

## Associations between Carotid Bifurcation Geometry and Atherosclerotic Plaque Vulnerability: A Chinese Atherosclerosis Risk Evaluation II Study

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### 1 Introduction

Carotid geometry has been suspected to be a risk factor for the initiation of atherosclerosis because of its influence on hemodynamics [1]. However, the relationships between carotid geometry and plaque vulnerability are not fully understood. This study aimed to determine the associations between carotid geometry and plaque vulnerability using magnetic resonance (MR) vessel wall imaging.

### 2 Methods

298 symptomatic patients with carotid atherosclerosis (< 30% stenosis) recruited from a cross-sectional, multicenter study, i.e. Chinese Atherosclerosis Risk Evaluation II (CARE-II) [2], were included in this study. All patients underwent carotid MR imaging, including 3D time-of-flight (TOF) and multi-contrast vessel wall imaging. Lumen boundaries of carotid artery were manually traced on TOF images and then the open-source tool Vascular Modeling Toolkit (VMTK) was used to extract a total of nine carotid geometry parameters, as illustrated in Figure 1. On the other hand, the presence of vulnerable plaque, which was defined as lesions with fibrous cap rupture, intraplaque hemorrhage, or large lipid core, was determined for each artery. Univariate and multivariate logistic regression were used to assess the differences in carotid artery geometric parameters between arteries with vulnerable and stable plaques.

### 3 Results

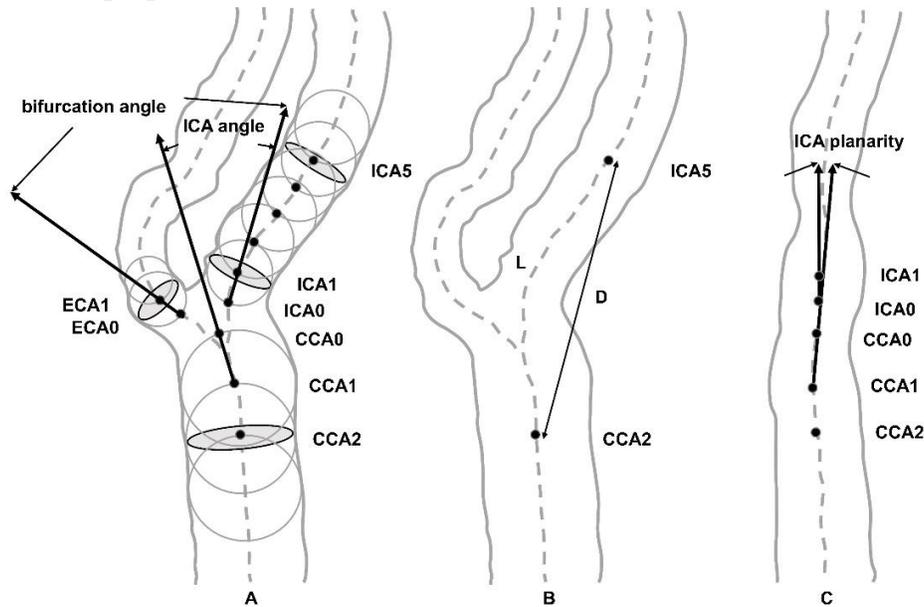
Of 298 recruited patients, 39 (13.1%) had vulnerable carotid plaques. Logistic regression revealed that larger ECA1: ICA1 area ratio (odds ratio [OR]: 1.79 per 1-SD increase, adj.  $P = 0.001$ ), smaller ICA1: ICA5 area ratio (OR: 0.35 per 1-SD increase, adj.  $P < 0.001$ ), and smaller proximal area ratio (OR: 0.47 per 1-SD increase, adj.  $P = 0.003$ ) were associated with the presence of vulnerable plaques. After adjustment for age, sex, history of smoking, and presence of stenosis, these three geometric parameters remained significantly associated with plaque vulnerability (all adj.  $P < 0.05$ ).

### 4 Discussion

We found patients with larger ECA1: ICA1 area ratio, smaller ICA1: ICA5 area ratio, and smaller proximal area ratio were more likely to have vulnerable plaques. These three geometric characteristics have previously been reported to be associated with higher wall shear stress [1, 3, 4]. Other studies have observed that higher wall shear stress is also associated with vulnerable plaque [5-7]. Thus, our results in combination of prior results are consistent with the hypothesis that wall shear stress is a mediating factor between carotid geometry and development of vulnerable plaque.

## 5 Conclusions

ECA1: ICA1 area ratio, ICA1: ICA5 area ratio and proximal area ratio may serve as additional risk factors for vulnerable plaque.



**Figure 1.** Representative carotid bifurcation illustrating calculation of geometric parameters. (A) Centerlines of ICA, ECA and CCA and the maximally-inscribed spheres along the vessel branches were automatically identified. ICA0, ECA0 and CCA0 are origins of the three vessels branches, while the other points (i.e. ICA1-ICA5, ECA1 and CCA1-CCA2) are centers of the identified maximally-inscribed spheres. Area ratios were calculated using the cross-sectional lumen areas through the points CCA2, ICA1, ICA5, and ECA1. (B) Between CCA2 and ICA5 the length of the centerline (L) and linear distance (D) were measured to calculate tortuosity as  $L/D-1$ . (A and C) The bifurcation plane and vectors of the branches were also defined, in order to calculate bifurcation angle, ICA angle and ICA planarity (cf. [1]).

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