Carotid Ultrasound for Assessment of Nonobstructive Carotid Atherosclerosis in Young Adults with Cryptogenic Stroke

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Background: The role of nonobstructive (<50% stenosis) carotid atherosclerosis (NOCA) in young adults with ischemic stroke is not well understood. In the present study, we investigated the prevalence and the ultrasonic characteristics of NOCA in a consecutive series of young adults with cryptogenic stroke (CS). *Methods:* Patients aged 18-54, consecutively treated in a tertiary hospital for first-ever CS (defined as an ischemic stroke without ASCOD (A: atherosclerosis; S: small-vessel disease; C: cardiac pathology; O: other causes) grade 1 potential cause) in the carotid artery territory, were prospectively enrolled. NOCA was assessed using carotid duplex ultrasonography. *Results:* Of 148 patients with first-ever ischemic stroke, 70 had CS, including 44 patients with carotid CS. NOCA was found in 22 of 44 (50%) patients. All but 1 plaque were echolucent. NOCA was bilateral in 15 patients and unilateral in 7 patients. All unilateral plaques were on the symptomatic side ($P = .02$). Plaque thickness, plaque length, and plaque volume were greater on the symptomatic side than on the asymptomatic side ($P = .001$, $P < .001$, and $P < .001$, respectively). Discrimination between the symptomatic and the asymptomatic side using any of these plaque metrics was good with areas under the curve (95% confidence interval) of .82 (.69-0.95), .85 (.74-0.96), and .87 (.75-0.99) for plaque thickness, plaque length, and plaque volume, respectively. *Conclusions:* NOCA is frequent in young adults with CS. Measurement of the plaque burden with carotid duplex may help to identify symptomatic NOCA. **Key Words:** Ultrasound—atherosclerosis—stroke in young adults—nonobstructive—cryptogenic stroke.

Introduction

Recent epidemiological studies indicate a growing incidence of ischemic stroke in young subjects.[1-3] Large artery atherosclerosis, defined as greater than or equal to 50% arterial stenosis, accounts for 8%–20% of strokes in adults under the age of 55.[4,5] According to current stroke-subtype classification systems, a nonobstructive (<50% stenosis) atherosclerotic plaque is not considered a potential cause of stroke, except in the rare case with a visible thrombus attached to the plaque.[6,7] Patients with such arterial lesions and no potential cause of stroke are thus classified as having cryptogenic stroke (CS). Retrospective studies have shown that non-obstructive carotid atherosclerosis (NOCA) is not uncommon in young adults with CS.[8,9] In the present study we sought to determine the prevalence of NOCA among prospectively enrolled young adults with CS in the carotid artery territory. We also analyzed the ultrasonic features of carotid plaques and compared the plaque burden between the symptomatic and asymptomatic carotid.

Methods

This was a single-center study, including patients aged 18-54 consecutively treated for first-ever CS in an academic stroke service between January 2016 and October 2016. Patients with cerebral venous thrombosis, subarachnoid hemorrhage with secondary brain ischemia, or transient ischemic attack as defined by transient neurological dysfunction without evidence of infarction on brain imaging were excluded.

The etiological workup of stroke was conducted using a predefined algorithm. Initial evaluation included brain magnetic resonance imaging (MRI) or computed tomography (CT), electrocardiography, routine blood studies, and noninvasive angiography of cerebral and cervical vessels using MR or CT angiography. Carotid stenoses were graded according to the North American Symptomatic Carotid Endarterectomy Trial criteria.[10] We used axial T1-weighted MRI scans with fat saturation for the diagnosis of arterial dissection. Inpatient telemetry and transesophageal echocardiography were performed in patients without definite cause of stroke after initial evaluation. Patent foramen ovale (PFO) was assessed at rest and during provocative maneuvers using intravenous injection of agitated saline. Additional investigations including 24-hour Holter monitoring, cerebrospinal fluid analysis, and testing for thrombophilia were performed in selected patients with suggestive findings on initial evaluation or without potential cause of stroke after completion of echocardiography.

All individual data were reviewed by a senior vascular neurologist and the causes of stroke were classified using the ASCOD (A: atherosclerosis; S: small-vessel disease; C: cardiac pathology; O: other causes) classification system.[7] In the present study, we only considered potential (ASCOD grade 1) causes of stroke. Patients with complete evaluation and no potential cause of stroke were classified as cryptogenic. According to this definition, CS encompassed patients without any possible cause of stroke and patients with abnormalities of uncertain significance such as PFO and NOCA.

Hypertension was defined as persistent elevation of systolic blood pressure at more than 140 mm Hg or diastolic blood pressure at more than 90 mm Hg documented before stroke, or treatment with antihypertensive drugs before stroke. Diabetes was defined as a previous diagnosis of type 1 or type 2 diabetes. Smoking was recorded in patients currently smoking or with a history of smoking.

Carotid duplex ultrasonography was performed to assess NOCA in patients with CS in the carotid artery territory. All examinations were performed on a Philips IU22 (Philips Medical Systems, Amsterdam, Netherlands) using a 9–13-MHz linear transducer without contrast agent. Plaque was defined as a focal structure encroaching into the arterial lumen and demonstrating a thickness of more than 2 mm, as measured from the media-adventitia interface to the intima–lumen interface.

The following characteristics were visually assessed for each plaque: echogenicity,[11] plaque ulceration,[12] and thrombus attached to the plaque. Nonobstructive plaques with superimposed thrombus are classified as potential cause of stroke according to ASCOD. However, for the purpose of the present study, plaques with thrombus were analyzed together with plaques without thrombus. The maximum thickness of plaque was measured in millimeter on a transverse view, perpendicular to the axis of the artery at the location of greatest plaque thickness. The absence of plaque and a focal thickening of less than 2 mm were scored as 0 mm. The maximum length (L) of plaque was determined on a longitudinal view and defined as the maximum distance in millimeter between 2 points on the plaque where the distance between the media–adventitia interface to the intima–lumen interface was more than 2 mm. The total artery diameter (TD) and residual lumen diameter (RD) were measured on a transverse view (Fig 1).

The plaque volume index (PVI) was calculated as follows: $\mathrm{PVI} = \left(\dfrac{\pi TD^2}{4} - \dfrac{\pi RD^2}{4} \right) \dfrac{L}{2}$

The PVI has been shown to correlate with the volume and weight of plaque measured on carotid endarterectomy specimens.[13]

All measurements were taken by the same senior neurosonologist. To evaluate interobserver variability, a second experienced neurosonologist repeated measurements masked to clinical data and to the findings of the first reader using recorded images.
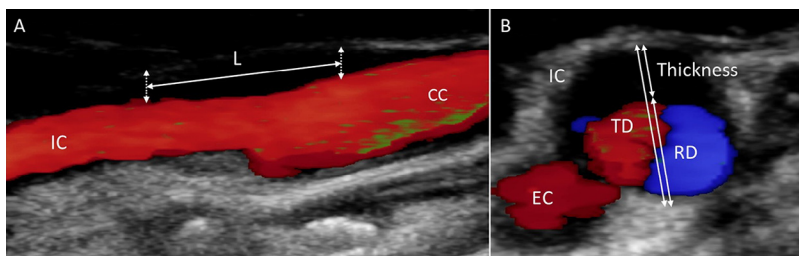

Figure 1. *Example of NOCA with measured parameters. Color-coded carotid duplex examination demonstrates an echolucent plaque ipsilateral to stroke. The plaque boundaries were delimited on a longitudinal view by dashed arrows of 2 mm in height on each end (A). The plaque thickness, and the total diameter and residual diameter of artery were measured on a transverse view at the location of greatest plaque thickness (B). Abbreviations: CC, common carotid artery; EC, external carotid artery; IC, internal carotid artery; L, plaque length; RD, residual diameter; TD, total diameter. (Color version of figure is available online.)*