Use of Carotid Ultrasound as a Surrogate for Coronary CT Angiography to Exclude Subclinical Coronary Atherosclerosis in Asymptomatic Patients with a Negative Coronary Calcium Study

Poster No.: C-0028
Congress: ECR 2012
Type: Scientific Exhibit
Authors: H. Y. Lee¹, S. M. Yoo², ¹Seoul/KR, ²Bundang/KR
Keywords: Ischaemia / Infarction, Arteriosclerosis, Contrast agent-intravenous, Ultrasound, CT-Angiography, Cardiac
DOI: 10.1594/ecr2012/C-0028

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Purpose

More than 50% of patients presenting with myocardial infarction are completely asymptomatic prior to the events [1, 2]. In addition, sudden cardiac death is the initial manifestation in approximately 20% of patients with cardiovascular disease [3, 4]. These catastrophic events are caused by the rupture of subclinical atherosclerotic plaque (i.e., asymptomatic but vulnerable plaque). Therefore, the presence of subclinical coronary atherosclerosis is a major determinant in predicting a future cardiovascular event [4]. Coronary calcium scoring CT (CAC CT) has the potential to identify subclinical coronary atherosclerosis. However, its value is limited because it does not identify non-calcified coronary plaque (i.e., the early changes of atherosclerosis) [5]. In fact, multiple recent studies have indicated that the number of patients with a significant coronary artery stenosis (#50%) and a zero calcium score are considerable [5-8]. Although coronary CT angiography (CTA) can precisely detect subclinical coronary atherosclerosis in asymptomatic subjects with a zero calcium score, it requires radiation exposure and the use of intravenous contrast material [5]. In contrast, carotid Doppler ultrasound has the potential to evaluate subclinical coronary atherosclerosis without radiation or contrast exposure [9-12]. However, no previous study exists in the English literature that assesses the diagnostic ability of carotid Doppler ultrasound examination to exclude the presence of subclinical coronary atherosclerosis in asymptomatic patients with a zero calcium score. Thus, the purpose of this study was to evaluate the diagnostic accuracy of carotid Doppler ultrasound to predict the presence of subclinical coronary atherosclerosis in asymptomatic subjects with a zero calcium score.
Methods and Materials

Study population

Our institutional review board approved this study and waived patient informed consent. We retrospectively reviewed the clinical and radiological data bases at a single institution. We identified 260 consecutive subjects in whom carotid Doppler ultrasound and coronary CTA including calcium score CT were performed for screening purposes from May 2006 to May 2011. Both examinations were performed within two weeks of each other in all subjects. Of the 260 subjects, 103 subjects had a calcium score of zero. Nine of the 103 subjects were excluded due to poor image quality in at least one of coronary artery segments on coronary CTA [poor enhancement (n=1) and coronary motion artifact (n=8)]. Seven subject were excluded due to known cardiovascular disease [(diabetes (n=6) and previous myocardial infarction (n=1)). Ultimately, eighty seven subjects [male, 60.9% (53/87); mean age, 50 ± 4.4] were enrolled in the study. These patients were divided into two groups: group 1 (n=12), subjects with at least one non-calcified plaque on coronary CTA; group 2 (n=75), subjects with normal coronary arteries. We analyzed several clinical and laboratory variables associated with coronary heart disease. These included a Framingham risk score (FRS), body mass index (BMI, kg/m²), waist circumference (cm), presence or absence of sedentary lifestyle, familial history of premature major adverse cardiovascular event (MACE), hypertension or dyslipidemia, systolic and diastolic blood pressure levels, smoking history if any including total pack-years of smoking, fasting blood glucose level, triglyceride, total cholesterol, and LDL and HDL cholesterol levels. FRS was calculated by using the following variables: age, sex, LDL and HDL cholesterol levels, systolic blood pressure level, presence or absence of smoking and diabetes [13]. A sedentary lifestyle was defined as no exercise or exercise less than 30 minutes per week. Familial history of premature MACE was considered to be present if the patient had a positive history in a first degree relative (<55 for men and <65 for women) [11]. Hypertension was defined as arterial blood pressure more than 140/90 mm Hg or a history of taking anti-hypertensive drugs. Dyslipidemia was considered to be present if there was a history of taking a lipid lowering medication or if the total serum cholesterol level was more than 250 mg/ml.

Carotid Doppler ultrasound protocol and analysis

Carotid intimo-media thickness (CIMT) was measured by using one of the two ultrasound systems (iU22, Philips Medical Systems,Bothell,WA,USA; LOGIQ E9, GE healthcares,Milwaukee,WI,USA) with 8-15 MHz linear transducer. Maximal CIMT was measured by one of two radiologists three times in the distal 1 cm of the far wall of each common carotid artery by using a manual reading technique. An averaged CIMT was used to determine the patient’s percentile by using an age, sex, and ethnicity-matched
CIMT as a reference value [11]. The measurement with the higher percentile of both mean CIMTs was used as the final percentile score. An abnormal CIMT was defined as >75 percentile or thickness # 1 mm [11]. Carotid plaque was defined as the presence of focal wall thickening at least 50% greater than that of the adjacent carotid wall.

**MDCT protocol and analysis**

A CAC score was measured on a 64-slice MDCT scanner (n=31) (Brilliance-64 scanner, Philips Medical Systems, Cleveland, OH, USA) or 256-slice MDCT scanner (n=56) (Brilliance iCT, Philips Medical Systems, Cleveland, OH, USA). The scanning parameters for CAC CT were prospective ECG-gating, 120 kV, 200 mA, and 3 mm slice thickness. The presence of coronary artery calcification was defined as a high density focus along the coronary arterial wall of >130 Hounsfield units (HU) using Agatston's method. Coronary CTA was performed using 120 kV. Variable tube current settings (mA) were used based on the patient's BMI. Prospective ECG-gating was used in patients with a heart rate <65 beats per minute. Otherwise, retrospective ECG-gated coronary CTA was performed. Tube current modulation was applied in all cases performed with retrospective ECG-gating to reduce radiation exposure. Intravenous injection of Iomeprol (Iomeron 400 mg/ml, Ilsung pharmaceuticals co, Seoul, Korea) was performed with a flow rate of 4-5 ml/s based on the patient's BMI. Scanning with 5 sec trigger delay was started when the contrast bolus arrived in the ascending aorta (>100 HU). Beta-blocker (Tenormin, 50 mg, Hyundae, Seoul, Korea) and sublingual nitrate (0.6 mg, Myungnum, Seoul, Korea) were administered in all patients without a contraindication.

Two radiologists (10 years of experience in cardiovascular imaging and 11 years of experience in body CT imaging) who were blinded to the clinical and carotid Doppler ultrasound data independently evaluated coronary CTA findings. If there was a disagreement on the MDCT findings, a final decision was reached by a consensus reading. Non-calcified coronary plaque was defined as the presence of a focal thickening of the coronary arterial wall with a low attenuation structure (> 1mm in diameter), in the absence of definite calcification on coronary CTA. We analyzed the following CT findings; presence and number of non-calcified coronary plaques, and degree of coronary artery stenosis [mild (#30%), moderate (30-50%), and significant (#50%)]. We analyzed diagnostic accuracy of carotid Doppler ultrasound to predict the presence of non-calcified coronary plaque and significant coronary stenosis (#50%) using coronary CTA as a gold standard.

**Statistical methods**

SAS version 4.1 (SAS Institute Inc., Cary, NC, USA) was used for statistical analysis. All continuous and categorical variables were expressed as mean ± standard deviation (SD) and percentage ratio, respectively. The unpaired t test and Fisher's exact test or chi-
square test were used to determine statistical significance of continuous and categorical variables between the two groups, respectively. Inter-observer agreement of CT findings was calculated by using kappa statistics. A p-value <0.05 was used as a cut-off value for statistical significance.
Results

There was a significant difference in gender ratio [group 1, male=91.7% (11/12) vs. group 2, male=44% (33/75), p=0.041], the incidence of hypertension [group 1=50% (6/12) vs. group 2=16% (12/75), p=0.021], and level of serum HDL [group 1, 44.3± 7.7 mg/dl vs. group 2, 55.4 ±11.4 mg/dl, p<0.001] between the two groups. There was no significant difference in other clinical characteristics. Abnormal CIMT in groups 1 and 2 was identified in 50% (6/12) and 29.3% (22/75), respectively (p>0.05). There was a significant difference in the presence of carotid plaque between the two groups [group 1, 66.7% (8/12) vs. group 2, 30.6% (23/75), p=0.036)]. There was no significant difference in the combined incidence of abnormal CIMT and carotid plaque between the two groups [group 1, 75% (9/12) vs. group 2, 48% (36/75), p>0.05]. There were 17 non-calcified coronary plaques in group 1. One patient had 3 plaques [significant stenosis in the proximal left anterior descending artery (LAD); mild stenosis in the mid-LAD and middle right coronary artery (mid-RCA)], and three patients had two coronary plaques [proximal LAD + mid-LAD (n=2) and proximal-LAD + mid-RCA (n=1)]. Overall, there were three significant, two moderate, and twelve mild coronary stenoses. All three patients with significant stenosis (Fig. 1) had multiple coronary plaques and were shown on carotid Doppler ultrasound to have carotid plaque and/or abnormal CIMT.
**Fig. 0:** Fig. 1A. A 48-year-old male with carotid plaque and significant coronary artery stenosis. The patient was an asymptomatic ex-smoker (15 pack-years) with dyslipidemia. He had a zero coronary calcium score and low Framingham risk score (8%). (A) Carotid Doppler ultrasound demonstrates both abnormal CIMT (>75 percentile) and an atherosclerotic plaque at the right carotid bulb (arrowheads). Volume rendering image (B) and curved multi-planar reformatted image (C) reveals a significant coronary artery stenosis (about 70%, arrows) with non-calcified plaque in the middle right coronary artery.

**References:** - Bundang/KR
Fig. 0: Fig. 1B. A 48-year-old male with carotid plaque and significant coronary artery stenosis. The patient was an asymptomatic ex-smoker (15 pack-years) with dyslipidemia. He had a zero coronary calcium score and low Framingham risk score (8%). (A) Carotid Doppler ultrasound demonstrates both abnormal CIMT (>75 percentile) and an atherosclerotic plaque at the right carotid bulb (arrowheads). Volume rendering image (B) and curved multi-planar reformatted image (C) reveals a significant coronary artery stenosis (about 70%, arrows) with non-calcified plaque in the middle right coronary artery.

References: - Bundang/KR
Fig. 0: Fig. 1C. A 48-year-old male with carotid plaque and significant coronary artery stenosis. The patient was an asymptomatic ex-smoker (15 pack-years) with dyslipidemia. He had a zero coronary calcium score and low Framingham risk score (8%). (A) Carotid Doppler ultrasound demonstrates both abnormal CIMT (>75 percentile) and an atherosclerotic plaque at the right carotid bulb (arrowheads). Volume rendering image (B) and curved multi-planar reformatted image (C) reveals a significant coronary artery stenosis (about 70%, arrows) with non-calcified plaque in the middle right coronary artery.

References: - Bundang/KR
The classification of the presence of non-calcified coronary plaque and degree of coronary artery stenosis was identical between two readers in all subjects (100%;
excellent inter-observer agreement, kappa=1.0). Total radiation dose for coronary CTA was 4.977 ± 1.662 mSv.

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of carotid Doppler ultrasound to identify subclinical coronary atherosclerosis on coronary CTA were 75% (9/12), 46.7% (38/75), 19.6% (9/46), and 92.7% (38/41), respectively. The sensitivity, specificity, PPV, and NPV of abnormal carotid Doppler ultrasound to detect significant coronary stenosis (#50%) on coronary CTA were 100% (3/3), 48.8% (41/84), 6.5% (3/46), and 100% (41/41), respectively. Three patients with a negative carotid Doppler ultrasound but positive coronary CTA had only mild coronary artery stenosis.
Fig. 0:  Fig. 1A. A 48-year-old male with carotid plaque and significant coronary artery stenosis. The patient was an asymptomatic ex-smoker (15 pack-years) with dyslipidemia. He had a zero coronary calcium score and low Framingham risk score (8%). (A) Carotid Doppler ultrasound demonstrates both abnormal CIMT (>75 percentile) and an atherosclerotic plaque at the right carotid bulb (arrowheads). Volume rendering image (B) and curved multi-planar reformatted image (C) reveals a significant coronary artery stenosis (about 70%, arrows) with non-calcified plaque in the middle right coronary artery.

© - Bundang/KR
**Fig. 0:** Fig. 1B. A 48-year-old male with carotid plaque and significant coronary artery stenosis. The patient was an asymptomatic ex-smoker (15 pack-years) with dyslipidemia. He had a zero coronary calcium score and low Framingham risk score (8%). (A) Carotid Doppler ultrasound demonstrates both abnormal CIMT (>75 percentile) and an atherosclerotic plaque at the right carotid bulb (arrowheads). Volume rendering image (B) and curved multi-planar reformatted image (C) reveals a significant coronary artery stenosis (about 70%, arrows) with non-calcified plaque in the middle right coronary artery.

© - Bundang/KR
Fig. 0: Fig. 1C. A 48-year-old male with carotid plaque and significant coronary artery stenosis. The patient was an asymptomatic ex-smoker (15 pack-years) with dyslipidemia. He had a zero coronary calcium score and low Framingham risk score (8%). (A) Carotid Doppler ultrasound demonstrates both abnormal CIMT (>75 percentile) and an atherosclerotic plaque at the right carotid bulb (arrowheads). Volume rendering image (B) and curved multi-planar reformatted image (C) reveals a significant coronary artery stenosis (about 70%, arrows) with non-calcified plaque in the middle right coronary artery.

© - Bundang/KR
Conclusion

In conclusion, a negative carotid Doppler ultrasound has a high negative predictive value excluding subclinical atherosclerosis on coronary CTA in asymptomatic subjects with a zero calcium score. Therefore, carotid Doppler ultrasound rather than coronary CTA appears to be a reasonable second-line examination in such subjects because it avoids radiation and contrast exposure.
References


