Basic biological and clinical research supports the role of inflammation in the initiation, growth, and rupture of atherosclerotic plaques.1 At every stage of atherosclerosis, monocyte-derived macrophages are the principal mediators of inflammation.2,3 Recent studies lend some clarity to the role of inflammation in driving the atherogenic response to hypercholesterolemia and suggest that this process is initiated in the bone marrow (BM) and spleen.4–6 In response to hypercholesterolemia, both the BM and spleen overproduce inflammatory monocytes that enter the circulation, accumulate in lesions, and differentiate into macrophages.7

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Acute myocardial ischemic injury8 and acute myocardial infarction (AMI)9 activate the sympathetic nervous system and trigger a cascade of hematopoietic stem and progenitor cell proliferation in the BM and emigration to the spleen, as well as peripheral monocytes.7 In this process, the spleen acts as an extramedullary hematopoietic reservoir, producing inflammatory monocytes that aggravate atherosclerosis.5 Thus, this inflammatory linkage among the BM, spleen, and blood after an acute cardiac event may intensify the chronic inflammatory process involved in atherosclerosis, independently from the primary myocardial wound site.7 This mechanism of systemic inflammation in atherosclerotic disease initiated by the BM and spleen has been studied in animal models but not in humans with coronary artery disease (CAD).

Activated inflammatory cells express high levels of glucose transporters and accumulate 18F-fluorodeoxyglucose (18F-FDG).10,11 For this reason, 18F-FDG positron emission tomography (PET) is a useful noninvasive imaging technique to evaluate the inflammatory status of atherosclerotic plaques.12,13

Background—Atherosclerosis is considered to be an inflammatory disease associated with the activation of hematopoietic and immune-related organs such as the bone marrow (BM) and spleen. We evaluated the metabolic activity of those organs and of the carotid artery with 18F-fluorodeoxyglucose positron emission tomography in patients with coronary artery disease, including acute myocardial infarction.

Methods and Results—Whole-body combined 18F-fluorodeoxyglucose positron emission tomography/computed tomography was performed in 32 patients with acute myocardial infarction, 33 patients with chronic stable angina, and 25 control subjects. The mean standard uptake value was calculated in the regions of interest in the spleen and the BM of lumbar vertebrae. The target-to-background ratio of the standard uptake values of the carotid artery and jugular vein was also calculated. In patients with acute myocardial infarction, the standard uptake values of the BM (1.67±0.16) and spleen (2.57±0.39), as well as the target-to-background ratio of the carotid artery (2.13±0.42), were significantly higher than the corresponding values of patients with angina (1.22±0.62; 2.03±0.35; 1.36±0.37; all P<0.001) and controls (0.80±0.44; 1.54±0.26; 1.22±0.22; all P<0.001), independent of traditional cardiovascular risk factors and high-sensitivity C-reactive protein. In all groups combined, the target-to-background ratio of the carotid artery was significantly associated with the standard uptake values of the BM (r=0.535; P<0.001), spleen (r=0.663; P<0.001), and high-sensitivity C-reactive protein (r=0.465; P<0.001).

Conclusions—The metabolic activity of the BM and spleen, as well as of the carotid artery, was highest in patients with acute myocardial infarction, intermediate in patients with angina, and lowest in control subjects. The activation of the BM and spleen was significantly associated with inflammatory activity of the carotid artery. (Circ Cardiovasc Imaging. 2014;7:454-460.)

Key Words: bone marrow ■ coronary artery disease ■ positron-emission tomography ■ spleen
plaque and periodontal disease. Theoretically, the metabolic activity of the BM and spleen can be also evaluated by PET using 18F-FDG.

This study has 3 objectives: to determine whether (1) the metabolic activation of the BM and spleen is associated with AMI, (2) the degree of metabolic activation of these organs is associated with inflammatory activity at carotid plaques remote from the coronary arteries, and (3) the activity in the BM and spleen is higher in patients with chronic stable angina (CSA) than in control subjects. We measured 18F-FDG uptake in the spleen, BM, and carotid artery using whole-body 18F-FDG-PET/computed tomography (CT) in patients with AMI and CSA and control subjects without a history of CAD.

Methods

Study Subjects

Between June 2008 and March 2009, we prospectively recruited patients at Korea University Guro Hospital who were diagnosed with AMI or CSA. AMI was defined as typical changes in biochemical markers of myocardial necrosis along with ≥1 of the following: ischemic symptoms, electrocardiographic changes indicative of new ischemia, development of pathological Q waves, or imaging evidence of new loss of viable myocardium or new regional wall motion abnormalities. CSA was defined as the presence of stable anginal symptoms for ≥6 months with ≥50% luminal narrowing in ≥1 major coronary artery on angiography. Criteria for exclusion from the control group were a history of cardiovascular disease (myocardial infarction, unstable angina, stroke, or cardiovascular revascularization), greater than stage 1 hypertension (resting blood pressure ≥160/100 mm Hg), uncontrolled diabetes mellitus (glycohemoglobin ≥9%), malignancy, or severe renal or hepatic disease. Subjects with a history of an inflammatory condition, or those taking inflammation-modulating medications within the prior 6 months, were excluded from the study. All participants provided written informed consent, and the Korea University Institutional Review Board approved this study protocol.

The following clinical and demographic parameters were recorded: age, sex, body mass index, waist circumference, the presence of hypertension (defined as those taking antihypertensive medications or ≥2 blood pressure recordings ≥140/90 mm Hg), the presence of diabetes mellitus (defined as those undergoing treatment with diet and medications or a fasting serum glucose ≥126 mg/dL), and dyslipidemia (defined as those taking lipid-lowering medications or a fasting serum total cholesterol ≥220 mg/dL, triglycerides ≥200 mg/dL, high-density lipoprotein cholesterol <40 mg/dL, or low-density lipoprotein cholesterol ≥160 mg/dL). Cardiac troponin-T and creatine kinase-MB fraction were measured using electrochemiluminescence immunoassays on the Elecsys 2010 analyzer (Roche Diagnostics, Indianapolis, IN). Concentrations of troponin-T ≥0.1 ng/mL and creatine kinase-MB ≥6.73 ng/mL in men or ≥3.77 ng/mL in women were used as cutoff values to diagnose AMI based on the instructions of the manufacturer.

18F-FDG-PET/CT Imaging

18F-PET/CT was performed using the Gemini TF 16-Slice PET/CT scanner (Philips Medical Systems, Cleveland, OH). Patients diagnosed with AMI, all of whom were successfully treated by primary percutaneous coronary intervention, underwent PET/CT within 10 days of the event when they were clinically stable (mean, 6.3 days; range, 1–10). The TF scanner is a new high-performance, time-of-flight-capable, fully 3-dimensional PET scanner that uses lutetium–yttrium oxyorthosilicate crystals. After ≥12 hours of fasting, FDG (5.19 MBq/kg) was injected intravenously, after which patients rested in a quiet room for 60 minutes. In patients with diabetes mellitus, who may have a different blood clearance from patients without diabetes, we determined blood glucose level before 18F-FDG administration and changed the PET schedule if it exceeded 180 mg/dL to reduce the metabolic effect on FDG uptake. Whole-body PET images (from below the cerebellum to the inguinal region) were acquired for 10 minutes (1 minute per bed position).

Analysis of PET Images

PET images were analyzed on a dedicated workstation (Extended Brilliance Workspace 3.5; 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 for a total of 8 consecutive PET/CT images for each subject. Arterial FDG uptake was quantified in the region of interest around each artery on every slice of the coregistered transaxial fusion PET/CT images. The highest standard uptake values (SUVRs) of the region of interests of all 8 slices within the right carotid artery were averaged together for each subject. Next, the arterial SUV was divided by the blood-pool SUV measured from the jugular vein for normalization. In this way, the arterial target-to-background ratio (TBR) was calculated for each subject. 18F-FDG uptake was measured in the spleen by placing a region of interest around the organ on all transaxial slices. The highest SUVRs from all transaxial slices were recorded, and their average was used as the mean SUV for the entire organ. BM 18F-FDG uptake was calculated under CT-guided anatomic reference from the third to fifth lumbar vertebrae, and the average of the highest SUVRs was used as the mean SUV for analysis. To determine the variability of the mean SUV measurements, images from 20 subjects were analyzed twice, several weeks apart, by 2 readers who were unaware of the clinical histories of subjects. The intra- and interobserver correlation coefficient values of the mean SUV measurements were <0.9.

Statistical Analysis

Baseline characteristics of the participants were analyzed according to the 3 main study groups. Frequencies and proportions were reported for categorical variables, and either mean±SD or median with interquartile range was reported for continuous variables based on normality of distribution. The Pearson χ² test, Fisher exact test, 1-way ANOVA, and Kruskal–Wallis test were used to compare variables among groups. Subsequent comparisons were performed by the Bonferroni post hoc test, Mann–Whitney U test, or Fisher exact test with Bonferroni-corrected P values. The SUVRs of the BM and spleen and the TBRs of the carotid artery were compared among the 3 groups using ANCOVA with Bonferroni multiple comparisons, in which the possible confounding effects of sex, waist circumference, hypertension, diabetes mellitus, dyslipidemia, smoking, statin use, and high-sensitivity C-reactive protein (hsCRP) were taken into account by including them in the model as covariates. Spearman correlation analysis was performed to identify the relationship between 18F-FDG uptake in multiple organs and hsCRP. Multiple linear regression analyses using the TBR of the carotid artery as a dependent variable were also performed to investigate whether there was an independent relationship between 18F-FDG uptake in each organ and uptake in the carotid artery. Data were analyzed using SPSS for Windows version 20.0 (SPSS, Chicago, IL). P<0.05 were considered statistically significant.

Results

Clinical and Laboratory Characteristics

The subjects included 51 men (56.7%) and 39 women (43.3%). Women comprised the majority of the control group, whereas men comprised the majority of the CSA and AMI groups. The mean age of subjects was 57.7±10.1 years and did not differ significantly among groups. Compared with the control group, most of the traditional cardiovascular risk factors, such as hypertension, diabetes mellitus, dyslipidemia, and smoking, were more prevalent in the CSA and AMI groups. The
prevalence of those risk factors was not significantly different among the CAD groups. Subjects taking statins comprised nearly a third of total subjects in both CAD groups on initial presentation. There were significant stepwise increases in white blood cell count and hsCRP from the control group to the AMI group (Table 1).

Comparison of FDG Uptake in the BM, Spleen, and Carotid Artery Among Groups

The mean maximum SUV levels in the spleen and BM were incrementally and significantly higher in the AMI and CSA groups compared with the control group (Table 1; Figures 1A, 2A, and 2B). The AMI group had higher carotid artery TBRs than did the CSA and control groups (Table 1; Figures 1B and 2C). Although the carotid artery TBR of the CSA and control groups did not differ significantly (Table 1; Figure 2C), it reached statistical significance after adjusting for sex, waist circumference, hypertension, diabetes mellitus, dyslipidemia, smoking, statin use, and hsCRP in ANCOVA analysis (for the carotid artery TBR, AMI versus CSA group, \( P < 0.001 \); CSA versus control group, \( P = 0.038 \)). The SUVs of the spleen and BM were also significantly different among groups after the same adjustments (for spleen SUV, AMI versus CSA group, \( P < 0.001 \); CSA versus control group, \( P < 0.001 \), for BM SUV, AMI versus CSA group, \( P = 0.003 \); CSA versus control group, \( P = 0.017 \)).

Correlation Between hsCRP and FDG Uptake in the BM, Spleen, and Carotid Artery

The TBR of the carotid artery and SUVs of the BM and spleen correlated significantly with each other in study subjects overall. Without adjustment, the TBR of the carotid artery was most highly correlated with the SUV of the spleen. HsCRP was also significantly correlated with FDG uptake in the BM.

Table 1. Baseline Characteristics of Study Subjects

<table>
<thead>
<tr>
<th></th>
<th>AMI (n=32)</th>
<th>CSA (n=33)</th>
<th>Control (n=25)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>56.9±11.6*</td>
<td>61.2±11.5*</td>
<td>57.1±7.5*</td>
<td>0.206</td>
</tr>
<tr>
<td>Men</td>
<td>21 (65.6)*</td>
<td>24 (72.7)*</td>
<td>6 (24.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.6±2.6†</td>
<td>26.0±4.0†</td>
<td>80.9±7.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WC, cm</td>
<td>83.4±16.3</td>
<td>92.3±11.4</td>
<td>94.0±7.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>15 (46.9)*</td>
<td>19 (57.6)*</td>
<td>1 (4.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>13 (40.6)*</td>
<td>13 (39.4)*</td>
<td>2 (8.0)</td>
<td>0.013</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>19 (59.4)*</td>
<td>16 (48.5)*</td>
<td>2 (8.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking</td>
<td>13 (40.6)*</td>
<td>13 (39.4)*</td>
<td>2 (8.0)</td>
<td>0.013</td>
</tr>
<tr>
<td>Statin use</td>
<td>9 (28.1)*</td>
<td>11 (33.3)*</td>
<td>0 (0)</td>
<td>0.006</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>187±44*</td>
<td>156±35</td>
<td>189±25*</td>
<td>0.001</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>137±142†</td>
<td>160±100*</td>
<td>87±44†</td>
<td>0.009</td>
</tr>
<tr>
<td>88 (58–168)</td>
<td>113 (85–254)</td>
<td>68 (56–122)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>45±12*</td>
<td>49±15*</td>
<td>59±16</td>
<td>0.001</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL</td>
<td>124±42*</td>
<td>92±30</td>
<td>115±24*</td>
<td>0.001</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>6.9±2.1*</td>
<td>7.0±1.6*</td>
<td>5.7±0.4</td>
<td>0.001</td>
</tr>
<tr>
<td>WBC, ( \times 10^{3}/\mu L )</td>
<td>10.9±3.3</td>
<td>6.5±1.2</td>
<td>5.0±1.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>hsCRP, mg/L</td>
<td>3.4±3.10</td>
<td>1.5±1.55</td>
<td>0.55±0.57</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>peak CK-MB, ng/mL</td>
<td>145.6±127.3</td>
<td>…</td>
<td>…</td>
<td>…</td>
</tr>
<tr>
<td>peak troponin-T, ng/mL</td>
<td>3.66±4.64</td>
<td>…</td>
<td>…</td>
<td>…</td>
</tr>
<tr>
<td>TBR</td>
<td>2.13±0.42</td>
<td>1.36±0.37*</td>
<td>1.16±0.09*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Spleen</td>
<td>2.57±0.39</td>
<td>2.03±0.35</td>
<td>1.54±0.26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>1.67±0.16</td>
<td>1.22±0.62</td>
<td>0.80±0.44</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are expressed as mean±SD, median with interquartile range in parenthesis, or number with percentage in parentheses. \( P \) values represent overall differences across groups as determined by ANOVA or the Kruskal–Wallis test for continuous variables and Pearson \( \chi^2 \) test or Fisher exact test for categorical variables. AMI indicates acute myocardial infarction; BMI, body mass index; CK-MB, creatine kinase-MB; CSA, chronic stable angina; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; hsCRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein; SUV, standard uptake value; TBR, target-to-background ratio; WBC, white blood cell; and WC, waist circumference.

*†The same letters indicate no statistical significance based on the Bonferroni post hoc test or Mann–Whitney \( U \) test, or separate Pearson \( \chi^2 \) test or Fisher exact test with Bonferroni-corrected \( P \) values.
spleen, and carotid artery (Table 2). In the AMI group, there was no correlation between peak serum creatine kinase-MB and troponin-T levels and FDG uptake in the BM, spleen, or carotid artery (data not shown).

**Relationship Between Carotid Artery TBR and BM FDG Uptake, Spleen FDG Uptake, and hsCRP**

Multiple linear regression analysis of the overall study population, which included age, sex, waist circumference, hypertension, diabetes mellitus, dyslipidemia, smoking, and statin use as covariates, revealed an independent relationship between carotid artery TBR, the SUVs of the spleen and BM, and hsCRP. The SUVs of the spleen and BM were significantly associated with carotid artery TBR even after further adjustment for hsCRP. In contrast, hsCRP did not maintain a significant association with carotid artery TBR when the SUV of the BM or spleen was entered into the model as an independent variable (Table 3).

**Discussion**

This study revealed significant associations between CAD, the metabolic activity of the spleen and BM, and the inflammatory activity of the carotid artery, independent of traditional cardiovascular risk factors and hsCRP level. Those activities were highest in patients with AMI, intermediate in patients with CSA, and lowest in the control group. The $^{18}$F-FDG uptake in the carotid artery was significantly associated with carotid artery TBR only after further adjustment for hsCRP. In contrast, hsCRP did not maintain a significant association with carotid artery TBR when the SUV of the BM or spleen was entered into the model as an independent variable (Table 3).

Most studies that support the association between inflammation and CAD have been based on epidemiological analysis of circulating biomarkers and animal experiments. Recent studies have identified the role of the spleen and BM in chronic and acute inflammation in atherosclerotic disease. In chronic inflammation of atherosclerosis, both the BM and spleen are involved. Hematopoietic stem and progenitor cells progressively relocate from the BM to the splenic red pulp, where they clonally expand with granulocyte macrophage colony-stimulating factor and interleukin-3 and differentiate into inflammatory monocytes. Monocytes born in the spleen intravasate, circulate, and accumulate into atherosclerotic lesions in murine models. Our findings are consistent with this knowledge, in that significantly higher activity was found in the BM, spleen, and carotid artery in the CSA group than in the control group.

Using $^{18}$F-FDG-PET, Assmus et al. found significantly higher metabolic activity in the BM and significantly larger populations of hematopoietic CD34$^+$ and CD133$^+$ cells in BM aspirates from patients within 7 days after AMI than in patients with chronic postischemic heart failure. The same authors reported that AMI induced by ligating a coronary artery or application of other stressors can activate stem cells in the BM in nonatherosclerotic mice. It has also been reported that acute ischemic myocardial injury triggers emergency hematopoiesis in the BM and spleen and that AMI liberates hematopoietic stem and progenitor cells from BM niches via signals from the sympathetic nervous system. The progenitors then seed the spleen and yield a sustained boost in monocyte production to meet demand in the infarcted myocardium. However, however, may have unintended consequences, such as acceleration of underlying atherosclerosis triggering reinfarction or stroke. Dutta et al. found that in apolipoprotein E-deficient mice, AMI accelerates underlying aortic atherosclerosis.

In light of these findings, our AMI group indeed demonstrated higher metabolic activity in the spleen and BM than the CSA group. The greater inflammatory activity in the carotid arteries of the AMI group compared with the CSA group may be evidence of this damaging accumulation of monocytes in atherosclerotic lesions. Moreover, we found that the metabolic activity of the carotid artery was closely associated with that of the spleen and BM, as well as with the level of hsCRP in the overall patient population. These findings suggest that the inflammatory status of atherosclerosis is influenced by systemic inflammation modulated by the spleen and BM.
Metabolic activation of the major organs that harbor inflammatory cells, such as the spleen, 8 has been revealed using 18F-FDG-PET in a variety of systemic conditions, including infection, 25 cancer, 16 connective tissue diseases, 26 and systemic autoimmune disorders. 27 However, few studies have demonstrated the metabolic activation of the BM and spleen in humans with CAD. To the best of our knowledge, this is the first in vivo human study showing the metabolic activity of the spleen and BM in patients with CAD using a molecular imaging tool.

In our study, the metabolic activity of the spleen and BM was high in patients with AMI even after a mean of 6.3 days from the event. Inflammatory monocytes, which have been found to be chronically expanded in the blood pool of atherosclerotic apolipoprotein E–deficient mice, impair infarct healing through prolonged presence in the infarct and deregulated resolution of inflammation. 28 This result suggests that patients with AMI who have underlying inflammation associated with atherosclerosis may have prolonged activation of the organs involved in inflammation. Further studies are needed to determine the time period during which activation of the spleen and BM persists after AMI in humans.

Our study has several limitations. First, its cross-sectional design, small sample size, and significant differences between subjects and controls may have introduced various levels of bias. Although we attempted to adjust for these differences and the small sample size, our model may not be sufficiently powered to support the results. Second, we did not perform coronary angiography in the control group to determine the time period during which activation of the spleen and BM persists after AMI in humans.

Table 2. Spearman Correlation Analysis Between hsCRP Level and FDG Uptake in the Carotid Artery, Spleen, and BM in the Overall Study Population

<table>
<thead>
<tr>
<th></th>
<th>SUV of BM</th>
<th>SUV of Spleen</th>
<th>hsCRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBR of carotid artery</td>
<td>0.535*</td>
<td>0.663*</td>
<td>0.465*</td>
</tr>
<tr>
<td>SUV of BM</td>
<td>...</td>
<td>0.637*</td>
<td>0.525*</td>
</tr>
<tr>
<td>SUV of spleen</td>
<td>0.637*</td>
<td>...</td>
<td>0.458*</td>
</tr>
</tbody>
</table>

BM indicates bone marrow; FDG, 18F-fluorodeoxyglucose; hsCRP, high-sensitivity C-reactive protein; SUV, standard uptake value; and TBR, target-to-background ratio.

*P < 0.001.

Table 3. Multiple Linear Regression Analysis Using the Carotid Artery TBR as a Dependent Variable

<table>
<thead>
<tr>
<th></th>
<th>β</th>
<th>P</th>
<th>R²</th>
<th>R² adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUV, bone marrow</td>
<td>0.438</td>
<td>&lt;0.001</td>
<td>0.329</td>
<td>0.245</td>
</tr>
<tr>
<td>SUV, spleen</td>
<td>0.688</td>
<td>&lt;0.001</td>
<td>0.461</td>
<td>0.394</td>
</tr>
<tr>
<td>hsCRP</td>
<td>0.011</td>
<td>0.040</td>
<td>0.192</td>
<td>0.088</td>
</tr>
</tbody>
</table>

hsCRP indicates high-sensitivity C-reactive protein; SUV, standard uptake value; and TBR, target-to-background ratio.

The association with the carotid artery TBR after adjustment for age, sex, waist circumference, hypertension, diabetes mellitus, dyslipidemia, smoking, and statin use.

The association with the carotid artery TBR after adjustment for the above covariates and hsCRP.

\[ R^2_{\text{adj}} = 1 - (1-R^2)(N-1)/(N-P-1) \], where \( R^2 = \text{sample } R^2 \), P = number of predictors, and N = total sample size.
confirm the presence of coronary atherosclerosis, and this may have affected our results. Third, we did not perform histopathologic analysis of tissue samples from the spleen or BM. However, it is already known that 18F-FDG accumulates in tissue macrophages, and its intensity correlates with the staining density of tissue macrophages in corresponding histological sections of specimens. Fourth, the patients with AMI may have had elevated levels of catecholamines and endogenous steroids associated with stress in addition to their underlying inflammatory state. However, we were not able to control for all factors affecting glucose metabolism and FDG uptake, including levels of insulin, catecholamines, steroids, and other substrates in plasma, which may have affected our results. Fifth, we did not control for other factors affecting systemic inflammation, such as lifestyle habits, low-grade chronic infections, and genetic predisposition. Finally, we did not measure the biomarkers of hematopoietic stem and progenitor cell in the BM or monocyte subsets in the peripheral blood. In short, this study was not designed to definitively prove an etiologic hypothesis but was an observational study designed to measure metabolic activity of the spleen and BM in patients with CAD as an indirect probe into a previously established condition.

In conclusion, the metabolic activity of the BM and spleen, as well as of the carotid artery, was highest in patients with AMI, intermediate in patients with CSA, and lowest in lowest in controls. The relationship between those parameters and CAD status was independent of traditional cardiovascular risk factors. The relationship between those parameters and CAD status was independent of traditional cardiovascular risk factors. Activation of the BM and spleen was closely associated with the activity in the carotid artery. Our results offer insights into risk stratification, monitoring of therapy, and physiological changes in the early stages of atherosclerosis, when intervention may be most effective.

Sources of Funding
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Disclosures
None.

References
This is the first in vivo human study showing the metabolic activity of the spleen, as well as bone marrow, in patients with coronary artery disease using 18F-fluorodeoxyglucose positron emission tomography. We demonstrated that the spleen and bone marrow are activated in coronary artery disease, especially after acute myocardial infarction. This finding confirms the results of animal studies that the hematopoietic organs are involved in atherosclerotic disease as a source of inflammatory cell production. Moreover, the high 18F-fluorodeoxyglucose uptake in the carotid artery in patients with coronary artery disease associated with increased activation of the bone marrow and spleen also suggests that the inflammatory status of atherosclerosis throughout the body is influenced by systemic inflammation modulated by the spleen and bone marrow. Although we did not investigate a causal relationship between these hematopoietic organs and coronary artery disease, our results provide insight into the pathophysiology, risk stratification, and therapeutic monitoring of atherosclerotic disease in humans.
Metabolic Activity of the Spleen and Bone Marrow in Patients With Acute Myocardial Infarction Evaluated by 18F-Fluorodeoxyglucose Positron Emission Tomographic Imaging
Eung Ju Kim, Sungeun Kim, Dong Oh Kang and Hong Seog Seo

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