Journal of Cardiology 67 (2016) 449–454

Contents lists available at ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Original article

Prevalence and distribution of coronary calcium in asymptomatic Japanese subjects in lung cancer screening computed tomography

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ARTICLE INFO

Article history:
Received 25 February 2015
Received in revised form 23 June 2015
Accepted 25 June 2015
Available online 23 July 2015

Keywords:
Coronary artery calcium
Epidemiology
Ethics
Risk factor

ABSTRACT

Background: Coronary artery calcium (CAC) is associated with a risk of coronary heart disease. The prevalence and distribution of the CAC score have been examined in Western countries, but few studies have been performed in Asia, and especially in Japan. The goal of this study was to investigate CAC scores in an asymptomatic Japanese population.
Methods: CAC score and risk factors were analyzed in 1834 asymptomatic subjects who underwent lung cancer screening computed tomography.
Results: CAC was present in 26.9% of all the subjects, 29.8% of the males, and 17.1% of the females. In all age groups, the CAC score was higher in males. In multivariate analysis, male gender [odds ratio (OR) 2.461, 95% confidence interval (CI) 1.361–4.452, $p = 0.002$], aging (OR 1.102, 95% CI 1.081–1.123, $p < 0.001$), dyslipidemia (OR 1.740, 95% CI 1.216–2.490, $p = 0.002$), and fasting glucose (OR 1.008, 95% CI 1.002–1.015, $p = 0.012$) were significantly associated with a CAC score >100.
Conclusion: The results of this study provide a pattern of CAC distribution based on age and gender in asymptomatic Japanese subjects. This pattern was similar to that in Western countries, although the absolute CAC scores were lower. High CAC scores were associated with male gender, aging, dyslipidemia, and fasting glucose.

Introduction

The coronary artery calcium (CAC) score is correlated with age and the presence and amount of coronary atherosclerotic plaque. The CAC score is a surrogate marker of coronary atherosclerosis and a strong predictor of future coronary events [1–7]. However, some studies have suggested differences in CAC scores among different ethnic groups [8–10]. Thus, the Multi-Ethnic Study of Atherosclerosis [9,10] was designed to examine the prevalence, risk factors, and progression of subclinical cardiovascular disease in a multiethnic cohort, including subjects of both genders and with a wide age range.

Most studies of CAC have been performed in Western countries, and the prevalence and distribution of CAC in Asian populations are still uncertain. A few small studies have been performed in asymptomatic Japanese subjects [11,12]. CAC scores have been evaluated by electrocardiogram (ECG)-ungated low-dose lung cancer screening CT [13,14], and use of this approach in Europe has shown a correlation with ECG-gated regular dose cardiac computed tomography (CT) and prognosis [15,16]. Thus, we investigated the prevalence and distribution of CAC in an asymptomatic Japanese population using low-dose lung cancer screening CT performed during a health checkup.

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http://dx.doi.org/10.1016/j.jjcc.2015.06.010
0914-5087/

Methods

Study population

The included subjects consisted of asymptomatic persons who voluntarily underwent a CT scan for lung cancer screening at a general health check up in Toranomon Hospital Health Management Center between January 2010 and March 2011. Of 1940 consecutive asymptomatic subjects, 106 were excluded from the study: 98 with a history of coronary artery disease, 7 with a pacemaker or valve implantation that could cause artifacts, and 1 with no record of a calcium score. A total of 1834 subjects were included in the analysis. Medical histories and current medications were derived from medical questionnaires. Hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg without medication in at the outpatient clinic in at least two separate measurements or antihypertensive medication use. Diabetes mellitus was defined as fasting blood glucose ≥126 mg/dl or HbA1c (NGSP) ≥6.5%, or use of medication for diabetes. Dyslipidemia was defined as total cholesterol ≥240 mg/dl or low-density lipoprotein (LDL) cholesterol ≥140 mg/dl and/or high triglyceride (TG) or lower high-density lipoprotein (HDL) cholesterol, or previous use of lipid-lowering medication. The cutoffs were plasma TG ≥150 mg/dl for high TG and HDL cholesterol <40 mg/dl for low HDL cholesterol. Hyperuricemia was defined as uric acid ≥7.1 mg/dl. Obesity was defined as a body mass index (BMI) ≥25 kg/m^2, according to the criteria in the World Health Organization Asia-Pacific guidelines [17]. Metabolic syndrome was classified using the US National Cholesterol Education Program Adult Treatment Panel III recommendations [18]. Smoking habits (never, former, and current) were obtained from a self-completed questionnaire. The study was approved by the Institutional Review Board of our hospital. Informed consent was obtained from all subjects.

Computed tomography for CAC scoring

All subjects underwent lung cancer screening with a multi-detector CT system (Acquilion 64; Toshiba Medical Systems, Tochigi, Japan). CT scans were acquired during one deep inspiratory breath hold, without use of contrast medium or ECG-gating. The low-dose lung CT scan was performed using a tube voltage of 120 kV, a tube current of 60–70 mA and 30–35 mAs based on the body size of the subject, and a 300–400 mm field of view. The technical parameters for lung cancer screening CT and reconstruction of images for CAC scoring have been documented previously [19]. In brief, the image was reconstructed using non-overlapping 3.0-mm slices with a 260-mm field of view, which is the standard method used in clinical practice based on electron beam CT [20]. Use of slice thickness and overlapping reconstruction has a major influence on CAC scoring [21], and thus we used the same reconstruction protocol as that used for cardiac CT for CAC scoring.

CAC assessment

Reconstructed images were transferred to a post-processing workstation for analysis. CAC scoring was performed with commercial software (ZIO station, Tokyo, Japan). Quantitative CAC scores were calculated as described by Agatston et al. [22]. The amount of coronary calcium can be quantified non-invasively using CT and calculation of the Agatston score [22] or the volume score [23] or calcium mass [24]. Among these techniques, we chose the Agatston score because large clinical risk stratification studies have been based on this score [1,25,26]. The Agatston score was obtained by multiplying the pixel area by the density score (1: 130–199 H; 2: 200–299 H; 3: 300–399 H; 4: ≥400 H) and summing the lesion scores [22]. The scores were rounded and classified in a binary manner to indicate the absence (Agatston score, 0) or presence (Agatston score, >0) of CAC.

Risk factor assessment

We assessed risk factors for CAC > 100 using multivariate analysis. Yamamoto et al. [11] showed that CAC scores of 100–399 and ≥400 were significantly associated with cardiac modality in high-risk Japanese patients. The subjects of the current study were asymptomatic, and therefore, their CAC scores were lower than those of patients in the previous study. Thus, we thought that a cut-off value of 100 for the CAC score was appropriate in the current study.

Statistical analysis

Data are expressed as mean ± SD for continuous variables, and as frequencies and percentages for categorical variables. The significance of differences in quantitative data was determined by Mann–Whitney *U*-test and Kruskal Wallis test. Univariate analyses were performed using a logistic regression model. Variables with a univariate $p < 0.20$ were included in multivariate analysis, which was carried out using the forward stepwise method. Statistical analysis was performed using SPSS for Windows, ver. 13.0 (Chicago, IL, USA), with $p < 0.05$ considered to indicate significance.

Results

Clinical characteristics of the subjects

The characteristics of the subjects are shown in Table 1. Of the 1834 subjects, 1425 (77.7%) were males, the mean age was 56 years, 26.2% had a history of hypertension, 51.6% had dyslipidemia, and 10.6% had diabetes mellitus. More than two-thirds of the subjects were current or former smokers. Twenty subjects (1.1%) had a history of cerebrovascular disease, with no significant difference between the genders. The prevalences of hypertension, dyslipidemia, diabetes mellitus, obesity (BMI ≥ 25), hyperuricemia, and low estimated glomerular filtration ratio (eGFR) (<60 ml/min/1.73 m^2) was higher in males than in females.

Distribution of CAC scores and factors associated with CAC

CAC was present in 26.9% of all the subjects, 29.8% of the males, and 17.1% of the females. The rates of CAC scores of 0, 0–99, 100–399, and ≥400 were 73.1%, 18.8%, 6.8%, and 1.4%, respectively, in the total population. In all age groups except <40 years, males had higher CAC scores than females, and the amount and prevalence of calcium increased steadily with age (all $p < 0.001$, except $p = 0.603$ for age <40 years; Tables 2 and 3). Baseline rates of hypertension, dyslipidemia, and diabetes mellitus were higher in males, and more males were current or former smokers.

The percentile curves for CAC scores in each 10-year age group are shown in Fig. 1. Each plot shows the curves for the 25th, 50th, 75th, 90th, and 95th percentiles across the age groups. In all subjects, the amount of CAC increased after age 50 years. Males and females showed a different pattern of increments in CAC scores, with a time-lag of about 10 years in females. Females showed a much steeper increase in CAC score after 60 years of age, whereas males showed a gradual pattern with earlier and greater increases in CAC score. The 95th percentiles for CAC scores in males aged >50 years and in females aged >60 years were >100, and that in males aged >70 years was >400 in our subjects.

Univariate regression analyses (Table 4) were performed to determine factors that affect the presence of CAC, as defined by a