Relationships Among Regional Arterial Inflammation, Calcification, Risk Factors, and Biomarkers

A Prospective Fluorodeoxyglucose Positron-Emission Tomography/Computed Tomography Imaging Study

James H.F. Rudd, MD, PhD, MRCP; Kelly S. Myers, MD; Sameer Bansilal, MD; Josef Machac, MD; Mark Woodward, PhD; Valentin Fuster, MD, PhD; Michael E. Farkouh, MD, MSc; Zahi A. Fayad, PhD

Background—Fluorodeoxyglucose positron-emission tomography (FDG PET) imaging of atherosclerosis has been used to quantify plaque inflammation and to measure the effect of plaque-stabilizing drugs. We explored how atherosclerotic plaque inflammation varies across arterial territories and how it relates to arterial calcification. We also tested the hypotheses that the degree of local arterial inflammation measured by PET is correlated with the extent of systemic inflammation and presence of risk factors for vascular disease.

Methods and Results—Forty-one subjects underwent vascular PET/computed tomography imaging with FDG. All had either vascular disease or multiple risk factors. Forty subjects underwent carotid imaging, 27 subjects underwent aortic, 24 subjects iliac, and 13 subjects femoral imaging. Thirty-three subjects had a panel of biomarkers analyzed. We found strong associations between FDG uptake in neighboring arteries (left versus right carotid, \( r=0.91 \), \( P<0.001 \); ascending aorta versus aortic arch, \( r=0.88 \), \( P<0.001 \)). Calcification and inflammation rarely overlapped within arteries (carotid artery FDG uptake versus calcium score, \( r=-0.42 \), \( P=0.03 \)). Carotid artery FDG uptake was greater in those with a history of coronary artery disease (target-to-background ratio, 1.83 versus 1.61, \( P<0.01 \)) and in males versus females (target-to-background ratio, 1.83 versus 1.63, \( P<0.05 \)). Similar findings were also noted in the aorta and iliac arteries. Subjects with the highest levels of FDG uptake also had the greatest concentrations of inflammatory biomarkers (descending aorta target-to-background ratio versus matrix metalloproteinase 3, \( r=0.53 \), \( P=0.01 \); carotid target-to-background ratio versus matrix metalloproteinase 9, \( r=0.50 \), \( P=0.01 \)). Nonsignificant positive trends were seen between FDG uptake and levels of interleukin-18, fibrinogen, and C-reactive protein. Finally, we found that the atheroprotective biomarker adiponectin was negatively correlated with the degree of arterial inflammation in the descending aorta (\( r=-0.49 \), \( P=0.03 \)).

Conclusions—This study shows that FDG PET imaging can increase our knowledge of how atherosclerotic plaque inflammation relates to calcification, serum biomarkers, and vascular risk factors. Plaque inflammation and calcification rarely overlap, supporting the theory that calcification represents a late, burnt-out stage of atherosclerosis. Inflammation in one arterial territory is associated with inflammation elsewhere, and the degree of local arterial inflammation is reflected in the blood levels of several circulating biomarkers. We suggest that FDG PET imaging could be used as a surrogate marker of both atherosclerotic disease activity and drug effectiveness. Prospective, event-driven studies are now underway to determine the role of this technique in clinical risk prediction. (Circ Cardiovasc Imaging. 2009;2:107-115.)

Key Words: atherosclerosis ■ imaging ■ inflammation ■ positron emission tomography ■ fluorodeoxyglucose ■ calcification

The complications of atherosclerosis are the commonest cause of death worldwide and an increasing burden to healthcare systems. Over the past 2 decades, however, several effective drugs have improved risk factor control and reduced mortality.1 In parallel, noninvasive techniques for imaging atherosclerosis have become more widely available. They can help to illuminate the underlying pathology of the disease and may improve the prediction of future clinical events. In addition, imaging can identify treatment-related changes in plaque structure and function that can serve as surrogate markers of drug efficacy.2

Clinical Perspective see p 115

Clinical events related to atherosclerosis are driven by inflammation within the plaque.3 Fluorodeoxyglucose

Received August 3, 2008; accepted December 23, 2008.

From the Imaging Science Laboratories (J.H.F.R., K.S.M., Z.A.F.), Cardiovascular Imaging Clinical Trials Unit (S.B., M.E.F.), Division of Nuclear Medicine (J.M.), Department of Radiology, Department of Medicine (M.W.), and The Zena and Michael A. Wiener Cardiovascular Institute and Marie Joseé and Henry R. Kravis Cardiovascular Health Center (V.F.), Mount Sinai School of Medicine, New York, NY.

Dr Rudd and Myers contributed equally to this work.

Correspondence to James H.F. Rudd, MD, PhD, MRCP, Division of Cardiovascular Medicine, Cambridge University, UK, jhfr2@cam.ac.uk or Zahi A. Fayad, Imaging Science Laboratories, Mount Sinai School of Medicine, New York, NY 10029. E-mail Zahi.Fayad@mssm.edu

© 2009 American Heart Association, Inc.

Circ Cardiovasc Imaging is available at http://circimaging.ahajournals.org

DOI: 10.1161/CIRCIMAGING.108.811752

107
PET can identify symptomatic lesions in the carotid\(^6\) and vertebral artery\(^7\) territories and can track the effect of anti-inflammatory plaque therapies in both human\(^8\) and animal\(^9\) models of disease.

This study used FDG PET imaging of atherosclerotic arteries to address several questions relating to the pathology of the disease. We investigated the extent to which the degree of arterial inflammation within the carotid arteries, aorta, and peripheral vasculature were correlated. Second, we examined the relationship between arterial inflammation and calcification. Third, we explored whether the presence of cardiovascular risk factors increased arterial inflammation, and finally we assessed the relationship between the level of several circulating inflammatory biomarkers and the degree of local arterial FDG uptake. We used a prospective study design and a vascular-specific PET imaging protocol that is highly reproducible.\(^{11,12}\)

**Methods**

**Patient Recruitment**

We prospectively recruited, at the Mount Sinai Medical Center, a heterogeneous group of 41 patients with either vascular disease (defined as previous myocardial infarction, stroke, or peripheral vascular disease) or at least 3 cardiovascular risk factors. Patients were identified in the catheter laboratory and in vascular outpatient clinics. All gave written informed consent and the study protocols were approved by the local institutional review board.

Baseline risk factor data were documented, including age, gender, ethnicity, history of coronary artery disease (defined as angina, previous myocardial infarction, or coronary artery disease at angiography), history of cerebrovascular disease (defined as transient ischemic attack or stroke), history of cigarette smoking, diagnosis or treated hypertension, history of diabetes, family history of heart disease, body mass index, and medication use.

**PET/Computed Tomography Imaging**

Of the 41 patients, 40 patients underwent carotid imaging, 27 patients underwent aortic imaging, 24 patients underwent iliac imaging, and 13 patients underwent femoral imaging. All studies were performed after at least 6 hours of fasting with a Lightspeed PET/computed tomography (CT) scanner (GE Healthcare, Milwaukeee, Wis) after injection of 370 MBq FDG. Subjects with prescan blood glucose of >200 mg/dl were excluded. Body scanning (encompassing the aorta, iliac, and femoral arteries) was performed first, 90 minutes after FDG injection in 2D mode, with 10 minute acquisitions at each bed position.

Carotid artery imaging was undertaken >2 hours after FDG injection, immediately after body imaging. The head and neck were placed into a soft-head holder and a single-bed position PET scan was acquired in 3D mode for 15 minutes. The external auditory meatus was the upper limit of the scan. CT was used for attenuation correction, anatomic coregistration, and quantification of arterial calcification. No CT contrast agent was administered.

**Image Reconstruction**

The 2D PET data were reconstructed using the ordered subset expectation maximization algorithm\(^{13}\) with a final voxel size of 4.25 mm. The 3D PET data had the same corrections applied, and were reconstructed using a 3D reprojection algorithm\(^{14}\) yielding the same voxel size.

**Calcification Quantification**

Calcium scores were calculated for the ascending aorta, aortic arch, descending aorta and both carotid arteries. Arterial calcification was measured from the CT images using the AW workstation (GE Healthcare) using Smart Score software. The method of Agatston et al\(^{15}\) was used with a threshold for calcium $\geq 130$ Hounsfield units.

**Biomarker Analysis**

Thirty-three patients had blood drawn for biomarker analysis. The remaining 8 patients had already undergone imaging before the facility to analyze the samples became available. Biomarkers were chosen to cover different aspects of the atherothrombotic process (inflammatory, thrombotic, and atheroprotective). The following biomarkers were measured: matrix metalloproteinases (MMP)-1, -3, -7, and -9, interleukins-6, -10, and -18, tumor necrosis factor-$\alpha$, adiponectin, plasminogen activator inhibitor-1, C-reactive protein (CRP), and a full lipid panel.

Venous blood samples were collected on the day of imaging, before FDG injection. The samples were centrifuged to obtain plasma and serum aliquots (3000 rpm for 20 minutes at 4°C for plasma and 3000 rpm for 10 minutes at 20°C for serum). The aliquots were stored at $\sim 80^\circ$C until the completion of the study. All biomarker analyses were carried out at the Molecular and Hemostasis Laboratory at the Center for Disease Control and Prevention (Atlanta, Ga). Fluorokine-MAIP MultiAnalyte Profiling Human Base kits were used with the BioPlex Luminex xMAP (BioRad, Austin, Tex) platform for biomarker quantification. Plasma samples were diluted in the appropriate calibrator diluent and incubated with the diluted microparticle analyte multiplex according to the manufacturer’s protocol. Analyte-specific antibodies were precoated onto color-coded microparticles. Microparticles, standards, samples, and appropriate controls were added to the wells. After washing, a biotinylated antibody cocktail specific to the analytes of interest was added to each well. After another wash to remove any unbound biotinylated antibody, streptavidin-phycocerythrin conjugate was added to each well. After a final wash, the microparticles were resuspended in buffer and read using the Luminex analyzer.

**Statistical Methods**

Continuous variables are summarized by their mean and SD, whereas dichotomous measures are given as percentages. To inves-
Arterial FDG Uptake Is Highly Correlated Across Different Arterial Territories
The average TBR value in each of the arterial territories is shown in Figure 3. It is clear that there are regional variations in inflammation, with the carotid and all regions of the aorta being more inflamed than the peripheral arteries. Associations between FDG uptake in each territory are shown in Table 2. We noted associations in the degree of FDG uptake across different arterial territories, more strongly between adjacent territories (neighboring aortic regions, carotid artery, and aorta) than between more distant regions (for example carotid versus femoral arteries). When analyzed individually, anatomic artery pairs had particularly strong correlations between their measured degrees of inflammation (left and right carotid, \( r=0.91, P<0.001 \); left and right femoral, \( r=0.96, P<0.001 \)).

Arterial FDG Uptake and Calcification Are Uncommon in the Same Artery
In those arteries in which both calcium scoring and FDG imaging was performed, there were negative correlations noted between inflammation and calcification. This was demonstrated in the carotid arteries (left carotid calcium versus left carotid FDG, \( r=-0.42, P=0.03 \); right carotid calcium versus right carotid FDG, \( r=-0.42, P=0.03 \)). A similar finding was noted in the ascending aorta but this did not reach statistical significance (calcium versus FDG, \( r=-0.30, P=0.13 \)).

Male Sex and the Presence of Coronary Artery Disease Are Associated With Arterial FDG Uptake
In the 40 subjects that underwent carotid imaging, FDG uptake was significantly greater in men (mean TBR in men, 1.83 versus 1.63 in women, \( P<0.05 \)). Arterial FDG uptake was also more marked in patients with a prior history of coronary artery disease (CAD) versus no history of CAD (mean TBR, 1.83 versus 1.61, \( P<0.01 \); Figure 4).

Aortic FDG uptake (n=27) was also associated with male gender (mean TBR, 1.81 versus 1.55, \( P<0.01 \)) and a trend toward higher FDG uptake in those with a history of CAD (mean TBR, 1.80 versus 1.64, \( P=0.06 \); Figure 5).

### Table 1. Patient Characteristics (n=41)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Percentage of Female Subjects (n=11)</th>
<th>Percentage of Male Subjects (n=30)</th>
<th>Percentage of Subjects Overall (n=41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>NA</td>
<td>NA</td>
<td>26.8</td>
</tr>
<tr>
<td>Age</td>
<td>64.7±7.2</td>
<td>63.7±8.6</td>
<td>64.0±8.2</td>
</tr>
<tr>
<td>Current or ex-smoker</td>
<td>27.2</td>
<td>56.7</td>
<td>48.8</td>
</tr>
<tr>
<td>History of coronary artery disease</td>
<td>45.5</td>
<td>83.3</td>
<td>73.2 (n=30)</td>
</tr>
<tr>
<td>History of other vascular disease</td>
<td>27.3</td>
<td>3.3</td>
<td>12.2 (n=5)</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>54.5</td>
<td>63.3</td>
<td>61.0</td>
</tr>
<tr>
<td>History of diabetes</td>
<td>27.3</td>
<td>40.0</td>
<td>36.6</td>
</tr>
<tr>
<td>Statin use</td>
<td>81.8</td>
<td>90.0</td>
<td>87.8</td>
</tr>
<tr>
<td>BMI</td>
<td>24.0±5.3</td>
<td>27.5±4.6</td>
<td>25.6±5.0</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>9.0</td>
<td>20.0</td>
<td>17.1</td>
</tr>
<tr>
<td>Black</td>
<td>9.0</td>
<td>16.7</td>
<td>14.6</td>
</tr>
<tr>
<td>Indian</td>
<td>9.0</td>
<td>13.3</td>
<td>12.2</td>
</tr>
<tr>
<td>White</td>
<td>72.7</td>
<td>50.0</td>
<td>56.1</td>
</tr>
</tbody>
</table>

Age and BMI are shown as mean±SD. BMI indicates body mass index.
FDG uptake in the iliac arteries (n=24) was similarly associated with male gender (mean TBR, 1.55 versus 1.33, P<0.05) and a prior history of CAD (mean TBR, 1.54 versus 1.29, P<0.01) but also was higher in those with a history of cigarette smoking (mean TBR, 1.59 versus 1.40, P<0.05; Figure 6).

Increased age, the presence of diabetes or hypertension, the use of statin medication, or ethnicity had no significant impact on FDG uptake in any arterial region.

Arterial FDG Uptake Positively Correlates With Levels of Several Circulating Inflammatory Biomarkers

Thirty-three patients from the cohort of 41 patients underwent both PET/CT imaging and biomarker analysis. The mean age of the biomarker subgroup (33 patients) was 64 years, with 73% men and 36% diabetic, similar to the overall patient group (41 patients).

Figure 1. Examples of FDG uptake. Top panel shows aortic arch imaging by FDG PET (left) and noncontrast CT (right). There is heterogeneous FDG uptake seen within the artery wall. Bottom panel demonstrates bilateral femoral artery FDG uptake on fused PET/CT images (arrows).

Figure 2. Aorta imaging with PET/CT. The left image is a noncontrast coronal CT image showing calcification of the abdominal aorta (group of 3 green arrows). The center and right images are coregistered PET and fused PET/CT images, respectively, demonstrating significant FDG uptake within the ascending aorta (single arrow) but relatively less FDG uptake in the calcified abdominal aorta. The green cross is in the inferior vena cava, where there is low FDG uptake.
There were significant correlations between MMP-3 levels and inflammation in 3 regions of the aorta: MMP-3 versus ascending aorta FDG uptake ($r=0.49$, $P=0.02$), arch ($r=0.44$, $P=0.05$), descending ($r=0.53$, $P=0.01$), and borderline significant in the abdominal aortic region ($r=0.41$, $P=0.07$). MMP-9 was significantly, positively associated with both carotid FDG uptake ($r=0.50$, $P=0.01$) and descending and abdominal aortic FDG uptake (descending aorta, $r=0.44$, $P=0.05$; abdominal aorta, $r=0.44$, $P=0.05$; Figure 7).

A strong positive trend was seen between levels of interleukin-18 and FDG uptake in the descending and abdominal aorta (descending, $r=0.41$, $P=0.06$; abdominal, $r=0.40$, $P=0.07$). In addition, nonsignificant trends were observed between serum fibrinogen levels and FDG uptake in the descending aorta ($r=0.41$, $P=0.06$), and between serum CRP levels and FDG uptake in the same territory ($r=0.43$, $P=0.06$).

We saw no relationships between arterial inflammation as assessed by FDG PET/CT and the other biomarkers measured, including serum lipid levels.

**Arterial FDG Uptake Is Inversely Related to Atheroprotective Biomarkers**

Serum levels of adiponectin were inversely related to inflammation in the descending aorta ($r=−0.49$, $P=0.03$), and plasminogen activator inhibitor-1 to inflammation in the carotid arteries ($r=−0.39$, $P=0.03$).

**Discussion**

We prospectively evaluated 41 subjects with either risk factors for, or established atherosclerosis using FDG PET/CT as a surrogate marker of vascular inflammation. Previous studies have established that the degree of arterial uptake of FDG correlates strongly with macrophage infiltration in 2 different animal models of disease and in patients with symptomatic carotid atherosclerosis. Most recently, it has been shown that arterial FDG PET imaging is capable of reporting on the reduction of vascular inflammation resulting from cardiovascular risk factor modification during a 1-year period. These intervention studies have set the stage for the use of FDG PET imaging as a potential surrogate marker for evaluating drug efficacy, analogous to its use in cancer therapy trials.

This study shows how FDG PET imaging can extend our insight into the disease process of atherosclerosis. We have shown that the presence of inflammation in one arterial territory is highly predictive of inflammation in others. This finding suggests a form of systemic arterial activation. There seems to be some degree of regionality, however, because inflammation across systemic arterial territories is more correlated than inflammation across arterial areas more anatomically remote from each other.

Supporting this theory of systemic activation, we also noted that the degree of arterial FDG uptake was associated with blood levels of several systemic inflammatory biomarkers, including those from the MMP family, and strong trends among both the interleukin group and CRP. A previous study demonstrated a link between carotid FDG uptake and level of MMP-1 in a group of patients with carotid disease awaiting surgery. We found no association in our population with this particular MMP, but did observe moderately strong correlations between FDG uptake and levels of both MMP-3 and MMP-9, which, along with MMP-1, have been implicated in plaque rupture. Overexpression of MMP-9 in ApoE knockout mice leads to rapid plaque destabilization, highlighting the key role of these macrophage-secreted enzymes. One particular advantage of FDG PET atheroma

---

**Table 2. Pearson Correlation Coefficient Values for FDG Uptake Between Various Arterial Regions**

<table>
<thead>
<tr>
<th></th>
<th>Ascending</th>
<th>Arch</th>
<th>Descending</th>
<th>Abdominal</th>
<th>Carotid</th>
<th>Iliac</th>
<th>Femoral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascending</td>
<td>...</td>
<td>0.88*</td>
<td>0.84*</td>
<td>0.88*</td>
<td>0.61*</td>
<td>0.79*</td>
<td>...</td>
</tr>
<tr>
<td>Arch</td>
<td>...</td>
<td>...</td>
<td>0.81*</td>
<td>0.89*</td>
<td>0.64*</td>
<td>0.84*</td>
<td>...</td>
</tr>
<tr>
<td>Descending</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>0.89*</td>
<td>0.48†</td>
<td>0.78*</td>
<td>...</td>
</tr>
<tr>
<td>Abdominal</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>0.62*</td>
<td>0.86*</td>
<td>...</td>
</tr>
<tr>
<td>Carotid</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>0.57*</td>
<td>0.43</td>
</tr>
<tr>
<td>Iliac</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>0.71*</td>
</tr>
<tr>
<td>Femoral</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

*P<0.01.
†P<0.05.
imaging over measurement of circulating biomarkers is the ability to pinpoint a particular arterial segment as being inflamed, allowing it to be targeted for treatment. Wu et al.\textsuperscript{19} demonstrated that arteries that were most highly inflamed on FDG PET before carotid intervention had the greatest release of harmful MMP-1 during the procedure.

We noted a modest relationship between arterial FDG uptake and serum CRP levels. Some previous publications have demonstrated positive correlations between FDG uptake and CRP, whereas others have not demonstrated any sort of relationship.\textsuperscript{4,8,19,24} Therefore, although this biomarker can help to refine the risk of future cardiovascular events at a population level,\textsuperscript{25} its role in individual subjects is not yet certain.

The lack of a relationship between arterial inflammation and serum low-density lipoprotein levels, and the inverse relationships between arterial inflammation and the biomarkers adiponectin and plasminogen activator inhibitor-1 are interesting. Adiponectin is known to act as a brake on inflammation in both healthy individuals and those with vascular disease,\textsuperscript{26,27} so it is intriguing that in those with the highest levels of this hormone, there were the lowest degrees of FDG arterial uptake. Serpins such as plasminogen activator inhibitor-1 have pro- or anti-inflammatory actions, depending on the degree of vascular activation.\textsuperscript{28} Other groups have previously noted no relationship between FDG uptake and low-density lipoprotein level,\textsuperscript{8,9,29} and it may be that oxidized low-density lipoprotein levels are more important in determining the amount of artery inflammation than low-density lipoprotein.

In this study, inflammation and calcification within arteries rarely overlapped. This has been previously suggested\textsuperscript{30}; but in a retrospective study of cancer patients where the degree of inflammation was not numerically quantified. Our finding

![Figure 4. Carotid artery inflammation variations among different risk factor groups. *P<0.05.](#)

![Figure 5. Aortic inflammation variations among different risk factor groups. *P<0.05.](#)
supports the view that plaques of different age might coexist in arteries, with episodes of inflammation leading to rupture events and having an end stage of calcification.

The observation that men have greater arterial FDG uptake than women suggests that atherosclerotic plaques in men may be more highly inflamed, perhaps providing a pathological link for their higher rate of cardiovascular events. Higher FDG uptake in the carotid and iliac arteries of patients with a prior history of CAD reinforces the global nature of atherosclerotic disease, whereas in patients with a history of cigarette smoking, FDG uptake was only increased in the iliac arteries. It is well known that iliac artery disease is common among smokers, and this result suggests a site-specific nature of the response to certain risk factors.

The fact that the small number of diabetic subjects in our study did not have higher FDG uptake than nondiabetics may be due to effective medical therapy in our study group, or to the competitive effect of hyperglycemia on FDG uptake. Some diabetic medications, such as glitazones, have been shown to have anti-inflammatory actions whereas metformin has been associated with a decreased risk of future cardiovascular events in obese type 2 diabetic patients. It is therefore plausible that taking these medications could reduce the degree of arterial inflammation detected by PET imaging.
Because we excluded patients with high blood glucose from the study, it is unlikely that significant competition between FDG and glucose would explain the lack of difference. Furthermore, it seems that FDG uptake into inflammatory lesions may be less sensitive to elevated serum glucose levels than tumor cells.34

Our study did not show an association of statin use and FDG uptake, in contrast to other work.8 This is most likely due to the small sample size in our nonstatin subgroup (as shown in Table 2, 88.8% of the subjects were taking statins).

Context and Conclusions

Our results are in broad agreement with the study published by Tahara et al in 2007.29 That study demonstrated higher FDG uptake in the arteries of men compared with women, and an association between FDG uptake and several components of the metabolic syndrome. However, their study was retrospective and limited to patients with cancer, was performed on a standalone PET scanner and did not include many patients with known cardiovascular disease. Our study specifically imaged patients with known vascular disease including a high proportion with CAD. We also used a vascular-tailored imaging protocol, and for the first time obtained data on risk factors, biomarkers, calcification, and FDG uptake at multiple sites within the same patient.

In conclusion, we have demonstrated that arterial FDG PET imaging can provide new insights into the pathobiology of atherosclerosis. We suggest future studies might test an arterial inflammation score derived from FDG PET and circulating biomarkers as a means of predicting clinical events in high-risk individuals. However, large, prospective event-driven studies of noninvasive inflammation imaging techniques are the best way to determine the place of these modalities in future clinical practice. Such studies are already underway (see http://www.hrpinitiative.com) and are due to report in 2011.

Sources of Funding

This work was supported by a British Heart Foundation International Fellowship (to J.H.F.R.) and Doris Duke Fellowship (to K.S.M.). Partial funding was provided by grant NIH/NHLBI ROI HL71021 (to Z.A.F.). This study was supported in part by the National Institute of Health Research Cambridge Biomedical Research Centre.

Disclosures

None.

References


---

**CLINICAL PERSPECTIVE**

Atherosclerotic plaque inflammation is thought to be central to plaque rupture and, by extension, clinical events such as acute coronary syndrome, stroke, and transient ischemic attack. By identifying such plaques before symptoms become apparent, preventive therapies such as statins might be initiated or intensified. Fluorodeoxyglucose positron-emission tomography/computed tomography is already established for cancer diagnosis, staging, and the prediction of tumor response to therapy. Our study applied this noninvasive imaging technology to atherosclerosis of the carotid, femoral, and iliac arteries and the aorta. We explored the links between plaque inflammation, arterial calcification, circulating biomarkers, and atherogenic risk factors. We found that there was strong symmetry in the distribution of arterial inflammation and that calcification was inversely linked with inflammation. We also confirmed previous work by demonstrating that arterial inflammation was greater in male patients and in those with a diagnosis of coronary artery disease. Clinical applications of this work may include the use of imaging for prediction of plaque rupture, insight into the pathobiology of atherosclerosis, and monitoring of antiatherosclerosis therapies. Underpinning these applications, studies are already underway that will link imaging findings with clinical events. In addition, fluorodeoxyglucose positron-emission tomography/computed tomography atherosclerosis imaging is already being used as a surrogate marker of antiatherosclerotic drug efficacy by several pharmaceutical companies seeking to exploit its uniquely high sensitivity and reproducibility.
Relationships Among Regional Arterial Inflammation, Calcification, Risk Factors, and Biomarkers: A Prospective Fluorodeoxyglucose Positron-Emission Tomography/Computed Tomography Imaging Study

James H.F. Rudd, Kelly S. Myers, Sameer Bansilal, Josef Machac, Mark Woodward, Valentin Fuster, Michael E. Farkouh and Zahi A. Fayad

Circ Cardiovasc Imaging, 2009;2:107-115; originally published online January 26, 2009; doi: 10.1161/CIRCIMAGING.108.811752

Circulation: Cardiovascular Imaging is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2009 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-9651. Online ISSN: 1942-0080

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circimaging.ahajournals.org/content/2/2/107

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Imaging can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Imaging is online at:
http://circimaging.ahajournals.org//subscriptions/