Heart Vessels (2010) 25:113–120
DOI 10.1007/s00380-009-1173-y



ORIGINAL ARTICLE

**Keishi Saihara · Shuichi Hamasaki · Sanemasa Ishida
Tetsuro Kataoka · Akiko Yoshikawa · Koji Orihara
Masakazu Ogawa · Naoya Oketani · Tsuyoshi Fukudome
Nobuhiko Atsuchi · Takuro Shinsato · Hideki Okui
Takuro Kubozono · Hitoshi Ichiki · So Kuwahata
Etsuko Mizoguchi · Shoji Fujita · Takuro Takumi
Yuichi Ninomiya · Kaai Tomita · Chuwa Tei**

# Enjoying hobbies is related to desirable cardiovascular effects

Received: July 14, 2008 / Accepted: May 7, 2009

**Abstract** An unhealthy lifestyle can increase the risk of cardiovascular disease. However, the mechanism by which lifestyle influences the development of cardiovascular disease remains unclear. Since coronary endothelial function is a predictor of cardiovascular prognosis, the goal of this study was to characterize the effect of enjoying hobbies on coronary endothelial function and cardiovascular outcomes. A total of 121 consecutive patients (76 men, 45 women) with almost normal coronary arteries underwent Doppler flow study of the left anterior descending coronary artery following sequential administration of papaverine, acetylcholine, and nitroglycerin. On the basis of responses to questionnaires, patients were divided into two groups; the Hobby group ($n$ = 71) who enjoyed hobbies, and the Non-hobby group ($n$ = 50) who had no hobbies. Cardiovascular outcomes were assessed at long-term follow-up using medical records or questionnaire surveys for major adverse cardiovascular events (MACE).The average follow-up period was 916 ± 515 days. There were no significant differences in demographics when comparing the two groups. The percent change in coronary blood flow and coronary artery diameter induced by acetylcholine was significantly greater in the Hobby group than in the Non-hobby group (49% ± 77% vs 25% ± 37%, $P < 0.05$, 4% ± 13% vs –3% ± 20%, $P < 0.05$, respectively). The MACE rate was significantly lower in the Hobby group than in the Non-hobby group ($P < 0.01$). Enjoyment of hobbies was the only independent predictor of MACE (odds ratio 8.1 [95% confidence interval 1.60, 41.90], $P = 0.01$) among the variables tested. In the early stages of arteriosclerosis, enjoying hobbies may improve cardiovascular outcomes via its favorable effects on coronary endothelial function.

**Key words** Hobby · Coronary · Endothelial function · Cardiovascular · Major adverse cardiovascular event

K. Saihara · S. Hamasaki (✉) · S. Ishida · T. Kataoka · A. Yoshikawa · K. Orihara · M. Ogawa · N. Oketani · T. Fukudome · N. Atsuchi · T. Shinsato · H. Okui · T. Kubozono · H. Ichiki · S. Kuwahata · E. Mizoguchi · S. Fujita · T. Takumi · Y. Ninomiya · K. Tomita · C. Tei
Department of Cardiovascular, Respiratory and Metabolic Medicine, Graduate School of Medicine, Kagoshima University, 8-35-1 Sakuragaoka, Kagoshima 890-8520, Japan
Tel. +81-99-275-5318; Fax +81-99-265-8447
e-mail: hamasksh@m.kufm.kagoshima-u.ac.jp

A portion of this study was presented at the 56th American College of Cardiology Meeting, 2007.

## Introduction

Endothelial dysfunction is present in the coronary and peripheral arteries in patients with chronic heart failure (CHF).[1,2] An important consequence of endothelial dysfunction is an impairment in nitric oxide (NO) release,[3] which results in the inability of a vessel to dilate in response to various physiological stimuli. Accumulating evidence suggests that endothelial dysfunction contributes to exercise intolerance, impaired myocardial perfusion, and left ventricular remodeling in patients with CHF. In patients with previous myocardial infarction, exercise training improves endothelium-dependent vasodilation, and this improvement is associated with a significant increase in exercise tolerance.[4] Further, NO has antiarteriosclerotic properties, and endothelial dysfunction is an independent risk factor for cardiovascular disease, including hypertension, peripheral vascular disease, and coronary artery disease.[5,6]

Endothelial function may also vary with lifestyle, including physical activity, stress, and quality of life. Indeed, interventions with an aggressive focus on lifestyle changes (smoking cessation, diet, exercise, and avoiding stress) produce favorable cardiovascular outcomes in patients treated with percutaneous coronary intervention.[7] Further, modifiable lifestyle factors (smoking, physical activity, and body mass index) in middle-aged men play an important role in long-term survival free of cardiovascular disease and diabetes.[8] Life stress is also thought to alter the dynamic regulation of the autonomic, neuroendocrine, and immune

systems, and high stress contributes to a higher risk of mortality from ischemic heart disease in younger men.[9]

Enjoying hobbies may relieve stress and increase quality of life. For example, Sivasankaran et al. reported that yoga and meditation programs improve endothelial function in patients with coronary artery disease.[10] However, the relationship among enjoying hobbies, coronary endothelial function, and cardiovascular prognosis remains unclear. Therefore, the goal of this study was to characterize the effect of enjoying hobbies on coronary endothelial function and cardiovascular outcomes.

## Subjects and methods

### Patients

One hundred and twenty-one patients (mean age ± SD 62.0 ± 12.8 years, age range 17–80 years; 76 men, 45 women) with angiographically normal or near-normal (% diameter stenosis <30%) epicardial coronary arteries characterized in the course of cardiac catheterization for investigation of chest pain or abnormal noninvasive examinations were enrolled in this study.

### Procedures

Pharmacologic-induced vasodilating function was assessed with a Doppler guide wire and represented as a change in coronary blood flow and coronary artery diameter. Study inclusion criteria were: (1) presence of angiographically smooth arteries, (2) mild irregularities with no coronary artery lesion >30% lumen diameter stenosis by visual assessment in major epicardial vessels, (3) proximal coronary arteries >2.0 mm, and (4) presence of single, discrete, and circular lesion with a smooth reference lesion.[11] Patients with previous myocardial infarction, previous coronary revascularization, or variant angina were excluded. Cardiac medications were withheld for at least 48 h before the study. Written informed consent was obtained from all patients before catheterization in accordance with guidelines established by the Committee for the Protection of Human Subjects at our institution. Diagnostic coronary angiography was performed using a 6-F Judkins catheter with a standard femoral artery percutaneous approach. Five thousand units of heparin were administered at the beginning of the procedure. Nonionic contrast material was used for all patients. No nitroglycerin was given prior to diagnostic procedures. Coronary blood flow (CBF) response to papaverine, acetylcholine (ACh), and nitroglycerin was studied according to protocols described previously.[12–14] After completion of the diagnostic catheterization, interventions were performed as follows: (1) introduction of a 0.014-inch Doppler guide wire (Cardiometrics, Santa Ana, CA, USA) into the left anterior descending coronary artery; (2) after obtaining a stable Doppler signal, a bolus of papaverine (an endothelium-independent vasodilator in resistance coronary arteries; 12.5 mg/5 ml) was injected through a catheter; and (3) infusion of ACh (an endothelium-dependent vasodilator in resistance and epicardial coronary arteries; 0.5 ml/min) at dosages of either 3 or 30 μg/min for 2 min via the catheter.[14,15] Drugs were infused at least 5 min apart. Coronary arteriography was performed before and immediately after infusion of each agent. Phasic coronary blood flow velocities, arterial blood pressure, and heart rate were monitored continuously and recorded. Measurements obtained during steady state conditions were used as control values for later analysis.

### Assessment of pharmacologic-induced coronary vasodilating function

Doppler flow velocity spectra were analyzed on-line to determine time-averaged peak velocity. Volumetric CBF was determined from the formula: CBF = cross-sectional area × average peak velocity × 0.5.[16] Coronary flow reserve to papaverine was calculated as the ratio of maximal CBF induced by papaverine to basal CBF, which was equivalent to the endothelium-independent function of the resistance coronary artery. Change in coronary artery diameter (CAD) in response to nitroglycerin, which reflects the endothelium-independent function of the epicardial coronary artery, was also calculated by similar methods. Endothelium-dependent function of the resistance coronary artery was calculated as the percent increase in CBF in response to ACh, and the percent increase in CAD induced by ACh was calculated as estimation of endothelium-dependent function of the epicardial coronary artery.[12–14]

### Long-term follow-up

Data for clinical long-term follow-up were obtained from hospital charts and through telephone interviews with patients, conducted by trained reviewers who were blinded to treatment assignment. Informed consent was obtained from all patients to allow use of these data for study analyses. Compliance was assessed and confirmed via patient interview by the physician upon hospital admission.

Study patients were assigned to either the "Hobby group" or "Non-hobby group" based on the response to the question, "Have you engaged in any pleasurable hobbies for more than one year?" The Hobby group was further subdivided into the Outdoor-hobby group and Indoor-hobby group. The following clinical events were reported as major adverse cardiovascular events (MACE): cardiac death, hospitalization due to heart failure, occurrence of fatal arrhythmia or myocardial infarction, or need for percutaneous coronary intervention or coronary artery bypass grafting. The first MACE was used for analysis. If a primary end point was reached, information regarding potential cardiovascular events was validated by review of source data. The decision that a patient had reached a primary end point was made only after reviewing the medical records. The relationship between questionnaire results, coronary endothelial function, and cardiovascular prognosis were fully examined.

### Coronary endothelial function and cardiovascular prognosis

Patients were divided into one of two groups according to ACh responsivity of epicardial and resistance coronary arteries. At the level of epicardial coronary artery, patients were subdivided into one of two groups: the Normal ACh CAD response group ($n$ = 65), reflecting an increased percent increase in CAD in response to ACh, and the Poor ACh CAD response group ($n$ = 56), reflecting a decreased percent increase in CAD in response to ACh. Further, at the resistance coronary vessel level, patients were subdivided into one of two groups: the Normal ACh CBF group, reflecting a percent increase in CBF >50% ($n$ = 37), and the Poor ACh CBF response group, reflecting a percent increase in CBF <50% ($n$ = 84). Cardiovascular outcomes were compared between the two groups.

### Statistical analysis

All measurements and analysis were performed in a blinded fashion. Statistical analysis was performed with StatView, version 5.0 (SAS Institute, Cary, NC, USA). Comparisons between variables and between groups were conducted by Student's regression analysis unpaired/paired $t$-test or the two-tailed multiple $t$-test with Bonferroni correction following analysis of variance. Event-free survival curve was analyzed with Kaplan–Meier methods, and the $P$ value was obtained using Cox regression analysis. Multivariate regression analysis was performed to identify the effects of enjoying hobbies and the classical risk factors for MACE as independent predictors of cardiovascular prognosis. A two-tailed probability value of less than 0.05 was considered statistically significant. Results are expressed as mean ± SD unless otherwise indicated.

## Results

A total of 121 patients were enrolled in this study (76 male, 45 female,). The mean age was 62.0 ± 12.8 years (range, 17–80 years). Questionnaire responders who enjoyed hobbies had a significantly greater MACE-free ratio and improved coronary endothelial function when compared with those that did not enjoy hobbies (97.2% vs 82.0%, $P < 0.05$). The Hobby group consisted of 71 patients who enjoyed hobbies, and the Non-hobby group consisted of 50 patients who did not have hobbies. Hobby details are summarized in Table 1. One hundred and twenty-one patients enjoyed a total of 157 hobbies; 81 of which were indoor hobbies and 76 of which outdoor hobbies (1.3 hobbies per patient). Twenty-one patients enjoyed only outdoor hobbies, 32 patients enjoyed only indoor hobbies, and 18 patients enjoyed both types of hobbies. Thirty-one patients, including 18 patients who enjoyed both types of hobbies, enjoyed outdoor hobbies (Outdoor-hobby group). Fifty patients, including 18 patients who enjoyed both types of hobbies, enjoyed indoor hobbies (Indoor-hobby group). The other 50 patients had no hobbies.

Patient characteristics of both groups are summarized in Table 2. There was no significant difference in age, sex, body mass index, classical coronary risk factors, and systemic blood pressure when comparing the two groups. There were no significant differences in the proportion of patients who were taking angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, statins, calcium channel blockers, and aspirin when comparing the two groups.

Clinical characteristics of the two groups are summarized in Table 3. There was no significant difference in the total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, fasting plasma glucose, hemoglobin A1c, and creatinine when comparing the two groups.

Table 4 shows the hemodynamic parameters of the two groups. There was no significant difference in left ventricular end-diastolic dimension, left atrial dimension, left ventricular ejection fraction, left ventricular mass, biventricular Tei index, heart rate, pulmonary capillary wedge pressure, mean pulmonary artery pressure, and cardiac index when comparing the two groups.

### Changes in coronary blood flow

The percent increase in CBF induced by ACh was significantly greater in the Hobby group than in the Non-hobby

**Table 1.** Hobby details

| | |
|---|---|
| Indoor hobby ($n$ = 81) | Outdoor hobby ($n$ = 76) |
| Reading books ($n$ = 19) | Farming, gardening ($n$ = 27) |
| Handicrafts, sewing ($n$ = 8) | Fishing ($n$ = 13) |
| Watching movies ($n$ = 6) | Playing golf ($n$ = 6) |
| Computer games ($n$ = 6) | Going for a drive ($n$ = 5) |
| Playing musical instruments ($n$ = 5) | Jogging, walking ($n$ = 4) |
| Playing the game of "Go" ($n$ = 5) | Ground-golf ($n$ = 3) |
| Taking care of a pet ($n$ = 4) | Taking pictures or movies ($n$ = 2) |
| Listening to music ($n$ = 4) | Softball ($n$ = 2) |
| Karaoke, chorus ($n$ = 5) | Mini-volleyball ($n$ = 2) |
| Cooking ($n$ = 2) | Japanese croquet ($n$ = 2) |
| Drawing pictures ($n$ = 2) | Japanese dancing ($n$ = 2) |
| Others ($n$ = 15) | Others ($n$ = 8) |

**Table 2.** Comparison of patient characteristics between two groups

| | Hobby group ($n$ = 71) | Non-hobby group ($n$ = 50) | $P$ value |
|---|---|---|---|
| Age (years) | 60.4 ± 11.9 | 64.3 ± 13.8 | 0.10 |
| Sex, male/female | 44/27 | 32/18 | 0.82 |
| BMI | 24.0 ± 3.4 | 23.0 ± 3.8 | 0.17 |
| Systolic BP/diastolic BP | 129 ± 21/75 ± 15 | 125 ± 23/72 ± 14 | 0.38 |
| Coronary risk factors | | | |
| Smoking (%) | 27 (38) | 21 (42) | 0.67 |
| Hypertension (%) | 41 (58) | 33 (66) | 0.60 |
| Hyperlipidemia (%) | 33 (46) | 23 (46) | 0.96 |
| Diabetes (%) | 13 (18) | 9 (18) | 0.97 |
| Medical profile | | | |
| ACEI (%) | 12 (17%) | 13 (34%) | 0.22 |
| ARB (%) | 15 (21%) | 18 (36%) | 0.07 |
| Statin (%) | 11 (18%) | 3 (8%) | 0.11 |
| CCB (%) | 28 (46%) | 19 (49%) | 0.87 |
| Aspirin (%) | 25 (41%) | 12 (31%) | 0.19 |

BSA, body surface area; BMI, body mass index; BP, blood pressure; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CCB, calcium channel blocker

**Table 3.** Comparison of clinical characteristics between two groups

| | Hobby group | Non-hobby group | $P$ value |
|---|---|---|---|
| Laboratory data | | | |
| Total cholesterol (mg/dl) | 195 ± 36 | 191 ± 32 | 0.57 |
| Triglyceride (mg/dl) | 116 ± 64 | 122 ± 68 | 0.62 |
| HDL-cholesterol (mg/dl) | 55 ± 16 | 57 ± 13 | 0.39 |
| LDL-cholesterol (mg/dl) | 119 ± 28 | 111 ± 30 | 0.16 |
| Fasting plasma glucose (mg/dl) | 105 ± 27 | 101 ± 16 | 0.47 |
| HbA1c (mg/dl) | 5.55 ± 1.07 | 5.56 ± 1.20 | 0.84 |
| Creatinine (mg/dl) | 0.80 ± 0.23 | 0.96 ± 0.86 | 0.15 |

HDL, high-density lipoprotein; LDL, low-density lipoprotein; HbA1c, hemoglobin A1c

**Table 4.** Comparison of hemodynamic parameters between two groups

| | Hobby group | Non-hobby group | $P$ value |
|---|---|---|---|
| Echocardiographic parameters | | | |
| LVDd (mm) | 52.5 ± 9.4 | 52.9 ± 9.0 | 0.81 |
| LAD (mm) | 39.9 ± 8.0 | 41.8 ± 10.2 | 0.26 |
| LVEF (%) | 60.6 ± 15.8 | 61.0 ± 14.1 | 0.88 |
| LV mass (g) | 261.6 ± 107.6 | 264.4 ± 81.0 | 0.87 |
| LV Tei index | 0.55 ± 0.24 | 0.54 ± 0.25 | 0.81 |
| RV Tei index | 0.34 ± 0.15 | 0.39 ± 0.18 | 0.14 |
| Hemodynamic parameter determined by Swan–Ganz catheter | | | |
| Heart rate (beats/min) | 70.1 ± 10.5 | 68.7 ± 13.7 | 0.52 |
| PCWP (mmHg) | 8.8 ± 4.4 | 8.7 ± 4.9 | 0.91 |
| MPAP (mmHg) | 14.8 ± 4.0 | 15.4 ± 4.6 | 0.45 |
| CI (l/min/m$^2$) | 2.97 ± 0.56 | 2.78 ± 0.60 | 0.08 |

LVDd, left ventricular end-diastolic dimension; LAD, left atrium dimension; LVEF, left ventricular ejection fraction; LV, left ventricle; RV, right ventricle; Tei, total ejection isovolemic; PCWP, pulmonary capillary wedge pressure; MPAP, mean pulmonary artery pressure; CI, cardiac index

group (49% ± 77% vs 25% ± 37%, $P < 0.05$), but the baseline CBF did not differ when comparing the two groups (76 ± 40 ml/min vs 90 ± 56 ml/min, $P$ not significant). The percent change in CBF induced by papaverine was comparable between the two groups (211% ± 109% vs 187% ± 112%, $P$ not significant) (Table 5).

Changes in coronary artery diameter

The baseline coronary artery diameter was similar when comparing the two groups (2.9 ± 0.7 mm vs 3.0 ± 0.6 mm, $P$ not significant). The percent change in CAD induced by ACh was significantly greater in the Hobby group than in

**Table 5.** Comparison of coronary hemodynamics between two groups

| | Hobby group | Non-hobby group | *P* value |
|---|---|---|---|
| CBF at baseline (ml/min) | 76 ± 40 | 90 ± 56 | 0.12 |
| CAD at baseline (mm) | 2.9 ± 0.7 | 3.0 ± 0.6 | 0.71 |
| % change in CBF induced by papaverine (%) | 211 ± 109 | 187 ± 112 | 0.24 |
| % change in CBF induced by ACh (%) | 49 ± 77 | 25 ± 37 | 0.04* |
| % change in CAD induced by ACh (%) | 4 ± 13 | –3 ± 20 | 0.02* |
| % change in CAD induced by NTG (%) | 17 ± 17 | 11 ± 12 | 0.05 |

Values are mean ± SD
CBF, coronary blood flow; CAD, coronary artery diameter; ACh, acetylcholine; NTG, nitroglycerine
*Significant *P* value vs non-hobby group

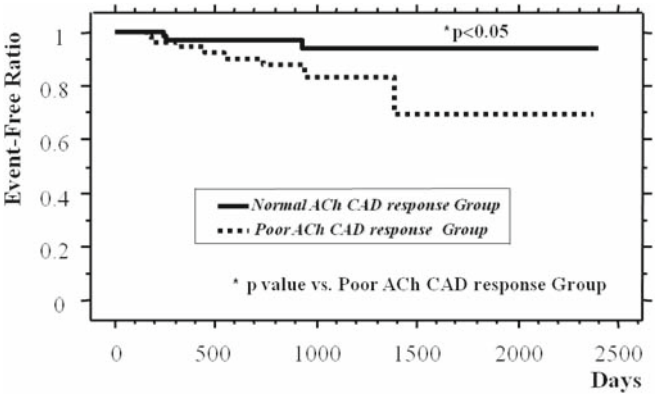



**Fig. 1.** Kaplan–Meier relationship between acetylcholine (*ACh*)-induced changes in coronary artery diameter (*CAD*) and outcomes; Normal ACh CAD response group versus Poor ACh CAD response group. *P* value was calculated with the log-rank test

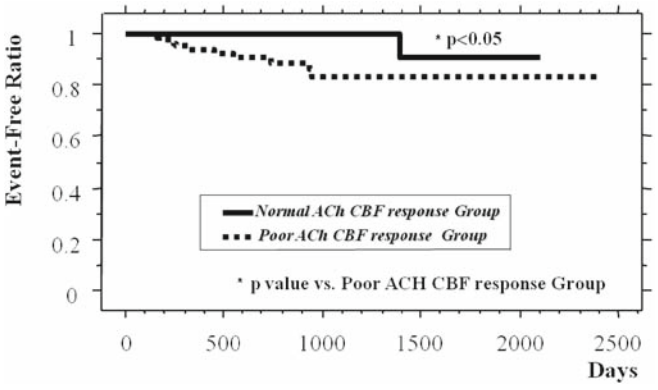



**Fig. 2.** Kaplan–Meier relationship between acetylcholine (*ACh*)-induced changes in coronary blood flow (*CBF*) and outcomes; Normal ACh CBF response group versus Poor ACh CBF response group. *P* value was calculated with the log-rank test

the Non-hobby group (4% ± 13% vs –3% ± 20%, $P < 0.05$). The percent change in CAD induced by nitroglycerin was not significantly different when comparing the two groups (17% ± 17% vs 11% ± 12%, *P* not significant) (Table 5).

## Cardiovascular outcomes and coronary endothelial function

Major adverse cardiovascular events occurred in 11 patients: hospitalization due to heart failure in 6 cases, fatal arrhythmia in 2 cases, acute myocardial infarction in 2 cases, and percutaneous coronary intervention in 1 case. At the epicardial coronary vessel level, MACE occurred in 3 cases (4.6%) in the Normal ACh CAD response group and in 8 cases (14.3%) in the Poor ACh CAD response group. The MACE-free ratio was significantly greater in the Normal ACh CAD response group than in the Poor ACh CAD response group ($P < 0.05$) (Fig. 1).

At the resistance coronary vessel level, MACE occurred in only one case (2.7%) in the Normal ACh CBF response group and in 10 cases (11.9%) in the Poor ACh CBF response group. The MACE-free ratio was significantly greater in the Normal ACh CBF response group than in the Poor ACh CBF response group ($P < 0.05$) (Fig. 2).

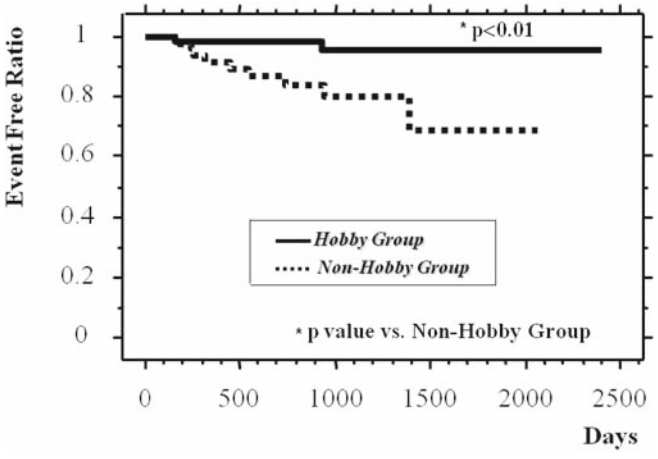



**Fig. 3.** Kaplan–Meier relationship between hobbies and outcomes; Hobby group versus Non-hobby group. *P* value was calculated with the log-rank test

## Cardiovascular outcomes and hobbies

There were two incidences of MACE in the Hobby group and 9 in the Non-hobby group. The MACE-free ratio was significantly greater in the Hobby group than in the Non-hobby group ($P < 0.05$) (Fig. 3).

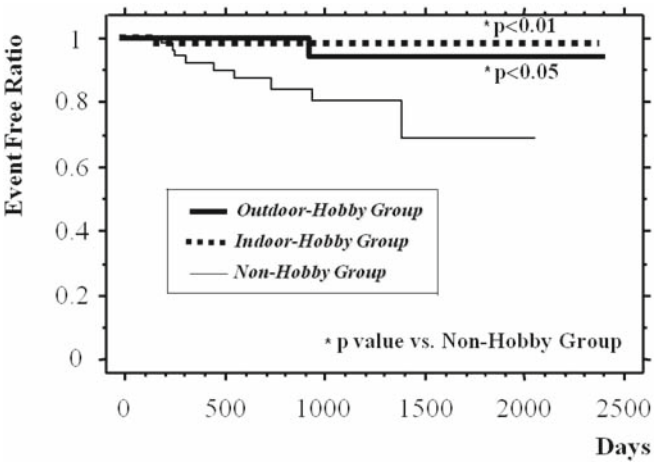



**Fig. 4.** Kaplan–Meier relationship between type of hobby and outcomes; Outdoor-hobby group versus Indoor-hobby group versus Non-hobby group. *P* value was calculated with the log-rank test

There was one incidence of MACE in the Outdoor-hobby group and one incidence of MACE in the Indoor-hobby group. The event-free ratio was significantly higher in the Outdoor-hobby group and Indoor-hobby group than in the Non-hobby group ($P < 0.05$ and $P < 0.01$, respectively) (Fig. 4).

## Multivariate analysis and Cox proportional hazards ratio of MACE

There were no significant differences in age, sex, body mass index, and major coronary risk factors when comparing the MACE group and Non-MACE group. However, the number of patients who enjoyed hobbies was significantly lower in the Non-MACE group than in the MACE group (18% vs 63%, $P < 0.01$) (Table 6). Of all the variables tested (age, sex, classical coronary risk factors, and hobbies), enjoying hobbies was the only independent predictor of MACE (odds ratio 6.74 [95% confidence interval 1.38, 32.91], $P = 0.02$) (Table 7).

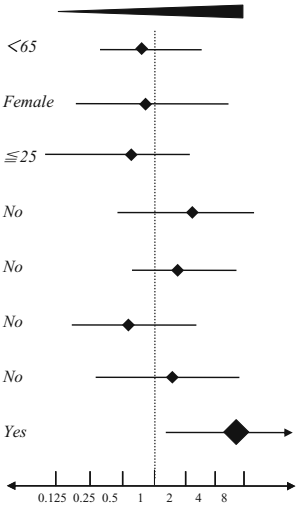
**Table 6.** Parameters in association with MACE

| Factor | MACE (+) $n = 11$ | vs | MACE (–) $n = 110$ | *P* value | |
|---|---|---|---|---|---|
| | | | | Univariate regression analysis | Multivariate regression analysis |
| Age | 64.7 ± 19.4 | vs | 61.7 ± 12.0 | 0.46 | 0.99 |
| Male | 8 (73%) | vs | 68 (62%) | 0.48 | 0.91 |
| Body mass index | 21.8 ± 3.1 | vs | 23.8 ± 3.6 | 0.09 | 0.27 |
| Current smoking | 7 (64%) | vs | 41 (37%) | 0.09 | 0.22 |
| Hypertension | 8 (73%) | vs | 66 (60%) | 0.41 | 0.59 |
| Hyperlipidemia | 4 (36%) | vs | 52 (47%) | 0.49 | 0.80 |
| Diabetes mellitus | 2 (18%) | vs | 20 (18%) | 0.99 | 0.80 |
| Hobby | 2 (18%) | vs | 69 (63%) | 0.004* | 0.01* |

MACE, major adverse cardiovascular events
*Significant *P* value vs MACE (+)

**Table 7.** Hazard ratio of parameters to MACE

| | | | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|---|---|
| | | | Hazard ratio | 95% CI | *P* value | Hazard ratio | 95% CI | *P* value |
| Age | <65 | 65≧ | 1.62 | (0.47–1.62) | 0.44 | 0.79 | (0.20–3.11) | 0.79 |
| Sex | Female | Male | 1.63 | (0.43–6.14) | 0.47 | 0.90 | (0.16–5.09) | 0.91 |
| BMI | ≦25 | 25< | 0.37 | (0.08–1.72) | 0.21 | 0.44 | (0.09–2.22) | 0.32 |
| Smoking | No | Yes | 2.56 | (0.75–8.76) | 0.13 | 2.21 | (0.46–10.61) | 0.32 |
| Hypertension | No | Yes | 1.64 | (0.43–6.20) | 0.47 | 1.79 | (0.44–7.36) | 0.42 |
| Hyperlipidemia | No | Yes | 0.60 | (0.18–2.06) | 0.42 | 0.62 | (0.15–2.44) | 0.48 |
| Diabetes | No | Yes | 1.03 | (0.22–4.83) | 0.97 | 1.51 | (0.29–7.86) | 0.62 |
| Hobby | Yes | No | 6.54 | (1.41–30.27) | 0.02 | 6.74 | (1.38–32.91) | 0.02 |




CI, confidence interval

## Discussion

Enjoying hobbies can improve quality of life by alleviating stress, improving daily activity, and normalizing automatic nervous system function. In the context of chronic life stress, an acute psychological challenge can provoke an exaggerated psychologic and sympathomedullary reactivity that is associated with decrements in individual natural killer cell function, and that persist beyond termination of the stressor and sympathomedullary recovery.[17] Mental stress cause an increase in platelet-dependent thrombin generation, which results in increased cardiovascular events.[18] However, the effect of enjoying hobbies on coronary function and cardiovascular prognosis has not yet been investigated. The association between endothelial dysfunction and the frequency of clinical events has been firmly established,[6,19] which is consistent with the present finding that the MACE ratio was significantly lower in the Normal ACh-responsive group than in the Poor ACh-responsive group.

### Mechanisms by which hobbies may affect endothelial function

In this study, physical activities were among the variety of hobbies and cultural activities that were enjoyed by patients. The current concept of shear stress-induced changes in endothelial nitric oxide synthase (eNOS) expression/activity is based on cell culture experiments or animal models. For example, a significant increase in eNOS expression was observed in human umbilical vein endothelial cells and bovine arterial endothelial cells after 6 h of laminar shear stress.[20] Further, exercise training increases eNOS expression in coronary conduit and resistance vessels in animals.[21] In humans, exercise training can alleviate endothelial dysfunction in symptomatic patients with coronary artery disease by increasing eNOS activity and potentiating endothelium-dependent increase in blood flow in the context of exercise training.[22] Therefore, enjoying outdoor hobbies may improve cardiovascular outcomes by promoting coronary endothelial function.

One cohort study reported that people who rarely visited the cinema, concerts, museums, or art exhibitions had a higher mortality risk when compared with people who participated in these activities. Thus, attendance at various types of cultural events may have a beneficial effect on longevity.[23] Further, Takahashi and Matsushita[24] reported that music therapy once weekly over 2 years reduced systolic blood pressure, and reduced physical and mental stress in elderly patients suffering from moderate to severe dementia. Thus, enjoying indoor hobbies may also result in improved cardiovascular outcomes.

### Relationship between lifestyle and mortality

Giltay et al.[25] reported that dispositional optimism is a relatively stable trait over 15 years, and is associated with a graded and inverse association with the risk of cardiovascular death in elderly men. Al-Khalili et al.[26] reported that important independent predictors of long-term all-cause mortality in middle-aged female patients surviving acute coronary syndrome included sedentary lifestyle, low physical exercise, and inadequate pulse rate and systolic blood pressure increase during exercise. In the present study, enjoying hobbies was the only predictor of MACE. Therefore, interventions to encourage enjoyable lifestyles during the early stage of atherosclerosis may result in improved cardiovascular outcomes.

### Study limitations

This study has several notable limitations. For example, the proportion of patients who were taking ACE inhibitors or angiotensin II receptor blockers was greater in the Non-hobby group than in the Hobby group. Angiotensin-converting enzyme inhibitors increase systemic and coronary blood flow via an endothelial-dependent, bradykinin-mediated NO pathway.[27] However, ACh-induced percent change in coronary diameter and coronary blood flow were significantly greater in the Hobby group than in the Non-hobby group.

Further, detailed information regarding concomitant medication use was not available, and misclassification of both clinical and lifestyle exposures could have occurred due to measurement error or biological variation, because data were collected prospectively. However, such errors would probably be random with respect to the outcomes, and cause underestimation of the observed associations.

The present study also cannot distinguish between the widespread effects of lifestyles on cardiovascular prognosis and its effect on coronary endothelial function. Lifestyle habits could have been partially driven by changes in response to chronic disease development and physician guidance. Finally, the study population was relatively small, so larger trials are needed to determine the validity of these results.

## Conclusion

In the early stage of arteriosclerosis, enjoying hobbies may improve cardiovascular outcomes via its favorable effects on coronary endothelial function.

## References

1. Kubo SH, Rector TS, Bank AJ, Williams RE, Heifetz SM (1991) Endothelium-dependent vasodilation is attenuated in patients with heart failure. Circulation 84:1589–1596
2. Drexler H, Hayoz D, Münzel T, Hornig B, Just H, Brunner HR, Zelis R (1992) Endothelial function in chronic congestive heart failure. Am J Cardiol 69:1596–1601
3. Hambrecht R, Fiehn E, Weigl C, Gielen S, Hamann C, Kaiser R, Yu J, Adams V, Niebauer J, Schuler G (1998) Regular physical exercise corrects endothelial dysfunction and improves exercise capacity in patients with chronic heart failure. Circulation 98: 2709–2715

4. Vona M, Rossi A, Capodaglio P, Rizzo S, Servi P, De Marchi M, Cobelli F (2004) Impact of physical training and detraining on endothelium-dependent vasodilation in patients with recent acute myocardial infarction. Am Heart J 147:1039–1046
5. Gokce N, Keaney JF Jr, Hunter LM, Watkins MT, Nedeljkovic ZS, Menzoian JO, Vita JA (2003) Predictive value of noninvasively determined endothelial dysfunction for long-term cardiovascular events in patients with peripheral vascular disease. J Am Coll Cardiol 41:1769–1775
6. Schächinger V, Britten MB, Zeiher AM (2000) Prognostic impact of coronary vasodilator dysfunction on adverse long-term outcome of coronary heart disease. Circulation 101:1899–1906
7. Lisspers J, Sundin O, Ohman A, Hofman-Bang C, Rydén L, Nygren A (2005) Long-term effects of lifestyle behavior change in coronary artery disease: effects on recurrent coronary events after percutaneous coronary intervention. Health Psychol 24:41–48
8. Wannamethee SG, Shaper AG, Walker M, Ebrahim S (1998) Lifestyle and 15-year survival free of heart attack, stroke, and diabetes in middle-aged British men. Arch Intern Med 158:2433–2440
9. Nielsen NR, Kristensen TS, Schnohr P, Grønbaek M (2008) Perceived stress and cause-specific mortality among men and women: results from a prospective cohort study. Am J Epidemiol 168: 481–491
10. Sivasankaran S, Pollard-Quintner S, Sachdeva R, Pugeda J, Hoq SM, Zarich SW (2006) The effect of a six-week program of yoga and meditation on brachial artery reactivity: do psychosocial interventions affect vascular tone? Clin Cardiol 29:393–398
11. Hamasaki S, Al Suwaidi J, Higano ST, Miyauchi K, Holmes DR Jr, Lerman A (2000) Attenuated coronary flow reserve and vascular remodeling in patients with hypertension and left ventricular hypertrophy. J Am Coll Cardiol 35:1654–1660
12. Nishimura RA, Lerman A, Chesebro JH, Ilstrup DM, Hodge DO, Higano ST, Holmes DR Jr, Tajik AJ (1995) Epicardial vasomotor responses to acetylcholine are not predicted by coronary atherosclerosis as assessed by intracoronary ultrasound. J Am Coll Cardiol 26:41–49
13. Hasdai D, Gibbons RJ, Holmes DR Jr, Higano ST, Lerman A (1997) Coronary endothelial dysfunction in humans is associated with myocardial perfusion defects. Circulation 96:3390–3395
14. Ninomiya Y, Hamasaki S, Saihara K, Ishida S, Kataoka T, Ogawa M, Orihara K, Oketani N, Fukudome T, Okui H, Ichiki T, Shinsato T, Kubozono T, Mizoguchi E, Ichiki H, Tei C (2008) Comparison of effect between nitrates and calcium channel antagonist on vascular function in patients with normal or mildly diseased coronary arteries. Heart Vessels 23(2):83–90
15. Egashira K, Inou T, Hirooka Y, Kai H, Sugimachi M, Suzuki S, Kuga T, Urabe Y, Takeshita A (1993) Effects of age on endothelium-dependent vasodilation of resistance coronary artery by acetylcholine in humans. Circulation 88:77–81
16. Doucette JW, Corl PD, Payne HM, Flynn AE, Goto M, Nassi M, Segal J (1992) Validation of a Doppler guide wire for intravascular measurement of coronary artery flow velocity. Circulation 85: 1899–1911
17. Pike JL, Smith TL, Hauger RL, Nicassio PM, Patterson TL, McClintick J, Costlow C, Irwin MR (1997) Chronic life stress alters sympathetic, neuroendocrine, and immune responsivity to an acute psychological stressor in humans. Psychosom Med 59:447–457
18. Kawano TA, Aoki N, Homori M, Kawano K, Maki A, Kimura M, Yanagisawa A, Ohsaki T, Takahashi R, Shiohara T, Ishikawa K, Yoshino H (2000) Mental stress and physical exercise increase platelet-dependent thrombin generation. Heart Vessels 15: 280–288
19. Suwaidi JA, Hamasaki S, Higano ST, Nishimura RA, Holmes DR Jr, Lerman A (2000) Long-term follow-up of patients with mild coronary artery disease and endothelial dysfunction. Circulation 101:948–954
20. Noris M, Morigi M, Donadelli R, Aiello S, Foppolo M, Todeschini M, Orisio S, Remuzzi G, Remuzzi A (1995) Nitric oxide synthesis by cultured endothelial cells is modulated by flow conditions. Circ Res 76:536–543
21. Sessa WC, Pritchard K, Seyedi N, Wang J, Hintze TH (1994) Chronic exercise in dogs increases coronary vascular nitric oxide production and endothelial cell nitric oxide synthase gene expression. Circ Res 74:349–353
22. Hambrecht R, Adams V, Erbs S, Linke A, Kränkel N, Shu Y, Baither Y, Gielen S, Thiele H, Gummert JF, Mohr FW, Schuler G (2003) Regular physical activity improves endothelial function in patients with coronary artery disease by increasing Phosphorylation of endothelial nitric oxide synthase. Circulation 107:3152–3158
23. Konlaan BB, Bygren LO, Johansson SE (2000) Visiting the cinema, concerts, museums or art exhibitions as determinant of survival: a Swedish fourteen-year cohort follow-up. Scand J Public Health 28:174–178
24. Takahashi T, Matsushita H (2006) Long-term effects of music therapy on elderly with moderate/severe dementia. J Music Ther 43:317–333
25. Giltay EJ, Kamphuis MH, Kalmijn S, Zitman FG, Kromhout D (2006) Dispositional optimism and the risk of cardiovascular death: the Zutphen Elderly Study. Arch Intern Med 166:431–436
26. Al-Khalili F, Janszky I, Andersson A, Svane B, Schenck-Gustafsson K (2007) Physical activity and performance predict long-term prognosis in middle-aged women surviving acute coronary syndrome. J Intern Med 261:178–187
27. Warren JB, Loi RK (1995) Captopril increases skin microvascular blood flow secondary to bradykinin, nitric oxide, and prostaglandins. FASEB J 9:411–418