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Original Article

Metabolic syndrome components and diabetes incidence according to the presence or absence of impaired fasting glucose: The Japan Epidemiology Collaboration on Occupational Health Study

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ABSTRACT

Background: We prospectively examined the association of diabetes risk with the number of metabolic abnormalities, as well as their combinations, according to the presence or absence of impaired fasting glucose (IFG) in a large-scale Japanese working population.
Methods: Participants included 55,271 workers at 11 companies who received periodic health check-ups between 2008 and 2013. The metabolic syndrome (MetS) components were defined using the 2009 Joint Interim Statement. IFG was defined as fasting plasma glucose 5.6–6.9 mmol/L. Diabetes newly diagnosed after the baseline examination was defined according to the American Diabetes Association criteria. We calculated the hazard ratios (HRs) for diabetes incidence using the Cox proportional hazards model.
Results: During the follow-up period (median 4.95 years), 3183 subjects developed diabetes. In individuals with normal fasting glucose levels, the risk of diabetes increased steadily with the increasing number of MetS components; the multivariable-adjusted HRs for incident diabetes for the number of MetS components were 2.0, 4.3, 7.0, and 10.0 for one, two, three, or four MetS components, respectively, compared with the absence of components. A similar association was observed among individuals with IFG; the corresponding HRs were 17.6, 23.8, 33.9, and 40.7. The combinations that included central

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obesity appeared to be more strongly associated with diabetes risk than other combinations with the same number of MetS components within the same glucose status.

Conclusions: Our findings indicate that risk stratification of individuals by the presence or absence of IFG and the number of MetS components can detect individuals with a high risk of diabetes.

Introduction

Metabolic syndrome (MetS) is a cluster of risk factors, including raised blood pressure, dyslipidemia, impaired fasting glucose (IFG), and central obesity.[1,2] Diabetes risk has been shown to increase with the number of MetS components.[3–6] Given that IFG is an early stage of developing diabetes[7] and a strong predictor of diabetes,[8] it would be preferable to treat the glucose component separately from other components in stratifying diabetes risk. Few studies, however, have adopted this analytic strategy in assessing diabetes risk in relation to the number of metabolic abnormalities.[9] In addition to the number of MetS components, it remains unclear whether specific combinations of the components confer higher risks of diabetes. Wilson et al reported that combinations that included central obesity and IFG were more strongly associated with diabetes risk than others with the same number of components.[5,10] However, that study was relatively small in size ($n \approx 2500$), so a larger study is required to provide a more stable risk estimate for each combination of metabolic components. Here, we prospectively examined the association of diabetes risk with the number of MetS components, as well as their combinations, according to the presence or absence of IFG in a large-scale multicenter cohort of Japanese male and female workers.

Materials and methods

Study procedure

The Japan Epidemiology Collaboration on Occupational Health (J-ECOH) Study is an ongoing multicenter epidemiologic study among workers of 12 companies in Japan.[11,12] In Japan, employees are obliged to undergo a general health examination at least once a year under the Industrial Safety and Health Act. As of March 2015, 11 of 12 participating companies provided data from health check-ups that were conducted between January 2008 and December 2013 or between April 2008 and March 2014. The date of the earliest examination (mostly in 2008) was regarded as the baseline, but if the 2008 dataset contained a large amount of missing data, the data of the 2009 or 2010 examination was used as the baseline (for two companies). Subjects were followed from the baseline until the date of the most recent examination (maximally December 2013 or March 2014). The study protocol was approved by the Ethics Committee of the National Center for Global Health and Medicine, Japan. The requirement for written informed consent was waived.

Subjects

Of the 95,040 subjects with baseline data, we excluded 1532 subjects aged under 20 years, 15,660 subjects with missing data regarding the diagnosis of diabetes, and 5339 subjects with diabetes, which was defined as a fasting plasma glucose level of ≥7.0 mmol/L (126 mg/dL), casual plasma glucose level of ≥11.1 mmol/L (200 mg/dL), hemoglobin A1c (HbA1c) of ≥48 mmol/mol (6.5%), or current use of an anti-diabetic drug, in accordance with the American Diabetes Association criteria.[13] After further exclusion of 13,695 subjects with missing data on waist circumference, fasting triglyceride, high density lipoprotein (HDL)-cholesterol, blood pressure, current use of cholesterol-lowering drugs and anti-hypertensive drugs, or smoking status, 58,814 subjects remained. We further excluded 3543 subjects who did not attend any subsequent health check-ups, leaving 55,271 subjects (47,160 men and 8111 women) for the analysis. Compared with those who were included in the present study, those who were excluded ($n = 3543$) were older and had higher levels of blood pressure and triglyceride and higher proportions of antihypertensive and hypolipidemic drug use.

Assessment of the MetS components

The MetS components were defined according to the 2009 Joint Interim Statement[1,14,15]: 1) waist circumference ≥90 cm in men and ≥80 cm in women (for Asians, including Japanese), 2) triglyceride level ≥1.7 mmol/L (150 mg/dL) or current medication for dyslipidemia, 3) HDL-cholesterol level <1.04 mmol/L (40 mg/dL) in men and <1.3 mmol/L (50 mg/dL) in women, 4) blood pressure ≥130 mm Hg systolic or ≥85 mm Hg diastolic or current use of antihypertensive drugs, and 5) fasting plasma glucose level ≥5.6 mmol/L (100 mg/dL). Additionally, IFG was defined as fasting plasma glucose 5.6–6.9 mmol/L (100–125 mg/dL).[16]

Laboratory measurements

In the participating companies, HbA1c was measured using a latex agglutination immunoassay, the HPLC method, or the enzymatic method. Plasma glucose was measured using the enzymatic method or the glucose oxidase peroxidative electrode method, and HDL-cholesterol and triglycerides were measured using the enzymatic method. All laboratories involved in the health checkup at the participating companies have received satisfactory results (rank A or score >95 out of 100) from external quality control surveillance.

Statistical analysis

We calculated the person-time from the date of the baseline examination to the first date when diabetes was confirmed at a follow-up examination or to the date of the most recent examination, whichever came first. We also calculated the hazard ratios (HRs) and 95% confidence intervals (CIs) for the incidence of diabetes using Cox proportional-hazards regression models by individual MetS component and by the number of MetS components according to the presence or absence of IFG. In the multivariable-adjusted model, we adjusted for age (years, continuous), sex, company, and smoking status (non-smoker or current smoker). We also calculated the HRs for each combination of MetS components. In that analysis, we created a dyslipidemia component if the subject had high triglyceride and/or low HDL-cholesterol level, in accordance with the definition of dyslipidemia in the 2009 Joint Interim Statement.[1] A two sided $P < 0.05$ was considered statistically significant. The SAS software package (version 9.3; SAS Institute, Cary, NC, USA) was used to perform all statistical analyses.

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