

**Long-Term Association of Brachial Artery Flow-Mediated Dilation and Cardiovascular Events in Middle-Aged Subjects with No Apparent Heart Disease**

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Background: Endothelial dysfunction is considered an important prognostic factor in atherosclerosis.

Methods and Results: To find out the long-term association of vascular endothelial function and adverse cardiovascular events (CVE), we prospectively assessed brachial artery endothelium-dependent flow-mediated dilation (FMD), using high-resolution linear array ultrasound, in 618 consecutive healthy subjects with no apparent heart disease: 387 (63%) men, mean age 54±11 years and body mass index 28±kg/m<sup>2</sup>. Subjects were divided into 2 groups: ≤ (n=309) and > (n=309) the median %FMD of 11.3%. The 2 groups were comparable in regard to cardiovascular risk factors, lipoproteins, fasting glucose, high-sensitivity C-reactive protein, concomitant medications and Framingham 10-year risk score. In a mean clinical follow-up of 3.6±1.8 years the composite CVE (all-cause mortality, non-fatal myocardial infarction, hospitalization for heart failure or angina pectoris, stroke, coronary artery bypass grafting and percutaneous coronary interventions) were significantly more common in subjects with %FMD ≤ rather than > the median of 11.3% (14.2% vs 1.0%, p=0.0001). Univariate analysis demonstrated that the median %FMD significantly predicted CVE [odds ratio (OR) of 2.78 and 95% CI (1.35 to 5.71) (p=0.003)]. After multivariate analysis that included traditional cardiovascular risk factors, median %FMD was the best independent predictor of long-term CVE [OR of 2.70 and 95% CI (1.16 to 6.32) (p<0.0001)] (Figure).

Conclusions: Brachial artery median %FMD independently predicts long-term adverse CVE in healthy subjects with no apparent heart disease in addition to those derived from traditional risk factor assessment.