Hypoadiponectinemia is Associated With Coronary Artery Spasm in Men

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Background The relationship between adiponectin and coronary spastic angina (CSA), both of which are closely involved in coronary endothelial dysfunction, has not been elucidated.

Methods and Results Plasma adiponectin concentrations were examined in 55 men with CSA and 55 with chest pain syndrome (CPS). The plasma log-adiponectin levels were significantly lower in patients with CSA than with CPS (0.61±0.28 vs 0.80±0.21 g/ml, p<0.0001). The prevalence of smoking was significantly higher in the CSA patients than in those with CPS (50.9% vs 29.1%, p=0.0195). In multiple logistic regression analysis, log-adiponectin (p=0.0008) and smoking (p=0.0210) were independent determinants of CSA.

Conclusions Hypoadiponectinemia is a potential risk factor for CSA in men, independent of smoking. (Circ J 2005; 69: 1154–1156)

Key Words: Adiponectin; Coronary artery spasm; Smoking
Results

Table 1 shows the clinical and biochemical characteristics of both groups. Plasma log-adiponectin levels were significantly lower in the CSA group compared with the CPS group (0.61±0.28 vs 0.80±0.21 µg/ml, p<0.0001). The prevalence of cigarette smoking was significantly higher in the CSA group than in the CPS group. High-density lipoprotein cholesterol (HDL-C) levels were significantly lower in the CSA group than in the CPS group.

Multiple logistic regression analysis revealed that hypo-adiponectinemia is a predictive risk factor for coronary artery spasm, even after adjustment for cigarette smoking and HDL-C, which were significant in the simple logistic regression (Table 2).

Discussion

The plasma adiponectin level is considered to be a marker of atheromatous vascular changes and smoking is a significant predictive risk factor for coronary artery spasm but the relationship between adiponectin and coronary artery spasm has not been determined to date. In this study, we showed that plasma adiponectin levels were significantly lower in the CSA group than in the CPS group and that low levels of plasma adiponectin were closely related to the presence of CSA, independent of cigarette smoking.

Endothelial dysfunction together with reduced endothelial vasodilatory function and smooth muscle hypercontraction in coronary arteries may play an important role in the pathogenesis of coronary artery spasm. In particular, NO, which is recognized as an endothelium-derived relaxing factor, is deficient in patients with CSA. Cigarette smoking is considered to be a major risk factor for CSA because the oxidative stress associated with cigarette smoking may be a source of free radicals, which may cause coronary artery spasm by reducing NO activity. On the other hand, a recent report indicates that adiponectin stimulates the production of NO in vascular endothelial cells and furthermore, that hypo-adiponectinemia is associated with impaired endothelium-dependent vasorelaxation, based on significantly re-
duced ACh-induced vasorelaxation in adiponectin-knockout mice compared with wild-type mice. In the present study, we demonstrated that adiponectin is a significant determinant of coronary artery spasm, irrespective of cigarette smoking, which suggests that the mechanism(s) by which hypoadiponectinemia impairs endothelium-dependent vasodilatation of the coronary arteries is different from that of cigarette smoking. Although the exact mechanism(s) of adiponectin-induced endothelium-dependent relaxation of coronary arteries is unknown, several potential mechanisms have been speculated. Hypoadiponectinemia is associated with insulin resistance and metabolic syndrome and adiponectin may restore impaired endothelial vasomotor function through improvement of insulin resistance and its associated metabolic abnormalities. Adiponectin may also increase NO production in coronary vascular endothelial cells by activating adenosine monophosphate-activated protein kinase, which in turn promotes eNOS via activation of phosphatidylinositol 3-kinase-Akt-dependent pathways in endothelial cells.

The potential limitation of this study is that the subjects were all men, who have significantly lower plasma adiponectin concentrations than BMI-adjusted women. Further studies are warranted to evaluate the significance of plasma adiponectin concentrations in the prevalence of coronary artery spasm in women.

In conclusion, low adiponectin level is associated with CSA in men, independent of cigarette smoking, and hypoadiponectinemia is a potential important risk factor for CSA.

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