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# Determinants of Extraaortic Arterial $^{18}\text{F}$ -FDG Accumulation in Asymptomatic Cohorts: Sex Differences in the Association with Cardiovascular Risk Factors and Coronary Artery Stenosis

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The objective of this study was to evaluate extraaortic arterial  $^{18}\text{F}$ -FDG accumulation in asymptomatic cohorts by sex and to clarify the association between extraaortic arterial  $^{18}\text{F}$ -FDG accumulation and cardiovascular risk factors (CRFs) and coronary artery stenosis (CAS). **Methods:** Five hundred twenty-one asymptomatic individuals (351 men and 170 women) who underwent cancer and CAS screening were enrolled. We evaluated extraaortic arterial  $^{18}\text{F}$ -FDG accumulation in the carotid artery (CA) and iliofemoral artery (IFA) and classified the accumulation patterns into 3 types. Type 1 patients had no extraaortic arterial  $^{18}\text{F}$ -FDG accumulation, type 2 had accumulation in either the CA or the IFA, and type 3 had accumulation in both the CA and IFA. CRFs (age, low-density lipoprotein [LDL] and high-density lipoprotein [HDL] cholesterol, triglyceride concentration, visceral abdominal fat, hypertension, diabetes, and smoking) and significant CAS were examined in relation to each accumulation type. **Results:** The men showed more extensive extraaortic arterial  $^{18}\text{F}$ -FDG accumulation than the women. Type 3 accumulation (60.4% vs. 37.1%,  $P < 0.0001$ ) was more frequently observed in men, whereas type 2 (34.2% vs. 44.7%,  $P = 0.02$ ) and type 1 (5.4% vs. 18.2%,  $P < 0.0001$ ) accumulation were more frequent in women. The CRFs other than smoking tended to be worse with extensive extraaortic arterial  $^{18}\text{F}$ -FDG accumulation. A multivariate logistic regression analysis showed that hypertension, age, LDL cholesterol, triglyceride, and visceral abdominal fat were significantly associated with type 3 accumulation in men, and LDL cholesterol and HDL cholesterol (inversely) were significantly associated with type 3 accumulation in women. CAS was found in 4.2% (9/212) of male patients and in 1.6% (1/63) of female patients with type 3 accumulation, whereas no CAS was found in the other 2 types. **Conclusion:** The men showed more extensive extraaortic arterial  $^{18}\text{F}$ -FDG accumulation than the women. LDL cholesterol was associated with extensive extraaortic arterial  $^{18}\text{F}$ -FDG accumulation in both sexes, but the other CRFs associated with extensive extraaortic  $^{18}\text{F}$ -FDG arterial accumulation differed between the sexes. The type 3 accumulation was con-

sidered to pose a risk of CAS, especially in male patients, whereas non-type 3 accumulation presented little risk.

**Key Words:** extraaortic arterial  $^{18}\text{F}$ -FDG accumulation; sex differences; cardiovascular risk factors coronary artery stenosis

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**A**therosclerosis is recognized as an inflammatory disorder, and previous studies showed that inflammation of atherosclerotic plaques could be evaluated by  $^{18}\text{F}$ -FDG PET imaging, especially in macrophage-related vascular inflammation (1–3). The prevalence and intensity of  $^{18}\text{F}$ -FDG accumulation in large arteries generally increase with aging (4,5).  $^{18}\text{F}$ -FDG accumulation in the abdominal aorta and iliofemoral artery (IFA) correlates with age and hypercholesterolemia (6). In addition, metabolic syndrome is also associated with carotid plaque  $^{18}\text{F}$ -FDG accumulation (7,8). A high prevalence of  $^{18}\text{F}$ -FDG accumulation in the femoral artery or carotid artery (CA) was also detected in patients with coronary artery disease (CAD) (6–8).

A histologic analysis of CA plaque revealed that men had more unstable CA plaque, including more features of inflammation, than did women (9). An in vivo carotid MR imaging-based study revealed that the presence of atherosclerotic components such as a thin or ruptured fibrous cap and lipid-rich necrotic core in CA was more common in men (10). Moreover, in CAD, sex differences in plaque morphology have been described that point to a higher prevalence of fresh thrombus and plaque rupture in men (11,12).

We hypothesized that extensive extraaortic arterial  $^{18}\text{F}$ -FDG accumulation such as that in CA and IFA may be associated with cardiovascular risk factors (CRFs) and coronary artery stenosis (CAS) and that male and female patients may show different extraaortic arterial  $^{18}\text{F}$ -FDG distribution. In addition different associations may also exist in extraaortic arterial  $^{18}\text{F}$ -FDG accumulation, CRFs, and CAS according to sex differences.

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The aims of this study were thus to explore sex differences in extraaortic arterial  $^{18}\text{F}$ -FDG distribution and to clarify such differences in the associations among extraaortic arterial  $^{18}\text{F}$ -FDG accumulation, CRFs, and CAS.

## MATERIALS AND METHODS

### Patients

This retrospective study was approved by the institutional review board of Koga Hospital 21, and direct informed consent was waived. This retrospective study included 521 asymptomatic consecutive patients (351 men and 170 women; age range, 28–84 y; mean age, 57.3 and 59.7 y, respectively) who were involved in a screening program using  $^{18}\text{F}$ -FDG PET/CT and coronary MR angiogram (MRA) run by our institution from November 2007 to May 2010. They underwent  $^{18}\text{F}$ -FDG PET/CT and coronary MRA to detect cancer and CAS, and these imaging modalities showed that none of the patients had a major disease. Thirteen patients had a history of curative operation for malignancy, and 2 patients had gastric and bladder cancer, which was found by the  $^{18}\text{F}$ -FDG PET/CT examination. No patients received oncologic treatment at the time of examination.

This study excluded the patients with a history of CAD or coronary revascularization, those who had received statin therapy for dyslipidemia, those who had uncontrolled diabetes (hemoglobin A1c  $> 9.0\%$ ) or had received insulin therapy for diabetes, and those who had had  $^{18}\text{F}$ -FDG accumulation in the cervical portion, which interfered with the evaluation of CA accumulation such as diffuse thyroidal accumulation or high sternomastoid muscle accumulation.

### $^{18}\text{F}$ -FDG PET/CT Protocol

The patients fasted for at least 6 h before  $^{18}\text{F}$ -FDG administration. All patients received an intravenous injection of  $^{18}\text{F}$ -FDG (3.7 MBq/kg) and then rested for 1 h before the scan started. Images were acquired using a True Point Biograph 40 PET/CT scanner (Siemens), which integrates 40-slice multidetector CT. Low-dose non-contrast-enhanced CT (tube voltage, 120 kV; effective tube current, 80 mA) that covered from the top of the skull to the proximal thigh was performed for attenuation correction and precise anatomic location, and then emission images for 2 min per position were obtained in 3-dimensional mode. The PET set was reconstructed using the Fourier rebinning ordered-subset expectation maximization 2-dimensional method, with 2 full iterations of 8 subsets, and the full width at half maximum was 4.2 mm.

### Coronary MRA and CT Angiography (CTA) Protocol

All patients ( $n = 521$ ) underwent cardiac MR imaging, performed with a 1.5-T scanner (Achieva; Philips) equipped with a 5-channel cardiac coil. Isosorbide dinitrate (5 mg) was administered sublingually to the patient before he or she underwent MR imaging. The whole-heart coronary MRAs were obtained using a free-breathing 3-dimensional segmented steady-state free precession sequence with electrocardiogram triggering. To compensate for the respiratory motion, prospective diaphragmatic navigator gating was used with no drift correction and the 5-mm gating window. The imaging parameters for the 3-dimensional segmented steady-state free precession sequence were as follows: repetition time/echo time, 4.0/2.0; flip angle,  $85^\circ$ ; field of view,  $300 \times 270$  mm; matrix,  $224 \times 220$ ; and slice thickness/reconstruction, 1.6/0.8 mm. Spectral presaturation with inversion recovery was applied to suppress epicardial fat signals. If available, a coronary CT angiogra-

phy (CTA) examination was performed in the patients who showed significant CAS on their MRA ( $n = 5$ ). Coronary CTA was performed using a LightSpeed VCT (GE Healthcare), which integrates a 64-slice multidetector CT scanner. The CTA protocol was the same as that used in our previous study (13). All patients underwent  $^{18}\text{F}$ -FDG PET/CT and coronary MRA within a 2-d period.

### $^{18}\text{F}$ -FDG PET/CT Findings

An experienced nuclear medicine physician, masked to the clinical characteristics of the patients, visually evaluated extraaortic arterial  $^{18}\text{F}$ -FDG accumulation in the CA and IFA. The scan was interpreted as positive if each artery showed linear activity of  $^{18}\text{F}$ -FDG accumulation higher than the background level. The accumulation pattern was classified into 3 types. Type 1 patients had no extraaortic accumulation, type 2 had accumulation in either the CA or the IFA, and type 3 had accumulation in both the CA and the IFA (Fig. 1).

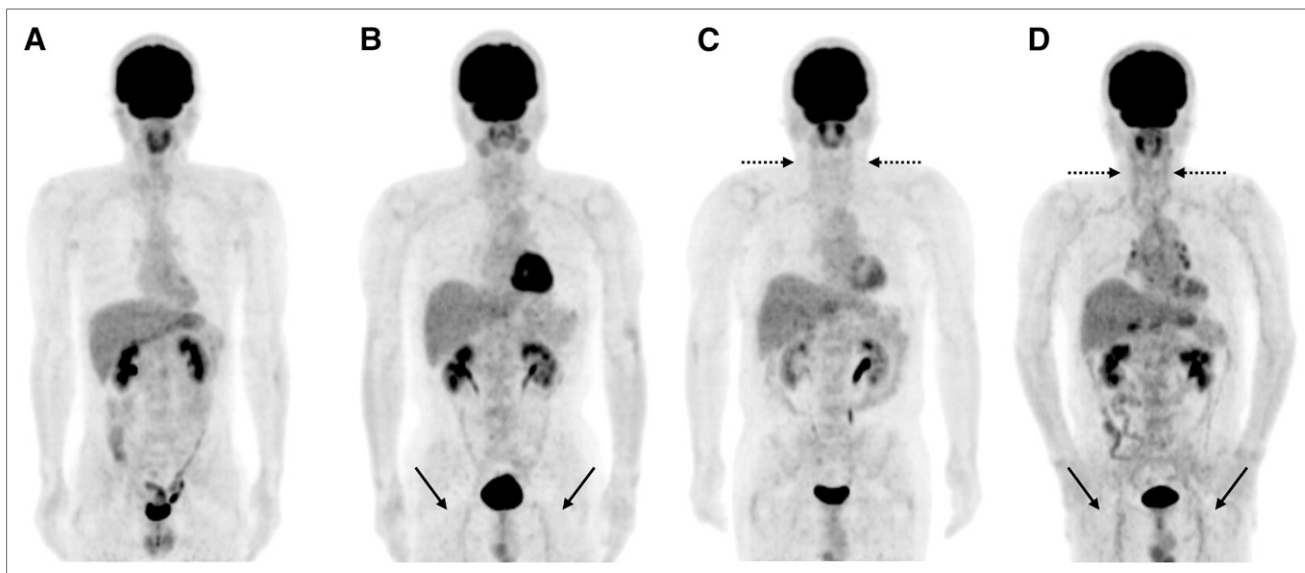
### Coronary MRA and CTA Findings

The following 9 segments of the coronary artery as defined in the guidelines of the American Heart Association were evaluated for stenosis (14): the proximal, middle, and distal segments of the right coronary artery (nos. 1–3); the left main coronary artery (no. 5); the proximal, middle, and distal segments of the left anterior descending artery (nos. 6–8); and the proximal and distal segments of the left circumflex artery (nos. 11 and 13). The segments were classified as having significant stenosis ( $\geq 75\%$ ) or no significant stenosis at visual assessment. The appearance of a reduction in segmental diameter or a loss of signal intensity on MR images was considered to be indicative of a significant CAS.

The subsequent CTA images were also assessed to compare them with the MRA findings, and any narrowing of the normal contrast-enhanced lumen to  $< 50\%$  that could be identified by multiplanar reconstructions or cross-sectional images was defined as significant CAS. Two observers independently evaluated the coronary MRA and CTA images. The observers were masked to the clinical character and  $^{18}\text{F}$ -FDG PET/CT findings of the patients. Disagreement between the 2 observers was settled by a consensus reading. The incidences of significant CAS were assessed and compared between the type 3 accumulation and the 2 other types in both sexes.

### CRFs

Eight CRFs (age, LDL cholesterol, HDL cholesterol, triglyceride concentration, visceral abdominal fat [VAT], hypertension, diabetes, and current smoking) were examined in relation to each accumulation type. Patients were classified as having hypertension if they had a systolic blood pressure  $\geq 140$  mm Hg or diastolic blood pressure  $\geq 90$  mm Hg (15) or were taking antihypertensive medications. Patients were classified as having diabetes if they had a fasting blood glucose  $\geq 126$  mg/dL or hemoglobin A1c  $\geq 6.5\%$  (16) or were taking oral antidiabetic medication. Hemoglobin A1c values were converted from Japan Diabetes Society values to National Glycohemoglobin Standardization Program values (17). VAT volumes were measured on the CT images obtained by the same PET/CT scanner. A cross-sectional 5-mm slice at the umbilical level was obtained, and the attenuation range of  $-60$  to  $-160$  Hounsfield units was used to identify adipose tissue. A computation of the surface area from the CT scans was conducted with volume analysis software (Fat Checker; J-MAC System). The total abdominal fat area was calculated using all pixels within the attenuation range, and VAT was defined as the area of adipose tissue



**FIGURE 1.** Maximum-intensity-projection images of PET/CT are shown. Extraaortic arterial  $^{18}\text{F}$ -FDG accumulation was classified into 3 types. (A) Type 1 is no extraaortic arterial  $^{18}\text{F}$ -FDG accumulation. (B and C) Type 2 is arterial  $^{18}\text{F}$ -FDG accumulation in either CA or IFA. (D) Type 3 is arterial  $^{18}\text{F}$ -FDG accumulation in both CA and IFA. In B–D, dotted arrows point to CA accumulation, and solid arrows point to IFA accumulation.

within the edge of the abdominal wall. The incidences or values of the 8 CRFs were compared among the 3 types of  $^{18}\text{F}$ -FDG accumulation, and the CRFs that were significantly associated with type 3 accumulation were assessed in both sexes.

### Statistical Analysis

Incidences were compared using a  $\chi^2$  test, and if necessary, a Bonferroni adjustment was added. Values were compared using the nonparametric Mann–Whitney  $U$  test or the Kruskal–Wallis test. A multiple logistic regression analysis examining the associations between CRFs and the type 3 accumulation pattern was performed. Probability values of less than 0.05 were considered significant.

### RESULTS

The clinical features of the patients are summarized in Table 1. The men showed more extensive extraaortic arte-

rial  $^{18}\text{F}$ -FDG accumulation than the women. Type 3 accumulation was more frequently observed in men than women (60.4% vs. 37.1%,  $P < 0.0001$ ), whereas type 2 (34.2% vs. 44.7%,  $P = 0.02$ ) and type 1 (5.4% vs. 18.2%,  $P < 0.0001$ ) accumulation were more frequent in women (Table 2).

The incidences of the CRFs other than smoking tended to be higher with extensive extraaortic arterial  $^{18}\text{F}$ -FDG accumulation, and the incidence of hypertension was significantly higher in male patients with type 3 accumulation than in the other 2 types (38.2% vs. 10.5% and 19.2%,  $P = 0.02$  and 0.0003, respectively; Table 3). In male patients with type 3 accumulation, the age, VAT, and triglyceride values were significantly higher than in male patients with the other 2 accumulation types, and the LDL cholesterol values of the men with type 3 accumulation were also

**TABLE 1**  
Clinical Features of Patients

Feature	Men	Women	$P$
No. of patients	351	170	
Age (y)			
Mean $\pm$ SD	57.3 $\pm$ 10.0	59.7 $\pm$ 9.6	0.03
Range	33–84	28–81	
Hypertension (%)	30.5	25.3	Not significant
Diabetes (%)	13.1	4.7	0.003
Smoking (%)	33.3	11.1	<0.0001
LDL cholesterol (mg/dL)	123.3 $\pm$ 29.5	126.6 $\pm$ 30.1	Not significant
HDL cholesterol (mg/dL)	52.5 $\pm$ 12.1	63.4 $\pm$ 15.4	<0.0001
Triglyceride (mg/dL)	132.4 $\pm$ 68.9	93.1 $\pm$ 49.6	<0.0001
VAT (cm <sup>2</sup> )	94.6 $\pm$ 43.2	56.8 $\pm$ 32.2	<0.0001

Data are mean  $\pm$  SD and %.

**TABLE 2**  
Sex Differences in Incidence of Each Accumulation Pattern

Type	Sex				P
	Men (n = 351)		Women (n = 170)		
	n	Percentage	n	Percentage	
1	19	5.4	31	18.2	<0.0001
2	120	34.2	76	44.7	0.02
3	212	60.4	63	37.1	<0.0001

significantly higher than those of the type 1 men ( $P = 0.03$ , Table 3). No significant difference was found in HDL cholesterol values (Table 3).

In the women, VAT and HDL cholesterol values were significantly higher and lower, respectively, in the type 3 patients than in patients with the other 2 types of accumulation, and the LDL cholesterol and triglyceride values were also significantly higher than those of the type 1 patients ( $P = 0.03$  to  $<0.0001$ , Table 3). The ages of the type 3 patients were significantly higher than those of the type 1 patients ( $P < 0.0001$ , Table 3), but no significant difference was found between the type 2 and type 3 patients.

The multivariate logistic regression analysis showed that hypertension, age, LDL cholesterol, triglyceride, and VAT were significantly associated with type 3 accumulation in men ( $P = 0.045$  to  $<0.0001$ , Table 4), and LDL cholesterol and HDL cholesterol (inversely) were significantly associated with type 3 accumulation in women ( $P = 0.047$  to  $0.02$ , Table 4).

Significant CAS was found in 4.2% (9/212) of the male type 3 patients and 1.6% (1/63) of the female type 3 patients, but no CAS was found in the patients with the other 2 accumulation types. A case of a male type 3 patient with significant CAS is shown in Figure 2. The incidence of CAS was significantly higher in type 3 than in non-type 3 patients ( $P = 0.01$ ) in the men but not in the women. We performed a subsequent coronary CTA in 5 patients, and we confirmed severe CAS in all 5. The details of the patients with significant CAS are given in Table 5.

## DISCUSSION

Arterial wall  $^{18}\text{F}$ -FDG accumulation in the vessel wall is related to macrophage infiltration, and it indicates vessel wall inflammation (3). In addition, arterial  $^{18}\text{F}$ -FDG accumulation is higher in plaque with a lipid-rich necrotic core than in plaques with collagen and calcification (18).

It has long been recognized that the incidence of CAD is significantly lower in women than in men, particularly women in the premenopausal stage. In premenopausal

**TABLE 3**  
Comparisons of CRFs Between Type 3 and Other Types of Patients

Feature	Type 1	Type 2	Type 3	P*
<b>Men</b>				
Hypertension (%)	10.5	19.2	38.2	0.02, type 1; 0.0003, type 2
Diabetes (%)	5.3	9.2	16	Not significant
Smoking (%)	52.6	33.3	31.6	Not significant
Age (y)	41.3 ± 9.9	55.5 ± 10.1	59.7 ± 8.3	<0.0001, type 1; 0.01, type 2
LDL cholesterol (mg/dL)	109.0 ± 25.1	118.9 ± 30.6	127.0 ± 28.6	0.03, type 1
HDL cholesterol (mg/dL)	55.8 ± 12.8	54.9 ± 13.5	50.9 ± 10.9	Not significant
Triglyceride (mg/dL)	105.8 ± 69.6	120.2 ± 57.4	141.7 ± 73.2	0.03, both
VAT (cm <sup>2</sup> )	49.5 ± 38.1	80.2 ± 41.1	107.3 ± 39.7	<0.0001, both
<b>Women</b>				
Hypertension (%)	9.7	27.6	30.2	Not significant
Diabetes (%)	0	9.2	9.5	Not significant
Smoking (%)	12.9	7.9	11.1	Not significant
Age (y)	51.3 ± 10.4	61.5 ± 8.5	61.7 ± 8.4	<0.0001, type 1
LDL cholesterol (mg/dL)	112.4 ± 23.9	126.4 ± 29.3	135.3 ± 32.7	0.03, type 1
HDL cholesterol (mg/dL)	66.6 ± 15.9	66.7 ± 15.8	57.7 ± 12.8	0.01, type 1; 0.001, type 2
Triglyceride (mg/dL)	76.9 ± 46.9	89.2 ± 42.4	105.9 ± 56.1	0.008, type 1
VAT (cm <sup>2</sup> )	37.3 ± 38.1	52.2 ± 30.7	70.1 ± 31.3	<0.0001, type 1; 0.004, type 2

\*P values between type 3 and types 1 and 2 accumulation were shown. Data are mean ± SD and %.

**TABLE 4**  
Odds Ratio and 95% Confidence Intervals for Type 3 Accumulation

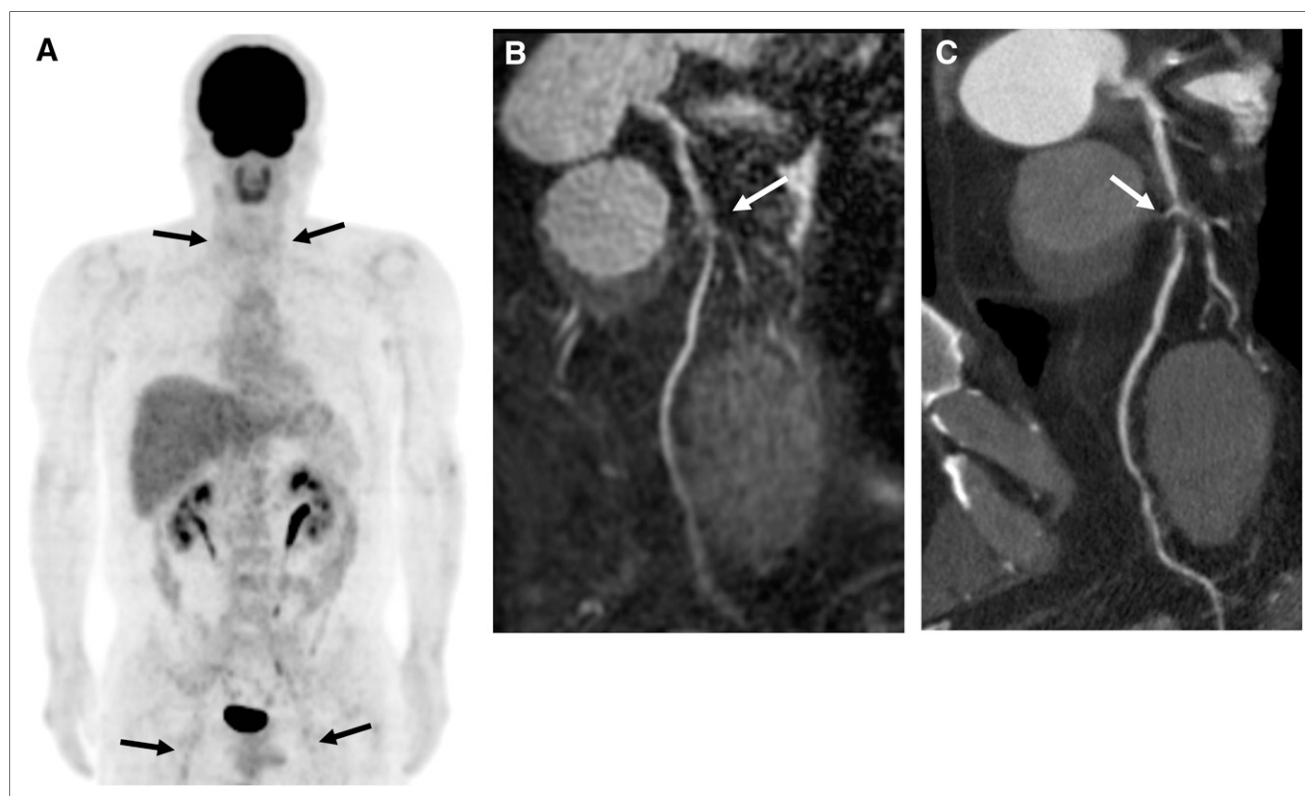
Feature	Men			Women		
	Odds ratio	95% Confidence interval	<i>P</i>	Odds ratio	95% Confidence interval	<i>P</i>
Hypertension	1.85	1.04–3.34	0.04	1.07	0.45–2.49	0.88
Diabetes	1.28	0.58–2.97	0.55	1.19	0.23–6.15	0.83
Smoking	0.82	0.47–1.43	0.48	1.33	0.36–4.89	0.66
Age	1.08	1.05–1.11	<0.0001	1.04	0.99–1.08	0.07
LDL cholesterol	1.01	1.00–1.02	0.004	1.01	1.00–1.03	0.047
HDL cholesterol	0.98	0.96–1.00	0.07	0.97	0.93–0.99	0.02
Triglyceride	1.00	1.00–1.01	0.045	1.00	0.99–1.01	0.93
VAT	1.02	1.01–1.03	<0.0001	1.01	0.999–1.03	0.05

women, compared with age-matched men, the lower prevalence of CAD has been explained by differences in body fat distribution, plasma lipoprotein levels, and indices of glucose-insulin homeostasis. Endogenous female sex hormones, especially estrogens, are thought to be cardioprotective via multiple mechanisms: increased HDL cholesterol, decreased LDL cholesterol, and release of vasodilators such as nitric oxide and prostacyclin from vessel walls (19). Additionally, estrogen seems to contribute to glucose homeostasis via increased glucose transport into the cell (19).

Hellings et al. revealed that CA plaques obtained from women contain less fat and macrophages and more smooth

muscle than those from men (9). Another study showed that men are more likely to have CA plaque characterized by the presence of lipid-rich necrotic core, a thin or ruptured fibrous cap, and intraplaque hemorrhage than women (10). Our present findings show that the men had more extensive extraortic arterial <sup>18</sup>F-FDG accumulation than the women, and our findings are in agreement with previous results.

Several studies showed that <sup>18</sup>F-FDG accumulation in the aorta and IFA correlated with age and hypercholesterolemia but not smoking, diabetes, hypertension, or obesity (6,20). On the other hand, Bucerius et al. reported that carotid <sup>18</sup>F-FDG accumulation was highly prevalent in



**FIGURE 2.** A 56-y-old man with significant CAS. (A) Maximum-intensity-projection image of PET/CT showed arterial <sup>18</sup>F-FDG accumulation in both CA and IFA, defined as type 3 accumulation (arrows). (B) Curved planar reconstruction of coronary MRA image showed significant stenosis in middle segment of left anterior descending artery (arrow). (C) Curved planar reconstruction of patient's coronary CTA images also showed significant stenosis in same artery (arrow).

**TABLE 5**  
Details of Patients with CAS

Patient no.	Sex	Age (y)	<sup>18</sup> F-FDG distribution	CAS on MRA*	CTA
1	M	56	Type 3	7	○
2	M	60	Type 3	7	○
3	M	63	Type 3	1, 5, 6, 11	×
4	M	64	Type 3	6	○
5	M	66	Type 3	7	×
6	M	69	Type 3	6, 7	○
7	M	72	Type 3	6, 7	○
8	M	79	Type 3	2, 7	×
9	M	80	Type 3	3, 7	×
10	F	61	Type 3	7	×

\*According to study of Scanlon et al. (14).

○ = CAS was confirmed by CTA; × = CTA was not performed.

the CAD population and was associated with obesity, age, smoking, hypertension, and male sex (8). In the present study, all of the CRFs examined except smoking tended to be worse with extensive extraaortic arterial <sup>18</sup>F-FDG accumulation, and significant differences were found in most of the CRFs between the type 3 and non-type 3 patients. Our results indicate that extraaortic arterial <sup>18</sup>F-FDG accumulation in the CA and IFA is related to many CRFs, and they also indicate that type 3 accumulation represents a state of more advanced atherosclerosis.

Our multivariate logistic regression analysis showed a male preponderance in several CRFs, which were significantly associated with extensive extraaortic arterial <sup>18</sup>F-FDG accumulation. A previous study showed that male sex is associated with carotid <sup>18</sup>F-FDG accumulation and other CRFs, such as obesity (8). Other research demonstrated sex differences in plaque morphology or the degree of arterial <sup>18</sup>F-FDG accumulation (9–12,21). We also speculated that male sex itself is an important CRF, and our present findings suggest that many other CRFs enhance extraaortic arterial <sup>18</sup>F-FDG accumulation in concert with male sex.

High serum levels of LDL cholesterol and low serum levels of HDL cholesterol are the major predictors of atherosclerotic CAD (22,23). Our present findings suggest that LDL cholesterol is the only common CRF that is significantly associated with extensive extraaortic arterial <sup>18</sup>F-FDG accumulation in both sexes. In our results, age and VAT were thought to have strong associations with extensive extraaortic arterial <sup>18</sup>F-FDG accumulation in men. Age was found to be the most significant and consistent factor correlated with arterial <sup>18</sup>F-FDG accumulation (6). Here we made comparisons by sex and found that age did not have a significant association with extraaortic arterial <sup>18</sup>F-FDG accumulation in women. We suspect that estrogen exposure earlier in life could be a cause of this result.

VAT is a key player in the development of metabolic syndrome (24). Lemieux et al. investigated sex differences of body fat distribution and reported that men had higher

VAT volume whereas women had higher subcutaneous fat tissue (25). Lear et al. claimed that VAT is the primary adiposity associated with atherosclerosis and likely represents an additional risk factor for carotid atherosclerosis in men (26). Shimizu et al. contended that VAT accumulation acts in concert with CRF accumulation to increase the risk for CAD (27). Our results showed that men had a higher VAT volume and a significant association with extensive extraaortic arterial <sup>18</sup>F-FDG accumulation and suggest that VAT both played a key role in the extensive extraaortic arterial <sup>18</sup>F-FDG accumulation in the men examined and was related to the development of CAD.

We found that diabetes was not significantly associated with extensive extraaortic arterial <sup>18</sup>F-FDG accumulation in either sex. Kim et al. reported that impaired glucose tolerance and type 2 diabetes were associated with vascular inflammation in carotid atherosclerosis detected by <sup>18</sup>F-FDG PET (28), a finding that differs from our results. However, they investigated the degree of <sup>18</sup>F-FDG accumulation using the target-to-background ratio in patients with different glucose tolerance levels (28) rather than arterial <sup>18</sup>F-FDG distribution. Our results suggest that diabetes may be associated with the degree of arterial <sup>18</sup>F-FDG accumulation rather than distribution.

In our study, significant CAS was found only in the type 3 patients (4.2% of the men and 1.6% of the women), and no CAS was found in the non-type 3 patients. Several studies have shown an association between CAD and CA inflammation (8,21). Carotid plaque morphology as assessed by either ultrasound or angiography has been related to coronary plaque morphology and coronary morbidity (29,30). Our present findings indicate that asymptomatic type 3 patients, especially male patients, had a risk of significant CAS. Conversely, non-type 3 patients were considered to have little risk of significant CAS.

Our study has some limitations. First, a major limitation of the present study is that it was retrospective, and further prospective studies would be beneficial. Second, we first evaluated CAS using coronary MRA. Although coronary

MRA is considered a useful modality that can noninvasively detect significant CAD with high sensitivity and moderate specificity, it also has a high negative predictive value (31). Third, we evaluated arterial  $^{18}\text{F}$ -FDG distribution but not the degree of arterial  $^{18}\text{F}$ -FDG accumulation (i.e., standardized uptake value or target to background) because we used 60-min  $^{18}\text{F}$ -FDG as the optimal circulation time point, as is commonly used in oncology PET studies. Previous studies recommended longer optimal circulation times, preferably at least 90 min (32), but an optimal circulation time point has not yet been standardized (32,33).

## CONCLUSION

Men showed more extensive extraaortic arterial  $^{18}\text{F}$ -FDG accumulation than women. LDL cholesterol was associated with extensive extraaortic arterial inflammation in both sexes, and the other CRFs associated with extensive extraaortic arterial inflammation differed between the sexes. The most extensive type 3 accumulation was considered to pose a risk of significant CAS, especially in male patients, whereas non-type 3 accumulation presented little risk.

## DISCLOSURE

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