STROKE

Plasma ADMA: a novel biomarker of subclinical brain injury?

Elevated plasma levels of asymmetrical dimethylarginine (ADMA) are associated with an increased prevalence of silent brain infarcts (SBIs), suggests research conducted by Pikula and colleagues as part of the Framingham Offspring Study. SBIs are recognized MRI markers of subclinical macrovascular and microvascular brain injury, leading the authors to speculate that ADMA might be a potentially useful new biomarker of subclinical vascular brain injury.

In blood vessels, nitric oxide is produced by endothelial nitric oxide synthase, which is inhibited by ADMA. Nitric oxide has a variety of biological functions and is a particularly important mediator of normal endothelial function. Raised plasma levels of ADMA decrease the bioavailability of nitric oxide, and can, as a consequence, affect blood flow. Perhaps not surprisingly, elevated plasma concentrations of ADMA are associated with an increased risk of developing

stroke or transient ischemic attack. SBIs are also associated with an increased risk of stroke, which prompted Pikula *et al.* to investigate a possible link between SBIs and plasma levels of ADMA in a community-based cohort.

“...an association exists between elevated plasma levels of ADMA and increased prevalence of SBIs”

The investigators took blood samples from 2,013 stroke-free individuals and measured concentrations of ADMA and its isomer—symmetrical dimethylarginine—by means of liquid chromatography–tandem mass spectrometry. The prevalence of SBIs and white-matter hyperintensities, which are also associated with subclinical vascular brain injury, was ascertained

by means of MRI. Analysis of the results indicated that an association exists between elevated plasma levels of ADMA and increased prevalence of SBIs. A corresponding association between white-matter hyperintensities and ADMA concentrations was not identified. Furthermore, no association was evident between symmetrical dimethylarginine, which does not inhibit endothelial nitric oxide synthase, and MRI markers of vascular brain injury.

These data indicate that an elevated plasma ADMA level is potentially a biomarker of subclinical brain injury, and Pikula *et al.* conclude that ADMA could represent a target for therapeutic interventions.

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Original article Pikula, A. *et al.* Association of plasma ADMA levels with MRI markers of vascular brain injury: Framingham offspring study. *Stroke* **40**, 2959–2964 (2009).