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Lifetime cigarette smoking is associated with abdominal obesity in a community-based sample of Japanese men: The Shiga Epidemiological Study of Subclinical Atherosclerosis (SESSA)

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ABSTRACT

Studies from Western countries suggest that smokers tend to display greater abdominal obesity than non-smokers, despite showing lower weight. Whether this holds true in a leaner population requires clarification. Using indices of abdominal obesity including visceral adipose tissue, we examined whether lifetime cigarette smoking is associated with unfavorable fat distribution among Japanese men.

From 2006 to 2008, we conducted a cross-sectional investigation of a community-based sample of Japanese men at 40–64 years old, free of cardiovascular diseases and cancer. Areas of abdominal visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) were calculated using computed tomography. We divided participants into four groups: never-smokers; and tertiles of pack-years of smoking among ever-smokers. Using multivariable linear regression, we calculated adjusted means of obesity indices (VAT, SAT, VAT-SAT ratio [VSR], and waist-hip ratio [WHR]) for each group, and mean differences between consecutive groups.

We analyzed 513 men (median age, 58.2 years; current smokers, 40.1%). Two-thirds showed body mass index (BMI) < 25 kg/m^2 (median, 23.5 kg/m^2). Overall, greater lifetime smoking group was associated with greater WHR and VSR. On average, one higher smoking group was associated with 0.005 higher WHR (95% CI, 0.001–0.008; $P = 0.005$) and 0.041 greater VSR (95% CI, 0.009–0.073; $P = 0.012$) after adjustment for potential confounders, including BMI. In this sample of relatively lean Japanese men, greater lifetime smoking was associated with a metabolically more adverse fat distribution. Although smoking is commonly associated with lower BMI, minimizing the amount of lifetime smoking should be advocated.

1. Introduction

Smokers tend to be leaner than non-smokers, although the long-term effects of smoking on weight remain unclear and can be variable (Audrain-McGovern and Benowitz, 2011; Chiolero et al., 2008). The idea that cigarette smoking is helpful in controlling body weight has remained popular (Audrain-McGovern and Benowitz, 2011), and the fear of gaining weight discourages smokers from quitting (Chiolero et al., 2008). Importantly, many population-based studies have suggested that cigarette smoking is associated with a greater degree of abdominal obesity (Bamia et al., 2004; Barrett-Connor and Khaw, 1989; Kim et al., 2012; Shimokata et al., 1989b), despite the lower weight/body mass index (BMI) observed in smokers (Canoy et al., 2005; Jee et al., 2002). In most of those studies, however, abdominal obesity was assessed using anthropometric measures such as waist

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circumference (WC) or waist-to-hip ratio (WHR). Whether smoking is associated with either visceral adipose tissue (VAT) or subcutaneous adipose tissue (SAT), or both thus remains unclear. This question is important, as VAT has been suggested to play a more important role than SAT in the pathogenesis of cardiometabolic derangements such as diabetes mellitus (DM) and atherosclerosis (Farb and Gokce, 2015; Perrini et al., 2008). In addition, most relevant studies have been conducted in the United States or Europe, where BMI is generally higher than in other regions, including Japan. We therefore aimed to examine cross-sectional associations between lifetime cigarette smoking and measures of abdominal obesity, including computed tomography (CT)-based assessments of VAT and SAT, in a population-based sample of Japanese men.

2. Methods

2.1. Subjects

This is a cross-sectional investigation of an observational population-based study. The subjects were male participants in a population-based cohort study conducted in Japan, the Shiga Epidemiological Study of Subclinical Atherosclerosis (SESSA). SESSA is a study of subclinical atherosclerosis and its determinants on a sample of Japanese residents, and details of the methods of enrollment have been reported previously (Kadota et al., 2013). In brief, from 2006 to 2008, we randomly selected and invited 2379 Japanese men aged 40 to 79 years who were residents of Kusatsu City, Shiga, based on the Basic Residents' Register of the city. The Register contains information on name, sex, birth date, and address of residents (Sekikawa et al., 2007). A total of 1094 men agreed to participate (The participation rate was 46%) (Kadota et al., 2013). The city, located in central Japan, has an industrial structure similar to the average of Japan: approximately two thirds and one-third are tertiary (i.e. service industries) and secondary (mining, manufacturing, construction industries) sectors, respectively, and the remaining few percent is primary sector (agriculture, forestry and fishery industry) according to the Ministry of Health, Labour and Welfare. For the present study, we limited our analyses *a priori* to those 40–64 years old who were free of cardiovascular disease and cancer at baseline (519 men). We chose the age cut-off of 64 years as an exclusion criterion to minimize the potential for older age to confound the association between smoking and obesity. Japanese men tend to start losing weight, as reflected by a decline in BMI, at around 60–69 years old (Yatsuya et al., 2011). According to the National Health and Nutrition Surveys in Japan, the proportion of current male smokers starts to decrease around the same age range (60–69 years), and continues to drop progressively with age (JAPAN HEALTH PROMOTION & FITNESS FOUNDATION, 2008). This simultaneous decline in body weight and smoking rates, likely rooted in both biological and socio-behavioral bases, may introduce further complexities and confounding to the relationship between exposure and outcome (Hu, 2008), which we therefore intended to avoid in our analyses.

The present study was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) and approved by the institutional review board of Shiga University of Medical Science (Nos. 17–19, 17–83).

2.2. Measurements

Data on medical history, use of medications, smoking, alcohol intake, and other lifestyle factors were collected from each participant using a self-administered questionnaire. Trained technicians confirmed the completed questionnaire with participants.

We assessed the amount of lifetime cigarette smoking in staged questions. First, participants were asked "Have you smoked in the past 30 days? (Yes/No)". Those answering "Yes" were categorized as current smokers, and queried the average number of cigarettes he smokes each day, and further asked the following question: "At what age did you start smoking cigarettes regularly? (Age)". For those who answered "No", the second question was "Have you smoked in the past?" If the answer was "No", we categorized the individual as a never-smoker, and if the answer was "Yes", we categorized him as a former smoker and asked for further information on the ages at which he started and ceased regular smoking, and the average number of cigarettes smoked each day during those periods. Based on the resulting information, we calculated the lifetime amount of cigarette smoking in pack-years, defined as the number of cigarettes smoked each day divided by 20, then multiplied by the number of years of smoking. Among the former smokers we categorized, three individuals reported same age for both initiation and cessation of smoking. We treated those individuals as former smokers with estimated pack-years of smoking of zero. The frequency of physical activity in leisure time was asked and categorized as "often", "occasional", or "rare to never."

Body weight and height were measured while the participant was wearing light clothing without shoes. Circumferences of the waist and hip were measured twice at the levels of the umbilicus and maximal protrusion of the hip, respectively, in the end-exhalation phase while the participant was standing upright. The mean of the two measurements was used for analysis. Blood pressure was measured twice consecutively in the right arm of the seated participant after sitting quietly for 5 min, using an automated sphygmomanometer (BP-8800; Colin Medical Technology, Komaki, Japan). The mean of these two measurements was used for analyses. Blood specimens were obtained early in the clinic visit after a 12-hour fast, and used for laboratory testing including lipids and glucose concentrations, and other detailed were reported previously. Serum lipid concentrations were determined at a single laboratory (Shiga Laboratory; MEDIC, Shiga, Japan) that had been certified for standardized lipid measurements according to the protocols of the US Centers for Disease Control and Prevention/Cholesterol Reference Method Laboratory Network. Concentrations of glycated hemoglobin (HbA1c) were measured using a latex agglutination inhibition assay according to the standardized method of the Japan Diabetes Society. DM was defined from a fasting serum glucose ≥126 mg/dL (≥6.99 mmol/L), HbA1c ≥6.1% (as per the Japan Diabetes Society protocol during the examination period; equivalent to ≥6.5% in the National Glycohemoglobin Standardization Program (Kashiwagi et al., 2012)), or current treatment for DM.

2.3. Abdominal adipose tissue areas

Areas of VAT and SAT were assessed using CT. Abdominal VAT was defined as the fat enclosed by the inner aspect of the abdominal wall. Abdominal SAT was defined as the fat outside the outer aspects of the abdominal wall, but not including that fat located within the muscular fascia. While participants were supine, serial CT images were obtained using a protocol similar to one described previously (Kadowaki et al., 2006). A single CT image of the L4–L5 vertebral space was selected to estimate areas of VAT and SAT. Adipose tissue was identified as showing attenuation between −190 and −30 Hounsfield units combined with anatomical interpretation by a reader. Studies of human cadavers have shown that the area measured by CT offers an accurate estimate of abdominal VAT,(Rossner et al., 1990) and the same or similar ranges of attenuation have been adopted to estimate VAT/SAT in population studies (DeNino et al., 2001; Ding et al., 2008; Fox et al., 2007; Wheeler et al., 2005). The inner and outer aspects of the abdominal walls were manually tracked, and respective areas were calculated using image analysis software (SliceOmatic; Tomovision, Montreal, Canada). Two types of CT scanner were used during the examination period: a GE-Imatron C150 Electron Beam Tomography system (EBCT; GE Medical Systems, South San Francisco, CA; slice thickness, 6 mm) for participants examined from May 2006 through to August 2007 and a 16-row multidetector row CT system (MDCT, Aquilion-16™; Toshiba Medical Systems, Tochigi, Japan; slice thickness, 7 mm) for participants examined thereafter. All CT images were analyzed at Shiga University of Medical Science by a trained