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Prevalence and Significance of Carotid Plaques in Patients With Coronary Atherosclerosis

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ABSTRACT

Background and Objectives: Carotid artery intima-media thickness (CIMT) has recently been recommended as a non-invasive tool for primary prevention of cardiovascular events; the association between CIMT and adverse cardiovascular events is well-known. We sought to evaluate the prevalence and significance of carotid artery plaque, especially in patients with coronary atherosclerosis. **Subjects and Methods**: The study population consisted of 1,705 consecutive patients {933 males (54.7%); mean age, 59.7±10.9 years} who underwent coronary angiography and carotid artery scanning using high-resolution ultrasonography. Carotid plaque was defined as a focal structure encroaching into the arterial lumen by at least 50% of the surrounding IMT value or a thickness >1.2 mm. **Results**: Carotid plaque was identified in 30.3% (516/1,705) of the patients. Of patients in whom the plaque location could be evaluated (n=1,027), carotid plaque was located at the common carotid artery {n=64/267 (24.0%)}, carotid bulb {n=194/267 (72.7%)}, and at both sites {n=9/267 (3.4%)}. The prevalence of hypertension (58.5% vs. 45.2%, p<0.001) and diabetes mellitus (30.6% vs. 23.5%, p=0.007) was higher in patients with carotid plaques. The patients with carotid plaques were older (65.4±8.9 years vs. 57.2±10.7 years, p<0.0001), had a thicker CIMT (0.89±0.20 mm vs. 0.77±0.16 mm, p<0.001), and higher fasting blood sugar (FBS) levels (132.1±60.7 mg/dL vs. 121.6±47.1 mg/dL, p<0.001) than those without carotid plaque. Patients with carotid plaque more frequently presented with acute coronary syndrome (32.4% vs. 23.9%, p<0.001) than those without carotid plaque. Significant coronary artery stenosis by coronary angiography (75.4% vs. 58.3%, p<0.001), especially multivessel disease (46.3% vs. 27.2%, p<0.001), was more frequent in patients with carotid plaques. On multivariate analysis, old age (≥65 years), hypertension, and increased CIMT (≥1.0 mm) were independent predictors of carotid plaque. Carotid plaque (odds ratio, 1.85; 95% confidence interval, 1.39-2.45; p<0.001) was an independent predictor of multivessel disease based on multivariate regression analysis. **Conclusion**: Carotid plaque was common (30.3%) in Korean patients with coronary atherosclerosis, but it is still relatively uncommon compared to Western populations. Carotid plaque was associated with old age, hypertension, and increased IMT, and was an independent predictor of multi-vessel disease. **(Korean Circ J 2009;39:317-321)**

KEY WORDS: Carotid arteries; Atherosclerosis; Coronary artery disease.

Introduction

Atherosclerosis is a systemic disease,[1] and carotid and coronary arteries are the two most common sites of involvement of atherosclerosis.[2)3)] High-resolution B-mode ultrasonography is useful non-invasive method to evaluate carotid atherosclerosis. Intima-media thickness (IMT) of the common carotid artery is a surrogate marker of atherosclerosis and associated with cardiovascular events.[4-6)] Recently, carotid IMT (CIMT) has been recommended as a non-invasive tool for primary prevention of cardiovascular events.[7)]

Carotid plaque is easily detected by B-mode ultrasonography and there are several studies which have shown that carotid plaque is associated with traditional cardiovascular risk factors[5)8-10)] and predicts cardiovascular events.[11-13)] Several studies have also shown that carotid plaque predicts the presence and extent of coronary artery disease (CAD).[14)15)]

In this study, we sought to evaluate the prevalence and clinical significance of carotid plaque, especially in

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patients with coronary atherosclerosis.

Subjects and Methods

Study population

Between January 2000 and June 2007, 1,705 consecutive patients {933 males (54.7%); mean age, 59.7±10.9 years} who underwent coronary angiography (CAG) and carotid artery scanning at the catheterization laboratory at Konyang University Hospital (Daejeon, Korea) were enrolled. The study subjects consisted of 919 patients who presented with stable angina, 182 patients with unstable angina, 269 patients with myocardial infarction, and 335 patients who underwent CAG to evaluate congestive heart failure and the risk for non-cardiac surgery. Those who were hemodynamically unstable and those with a poor quality of their carotid image or declined to study were excluded. The baseline demographic, clinical, and angiographic data were gathered by trained research technicians.

Coronary angiography

CAG was performed through the femoral or radial artery using a standard technique. Significant coronary artery stenosis was defined as a >50% reduction of the internal diameter and evaluated at the major epicardial coronary arteries and side branches with a diameter ≥2.5 mm.

Carotid artery scanning

Before or within 2 days after CAG, carotid artery scanning was performed with a high-resolution ultrasonographic unit (Hewlett-Packard Sonos-5500), equipped with a 7.5 MHz linear array transducer. The subjects were assessed in the supine position. All ultrasonographic examinations were performed by one specially trained technician who was unaware of the study subject's clinical and angiographic information.

The IMT was measured in 1 cm long segments just proximal to the carotid bulb in the common carotid artery using a semi-automatic technique with MATH® software (version 2.01; METRIS CO., Argenteuil, France). In the presence of plaque, the IMT was measured at the segment without plaque. Carotid plaque was defined as a focal structure encroaching into the arterial lumen by at least 50% of the surrounding IMT value,[16] or with a thickness >1.2 mm.[9][17] The bilateral common carotid arteries (CCAs) and bulb (bifurcation) were scanned to evaluate the presence of plaque. From January 2005, we evaluated the locations (left or right side, CCA or carotid bulb) of the carotid plaque.

Statistical analysis

The data are expressed as the means±SDs or frequencies (percentages). The patient characteristics between groups were compared using a t-test for continuous variables and a chi-square test for categorical variables. Cox regression analysis was performed to determine the variables that were independently associated with carotid plaque. A $p<0.05$ was considered statistically significant. All analyses were conducted with Statistical Package for Social Science (SPSS, version 12; SPSS, Inc., Chicago, IL, USA).

Results

Patient characteristics

The prevalence of hypertension (58.5% vs. 45.2%, $p<0.001$) and diabetes mellitus (30.6% vs. 23.5%, $p=0.007$) was higher in patients with carotid plaque than in those without carotid plaque. The patients with carotid plaque were older (65.4±8.9 years vs. 57.2±10.7 years, $p<0.0001$), had a thicker right CIMT (0.89±0.20 mm vs. 0.77±0.16 mm, $p<0.001$), and higher fasting blood sugar (FBS) levels (132.1±60.7 mg/dL vs. 121.6±47.1 mg/dL, $p<0.001$) than those without carotid plaque. The baseline characteristics are summarized in Table 1. Patients with carotid plaque were more frequently presented with acute coronary syndrome (ACS, 32.4% vs. 23.9%, $p<0.001$) than those without carotid plaque. On multivariate regression analysis, old age (≥65 years), hypertension, and increased carotid IMT

Table 1. Baseline characteristics of the study subjects

	Plaque (-) n=1,189	Plaque (+) n=516	p
Age (years)	57.2±10.7	65.4±8.9	<0.001
Male (%)	54.8	54.5	NS
Medical history (%)			
Hypertension	45.2	58.5	<0.001
Diabetes mellitus	23.5	30.6	0.002
Current smoking	30.0	33.1	NS
Dyslipidemia	35.8	37.2	NS
Old MI	7.6	8.3	NS
ACS (%)	23.9	32.4	<0.001
Rt. CIMT (mm)	0.77±0.16	0.89±0.20	<0.001
BMI (kg/m^2)	25.1	24.2	<0.001
Laboratory data			
T-cholesterol (mg/dL)	188.4±40.0	189.8±46.5	NS
Triglycerides (mg/dL)	178.8±119.5	169.7±111.0	NS
HDL-C (mg/dL)	43.3±16.2	41.8±10.8	NS
LDL-C (mg/dL)	117.0±31.1	119.0±35.3	NS
FBS (mg/dL)	121.6±47.1	132.1±60.7	<0.001
hs-CRP (mg/L)	2.28±2.84	2.68±3.08	0.017
EF (%)	65.1±9.4	63.1±11.9	<0.001

Values are the means±SD. MI: myocardial infarction, ACS: acute coronary syndrome, Rt. CIMT: right carotid intima-media thickness, BMI: body mass index, T-cholesterol: total-cholesterol, HDL-C: high density lipoprotein-cholesterol, LDL-C: low density lipoprotein-cholesterol, hs-CRP: high-sensitivity C-reactive protein, EF: ejection fraction. NS: not significant

Table 2. Independent predictors of carotid plaque in patients with coronary atherosclerosis

	OR	95% CI	p
Old age (≥65 years)	3.72	2.86-4.83	<0.001
Hypertension	1.59	1.21-2.08	0.001
Thick IMT (≥1.0 mm)	2.55	1.76-3.68	<0.001

Relevant baseline clinical characteristics were included in the multiple logistic regression analysis model. The variables in this model included male gender, old age (≥65 years), a history of hypertension, myocardial infarction, and diabetes mellitus, current smoker, dyslipidemia (total cholesterol ≥220 mg/dL), increased IMT (Rt. CCA-IMT ≥1 mm), increased hs-CRP (≥3 mg/L), obesity (BMI ≥25), and decreased HDL-C (<45 mg/dL). OR: odds ratio, CI: confidence interval, IMT: intima-media thickness, Rt. CCA: right common carotid artery, hs-CRP: high-sensitivity C-reactive protein, BMI: body mass index, HDL-C: high density lipoprotein-cholesterol

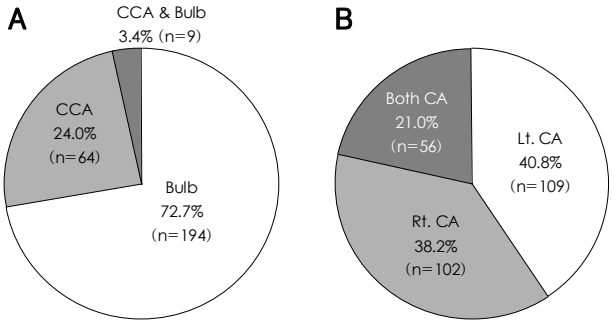

Fig. 1. Location of carotid plaque. Carotid plaque was founded more frequently in the carotid bulb (72.7%, n=194) than the common carotid artery (24.0%, n=64). Carotid plaque was found at the left carotid artery (40.8%, n=109) as well as the right carotid artery (38.2%, n=102) and at both carotid arteries (21.0%, n=56). CCA: common carotid artery, Lt. CA: left carotid artery, Rt. CA: right carotid artery.

(≥1.0 mm) were independent predictors of carotid plaque (Table 2).

Prevalence and site of carotid plaque

Five hundred sixteen patients (30.3%) had carotid plaque. Of 1,027 patients who were evaluated for the location of carotid plaque, 267 patients (26.0%) had carotid plaque. Carotid plaque was more frequently founded in the carotid bulb than the CCAs (Fig. 1).

Coronary angiographic findings according to the presence of carotid plaque

Significant coronary artery stenosis by coronary angiogram (75.4% vs. 58.3%, p<0.001), especially multi-vessel disease (46.3% vs. 27.2%, p<0.001), was more frequent in patients with carotid plaque (Fig. 2). Based on multiple logistic regression analysis, carotid plaque was an independent predictor of multi-vessel disease {odds ratio (OR), 1.85; 95% confidence interval (CI), 1.39-2.45; p<0.0001} (Table 3).

In subgroup analysis, patients with carotid plaque in the CCAs had a higher incidence of significant coronary artery stenosis than those with plaque in the bulb

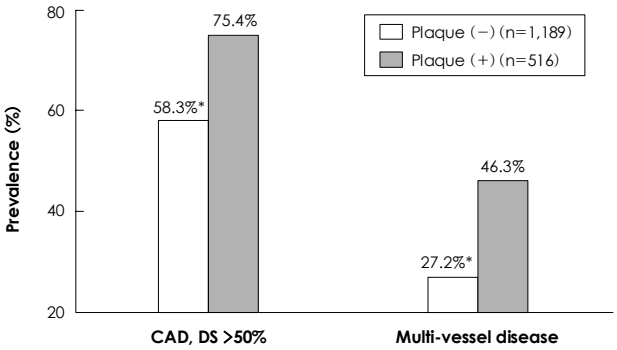

Fig. 2. Coronary artery disease according to carotid plaque. Significant coronary artery stenosis by coronary angiogram (75.4% vs. 58.3%, p<0.001), especially multi-vessel disease (46.3% vs. 27.2%, p<0.001), were more frequent in patients with carotid plaque. *p<0.001. CAD: coronary artery disease, DS: diameter stenosis.

Table 3. Independent predictors of multi-vessel disease in patients with coronary atherosclerosis

	OR	95% CI	p
Male	1.37	1.02-1.82	0.035
Plaque (+)	1.85	1.39-2.45	<0.001
Diabetes mellitus	1.96	1.47-2.61	<0.001
Hypertension	1.47	1.12-1.92	0.005
Hypercholesterolemia (total cholesterol ≥220 mg/dL)	1.43	1.09-1.87	0.010
History of myocardial infarction	2.11	1.33-3.33	0.001
Acute coronary syndrome	3.46	2.60-4.61	<0.001
Low HDL-C (<45 mg/dL)	1.56	1.18-2.07	0.002

Relevant baseline clinical characteristics were included in the multiple logistic regression analysis model. The variables in this model included male gender, carotid plaque, old age (≥65 years), history of hypertension, myocardial infarction and diabetes mellitus, current smoker, dyslipidemia, increased IMT (Rt.CCA-IMT ≥1 mm), increased hs-CRP (≥3 mg/L), obesity (BMI≥25), and decreased HDL-C. OR: odds ratio, CI: confidence interval, IMT: intima-media thickness, Rt. CCA: right common carotid artery, hs-CRP: high-sensitivity C-reactive protein, BMI: body mass index, HDL-C: high density lipoprotein-cholesterol

(89.1% vs. 66.0%, p<0.001). Patients with plaques in both carotid arteries had a higher incidence of significant coronary artery stenosis (83.9% vs. 69.2%, p=0.03) and multi-vessel disease (67.9% vs. 42.7%, p=0.001) than those with plaque in a single carotid artery (Fig. 3). In patients who presented with stable angina, those with carotid plaque had a higher chance for significant coronary artery stenosis (78.4% vs. 61.6%, p<0.001) than those without carotid plaque.

Discussion

The prevalence of carotid atherosclerotic stenosis, which is defined as an IMT >1.2 mm in Korean adults who volunteered for a routine heath check-up, has been reported to be 8.2%.[9] The prevalence of carotid plaque in Western general populations has been reported to be 15.7-26%[16] and 57-58% in patients with coronary

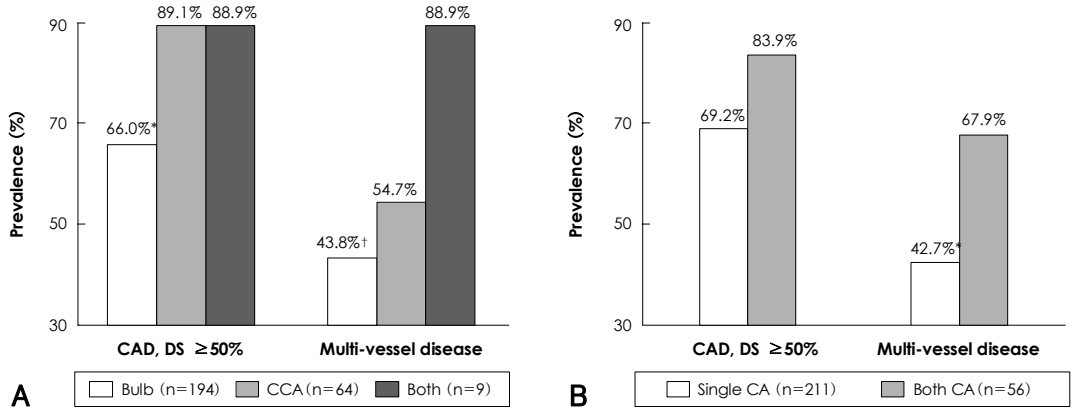

Fig. 3. Coronary artery disease according to the location of plaque. A: patients with carotid plaque in the bulb had a higher incidence of significant coronary artery stenosis than those with plaque in the CCA (66.0% vs. 89.1%, p<0.001), and multi-vessel disease was more frequent in patients with plaque involving the CCA and bulb than those with plaque involving the bulb (43.8% vs. 88.9%, p=0.012). B: patients with plaques in both carotid arteries had a higher incidence of significant coronary artery stenosis (83.9% vs. 69.2%, p=0.03) and multi-vessel disease (67.9% vs. 42.7%, p=0.001) than those with plaque in a single carotid artery. *p<0.001, †p=0.012, ‡p=0.03. CCA: common carotid artery, CAD: coronary artery disease, DS: diameter stenosis.

heart disease risk.[17] Carotid plaque is defined as a distinct area that can be identified with either mineralization or focal protrusion into the lumen in the former study and a localized thickening >1.2 mm in the latter study. Our study showed that carotid plaque was common (30.3%) in Korean patients who underwent CAG to evaluate CAD and a relatively lower incidence compared with Western populations, even using the same plaque definition.

Carotid plaque was associated with cardiovascular risk factors. The Framingham study[10] showed that age, smoking, systolic blood pressure, and cholesterol levels were independent predictors of carotid atherosclerosis and Cho et al.[9] reported that carotid plaque was associated with a history of stroke, hypertension, heart disease, hyperlipidemia, elevated $HbA1_C$, older age, a wider pulse pressure, lower high density lipoprotein-cholesterol (HDL-C), and heavy smoking. In this study, independent predictors of carotid plaque were old age (≥65 years), hypertension, and increased IMT (≥1.0 mm). The study subjects consisted of patients with coronary atherosclerosis, which may explain the different risk factors from previous reports.

Another main finding of this study was the association of carotid plaque and CAD. Many studies have shown a relationship between carotid and coronary atherosclerosis. Hallerstam et al.[15] reported a correlation between carotid atherosclerosis and the extent and severity of CAD. In the current study, we found that carotid plaque is an independent risk factor of multivessel disease of coronary arteries in patients with coronary atherosclerosis. Carotid plaque was more frequently founded at the carotid bulb which is one of the most common sites of atherosclerotic plaque,[18][19] and is thought to originate from endothelial damage caused by disturbances in local blood flow,[20] which are influenced by bifurcation anatomy.[21][22] However, the incidence of significant CAD was higher in patients with CCA plaque. This result suggests that CCA plaque may be more closely related to systemic atherosclerosis.

This study was a single center study that was limited to the prevalence of carotid plaque in Koreans who have coronary atherosclerosis. A multi-center study in several areas of Korea is needed to evaluate the prevalence of carotid plaque and the value of carotid scanning as a screening test in predicting coronary atherosclerosis in Koreans. However, our study had a relatively large study population and all study subjects were documented to have coronary atherosclerosis by CAG. Second, we did not evaluate the plaque involving the internal carotid artery, known to be the second most common site of carotid plaque,[19] and the total number of carotid plaques. So, further study is needed to evaluate the risk stratification of CAD depending on the location of the carotid plaque.

In conclusion, carotid plaque was common in Korean patients with coronary atherosclerosis, but it is still relatively uncommon compared to those of Western populations. It was associated with cardiovascular risk factors, including hypertension, diabetes, and increased CIMT and independent predictors of multi-vessel disease in patients with coronary atherosclerosis. Therefore, the patients with carotid plaque, especially who presented with ischemic heart disease, should be evaluated for significant CAD.

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