Adrenomedullin as a Molecular Biomarker of Cardiovascular Disease

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Adrenomedullin (AM) is a potent vasodilator peptide that was originally discovered from human pheochromocytoma. AM is widely distributed in various organs and tissues, including the cardiovascular system. AM is not only a potent vasodilator peptide, but also has protective effects against vascular and cardiac cell injury and excessive growth. Plasma AM levels are elevated in various cardiovascular disorders. The present study examined the association between plasma AM and atherosclerotic disease, and investigated the predictive value of AM for future cardiovascular events. In 121 patients with cardiovascular risks and/or diseases including ischemic heart disease (IHD) and peripheral arterial disease (PAD), plasma concentrations of AM, high sensitive C-reactive protein (hs-CRP), and interleukin (IL)-6 were measured. The patients with IHD and/or PAD had significantly higher levels of AM than those without. Among AM, hs-CRP, and IL-6, AM was most strongly associated with both IHD and PAD in multivariate analysis. During follow-up periods (mean, 3.5 years) after the baseline assessment, 28 patients newly experienced cardiovascular events (stroke/TIA, n=12; acute coronary syndrome, n=7; and congestive heart failure, n=9). When the patients were divided into three groups by tertiles of basal levels of plasma AM, cumulative event-free rates by the Kaplan-Meier method were decreased according to the increase in basal AM levels. By multivariate Cox regression analysis, high AM, but not hs-CRP or IL-6, was an independent determinant of cardiovascular events during follow-up. These results indicate that plasma AM is a sensitive bio-molecular marker for the presence of atherosclerotic vascular lesions, and also is useful as a predictor of future cardiovascular events in high-risk patients.