Research Article

Sex and age differences in the effect of obesity on incidence of hypertension in the Japanese population: A large historical cohort study

Misuzu Fujita, PhD* and Akira Hata, MD, PhD

Department of Public Health, Chiba University, Chiba, Japan

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Abstract

Elevated risk of death from any cause and stroke associated with high body mass index (BMI) values decline with aging. However, it is not clear whether the effect of obesity on the incidence of hypertension varies by sex or age. Cox regression analyses were performed using a large historical cohort composed of 6803 men and 22,800 women. In the final model, which included the main effect (sex, age, and BMI), all two-way interactions (sex*age, sex*BMI, and age*BMI), a three-way interaction (sex*age*BMI), and adjusted variables determined by backward elimination, the three-way interaction and two of the two-way interactions (age*sex and age*BMI) were not significant; the remaining two-way interaction between sex and BMI was significant ($P = .016$). In the next step, the effect of BMI on the incidence of hypertension stratified by sex was evaluated. Hazard ratios (HRs) were significantly higher for BMI 27.0 to <29.0 and ≥29.0 kg/m^2 than for the HR for BMI 21.0 to <23.0 kg/m^2 in women (HR, 1.45; 95% confidence interval [CI], 1.32–1.59 and HR, 1.46; 95% CI, 1.29–1.65, respectively), but not in men (HR, 1.14; 95% CI, 0.98–1.33 and HR, 1.01; 95% CI, 0.77–1.32, respectively). The effect of obesity on the incidence of hypertension is stronger in women than in men. J Am Soc Hypertens 2014;8(1):64–70. © 2014 American Society of Hypertension. All rights reserved.

Keywords: Incidence of hypertension; sex difference; age difference; obesity.

Introduction

Hypertension is a leading risk factor for cardiovascular disease, stroke,[1–3] and all-cause mortality.[3,4] During the 1960s, stroke mortality in Japan was markedly high compared with international standards, but has drastically reduced.[5] The major reason for this change is regarded to be an overall decline in blood pressure levels among the Japanese population.[6] However, hypertension continues to pose an important public health challenge: it remains a common disease in Japan[7] and other countries,[8,9] but is one that can be prevented by lifestyle changes.[10]

Many cross-sectional studies have reported a significant positive association between the prevalence of hypertension and body mass index (BMI).[7,11,12] Prospective studies have also confirmed the influence of obesity on the incidence of hypertension.[13–16] However, sex-related differences in the association between obesity and hypertension are unclear because previous studies have reported the association only in men,[13] only in women,[16] and in both men and women.[14,15] Large prospective studies have indicated that high BMI values associated with the elevated risk of death from any cause,[17–20] stroke,[1,21] and cardiovascular disease[19] decline with aging. We therefore hypothesized that the association between obesity and the incidence of hypertension might vary by age.

In 2008, the Japanese Ministry of Health, Labour, and Welfare (MHLW) began a system of annual health examinations focused specifically on metabolic syndrome. The MHLW-published guidelines indicated that the effect of lifestyle changes (ie, weight reduction) on prevention of lifestyle-related diseases was larger in a group aged 40 to 60 years than in an older age group. This statement is consistent with the aforementioned findings of the declining effect of obesity with age on death from any cause,[17–20] stroke,[1,21] and cardiovascular disease.[19] However, it is unclear whether the effect of obesity on incidence of hypertension varies with age. Therefore, this study aimed to reveal the interactions

between sex and BMI and between age and BMI on the incidence of hypertension in Japanese men and women.

Methods

Subjects

Subjects were residents of Chiba City, Chiba prefecture, Japan. We constructed a historical cohort using data from annual health examinations carried out between 1996 and 2004 collected in accordance with the Health and Medical Service Law for the Aged. In 1996, 60,826 participants aged 40 to 79 years (17,210 men, 43,616 women) attended the annual health examination. We excluded 1019 participants (374 men, 645 women) with missing information and 27,979 participants (9430 men, 18,549 women) with hypertension diagnosed according to the criterion of the Japanese Society of Hypertension (JSH)—systolic blood pressure (SBP) $\geq$140 mm Hg and/or diastolic blood pressure (DBP) $\geq$90 mm Hg—and/or anamnesis for hypertension according to a self-reported questionnaire completed at baseline in 1996. This left 31,828 subjects (7406 men, 24,422 women), of whom 29,603 (6803 men, 22,800 women) could be followed at least once.

Since this cohort was obtained from the annual health examinations conducted in accordance with the Health and Medical Service Law for the Aged, consent was not obtained from the subjects. Therefore, in order to convert the health examination data into anonymous data, personal information (eg, name, date of birth, address, and telephone number) were removed from the records at Chiba City health centers. The Institutional Review Board of Chiba University approved this study. All procedures were followed in accordance with the Ethical Guidelines for Epidemiological Research of the Japanese Ministry of Education, Culture, Sports, Science, and Technology and the Japanese MHLW.

Baseline Examination

We defined the annual health examination conducted in accordance with the Health and Medical Service Law for the Aged in 1996 as baseline. The examinations were performed at designated clinics or hospitals in Chiba City. Height, weight, SBP, and DBP were measured, and blood samples were drawn during periods of fasting or non-fasting. Blood pressure measurements were performed in accordance with the diagnostic procedure of circulatory disease of the Japanese Circulation Management Research Council. Briefly, the examination room was kept quiet and the room temperature maintained at 20 to 25°C. Blood pressure measurements were taken after 5 minutes of rest with the subjects in a sitting position. Manchette width was approximately 13 cm, and length was 22 to 24 cm. The mercury sphygmomanometer or automatic sphygmomanometer was checked before use. Plasma glucose, serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyltransferase (GGT), and creatinine levels were determined by commercial clinical laboratories. Either fasting plasma glucose (glucose level after fasting, except for water, for $\geq$8 hours before blood drawing) or non-fasting plasma glucose (those who had not fasted) was measured for all subjects. On the basis of fasting or non-fasting plasma glucose level at baseline, subjects were categorized into two groups according to the guidelines of the Japanese Diabetes Society[22]: non-diabetic type (fasting plasma glucose <7.0 mmol/L or non-fasting plasma glucose level <11.1 mmol/L) and diabetic type (fasting plasma glucose $\geq$7.0 mmol/L or non-fasting plasma glucose level $\geq$11.1 mmol/L). Estimated glomerular filtration rate (eGFR) was calculated from serum creatinine, sex, and age using the Japanese coefficient-modified CKD Epidemiology Collaboration (CKD-EPI) equation.[23] We calculated AST category (<30 IU/L, $\geq$30 IU/L), ALT category (<30 IU/L, $\geq$30 IU/L), and GGT category (<50 IU/L, $\geq$50 IU/L) according to the standard program for health checkups and health guidance published by the Japanese MHLW, because the distributions of these variables were not normal. From each subject's self-reported questionnaire, we obtained anamnestic history of diabetes, liver disease, and kidney disease (presence or absence), smoking habit (non-smoker, smoker of 1–19, or >20 cigarettes/day), and alcohol consumption (non-drinker, drinker of 1 unit alcohol/day, or >1 unit alcohol/day). We defined one unit of alcohol as one glass of Japanese sake (180 mL), beer (633 mL), or whiskey (60 mL), roughly equivalent to 21, 23, and 20 g ethanol, respectively, according to the Standard Table of Food Composition in Japan. We asked the subjects the number of such glasses they drank every day. Subjects were categorized into three age groups (40 to 59, 60 to 69, and 70 to 79 years) and into seven BMI groups (<18.5, 18.5 to <21, 21 to <23, 23 to <25, 25 to <27, 27 to <29, and $\geq$29 kg/m^2).

Criteria for Incidence of Hypertension During the Follow-up Period

The 1997 to 2004 annual health examinations were defined as follow-up examinations. SBP and DBP were measured at clinics or hospitals, and anamnestic history of hypertension was examined using a self-report questionnaire at each follow-up examination. Subjects were defined as having hypertension according to the JSH criterion (SBP $\geq$140 mm Hg, DBP $\geq$90 mm Hg)[24] and/or being newly diagnosed as having hypertension by a physician during the follow-up period according to the self-report questionnaire.

Statistical Analysis

Continuous variables are presented as mean and standard deviation or as median (25th and 75th percentile) values. Comparisons of variables between men and women were