Association of Adiponectin, Resistin, and Vascular Inflammation
Analysis With $^{18}$F-Fluorodeoxyglucose Positron Emission Tomography

Hae Yoon Choi, Sungeun Kim, Sae Jeong Yang, Hye Jin Yoo, Ji A. Seo, Sin Gon Kim, Nan Hee Kim, Sei Hyun Baik, Dong Seop Choi, Kyung Mook Choi

Objective—Adiponectin and resistin are adipokines that are linked to obesity, inflammation, and atherosclerosis. $^{18}$F-Fluorodeoxyglucose (FDG) positron emission tomography is a promising imaging technique that can be used to evaluate vascular inflammation.

Methods and Results—We measured adiponectin and resistin levels, as well as traditional cardiovascular risk factors, in 60 obese subjects and 60 nonobese controls. In addition, we compared carotid intima-media thickness and target-to-background ratio (TBR) measured using $^{18}$F-fluorodeoxyglucose–positron emission tomography/computed tomography. The mean TBR values were significantly higher in the obese group compared with normal subjects, although their mean carotid intima-media thickness levels were not significantly different. Serum adiponectin levels showed a significant negative correlation with mean TBR values ($r=−0.215$, $P=0.020$), whereas resistin levels were positively correlated with mean TBR values ($r=0.214$, $P=0.021$). Multiple linear regression analysis showed that mean TBR values were independently associated with body mass index, high-sensitivity C-reactive protein, and resistin levels ($R^2=0.308$).

Conclusion—Adiponectin and resistin may be useful as biomarkers to reflect vascular inflammation. In particular, resistin levels were independently associated with vascular inflammation even after adjusting for other cardiovascular risk factors. (Arterioscler Thromb Vasc Biol. 2011;31:944-949.)

Key Words: positron emission tomography ■ adiponectin ■ inflammation ■ resistin

Atherosclerosis is a chronic inflammatory process resulting from the interaction of modified lipoproteins, monocyte-derived macrophages, T cells, and the normal cellular elements of the arterial wall.1 Atherosclerotic plaques contain many inflammatory cells, such as macrophages, which secrete several cytokines that cause weakening of the fibrous plaque cap.2,3 The rupture of an atherosclerotic plaque and the subsequent formation of the thrombi are the main factors responsible for myocardial infarction and cerebral infarctions. The biological compositions and inflammatory state of an atherosclerotic plaque, rather than the degree of stenosis or its size, are the major determinants of acute clinical events.4

Adiponectin is a metabolically active adipokine that is inversely associated with obesity, insulin resistance, and atherosclerosis.5,6 Previous studies have indicated that adiponectin has antiinflammatory, antiatherogenic, and antidiabetic properties.7 Adiponectin is independently associated with a reduced risk of type 2 diabetes8 and a decreased coronary heart disease risk in diabetic men.9 Moreover, high plasma adiponectin levels were associated with a lower risk of myocardial infarction in men during the 6 years of follow-up in the Health Professionals Follow-Up Study.10 On the other hand, resistin was originally discovered as an adipokine that was suggested to be a link between obesity and insulin resistance in rodents.11 In contrast to rodents, human resistin is expressed primarily in inflammatory cells and has been shown to be involved in obesity-related subclinical inflammation, atherosclerosis, and cardiovascular disease (CVD).12 Reilly et al13 showed that circulating resistin levels are correlated with inflammation markers and are predictive of coronary atherosclerosis measured using coronary artery calcification scores, independent of C-reactive protein.

Recently, positron emission tomography (PET) with $^{18}$F-fluorodeoxyglucose (FDG) has emerged as a novel imaging technique to identify vascular inflammation.14 FDG accumulates in plaque macrophages, and its uptake is correlated with macrophage density. Tawakol et al15 reported a significant

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944
correlation between the PET signal from carotid plaques and macrophage staining from the corresponding histological sections ($r=0.70$; $P<0.001$). Rudd et al demonstrated that atherosclerotic plaque inflammation can be imaged with FDG-PET and that symptomatic, unstable plaques accumulate more FDG than do asymptomatic lesions. Recently, we found that FDG uptake values measured using FDG-PET/computed tomography (CT) were significantly increased in patients with impaired glucose tolerance or type 2 diabetes compared with the normal subjects and correlated with cardiovascular risk factors. Therefore, FDG-PET has been recognized as one of the advanced imaging approaches that can be used to evaluate vascular inflammation.

In this study, we examined the associations among circulating adiponectin, resistin levels, and vascular inflammation using FDG-PET/CT in healthy volunteers without known CVD or diabetes. In addition, we compared carotid intima-media thickness (CIMT) and target-to-background ratio (TBR) measured using FDG-PET/CT in obese and nonobese groups.

Materials and Methods

Study Design and Participants

We prospectively enrolled 120 apparently healthy participants who underwent a medical checkup in the health promotion center in Korea University Guro Hospital using predefined inclusion and exclusion criteria. Participants included 60 obese subjects (body mass index [BMI] $\geq 25$ kg/m$^2$) and 60 nonobese controls (BMI <25 kg/m$^2$). No participants had history of CVD (myocardial infarction, unstable angina, stroke, peripheral artery disease, or cardiovascular revascularization), diabetes, stage 2 hypertension (resting blood pressure $\geq 160/100$ mm Hg), malignancy, or severe renal or hepatic disease. Participants were free of any lipid-lowering therapies and postmenopausal hormone replacement therapy for at least the previous 6 months. All participants provided written informed consent, and the Korea University Institutional Review Board, in accordance with the Declaration of Helsinki of the World Medical Association, approved this study protocol.

Anthropometric and Laboratory Measurements

BMI was calculated as weight/height$^2$ (kg/m$^2$), and waist circumference was measured at the midpoint between the lower border of the rib cage and iliac crest. All blood samples were obtained in the morning after a 12-hour overnight fast and were immediately stored at $-80^\circ$C for subsequent assays. Serum triglycerides and high-density lipoprotein (HDL) cholesterol levels were determined enzymatically using a chemistry analyzer (Hitachi 747, Hitachi, Tokyo, Japan), and the low-density lipoprotein (LDL) cholesterol concentration was estimated using the Friedewald formula. A glucose oxidase method was used to measure plasma glucose, insulin resistance (IR) was calculated using the homeostasis model assessment (HOMA), and high-sensitivity C-reactive protein (hsCRP) levels were determined via a chemiluminescence immunoassay (Beckman Coulter, Brea, CA). Serum adiponectin levels were measured using ELISA (Mesdia, Seoul, Korea), and the intraassay and interassay variations were 5.0% and 4.6%, respectively. Serum resistin levels were measured using ELISA (AdipoGen, Incheon, Korea), and the intraassay and interassay variations were 3.7% and 5.6%, respectively.

Measurement of CIMT

The intima-media thickness (IMT) of the common carotid artery was determined using high-resolution B-mode ultrasonography (EnVisor, Philips Medical Systems, Andover, MA) with a 5- to 12-MHz transducer. Measurements of CIMT were made using the IMT measurement software Intimascope (Media Cross Co, Tokyo, Japan) at 3 levels of the lateral and medial walls, 1 to 3 cm proximal to the carotid bifurcation. The mean IMT was the average value of 99 computer-based points in the region, and the maximal IMT was the IMT value at a maximal point of the region. All measurements were recorded by a single trained technician who was blinded to the subject’s anthropometric and laboratory data.

$^{18}$F-FDG PET/CT Imaging

PET/CT was performed using the Gemini TF 16-Slice PET/CT scanner (Philips Medical Systems). The TF scanner is a new high-performance, time-of-flight–capable, fully 3-dimensional PET scanner using lutetium-yttrium oxyorthosilicate crystals. After at least 12 hours of fasting, $^{18}$F-FDG (370 to 550 MBq) was injected intravenously, and then the patients rested in a quiet room for 60 minutes. A whole body PET image (below cerebellum to inguinal) was acquired for 10 minutes (11-minute per bed), and PET image analysis was performed on a dedicated workstation (Extended Brilliance Workspace 3.5 with PET/CT viewer for automated image registration, Philips). Right carotid FDG uptake was measured along the length of the right carotid vessel, starting at the bifurcation and extending inferiorly and superiorly every 4 mm. Arterial FDG uptake was quantified in a region of interest around each artery on every slice of the coregistered transaxial PET/CT images. The region of interest was fitted to the artery wall on each axial slice, and coronal and sagittal views were used to ensure that the FDG uptake occurred in the artery. The standardized uptake value (SUV) was the decay-corrected tissue concentration of FDG (in kBq/mL) divided by the injected dose per body weight (kBq/g). The arterial SUV value was normalized to the blood pool SUV value measured from the jugular vein (standardized circular regions of interest; right carotid artery, area $=77.9\pm3.42$ mm$^2$, 9 pixels; right jugular vein, area $=95.0\pm12.7$ mm$^2$, 9 pixels). Afterward, a TBR was calculated as the right carotid vessel plaque SUV divided by the venous blood SUV, and a mean and maximum value of TBR was calculated for each patient. To determine the variabilities in the mean and maximum TBR measurements, images from 20 subjects were twice analyzed, several weeks apart, by 2 readers blinded to the subject’s clinical history. The intra- and interobserver correlation coefficient values of the mean and maximum TBR measurements were $>0.8$.

Statistical Analysis

Data are expressed as mean±SD or median (interquartile range). Differences between groups were tested using the independent 2-sample $t$ test, Mann–Whitney $U$ test, or $\chi^2$ test. Spearman rank correlation tests were performed to determine the relationships between TBR, hsCRP, CIMT values, and other cardiovascular risk variables. To test adipokine trends according to serum mean TBR tertiles, 1-way ANOVA and the Kruskal–Wallis test were performed. Multiple regression analysis was conducted using the mean TBR as a dependent variable. Age, gender, BMI, waist circumference, smoking, systolic blood pressure, diastolic blood pressure, HDL cholesterol, LDL cholesterol, triglyceride, serum fasting glucose level, homocysteine, serum adiponectin level, serum resistin level, and hsCRP level were adopted as independent variables. Data were analyzed using SPSS for Windows (version 12.0, SPSS Inc., Chicago, IL), and a probability value $<0.05$ indicated statistical significance.

Results

Patient Characteristics

Clinical and biochemical characteristics of the study subjects are shown in Table 1. The obese group, which had a higher BMI ($\geq 25$ kg/m$^2$), had decreased HDL cholesterol and...
Table 1. Clinical and Laboratory Characteristics of the Study Subjects

<table>
<thead>
<tr>
<th></th>
<th>Nonobese Group (n=60)</th>
<th>Obese Group (n=60)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>51.2±9.8</td>
<td>48.2±10.1</td>
<td>0.096</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>37/23</td>
<td>37/23</td>
<td>1.000</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.1±2.1</td>
<td>27.4±2.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>80.0±7.1</td>
<td>89.9±6.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>120.5±13.4</td>
<td>127.6±13.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>79.3±10.0</td>
<td>84.4±9.9</td>
<td>0.006</td>
</tr>
<tr>
<td>Fasting glucose (mmol/L)</td>
<td>4.65±0.87</td>
<td>5.40±0.78</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HOMA-IR*</td>
<td>0.49 (0.18, 0.89)</td>
<td>1.49 (0.62, 2.16)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>4.37±1.05</td>
<td>5.20±1.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/L)</td>
<td>2.66±0.91</td>
<td>3.40±0.98</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>1.27±0.36</td>
<td>1.12±0.28</td>
<td>0.045</td>
</tr>
<tr>
<td>Triglyceride (mmol/L)*</td>
<td>0.83 (0.62, 1.31)</td>
<td>1.42 (1.08, 2.27)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>hsCRP (mg/L)*</td>
<td>0.48 (0.20, 1.16)</td>
<td>2.16 (0.60, 3.30)</td>
<td>&lt;0.000</td>
</tr>
<tr>
<td>Mean IMT (mm)*</td>
<td>0.87 (0.54, 0.72)</td>
<td>0.65 (0.57, 0.79)</td>
<td>0.107</td>
</tr>
<tr>
<td>Maximum IMT (mm)*</td>
<td>0.71 (0.65, 0.86)</td>
<td>0.80 (0.67, 0.93)</td>
<td>0.038</td>
</tr>
<tr>
<td>Mean TBR*</td>
<td>1.09 (1.06, 1.19)</td>
<td>1.23 (1.09, 1.36)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximum TBR*</td>
<td>1.18 (1.13, 1.31)</td>
<td>1.34 (1.18, 1.54)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adiponectin (ng/ml)*</td>
<td>9.86 (4.75, 14.41)</td>
<td>4.79 (3.60, 7.11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Resistin (ng/ml)*</td>
<td>5.38 (3.40, 8.43)</td>
<td>4.84 (3.17, 6.95)</td>
<td>0.295</td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure; DBP, diastolic blood pressure; FGB, fasting blood glucose.

*P values represent overall differences across groups as determined using the t test for linear comparisons or the Mann–Whitney test.

adiponectin levels and increased waist circumference, blood pressure, fasting glucose level, HOMA-IR, total cholesterol, LDL cholesterol, triglyceride, and hsCRP levels compared with those of the lower BMI (<25 kg/m²) group. Furthermore, mean/maximal TBR values and maximal IMT values were significantly higher in the obese group compared with those of the nonobese group (Table 1, Figure 1A). However, there were no significant differences in mean IMT or resistin levels between the obese and nonobese groups (Table 1, Figure 1B).

### Discussion

Using FDG-PET/CT, we found that patients in the obese group had increased TBR values, reflecting vascular inflammation, compared with those of the nonobese group. Furthermore, vascular inflammation was positively correlated with resistin and negatively correlated with adiponectin. In particular, resistin showed an independent association with vascular inflammation, even after consideration of other risk factors associated with atherosclerosis.

Resistin is derived almost exclusively from adipose tissue in rodents, but it is expressed primarily in inflammatory cells, especially macrophages, in humans. In the rodent model, resistin was initially suggested to be a link between obesity and insulin resistance, but this has not been shown in humans. Instead, resistin expression was found to be abundant in monocytes/macrophages, which play an important role in inflammation and atherosclerosis. Kawamura et al. found that resistin induces the expression of adhesion molecules such as vascular cellular adhesion molecule-1, and that intercellular adhesion molecule-1 and adiponectin inhibit the effect of resistin in the vascular endothelial cells. Lee et al. observed that resistin promotes foam cell formation via dysregulation of scavenger receptors.
obesity or insulin resistance status.27 In men with acute myocardial infarction, a multivariate model revealed that obesity and C-reactive protein were independent variables associated with higher resistin levels.28 Moreover, Weikert et al29 reported that among 26 490 middle-aged subjects, individuals in the highest quartile of resistin level, compared with those in the lowest quartile of resistin level, had a significantly increased risk of myocardial infarction after adjustment for cardiovascular risk factors, including C-reactive protein (relative risk, 2.09; 95% confidence interval, 1.01 to 4.31). Recently, in 397 Korean patients with acute myocardial infarction, high resistin levels were predictors for all-cause mortality, independent of other risk factors.30 These studies suggest that resistin may represent a novel link of metabolic signals, inflammation, and atherosclerosis. The present study demonstrates the association of resistin level and the TBR

Table 2. Clinical and Laboratory Variables According to Mean TBR Tertiles

<table>
<thead>
<tr>
<th>Variable</th>
<th>1st Tertile (n=44)</th>
<th>2nd Tertile (n=38)</th>
<th>3rd Tertile (n=38)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean TBR</td>
<td>1.03±0.07</td>
<td>1.16±0.05</td>
<td>1.39±0.18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (years)</td>
<td>51.11±9.71</td>
<td>49.4±10.9</td>
<td>48.4±9.5</td>
<td>0.463</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>23/21</td>
<td>22/16</td>
<td>29/9</td>
<td>0.070</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.2±3.1</td>
<td>24.9±3.4</td>
<td>26.5±3.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>82.2±8.5</td>
<td>84.3±8.2</td>
<td>88.7±6.5</td>
<td>0.001</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>122.2±13.0</td>
<td>125.6±14.5</td>
<td>124.4±13.7</td>
<td>0.518</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>79.5±8.4</td>
<td>83.47±11.5</td>
<td>82.8±10.7</td>
<td>0.171</td>
</tr>
<tr>
<td>FBG (mmol/L)</td>
<td>4.78±1.05</td>
<td>4.99±0.74</td>
<td>5.34±0.78</td>
<td>0.019</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>0.98±1.10</td>
<td>0.90±0.78</td>
<td>1.33±0.99</td>
<td>0.072</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>4.54±1.19</td>
<td>4.60±0.99</td>
<td>5.24±1.12</td>
<td>0.009</td>
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<tr>
<td>LDL cholesterol (mmol/L)</td>
<td>2.79±0.97</td>
<td>2.86±0.93</td>
<td>3.48±1.02</td>
<td>0.003</td>
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<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>1.21±0.36</td>
<td>1.24±0.32</td>
<td>1.18±0.29</td>
<td>0.728</td>
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<td>Triglyceride (mmol/L)</td>
<td>1.35±1.19</td>
<td>1.38±0.84</td>
<td>1.58±0.87</td>
<td>0.104</td>
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<tr>
<td>hsCRP (mg/L)</td>
<td>0.86±1.40</td>
<td>1.65±1.94</td>
<td>3.88±3.37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean IMT</td>
<td>0.64±0.18</td>
<td>0.65±0.13</td>
<td>0.66±0.12</td>
<td>0.074</td>
</tr>
<tr>
<td>Maximum IMT</td>
<td>0.77±0.22</td>
<td>0.78±0.15</td>
<td>0.82±0.15</td>
<td>0.037</td>
</tr>
<tr>
<td>Adiponectin (µg/ml)</td>
<td>9.65±5.13</td>
<td>7.75±5.97</td>
<td>6.61±4.81</td>
<td>0.007</td>
</tr>
<tr>
<td>Resistin (ng/ml)</td>
<td>5.50±4.32</td>
<td>5.67±3.16</td>
<td>7.57±5.26</td>
<td>0.014</td>
</tr>
</tbody>
</table>

SE indicates standard error; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose.

Table 3. Univariate and multivariate analyses for Mean TBR Values

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate Coefficients</th>
<th>Univariate SE</th>
<th>Univariate P</th>
<th>Multivariate Coefficients</th>
<th>Multivariate SE</th>
<th>Multivariate P</th>
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<td>Age</td>
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<tr>
<td>Gender</td>
<td>-0.025</td>
<td>0.011</td>
<td>0.021</td>
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<td>BMI</td>
<td>0.006</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>0.004</td>
<td>0.001</td>
<td>0.014</td>
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<td>Waist circumference</td>
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<td>...</td>
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<td>...</td>
</tr>
<tr>
<td>SBP</td>
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<td>0.000</td>
<td>0.718</td>
<td>...</td>
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<tr>
<td>DBP</td>
<td>0.001</td>
<td>0.001</td>
<td>0.243</td>
<td>...</td>
<td>...</td>
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</tr>
<tr>
<td>FBG</td>
<td>0.001</td>
<td>0.000</td>
<td>0.031</td>
<td>...</td>
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<td>...</td>
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<tr>
<td>HOMA-IR</td>
<td>0.026</td>
<td>0.012</td>
<td>0.029</td>
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<tr>
<td>LDL cholesterol</td>
<td>0.000</td>
<td>0.000</td>
<td>0.002</td>
<td>...</td>
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<td>...</td>
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<tr>
<td>HDL cholesterol</td>
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<td>0.000</td>
<td>0.221</td>
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<td>Triglyceride</td>
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<td>0.008</td>
<td>0.022</td>
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<td>...</td>
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<tr>
<td>hsCRP</td>
<td>0.023</td>
<td>0.004</td>
<td>&lt;0.001</td>
<td>0.015</td>
<td>0.004</td>
<td>0.001</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.044</td>
<td>0.038</td>
<td>0.249</td>
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<td>...</td>
</tr>
<tr>
<td>Adiponectin</td>
<td>-0.019</td>
<td>0.008</td>
<td>0.016</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Resistin</td>
<td>0.021</td>
<td>0.008</td>
<td>0.015</td>
<td>0.016</td>
<td>0.016</td>
<td>0.07</td>
</tr>
</tbody>
</table>

Adiponectin, Resistin, and Vascular Inflammation

Figure 2. Correlations between adiponectin (µ/mL) (A), resistin (ng/mL) (B), and mean TBR level.
values that reflect vascular inflammation, even after adjusting for other cardiovascular risk factors, including hsCRP.

Adiponectin, a circulating adipose tissue-derived hormone, is downregulated in obese individuals. Experimental studies have shown that adiponectin plays a protective role in the development of insulin resistance, inflammation, and atherosclerosis. Hypoadiponectinemia has been established as an independent risk factor for type 2 diabetes and CVD. The present study confirmed that circulating adiponectin levels were negatively correlated with cardiovascular risk profiles, such as BMI, waist circumference, lipid profiles, insulin resistance, and hsCRP levels. Although the role of adiponectin is attractive as a biomarker for estimating the risk of atherosclerotic CVD, several recent studies have reported conflicting results. Wannamethee et al reported that high adiponectin levels were associated with increased all-cause and CVD mortality in older men with heart failure. Hajer et al also reported that lower adiponectin levels were associated with a lower cardiovascular risk in patients with clinical evident vascular disease. There is no clear explanation for this discrepancy. In this study including middle-aged participants without known CVD, adiponectin levels were correlated negatively with vascular inflammation measured using FDG-PET/CT. However, this relationship was attenuated after adjusting for other cardiovascular risk factors, including hsCRP, a marker of systemic inflammation that predicts the risk of CVD.

There is growing evidence that vascular inflammation is involved in atherosclerosis. Epidemiological and experimental studies have established that intima-media thickness of the carotid and femoral arteries is a valid surrogate marker for the progression of atherosclerotic disease. However, CIMT does not provide information about plaque composition or inflammatory state; FDG-PET may effectively detect the inflammatory state of an atherosclerotic plaque. Ogawa et al reported that macrophages are responsible for the accumulation of FDG in atherosclerotic lesions, and FDG uptake is correlated with macrophage density. Silvera et al evaluated the relationship between atherosclerotic plaque inflammation, as assessed by FDG-PET/CT, and plaque morphology and composition, as assessed by magnetic resonance imaging. They found that the TBR value was higher in the lipid-necrotic core group compared with collagen and calcium groups in 16 patients with cardiovascular risk factors. On the other hand, FDG-PET imaging of atherosclerotic plaque inflammation is highly reproducible, with favorable inter- and intraobserver agreement. In addition, Tahara et al showed inflammation is highly reproducible, with favorable inter- and intraobserver agreement.

In this study including middle-aged participants without known CVD, adiponectin levels were correlated negatively with vascular inflammation measured using FDG-PET/CT. However, this relationship was attenuated after adjusting for other cardiovascular risk factors, including hsCRP, a marker of systemic inflammation that predicts the risk of CVD.

Serum adiponectin and resistin levels showed significant correlation with vascular inflammation, as represented by TBR values measured using FDG-PET/CT. These results suggest that adiponectin and resistin may be useful circulating biomarkers that reflect vascular inflammation. Additional prospective studies are needed to support the use of adiponectin, resistin levels, and FDG-PET imaging as predictors of risk for developing atherosclerosis and CVD.

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Disclosures

None.

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Adiponectin, Resistin, and Vascular Inflammation


Association of Adiponectin, Resistin, and Vascular Inflammation: Analysis With 18F-Fluorodeoxyglucose Positron Emission Tomography

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Figure: PET-CT images from each group. (A) obese subjects (B) non-obese controls.
Summary

목적
Adiponectin과 resistin은 비만 및 즉상경화와 연관된 adipokine들이다. \textsuperscript{18}F-Fluorodeoxyglucose(FDG) positron emission tomography 영상은 혈관의 염증을 평가하는데 장점을 보이는 지표이다.

방법 및 결과
연구진은 기타 심혈관질환의 위험인자들과 함께 adiponectin과 resistin 수치를 측정하였으며, 경동맥의 혈관중막 두께(carotid intima-media thickness)를 \textsuperscript{18}F-fluorodeoxyglucose-positron emission tomography/computed tomography 기법으로 측정하여 target-to-background ratio(TBR)를 구하였다. 총 60명의 비만환자를 60명의 정상환자로 대조군과 비교하였다.

평균 TBR 수치는 정상군에 비하여 비만군에서 유의하게 높았으며, 혈중 adiponectin 수치와는 유의한 음의 상관관계를 나타내었고(r=-0.215, P=0.020), resistin 수치와는 유의한 양의 상관성을 나타내었다(r=0.241, P=0.021). Multiple linear regression 분석 시 TBR 평균치는 body mass index, high-sensitivity C-reactive protein, 그리고 resistin 수치와 독립적인 관련성을 나타내었다(R'=0.308).

결론
Adiponectin과 resistin은 혈관의 염증 정도를 반영하는 생체표지자로 생각된다. 특히 resistin 수치는 기타 위험인자들의 영향을 보정한 이후에도 혈관의 염증과 독립적인 관련성이 존재한다.
Commentary

특별한 증상이 없는 상태에서 주요혈관의 족상경화의 정도를 측정할 수 있다면 정명의 결과에서부터 처방의 변화를 단순히 검증할 수 있다거나, 모든 부분에 지급까지의 개념을 뛰어넘는 둘을 제공하는 것이다.

Table 1과 Figure 1에서와 같이 Fluorodeoxyglucose (FDG) positron emission tomography라는 신경내부의 방법인 활발하였을 때의 '단지 비만도가 증가되어 있다'는 생각으로 적절한 많은 burden의 족상경화가 관찰되었으며, 이는 비만상관 혈중표지자인 resistin 및 adiponectin 등이 높은 유발성을 나타내었다.

네분비 또는 심장질환의 식단을 다소 가지고 있다면 이들 사이의 연관성은 많은 논문에서 언급되며 여분의 할당된 지역에서의 Fluorodeoxyglucose(FDG) positron emission tomography에 대하여 고찰을 하는 것이 좋은 것으로 보인다.

기존의 방법들

A. Intravascular Ultrasound

당연히 이미지의 관점에서 족상경화류의 성장을 측정할 수 있다. 단 carotid IMT, plaque 등의 확장면에서는 간단하고 신뢰성을 높은 방법으로 판단된다.

최근에는 이를 보완하기 위하여 Contrast-enhanced ultrasound(CESUS)라는 기법을 이용하기도 한다. 이는 lipid 또는 albumine 등의 성질을 가지고 있는 microbubble을 주입한 후, washout phase 이후에 plaque에 도달하는 소혈관들의 영상이 가능한 것으로 판명되어 있으며, 최근에는 plaque의 폐증도 역시 반영되는 주장이다.

이런 소혈관의 영상도를 높이기 위하여 최근에는 VCAM-1, 기타 adhesion molecule들을 conjugation하여 영상을 시도하기도 한다.
B. Computed Tomography
Electron-beam CT와 multiple-row detector CT(MDCT) 등의 두 가지 방법이 존재한다. 간단히 말하여 전자는 3mm 간격의 영상으로 석회화 정도를 판정 가능하고, 추자는 0.5mm까지의 영상으로 조영제를 사용하면 혈관의 조영이 가능한 정도로 정밀도가 높다. 최근 512-slice 등으로 기법이 향상되고 있으며 영상학적 진단이 있기 때문에 MR 등과의 동시 영상으로 가능한면에서 보완 가능성이 높다. 그러나 임의 발생체에서 줄이기 위해 괴목량을 줄여야 하며, 항후 반복 시행간격 설정 등의 표준치료 지침이 설정되어야 한다. 그러나 negative predictive value가 높은 장점이 있다.

C. MRI
영상취득의 문제로 아직 괴목량의 조영이 어려우나, 고신호선 T1, T2, proton-density weighting 이미지의 적용으로 plaque의 성상 추정이 가능하다. 괴목등은 괴목적에서 fibrous cap(또는 integrity), lipid-rich/necrotic core, intraplaque hemorrhage, and calcification 등의 면발이 가능하며 소위 vulnerable plaque의 판단이 가능하다. 최근에는 특히 iron oxide를 이용한 plaque의 영상을 획득하고 있으며 이의 ultrasmall particle 또는 VCAM-1 등의 리간도를 혈합시킨 macroparticle 등을 이용하기도 한다.

D. FDG positron emission tomography
PET, SPECT 공히 혈관내질병절단도가 5-15mm로 낮기 때문에 진단을 받지 못한 경우가 많아서 흔히 수술적 방법으로 치료가 매우 높다. PET를 이용하면 rupture, chemotaxis, angiogenesis, lipoprotein accumulation, proteolysis, and thrombogenicity 등의 평가가 이론적으로 가능하며, PET를 이용하면 18F-FDG, TSPO(translocator protein), ligands, choline ligands 등의 세포 내 활성영상을 얻을 수 있다.

- Fluorodeoxyglucose(FDG)
이중 PET에서 각광을 받는 것이 FDG이다. 이는 당류의 대화로 세포합성을 hexokinase에 의하여 세포탈출이 불가능하기 때문에 영상 표지자로 이용가능하다. 따라서 세포활성이 높은 대식세포 등의 영상이 주로 이루어 지게 된다. 실장에서의 문제점은 아직 PET 자체의 성장 포화가 아직 어렵다는 점과, 심근으로의 FDG 병합 영상이 선명하지 않다는 점이다.

이외 최근에는 대식세포에만 특이하게 함유하는 18-kDa translocator protein(TSPO/the peripheral benzodiazepine receptor(18PBR)) 또는 풍속하는 세포에 주로 함유하여 전립선의 영상에 이용되었던 18F-labeled fluorocholine(FCH) 등의 용용이 시도되고 있다.

REFERENCE