JACC: CARDIOVASCULAR IMAGING
VOL. 4, NO. 5, 2011

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER INC.
DOI:10.1016/j.jcmg.2011.03.003

EDITORIAL COMMENT

Wear and Tear*

Arnold P. G. Hoeks, PhD,† Marianne Eline Kooi, PhD‡
Maastricht, the Netherlands

The natural history of ruptured plaques in humans still remains a mystery, especially in the final stages before rupture. No clear signs have yet been distinguished that may indicate that the plaque is about to fracture. To our knowledge, only a few cases have been documented where a carotid plaque was investigated a few months before and after rupture (1–3). The evaluation of plaque morphology and composition using magnetic resonance imaging (MRI) (4) reveals a high content of intraplaque hemorrhage. On the basis of computational fluid dynamics (CFD), it has been concluded that plaque rupture occurs in the region with the highest wall shear stress (1). Similarly, the application of patient-specific morphology and CFD to a group of 20 subjects with a distinct ulcerative lesion in the context of an acute coronary syndrome (5) showed that sites with high mean wall shear stresses corresponded to sites of plaque rupture. However, this conclusion was later questioned because only steady states were considered (no pulsatile blood flow conditions), and the associated effects of transmural and longitudinal pressure gradients were ignored (6,7). No direct information is yet available about the dynamic stress distribution within plaques. The dynamic interaction between pulsatile blood flow and wall mechanics is generally inferred from computational models, assuming simplifications, for example, a homogeneous wall thickness and composition with modeled mechanical characteristics (8).

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The absence of detailed knowledge about blood flow and wall structure complicates any discussion about plaque vulnerability. In this issue of *iJACC*, Beaussier et al. (9) approach the problem from the other side: how do morphology and composition relate to the observed mechanical characteristics of symptomatic and asymptomatic plaques located in the common carotid artery (CCA)? Data regarding the 3-dimensional lumen, plaque morphology, and composition (lipid, calcium, hemorrhage, fibrous aspects) were acquired with dedicated MRI protocols. Within a plane through the plaque, a noninvasive ultrasound echotracking system provided the posterior intima-media wall thickness (IMT) and diameter (distance between anterior and posterior media/adventitia interfaces) in real time. The study explored the relationship between the MRI plaque characterization (14 complex plaques with American Heart Association [AHA] stages IV to VIII vs. 32 simple plaques, AHA stages I to III) and the observed cyclic diameter change, at the level of the plaque compared with that of a nonaffected reference site in the CCA. Finally, it addressed the question as to what extent the variation along the artery differs between subjects with ischemic events (9 plaques of 9 symptomatic patients at the ipsilateral side) and asymptomatic patients (30 plaques from 18 patients). The investigators concluded that, for complex plaques, the cyclic diameter change is reduced ($p = 0.046$) while the artery exhibits outward modeling to retain lumen area. Unfortunately, a reduced cyclic diameter change did not distinguish between simple and complex plaques, or between symptomatic and asymptomatic plaques.

The strain along one dimension is by definition the relative change in length, which for a wall with thickness h can be approximated by the wall strain $\Delta h/h$, where Δh is the (negative!) change in wall

*Editorials published in *JACC: Cardiovascular Imaging* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Imaging* or the American College of Cardiology.

From the †Department of Biomedical Engineering, Cardiovascular Research Institute Maastricht, Maastricht, the Netherlands, and the ‡Department of Radiology, Cardiovascular Research Institute Maastricht, Maastricht, the Netherlands. The authors have reported that they have no relationships to disclose.

thickness from diastole to systole (Fig. 1) (10). The wall strain relates directly to the relative change in lumen diameter $\Delta d/d$, where Δd is the absolute change in diameter d from diastole to systole (distension). Hence, the pulsatile relative diameter change can also be regarded as an estimate for the wall strain. This approach was followed in a previous article by the same group (11). However, for arterial segments with a reduced lumen area (inward modeling) or the same lumen area but a nonuniform wall thickness (outward modeling), the direct relationship between relative lumen diameter and relative wall thickness is lost. For an inward remodeled artery, a normal "lumen strain" translates into a considerably reduced wall strain. Moreover, in the perpendicular plane, the absolute pulsatile diameter change might be the same while the relative change is diminished. For this reason, the investigators adopted the policy of considering distension rather than the relative change in diameter as a measure for local strain (12). However, neither approach is able to unequivocally characterize the strain within the plaque.

The poor concordance between the plaque characteristics at echotracking and MRI might be traced back to the way the plaque strain characteristics are derived. The observed strain values, reported as median and quartiles, exhibited a wide spread. For example, in Beaussier et al. (9), Table 4 complex plaques had a median distension of 360 μm (quartile: 308; 462), whereas the reference CCA section had a distension of 458 μm (quartile: 388; 604), which is a nonsignificant difference ($p = 0.2$). Simple plaques exhibited a similar pattern, but the distension gradient along the artery had a distribution that was twice as wide, reaching even negative values of 180 μm. Unfortunately, no scatter plots were included to relate the observed gradients to both plaque type and inward/outward remodeling.

The distensibility at the site of a complex plaque was 16.3 MPa^{-1} (quartile: 13.3; 17.8) and differed significantly ($p = 0.007$) from the distensibility at the reference site, which was 21.1 MPa^{-1} (quartile: 15.6; 24.6). In this study, simple plaques had a similar distensibility as the reference site—a finding that contradicts the notion that distensibility could be indicative for atherosclerosis. The observed distributions are surprisingly narrow considering that the distensibility is defined as the ratio of the relative change in diameter and the local pulse pressure (10). The pulse pressure assumed at the site of the plaque might be questionable because within a relatively narrow orifice, pressure is (temporarily) converted to velocity, reducing the transmural pressure.

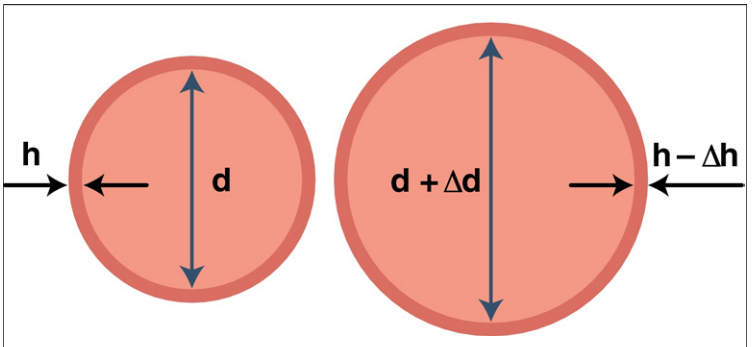

Figure 1. Relationship Between Lumen Distension and Wall Strain

The wall area in diastole (**left**) equals πdh, where d is the end-diastolic diameter and h is the wall thickness, and should remain constant while the artery lumen expands to systole (**right**). Hence, a relative increase in diameter of $\Delta d/d$ converts to a similar relative increase in circumference (circumferential strain) and is accompanied by a relative decrease in wall thickness of approximately $\Delta h/h$, in other words, a negative wall strain. For an older subject group, the relative diameter change is on the order of 6% (10).

Characterization of MRI plaque plays a dominant role in the analysis. Because of the low number of enrolled subjects, AHA categories I to III and IV to VIII were grouped so that an increase in wall thickness acts as a major determinant of distensibility. The advanced group contains plaques with a high lipid content, probably exhibiting a high distension, and plaques with calcifications and fibrous tissue, which are likely to be stiffer than those with a lipid pool. This combination of elastic and stiff plaques in a single group may disguise possible differences.

Another explanation for the poor concordance might be the time elapsed between the ischemic event and the echotracking/MRI evaluation (3 ± 3 months), allowing some degree of plaque stabilization. Unfortunately, the study does not report MRI estimates for lumen and wall areas to compare with echotracking estimates.

In conclusion, the study demonstrates that complex plaques exhibit a reduced strain pattern, but not the reverse. The poor specificity probably results from the way strain was defined. It was not expressed as a relative stretch/compression, neither was it selectively applied to the region of interest. Future studies might benefit from a direct assessment of the strain in the wall and in the plaque, and studies involving a larger number of subjects will allow detailed plaque differentiation.

Reprint requests and correspondence: Dr. Arnold P. G. Hoeks, Biomedical Engineering, Maastricht University, P.O. Box 616, Maastricht 6200 MD, the Netherlands. *E-mail: a.hoeks@maastrichtuniversity.nl.*

JACC: CARDIOVASCULAR IMAGING, VOL. 4, NO. 5, 2011
MAY 2011:478–80

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Key Words: carotid artery ■ distension ■ MRI ■ plaque ■ strain ■ ultrasound.