Association of Adiponectin, Resistin, and Vascular Inflammation
Analysis With 18F-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. 18F-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 18F-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 (R2 = 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 diabetes 8 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 al 13 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 18F-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 al 15 reported a significant

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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/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 6-month period before enrollment. We also excluded subjects with a history of inflammatory condition or those taking medications that might affect the inflammatory status within 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 5.6%, 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.

**18F-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–compatible, 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±3.42 mm$^2$, 9 pixels; right jugular vein, area=95.0±12.7 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, HOMA-IR, 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...
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).

Imaging and Clinical Parameters

In a Spearman correlation analysis, adiponectin levels were negatively correlated with BMI, waist circumference, total cholesterol, LDL cholesterol, triglyceride, fasting plasma glucose, HOMA-IR, and hsCRP levels and positively correlated with HDL cholesterol level and age (all P<0.05). Importantly, adiponectin levels showed a negative relationship with mean TBR values (r = −0.215, P = 0.020), whereas resistin levels showed a positive relationship with mean TBR values (r = 0.214, P = 0.021) (Figure 2). Resistin levels showed a positive relationship with IMT values, whereas adiponectin levels had no significant correlation with IMT values. In the present study, there was a significant positive relationship between mean TBR and CIMT values (r = 0.207, P = 0.024).

Table 2 shows the clinical and laboratory variables stratified by tertiles of mean TBR levels. Significant differences in BMI, waist circumference, fasting glucose, total cholesterol, LDL cholesterol, hsCRP, maximal IMT, adiponectin, and resistin levels between groups were noted (all P<0.05).

Univariate analysis showed that mean TBR values were significantly associated with gender, BMI, waist circumference, fasting glucose, HOMA-IR, LDL cholesterol, triglyceride, hsCRP, adiponectin, and resistin levels (Table 3). When multiple stepwise regression analysis was performed using mean TBR as a dependent variable, hsCRP (P = 0.01), BMI (P = 0.014), and resistin levels (P = 0.046) were independently associated with mean TBR values (R² = 0.308) (Table 3).

**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. Kawanami 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.
(SR-A and CD36) and ATP-binding cassette transporter-A1 in macrophages. In a population-based cross-sectional study of 3193 Chinese subjects, resistin was more strongly associated with inflammatory and fibrinolytic markers than with 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>Tertile</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>51.1±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>
</tr>
<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>
</tr>
<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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<tr>
<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>
</tr>
<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>
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<tr>
<td>Mean IMT</td>
<td>0.64±0.18</td>
<td>0.65±0.13</td>
<td>0.68±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>

SBP indicates 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></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>
</tr>
</thead>
<tbody>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Age</td>
<td>-0.001</td>
<td>0.001</td>
<td>0.103</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Gender</td>
<td>-0.025</td>
<td>0.011</td>
<td>0.021</td>
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</tr>
<tr>
<td>BMI</td>
<td>0.006</td>
<td>&lt;0.001</td>
<td>0.004</td>
<td>0.001</td>
<td>0.014</td>
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<tr>
<td>Waist circumference</td>
<td>0.002</td>
<td>0.001</td>
<td>0.001</td>
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<tr>
<td>SBP</td>
<td>0.000</td>
<td>0.000</td>
<td>0.718</td>
<td></td>
<td></td>
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</tr>
<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>
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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>
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<tr>
<td>HDL cholesterol</td>
<td>-0.001</td>
<td>0.000</td>
<td>0.221</td>
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<td>Triglyceride</td>
<td>0.020</td>
<td>0.008</td>
<td>0.022</td>
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<tr>
<td>hsCRP</td>
<td>0.023</td>
<td>&lt;0.001</td>
<td>0.015</td>
<td>0.004</td>
<td>0.001</td>
<td></td>
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<tr>
<td>Smoking</td>
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<td>0.038</td>
<td>0.249</td>
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<tr>
<td>Adiponectin</td>
<td>-0.019</td>
<td>0.008</td>
<td>0.016</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Resistin</td>
<td>0.021</td>
<td>0.008</td>
<td>0.015</td>
<td>0.016</td>
<td>0.07</td>
<td>0.046</td>
</tr>
</tbody>
</table>

SE indicates standard error; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose.
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. Hajej 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. CIMT does not provide information about plaque composition or progression 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. Hajej 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 characterized by an inflammatory process irrespective of the dominant plaque morphology. Circulation. 1994;89:36–44.


Conclusions

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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**Figure:** PET-CT images from each group. (A) obese subjects (B) non-obese controls.
즉상경화의 접근에 있어서의 FDG-PET의 유용성

한 기훈 교수
서울아산병원 심장내과

Summary

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

방법 및 결과
연구대상은 각기 실험실에서의 혈액검사에서 양성 impedence, 체질량지수(body mass index, BMI), 고지혈증, 당뇨병, 고혈압, 비만, 고밀도리प로프로틴, low-density lipoprotein(LDL), high-density lipoprotein(HDL), 총コレ스테롤, cholesterol, 중성지방, triglyceride, C-reactive protein(CRP), D-dimer, homocysteine, D-dimer, homocysteine, D-dimer의 혈액검사에서 양성의 대상자들을 대상으로 하였다. 60명의 대상자를 대상으로 하였다. 60명의 대상자들을 대상으로 하였다.

평균 TBR 수치는 정상군에 비하여 비망군에서 유의하게 높았으며, 혈중 adiponectin 수치와는 유의한 음의 상관관계를 나타내었고($r=-0.215$, $P=0.020$), resistin 수치와는 유의한 양의 상관성을 나타내었다($r=0.214$, $P=0.021$). Multiple linear

결론
Adiponectin과 resistin은 혈관의 염증 정도를 반영하는 생체표지자로 생각된다. 특히 resistin 수치는 각 기 혈액학자의 영향을 보정한 이후에도 혈관의 염증과 독립적인 관련성을 존재한다.
고혈압의 증상이 없는 경우에서 주요혈관의 죽상경화의 정도를 측정할 수 있는데 그 증상의 결과에서부터 치료적인 면까지, 모든 부분에 지급까지의 개념을 둘어낸 뿐을 제공하는 것이다.

Table 1과 Figure 1에와 같이 Fluorodeoxyglucose (FDG) positron emission tomography는 신경의 방법들을 적용하였을 때 '단지 비만도가 상승되어 있는' 대상자들에게만 많은 burden의 죽상경화가 관찰되었으며, 이는 비만유전 결합표지자인 mediator인 resistin 및 adiponectin 등의 농도와 연관성을 나타내었다.

네번 비 또는 심장질환의 식전을 다소 가지고 있다면 이들 사이의 연관성을 많이 논문에서 언급되므로 현재의 혈관이에서는 Fluorodeoxyglucose (FDG) positron emission tomography에 대하여 고찰을 하는 것이 좋을 것으로 보인다.

기존의 방법들
A. Intravascular Ultrasound
만약 이때의 영상을 인하여 죽상경화반의 성장을 측정할 수 있다. 단 carotid IMT, plaque 등의 포착면에서는 간단하고 신뢰성 높은 기법으로 판단된다.

최근에는 이를 보완하기 위하여 Contrast-enhanced ultrasound(CEUS)라는 기법을 이용하기도 한다. 이는 lipid 또는 albumin 등의 생체를 가지는 microbubble을 주입함으로써 washout phase 후에 plaque에 도달하는 소혈관들의 영상이 가능한 것으로 알려져 있으며, 최근에는 plaque의 병증도 역시 반영되는 주장이 있다. 이러한 소혈관의 영상도를 높이기 위하여 최근에는 VCAM-1, 기타 adhesion molecule들을 conjugation하여 영상을 시도하기도 한다.

Table 1. TNR 테트리 분포에 따른 임상적, 실험실 수치의 분포

<table>
<thead>
<tr>
<th></th>
<th>1st Tetrac (n=44)</th>
<th>2nd Tetrac (n=38)</th>
<th>3rd Tetrac (n=36)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size of IMT</td>
<td>1.04 ± 0.03</td>
<td>1.01 ± 0.05</td>
<td>1.04 ± 0.03</td>
<td>&lt;0.04</td>
</tr>
<tr>
<td>Age (years)</td>
<td>62.7 ± 7.7</td>
<td>62.4 ± 7.5</td>
<td>63.1 ± 8.2</td>
<td>0.89</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>73/27</td>
<td>71/36</td>
<td>73/33</td>
<td>0.60</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.5 ± 3.1</td>
<td>24.3 ± 3.5</td>
<td>23.6 ± 3.2</td>
<td>0.03</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>82.6 ± 8.5</td>
<td>84.3 ± 8.9</td>
<td>82.7 ± 8.4</td>
<td>0.03</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>0.06</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>82.4 ± 8.4</td>
<td>83.4 ± 9.1</td>
<td>82.8 ± 8.7</td>
<td>0.13</td>
</tr>
<tr>
<td>FPG (mmol/L)</td>
<td>4.78 ± 0.05</td>
<td>4.95 ± 0.31</td>
<td>5.34 ± 0.78</td>
<td>0.09</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>1.62 ± 1.9</td>
<td>0.80 ± 7.1</td>
<td>1.33 ± 0.99</td>
<td>0.07</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>4.41 ± 1.9</td>
<td>4.60 ± 0.98</td>
<td>5.24 ± 1.72</td>
<td>0.09</td>
</tr>
<tr>
<td>LDL, cholesterol (mmol/L)</td>
<td>2.79 ± 1.97</td>
<td>2.86 ± 1.01</td>
<td>3.40 ± 1.20</td>
<td>0.03</td>
</tr>
<tr>
<td>HDL, cholesterol (mmol/L)</td>
<td>1.21 ± 0.36</td>
<td>1.24 ± 0.32</td>
<td>1.19 ± 0.29</td>
<td>0.72</td>
</tr>
<tr>
<td>triglyceride (mmol/L)</td>
<td>1.35 ± 1.10</td>
<td>1.38 ± 0.24</td>
<td>1.56 ± 0.07</td>
<td>0.10</td>
</tr>
<tr>
<td>hsCRP (mg/L)</td>
<td>0.64 ± 0.16</td>
<td>0.68 ± 0.12</td>
<td>0.66 ± 0.13</td>
<td>0.04</td>
</tr>
<tr>
<td>Mean IMT</td>
<td>0.64 ± 0.10</td>
<td>0.68 ± 0.12</td>
<td>0.66 ± 0.13</td>
<td>0.04</td>
</tr>
<tr>
<td>Maximum IMT</td>
<td>0.77 ± 0.22</td>
<td>0.78 ± 0.11</td>
<td>0.80 ± 0.15</td>
<td>0.07</td>
</tr>
<tr>
<td>Adiponectin (ng/mL)</td>
<td>0.64 ± 0.13</td>
<td>0.65 ± 0.97</td>
<td>0.61 ± 0.49</td>
<td>0.07</td>
</tr>
<tr>
<td>Resistin (ng/mL)</td>
<td>5.50 ± 3.22</td>
<td>5.67 ± 3.14</td>
<td>7.5 ± 5.20</td>
<td>0.01</td>
</tr>
</tbody>
</table>

SIP indicates systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose.

Figure 1. Plot of TNR value and log resistin (ng/mL) value.
B. Computed Tomography

Electron-beam CT와 multiple-row detector CT(MDCT) 등의 두 가지 방법이 존재한다.
간단히 말하면 전자는 3mm 간격의 영상으로 석회화 정도를 판정 가능하고, 후자는 0.5mm까지의 영상으로 조영제를 사용하면 혈관의 조영이 가능한 정도로 정밀도가 높다. 최근은 512-slice 등으로 기법이 향상되고 있으며 영상력의 강점이 있기 때문에 PET 등과의 동시 영상으로 가능정한 면에서 보완 가능성이 높다.

그러나 앞의 발생유형을 줄이기 위해 폐포양을 줄여야 하며, 항후 반복 시행간격 설정 등의 표준 치료 지침이 설정되어야 한다. 그러나 negative predictive value가 높은 장점이 있다.

C. MRI

영상층득의 문제로 아직 공동의 조영이 어려우나, 고석적인 T1, T2, proton-density weighting 이미지의 종합으로 plaque의 성상 추정이 가능하다. 적어도 공동영역에서는 fibrous cap (and its integrity), lipid-rich/necrotic core, intraplaque hemorrhage, and calcification 등의 판별이 가능하여 소위 vulnerable plaque의 판단이 가능하다.

보존적 이러한 iron oxide를 이용한 plaque의 양상의 각각을 바꾸고 있으며 이의 ultrasmall particle 또는 VCAM-1 등의 리간드를 접합시킨 macroparticle 등을 이용하기도 한다.

D. FDG positron emission tomography

PET, SPECT 공히 하부환적 정밀도가 5-15mm로 높기 때문에 재현을 받지만 소위 기능적인 이미지로 취득할 수 있기 때문에 확률적으로 가치가 매우 높다. SPECT를 이용하면 rupture, chemotaxis, angiogenesis, lipoprotein accumulation, proteolysis, and thrombogenicity 등의 평가가 가능하며, PET를 이용하면 $^{18}$F-FDG, TSPO(translocator protein), ligands, choline ligands 등의 세포 내 함유영상을 얻을 수 있다.

- Fluorodeoxyglucose(FDG)

이중 PET에서 각광을 받는 것이 FDG이다. 이는 당류의 흡수로 세포합합 후 hexokinase에 의하여 세포탈출이 불가능하기 때문에 영상 표지자로 이용이 가능하다. 따라서 세포활성의 높은 대식세포 등의 영상이 주로 이루어지게 된다.

심장에서의 문제점은 아직 PET 자체의 성장 황작이 아직 어렵다는 점과, 심근으로의 FDG 질병 영상이 선명하지 않다는 점이다.

이외 최근에는 대식세포에만 특이하게 합입하는 18-kDa translocator protein(TSPO)의 peripheral benzodiazepine receptor(PBR). 또는 평활성 세포에 주로 합합하여 전립선의 영상에 이용되었던 $^{18}$F-labeled fluorocholine(FCH) 등의 응용이 시도되고 있다.

REFERENCE