Atherosclerosis 242 (2015) 515–520

Contents lists available at ScienceDirect

Atherosclerosis

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

Colorectal adenoma is associated with coronary artery calcification in a Korean population

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ARTICLE INFO

Article history:
Received 24 April 2015
Received in revised form
20 June 2015
Accepted 6 August 2015
Available online 8 August 2015

Keywords:
Colorectal adenoma
Coronary artery calcification
Screening

ABSTRACT

Objective: Colorectal adenoma and coronary atherosclerosis have similar risk factors. The aim of this study was to investigate the association between colorectal adenoma and coronary artery calcification (CAC), which is used as a surrogate marker for coronary atherosclerosis.
Methods: This is a cross-sectional study of 398 Koreans (290 males, mean age of 56.8 ± 8.1 years) who underwent CAC scoring by multi-slice computed tomography and colonoscopy on the same day as the screening examination. The CAC scores were divided into the following three categories according to severity: absent (CAC score = 0), mild (0 < CAC score ≤ 100), and moderate-to-severe CAC (CAC score > 100).
Results: Colorectal adenoma was detected in 149 (37.4%) subjects and was significantly associated with a CAC score of >0 (OR = 1.66, 95% CI = 1.05–2.64, $P = 0.032$), including both mild (OR = 1.80, 95% CI = 1.06–3.03, $P = 0.029$) and moderate-to-severe CAC (OR = 1.95, 95% CI = 1.05–3.63, $P = 0.035$), in multivariate analysis after adjusting for age, gender and other risk factors. The proportion of subjects with colorectal adenoma and advanced adenoma progressively increased with increasing CAC score (colorectal adenoma 28.9%–54.1%, P for trend < 0.001; advanced adenoma 7.0%–16.4%, P for trend = 0.026).
Conclusion: Colorectal adenoma is related to coronary artery calcification independent of traditional risk factors for asymptomatic Koreans. The prevalence of advanced adenoma is more common in individuals with severe coronary atherosclerosis.

1. Introduction

The incidence and resulting mortality of colorectal cancer and cardiovascular disease, including coronary artery disease, have increased rapidly in Asia in recent decades [1–3]. Colorectal adenoma is the precursor lesion of colorectal adenocarcinoma, and removal of adenomatous polyps by colonoscopy is important to prevent colorectal cancer [4,5]. In addition, asymptomatic atherosclerotic changes can progress to symptomatic coronary artery disease over time [6]. Therefore, it is important to diagnose colorectal adenoma and coronary atherosclerosis and to recommend lifestyle modifications in asymptomatic patients.

Colorectal neoplasm and coronary atherosclerosis share similar risk factors, such as male gender, obesity, diabetes mellitus and smoking status [7–9]. Several studies have reported inconsistent results with regard to the association of colorectal neoplasm with coronary artery disease [9–13]. Moreover, most of these studies have used invasive coronary angiography or coronary computed tomography (CT) angiography, which are not appropriate for the screening of asymptomatic subjects. The coronary artery calcium (CAC) score reported by CT scan is widely accepted as a specific parameter of subclinical coronary atherosclerosis [14,15]. It is useful for the screening of asymptomatic subjects, providing reasonably

Abbreviations: CT, computed tomography; CAC, coronary artery calcification; BP, blood pressure; BMI, body mass index; TC, total cholesterol; TG, triglycerides; LDL, low-density lipoprotein; HDL, high-density lipoprotein; CRP, C-reactive protein; HbA1c, hemoglobin A1c; NSAID, non-steroidal anti-inflammatory drug; SD, standard deviation; OR, odds ratio; CI, confidence interval.

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http://dx.doi.org/10.1016/j.atherosclerosis.2015.08.004
0021-9150/

good prognostic information with a relatively low dose of radiation, and it is a noninvasive technique.

Knowledge of the relationship between colorectal neoplasm and coronary atherosclerosis independent of other traditional risk factors is important for performing health assessments of asymptomatic subjects. Therefore, we aimed to investigate whether colorectal adenoma is associated with CAC, which is used as a surrogate marker for coronary atherosclerosis in the asymptomatic population.

2. Subjects and methods

2.1. Subjects

We performed a retrospective, cross-sectional study. The clinical records of 414 consecutive subjects who underwent colonoscopy and CAC scoring on the same day during routine health check-ups between January 2009 and December 2014 at the Seoul National University Hospital Healthcare System Gangnam Center were reviewed. We excluded 16 subjects with a history of colorectal cancer or inflammatory bowel disease, a history of colon resection, or a history of angina pectoris or myocardial infarction. Finally, 398 subjects were enrolled in the study and further analyzed. The study data included information provided by a questionnaire, anthropometric assessment, colonoscopy, laboratory data, histopathological data and CAC as measured by multi-slice CT scan. The study protocol was approved by the Institutional Review Board of Seoul National University Hospital. Written informed consent was obtained from all subjects prior to undergoing the procedures.

2.2. Clinical and laboratory evaluations

Laboratory evaluation included measurements of total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, C-reactive protein (CRP), fasting glucose and hemoglobin A1c (HbA1c) levels. Venous blood samples were collected before 10 AM after a 12-h overnight fast. Height and body weight were measured using a digital scale. Body mass index (BMI, kg/m^2) was calculated as weight divided by height squared, and waist circumference was measured at the midpoint between the lower costal margin and the iliac crest by a well-trained nurse. Current smokers were defined as those who had been smoking for at least 1 year. Hypertension was defined as a systolic blood pressure of $\geq$140 mmHg, a diastolic blood pressure of $\geq$90 mmHg and/or the current use of antihypertensive agents. Subjects with a fasting plasma glucose level of $\geq$126 mg/dL or those who were currently on anti-diabetic treatment were defined as having diabetes mellitus.

2.3. Detection of colorectal adenoma by colonoscopy

Conventional white light colonoscopy (CF-H260 series; Olympus, Tokyo, Japan and EC 590 ZW series; Fujinon, Inc., Saitama, Japan) was used for all procedures. Bowel preparations were performed using 4 L polyethylene glycol lavage (Colonlyte; Meditech Korea Pharm., Seoul, Korea). All colonoscopies were performed by board-certified gastroenterologists. All polyps were biopsied or resected and sent for histopathological assessment. Polyp sizes were estimated using 7-mm diameter open-biopsy forceps. An adenoma was defined as a polyp with adenomatous tissue, including sessile serrated adenoma and advanced adenoma, as confirmed by pathology, but not invasive cancer. Colorectal adenoma was classified as advanced for polyps of $\geq$10 mm in diameter or the presence of a villous component, high-grade dysplasia or three or more adenomas.

2.4. Measurement of CAC by multi-detector CT

Coronary CT was performed using a 16-slice multi-detector CT system (Somatom Sensation 16; Siemens Medical Solutions, Forchheim, Germany) and a 64-channel multi-detector CT system (Brilliance 64; Philips Medical Systems, Best, Netherlands). CAC scans were performed according to the standard procedure of prospective ECG-triggered scan acquisition with a tube voltage of 120 kV and 110 effective mA with a 200-mm field of view [16]. The data were reconstructed to a 3-mm thick slice with a 400-ms acquisition window. The CAC score was calculated using CT software program (Rapidia 2.8; INFINITT, Seoul, Korea) with the Agatston method [17].

2.5. Statistical analysis

Baseline characteristics were compared using the chi-squared test and Student's t-test for categorical and continuous variables, respectively. The CAC scores were stratified into three groups according to severity for use in ordinal logistic regression analysis to determine whether colorectal adenoma was associated with an increased CAC score [18–20]. The severity categories were as follows: absent (CAC score = 0), mild (0 < CAC score $\leq$ 100) and moderate-to-severe CAC (CAC score > 100). Multivariable analysis was used to control for the influences of age, sex, and other possible factors on colorectal adenoma. For each variable, the odds ratio (OR) and 95% confidence interval (CI) were calculated. Statistical analysis was performed using Statistical Package for the Social Sciences version 22.0 (SPSS, Inc., Chicago, IL, USA). Statistical significance was established for two-sided P values of <0.05.

3. Results

3.1. Clinical characteristics with regard to colorectal adenoma

A total of 398 subjects (290 males, mean age of 56.8 ± 8.1 years) were analyzed in this study. Colorectal adenoma was detected in 149 (37.4%) subjects. The baseline characteristics of the subjects with and without colorectal adenoma are provided in Table 1. The subjects in the colorectal adenoma group were older than those in the non-adenoma group, and a higher proportion of them were male. The adenoma group had a significantly higher systolic blood pressure, BMI, waist circumference, fasting glucose and number of subjects with hypertension. There were no significant differences between the groups with respect to current smoking status, alcohol use, diabetes mellitus, most of the laboratory test results (except for fasting glucose) and medications used. The mean CAC score was higher in the adenoma group than in the non-adenoma group, but this difference was not significant ($P = 0.096$). The subjects with colorectal adenoma had a significantly higher prevalence of CAC presence (CAC score > 0, $P < 0.001$) and moderate-to-severe CAC (CAC score > 100, $P = 0.003$) than those without adenoma.

3.2. Clinical characteristics according to CAC score

The subjects were divided into two groups according to their CAC scores. Two-hundred and forty-two subjects had no demonstrable calcification in the coronary arteries (CAC score = 0), whereas the remaining 156 had evidence of coronary calcification (CAC score > 0). The clinical characteristics of each group are displayed in Table 2. The two groups differed significantly with respect to mean age, gender, diabetes prevalence, hypertension prevalence, BMI, waist circumference, HbA1c, and the use of aspirin and lipid-lowering medications. The prevalence of colorectal adenoma was significantly higher in subjects in the CAC > 0 group ($P < 0.001$).