Volumetric Analysis of Carotid Plaque Components and Cerebral Microbleeds: A Correlative Study

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Purpose: The purpose of this work was to explore the association between carotid plaque volume (total and the subcomponents) and cerebral microbleeds (CMBs). *Materials and Methods:* Seventy-two consecutive (male 53; median age 64) patients were retrospectively analyzed. Carotid arteries were studied by using a 16-detector-row computed tomography scanner whereas brain was explored with a 1.5 Tesla system. CMBs were studied using a T2*-weighted gradient-recalled echo sequence. CMBs were classified as from absent (grade 1) to severe (grade 4). Component types of the carotid plaque were defined according to the following Hounsfield unit (HU) ranges: lipid less than 60 HU; fibrous tissue from 60 to 130 HU; calcification greater than 130 HU, and plaque volumes of each component were calculated. Each carotid artery was analyzed by 2 observers. *Results:* The prevalence of CMBs was 35.3%. A statistically significant difference was observed between symptomatic (40%) and asymptomatic (11%) patients (*P* value = .001; OR = 6.07). Linear regression analysis demonstrated an association between the number of CMBs and the symptoms (*P* = .0018). Receiver operating characteristics curve analysis found an association between the carotid plaque subcomponents and CMBs (A_z = .608, .621, and .615 for calcified, lipid, and mixed components, respectively), and Mann–Whitney test confirmed this association in particular for the lipid components (*P* value = .0267). *Conclusions:* Results of this study confirm the association between CMBs and symptoms and that there is an increased number of CMBs in symptomatic patients. Moreover, we found that an increased volume of the fatty component is associated with the presence and number of CMBs. **Key Words:** Cerebral microbleeds—carotid artery plaque—MRI—CTA.

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Introduction

Cerebral microbleeds (CMBs) are small and round hypointense areas on T2*-weighted gradient-recalled echo (GRE) sequence.[1] In the last years, an increasing interest in the clinical relevance of CMBs in individuals with cerebrovascular disease or dementia as well as in normal aging has been manifested,[2-4] and it has been suggested that CMBs may be a reliable biomarker for pathologic damage to small vessels from hypertension or cerebral amyloid angiopathy.[5] Moreover, CMBs are a common finding in stroke patients, especially those with hemorrhage, and some authors thought that they may be a marker of future cerebral hemorrhage.[6]

Recently Saba et al[7] found that there is an association between the presence of carotid artery fatty plaque and CMBs by suggesting that the composition of carotid artery may be considered as a marker of the presence of CMBs.

Recent investigations demonstrated that the computed tomography angiography (CTA), other than the quantification of the degree of stenosis and the characterization of the plaque's morphology, can evaluate the volume of the total volume of the carotid artery plaque as well as the volume of the subcomponents of the plaque (namely the fatty, mixed, and calcified tissues).[8,9]

The purpose of this work was to assess the potential association between carotid plaque volume (total and the subcomponents) and CMBs.

Materials and Methods

Study Design and Patient Population

The institutional review board approval for this study was obtained. Based on a power calculation (type I error, $\alpha = .05$; type II error, $\beta = .1$; A_z null hypothesis value = .5; A_z significant value = .7, pooled group), we estimated that a sample size of at least 100 carotids would be sufficient to investigate the relationship between carotid artery plaque type and CMBs. Therefore, we included all the patients who underwent multidetector CTA (MDCTA) of supra-aortic vessels and brain magnetic resonance imaging (MRI) in our hospital from July 2010 to March 2011 for a total of 72 consecutive patients (53 male, 19 female; mean age 68 years; age range 48-83 years).

Part of the examined population (n = 34) was included in previously published studies [Blinded for peer review], and the criteria we adopted to perform MDCTA of carotid arteries and brain MRI were published in previous investigations [Blinded for peer review].[10,11]

In brief, in our institutions, MDCTA of carotid arteries is performed in 2 different types of patients: (1) symptomatic and (2) asymptomatic. The classification of the symptomatic patients is described in the next section whereas asymptomatic patients are recruited from those patients where screening ultrasound analysis of carotid arteries showed the following: (1) presence of a carotid stenosis greater than 50% (according to the NASCET [North American Symptomatic Carotid Endarterectomy Trial] criteria[12]); (2) evidence of plaque alteration (an irregular surface, intraplaque hemorrhage, ulceration); and (3) when ultrasound could not provide adequate information about the degree of stenosis and plaque type because of anatomical conditions. In our institute is protocol to assess the carotid arteries of asymptomatic patients who undergo cardiac interventions for coronary artery disease, aortic interventions, and lower leg artery surgery, and in diabetics aged more than 50 years. All patients that perform CTA of carotid arteries are invited to underwent MRI exam of the brain. The brain MRI is also performed, as protocol, in all patients candidates to the carotid endarterectomy (CEA) procedure.

Classification of Cerebrovascular Symptoms

Vascular risk factors and coexisting comorbidities and treatment known before stroke or transient ischemic attack (TIA) are systematically recorded in our institution, and the TOAST (Trial of Org 10172 in Acute Stroke Treatment) criteria were used to classify the causes of stroke.[13] Patients were considered as ***symptomatic*** when they suffered TIA or stroke. In this study, we considered 3 months for the time window to be included in the symptomatic group.

For the purpose of this analysis, we considered as independent unit the carotid and the cerebral hemisphere of each side, and in symptomatic patients we considered the ipsilateral carotid artery and brain hemisphere as "symptomatic" and the contralateral carotid artery and brain hemisphere as "asymptomatic." In asymptomatic patients, we considered both carotids and brain hemispheres as "asymptomatic." Therefore, in symptomatic patients, according to the clinical symptoms, we considered a symptomatic side and an asymptomatic side whereas in asymptomatic patients both sides were considered asymptomatic.

MDCTA Technique

All patients underwent MDCTA of the supra-aortic vessels with a 16-multidetector-row computed tomography (CT) system (Philips Brilliance, Eindhoven, Netherlands), according to a previously described methodology [Blinded for peer review].[10,11] Examination was performed from the aortic arch to the carotid siphon by delivering a bolus of 80 mL of contrast medium (Ultravist 370; Bayer, Leverkusen, Germany) at a flow rate of 5 mL/s. The correct timing of the scan was selected with a bolus tracking technique. CT technical parameters included the following: matrix 512×512; field of view (FOV) 14-19 cm; 180-220 mAs; 120-140 kV. C-filter algorithm was applied.

Brain MRI Technique

Imaging examinations were performed with a Gyroscan 1.5-T superconducting magnet (Philips, Best, The Netherlands) with a head coil, according to a standardized protocol [Blinded for peer review]. For each patient, a two-dimensional T2*-weighted GRE sequence was performed (repetition time (TR) shortest; echo time (TE) 23 ms; flip angle 15°; in-plane resolution $.9 \times .9$ mm; FOV 230 mm; matrix 512×512; slice thickness 5 mm; interslice gap .5 mm).

Definition and Rating of CMBs

All datasets were anonymized and 2 experienced radiologists reviewed in consensus all images for the presence