus, hyperlipidaemia, parental coronary heart disease, job type, and sedentary job; p values are based on the likelihood ratio test.

Table 6 The ORs (95% CIs) of acute myocardial infarction relative to few days off, and insufficient sleep according to weekly working hours in the recent past

Days off or sleep	Weekly working hours in the past month		p Value for interaction
	≤60 OR (95%CI)	≥61 OR (95%CI)	
Days off in the past month:			
≥2	1.0 (referent)	1.3 (0.7 to 2.3)	0.85
<2	2.1 (0.7 to 6.1)	3.7 (1.2 to 11.8)	
Days of <5 h sleep in the past week:			
≤1	1.0 (referent)	1.8 (1.0 to 3.2)	0.98
≥2	3.6 (1.8 to 7.5)	3.1 (0.8 to 12.2)	

Adjusted for cigarette-year, alcohol drinking, overweight, hypertension, diabetes mellitus, hyperlipidaemia, parental coronary heart disease, job type, and sedentary job; p values are based on the likelihood ratio test.

increased risk. Higher ORs for few days off in the past month rather than in the past year and for frequent lack of sleep in the past week rather than in the past year indicate that sleep deprivation and lack of rest in the very recent past may exert a trigger effect on the onset of AMI.

A previous case-control study in Japan showed that working >11 hours compared with working 7.1–9.0 hours a day in the past month was associated with a twofold increased risk of AMI.¹⁰ In that study a much higher risk was found among those working 7 hours a day or less.¹⁰ In the present study, the relation between working hours and the risk of AMI was monotonic. The lowest category of working hours in the present study was 40 hours or less a week. Even when the lowest category was divided into <35 and 35–40 hours a week, an almost monotonic, positive relation remained; adjusted ORs for the categories of <35, 35–40, 41–60, and >61 were 1.0 (referent), 1.5, 1.7, and 2.9, respectively. In the previous study of Japanese men,¹⁰ cases were patients admitted to hospital, and controls were selected from among those receiving routine medical examinations at the work place; it was thus possible that cases had shortened working hours because of pre-morbid conditions whereas controls were healthy workers who worked as usual. In the present study, control subjects were selected from among community residents, and thus selection bias due to the healthy worker effect was unlikely.

Several studies have shown an association between job strain and ischaemic heart disease.^{8, 16–18} It was supposed that job strain, especially high job demand, was related to long working hours and sleep debt, resulting in CHD through overtime work and insufficient sleep. In the present study, job demand score was associated positively with working hours

Main messages

- Longer working hours were related to progressively increased risks of AMI.
- Insufficient sleep was also associated with an increased risk of AMI.
- Long working hours and insufficient sleep in the recent past were more strongly related to an increased risk of AMI.

Policy implications

- Restricting working hours to 40 or less a week is desirable.
- Those working for a prolonged time should take sufficient sleep or take at least 2 days rest a month.

and negatively with hours of sleep, but the associations were rather weak (data not shown). Shift work is another risk factor for AMI,^{19, 20} which may exert its influence through poor or short sleep time. Among controls, mean hours of sleep on working days in the past year were 6.8 in the shift workers and 7.0 in non-shift workers. Additional adjustment for high job demand and shift work did not alter the reported results.

Overtime work deprives people of sleep time and holidays. However, insufficient sleep itself might be part of the syndrome of vital exhaustion.^{21, 22} The present study did not consider quality of sleep. It has been suggested that poor quality of sleep may increase the risk of AMI.^{23–25} However, a cross sectional study and a prospective study indicated that increased risk of CHD associated with short sleep time was independent of sleep quality.^{12, 13}

As the participation rate in controls was not sufficiently high, the selection bias needs to be considered carefully. It could be anticipated that men working longer were more likely to be reluctant to participate in the study. However, the pilot investigation found no material difference between the participant controls and non-participant control candidates for working hours and days off but non-participants slept longer than participants. It is thus unlikely that the increased risks of AMI associated with overtime work, short sleep time, frequent lack of sleep, and few days off were overestimated. It is possible that having an AMI may have influenced patients' perception or recall of work and sleep before the onset of the AMI. Therefore, caution needs to be exercised in interpretation. The present study was based only on non-fatal AMI, and cannot consider the effect of working hours and duration of sleep on the occurrence of fatal AMI. Generalisation of the present findings is thus limited.

Several biological explanations are possible for the increased risk of AMI associated with overtime work. Overtime

work is known to increase blood pressure and heart rate,^{26,27} and induce cardiac or psychological symptoms—such as chest pain, depression, and fatigue.²⁸ Chronic stress or fatigue resulting from extensive overtime work causes a sympathodominant state which may induce cardiovascular abnormalities or dysfunctions resulting in the onset of AMI.²⁹ It is also known that lack of sleep increases activity in the sympathetic nervous system, leading to an increase of blood pressure and heart rate.^{30–32} Furthermore, people with sleep deprivation were shown to be more likely to develop malignant hypertension than those without.³³ The combined effect of overtime work and insufficient sleep may increase sympathetic nervous system activity to such a critical level as to induce the onset of an AMI.

In summary, overtime work and insufficient sleep in the past year were each related to an increased risk of AMI, and insufficient sleep and few days off in the very recent past were associated with a profound increase in the risk. These findings suggest that chronic overwork and sleep deprivation confer increased risk of AMI, and that recent lack of rest and sleep deprivation may further enhance the risk of infarction.

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APPENDIX: MEMBERS OF THE FUKUOKA HEART STUDY GROUP LISTED IN ALPHABETICAL ORDER AT EACH AFFILIATION

Hiroko Kodama, Suminori Kono*, Ying Liu, Yoshihiro Miyake, Shizuka Sasazuki, Keitaro Tanaka, Shoji Tokunaga, Kouichi Yoshimasu, Masakazu Washio (Department of Preventive Medicine, Graduate School of Medical Sciences, Kyushu University; these are also the members of the working group); Masahiro Mohri†, Akira Takeshita (Department of Cardiovascular Medicine, Graduate School of Medical Sciences, Kyushu University); Kikuo Arakawa, Munehiro Ideishi, Takanobu Nii, Kazuyuki Shirai (Second Department of Internal Medicine, School of Medicine, Fukuoka University); Koichi Handa, Keiichi Tanaka (Department of Emergency and Critical Care Medicine, School of Medicine, Fukuoka University); Hidekazu Arai (Tokushukai Fukuoka Hospital); Yoshitaka Doi, Tomoki Kawano, Osamu Nakagaki, Kazuyuki Takada (Saiseikai Fukuoka General Hospital); Yasushi Sasaki (Ishihara Cardiovascular Disease Hospital); Yasushi Ishihara (Odo Ishihara Hospital); Tetsuji Inoh (Fukuoka Red Cross Hospital); Fumio Oshima (Fukuoka Medical Association Hospital) Tomoki Honma, Samon Koyanagi (National Kyushu Medical Center Hospital); Yasuo Hayashi, Yuji Taira (Hara Sanshin General Hospital); Yuji Maruoka (Hamanomachi Hospital); Ken Abe (Chihaya Hospital); Shunji Miake, Suguro Mori, Shinya Oda (Hakujuji Hospital); Ryuichi Nagashima, Ichiro Ohmura (National Sanatorium Fukuokahigashi Hospital); Tadayuki Hiroki, Ryuichiro Miyawaki (Fukuoka University Chikushi Hospital); Juzabu Jinnouchi (Sasaguri Hospital); Shinichiro Ito, Kazuyuki Saito (Fukuoka Seishukai Hospital); Terutoshi Tanioka (Munakata Suikokai Hospital); Kohzo Iino (Itoshima Medical Association Hospital); Yasuhiro Maeda (Munakata Medical Association Hospital); Yasuhiko Orita (Fukuoka Kameyamae-eikoh Hospital); Yohsuke Katsuta, Hidero Nakazono (Saiseikai Futusukaichi Hospital); Naotaka Hamasaki (Department of Clinical Chemistry and Laboratory Medicine, Graduate School of Medical Sciences, Kyushu University); Hitomi Hayabuchi (Fukuoka Womens' University); Sumie Jingu, Ryoko Hayashi, Masako Sakamoto (Fukuoka City Office); Yoshiki Egashira, Tadashi Enomoto, Masanori Fujino, Keisuke Fukuda, Masakazu Gondo, Shouhei Hata, Satoshi Hiratsuka, Takashi Ichiki, Nariaki Ikeda, Yasuto Iwanaga, Hisashi Kanaya, Yoshihiro Kato, Masaki Kohara, Nobuo Masuda, Hideyo Matsuguchi, Eiichi Murayama, Masatsugu Ohga, Hideaki Ogushi, Nobuo Ouchi, Hiroshi Saku, Teizo Sata, Kuninori Soejima, Hiroshi Takamiya, Shinsuke Takei, Masafumi Tanaka, Noritami Tashiro, Takehiko Yamada, Tsutomu Yamamoto, Masato Yoshida (general practitioners in Fukuoka City).

*Principal investigator; †Coprincipal investigator.

Authors' affiliations

Y Liu, Graduate student of Department of Preventive Medicine, Graduate School of Medical Sciences, Kyushu University, Fukuoka 812-8582, Japan

H Tanaka, Department of Epidemiology, Medical Research Institute, Tokyo Medical and Dental University, Tokyo 101-0062, Japan

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