Serum adiponectin in coronary heart disease: ethnic differences and relation to coronary artery disease severity

H S Lim, M H Tayebjee, K T Tan, J V Patel, R J Macfadyen, G Y H Lip


Adiponectin is a collagen-like protein secreted predominantly by adipose tissue. In humans, plasma adiponectin concentrations are inversely related to measures of insulin resistance, with reduced adiponectin concentrations reported in obesity and patients with essential hypertension, dyslipidaemia, diabetes, and coronary artery disease (CAD). Low serum adiponectin concentrations appear to be associated with an increased risk of myocardial infarction, but it is not clear if this increased risk is related to increased coronary disease burden.

People of South Asian descent have increased susceptibility to glucose intolerance, dyslipidaemia, and CAD, the cause(s) of which are complex and multiple. One small study suggested lower adiponectin concentrations in South Asians compared to body mass index (BMI) matched white people, but ethnic differences in plasma adiponectin among patients with CAD have not been reported. We hypothesised that serum adiponectin is lower in CAD patients of South Asian descent compared to white counterparts, and secondly, that there was a relation between serum adiponectin and coronary disease severity by angiography. To test these hypotheses, we performed a cross-sectional study of consecutive white and South Asian patients undergoing cardiac catheterisation.

METHODS

Consecutive patients attending outpatient diagnostic cardiac catheterisation for the investigation of CAD were recruited. The South Asian patients attending our unit are almost exclusively of Punjabi origin, and their ethnic group was confirmed by direct enquiry. Patients with angiographically normal coronary arteries, concurrent inflammatory or neoplastic disease, haemodynamically significant valvar heart disease, prior revascularisation, or recent (≤ 3 months) admission for coronary ischaemia were excluded. Data from these patients were compared with healthy controls.

All patients underwent conventional coronary angiography, with each angiogram reviewed independently by two experienced observers blinded to the clinical details for the patient; the intra- and inter-observer coefficient of variation was < 5%. The coronary atheroma score (CAS) and coronary stenosis score (CSS) were calculated for each patient, as previously established. Left ventricular systolic function was qualitatively assessed as normal or abnormal by visual inspection and quantitative analysis of the ventriculogram (defined as a calculated ejection fraction < 40%).

Venous blood was centrifuged at 1000 g and 4 °C for 20 minutes. Serum was aliquoted and stored at −70 °C for batch analysis. Serum adiponectin was measured by ELISA using commercial kits and reagents (R&D Systems, Abingdon, UK). Intra-assay coefficients of variation were < 5% and inter-assay variance < 10%.

Analyses and power calculations were performed using Minitab 13 (Minitab Inc, State College, Pennsylvania, USA). A stepwise multiple regression analysis was performed to determine independent predictors of serum adiponectin. Variables that were significantly different between patient groups or related on univariate analysis were included in the analysis.

RESULTS

We recruited 139 patients (90 white, 49 South Asians) with angiographically confirmed CAD and 31 comparable normal healthy white controls (table 1). Systolic and diastolic blood pressures and total cholesterol were highest in the white controls, reflecting the use of lipid lowering therapy (statins) in the patient groups. There were no significant differences in CAS or CSS between patient groups.

Serum adiponectin was highest in the control group, intermediate in the white patients, and lowest among South Asian patients (Kruskal Wallis test, p < 0.001; Tukey’s post hoc test for inter-group differences after log transformation, p < 0.05).

There was no difference in CAS (0.888 (0.483–1.650) vs 0.915 (0.270–1.900), p = 0.616) or CSS (0.867 (0.384–1.498) vs 0.688 (0.158–1.415), p = 0.515) between the lowest and the highest tertile of serum adiponectin. Similarly, there was no difference in serum adiponectin concentrations between the highest and lowest tertiles of CAS (3.0 (2.0–4.4) vs 2.7 (2.1–3.5) μg/ml, p = 0.570) or CSS (3.0 (1.9–4.1) vs 2.5 (2.0–3.4) μg/ml, p = 0.391).

There were no significant differences in serum adiponectin between males and females (p = 0.243), and patients with normal and abnormal left ventricular ejection fraction (LVEF) (p = 0.360) and with or without statin treatment (p = 0.380) (full data not shown).

On univariate analysis, serum adiponectin correlated positively with age in both patient groups (Spearman r = 0.225, p = 0.033, and r = 0.525, p < 0.001 in white and South Asian respectively), but correlated positively with high density lipoprotein (HDL) cholesterol (r = 0.379, p < 0.001) and inversely with serum triglycerides (r = −0.333, p = 0.011) in the white patients. Serum adiponectin did not correlate with CAS or CSS in either patient groups or the whole patient cohort (CAS: r = −0.054, p = 0.541; CSS: r = 0.018, p = 0.837).

For a multivariate analysis, we included variables that were significantly different between white and South Asians and variables which correlated with serum adiponectin on univariate analysis (that is, age, systolic and diastolic blood pressures, ethnicity, diabetes, statin use, serum triglycerides, and HDL cholesterol). Ethnic group (p = 0.044) and HDL cholesterol (p = 0.015) were independent predictors of serum adiponectin in patients with CAD.

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CAS, coronary atheroma score; CSS, coronary stenosis score; HDL, high density lipoprotein; LVEF, left ventricular ejection fraction
DISCUSSION
South Asians living in Britain suffer from an increased risk of coronary events and mortality compared to age matched white patients. Insulin resistance and associated metabolic abnormalities may be contributory factors. Serum adiponectin concentrations correlate well with measures of insulin resistance and accumulating data suggest that adiponectin may have anti-atherogenic properties. Hence, low adiponectin concentrations may be a link between increased prevalence of insulin resistance and coronary events among South Asians. One small study suggested lower serum valence of insulin resistance and coronary events among South Asians. However, our larger study extends this finding to a population with angiographically proven CAD, suggesting that adiponectin may contribute to disease development in these patients, independently of age, diabetes, and dyslipidaemia. In conclusion, serum adiponectin is lower in South Asian patients with CAD compared to their white counterparts, but was not significantly related to angiographic coronary disease. The lower adiponectin concentrations may contribute to the development of CAD, especially in the South Asian population.

AUTHORS’ AFFILIATIONS
H S Lim, M H Tayebjee, K T Tan, J V Patel, R J Macfadyen, G Y H Lip, Haemostasis Thrombosis and Vascular Biology Unit, University Department of Medicine, City Hospital, Birmingham, UK

Correspondence to: Professor Gregory Y H Lip, Haemostasis Thrombosis and Vascular Biology Unit, University Department of Medicine, City Hospital, Birmingham, B18 7QH, UK; g.y.h.lip@bham.ac.uk

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REFERENCES

Table 1 Characteristics of study participants

<table>
<thead>
<tr>
<th></th>
<th>Controls (n = 31)</th>
<th>White CAD (n = 90)</th>
<th>South Asian CAD (n = 49)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65 (10)</td>
<td>62 (6)</td>
<td>61 (9)</td>
<td>0.068</td>
</tr>
<tr>
<td>Males (%)</td>
<td>15</td>
<td>61</td>
<td>34</td>
<td>0.108</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>131 (12)</td>
<td>142 (22)</td>
<td>130 (17)</td>
<td>0.001*</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>76 (10)</td>
<td>79 (10)</td>
<td>74 (10)</td>
<td>0.022†</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29 (28–31)</td>
<td>29 (26–34)</td>
<td>28 (25–30)</td>
<td>0.444</td>
</tr>
<tr>
<td>Cholesterol (mmol/l)</td>
<td>5.5 (1.1)</td>
<td>4.5 (1.1)</td>
<td>4.5 (1.0)</td>
<td>0.001†</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>1.3 (0.8–2.0)</td>
<td>1.7 (1.2–2.6)</td>
<td>1.5 (1.1–2.4)</td>
<td>0.128</td>
</tr>
<tr>
<td>HDL (mmol/l)</td>
<td>1.55 (0.35)</td>
<td>1.28 (0.36)</td>
<td>1.25 (0.25)</td>
<td>0.001†</td>
</tr>
<tr>
<td>Smokers (%)</td>
<td>13</td>
<td>3</td>
<td>3</td>
<td>0.142</td>
</tr>
<tr>
<td>Previous MI (%)</td>
<td>36</td>
<td>22</td>
<td>22</td>
<td>0.5765</td>
</tr>
<tr>
<td>LV dysfunction (%)</td>
<td>25</td>
<td>13</td>
<td>13</td>
<td>0.582†</td>
</tr>
<tr>
<td>Patients with diabetes (%)</td>
<td>23</td>
<td>22</td>
<td>22</td>
<td>0.020†</td>
</tr>
<tr>
<td>Statin treatment (%)</td>
<td>78</td>
<td>33</td>
<td>33</td>
<td>0.007†</td>
</tr>
<tr>
<td>ACE inhibitor (%)</td>
<td>35</td>
<td>21</td>
<td>21</td>
<td>0.649</td>
</tr>
<tr>
<td>CAS</td>
<td>1.04 (0.50–1.80)</td>
<td>0.82 (0.43–1.62)</td>
<td>0.82 (0.43–1.62)</td>
<td>0.4815</td>
</tr>
<tr>
<td>CSS</td>
<td>0.90 (0.38–1.61)</td>
<td>0.77 (0.40–1.32)</td>
<td>0.77 (0.40–1.32)</td>
<td>0.3965</td>
</tr>
<tr>
<td>Adiponectin (µg/ml)</td>
<td>5.2 (3.7–6.2)</td>
<td>3.0 (2.0–4.2)</td>
<td>2.3 (1.8–3.0)</td>
<td>&lt;0.001†</td>
</tr>
</tbody>
</table>

*White CAD v South Asians CAD and controls; †white CAD v South Asian CAD; ‡controls v CAD patients; §comparisons between patient groups only; ¶controls v white CAD v South Asian CAD. ACE, angiotensin converting enzyme; BMI, body mass index; CAD, coronary artery disease; CAS, coronary artery stenosis score; CSS, coronary stenosis score; DBP, diastolic blood pressure; HDL, high density lipoprotein; LV, left ventricular; MI, myocardial infarction; SBP, systolic blood pressure.
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