Atherosclerosis 233 (2014) 584–589

Contents lists available at ScienceDirect

Atherosclerosis

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

Family history of coronary heart disease is more strongly associated with coronary than with carotid atherosclerosis in healthy asymptomatic adults

Beomseok Suh [a], Dong Wook Shin [a,b,*], Seung-Pyo Lee [c], Haewon Lee [a], Hyejin Lee [a], Eun-Ah Park [d], BeLong Cho [a,b]

[a] Department of Family Medicine, Seoul National University Hospital, Seoul, Republic of Korea
[b] Health Promotion Center, Seoul National University Hospital, Seoul, Republic of Korea
[c] Cardiovascular Center and Department of Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea
[d] Department of Radiology and Institute of Radiation Medicine, Seoul National University Hospital, Seoul, Republic of Korea

ARTICLE INFO

Article history:
Received 28 June 2013
Received in revised form
31 December 2013
Accepted 21 January 2014
Available online 29 January 2014

Keywords:
Subclinical atherosclerosis
Coronary computed tomography angiography
Coronary artery stenosis
Carotid ultrasonography
Carotid intima media thickness
Family history of coronary heart disease

ABSTRACT

Objective: To investigate the potentially different relationship between family history (FH) of coronary heart disease (CHD) and carotid or coronary atherosclerosis.
Methods: Asymptomatic healthy Korean adults older than 30 years who received both coronary CTA and carotid USG as part of a self-referred health check-up were retrospectively investigated ($N = 662$). Multivariable logistic regression analysis was employed to investigate the relationship between FH of CHD and either coronary CTA or carotid USG results.
Results: Adjusted for major CVD risk factors, FH of CHD was significantly associated with presence of any plaque in coronary arteries (aOR 2.10, 95% CI 1.07–4.16) and significant coronary stenosis (aOR 4.92, 95% CI 1.58–15.4), but was not associated with presence of any plaque in carotid arteries (aOR 1.27, 95% CI 0.61–2.63) and increased carotid IMT (aOR 1.44, 95% CI 0.40–5.22). Addition of FH of CHD had significant incremental predictive value to models for any coronary plaque (AUC 0.781 vs. 0.786, $p = 0.0351$), and significant coronary stenosis (AUC 0.772 vs. 0.808, $p = 0.0129$), but not for any carotid plaque (AUC 0.748 vs. 0.748, $p = 0.528$), and increased carotid IMT (AUC 0.778 vs. 0.783, $p = 0.591$).
Conclusion: To our knowledge, our study is the first to show specific comparative evidence that FH of CHD is more strongly associated with coronary than with carotid atherosclerosis. Our results suggest FH of CHD adds predictive value specifically to coronary atherosclerosis, but not carotid atherosclerosis, and suggest the possibility that screening for coronary atherosclerosis (via CAC) among low to intermediate risk asymptomatic adults with FH of CHD may be beneficial, who otherwise would not be screened according to traditional risk algorithms.

1. Background

Early detection for cardiovascular disease (CVD) may be beneficial because the majority of patients with sudden cardiac death or nonfatal myocardial infarction are silent prior to the attacks [1]. Traditional CVD risk assessment algorithms are clinically applied to estimate the future event risk [2,3], but often have limited predictive power.

Noninvasive measures of subclinical atherosclerosis, such as coronary artery calcium (CAC), coronary computed tomography angiography (CTA) and carotid ultrasonography (USG), are associated positively and strongly with future incidence of cardiovascular disease (CVD), and improve predictive power [4–6]. With the recent addition of evidence, these noninvasive tests have been considered to be implemented into traditional risk algorithms; in particular, CAC has been suggested for use in risk stratification of intermediate risk, low to intermediate risk, and diabetic individuals in recent guidelines [7,8].

However, an interesting observation is that these tests often do not concur and do not necessarily have overlapping outcomes and clinical implications. The results of CAC and carotid intima media thickness (CIMT) have only moderate degree of agreement within

* Corresponding author. Department of Family Medicine & Health Promotion Center, Seoul National University Hospital, 101 Daehakro, Jongnogu, Seoul 110-744, Republic of Korea. Tel.: +82 2 2072 0847; fax: +82 2 766 3276.
E-mail address: dwshin.snuh@gmail.com (D.W. Shin).

0021-9150/$ – see front matter © 2014 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.atherosclerosis.2014.01.046

individuals [9–11], and each test has some variability in the potential for predicting future CVD [12]: for example, CAC has higher predictive value of incident CHD than CIMT [6,13]. Therefore, whether and how to use these tests for early detection in clinical practice remains a matter of debate [14,15].

Family history (FH) of coronary heart disease (CHD) is a major risk factor for CVD [16,17], with a conservative estimate of 2-fold increase in risk [18,19]. However, studies suggest stronger association between FH of CHD with CHD compared to ischemic stroke [20], suggesting different genetic effects on CHD versus ischemic stroke.

FH of CHD has also been positively associated with presence of coronary plaques and significant stenosis [21], and increased CIMT [22]. If the association between FH of CHD and subclinical atherosclerosis is different between sites, it may provide useful information in the selection of appropriate methods for a given individual. However, to our knowledge there has been no previous study on the direct comparison of the association of FH of CHD with coronary and carotid atherosclerosis.

In this study, we investigated the comparative association of FH of CHD to different aspects of subclinical atherosclerosis by simultaneously measuring coronary CTA and carotid USG.

2. Methods

2.1. Study population

We retrospectively enrolled 732 consecutive Korean individuals older than 30 years who simultaneously received both CTA with 64-slice multidetector row computed tomography (MDCT) and Carotid Ultrasonography (Carotid USG) for general routine self-referred health evaluation in Seoul National University Hospital (SNUH) from January 2010 to December 2011. Subjects with atypical chest pain ($n = 12$) and cardiac type chest pain ($n = 7$), those with previous history of myocardial infarction/angina, coronary revascularization, or coronary bypass surgery history ($n = 43$), and those with insufficient medical records ($n = 7$) were excluded. As a result, a total of 662 asymptomatic Korean adults older than 30 years were enrolled. This retrospective study was approved by the SNUH institutional review board and the requirement for informed consent was waived.

2.2. Major CVD risk factor assessment

All subjects were asked whether they had chest pain and was categorized as non-cardiac, atypical, and typical, according to the Rose angina questionnaire [23]. Medical history of myocardial infarction, angina, stroke, hypertension, diabetes mellitus, hyperlipidemia, FH of CHD, current medication profile, and smoking status were inquired by self-reported questionnaire and medical interview prior to health screening (which was reviewed by retrospective chart review). FH of CHD was defined as history of CHD among first degree relatives (including both parents and siblings) at any age. Total cholesterol (TC), triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol (LDL-C), fasting plasma glucose, hemoglobin A1c level were measured after at least 12-h fasting period on the same day of the study. Hypertension was defined as history of hypertension and/or use of antihypertensive medication or a blood pressure ≥140/90 mmHg. Diabetes was defined as history of diabetes and/or use of oral hypoglycemic medication or subcutaneous insulin or a fasting plasma glucose ≥126 mg/dL or hemoglobin A1c ≥6.5%. Hyperlipidemia was defined as history of hyperlipidemia and/or use of lipid lowering agents or LDL-C ≥160 mg/dL or TC ≥ 240 mg/dL. Framingham risk score of subjects was calculated, and risk groups were categorized into low (<10%), intermediate (10–20%), and high (>20%), as described previously [24].

2.3. Coronary CTA data acquisition & analysis

Methods used for coronary CTA data acquisition and analysis in this study have been described elsewhere [25]. In brief, all CT examinations were performed using a dual source scanner (Somatom Definition; Siemens Medical Solutions, Germany), scans performed using the retrospective ECG-gated mode with ECG pulsing. Data were processed using three-dimensional software (Rapidia; INFINITT, Korea) and the images were in consensus assessed by 2 experienced radiologists. The presence of coronary stenosis and/or plaques was anatomically assessed based on a modified model of the coronary tree with 15 segments [26]. The stenoses were evaluated semi-quantitatively and described as the percentage of lumen diameter reduction (estimated as multiples of 5%). Each segment was categorized as significant (≥50% lumen diameter reduction) or non-significant (<50% lumen diameter reduction), as previously implemented [27,28]. Plaques were defined as structures >1 mm^2 within and/or adjacent to the vessel lumen, clearly distinguished from the lumen and surrounding pericardial tissue, and were visually classified for character of the atherosclerotic plaque in each arterial segment, in which the most stenotic portion was characterized if there were multiple plaque lesions per segment, into one of following: non-calcified, calcified, or mixed plaque.

2.4. Carotid USG data acquisition & analysis

Carotid USG was performed using the LOGIQ 7.0 system (GE Medical Systems, USA) to measure IMT and carotid plaques. Both common carotid arteries were thoroughly scanned from proximal to distal to the bifurcation. IMT was measured at the far wall of each common carotid artery about 1 cm proximal to the carotid bulb. If IMT was increased at both sides, the thicker measurement was selected. Increased IMT was defined when the average IMT was ≥1.0 mm, as a criterion previously reported [29], and also confirmed to be more than 2 standard deviations higher than age-specific average IMT among healthy Korean subjects [30]. Carotid plaques were defined according to the Mannheim Consensus, as focal structures encroaching into the arterial lumen of at least 0.5 mm or 50% of the surrounding IMT value, or demonstrates a thickness >1.5 mm as measured from the media-adventitia interface to the intima–lumen interface [29]. When a plaque was present, IMT was measured at the nearest plaque-free point. All measurements were taken by specialized radiologists.

2.5. Statistical analysis

Multivariable logistic regression models consisting of FH of CHD as the main independent variable, adjusted for age, sex, BMI, smoking status, hypertension, diabetes, and hyperlipidemia as independent covariates were constructed to predict the following 4 separate dependent variables (as measures of coronary or carotid atherosclerosis): (1) presence of any plaque type at any coronary artery segment on coronary CTA, (2) significant coronary stenosis (defined as stenosis ≥50%) on coronary CTA, (3) presence of any plaque in either common carotid artery on carotid USG, and (4) significantly increased IMT (defined as IMT ≥1.0 mm) on carotid USG. Kappa (κ) coefficients were determined to evaluate the magnitude of agreement between the four different aspects of coronary and carotid atherosclerosis investigated in this study. Incremental predictive values of adding FH of CHD into the multivariable logistic regression models for presence of coronary plaque,