American Dietetic Association

RESEARCH

Research and Professional Briefs

Fruit Consumption Is Associated with Lower Carotid Intima-Media Thickness and C-Reactive Protein Levels in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Preliminary evidence in support of fruit intake for the prevention of cardiovascular disease in patients with type 2 diabetes mellitus (T2DM) is still limited. The objective of this study was to evaluate the association between fruit consumption and cardiovascular risk factors such as carotid intima-media thickness (CIMT) and high-sensitive C-reactive protein (hsCRP) in patients with T2DM. In this cross-sectional study, 407 patients with T2DM were recruited from August 2007 to December 2009. Dietary assessment based on 3-day 24-hour recall interviews, hsCRP levels, and CIMT were examined. Participants were categorized into three tertiles based on fruit intake. Comparisons of the participants' clinical characteristics among the three categories were performed using either one-way analysis of variance or analysis of covariance. In patients with type 2 diabetes with CIMT $\geq$1 mm, the intake of fruit was lower (P=0.001), whereas the serum hsCRP level was higher (P<0.001) compared with patients showing CIMT <1 mm. Results of the multivariable logistic regression analysis showed that the odds ratios of CIMT and hsCRP were 8% and 31% lower, respectively, in participants in the top tertile compared with those in the lowest tertile (P=0.018 and P<0.001, respectively) after adjustment for potential confounders. Hence, a reduction in hsCRP concentration and CIMT were found to be associated with an increase in fruit intake. Sufficient daily intake of fruits should, therefore, be considered as an important component of a medical nutritional therapy strategy for the prevention of cardiovascular diseases in patients with T2DM.

J Am Diet Assoc. 2011;111:1536-1542.

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Manuscript accepted: May 6, 2011.

0002-8223/$36.00

doi: 10.1016/j.jada.2011.07.010

Atherosclerosis is the trigger for a number of the major cardiovascular events responsible for the high mortality rates in patients with diabetes (1). Atherosclerosis in patients with diabetes can develop at the prediabetic stage, progress silently, and present eventually as a serious clinical event, such as myocardial infarction and stroke. Carotid intima-media thickness (CIMT) has been widely used to predict the early pathological changes of atherosclerosis in patients, including those with type 2 diabetes mellitus (T2DM) (2,3). In two previous case-control studies, the CIMT was found to be considerably greater in type 2 diabetic patients with cardiovascular disease (CVD) and stroke than those without these complications (4,5). In addition, a 0.1-mm increase in the CIMT has been suggested to be associated with a 1.8-fold increase in the risk of stroke in patients with T2DM (5). In addition to carotid artery stenosis, inflammation has also been implicated in the etiology of atherosclerosis and T2DM. For example, C-reactive protein, one of the acute-phase proteins in inflammation, is predictive of atherosclerosis in patients with T2DM (6,7).

A large number of studies have shown that the consumption of fruit and vegetables is negatively associated with the incidence of CVD and diabetes mellitus (8-10). Several large-scale investigations have further shown that fruit intake is inversely associated with the CIMT and high-sensitive C-reactive protein (hsCRP) levels in the general population (11-13). Patients with T2DM, compared with the general population, may therefore need to pay closer attention to their dietary habits and adjust their behaviors in this regard, including eating in moderation and making healthier food choices. For example, diets that are high in fruits, vegetables, whole grains, and nuts are often recommended to patients with T2DM in order to reduce the risk of CVD (14). These food types are important sources of dietary fiber, vitamins, and polyphe-

nols, components that play important roles in inhibiting the risk for CVD by acting as antioxidants or improving the lipid profile (15-17). At present, there have been few investigations about fruit intake and its association with the risk factors for CVD in patients with T2DM. Therefore, a cross-sectional study was conducted to evaluate fruit intake and its association with cardiovascular risk factors, including hsCRP and CIMT in patients with T2DM.

METHODS

Study Population

Diagnosis and typing of diabetes mellitus was conducted in accordance with 1999 World Health Organization guidelines (18). Six hundred and ninety-two participants were originally enrolled in Guangzhou First Municipal People's Hospital and the First Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China between August 2007 and December 2009. Eligible participants included both inpatients and outpatients aged from 45 to 69 years with a 3- to 10-year history of T2DM. Participants were excluded if they had an acute infection, inflammatory bowel disease, osteoarthritis, rheumatoid arthritis, chronic hepatitis, gout, asthma, angina pectoris, acute myocardial infarct, cerebral infarct, peripheral arterial disease, or a >5 kg change in body weight during the previous 3 months. In addition, eligible participants were divided into two groups according to CIMT—one group included those with CIMT ≥1 mm and the other included those with CIMT <1 mm. Informed consent was obtained from each patient and this study was approved by the Ethics Association of Sun Yat-Sen University.

Questionnaire Interview

All participants completed a questionnaire that requested information on the history of T2DM, CVD, and medication use, as well as smoking status, physical activities, and sociodemographic factors, such as education and economic status. The history of medication use was further confirmed by comparisons with medical records. Dietary intake was evaluated on the basis of a 3-day 24-hour recall interview (also known as a 72-hour dietary recall). Participants were requested by trained nutrition students to list the name and quantity of all foods, drinks, and dietary supplements consumed during the previous 3 days, which consisted of 2 working days and 1 weekend day. Common sets of household measures, photographs, and/or drawings of typical foods were shown to participants to help them estimate portion sizes. Probing questions about snacks, drinks, type of milk, fat, supplements, and other foods were also used to elicit more detailed information about dietary habits. Daily intakes of cereals, fish, vegetables, fruit, energy, and nutrients were compared between participants with CIMT ≥1 mm and <1 mm after being calculated according to previously devised food composition data (China Food Composition, version 1, 2002, Peking Medical University, Beijing, China). Validity of the food consumption data was investigated by comparing the results obtained using the 3-day 24-hour recall interview and those obtained via the food frequency questionnaire from 65 patients with T2DM. The results showed that the correlation coefficients between the two sets of data were 0.67 for fruit, 0.63 for vegetables, 0.59 for total energy, and 0.64 for dietary fiber.

Anthropometric Measurements

All participants underwent anthropometric measurements including height, weight, and circumferences of the waist and hip. The mean of two parallel measurements was recorded as the final value with a precision of 0.1 cm. The body mass index was (BMI) calculated as kg/m^2, and the waist-to-hip ratio as the waist circumference/hip circumference. Postprandial blood glucose measurements were made at 2 hours after asking patients to consume a typical breakfast meal. No other measures were used to ensure meal standardization. Two consecutive measurements of blood pressure were taken from the right arm after each participant had rested for at least 10 minutes. Systolic blood pressure and diastolic blood pressure were recorded to the nearest 2 mmHg. The averages of these two blood pressure values were used for subsequent analysis.

Measurement of CIMT

The CIMT was measured as described previously (4) at the common carotid artery (CCA; 20 mm proximal to the bifurcation) with a 10.0-MHz linear-array transducer (Technos MPX DU8, Esaote, Genoa, Italy). Briefly, far-wall IMT of both CCAs was examined at three sites (the thickest point and at 1 cm upstream and downstream, free-form plaques) on the longitudinal view by a single trained technician. The maximum CCA-IMT was defined as the mean of the thickest wall of the right and left CCA, calculated from three measurements on each side. To assay the quality of the ultrasonic protocol, 65 patients with T2DM underwent a repeat scan 2 weeks later. The ultrasonic scans were performed by the same sonographer (intra-observer repeatability), or by different sonographers (inter-observer repeatability). The inter- and intra-assay coefficients of variation for CIMT were 3.7% and 5.9%, respectively.

Biochemical Analyses

Blood samples were drawn from all study participants after they had fasted overnight for 12 hours. Serum and plasma were collected after centrifugation at 1,500*g* for 15 minutes at 4°C within 2 hours and stored at −80°C until testing. Plasma total cholesterol, triglycerides, high-density lipoprotein cholesterol, and high-density lipoprotein cholesterol were measured using commercial colorimetric kits (Biosino Biotechnology Company Ltd, Beijing, China) and an automated analyzer (AU2700; Olympus Co Ltd, Tokyo, Japan). Plasma fasting glucose and 2-hour postprandial glucose were assayed on the day of blood collection with an enzymatic colorimetric method using glucose oxidase. Plasma glycosylated hemoglobin level was analyzed using a Bio-Rad Variant analyzer that utilizes ion-exchange high-performance liquid chromatography (Diamat System; Bio-Rad Laboratories, Richmond, CA). The serum hsCRP concentration was determined using enzyme-linked immunosorbent assay kits