

Plaque Rupture in the Carotid Artery Is Localized at the High Shear Stress Region

A Case Report

Harald C. Groen, MSc; Frank J.H. Gijssen, PhD; Aad van der Lugt, MD, PhD;
Marina S. Ferguson, MT; Thomas S. Hatsukami, MD; Anton F.W. van der Steen, PhD;
Chun Yuan, PhD; Jolanda J. Wentzel, PhD

Background and Purpose—Cerebrovascular events are related to atherosclerotic disease in the carotid arteries and are frequently caused by rupture of a vulnerable plaque. These ruptures are often observed at the upstream region of the plaque, where the wall shear stress (WSS) is considered to be highest. High WSS is known for its influence on many processes affecting tissue regression. Until now, there have been no serial studies showing the relationship between plaque rupture and WSS.

Summary of Case—We investigated a serial MRI data set of a 67-year-old woman with a plaque in the carotid artery at baseline and an ulcer at 10-month follow up. The lumen, plaque components (lipid/necrotic core, intraplaque hemorrhage), and ulcer were segmented and the lumen contours at baseline were used for WSS calculation. Correlation of the change in plaque composition with the WSS at baseline showed that the ulcer was generated exclusively at the high WSS location.

Conclusions—In this serial MRI study, we found plaque ulceration at the high WSS location of a protruding plaque in the carotid artery. Our data suggest that high WSS influences plaque vulnerability and therefore may become a potential parameter for predicting future events. (*Stroke*. 2007;38:2379-2381.)

Key Words: carotid artery ■ MRI ■ shear stress ■ ulceration

Cerebrovascular events are related to atherosclerotic disease in the carotid arteries and are frequently caused by rupture of a vulnerable plaque. These plaques are characterized by the presence of a large lipid pool covered by a thin fibrous cap with infiltration of macrophages and a scarcity of smooth muscle cells. Plaque rupture has been more frequently observed at the proximal, upstream side of the minimal lumen diameter,¹ which is supposedly exposed to higher wall shear stress (WSS). There is ample evidence that the endothelium responds to high WSS such that it induces antiproliferative action,² which may lead to cap thinning. For that reason, we hypothesized that high WSS at the upstream side of the plaque has a biological effect on the fibrous cap and therefore enhances plaque vulnerability.³ We present a case study in which we demonstrate the relation between high WSS and plaque rupture.

Materials and Methods

Patient

Serial carotid MRI examinations were performed on a 67-year-old individual who was found to have moderate carotid stenosis by

duplex ultrasonography. The institutional review committee approved the study and the patient gave informed consent. The patient's baseline MRI showed a plaque in the right carotid artery and the 10-month follow-up MRI showed plaque rupture with an ulcer.⁴

MRI

The high-resolution, multisequence MRI protocol at baseline and follow up included 4 sequences: 3-dimensional time of flight, T1, T2, and proton density weightings. The in-plane resolution was 0.3×0.3 mm with a slice thickness of 2 mm. The image segmentation was based on the signal intensities relative to the adjacent sternocleidomastoid muscle. A validated scheme⁵ of hyper-, iso-, and hypointense signal intensities from the time of flight, T1, T2, and proton density images was used to identify the lumen, plaque components (lipid/necrotic core, intraplaque hemorrhage), and ulcer (Figure 1).

Computational Fluid Dynamics

In preparation for the WSS calculation, the baseline lumen contours were imported into GAMBIT (Fluent Inc.) from which a 3-dimensional meshed volume was created. At the entrance and exit of the carotid bifurcation, circular segments were added to minimize the influence of the boundary conditions. A static parabolic inflow profile with a

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From Biomedical Engineering (H.C.G., F.J.H.G., A.F.W.v.d.S., J.J.W.), Erasmus MC, Rotterdam, The Netherlands; Interuniversity Cardiology Institute of the Netherlands (H.C.G., A.F.W.v.d.S., J.J.W.), Utrecht, The Netherlands; Radiology (H.C.G., A.v.d.L.), Erasmus MC, Rotterdam, The Netherlands; and Radiology (M.S.F., C.Y.) and Surgery (T.S.H.), University of Washington, Seattle, Wash.

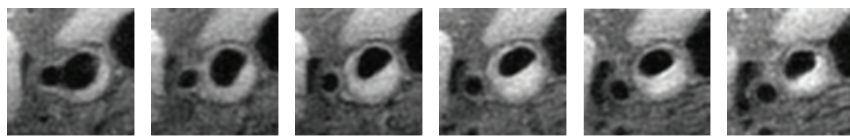
Correspondence to Jolanda Wentzel, Biomedical Engineering, Biomechanics Laboratory, Ee2322, Erasmus MC, PO Box 2040, 3000 CA Rotterdam, The Netherlands. E-mail j.wentzel@erasmusmc.nl

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Baseline



Follow-up

■ Lipid/necrotic core ■ Intraplaque hemorrhage ■ Ulcer

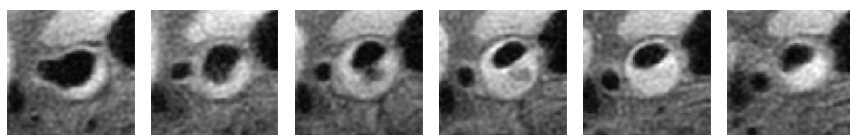
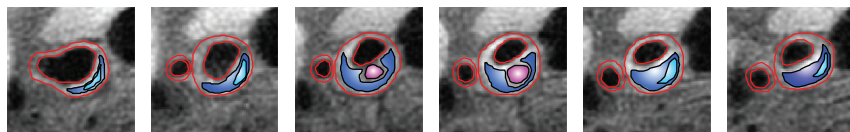


Figure 1. Matched MRI images (T1) with and without superimposed vessel wall segmentation at baseline (top) and 10-month follow up (bottom).

peak velocity of 0.6 m/s was chosen to obtain physiological shear stress values (1.2 Pa) at the common carotid artery. FIDAP (Fluent Inc.) was used to compute the flow velocities and WSS distribution by using free outflow for the internal and external arteries; no slip at the wall and blood was simulated as an incompressible Newtonian fluid (viscosity 3.5 mPa/s, density 1050 kg/m³).

Analysis

The segmentations at baseline and follow up were matched using the bifurcation as a marker to align the slices in the superior direction and the center of the lumen in the transversal direction. The slices containing plaque at baseline and/or follow up were selected for further analysis. For each slice, the wall was divided into 256 parts such that each baseline lumen contour was divided into 256 equidistant sections. In each part, the average baseline WSS and the baseline wall component volumes (ie, area×slice thickness) were

calculated using in-house created software. Subsequently, in each part, the volumes of the wall components at follow up were determined.

Results

Six matched pairs of MRI images were available for analysis (Figure 1). At baseline, the lipid/necrotic core volume was 308 mm³, from which 34% consisted of intraplaque hemorrhage, and increased to 335 mm³ with 16% intraplaque hemorrhage during the 10-month follow-up period. The average WSS at baseline in the carotid bifurcation was 3.2 ± 2.0 Pa and the site of ulceration was observed at the highest WSS (Figure 2). To quantify this observation, the data, linking plaque composition to WSS, was divided into

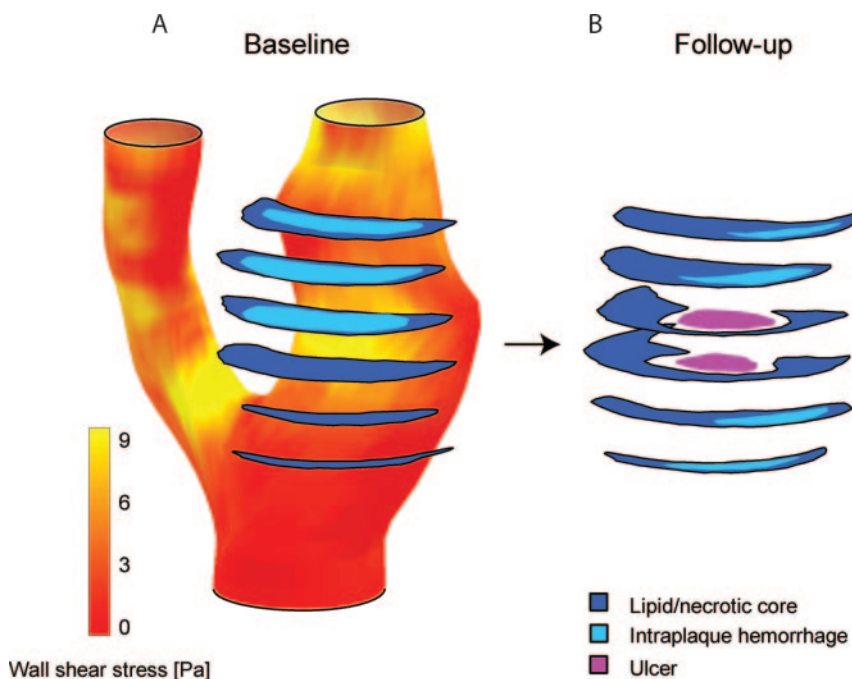


Figure 2. A, Baseline wall shear stress mapped at baseline 3-dimensional lumen geometry of a carotid bifurcation including plaque segmentation. B, Plaque segmentation at 10-month follow up, including the ulcer.

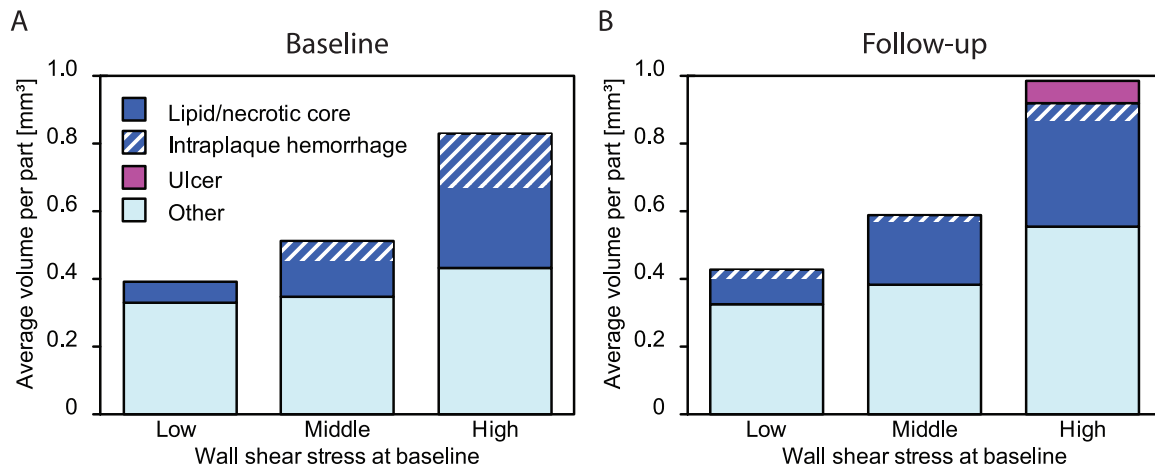


Figure 3. Vessel wall composition at baseline (A) and 10-month follow up (B) as function of baseline wall shear stress (low: 0.1 to 2.1; middle: 2.1 to 3.8; high: 3.8 to 8.8 Pa).

tertiles with respect to their WSS value (low, middle, and high). For each tertile, the average volume of wall component per part at baseline (Figure 3A) and follow up (Figure 3B) was computed. The total volume and the lipid/necrotic volume increased both with WSS and time and the ulcer at follow up was found in the highest WSS tertile (Figure 3).

Discussion

This case report shows the colocalization of high WSS at baseline and a subsequent ulceration 10 months later using serial MRI. Little is known about the mechanisms that make the vulnerable plaque susceptible to rupture. In a recent review,³ a number of biological pathways were proposed, which could explain the important role of high WSS in destabilization of the vulnerable plaque. In this case study, the weakest location appeared at the upstream highest WSS region of the plaque (Figures 2 and 3). This agrees with observations that plaque-destabilizing components, including macrophages and matrix metalloproteinase-9, are highest in concentration at the upstream (high WSS) region of the plaque.³

Assumptions were made for calculating the WSS distribution. Although the assumptions could have influenced the absolute WSS, several studies showed that they are of second order of importance. Moreover, we used the distribution rather than the absolute WSS so that the assumptions most likely did not influence the final conclusion of the study.

Intraplaque hemorrhage is known to be involved in plaque progression and cerebral events. The observed intraplaque hemorrhage at baseline could have accelerated the destabili-

zation of the plaque; however, in this case, the site of rupture was precisely at the highest WSS region (Figures 2 and 3). More patients will be required to confirm this preliminary finding that high WSS is involved in plaque destabilization leading to plaque rupture and to prove the value of this technology in risk prediction.

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Disclosures

None.

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