Asymmetrical Dimethylarginine: A Novel Risk Factor for Coronary Artery Disease

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Summary

Background: Asymmetrical dimethylarginine (ADMA) is an endogenous competitive inhibitor of nitric oxide synthase and has been associated with systemic atherosclerosis; however, the role of ADMA in patients with coronary artery disease (CAD) has not been investigated.

Hypothesis: The present study was designed to determine whether the plasma ADMA level predicts the presence of CAD independently, and whether the plasma ADMA level correlates with the extent and severity of coronary atherosclerosis.

Methods: In all, 97 consecutive patients with angina and positive exercise stress test were enrolled prospectively for coronary angiography. According to the result of angiography, the subjects were divided into two groups: Group 1 (n = 46): patients with normal coronary artery or mild CAD (<50% stenosis of major coronary arteries); Group 2 (n = 51): patients with significant CAD (≥50% stenosis of major coronary arteries). Plasma levels of ADMA and L-arginine were determined by high-performance liquid chromatography. In addition, we used coronary atherosclerotic score to assess the extent and severity of CAD.

Results: The plasma levels of ADMA in Group 2 patients were significantly higher than those in Group 1 patients (0.66 ± 0.17 µM vs. 0.44 ± 0.09 µM, p < 0.001); these were accompanied by significantly lower plasma L-arginine/ADMA ratio in patients with significant CAD (Group 1 vs. 2: 194.0 ± 55.3 vs. 136.7 ± 50.3, p < 0.001). In a multivariate stepwise logistic regression analysis, both plasma ADMA level and plasma L-arginine/ADMA ratio were identified as independent predictors for CAD. Moreover, there were significant positive and negative correlations between coronary atherosclerotic score and plasma ADMA level as well as plasma L-arginine/ADMA ratio, respectively (plasma ADMA level: r = 0.518, p < 0.001; L-arginine/ADMA ratio: r = 2 0.430, p < 0.001).

Conclusions: Both plasma ADMA level and plasma L-arginine/ADMA ratio were useful in predicting the presence of significant CAD and correlated significantly with the extent and severity of coronary atherosclerosis. Our findings suggest that plasma ADMA level may be a novel marker of CAD.

Key words: asymmetrical dimethylarginine, coronary artery disease, nitric oxide