

Leisure Time and Job Related Physical Activity and the Risk of Non-Fatal Acute Myocardial Infarction in Japanese Men and Women – A Population Based Case-Control Study

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ABSTRACT

Physical activity is regarded to reduce the risk of coronary heart disease. However, vigorous physical activity can transiently increase the risk of acute myocardial infarction. The present study examined the relationship of physical activity to nonfatal acute myocardial infarction (AMI) in a Japanese population. A total of 660 cases with their first episode of AMI aged 40-79 years living in Fukuoka City or adjacent areas and 1277 controls matched for age, sex and residence were surveyed on lifestyle including physical activity. Among them, 625 cases and 1166 individually matched controls were used in the final analysis. Physical activity showed a decreased trend of crude relative risk of AMI in heavier job type, spending longer time on sports activity, higher frequency of sports activity, higher frequency of moderate or strenuous sports activity and having hard sports activity in men, while spending longer time on sports activity showed a decreased crude relative risk of AMI in women. Even after controlling for confounding factors, higher frequency of sports activity and having hard sports activity were associated with a decreased risk of AMI in men. Playing any sports was associated with lower adjusted risk of AMI, and higher frequency of moderate or strenuous sports activity showed a trend toward a decreased adjusted relative risk of AMI in women. The present study suggests that sports activity may be inversely associated with the risk of AMI in both Japanese men and women.

Keywords: Physical activity; Acute myocardial infarction; Japanese; Case-control study

INTRODUCTION

Cardiovascular disease is the second leading cause of death in Japan, which was more than 360, 000 deaths in 2013[1]. Most cases of cardiovascular disease are those with stroke or coronary heart disease. In Japan, the incidence of stroke is decreasing while the incidence of coronary heart disease is increasing [2].

Physical activity is regarded to reduce the risk of coronary heart disease in Western countries [3, 4, 5, 6], and regular physical activity is advocated by the medical community because physical activity and exercise training are suggested to reduce the incidence of coronary heart disease events [3,4,5,6]. However, vigorous physical activity can transiently increase the risk of acute myocardial infarction [7]. Furthermore, Holterman et al [8] reported that high occupational physical activity may increase the risk of acute myocardial infarction among those with low leisure time physical activity in a Western population.

In Japan, Noda et al[9] reported that physical activity reduced the risk of coronary heart disease while Shibata et al[10] reported that physical activity failed to reduce the risk of coronary heart disease after controlling other factors. Therefore, the impact of physical activity on coronary heart disease should be examined carefully in Japan. Here, we examined the relationship between physical activity and the risk of acute myocardial infarction (AMI) using the anonymized data from a large scale multicenter case control study in Japan [11, 12, 13, 14, 15, 16].

SUBJECTS AND METHODS

Subjects

The selection criteria and study design of the Fukuoka Heart Study have been described previously [11,12,13,14,15,16]. Consecutive cases of a first episode of acute myocardial infarction (AMI) that were admitted within 1 month of onset were identified in 22

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collaborating hospitals during the period September 1996 to September 1998. Cases were restricted to residents of Fukuoka City at the inception of the study, and extended to include those in 21 adjacent municipalities after June 1997. Thirteen hospitals were originally selected to cover Fukuoka City, and 9 hospitals subsequently joined the study. These collaborating hospitals were staffed with one or more expert cardiologists and equipped with the facilities for treating AMI. The cardiologists made the diagnosis of AMI, which was based on ECG, ischemic cardiac pain and enzyme changes, in accordance with the criteria used the Lipid Research Clinical Program. Research nurses visited each hospital weekly and checked all admissions with a diagnosed or suspected AMI. They asked eligible patients to participate in the study with the permission of the attending doctors. A total of 660 of 756 eligible patients (87%; age range, 40-79 years) were surveyed with regard to lifestyle and other factors.

Community controls were recruited by referring to the residents registers of the municipalities where the corresponding cases resided. For each case, we selected at most 2 controls matched for birth year (within 2 years), sex, and proximity in residence. Candidates were first approached by mail. Two reminders were sent, and contact by telephone was attempted in last if the telephone number was listed in the telephone directory. Of 2613 subjects approached, 53 were returned as undeliverable mail, 22 were dead, 26 were found to be non-residents, 79 had prior history of MI; 889 refused. Thus a net participation rate was calculated as 52% (1277/2433). 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.

The final analysis included 625 sets of 625 cases and 1166 individually matched controls excluding one case for whom no matched control was selected, 32 cases with incomplete data and their 64 controls, and 47 controls with incomplete data and their matched 2 cases. As reported previously [11], nonparticipating control candidates were almost similar in characteristics to control subjects.

Physical Activity Indexes and Risk Factors

A questionnaire-based interview ascertained personal characteristics such as smoking habit, alcohol consumption, occupational and leisure time physical activities, medical history of

hypertension, hyperlipidemia, diabetes mellitus, or angina pectoris, and family history of AP or MI. The questionnaire was distributed to the patients with AMI before interview and was completed with the assistance of research nurses during the hospital admission. The median time from admission to interview was 14 days. Control subjects also received the questionnaire by mail beforehand, and research nurses and members of the working group (physicians and a public health nurse) interviewed them at a clinic, medical office or the subjects' workplaces or home (72.7%, 8.7%, 6.8%, and 11.7%, respectively). Control subjects under medical treatment were usually interviewed at their own doctor's clinic.

The interview elicited details of work related and leisure-time physical activities before AMI incases and before interview in controls. Questions on leisure-time physical activity asked about the number of days on which subjects had exercised per week on weekdays and per month on weekends or holidays on average over the past year, the type of regular activity, and the average amount of time spent in each activity. Leisure-time physical activity was classified into 4 levels of intensity by referring to MET values (ratio of working metabolic rate/resting metabolic rate) in the published literature [17] The MET score (light=1.5, moderate=4, hard=6 and very hard=8) was multiplied by the number of hours per week engaged in each activity to yield the MET-hours per week as an index of energy expenditure (kcal/kg/week) for leisure-time physical activity. Questions on job related physical activity asked about mean working hours each week, number of days off a year, the intensity of physical activity at working and yearly mean time for commuting on foot or bicycle. The MET score (sedentary work=1.5, light mobile=4 and Heavy, strenuous work=6) multiplied by the working hours per week was added to the MET score of 4 multiplied by the commuting hours per week to get the MET-hours per week as an index of energy expenditure for work related physical activity. Subjects who were unemployed were classified as occupationally inactive. An index of total energy expenditure was yielded by adding the MET-hours per week for leisure-time physical activity and that for work-related physical activity.

Cigarette smokers were defined as those who had ever smoked daily for 1 year or longer, and alcohol drinkers were defined as those who had

drunk at least once per week for 1 year or more. Former smokers (or former alcohol drinkers) were those who had ceased smoking (or alcohol drinking) for 1 or more years before the onset of AMI or the interview. Ethanol intake (mL/day) was assessed for current drinkers based on reported consumption frequencies and amounts of 4 alcoholic beverages (sake, shochu, beer, and spirits). History of diseases related to AMI (hypertension, hyperlipidemia, 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 to calculate a body mass index (kg/m^2) of 25 or greater was defined as overweight.

Ethics

The Fukuoka Heart Study was designed and implemented in accordance with the Declaration of Helsinki adopted by the 18th World Medical Assembly; observational studies were not the subject of review by the institutional ethical committee at the time of the survey. Study subjects were patients with a first episode of AMI and matched community controls. Written informed consent was given by all participating individuals. The anonymized data were used for analysis in the present study. The present study was approved by the institutional review boards of St. Mary's College (IRB# H19-031).

Statistical Analyses

Chi-squared test and unpaired t test were used to compare the frequencies and means of the characteristics between cases and controls. Relative risks (RRs) and their 95% confidence intervals (CIs) were estimated with multiple conditional logistic regression analysis to show the association between the risk of AMI and the factors related to physical activity adjusting for the selected potential confounding factors. Trend of the association was tested by including the median of each category of the covariate to the conditional logistic model.

As indexes of leisure-time physical activity (LTPA), the MET-hours per week for LTPA was categorized into 3 levels in men (29 to 32, 33 to 35 and 36 to 95) in women (23 to 32, 33 to 34 and 35 to 83). Job physical activity (kcal/ kg/ week) and leisure-time physical activity (kcal/kg/week), respectively, were categorized into 3 levels in men (0, 2 to 84 and 85 to 581) in

women (0, 2 to 81 and 82 to 480), and in men (0, 1 to 14 and 15 to 128) and in women (0, 1 to 12 and 13 to 168). Additionally, length of any sports (min/week), frequency of any sports (time/week), length of moderate or more strenuous sports (min/week) were categorized into 3 levels (see tables 2 and 3 for detail). Binary variables for hard sports (no/yes) and moderate or more strenuous sports (no/yes) also were generated and statistically analyzed.

Covariates included in the model were age, overweight, cigarettes smoking, alcohol intake, hypertension, diabetes mellitus, hyperlipidemia, angina pectoris, and parental CHD (angina pectoris and myocardial infarction). In addition, the factor regarding the leisure-time physical activity or the factor regarding job-related physical activity was adjusted for when analyzing the other. Smoking status was categorized into 4 levels in men (never, past, and current smoking of 1-20 or 21+ cigarettes per day) and into 2 levels in women (never, and past combined and current smoking). Alcohol consumption was categorized into 4 levels in men (never, past, and current drinking of 1-30 or 31+ ml of alcohol per day) and into 2 levels in women (never, and past combined and current drinking) because alcohol use was much less. Indicator variables were created for these covariates and included as explanatory variables in the logistic regression models. Two-sided P values less than 0.05 were considered statistically significant. All statistical analyses were performed using Stata Release 12 (Stata Corporation, College Station, TX).

RESULTS

Table 1 shows the characteristics of cases and controls. Compared with control subjects, patients with acute myocardial infarction (AMI) showed less frequent current alcohol use and more prevalent current smokers. More AMI patients had family history of ischemic heart diseases and suffered from hypertension and diabetes mellitus than controls. AMI patients showed a greater proportion of angina pectoris and hyperlipidemia than controls in men, but the difference did not show statistical significance in women. There was no significant difference in age, body mass index and the proportion with regular job between cases and controls in either men or women.

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Table1. Characteristics of cases and controls

	Men				Women					
	Case(n=453)		Control(n=846)		Case(n=172)		Control(n=320)			
	Mean	(SD)	Mean	(SD)	p for difference	Mean	(SD)	Mean	(SD)	p for difference
Age (years)	61.9	(9.6)	62.4	(9.4)	0.37	67.6	(8.3)	67.8	(8.2)	0.76
Body mass index (kg/m ²)	23.3	(3.0)	23.1	(3.0)	0.20	23.2	(3.5)	23.1	(3.4)	0.76
	%		%			%		%		
Regular job	61.1		65.5		0.11	20.9		15.9		0.17
Current alcohol use	45.3		65.7		<0.001	8.7		22.2		<0.001
Current smoking	60.9		45		<0.001	20.9		10.3		<0.01
Family history ¹	16.8		12.1		0.02	18.0		9.4		<0.01
Hyperlipidemia	12.1		6.7		<0.001	14.5		13.4		0.74
Angina pectoris	7.3		2.7		<0.001	7.6		3.8		0.07
Hypertension	30.7		19.5		<0.001	47.7		26.6		<0.001
Diabetes mellitus	16.1		8.0		<0.001	19.8		5.6		<0.001

¹Parents with angina pectoris or myocardial infarction.

Table 2 gives the crude and adjusted relative risks of AMI according to the physical activity in men. Physical activity showed a decreased trend of crude relative risk of AMI in heavier job type, spending longer time on sports activity, higher frequency of sports activity, higher frequency of moderate or strenuous sports activity, and having hard sports activity. Even after adjusting for cigarette smoking, alcohol

drinking, overweight, family history of coronary heart diseases, medical histories of hypertension, diabetes mellitus, hyperlipidemia and angina pectoris, higher frequency of sports activity was associated with a decreased trend of relative risk of AMI (P = 0.03). Having hard sports activity showed low risk of AMI; adjusted relative risk (95% confidence interval) was 0.55 (0.32 to 0.94).

Table2. Relative risks (RR) and their 95% confidence intervals (CI) of acute myocardial infarction according to physical activity in middle-aged and older men in the Fukuoka Heart Study, September 1996 to March 1998.

Men	Case (n=453)	Control (n=846)	Crude matched RR (95% CI)		P for trend	Adjusted matched RR* (95% CI)		P for trend
Total physical activity (kcal/kg/week)								
29 - 32	213	361	1.00 (referent)			1.00 (referent)		
33 - 35	121	222	0.91	(0.68 to 1.22)	0.06	1.01	(0.73 to 1.40)	0.44
36 - 95	119	263	0.75	(0.57 to 1.00)		0.89	(0.65 to 1.23)	
Occupational physical activity (kcal/kg/week)								
0	172	282	1.00 (referent)			1.00 (referent)		
2 - 84	143	284	0.75	(0.54 to 1.04)	0.10	0.74	(0.52 to 1.07)	0.26
85 - 581	138	280	0.71	(0.51 to 1.00)		0.75	(0.52 to 1.09)	
Job intensity type								
No+sedentary job	355	623	1.00 (referent)			1.00 (referent)		
Light mobile	72	136	0.91	(0.66 to 1.27)	<0.01	1.04	(0.72 to 1.50)	0.07
Heavy work	26	87	0.49	(0.30 to 0.80)		0.53	(0.31 to 0.90)	
Leisure-time physical activity (kcal/kg/week)								
0	281	489	1.00 (referent)			1.00 (referent)		
1 - 14	91	188	0.84	(0.63 to 1.13)	0.21	0.92	(0.66 to 1.28)	0.87
15 - 128	81	169	0.82	(0.60 to 1.13)		0.97	(0.69 to 1.38)	
Length of sports activity (min/week)								
0	164	235	1.00 (referent)			1.00 (referent)		
5 - 210	160	317	0.70	(0.52 to 0.94)	<0.01	0.81	(0.59 to 1.12)	0.15
213 - 1920	129	294	0.61	(0.45 to 0.82)		0.75	(0.54 to 1.06)	
Frequency of sports activity (times/week)								
0	164	237	1.00 (referent)			1.00 (referent)		
0.2 - 3.2	168	315	0.75	(0.56 to 1.00)	<0.01	0.88	(0.64 to 1.21)	0.03
3.4 - 10	121	294	0.57	(0.42 to 0.78)		0.68	(0.48 to 0.97)	
Frequency of moderate or more strenuous sports activity (times/week)								
0	281	487	1.00 (referent)			1.00 (referent)		

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0.2 - 1.9	95	176	0.92	(0.68 to 1.25)	0.05	1.01	(0.72 to 1.41)	0.36
1.9 - 8.2	77	183	0.73	(0.54 to 1.00)		0.85	(0.60 to 1.21)	
Length of moderate or more strenuous sports activity (min/week)								
0	281	487	1.00 (referent)			1.00 (referent)		
5 - 182	89	184	0.83	(0.62 to 1.12)	0.20	0.92	(0.66 to 1.28)	0.74
187 - 1920	83	175	0.82	(0.60 to 1.11)		0.94	(0.67 to 1.32)	
Hard sports activity								
No	431	764	1.00 (referent)			1.00 (referent)		
Yes	22	82	0.45	(0.27 to 0.74)		0.55	(0.32 to 0.94)	
Moderate or more strenuous sports activity								
No	281	487	1.00 (referent)			1.00 (referent)		
Yes	172	359	0.82	(0.65 to 1.05)		0.93	(0.71 to 1.21)	
Estimation from conditional logistic regression; * adjusted for cigarette smoking, alcohol drinking, overweight, parent coronary heart diseases, hypertension, diabetes mellitus, hyperlipidemia and angina pectoris.								

Table 3 illustrates the crude and adjusted relative risks of AMI according to the physical activity in women. Having sports activity was associated with a reduced crude relative risk of AMI in women. Longer time spending on sports activity showed a decreasing trend of crude relative risk of AMI (P = 0.04). After adjusting for the above confounding factors, women who engage in any sports showed a low adjusted relative risk of AMI and the adjusted relative risks (95% confidence interval) of AMI for

women who play any sports 0.2 to 4.0 times per week and 4.2 to 8.9 times per week, respectively, were 0.46 (0.27 to 0.79) and 0.58 (0.34 to 0.98) compared to women without any sports. Higher frequency of moderate or more strenuous sports activity was associated with a trend toward reduced adjusted relative risk of AMI. The association between hard sports activity and relative risk of AMI was not statistically significant in women.

Table 3. Relative risks (RR) and their 95% confidence intervals (CI) of acute myocardial infarction according to physical activity in middle-aged and older women in the Fukuoka Heart Study, September 1996 to March 1998.

Women	Case (n=172)	Control (n=320)	Crude matched RR (95% CI)		P for trend	Adjusted matched RR* (95% CI)		P for trend
Total physical activity (kcal/kg/week)								
29 - 32	104	181	1.00 (referent)			1.00 (referent)		
33 - 34	36	79	0.81	(0.51 to 1.30)	0.83	0.77	(0.46 to 1.29)	0.89
35 - 83	32	60	0.90	(0.53 to 1.53)		0.91	(0.50 to 1.65)	
Occupational physical activity (kcal/kg/week)								
0	132	239	1.00 (referent)			1.00 (referent)		
2 - 81	20	39	0.94	(0.52 to 1.72)	0.54	1.25	(0.62 to 2.52)	0.84
82 - 480	20	42	0.81	(0.42 to 1.58)		0.90	(0.43 to 1.91)	
Job intensity type								
No+sedentary job	154	275	1.00 (referent)			1.00 (referent)		
Light mobile	12	28	0.73	(0.35 to 1.50)	0.20	0.72	(0.31 to 1.63)	0.18
Heavy work	6	17	0.57	(0.20 to 1.61)		0.48	(0.15 to 1.55)	
Leisure-time physical activity (any type) (kcal/kg/week)								
0	123	218	1.00 (referent)			1.00 (referent)		
1 - 12	19	54	0.63	(0.36 to 1.09)	0.91	0.56	(0.30 to 1.04)	0.89
13 - 168	30	48	1.13	(0.67 to 1.91)		1.19	(0.65 to 2.20)	
Length of any sports activity (min/week)								
0	74	93	1.00 (referent)			1.00 (referent)		
4 - 180	46	115	0.49	(0.30 to 0.79)	0.04	0.44	(0.26 to 0.75)	0.14
186 - 2520	52	112	0.55	(0.35 to 0.89)		0.61	(0.36 to 1.04)	
Frequency of any sports activity (times/week)								
0	74	93	1.00 (referent)					
0.2 - 4.0	47	118	0.49	(0.30 to 0.78)	0.06	0.46	(0.27 to 0.79)	0.09
4.2 - 8.9	51	109	0.56	(0.35 to 0.89)		0.58	(0.34 to 0.98)	
Frequency of moderate or more strenuous sports activity (times/week)								
0	123	216	1.00 (referent)			1.00 (referent)		
0.2 - 3.2	24	53	0.80	(0.48 to 1.34)	0.50	0.80	(0.44 to 1.44)	0.03
3.9 - 8.0	25	51	0.85	(0.51 to 1.43)		0.76	(0.42 to 1.39)	

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Length of moderate or more strenuous sports activity (min/week)							
0	123	216	1.00 (referent)			1.00 (referent)	
6 - 180	21	61	0.61	(0.36 to 1.04)	0.88	0.54	(0.29 to 0.97) 0.88
186 - 2520	28	43	1.18	(0.68 to 2.05)		1.27	(0.66 to 2.43)
Hard sports activity							
No	166	302	1.00 (referent)			1.00 (referent)	
Yes	6	18	0.59	(0.23 to 1.52)		0.64	(0.21 to 1.93)
Moderate or more strenuous sports activity							
No	123	216	1.00 (referent)			1.00 (referent)	
Yes	49	104	0.83	(0.56 to 1.22)		0.78	(0.50 to 1.22)
Estimation from conditional logistic regression; * adjusted for cigarette smoking, alcohol drinking, overweight, parent coronary heart diseases, hypertension, diabetes mellitus, hyperlipidemia and angina pectoris.							

DISCUSSION

Physical activity is reported to reduce the risk of coronary heart disease in Western countries [3,4,5, 6], and regular physical activity is advocated to reduce the incidence of coronary heart disease events[3,4,5, 6]. In a Danish adult population, Petersen et al.[18] demonstrated that total sitting time is associated with an increased risk of AMI death after controlling for other factors. In addition, the INTERHEART study[6] also demonstrated that physical inactivity increased the risk of AMI after adjusting for other risk factors such as smoking, lack of alcohol intake, hypertension, diabetes, abdominal obesity, and high risk diet. In the present study, frequency of any sports was associated with a decreased risk of AMI in both men and women even after controlling known risk factors for AMI, which suggests that regular physical activity may reduce the risk of AMI in the Japanese population.

Although obesity is reported as an independent risk factor for coronary heart diseases [6, 19], Liu et al [20] reported that body mass index was positively associated with hypertension, diabetes mellitus, and dyslipidemia in the Japanese population. Kaplan proposed the term “deadly quartet” as a profile of a person having high risk of coronary heart disease with a combination of upper-body obesity, glucose intolerance, hypertriglyceridemia, and hypertension [21]. Moerkedal et al [22] demonstrated that metabolically healthy persons with obesity failed to show an increased risk of AMI although metabolically unhealthy individuals without obesity increased the risk of AMI in the Nord-Troendelag study[22] while Ninomiya et al[23] reported that metabolic syndrome increased the risk of coronary artery diseases and the risk increased with the components of metabolic syndrome (i.e., obesity, high blood pressure, elevated fasting glucose level, dyslipidemia) in a Japanese population in the

Hisayama study. In addition, Washio et al [24] reported that metabolic syndrome and each of hypertension, diabetes mellitus, hypertriglycemia and hypo-HDL-cholesterolemia increased the risk of coronary artery sclerosis but obesity did not increase the risk of coronary atherosclerosis. These findings and the result of the present study suggest that persons with physical inactivity may increase the risk of AMI because they are not only obese but also have other AMI risk factors such as hypertension, diabetes mellitus and dyslipidemia.

Regular physical activity is recommended for the prevention of coronary heart diseases. However, too high physical activity is reported to increase the risk of AMI in Western populations [7].In the present study, hard sport was associated with a decreased risk of AMI only in men. Hard sport showed lower relative risk than the unity but it failed to reach statistical significance in women. The present study, however, cases were recruited from AMI patients in hospitals, and we did not obtain the information from AMI patients who died before the interview. If hard exercise was more strongly associated with fatal AMI than with nonfatal AMI, the present study may underestimate the overall risk of AMI associated with hard exercise. Further studies are recommended to answer whether the hard sport may decrease the risk of AMI in Japanese population.

There are certain limitations in the current study. Although the use of community controls was an advantage, the participant rate of control candidate was just over 50%, which raise concerns about the representativeness of control subjects. However, the survey of nonparticipating control candidates revealed that nonparticipating control candidates were almost similar in characteristics to control subjects [11].

In the present study, even after adjusting for confounding factors, high frequency of sports

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activity and high frequency of moderate or strenuous sports activity showed a decreased risk of AMI in both men and women. These findings suggest that sports activity may be inversely associated with the risk of AMI in both male and female Japanese population. The Japanese Ministry of Health, Labour and Welfare proposed "Health Japan 21" [25], analysis and assessment project for national health promotion with quantitative target for healthy life style. In the plan, physical activity is proposed as one of the main theme for health promotion. The results of this study provide a supporting evidence to construct this type of public health project.

CONCLUSIONS

Playing any sports was associated with lower risk of acute myocardial infarction (AMI). Higher frequency of moderate or strenuous sports activity showed a trend toward a decreased relative risk of AMI in women. The present study suggests that sports activity may be inversely associated with the risk of AMI in both Japanese men and women.

ACKNOWLEDGMENTS

We thank the following medical associations for their valuable support: Fukuoka City Medical Association, Division of Internal Medicine of the Fukuoka City Medical Association, Chikushi Medical Association, Itoshima Medical Association, Kasuya Medical Association, and Munakata Medical Association. This study was financially supported by Sankyo, Co Ltd, Japan.

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APPENDIX 1

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Citation: Shoji Tokunaga et.al, “Leisure Time and Job Related Physical Activity and the Risk of Non-Fatal Acute Myocardial Infarction in Japanese Men and Women – A Population Based Case-Control Study”, *International Journal of Research Studies in Medical and Health Sciences*. 2019; 4(4): 15-23.

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