ELSEVIER

Atherosclerosis 187 (2006) 123–130

ATHEROSCLEROSIS

www.elsevier.com/locate/atherosclerosis

Multiple metabolic risk factors and total and cardiovascular mortality in men with low prevalence of obesity

Hye Soon Park [a], Sung-Il Cho [b,*], Yun-Mi Song [c], Joohon Sung [d]

[a] *Department of Family Medicine, University of Ulsan College of Medicine, Seoul, South Korea*
[b] *Institute of Health and Environment, School of Public Health, Seoul National University, 28 Yongon-Dong, Chogno-Gu, Seoul 110-799, South Korea*
[c] *Department of Family Medicine, Sungkyunkwan University School of Medicine, Suwon, South Korea*
[d] *Department of Preventive Medicine, Kangwon National University Medical School, Chuncheon, South Korea*

Received 3 December 2004; received in revised form 1 August 2005; accepted 22 August 2005
Available online 28 September 2005

Abstract

We investigated the association between the multiple metabolic risk factors and cardiovascular and overall mortality among Korean men, a population with a low prevalence of obesity. This prospective cohort study involved 682,597 Korean men, aged 30–69 years at baseline (1992), who were initially without cancer or debilitating diseases. Death due to ischemic heart disease (IHD), stroke, cardiovascular disease (CVD), and any cause among men relative to metabolic risk factors, including overweight, high blood pressure, high fasting glucose, and high total cholesterol was analyzed. There were 17,785 deaths during the 8.5-year follow-up, of which 874 were due to IHD, 1644 to stroke, and 3306 to CVD. As a function of the number of metabolic risk factors, the relative risk of death from CVD was 2.0 (1.7–2.2), 2.9 (2.5–3.3), 3.5 (3.0–4.1), and 5.0 (3.9–6.4) for 1, 2, 3, and 4 risk factors, respectively, whereas the relative risk of death from all causes was 1.3 (1.2–1.4), 1.5 (1.4–1.6), 1.6 (1.5–1.7), and 1.9 (1.6–2.2) for 1, 2, 3, and 4 risk factors, respectively. The relative risk of IHD, stroke, CVD and all-cause mortality increased linearly with the number of metabolic risk factors. Early identification and strict management of metabolic risk factors should be reinforced in Koreans, even though there is a low prevalence of obesity among this population.

Keywords: Metabolic risk factors; Cardiovascular mortality; Body mass index; Korean

1. Introduction

Overweight, high blood pressure, impaired glucose tolerance, and dyslipidemia are widely recognized as major risk factors for atherosclerosis [1,2]. Furthermore, concomitant occurrence of these risk factors is considered to indicate a particularly high risk of cardiovascular disease (CVD) [3,4].

The results of the Multiple Risk Factor Intervention Trial [1,4] have demonstrated the importance of the presence of multiple risk factors. The association between the presence of multiple risk factors with cardiovascular and overall mortality has been assessed through population-based, cohort studies in Western populations [1,4,5] with a high prevalence of obesity. In addition, cardiovascular mortality associated with the metabolic syndrome [6] and mortality from coronary heart disease related with cardiovascular risk factor clustering in patients with type 2 diabetes [7] has been investigated.

The Asia-Pacific region currently accounts for approximately half the global burden of CVD, and future projections suggest this proportion will increase [8,9]. In Eastern Asia, the incidence of ischemic heart disease (IHD) is lower than in most Caucasian populations, whereas the incidence of stroke is higher [10,11]. There are data indicating that population-wide levels of risk factors for CVD are rising substantially in many countries in Asia [12]. In addition, several studies among Asian populations have established continuous linear associations between blood pressure [13], diabetes mellitus [14], or serum cholesterol [15] with CVD.

Despite this, however, little is known about the relationship between the presence of multiple metabolic risk factors and cardiovascular and overall mortality in Asian popula-

* Corresponding author. Tel.: +82 2 740 8868; fax: +82 2 743 8240.
E-mail address: scho@snu.ac.kr (S.-I. Cho).

0021-9150/$ – see front matter © 2005 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.atherosclerosis.2005.08.027

tions. At present, CVD is the leading cause of death in South Korea, with stroke ranked second [16]. Moreover, the death rate from IHD has increased 106.7% over 10 years [16]. We therefore prospectively assessed this association over 8.5 years in a population-based cohort of South Korean men.

2. Methods

2.1. Study subjects

We investigated 682,597 South Korean men, aged 30–69 years, selected from the database of the Korean Medical Insurance Corporation and who had undergone health examination in 1992. The Korean Medical Insurance Corporation provides all civil service personnel, including office workers and teachers, with medical expenses as well as biennial health examinations.

Among the total of 711,145 men aged 30–69 years, we excluded those who had a history of alleged cancer, weight gain or loss due to endocrine disease or infectious disease, or another debilitating disease (1174), and those with inadequate or missing data (27,374). This left a total of 682,597 men.

2.2. Basic questionnaire

A questionnaire was administered to each participant a few days before the examination. Participants were asked to record their medical history, family history, smoking habits, alcohol consumption, exercise habits, economic level, and weight change status. Family history was assessed by the presence or absence of a family history of hypertension, diabetes, stroke, or heart diseases in first degree relative as dichotomous variables. Study subjects were categorized into three groups by smoking habit: non-smokers (never smoked), former smokers (smoked previously, but do not currently smoke), and current smokers (have smoked until now). Subjects were also categorized into three groups by frequency of alcohol intake: light drinkers (<1 session per week), occasional drinkers (2–3 sessions per week), and frequent drinkers (>3 sessions per week). Since detailed information was not available regarding physical exercise, subjects were categorized into two groups: those who did and those who did not engage in regular exercise. Economic status was categorized into five levels based on monthly salary (<$ 560, $ 560–1120, $ 1120–1680, $ 1680–2240, and ≥$ 2240). Weight change status was assessed by the presence or absence of weight gain or loss during the past year.

2.3. Metabolic risk factors

Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Blood pressure was measured in the seated position using a standard mercury sphygmomanometer or automatic manometer. A blood sample was obtained from each subject after fasting for 12 h overnight, and the resultant serum was analyzed for fasting glucose and total cholesterol.

We assessed four metabolic risk factors: overweight, high blood pressure, high fasting glucose, and high total cholesterol. Overweight was defined as a BMI of at least 25 kg/m^2 [17,18], high blood pressure was defined as systolic blood pressure of at least 130 mmHg or diastolic blood pressure of at least 85 mmHg [19,20], with participants having a medical history of hypertension included in the high blood pressure group; high fasting glucose was defined as a fasting serum glucose concentration of 6.05 mmol/l (110 mg/dl) or higher [20,21], with participants having a medical history of diabetes included in the high fasting glucose group; and high total cholesterol was defined as a serum cholesterol level of at least 5.7 mmol/l (220 mg/dl).

2.4. Determination of IHD, stroke, CVD, and all causes of death

Mortality follow-up between 1992 and 2000 was mainly based on nationwide death certificate data of the Korea National Statistical Office, supplemented by death benefit records of the Korean Medical Insurance Corporation. The vital status of study subjects between 1992 and 2000 was confirmed through exact data linkage on the basis of the unified 13-digit identification number. In Korea, professionally trained and certified medical chart recorders abstract, chart and complete death certificates using information provided by physicians. All records of death certificates in Korea are registered with the Korea National Statistical Office. In the present study, computerized searches of death certificate data from the Korea National Statistical Office were performed for each of the Korean Medical Insurance Corporation enrollees; therefore, in terms of mortality, follow-up is likely to be almost 100% complete. The participants who remained alive at the end of follow-up were treated as censored cases. The principal outcome variables were mortality from (1) IHD alone (*International Classification of Diseases*, *Ninth Revision* [*ICD-9*] codes 410–414); (2) stroke alone (*ICD-9* codes 430–438); (3) all CVD, including hypertensive disease (*ICD-9* codes 401–405), IHD (*ICD-9* codes 410–414), stroke (*ICD-9* codes 430–438), other heart diseases likely related to atherosclerosis (*ICD-9* codes 426–429), sudden death (*ICD-9* code 798), and other vascular diseases (*ICD-9* codes 440–444); (4) all causes. To exclude the effect of preexisting occult disease on the relationship between metabolic risk factors and mortality, subjects who died within the first 3 years were disregarded. The follow-up period lasted 8.5 years from January 1992 to June 2000.

2.5. Statistical analysis

The un-adjusted risk of mortality associated with each risk factor including family history, smoking, alcohol consumption, and exercise habits was derived from the Cox pro-