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Is the association between healthy lifestyle behaviors and cardiovascular mortality modified by overweight status? The Japan Collaborative Cohort Study

Eri Eguchi [a], Hiroyasu Iso [b,*], Naohito Tanabe [c], Hiroshi Yatsuya [d], Akiko Tamakoshi [e], on behalf of the Japan Collaborative Cohort Study Group

[a] Department of Public Health, Social Medicine and Medical Informatics, Ehime University Graduate School of Medicine, Toon, Japan
[b] Public Health, Department of Social and Environmental Medicine, Osaka University Graduate School of Medicine, Osaka, Japan
[c] Division of Health Promotion, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan
[d] Department of Public Health, Fujita Health University, Toyoake, Japan
[e] Department of Public Health, Hokkaido University Graduate School of Medicine, Sapporo, Japan

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ABSTRACT

Objective: To examine the modifying effects of overweight status on the association of healthy lifestyle behaviors with cardiovascular mortality in the Japanese population.

Methods: A community-based, prospective cohort of 18,730 men and 24,216 women aged 40–79 years without a history of cardiovascular disease (CVD) or cancer at baseline (1988–1990) was followed until 2009. Healthy lifestyle behaviors included intake of fruits, fish, and milk; exercise; avoidance of smoking; moderate alcohol intake; and moderate sleep duration.

Results: During the median of 19.3 years of follow-up, there were 2412 deaths from total CVD. Inverse associations between healthy lifestyle scores and mortality from stroke, total CVD, and coronary heart disease (CHD) were observed for non-overweight and overweight (body mass index ≥25 kg/m2) individuals, although the association was weaker for overweight individuals. The multivariable hazard ratios (HRs, 95% confidence interval) of mortality from total CVD for the highest (6–7) versus the lowest (0–2) scores were 0.44 (0.37–0.54) for non-overweight and 0.56 (0.39–0.81) for overweight individuals. Especially for CHD mortality, such association was more evident for non-overweight compared to that for overweight individuals.

Conclusions: Our findings suggest that lifestyle modification may be beneficial in the prevention of cardiovascular mortality for persons who are and are not overweight.

Introduction

We previously reported that conforming to a number of lifestyle behaviors reduces the likelihood of dying from cardiovascular disease (CVD) (Eguchi et al., 2012a). These behaviors are maintaining a normal body mass index (BMI); having moderate physical activity; having a moderate alcohol intake; avoiding smoking; having a moderate sleep duration; and consuming fruits, fish, and milk. Among the eight behaviors studied, the maintenance of a normal BMI is important. In Japan and in other countries, the prevention of CVD in adults is characterized by its emphasis on obesity: overweight or obesity or its absence determines if individuals have metabolic syndrome or not.

And in Japan, the existence of metabolic syndrome (overweight/obesity and two other components) determines subsequent health counseling and clinical intervention (Alberti et al., 2006). Therefore, examining the association of healthy lifestyle behaviors with CVD stratified according to overweight status is relevant, as it reveals whether individuals who are not overweight experience the direct effects of healthy lifestyle behaviors, and whether overweight leads to no or weak association between such behaviors and CVD. Before, there were several reports regarding the association between the combination between lifestyle behaviors and mortality from CVD. Nurses' Health study showed that the combination of five healthy lifestyle behaviours was associated with an 83% reduction in the incidence of coronary heart disease (CHD), and a 75% reduction in the incidence of CVD among American women (Stampfer et al., 2000). Similarly, a health professional study reported that the combination of five healthy lifestyle behaviours was associated with a 69–79% reduction in the incidence of stroke among American men and women (Chiuve et al., 2008); and the EPIC Norfolk study demonstrated that a combination of four bad lifestyle behaviors was associated with a 45–240% increase in the incidence of stroke among European men and women (Myint et al., 2009). However, to our knowledge, no prospective study has reported a

* Corresponding author at: Public Health, Department of Social and Environmental Medicine, Osaka University Graduate School of Medicine, 2-2, Yamadaoka, Suita, Osaka 565-0871, Japan. Fax: +81 6 6879 3919.
E-mail address: iso@pbhel.med.osaka-u.ac.jp (H. Iso).

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modification effect of overweight status on the association of healthy lifestyle behaviors with mortality from or incidence of CVD.

Hence, the investigation of the association between healthy lifestyle behaviors and mortality from CVD stratified according to overweight status is important in formulating public health strategies. The present work was a large, prospective cohort study of Japanese men and women from the general population. We examined the effect of overweight status on the association between healthy lifestyle behaviors and mortality from CVD.

Methods

A baseline survey of the JACC Study was conducted in 1988–90. A total of 110,585 subjects (46,395 men and 64,190 women) aged 40–79 years in 45 areas in Japan completed self-administered questionnaires, including lifestyle information and medical histories pertaining to CVD and cancer. The details of the study procedure were described previously (Ohno et al., 2001). This study was approved by the ethics committees of the Nagoya University School of Medicine, the University of Tsukuba, and Osaka University.

Out of all the subjects, 2574 men and 3276 women were excluded because of positive histories of stroke, coronary heart disease (CHD), or cancer. Similarly, another 25,091 and 36,698, respectively, were excluded because of lacking information for calculating the healthy lifestyle score. A total of 42,946 participants (18,730 men and 24,216 women) were eligible for the present study. There was no substantial difference in CVD risk factors between individuals with complete healthy lifestyle scores and those with missing information (Eguchi et al., 2012a).

Mortality surveillance

The cause and date of death of participants were identified by reviewing all death certificates in each area. According to the International Classification of Diseases, 10th revision, cause-specific mortality was determined in terms of stroke (I60 to I69), CHD (I20 to I25), and total CVD (I01 to I99). By the 31st of December 2009, except for several areas where follow-up was terminated at the end of 1999 (six areas), 2003 (five areas), and 2008 (two areas), a total of 8464 subjects had been censored because of death, and 2,483, because of moving out. The median follow-up period was 19.3 years (interquartiles: 11.4 to 21.0).

Overweight status and non-overweight status

Overweight status was defined as BMI $\geq$ 25 kg/m^2, and non-overweight status was defined as <25 kg/m^2.

Healthy lifestyle score

The healthy lifestyle score was defined by eight healthy lifestyle behaviors (Eguchi et al., 2012a), namely: 1) fruit intake per day ($\geq$1); 2) fish intake per day ($\geq$1); 3) milk consumption per day (almost every day); 4) maintaining a BMI ranging from 21 to 25 kg/m^2; 5) number of hours spent on walking ($\geq$0.5 per day and/or sports ($\geq$5 h per week); 6) avoidance of smoking (nonsmokers including past smokers); 7) alcohol consumption (<46.0 g ethanol/day); and 8) sleep duration (5.5–7.4 h/day). We used seven healthy lifestyle behaviors except for maintaining a BMI ranging from 21 to <25 kg/m^2.

The total allocated points of lifestyle behaviors were used to compute the healthy lifestyle score, which ranged from 0 to 7. The scores were grouped into six categories (0–1, 2, 3, 4, 5, and 6–7 points) for analyses to keep the number in both men and women balanced in each category.

Statistical analyses

We first calculated mean age, age and sex-adjusted mean BMI, prevalence of healthy lifestyle behaviors and prevalence of cardiovascular risk factors according to healthy lifestyle score and overweight status, using the analysis of covariance for mean values and the logistic regression model for prevalence (Eguchi et al., 2012a,b).

Survival probability of mortality from stroke, CHD, and total CVD for non-overweight and overweight individuals was calculated, and Kaplan–Meier's survival curves were constructed.

We also calculated multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) to determine the sex-specific associations between eight individual lifestyle behaviors and mortality from stroke, CHD, and total CVD, and between the combination of lifestyle behaviors and mortality from stroke, CHD, other CVDs, and total CVD during the follow-up period, stratified by BMI. Mortality from other CVDs is the CVD mortality except for mortality from stroke and CHD. We used Cox proportional hazard models using, as reference, the healthy lifestyle score categories of 0–2. Effect modifications by BMI category were tested using cross-product terms of BMI category (BMI< and $\geq$25 kg/m^2) by healthy lifestyle score (continuous). To evaluate the impact of age on the BMI-specific associations between healthy lifestyle score and mortality from CVD, we conducted an age ($\geq$65 and <65 years old) stratified analysis. Also, to evaluate the impact of lifestyle behaviors on CVD mortality only for nonsmokers, we conducted the same analysis without smokers since the impact of smoking for CVD mortality is the biggest among the lifestyle behaviors.

Covariates for multivariable analyses were age (years), sex for total subjects, BMI, histories of hypertension and diabetes mellitus (yes or no), education level (school attendance until 13, 13–15, 16–18, or beyond 19 years old), perceived mental stress (high, medium, or low), and regular employment (yes or no) (Eguchi et al., 2012a,b).

We repeated the same analyses after excluding early death that occurred within five years from the baseline to examine the possibility of reverse causation.

We used the Statistical Analysis Software (SAS) program v. 9.2 (SAS Institute Inc., Cary, NC, USA) for all statistical analyses. All probability values for statistical tests were two-tailed, and P values less than 0.05 were regarded as statistically significant (Eguchi et al., 2012a,b).

Results

The proportion of overweight individuals (BMI $\geq$ 25 kg/m^2) was 17.9% in men and 21.3% in women. Mean ages of non-overweight and overweight men were 56.0 and 53.6, respectively, whereas the corresponding ages for women were 56.0 and 56.3, respectively. The number of deaths from stroke, CHD, other CVDs and total CVD was 539, 304, 416, and 1259, respectively, in men; and 523, 200, 430, and 1153, respectively, in women.

Figs. 1 to 3 illustrate Kaplan–Meier survival curves of mortality from stroke, CHD, and total CVD, respectively, according to the healthy lifestyle scores of non-overweight and overweight participants. There is a larger decline in survival rate for the lower healthy lifestyle score categories compared with those for the higher score categories for mortality from stroke and total CVD in both non-overweight and overweight individuals (P values for logrank were <0.0001 for non-overweight and 0.002 for overweight individuals for mortality from stroke, and were <0.0001 and <0.0001, respectively, for mortality from total CVD). For mortality from CHD, such trend was evident in non-overweight individuals, but not in overweight individuals (P values for logrank were <0.0001 for non-overweight and 0.28 for overweight individuals).

Table 1 shows multivariable-adjusted HRs of mortality from stroke, CHD, other CVDs and total CVD according to healthy lifestyle scores for non-overweight and overweight men and women. There were inverse associations of healthy lifestyle score with mortality from stroke, CHD, other CVDs and total CVD in all subjects that are both non-overweight and overweight. These associations did not vary materially between men and women (P values for interaction by sex were 0.99, 0.31, 0.98, and 0.68, respectively). When stratified by overweight status, as the table shows, the HRs of mortality from stroke, CHD, and total CVD became lower as lifestyle score category became higher among non-overweight individuals while that relationship for overweight was not evident compared to non-overweight individuals. For example, in total subjects, the magnitude of HRs (95% CIs) of total CVD mortality for healthy lifestyle categories of 6–7 compared to that of 0–2 was 0.44 (0.37–0.54) for non-overweight and 0.56 (0.39–0.81) for overweight individuals. There was no interaction of overweight status on the association between lifestyle behaviors and mortality from stroke, and total CVD (P values for interaction were 0.89 in men and 0.17 in women for stroke, and 0.33 in men and 0.58 in women for