

Physical Conditioning and Vascular Function

Walking and Sports Participation and Mortality From Coronary Heart Disease and Stroke

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OBJECTIVES	We aimed to examine the impact of exercise on mortality from cardiovascular disease (CVD) in Asian populations.
BACKGROUND	Few data have been available in Asian countries, where job-related physical activity is higher than that in Western countries.
METHODS	Between 1988 and 1990, 31,023 men and 42,242 women in Japan, ages 40 to 79 years with no history of stroke, coronary heart disease (CHD), or cancer, completed a self-administered questionnaire. Systematic mortality surveillance was performed through 1999, and 1,946 cardiovascular deaths were identified. We chose the second lowest categories of walking and sports participation as the reference to reduce a potential effect of ill health.
RESULTS	Men and women who reported having physical activity in the highest category (i.e., walking ≥ 1 h/day or doing sports ≥ 5 h/week) had a 20% to 60% lower age-adjusted risk of mortality from CVD, compared with those in the second lowest physical activity category (i.e., walking 0.5 h/day, or sports participation for 1 to 2 h/week). Adjustment for known risk factors, exclusion of individuals who died within two years of baseline inquiry, or gender-specific analysis did not substantially alter these associations. The multivariate-adjusted hazard ratios (95% confidence interval) for the highest versus the second lowest categories of walking or sports participation were 0.71 (0.54 to 0.94) and 0.80 (0.48 to 1.31), respectively, for ischemic stroke (IS); 0.84 (0.64 to 1.09) and 0.51 (0.32 to 0.82), respectively, for CHD; and 0.84 (0.75 to 0.95) and 0.73 (0.60 to 0.90), respectively, for CVD.
CONCLUSIONS	Physical activity through walking and sports participation might reduce the risk of mortality from IS and CHD. (J Am Coll Cardiol 2005;46:1761-7) © 2005 by the American College of Cardiology Foundation

Previous prospective studies have shown an inverse association between physical activity and the risk of developing coronary heart disease (CHD) (1-4) and total or ischemic stroke (IS) (5-7) among whites and Japanese Americans.

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Manuscript received January 6, 2005; revised manuscript received June 13, 2005, accepted July 11, 2005.

The benefits of physical activity include lowered blood pressure (8,9), increased insulin sensitivity (10,11), elevated HDL-cholesterol levels (12), and improved endothelial function (13). To our knowledge, however, no prospective study has reported these effects of exercise in Asian countries, where the prevalence of job-related physical activity has been reported to be high (14).

In the current study we examined the relationship between physical activity through walking and sports participations and the mortality due to stroke, CHD, and total cardiovascular disease (CVD) among Japanese men and women in a large cohort study.

METHODS

Study cohort and baseline questionnaire. The Japan Collaborative Cohort Study for Evaluation for Cancer Risk (JACC), sponsored by Ministry of Education, Science, Sports and Culture of Japan, was undertaken from 1988 to 1990, when 110,792 individuals (46,465 men and 64,327 women) ages 40 to 79 years and living in 45 communities across Japan participated in municipal health screening examinations and completed self-administered questionnaires about their lifestyles and medical histories of previous

Abbreviations and Acronyms

CHD	= coronary heart disease
CI	= confidence interval
CVD	= cardiovascular disease
HR	= hazard ratio
IPH	= intraparenchymal hemorrhage
IS	= ischemic stroke
SAH	= subarachnid hemorrhage

CVD and cancer (15). Informed consent was obtained from all subjects before completing the questionnaire. Of these subjects, 77,676 individuals (32,953 men and 44,723 women) provided a valid response to questions about the average daily time spent walking: "How long on average do you spend walking indoors or outside on a daily basis?" The list of possible answers was: "<0.5 h," "0.5 h," "0.6 to 0.9 h," and "≥1.0 h." Subjects were also questioned about the average weekly time spent in athletic and sporting events: "What is the average amount of time you spend engaging in sports on a weekly basis?" The list of possible answers were: "<1 h," "1 to 2 h," "3 to 4 h," and "≥5 h."

The validity of the estimated time spent participating in sports and leisure time physical activity was examined in a random sample of 739 men and 991 women from the baseline participants (16). The Spearman rank correlation reported that time spent participating in sports with leisure-time physical activity as reported during the previous 12 months, estimated from a structured interview on the basis of the Minnesota leisure-time physical activity questionnaire (17), was 0.53 in men and 0.58 in women. The reliability for time spent walking and engaging in sports was examined 12 months apart in a random sample of 416 men and 636 women. We obtained modest kappa coefficients: 0.32 in men and 0.31 in women for time spent walking (four categories), and 0.45 in men and 0.40 in women for time spent participating in sports (four categories).

We excluded 1,930 men and 2,481 women from the analysis because of a previous history of stroke, CHD, or cancer at the time of baseline inquiry. Therefore, a total 73,265 individuals (31,023 men and 42,242 women) were enrolled in the present study.

Mortality surveillance. To find cohort deaths, the investigators conducted a systematic review of death certificates, all of which were forwarded to the local public health center in each community. It is believed all deaths that occurred in the cohort were ascertained, except for subjects who died after they had moved from their original community, in which case the subject was treated as a censored case. Mortality data were sent centrally to the Ministry of Health and Welfare, and the underlying causes of death were coded for the National Vital Statistics according to the International Classification of Disease, 10th revision. The mortality follow-up inquiry for this study was conducted until the end of 1999, and the average follow-up was 9.7 years. Only 3.4% of the subjects had moved out of the communities and were

treated as censored. The Ethics Committee of the University of Tsukuba approved this study.

Statistical analysis. Statistical analysis was made on the basis of cause-specific mortality rates. Person-years of follow-up were calculated from the date of the baseline questionnaire to the date of death, moving from the community, or the end of 1999, whichever occurred first. The hazard ratio (HR) of mortality from CVD was defined as the death rate for the participants within the four categories of walking time divided by the corresponding rate among those who reported 0.5 h/day of average walking time and for the participants within the four categories of sports participation time divided by the corresponding rate among those who reported 1 to 2 h/week average time in sports.

Age-adjusted means and proportions of selected cardiovascular risk factors were presented among the categories of walking and sports participation. Differences from the second lowest category in gender-specific, age-adjusted mean values and proportions of baseline characteristics were examined with a *t* test or chi-square test. The age-adjusted and multivariate-adjusted HRs and the 95% confidence intervals (CIs) were calculated after adjustment for age, gender, and potential confounding factors with the Cox proportional hazards model. These factors included body mass index (gender-specific quintiles), history of hypertension (no versus yes), history of diabetes (no versus yes), smoking status (never, ex-smoker, and current smokers of 1 to 19 and ≥20 cigarettes/day), alcohol intake category (never, ex-drinker, and current drinker of ethanol at 1 to 22, 23 to 45, 46 to 68, and ≥69 g/day), hours of sleep (<6.0, 6.0 to 6.9, 7.0 to 7.9, 8.0 to 8.9, and ≥9.0 h/day), age of completed education (<13, 13 to 15, 16 to 18, and ≥19 years old), job style (manual worker, non-manual worker, and non-worker), perceived mental stress (low, medium, and high), and frequency of fish intake (0, <1, 1 to 2, 3 to 4, and ≥5 times/week). These factors had been known as cardiovascular risk factors and associated with walking and sports participation at baseline inquiry in this cohort. In the analysis of walking time, we also adjusted for time spent participating in sports, and in the analysis of sports participation, we adjusted for time spent walking.

Because the individuals in the lowest categories were more likely to have ill health and the goal of this study was to study physical activity in healthy subjects, we chose the second lowest categories of walking and sports participation as the reference.

Cause-specific mortality was determined by the total deaths due to stroke (International Classification of Disease, 10th revision, codes I60 to 69), CHD (codes I20 to I25), and total CVD (codes I01 to I99). Stroke was further categorized as subarachnid hemorrhage (SAH) (code I60), intraparenchymal hemorrhage (IPH) (code I61), and IS (code I63). The analysis was repeated by excluding deaths within the first two years after the baseline (476 men and 267 women), to examine the potential effect of any existing

pre-clinical disorders that might have interfered with participation in walking and sports.

RESULTS

A total of 73,265 individuals (31,023 men and 42,242 women) were followed up for an average of 9.7 years, and 1,946 subjects (1,081 men and 865 women) died from CVD. These deaths among men included a total of 499 from stroke (127 IPH, 57 SAH, and 186 IS) and 244 from CHD. The number of deaths among women included a total of 424 from stroke (92 IPH, 98 SAH, and 141 IS) and 153 from CHD.

Table 1 shows gender-specific, selected cardiovascular risk factors according to the four categories of walking time and sports participation time. Compared with men and women who reported 0.5 h/day of walking (second lowest category), those who reported ≥ 1.0 h/day of walking (highest category) were more likely to be manual workers, have a high dietary intake of fish, participate in sports, and were less educated, less likely to have perceived mental stress, and had little history of hypertension and diabetes and a lower mean of body mass index. Men who reported ≥ 1.0 h/day of walking smoked, drank more, and slept more, as compared with those who reported 0.5 h/day of walking. Similar associations were observed according to sports participation categories.

Compared with men and women who reported 0.5 h/day of walking, those who reported ≥ 1.0 h/day walking had a 17% to 33% lower age-adjusted mortality from total stroke, IS, CHD, and total CVD (Table 2). Adjustment for cardiovascular risk factors somewhat attenuated these relationships; however, the risk reduction for IS and total CVD remained statistically significant for men and women combined. The multivariate HR (95% CI) among men and women (combined) who reported a walking time of ≥ 1.0 versus 0.5 h/day was 0.71 (0.54 to 0.94), $p = 0.02$ for IS; 0.84 (0.64 to 1.09), $p = 0.19$ for CHD; and 0.84 (0.75 to 0.95), $p = 0.006$ for total CVD. These inverse associations were similarly observed for each gender, although not statistically significant in either gender.

Strong inverse associations within the sports participation categories were found for mortality from CHD and total CVD (Table 3). The multivariate HR (95% CI) among men and women who reported time spent participating in sports for ≥ 5 versus 1 to 2 h/week was 0.51 (0.32 to 0.82), $p = 0.005$ for CHD and 0.73 (0.60 to 0.90), $p = 0.003$ for total CVD.

We evaluated the HR of death for the lowest versus second lowest categories of time spent walking. The multivariate HR (95% CI) was 1.37 (1.10 to 1.72), $p = 0.005$ for total stroke mortality, and 1.35 (1.16 to 1.57), $p < 0.001$ for total CVD mortality.

These inverse associations for walking and sports participation time with mortality were not altered substantially when deaths occurring within two years after baseline were

Table 1. Gender-Specific Age-Adjusted Mean Values or Prevalence of Cardiovascular Risk Factors at Baseline According to Walking Time and Sports Time

	Walking Time (h/Day)								Sports Time (h/Week)							
	Men				Women				Men				Women			
	<0.5	0.5	0.6-0.9	≥ 1.0	<0.5	0.5	0.6-0.9	≥ 1.0	<1	1-2	3-4	≥ 5	<1	1-2	3-4	≥ 5
No. at risk	3,865	5,770	5,962	15,426	4,644	7,404	8,595	21,599	21,133	5,299	2,211	2,380	31,921	5,934	2,299	2,088
Percentage at risk	12.5	18.6	19.2	49.7	11.0	17.5	20.3	51.1	68.1	17.1	7.1	7.7	75.6	14.0	5.4	4.9
Age, yrs	56.1*	57.2	57.8†	57.5‡	56.7*	57.9	57.8	57.5†	56.8‡	56.5	59.2*	62.1*	57.1	57.4	59.8*	62.4*
Body mass index, kg/m ²	22.9‡	22.8	22.7	22.5†	23.1†	22.9	22.9	22.8†	22.6	22.7	22.7	22.7	22.9	22.9	22.8	22.9
History of hypertension, %	19.4	19.8	20.3	17.0*	21.3	21.1	20.9	19.4†	18.1	19.2	20.0	18.6	20.2	21.1	19.8	19.1‡
History of diabetes, %	6.9	7.5	6.0*	5.0*	4.2	4.6	4.0‡	2.8*	5.6*	6.6	6.5	6.4	3.4‡	4.0	4.1	4.0
Ethanol intake, g/day	35.6*	31.8	32.9‡	35.3*	12.9*	10.3	9.4	10.4	34.9*	32.2	32.7	34.4†	10.6	9.8	9.9	10.4
Hours of sleep, h/day	7.45†	7.39	7.41	7.48*	7.14†	7.08	7.07	7.08	7.46†	7.41	7.41	7.51*	7.09	7.07	7.05	7.12
Current smoker, %	49.4	49.1	49.3	52.4*	5.5†	4.4	4.3	4.3	52.1*	48.0	47.3	49.1	4.6*	3.5	4.5‡	4.3
College or higher education, %	14.0*	20.9	19.6	12.3*	7.5*	10.6	9.7	8.6*	13.5*	20.3	21.3	16.9*	8.3*	11.9	12.0	9.8†
Office worker, %	15.4*	23.6	18.7*	7.0*	7.5*	9.0	7.4*	4.3*	11.6*	18.5	18.9*	12.8	5.7*	7.9	6.7‡	5.6*
Manual worker, %	38.1*	29.1	34.0*	47.6*	23.8*	18.4	18.0	22.9*	43.2*	34.9	30.7	36.5*	22.0*	18.5	17.4	20.8‡
High perceived mental stress, %	26.9	26.8	23.4*	20.5*	22.2	20.8	19.6	19.5†	23.2	22.9	21.1	22.7	20.6*	18.4	18.7	17.9
Frequency of fish intake, n/week	6.7†	6.5	6.8*	7.1*	6.8	6.9	7.0	7.2*	6.9	6.8	6.8	7.2*	7.0*	7.2	7.1	7.4
Sports 5 h/week and more, %	1.6*	3.6	6.1*	11.3*	1.1	1.6	3.3*	7.6*	—	—	—	—	—	—	—	—
Walking 1.0 h/day and more, %	—	—	—	—	—	—	—	—	48.6*	44.1	47.9†	73.8*	49.4	48.6	56.6*	78.7*

†p < 0.001; ‡p < 0.01; §p < 0.05.

Table 2. Hazard Ratios (95% CI) of Mortality from Cardiovascular Disease According to Walking Time

	Walking Time (h/Day)											
	Men				Women				Men and Women			
	<0.5	0.5	0.6-0.9	≥1.0	<0.5	0.5	0.6-0.9	≥1.10	<0.5	0.5	0.6-0.9	≥1.0
Person-yr	36,354	54,499	56,595	148,929	44,804	71,557	83,491	211,995	81,158	126,056	140,085	360,924
Total stroke												
n	70	103	89	237	72	82	76	194	142	185	165	431
Age-adjusted HR	1.24 (0.91-1.68)	1.0	0.76 (0.57-1.01)	0.81 (0.64-1.02)	1.69 (1.23-2.32)	1.0	0.81 (0.59-1.10)	0.87 (0.67-1.13)	1.44 (1.16-1.79)	1.0	0.78 (0.63-0.96)	0.83 (0.70-0.99)
Multivariate HR*	1.15 (0.84-1.57)	1.0	0.79 (0.59-1.05)	0.84 (0.67-1.07)	1.66 (1.20-2.30)	1.0	0.82 (0.60-1.12)	0.93 (0.72-1.21)	1.37 (1.10-1.72)	1.0	0.80 (0.65-0.99)	0.88 (0.74-1.05)
IPH												
n	19	29	27	52	17	17	18	40	36	46	45	92
Age-adjusted HR	1.12 (0.63-1.99)	1.0	0.84 (0.50-1.43)	0.64 (0.41-1.00)	1.87 (0.95-3.66)	1.0	0.92 (0.47-1.78)	0.85 (0.48-1.50)	1.39 (0.90-2.15)	1.0	0.87 (0.57-1.31)	0.71 (0.50-1.02)
Multivariate HR*	1.12 (0.62-2.02)	1.0	0.88 (0.52-1.49)	0.73 (0.46-1.16)	1.89 (0.95-3.76)	1.0	0.95 (0.49-1.84)	0.93 (0.52-1.66)	1.38 (0.89-2.15)	1.0	0.90 (0.60-1.37)	0.80 (0.56-1.15)
SAH												
n	6	10	7	34	11	15	20	52	17	25	27	86
Age-adjusted HR	0.93 (0.34-2.55)	1.0	0.67 (0.25-1.76)	1.24 (0.61-2.51)	1.32 (0.61-2.87)	1.0	1.14 (0.58-2.23)	1.21 (0.68-2.15)	1.15 (0.62-2.14)	1.0	0.95 (0.55-1.64)	1.21 (0.78-1.89)
Multivariate HR*	0.97 (0.35-2.73)	1.0	0.67 (0.25-1.77)	1.26 (0.61-2.60)	1.40 (0.64-3.08)	1.0	1.08 (0.55-2.11)	1.22 (0.68-2.19)	1.24 (0.66-2.31)	1.0	0.93 (0.54-1.61)	1.25 (0.80-1.97)
Ischemic stroke												
n	26	45	28	87	26	34	21	60	52	79	49	147
Age-adjusted HR	1.12 (0.69-1.81)	1.0	0.54 (0.33-0.86)	0.67 (0.47-0.96)	1.53 (0.92-2.55)	1.0	0.54 (0.32-0.94)	0.67 (0.44-1.03)	1.30 (0.92-1.85)	1.0	0.54 (0.38-0.76)	0.67 (0.51-0.88)
Multivariate HR*	1.03 (0.63-1.69)	1.0	0.56 (0.35-0.91)	0.71 (0.49-1.02)	1.38 (0.82-2.33)	1.0	0.56 (0.32-0.97)	0.73 (0.48-1.13)	1.18 (0.82-1.69)	1.0	0.56 (0.39-0.80)	0.71 (0.54-0.94)
CHD												
n	39	48	48	109	21	36	34	62	60	84	82	171
Age-adjusted HR	1.45 (0.95-2.22)	1.0	0.89 (0.60-1.33)	0.80 (0.57-1.13)	1.12 (0.66-1.93)	1.0	0.82 (0.52-1.32)	0.64 (0.42-0.97)	1.32 (0.95-1.84)	1.0	0.85 (0.63-1.16)	0.73 (0.56-0.95)
Multivariate HR*	1.56 (1.01-2.41)	1.0	0.91 (0.61-1.36)	0.93 (0.66-1.32)	1.04 (0.60-1.80)	1.0	0.82 (0.51-1.32)	0.74 (0.49-1.13)	1.34 (0.96-1.89)	1.0	0.89 (0.65-1.21)	0.84 (0.64-1.09)
Total CVD												
n	155	225	202	499	145	176	173	371	300	401	375	870
Age-adjusted HR	1.24 (1.01-1.52)	1.0	0.79 (0.66-0.96)	0.78 (0.67-0.92)	1.59 (1.28-1.99)	1.0	0.86 (0.70-1.06)	0.79 (0.66-0.94)	1.40 (1.20-1.62)	1.0	0.82 (0.71-0.94)	0.78 (0.69-0.88)
Multivariate HR*	1.21 (0.98-1.49)	1.0	0.83 (0.68-1.00)	0.85 (0.72-1.00)	1.50 (1.20-1.87)	1.0	0.87 (0.70-1.07)	0.85 (0.70-1.02)	1.35 (1.16-1.57)	1.0	0.85 (0.74-0.98)	0.84 (0.75-0.95)

*Adjusted for age, gender, sports time, and cardiovascular risk factors.

CHD = coronary heart disease; CI = confidence interval; CVD = cardiovascular disease; HR = hazard ratios; IPH = intraparenchymal hemorrhage; SAH = subarachnoid hemorrhage.

Table 3. Hazard Ratios (95% CI) of Mortality from Cardiovascular Disease According to Sports Time

	Sports Time (h/Week)											
	Men				Women				Men and Women			
	<1	1-2	3-4	≥5	<1	1-2	3-4	≥5	<1	1-2	3-4	≥5
Person-yr	201,833	50,934	20,946	22,663	311,184	58,081	22,287	20,294	513,017	109,015	43,233	42,958
Total stroke												
n	337	70	46	46	317	61	25	21	654	131	71	67
Age-adjusted HR	1.37 (1.06-1.77)	1.0	1.17 (0.80-1.70)	0.88 (0.60-1.27)	1.04 (0.79-1.37)	1.0	0.79 (0.50-1.26)	0.60 (0.36-0.98)	1.23 (1.02-1.48)	1.0	1.00 (0.75-1.33)	0.75 (0.56-1.01)
Multivariate HR*	1.26 (0.97-1.64)	1.0	1.17 (0.81-1.71)	0.87 (0.59-1.27)	0.88 (0.67-1.17)	1.0	0.79 (0.49-1.26)	0.57 (0.35-0.95)	1.09 (0.90-1.32)	1.0	1.01 (0.76-1.35)	0.75 (0.55-1.01)
IPH												
n	91	17	12	7	72	13	4	3	163	30	16	10
Age-adjusted HR	1.42 (0.85-2.39)	1.0	1.36 (0.65-2.84)	0.61 (0.25-1.48)	1.10 (0.61-1.98)	1.0	0.63 (0.20-1.92)	0.44 (0.12-1.53)	1.29 (0.88-1.91)	1.0	1.05 (0.57-1.92)	0.53 (0.26-1.09)
Multivariate HR*	1.41 (0.83-2.40)	1.0	1.41 (0.67-2.97)	0.67 (0.27-1.64)	0.84 (0.46-1.55)	1.0	0.61 (0.20-1.87)	0.40 (0.11-1.41)	1.17 (0.78-1.74)	1.0	1.08 (0.59-1.99)	0.56 (0.27-1.16)
SAH												
n	34	14	4	5	67	17	10	4	101	31	14	9
Age-adjusted HR	0.60 (0.32-1.13)	1.0	0.66 (0.22-2.02)	0.71 (0.25-1.98)	0.78 (0.46-1.32)	1.0	1.29 (0.59-2.81)	0.49 (0.16-1.45)	0.70 (0.47-1.05)	1.0	0.99 (0.53-1.86)	0.57 (0.27-1.21)
Multivariate HR*	0.56 (0.30-1.07)	1.0	0.66 (0.22-2.03)	0.65 (0.23-1.85)	0.70 (0.41-1.21)	1.0	1.23 (0.56-2.70)	0.45 (0.15-1.36)	0.64 (0.43-0.97)	1.0	0.95 (0.51-1.80)	0.53 (0.25-1.12)
Ischemic stroke												
n	126	25	18	17	109	18	6	8	235	43	24	25
Age-adjusted HR	1.50 (0.97-2.30)	1.0	1.21 (0.66-2.22)	0.84 (0.45-1.55)	1.23 (0.75-2.03)	1.0	0.61 (0.24-1.53)	0.71 (0.31-1.62)	1.41 (1.02-1.96)	1.0	0.97 (0.59-1.60)	0.78 (0.47-1.27)
Multivariate HR*	1.34 (0.86-2.08)	1.0	1.22 (0.66-2.25)	0.84 (0.45-1.57)	1.07 (0.64-1.77)	1.0	0.62 (0.25-1.58)	0.73 (0.31-1.70)	1.26 (0.90-1.75)	1.0	1.00 (0.61-1.66)	0.80 (0.48-1.31)
CHD												
n	153	49	22	20	118	23	8	4	271	72	30	24
Age-adjusted HR	0.88 (0.64-1.21)	1.0	0.83 (0.50-1.37)	0.57 (0.34-0.96)	1.04 (0.67-1.63)	1.0	0.67 (0.30-1.49)	0.30 (0.10-0.86)	0.95 (0.73-1.23)	1.0	0.77 (0.50-1.18)	0.49 (0.31-0.78)
Multivariate HR*	0.84 (0.60-1.17)	1.0	0.86 (0.52-1.43)	0.60 (0.36-1.03)	0.91 (0.58-1.44)	1.0	0.71 (0.31-1.59)	0.30 (0.10-0.87)	0.89 (0.68-1.16)	1.0	0.80 (0.52-1.22)	0.51 (0.32-0.82)
Total CVD												
n	720	183	87	91	660	107	49	49	1380	290	136	140
Age-adjusted HR	1.11 (0.94-1.30)	1.0	0.86 (0.66-1.11)	0.68 (0.53-0.87)	1.24 (1.01-1.52)	1.0	0.88 (0.63-1.23)	0.78 (0.56-1.10)	1.18 (1.04-1.33)	1.0	0.86 (0.70-1.06)	0.71 (0.58-0.87)
Multivariate HR*	1.05 (0.89-1.24)	1.0	0.87 (0.67-1.12)	0.70 (0.54-0.90)	1.09 (0.88-1.34)	1.0	0.89 (0.63-1.25)	0.81 (0.57-1.14)	1.07 (0.94-1.22)	1.0	0.88 (0.72-1.08)	0.73 (0.60-0.90)

*Adjusted for age, gender, walking time, and cardiovascular risk factors.
Abbreviations as in Table 2.

excluded (data not shown). The multivariate HR (95% CI) among men and women (combined) for time spent walking for ≥ 1.0 versus 0.5 h/day was 0.73 (0.54 to 0.97), $p = 0.032$ for mortality due to IS; 0.85 (0.64 to 1.13), $p = 0.263$, for CHD; and 0.87 (0.76 to 0.99), $p = 0.028$ for total CVD. The multivariate HR (95% CI) among men and women (combined) for time spent participating in sports for ≥ 5 versus 1 to 2 h/week was 0.47 (0.28 to 0.78), $p = 0.004$ for mortality due to CHD and 0.78 (0.63 to 0.97), $p = 0.03$ for total CVD mortality.

DISCUSSION

In the present large prospective study of Japanese men and women, we observed approximately a 20% to 50% reduction in mortality due to IS, CHD, and total CVD associated with higher physical activity through walking and sports participation. These relationships were not substantially altered after adjustment for known risk factors or when deaths that occurred within two years were excluded from the analysis.

Our findings are consistent with previous reports of Americans (1,2,5,6), Japanese-Americans (4,7), and Europeans (3) and meta-analyses (18,19). Total physical activity (>21.7 vs. 0 to 2.0 MET-h/week), physical activity through walking (≥ 10 vs. ≤ 0.5 MET-h/week), and walking pace (≥ 3 vs. < 2 mph) were associated with 34%, 35%, and 36% respective reductions in the risk of developing CHD (1), and 48%, 40%, and 53% respective reductions in risk of IS (5) for American nurses. Similar risk reductions (approximately 30% to 50%) for CHD (3,4) and IS (7) associated with walking and leisure-time physical activity were found for Japanese-American men and European men. In previous meta-analyses, high activity and moderate activity were associated with 37% and 10% respective risk reduction of mortality from CHD (18), and high activity and moderate activity were associated with 21% and 9% respective risk reduction of incidence or mortality from IS (19), compared with low activity.

We did not find any significant inverse association between physical activity and mortality from IPH or SAH. This finding is consistent with the results of studies examining American nurses (5) but not of American male physicians (6) and Japanese-American men (7). American male physicians (6) who exercised ≥ 5 versus < 1 time/week had a 46% lower risk for hemorrhagic stroke, but this association was observed only among subjects ages 55 to 68 years but not for those 40 to 54 years of age. Japanese-American men who were physically active had a 73% lower risk of hemorrhagic stroke mortality (7), compared with non-active men.

Furthermore, our data suggest a potential differential effect of walking versus sports participation on IS and CHD risk. We found that participation in sports was associated with a reduced mortality due to CHD, but this association did not exist with walking time. Walking time, however,

was associated with a reduced risk for mortality from IS, but sports participation was not. A similar pattern of association between physical activity and CHD was observed in previous studies (2,3). In a study of American male health professionals (2), average exercise intensity was associated with reduced risk of CHD, independent of total physical activity. In European men (3), energy expenditure during engagement in leisure-time physical activity was associated with a lower risk of CHD, whereas walking or cycling to work was not. A reason for reduced mortality from IS by walking but not by sports participation in our study is uncertain. One of the potential mechanisms for the differential association might be a differential effect of physical activity intensity on insulin resistance. Reduced insulin resistance by moderate-intensity exercise was larger than by high-intensity exercise, when the amount of physical activity was not large (11). Insulin resistance raises the risk of IS more than that of CHD (20,21). Therefore, moderate intensity physical activity similar to walking (17) is more likely to improve insulin resistance and might reduce the risk of IS to a greater degree than the risk of CHD.

Common mechanisms for a reduced risk of IS and CHD associated with walking or sports participation include improved endothelial function (13), an increase in HDL-cholesterol levels (12), and the lowering of ambulatory blood pressure through decreased sympathetic nervous activity (8,9). Previous cohort studies revealed that glucose intolerance (22,23), low HDL-cholesterol levels (24,25), and high blood pressure (26, 27) raised the risk of IS and CHD, and in hypertensive patients, endothelial dysfunction raised the risk of cardiovascular events (28). In the present study, the prevalence of a history of hypertension and diabetes was lower for subjects of both genders who spent more time walking or participating in sports.

Limitations of the present study included the fact that we did not have systematic information on pre-clinical disorders that prevented the participants from walking or participating in sports. This might have lead to a bias of cause-effect reversal, even though most of the subjects were apparently healthy. To avoid the potential bias due to pre-clinical disorders and/or psychosocial distress, we chose the second lowest physical activity categories as a reference. In fact, persons with the lowest categories of physical activity were more overweight, drank more, were more mentally stressed, and less educated. This probably leads to an underestimate of HRs. We also repeated the data analysis by excluding early deaths, which would also reduce the potential confounding effect of pre-clinical disorders.

A second limitation of the current study was that we did not have incidence data. We used the death certificate and did not validate causes of death; however, previous studies have shown that death certificate diagnosis with regard to stroke subtypes is valid, owing to the high prevalence of CT scan or MRI use in hospitals in Japan (29,30).

The strength of the present study is a statistical power sufficient to detect the effects of physical activity on mor-

tality from CVD. We found a significant inverse association between time spent walking and the risk of IS in addition to an inverse relationship between sports participation and risk of CHD in Asian countries, where job-related physical activity is generally higher than in Western countries (14).

In conclusion, the present study provides epidemiological evidence that engaging in physical activity through walking and sports participation might reduce risk of mortality from IS and CHD among Japanese men and women.

Acknowledgments

The authors sincerely express their appreciation to Dr. Kunio Aoki, Professor Emeritus, Nagoya University School of Medicine and the former chairman of the JACC Study, and to Dr. Haruo Sugano, the former Director, Cancer Institute, Tokyo, who greatly contributed to the initiation of the JACC Study. We thank Dr. Aaron R. Folsom, University of Minnesota, for his valuable scientific suggestions.

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