Plasma adiponectin levels increase after coronary artery bypass grafting

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BACKGROUND/OBJECTIVE: Adiponectin (APN) is an adipokine, and low APN levels are associated with cardiovascular disease. Plasma APN levels were evaluated before and after coronary artery bypass grafting (CABG) and compared with the presence of coronary artery disease (CAD).

METHODS: Patients with CAD (n=40) and patients without CAD (n=40) were examined. Peripheral venous plasma APN levels were measured before and after surgery (at one, seven and 30 days). Tumour necrosis factor-alpha (TNF-α) and high-sensitivity C-reactive protein (hs-CRP) levels were measured before surgery and after surgery at 30 days.

RESULTS: Before surgery, APN levels were 57% lower in patients with CAD compared with patients without CAD. Seven days after CABG, APN levels significantly increased in patients with CAD but not patients without CAD. Plasma TNF-α and hs-CRP decreased after CABG in both groups.

CONCLUSION: Patients with coronary heart disease have increased plasma levels of APN and decreased levels of TNF-α and hs-CRP after coronary revascularization.

Key Words: Adiponectin; Coronary artery bypass graft; Coronary artery disease; Tumour necrosis factor


Anthropometric measurements
Body mass index was calculated as body weight (kg) divided by height (m) squared. Waist circumference (cm) was accurately measured as the largest diameter between lower rib margin and iliac crest.

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TABLE 1
Comparison of clinical and laboratory characteristics between coronary artery disease (CAD) and non-CAD groups

<table>
<thead>
<tr>
<th></th>
<th>Non-CAD (n=40)</th>
<th>CAD (n=40)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>60.3±5.6</td>
<td>62.9±6.6</td>
<td>ns</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.8±3.4</td>
<td>26.6±3.2</td>
<td>ns</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>81.3±6.0</td>
<td>91.2±6.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Fasting glucose, mmol/L</td>
<td>4.36±0.41</td>
<td>4.42±0.35</td>
<td>ns</td>
</tr>
<tr>
<td>Insulin (mUI)</td>
<td>14.2±2.4</td>
<td>14.9±3.1</td>
<td>ns</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>4.59±0.58</td>
<td>4.88±0.69</td>
<td>ns</td>
</tr>
<tr>
<td>HDL, mmol/L</td>
<td>1.15±0.07</td>
<td>1.02±0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.49±0.09</td>
<td>1.74±0.19</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>hsCPR, mg/L</td>
<td>6.5±1.5</td>
<td>9.2±1.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>APN, mg/L</td>
<td>11.9±2.3</td>
<td>6.8±1.6</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD unless otherwise indicated. APN Adiponectin; HDL High-density lipoprotein; hsCPR High-sensitivity C-reactive protein; HOMA-IR Homeostasis model assessment-insulin resistance. ns Not significant

RESULTS

Clinical and laboratory characteristics

The clinical and laboratory characteristics of the CAD and non-CAD subjects are summarized in Table 1. No significant differences were evident between the two groups in terms of body mass index, blood pressure, total and high-density lipoprotein cholesterol levels, age, smoking incidence, fasting insulin and glucose levels, and plasma lipid patterns (P = not significant for all). CAD subjects had higher waist circumferences and triglyceride levels compared with the non-CAD subjects (both P < 0.05). None of the patients were diabetic and none were taking thiazolidinediones. These anthropometric and biochemical parameters were unchanged after cardiac surgery.

Plasma APN, TNF-α and hs-CRP levels before cardiac surgery

There were no significant changes in peripheral plasma APN levels 24 h after CABG. In non-CAD subjects, peripheral plasma APN levels did not significantly change before cardiac surgery or at days one, seven and 30 after valve replacement surgery. In CAD subjects, peripheral plasma APN levels increased seven days after CABG. There were no significantly changed in peripheral plasma APN levels from seven to 30 days after CABG (Figure 1).

Peripheral plasma APN levels were significantly lower in CAD than non-CAD patients before cardiac surgery, while peripheral plasma TNF-α and hs-CRP levels were higher in CAD than non-CAD patients before cardiac surgery. Before and after cardiac surgery, there were no significantly changes in peripheral plasma TNF-α levels in control non-CAD subjects. In CAD subjects, peripheral plasma TNF-α and hs-CRP levels decreased 30 days after CABG (Table 2).

DISCUSSION

In the present study, we showed that patients with CAD have lower APN levels compared with control subjects. By seven days after surgical revascularization, there was a rapid increase in plasma APN concentrations in the CAD patients.

Pischon et al (12) reported that decreased serum APN levels were associated with a higher risk of myocardial infarction. Others have shown that after coronary revascularization, coronary plasma APN levels increase rapidly (13,14). In our control group of selected valvular patients, plasma APN levels did not change significantly before and after cardiac surgery; while in the CAD group, surgical revascularization may explain the increased APN levels. Coronary venous APN concentrations were significantly higher than coronary artery levels, suggesting that epicardial fat may serve as an important source of coronary APN (15). In patients with CAD, epicardial fat APN levels are 40% lower than normal levels (16).

TNF-α is a multifunctional inflammatory response factor produced by macrophages, which are highly abundant in adipose tissue. TNF-α, interleukin-1 and interleukin-6 can stimulate the production of additional inflammatory cytokines, as well as promote expression of the chemokotactic factor monocyte chemoattractant protein-1 and interleukin-8 (17). Hector et al (18) found that TNF-α can inhibit APN messenger RNA expression in human visceral adipose tissue.

Inflammation contributes to cardiovascular disease and hs-CRP is a reliable marker of systemic inflammation (19). Emerging evidence suggests that hs-CRP may be directly involved in atherogenesis, and arterial plaques have increased hs-CRP levels (20). The reciprocal association of adiponectin and hs-CRP levels in both plasma and adipose tissue was demonstrated (11,21). Thus, adiponectin may directly or indirectly alter the hs-CRP levels in plasma and adipose tissue by modulating the inflammatory cascade.

Matsuda et al (22) proposed the fat-vascular regulation axis theory, whereby adipocytokines can directly affect vascular endothelial cells,
arterial smooth muscle cells, and macrophages, as well as alter other functions to regulate the metabolic balance in blood vessel walls to affect atherosclerosis, inflammation and thrombosis rates. This close contact among factors, vascular structure and adipocyte function is known as the 'adipocytokines-vascular axis adjustment'.

Study limitations
The present study had several limitations and caution should be exercised when interpreting the results. First, the sample size of the present study was relatively small and further investigations on a larger population will be necessary. A larger trial will also need to include patients with diabetes and obesity. Second, the exact mechanism whereby APN increases following CABG surgery also remains to be explored. Third, the present study measured plasma APN levels but did not explore other adipokines such as leptin.

REFERENCES

CONCLUSIONS
Higher plasma APN levels may have a protective role against initiation and progression of atherosclerosis in either native coronary arteries or vascular grafts in atherosclerotic patients who undergo surgical revascularization. It may be through modifying the adipocytokine-vascular adjustment axis feedback to stimulate local epicardial fat, increased APN levels, and reduced TNF-α and hs-CRP levels.

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