Impact of shear stimulus, risk factor burden and early atherosclerosis on the time-course of brachial artery flow-mediated vasodilation
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**Objectives** Our aim was to analyze flow-mediated dilation (FMD) time-course in response to forearm occlusion in the clinical setting.

**Methods and results** In 50 asymptomatic subjects, monitoring software measuring continuous beat-to-beat change in brachial artery diameter was used to determine FMD magnitude in percentage change in peak diameter from baseline (FMD-\(\Delta D\), time to peak diameter after occlusion release (FMD-\(t_{\text{peak}}\)), integrated FMD response calculated as area under dilation curve (FMD-AUC), maximum FMD rate calculated as maximal slope of dilation (FMD-MDR). FMD-\(\Delta D\) and FMD-MDR correlated positively with peak wall shear stress (\(P<0.05, P<0.01\)). FMD-MDR correlated negatively with age (\(P<0.001\)). Framingham risk score (\(P<0.01\)) and carotid intima–media thickness (\(P<0.05\)), while FMD-\(\Delta D\) correlated negatively with Framingham risk score only (\(P<0.01\)). After adjustment, all these correlations were independent of antihypertensive, lipid-lowering and antidiabetic therapies. All but that of FMD-MDR with intima–media thickness were also found in a subgroup of 29 untreated subjects and in a subgroup of 24 untreated and low-risk (FRS<10%) subjects. FMD-\(t_{\text{peak}}\) and FMD-AUC were not associated with shear stimulus, Framingham risk score, and intima–media thickness.

**Conclusion** The kinetics of dilation (maximum rate) seem more sensitive than their magnitude in assessing FMD performance and its determinants. *J Hypertens* 26:508–515

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**Keywords:** atherosclerosis, endothelial function, flow-mediated vasodilation, risk factors, shear stress, ultrasound

**Abbreviations:** FMD, Flow-mediated dilation; FMD-AUC, Integrated FMD response calculated as area under dilation curve; FMD-\(\Delta D\), Magnitude in percent change in peak diameter from baseline; FMD-MDR, Maximum FMD rate calculated as maximal slope of dilation; FMD-\(t_{\text{peak}}\), Time to peak diameter after occlusion release; FRS, Framingham risk; IMT, Intima-media thickness

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**Introduction**
Flow-mediated dilation (FMD) describes the vasodilation in a conduit vessel, generally the brachial artery, in response to acute elevation in flow-associated shear stimulus [1]. The arterial diameter response to flow change can be assessed noninvasively by ultrasound after temporary forearm ischemia by cuff occlusion [2]. The magnitude of dilation response, expressed as the percentage change between diameter at maximal dilation within the 60 s after occlusion release and baseline diameter, is traditionally used for estimating FMD performance [2]. In subjects without overt clinical arterial disease, FMD magnitude was found to be inversely associated with various cardiovascular risk factors [3–5] and subclinical atherosclerosis [6,7]. Recently we developed new monitoring software allowing measuring continuously beat-to-beat brachial artery diameter during the entire FMD time course [8]. The present study used this method in 50 asymptomatic subjects with the aim to determine new parameters of FMD time course and their potential relationships with shear stimulus, cardiovascular risk factor burden, and early carotid atherosclerosis.

**Methods**

**Study subjects**
Fifty asymptomatic subjects without known cardiovascular disease, referred for cardiovascular risk stratification, were included consecutively in the study. Body mass index was calculated as weight to height squared ratio. Resting brachial blood pressure was the mean of three sphygmomanometric measurements, with a arm size-adapted cuff by a trained physician. Hypertension was defined as blood pressure at or above 140 or 90 mmHg or presence of current antihypertensive treatment. Fasting blood lipids and glucose were measured by enzymatic methods [after precipitation of low-density lipoprotein (LDL) and very-low-density lipoprotein for high-density lipoprotein (HDL) measurement]. Hypercholesterolemia was defined as total cholesterol at or above 5.2 mmol/l or presence of current lipid-lowering drug treatment. Diabetes was defined as fasting blood glucose at or above 7 mmol/l or current antidiabetic treatment. Current smoking was defined as daily consumption of at least one cigarette for at least 3 months. We estimated the risk of coronary heart disease by entering age, male sex, systolic