JNN

ORIGINAL ARTICLE

pISSN 2635-425X eISSN 2635-4357
https://doi.org/10.31728/jnn.2024.00164

Association between Coronary Artery Calcification and Carotid Plaque Using Health Check-Up Data

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Background: Coronary artery calcification and carotid plaque are recognized indicators of atherosclerosis, both linked to elevated cardiovascular and cerebrovascular risks. This study investigates the association between coronary artery calcification and carotid plaque and examines key risk factors associated with carotid plaque presence.

Methods: We enrolled 2,620 participants who underwent coronary artery calcium scoring via computed tomography and carotid ultrasound for health check-up from January 2017 to December 2022. Patient data, including age, sex, hypertension, diabetes mellitus, dyslipidemia, smoking history, body mass index, glucose, cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and lipoprotein(a), were collected. Logistic regression analyses were performed to explore the relationship between coronary artery calcification and carotid plaque, adjusting for major cerebrovascular risk factors.

Results: Coronary artery calcification was present in 44.7% of participants, and carotid plaque was detected in 43.5%. Univariable analysis showed a significant association between coronary artery calcification and carotid plaque (unadjusted odds ratio: 4.393, $p<0.001$). In the multivariable model, which included age, sex, hypertension, dyslipidemia, glucose, low-density lipoprotein cholesterol, and coronary artery calcification presence, coronary artery calcification remained an independent predictor of carotid plaque (adjusted odds ratio: 2.327, $p<0.001$). The model's area under the receiver operating characteristic curve was 0.768.

Conclusion: Our study demonstrates that coronary artery calcification is independently and significantly associated with carotid plaque in a health check-up population. Carotid imaging, such as carotid ultrasound, may be beneficial for early detection and management of carotid atherosclerosis in patients with coronary artery calcification.

J Neurosonol Neuroimag 2024;16(2):86-92

Key Words: carotid stenosis; coronary artery disease; carotid ultrasound

Received: November 20, 2024
Revised: December 21, 2024
Accepted: December 23, 2024

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INTRODUCTION

Coronary artery calcification (CAC) and carotid plaque are recognized markers of atherosclerosis, each associated with an elevated risk of cardiovascular and cerebrovascular events.[1-3] While CAC reflects coronary atherosclerosis, and carotid plaque indicates carotid atherosclerosis, both conditions are manifestations of systemic vascular disease. Understanding the relationship between CAC and carotid plaque could enhance early detection and risk assessment, especially given the potential for these markers to identify patients with a high burden of atherosclerosis.

Previous studies have examined CAC and carotid plaque independently, but few studies using health check-up data have explored their association.[4-8] Clarifying this

association could support CAC as a useful marker for identifying patients who may benefit from further cerebrovascular evaluation, such as carotid ultrasound.

This study investigates the association between CAC and carotid plaque, using multivariable logistic regression to account for major cerebrovascular risk factors. By focusing on CAC as a predictor of carotid atherosclerosis, we aim to contribute to a more integrated approach in assessing vascular health and improving preventive care strategies.

SUBJECTS AND METHODS

1. Data collection

We enrolled participants who underwent coronary artery calcium score computed tomography (CT) and carotid ultrasound for health check-up at Gangnam Severance Hospital from January 2017 to December 2022.

Data on the patients, including their sex, age, presence of hypertension, dyslipidemia, diabetes mellitus (DM), and smoking history, were collected. Additionally, Body mass index (BMI), glucose, cholesterol, triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and lipoprotein(a) (Lp(a)) data were collected.

2. Carotid artery ultrasound

Board-certified radiologists conducted carotid artery ultrasound examinations using multiple ultrasound devices, including the Philips iU22 and Philips EPIQ 5G. Separate longitudinal images were obtained of both the proximal and distal sections of the common carotid arteries and the internal carotid arteries on each side. Carotid plaque was identified as a focal structure that protruded into the arterial lumen by at least 0.5 mm or 50% more than the adjacent intima-media thickness, or that had a thickness of 1.5 mm or more.[9,10]

3. Coronary artery calcium scores

CT scans were conducted using a 64-slice multi-detector CT scanner (Revolution CT; GE Healthcare, Milwaukee, WI, USA). Patients with an initial heart rate of 60 beats per minute or higher were given an oral dose of 40 mg metoprolol to lower their heart rate to the target range of 50 to 60 beats per minute. Sublingual nitroglycerin was administered right before the scan. A bodyweight-adjusted dose (0.6–0.7 mL/kg) of an iodine-based contrast agent (iopamidol 370 mg iodine per mL, Iopamiro; Bracco, Milan, Italy) was injected into the antecubital vein over 10 seconds, followed by 25 mL of saline injected at a rate of 5.0 mL per second. The reconstructed CT images were transferred to a GE Centricity system (GE Healthcare Bio-Sciences Corp., Piscataway, NJ, USA) for post-processing and image analysis. Coronary arteries were assessed using rapid acquisition of 30 to 40 contiguous slices (each 3 mm thick) in end-diastole, with ECG-triggered imaging during a single 30 to 35 second breath-hold. Each scan was independently reviewed by a radiologist at a centralized reading center. Coronary artery calcium scores (CACS) were calculated according to the Agatston method.[11] A CACS greater than 0 indicated the presence of CAC.

4. Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 26 (IBM Co., Armonk, NY, USA). Logistic regression analysis was used to examine the relationship between the presence of coronary artery calcification and carotid plaque. Univariable analysis was conducted for coronary artery calcification and carotid plaque, with carotid plaque as the dependent variable. Multivariable analysis, which included variables such as sex, age, hypertension, dyslipidemia, DM, smoking, BMI, glucose, HDL-C, LDL-C, and Lp(a) was also performed. A *p*-value of less than 0.05 was considered statistically significant. The logistic regression model with the highest Receiver Operating Characteristic (ROC) curve was identified, and it was used to calculate the Area Under the Curve (AUC). The optimal cutoff value was determined, and sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

RESULTS

A total of 2,620 participants were included in this analysis, with a mean age of 57.2±10.1 years, and 64.6%

were male. The prevalence of hypertension, DM, dyslipidemia, and smoking was 31.9%, 10.8%, 26.9%, and 16.0%, respectively. The mean BMI was 25.0±3.6 kg/m^2. Mean levels of glucose, cholesterol, TG, HDL-C, and LDL-C were 106.5±24.1 mg/dL, 202.8±43.5 mg/dL, 137.7±88.1 mg/dL, 55.0±13.1 mg/dL, and 124.8±36.8 mg/dL, respectively. The mean Lp(a) level was 15.9±18.9 mg/dL. CAC was present in 44.7% of participants, and carotid artery plaque was detected in 43.5% (Table 1).

A comparison of participants based on the presence or absence of CAC (CACS>0 vs. CACS=0) revealed that those with the presence of CAC were significantly older than those without CAC. A significantly higher proportion of male was observed in the presence of CAC group compared to the absence of CAC group. Furthermore, the prevalence of hypertension, DM, and dyslipidemia was markedly elevated in the CAC group compared to the absence of CAC group. No significant difference was observed in smoking status between the two groups. With regard to metabolic markers, participants with the presence of CAC exhibited significantly elevated glucose levels and TG levels. HDL-C levels were observed to be lower. Contrary to expectations, cholesterol and LDL-C levels were found to be lower in the presence of CAC group than in the absence of CAC group. Participants with the presence of CAC also had significantly higher Lp(a) levels compared to those without CAC. Carotid plaque was significantly more prevalent among those with the presence of CAC than in those without (62.9% vs. 27.8%, $p<0.05$).

A similar pattern was observed when comparing participants based on the presence or absence of carotid plaque. The group with carotid plaque exhibited a higher proportion of males, a higher mean age, and a higher prevalence of hypertension, DM, and dyslipidemia. As with the CAC group, glucose, triglyceride, and Lp(a) levels were elevated, while HDL-C, cholesterol, and LDL-C levels were lower in the group with carotid plaque. Furthermore, the prevalence of coronary artery calcification was significantly higher in the group with carotid plaque compared to those without (64.6% vs. 29.4%, $p<0.05$).

Table 1. Characteristics and comparison based on coronary artery calcification and carotid plaque presence

Characteristic	Total (n=2620) Mean±1SD or n (%)	Coronary artery calcification			Carotid plaque		
		Presence (n=1,172)	Absence (n=1,448)	*p*-value	Presence (n=1,140)	Absence (n=1,480)	*p*-value
Age	57.2±10.1	61.45±8.9	53.8±9.8	<0.05	61.5±8.9	53.9±9.7	<0.05
Sex: Male	1,692 (64.6%)	909 (77.6%)	783 (54.1%)	<0.05	793 (69.6%)	899 (60.7%)	<0.05
Hypertension	836 (31.9%)	553 (47.2%)	283 (19.5%)	<0.05	507 (44.5%)	329 (22.2%)	<0.05
Diabetes mellitus	284 (10.8%)	220 (18.8%)	64 (4.4%)	<0.05	190 (16.7%)	94 (6.4%)	<0.05
Dyslipidemia	706 (26.9%)	452 (38.6%)	254 (17.5%)	<0.05	412 (36.1%)	294 (19.9%)	<0.05
Smoking	418 (16.0%)	189 (16.1%)	229 (15.8%)	0.82	170 (14.9%)	248 (16.8%)	0.20
Body mass index	25.0±3.6	25.6±3.4	24.6±3.7	<0.05	25.3±3.3	24.9±3.8	<0.05
Glucose	106.5±24.1	112.8±29.5	101.4±16.9	<0.05	111.5±27.9	102.6±19.8	<0.05
Cholesterol	202.8±43.5	195.7±47.1	208.5±39.4	<0.05	198.5±46.8	206.0±40.5	<0.05
Triglycerides	137.7±88.1	143.6±95.8	132.9±81.1	<0.05	142.8±92.9	133.8±84.1	<0.05
High-density lipoprotein cholesterol	55.0±13.1	53.1±12.5	56.6±13.4	<0.05	53.9±12.8	55.9±13.3	<0.05
Low-density lipoprotein cholesterol	124.8±36.8	119.6±39.8	129.0±33.6	<0.05	121.4±39.6	127.4±34.3	<0.05
Lipoprotein(a)	15.9±18.9	17.0±20.6	14.9±17.3	<0.05	17.1±20.3	14.9±17.6	<0.05
Coronary artery calcium score	102.5±317.7	226.2±443.6	0±0		192.2±439.3	33.4±138.6	<0.05
Presence of coronary artery calcification	1,172 (44.7%)	1,172 (100%)	0 (0%)		737 (64.6%)	435 (29.4%)	<0.05
Carotid plaque	1,140 (43.5%)	737 (62.9%)	403 (27.8%)	<0.05	1140 (100%)	0 (0%)	

A logistic regression analysis was conducted to examine the association between the presence of CAC and carotid plaque. The univariate logistic regression analysis, with carotid plaque as the dependent variable, revealed a significant association between the presence of CAC and carotid plaque, with an unadjusted odds ratio (OR) of 4.393 (p<0.001, 95% Confidence Interval [CI]: 3.725–5.182). A multivariable analysis was performed with carotid plaque as the dependent variable, including CAC presence, age, sex, hypertension, DM, dyslipidemia, smoking, BMI, glucose, HDL-C, LDL-C, and Lp(a) as independent variables. Due to strong correlations with LDL-C, cholesterol and TG were excluded from the model. The stepwise method was employed to remove variables while selecting the model with the highest ROC curve. Using the stepwise method, DM, smoking, BMI, HDL-C, and Lp(a) were removed. Consequently, the final model included the variables age, sex, HTN, dyslipidemia, glucose, LDL-C, and the presence of CAC. The presence of CAC was significantly associated with the presence of carotid plaque, with an adjusted OR of 2.327 (p<0.001, 95% CI: 1.924–2.814) (Table 2). The predicted probabilities were calculated using the final logistic regression model, and the ROC curve was generated by assessing the true positive and false positive rates at different thresholds. The AUC of the model was 0.768 (95% CI: 0.750–0.786) (Fig. 1). The optimal threshold was determined, yielding a sensitivity of 67.98% and a specificity of 72.70%. The corresponding PPV and NPV were calculated as 2.49 and 0.44, respectively (Table 3).

DISCUSSION

This study aimed to investigate the association between CAC and carotid artery plaque and to identify risk factors associated with the presence of carotid plaque using multivariable logistic regression analysis. Our findings indicate a significant association between the presence of CAC and carotid plaque, suggesting that participants with CAC are more likely to have carotid atherosclerosis. This association was robust across both univariable and multivariable analyses, with CAC presence yielding an unadjusted OR of 4.393 in the univariable model and an adjusted OR of 2.327 in the multivariable model, even after adjusting

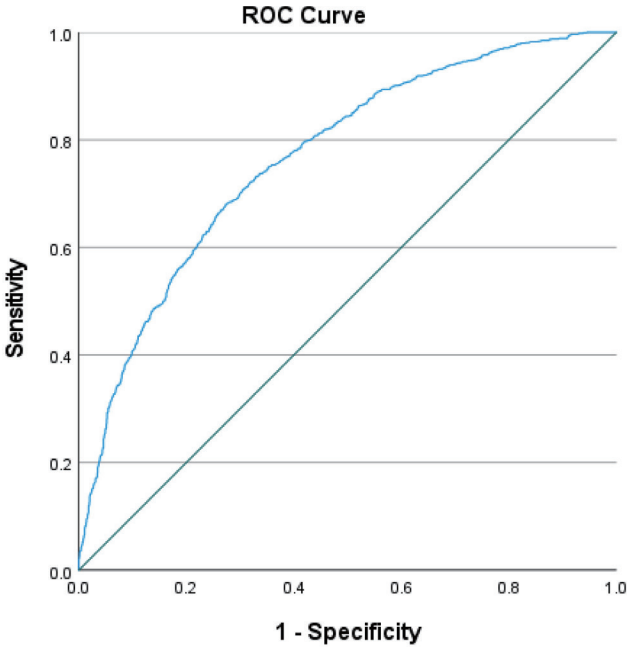

Fig. 1. Receiver operating characteristic (ROC) curve for the predictive model of carotid plaque presence. The ROC curve illustrates the discriminative ability of the multivariable logistic regression model, which includes CAC presence, age, sex, hypertension, dyslipidemia, glucose, and LDL-C as predictors. The area under the curve (AUC) is 0.768.

Table 2. Results of multivariate logistic regression analysis with carotid plaque as the dependent variable

Variable	Adjusted odds ratio	95% Confidence Interval		p-value
		Lower limit	Upper limit	
Age	1.073	1.062	1.085	<0.001
Sex: male	1.306	1.073	1.588	0.008
Hypertension	1.517	1.244	1.850	<0.001
Dyslipidemia	1.332	1.075	1.651	0.009
Glucose	1.008	1.004	1.011	<0.001
Low-density lipoprotein cholesterol	1.004	1.001	1.006	0.007
Presence of coronary artery calcification	2.327	1.924	2.814	<0.001

for other cerebrovascular risk factors.

These results align with previous studies that have highlighted CAC and carotid plaque as markers of atherosclerosis and predictors of cerebrovascular events.[12-14] Both coronary and carotid atherosclerosis are manifestations of systemic atherosclerosis, and the coexistence of these conditions in participants may indicate a higher overall burden of vascular disease. Importantly, in our study, even after adjusting for key risk factors such as age, sex, hypertension, dyslipidemia, glucose, and LDL-C, CAC remained independently associated with carotid plaque presence. This suggests that CAC may serve as a unique and independent indicator of carotid atherosclerosis beyond the traditional risk factors, highlighting its potential role in comprehensive cerebrovascular risk assessment. Additionally, this suggests that patients with CAC may require further evaluation for carotid atherosclerosis, such as carotid ultrasound.

In this study, contrary to expectations, the group with both CAC and carotid plaque had significantly lower cholesterol and LDL-C levels. This result is presumed to be

Table 3. Final logistic regression model: Sensitivity, specificity, positive predictive value, and negative predictive value

Metric	Value	95% confidence interval
Sensitivity	67.98%	65.19% to 70.69%
Specificity	72.70%	70.36% to 74.96%
Positive predictive value	2.49	2.27 to 2.73
Negative predictive value	0.44	0.40 to 0.48

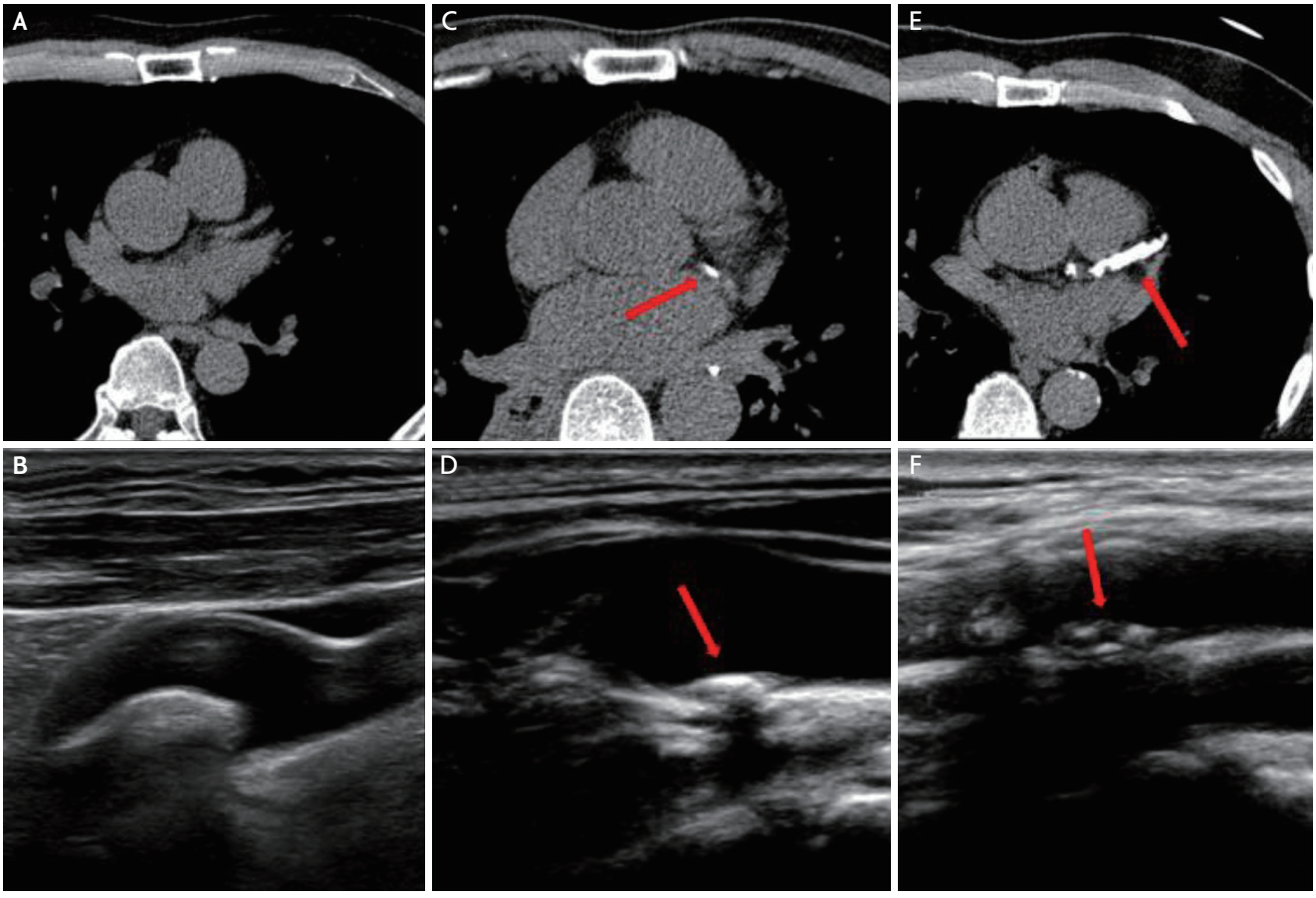

Fig. 2. (A, B) Patient with a coronary artery calcium score of 0. (A) No calcification observed on coronary artery calcium score computed tomography. (B) No plaque was identified on the carotid ultrasound. (C, D) Patient with a coronary artery calcium score of 113.65. (C) Coronary artery calcification is observed (red arrow). (D) Calcified plaque is detected with mild stenosis (red arrow). (E, F) Patient with a coronary artery calcium score of 1007.1. (E) Severe coronary artery calcification is observed (red arrow). (F) Heterogeneous plaque is detected with moderate stenosis (red arrow).

due to a higher prevalence of dyslipidemia in the group with both CAC and carotid plaque, leading to increased use of lipid-lowering medications such as statins. Indeed, in the multivariable analysis, including dyslipidemia, the likelihood of having carotid plaque increased with higher LDL-C levels. However, our study only confirmed the presence of dyslipidemia without assessing the use of lipid-lowering medications, making it difficult to establish a precise causal relationship. This represents a limitation of our study.

In our study, we used only the presence or absence of CAC to predict the presence of carotid plaque. However, it is well established that as the CACS increases, the risk of carotid plaque rises in proportion.[8] A similar trend was observed among our study participants, although limitations in our analytical methods prevented us from further investigating this relationship (Fig. 2).

Our study has several strengths that lend robustness to our findings. First, we conducted a comprehensive analysis using a broad set of cardiovascular and cerebrovascular risk factors, allowing for an in-depth examination of the association between CAC and carotid plaque. By including variables such as age, sex, hypertension, DM, dyslipidemia, smoking, BMI, glucose, HDL-C, LDL-C, and Lp(a), we were able to create a well-adjusted model to assess this relationship. Second, our use of both univariable and multivariable logistic regression analyses strengthens the validity of our results. Even after adjusting for potential confounders, the association between CAC and carotid plaque remained significant, suggesting that CAC may serve as an independent marker of carotid atherosclerosis. The clinical relevance of these findings lies in the potential role of CAC as a useful indicator in risk stratification, aiding in the identification of patients who may benefit from further screening for carotid atherosclerosis. Third, the large sample size (2,620 participants) enhances the statistical power of our study, making our findings more reliable and potentially generalizable to similar populations.

However, our study also has limitations that should be considered. First, one notable limitation is the lack of data on lipid-lowering medication use. Although we accounted for dyslipidemia, we were unable to determine whether participants were using statins or other lipid-lowering medications, which may have influenced LDL-C and cholesterol levels. This limitation restricts our ability to fully understand the relationship between lipid profiles and atherosclerosis in patients with CAC and carotid plaque. Second, the cross-sectional design of our study limits causal inferences, as we cannot determine whether CAC directly contributes to the development of carotid plaque. Future longitudinal studies are needed to clarify the temporal relationship between these markers of atherosclerosis. Third, as a single-center study, our findings may not be generalizable to other populations or clinical settings. Multi-center studies across diverse demographic and clinical environments are recommended to confirm these associations. Fourth, although we included a range of cerebrovascular risk factors, other potential confounders such as genetic predispositions, lifestyle factors, or the absence of homocysteine test results were not accounted for and may influence the observed associations.

In conclusion, our study demonstrates a strong association between CAC and carotid plaque, with CAC serving as an independent predictor of carotid atherosclerosis even after adjusting for other risk factors. These findings emphasize the importance of comprehensive cardiovascular risk assessment, incorporating both CAC and traditional risk factors, to improve early detection and prevention of carotid atherosclerosis.

Ethics Statement

This study was approved with a waiver of informed consent by the Gangnam Severance Hospital, Yonsei University Health System Institutional Review Board (3-2023-0157), ensuring adherence to ethical guidelines and the protection of participants' rights and welfare.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author upon reasonable request.

Author Contributions

Minsoo Sung and Kyung-Yul Lee designed the study; Minsoo Sung and Young Hoon Yoon were responsible for data acquisition; Minsoo Sung analyzed the data; Minsoo Sung wrote the first draft; Yo Han Jung and Kyung-Yul Lee critically reviewed the manuscript; Kyung-Yul Lee supervised the project. All authors have read and approved the final manuscript.

Acknowledgements

None.

Sources of Funding

None.

Conflicts of Interest

No potential conflicts of interest relevant to this article was reported.

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