Longitudinal Distribution of Mechanical Stresses in Carotid Plaques of Symptomatic Patients

Samuel A. Thrysøe, PhD; Minako Oikawa, PhD, MD; Chun Yuan, PhD; Nikolaj Eldrup, PhD, MD; Anette Klarke, MD; William P. Paaske, PhD, MD; Erling Falk, PhD, MD; W. Yong Kim, PhD, MD; Jens Vinge Nygaard, PhD

Background and Purpose—Mechanical stress may contribute to plaque rupture in patients with carotid atherosclerosis. We determined longitudinal mechanical stresses in carotid atherosclerotic plaques and compared them with known markers of plaque vulnerability.

Methods—Nineteen symptomatic patients scheduled for carotid endarterectomy underwent carotid MRI with a multicontrast protocol to characterize plaque morphology and geometry. Longitudinal 2-dimensional computational models were generated from the MRI data, and the mechanical stresses were calculated.

Results—Peak longitudinal mechanical stresses occurred predominantly in the shoulder regions of the carotid plaque and correlated inversely with fibrous cap thickness (r = −0.61; P = 0.01), and increasing degrees of stenosis (r = 0.71; P = 0.003). Peak stress levels were asymmetrically distributed longitudinally, with 50% occurring proximal to the maximal stenosis, 25% at the point of maximal stenosis, and 25% distal to the maximal stenosis.

Conclusion—The peak longitudinal mechanical stresses in the fibrous caps of symptomatic patients with carotid atherosclerotic stenosis were located at known predilection sites for plaque rupture, suggesting that mechanical stresses may play a role in plaque destabilization. (Stroke. 2010;41:1041-1043.)

Key Words: atherosclerosis ▶ carotid artery ▶ computational fluid dynamics ▶ fluid structure interaction ▶ plaque rupture

The mechanical stresses on the atherosclerotic plaques may influence the risk of plaque rupture.1–3 Stress level differences have been found between symptomatic and asymptomatic carotid plaques2 and between ruptured and nonruptured coronary lesions.3 These studies relied on time-consuming 3-dimensional computational simulations1 or cross-sectional 2-dimensional simulations,3 disregarding effects of fluid structure interaction. We determined the longitudinal mechanical stresses using a more time-efficient longitudinal 2-dimensional model based on MRI and incorporating effects of plaque morphology, plaque geometry, blood pressure, and the local flow field.

Subjects and Methods

Study Population

Nineteen symptomatic, nonconsecutive patients (enrollment based on scanner availability) scheduled for carotid endarterectomy were included after having given informed consent. The study was approved by the local ethics committee.

MRI Protocol

Patients were scanned using a 1.5-T MRI scanner (Philips Intera Achieva 1.5-T R1.5.4; Philips) equipped with a surface coil. The symptomatic carotid artery was examined using T1-weighted, T2-weighted, proton-density weighted, and time-of-flight scans.4 To minimize digitization errors and facilitate accurate segmentations, the images were interpolated using zero-filled Fourier Transforms yielding an interpolated in-plane resolution of 0.31 × 0.31 mm. Flow velocities were measured using a phase-contrast turbo field echo sequence, whereas vessel wall deformation was depicted using a balanced gradient echo sequence.5

Computational Simulation

A semi-automated software (CASCADE; Vascular Imaging Laboratory) was used for segmentation of lipid-rich necrotic core, fibrous cap, vessel lumen, and vessel wall.4 Two curved lines were created through the center of the common carotid trunk and the internal and external carotid arteries, respectively. A curved plane was defined between these 2 lines, which were extended outward to ensure completion of the model. Finally, the curved plane was projected onto a 2-dimensional plane parallel to the bifurcation, constituting the 2-dimensional computational model.3 Intersections between the curved plane and outlines of the individual components of the carotid atherosclerotic plaques were extracted, constituting the longitudinal 2-dimensional model. Patient-specific blood velocities measured by MRI were applied to both outlets. Time-resolved blood pressure was applied at the inlet and measured using an applation tonometry transducer (SPT-301; Millar Instruments). The pressure profile was

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From the MR-Center (S.A.T., W.Y.K.), Aarhus University Hospital Skejby, Aarhus N, Denmark; Vascular Imaging Lab (C.Y., M.O.), University of Washington, Seattle, Wash; Department of Cardiothoracic and Vascular Surgery (N.E., A.K., W.P.P.), Department of Cardiology (E.F., W.Y.K.), Interdisciplinary Nanoscience Center (J.V.N.), Aarhus University, Aarhus N, Denmark.

Correspondence to Samuel Alberg Thrysøe, Aarhus University Hospital Skejby, MR-Center, Brendstrupgaardsvej 100, DK-8200, Aarhus N, Denmark. E-mail Samuel@mr.au.dk.

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scaled to the systolic and diastolic blood pressures of the individual patient.

A fluid–structure interaction simulation was used to calculate the mechanical principal stress levels in the plaque, which are caused by forces exerted by the flowing blood. The simulations were performed using a commercially available finite element solver (COMSOL 3.4; Comsol AB).

**Data Analysis**

Minimal fibrous cap thickness, defined as the thinnest tissue between the blood and the lipid-rich necrotic core, and the lipid-rich necrotic core area were measured. Correlations were estimated using Spearman-rank correlation coefficients with corresponding probabilities using 5% significance level. A $z$ distribution was used to calculate 95% CI.

**Results**

Two patients were excluded from the study because of poor image quality caused by motion artifacts, and 1 was excluded because of data loss, leaving 16 patients for analysis. Figure 1 shows the results of a typical simulation. Four patients displayed recent infarcts, whereas 3 patients exhibited older infarcts.

**Correlations**

Significant correlations were found between minimal fibrous cap thickness and degree of stenosis ($r_s = -0.64; P = 0.009$; Figure 2A), peak principal stress and degree of stenosis ($r_s = 0.71; P = 0.003$; Figure 2B), and peak principal stress and minimal fibrous cap thickness ($r_s = -0.61; P = 0.014$; Figure 2C).

**Figure 2.** Correlations between the degree of stenosis, minimal fibrous cap thickness, peak principal stresses, lipid-rich necrotic core area, and systolic blood pressure. A, B, and C were statistically significant. Results depicted at time of systole.
Peak Principal Stresses
Maximal stresses occurred at the minimal fibrous cap thickness in 11 of the 16 patients (69%). The shoulder region, defined as the junction between normal vessel wall and atherosclerotic plaque, was the location of peak principal stresses and a thin fibrous cap in 12 of 16 patients (75%). Eight patients (50%) showed maximal stresses proximal to the area of maximal stenosis, 4 (25%) had maximal stresses distal to this area, and in the remaining 4 patients (25%) stresses were largest at the area of maximal stenosis.

Discussion
Histopathologic studies have indicated that lipid-rich necrotic core size and fibrous cap thickness are key morphological determinants of plaque vulnerability. However, principal stresses may be of additional significance, combining the effects of morphology, anatomy, and hemodynamics into a single comprehensive aggregate of the local maximal mechanical forces that act on the plaque and vessel wall.

A significant correlation was found between peak principal stresses and the degree of stenosis and also between peak principal stresses and minimal fibrous cap thickness (Figure 2A–C). However, there was a marked variation of stress levels, particularly in patients with thin fibrous caps and large degrees of stenosis.

Longitudinal 2-dimensional models will inherently disregard plaque morphology out of the chosen plane, which could affect the obtained stress levels. However, the location of maximal longitudinal stress levels in this study showed an asymmetrical distribution in accordance to a previous angiographic study of plaque ulceration, with 50% of the patients displaying maximal stress levels proximal to the plaque, 25% with maximal stresses at the center of the plaque, and 25% with maximal stresses distal to the plaque.

Conclusion
This study introduces a time-efficient method of performing longitudinal principal stress simulations. Peak principal stresses occurred predominantly at the regions with minimal fibrous cap thickness and within the shoulder region of the carotid plaque, a known predilection site of plaque rupture.

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Disclosure
S.A.T., W.Y.K., and J.V.N. are seeking a patent on the technology involved in this study, and E.F. is affiliated with a plaque study. There are no other conflicts to report.

References
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