In this edition of *Hypertension*, the Framingham Heart Study group reports on the relationship between diastolic shear stress and brachial artery flow-mediated dilation (FMD) in 2045 participants of the Framingham Offspring group.\(^1\) Clinical correlates and heritability of FMD in the participants have been published previously.\(^2\) The new report\(^1\) challenges conventional concepts on endothelial function and on modification of endothelial function by risk factors of cardiovascular disease. The authors conclude that when present, impaired FMD of the brachial artery may be due not to impaired release of NO from the vascular endothelium, but from a lesser stimulus to NO release as a consequence of decreased flow velocity (and shear stress) during reactive hyperemia caused by impaired microvascular response. Are there fewer peripheral vessels capable of responding to local ischemia?

The method used by the authors differed from those previously applied in that they related FMD to systolic dilation to diastolic shear stress (DSS), not to systolic shear stress or to shear stress averaged over the whole cardiac cycle. They calculated shear stress from constant blood viscosity, mean diastolic flow velocity, and baseline end-diastolic diameter, assuming a parabolic velocity profile. Expressed this way, they found a close relationship between DSS and FMD that was not related to most conventional risk factors, including gender. These results\(^1\) add a new twist to the study of endothelial function and NO production, and raise other possibilities as to how disease, drugs, and/or risk factors affect arteries that are not subject to atherosclerosis. Present techniques of measuring FMD are time consuming, have low reproducibility, and are imprecise (because dilation is so small, averaging just 2.3% in the males of this series). If a fault lies in the peripheral circulation, then more attention should be given to absolute flow in the smaller vessels, using old-fashioned, conventional venous occlusive plethysmography. Many investigators have done this previously; Irace et
concluded that endothelial function could be reliably evaluated by plethysmography or by FMD and that the 2 methods correlated. Alternatively, one might consider other techniques of pulse waveform analysis, which evaluate global endothelial function, but also appear to correlate with the conventional measures.

In the present study, FMD was related to DSS, whereas others have related FMD to maximal (systolic) shear stress. Flow is much higher in systole than in diastole, but the relationship varies with cardiac and vascular disease and with aging. It is not established whether conventionally measured peak (systolic) or diastolic shear stress is the stimulus to NO production and to FMD. Further, investigators assumed laminar flow and a parabolic velocity profile when measuring wall stress. This is not strictly correct. The flow velocity varies across the vessel lumen during the cardiac cycle so that wall stress varies in a complex way with time during pulsatile flow. This was calculated by McDonald and Womersley, whose velocity profiles are shown in the Figure for an artery of similar caliber to the brachial artery in humans and concur with those measured experimentally.

Clearly, this field remains controversial and requires new and different approaches. The beauty of the present study is that it was conducted in a large, well characterized group of normal subjects as part of an extensive screening process during a half-day period. It was also conducted under modest circumstances. Framingham is famous for its frugality as well as its inventiveness and has shown that major advances do not require expensive premises and budget, just adequate funding, good planning and supervision, readiness to innovate, cooperation and coordination between staff and community, and above all, perseverance.

References
Shear Stress and Flow-Mediated Dilation
Michael F. O’Rourke and Wilmer W. Nichols

Hypertension. 2004;44:119-120; originally published online July 12, 2004;
doi: 10.1161/01.HYP.0000137301.99716.e8

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://hyper.ahajournals.org/content/44/2/119

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/