Relation between carotid artery FDG uptake and cardiovascular risk in asymptomatic adults

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- ABSTRACT -

Relation between carotid artery FDG uptake and cardiovascular risk in asymptomatic adults

We investigated the relation between carotid artery FDG uptake and cardiovascular risk based on the Framingham risk score (FRS), and evaluated the possible role of FDG uptake in terms of risk stratification of asymptomatic adults. We evaluated 290 adults who underwent FDG PET/CT as part of general health screens. We calculated target-to-background ratios, corrected for pre-scan blood glucose levels, and obtained "TBRglu" values for both common carotid arteries. The FRS and the presence/absence of metabolic syndrome were recorded for each subject. Relationships among TBRglu values, metabolic syndrome status, and clinical parameters were assessed. Carotid artery FDG uptake was significantly associated with clinical risk factors. Stepwise multiple regression analysis revealed that triglyceride levels, diabetes, and metabolic syndrome were independent determinants of high TBRglu. Of subjects with metabolic syndrome, those exhibiting high carotid artery FDG uptake had significantly higher levels of high sensitivity C-reactive protein (hsCRP). In subjects who did not have metabolic syndrome, FRS were significantly elevated in those exhibiting high carotid artery FDG uptake compared to those with low uptake (13.1 ± 7.0 vs. 8.2 ± 7.4), as was also true of subjects with the syndrome (21.8 ± 16.0 vs. 13.5 ± 11.9). High carotid FDG uptake is significantly associated with clinical risk factors and a greater FRS. Of subjects with metabolic syndrome, those with high carotid uptake had significantly higher hsCRP concentrations and FRSs. Therefore, carotid artery FDG activity may serve as a possible biomarker

allowing cardiovascular risk stratification of asymptomatic populations.

Key words: atherosclerosis, carotid arteries, 18F-FDG, risk assessments, metabolic syndrome, cardiovascular disease

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I. INTRODUCTION

Atherosclerosis is a leading cause of adverse cardiovascular events including angina, myocardial infarction, and stroke. These complications increasingly burden healthcare systems and impair the quality of life. Prevention of cardiovascular disease (CVD) is a serious health issue, and screening for cardiovascular risk is important in clinical practice. However, risk stratification of asymptomatic subjects remains challenging. Although several risk-scoring models have been developed, additional indicators of risk are needed (Berger et al, 2010). Recently, [18F]-fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) has emerged as a powerful noninvasive imaging technique of measuring vascular inflammation associated with atherosclerosis (Lee et al, 2008; Oh et al, 2010; Bucerius et al, 2011; Yoo et al, 2011; Wu et al, 2012; Cocker et al, 2012; Kaneko et al, 2013). Atherosclerosis is a chronic disease in which several processes interact in the vascular endothelium, and development of inflammation is important if atherogenic plaque is to evolve to become vulnerable plaque (Hansson, 2005). Inflammation caused by an increase in the number of activated macrophages within plaque is the key feature increasing the level of vascular FDG uptake in atherosclerosis (Rudd et al, 2002; Tawakol et al, 2006). Imaging of atherosclerosis using FDG PET yields cellular and molecular information, and the activity of FDG uptake in large arteries and/or aortas may reflect the global plaque burden. Further, increased vascular FDG uptake is associated with traditional cardiovascular risk factors (Bucerius et al, 2011; Kaneko et al, 2013) and regression of FDG uptake has been observed after prescription of statins (Wu et al, 2012; Tahara et al, 2006) or lifestyle modification (Lee et al, 2008). Therefore, FDG PET/CT

shows promise for evaluation and monitoring of atherosclerosis in both symptomatic and asymptomatic subjects. The prevalence of metabolic syndrome has increased worldwide as more subjects become overweight and obese (Dekker et al, 2005; Ford et al, 2010). Metabolic syndrome is a cluster of interrelated features of metabolic origin, many of which are detectable only in the laboratory, and patients with the syndrome usually have no symptoms. Metabolic syndrome is a potent predictor of future cardiovascular disease and death (Wilson et al, 2005). Recently, one study found that carotid artery FDG uptake was elevated in subjects with metabolic syndrome, and it was suggested that the syndrome was associated with inflammatory carotid atherosclerosis (Tahara et al, 2007). However, few studies have been performed to evaluate an association between vascular FDG uptake for the metabolic syndrome and cardiovascular risk in asymptomatic populations. We thus investigated the relationship between carotid artery FDG uptake and cardiovascular risk estimated using the Framingham Heart Study risk scoring system (FRS). Further, we evaluated the possible utility of FDG PET/CT data for risk stratification in asymptomatic adults.

II. MATERIALS AND METHODS

A. STUDY SUBJECTS AND DATA COLLECTION

The study subjects were 293 consecutive asymptomatic adults who underwent FDG PET/CT as part of general health screening at our institution between January 2012 and July 2012. Of these subjects, we excluded two for whom serum high sensitivity C-reactive protein (hsCRP) measurements were lacking and one showing intense neck muscle uptake on PET/CT. No subject had any known malignancy, vasculitis, or cerebrovascular or coronary artery disease. The Ethics Committee of our institution approved this retrospective study.

All 290 subjects answered a medical questionnaire assessing smoking status, and past medical and current medication history. Height, weight, blood pressure (BP), and waist circumference were measured, and body mass index (BMI) was calculated as the weight/height2 (kg/m2). Blood tests included measurement of the levels of fasting plasma glucose, hsCRP, total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, and γ-glutamyl transpeptidase (γ-GT). All measurements and tests were conducted on the same day on which FDG PET/CT was performed.

Hypertension was defined as a systolic BP ≥140 mmHg, a diastolic BP ≥ 90 mmHg, or use of any anti-hypertensive medication. Diabetes mellitus was defined as a fasting blood glucose level ≥126 mg/dl or use of any hypoglycemic medication. Metabolic syndrome was diagnosed using the criteria established by the American Heart Association/National Heart, Lung, and Blood Institute, using waist circumferences adjusted for Asians. Thus, the

syndrome was diagnosed when three or more of the following were present: 1) waist circumference ≥90.0 cm in males and ≥80.0 cm in females; 2) fasting triglycerides ≥150 mg/dl; 3) HDL cholesterol <40 mg/dl in males and <50 mg/dl in females; 4) systolic BP ≥130 mmHg or diastolic BP ≥85 mmHg, or use of antihypertensive medication; and, 5) fasting plasma glucose ≥100 mg/dl or use of diabetes medication (Grundy et al, 2005). Individual 10-year general cardiovascular disease risks were estimated using FRS predictive criteria (D'Agostino et al, 2008).

B. FDG PET/CT

All subjects fasted for at least 6 h before imaging and the blood glucose level at the time of FDG injection was less than 200 mg/dl in all subjects. PET/CT was performed using Discovery ST (n = 142; GE Healthcare, Milwaukee, WI, U.S.A.) or Discovery STe scanners (n = 148; GE Healthcare). Unenhanced CT scans were collected 60 min after injection of 5 MBq/kg FDG, using an 8- or 16-slice helical CT (120 KeV; 30 - 100 mA in the AutomA mode; section width of 3.75 mm). After CT scanning, emission scans were obtained from the thigh to the skull base, for 2.5 min per frame, in the three-dimensional (3D) mode. Attenuation-corrected PET images obtained using CT data were reconstructed by a 3D ordered-subsets expectation maximization algorithm (20 subsets, two iterations).

C. IMAGE ANALYSIS

All PET/CT images were reviewed on a workstation (GE Advantage Workstation 4.4, GE Healthcare) by two experienced nuclear medicine

physicians. First, we defined the range of the common carotid artery (CCA) on fusion images, beginning from the brachiocephalic trunk or aortic arch, and continuing to below the bifurcation site. Next, we manually placed circular or ellipsoidal regions of interest (ROIs) on every slice of transaxial PET images showing the CCA. We included all arterial wall and lumen tissue but excluded adjacent soft tissues. The maximum standardized uptake values (SUVs) of the bilateral CCAs were recorded. Mean SUV values were derived by averaging the maximum SUVs of all slices containing CCAs. To calculate the background activity, the mean SUVs of pooled blood were measured by placing circular ROIs at the mid levels of both jugular veins, and the data were averaged. Target-to-background ratios (TBRs) were calculated by dividing each mean CCA SUV by the blood pool activity. For glucose-corrected parameters, mean SUVs were corrected by individual fasting blood glucose levels prior to scanning to account for a competitive impact of glucose and FDG uptake using an established formula; mean SUVglu = mean SUV × individual blood glucose level (mmol/l)/5.0 mmol/l [19, 20]. Finally, the target-to-background ratio corrected by blood glucose level (TBRglu) was calculated by dividing the mean SUVglu by blood pool activity.

D. STATISTICAL ANALYSIS

Continuous variables are expressed as means ± standard deviations in tables and as means ± standard errors in histograms. To compare between-group differences, Student's t-test or the Mann-Whitney U test were used as appropriate when variables were continuous, and the Chi-squared or Fisher's exact test when variables were categorical.

Correlations were sought using Pearson's or Spearman's test. To determine factors affecting TBRglu values, multiple stepwise regression analysis was performed using SPSS (IBM SPSS Statistics version 18, IBM Inc., New York, NY, U.S.A.). A P value <0.05 was considered to reflect statistical significance.

III. RESULTS

The clinical characteristics of the 290 subjects are summarized in Table 1.

Table 1. Clinical Variables of Study Subjects

Variables	Total (n=290)	TBRglu<1.5 (n=225)	TBRglu≥1.5 (n=65)	*P* value
Male/Female	158/132	112/113	46/19	0.003
Age (year)	54.5 ± 8.7	54.4 ± 8.8	55.1 ± 8.3	NS
Body weight (kg)	66.4 ± 12.2	65.2 ± 12.3	70.4 ± 11.3	0.003
Body mass index (kg/m^2)	24.6 ± 3.1	24.3 ± 3.0	25.8 ± 3.2	0.001
Waist circumference (cm)	86.9 ± 7.8	86.2 ± 7.7	89.3 ± 7.6	0.004
Systolic BP (mmHg)	119.5±15.1	117.8±14.5	125.3±15.8	<0.001
Diastolic BP (mmHg)	76.3 ± 11.2	75.3 ± 10.7	80.1 ± 11.9	0.002
Fasting glucose (mg/dl)	101.1 ± 23.6	94.0 ± 14.5	126.5 ± 31.0	<0.001
Total cholesterol (mg/dl)	193.2 ± 37.6	192.4 ± 36.6	195.7 ± 41.0	NS
HDL cholesterol (mg/dl)	51.2 ± 12.6	52.5 ± 12.4	46.6 ± 12.5	0.001
LDL cholesterol (mg/dl)	115.2 ± 31.2	116.1 ± 31.0	112.2 ± 31.6	NS
Triglyceride (mg/dl)	133.9 ± 95.2	119.5 ± 70.0	185.0 ± 143.8	0.001
γ-GT (U/L)	34.8 ± 33.2	32.3 ± 32.9	43.8 ± 32.7	0.014
hsCRP (mg/dl)	0.12 ± 0.18	0.10 ± 0.17	0.17 ± 0.18	0.009
Hypertension	71 (24.5%)	44 (19.6%)	27 (41.5%)	<0.001
Diabetes mellitus	42 (14.5%)	8 (3.6%)	34 (52.3%)	<0.001
Current smoking	54 (18.6%)	37 (16.4%)	17 (26.2%)	NS
Metabolic syndrome	93 (32.1%)	55 (24.4%)	38 (58.5%)	<0.001
Statin medication	28 (9.7%)	20 (8.9%)	8 (12.3%)	NS
Framingham risk score	12.0 ± 3.4	9.4 ± 9.0	18.2 ± 13.7	<0.001

TBRglu, target-to-background ratio normalized with blood glucose level; BP,

blood pressure; HDL, high density lipoprotein; LDL, low density lipoprotein; hsCRP, high sensitive C-reactive protein; γ-GT, gamma glutamyl transpeptidase; NS, not significant. Data are present as mean ± SD.

The mean age was 54.5 years. Of all subjects, 71 (24.5%) had hypertension, 42 (14.5%) diabetes, 123 (42.4%) were current smokers, and 28 (9.7%) took statins. The mean FRS was 12.0 ± 3.4%. The mean TBR and TBRglu were 1.3 ± 0.1 and 1.6 ± 1.2, respectively. In the present study, we did not aim to compare TBR and TBRglu, thus we focus on TBRglu in the article. Ninety-three subjects (32.1%) were diagnosed with metabolic syndrome by health screening. Their mean TBRglu was significantly greater than that of subjects without the syndrome (1.5 ± 0.3 vs. 1.3 ± 0.2, $P < 0.001$). The 75th percentile of TBRglu in all subjects was 1.5, and we chose the value as threshold for data analysis. Two groups, showing high and low FDG uptake by the carotid arteries, could be distinguished using a TBRglu threshold of 1.5 (Table 1).

More members of the high uptake group were male (70.8 vs. 49.7%, $P = 0.003$) and more obese (high body weight, $P = 0.003$; BMI, $P = 0.001$; waist circumference, $P = 0.004$) than the low uptake group. The former subjects had significantly higher BP ($P < 0.005$); elevated levels of fasting plasma glucose ($P < 0.001$), triglycerides ($P = 0.001$), γ-GT ($P = 0.014$), and hsCRP ($P = 0.009$); and lower levels of HDL cholesterol ($P = 0.001$).

Also, these subjects exhibited more hypertension ($P < 0.001$), diabetes ($P < 0.001$), and metabolic syndrome ($P < 0.001$), than the low uptake group. In addition, their FRSs were significantly higher ($P < 0.001$).

Correlation analysis showed that TBRglu was significantly associated with body weight ($P = 0.001$); BMI ($P < 0.001$); BP ($P < 0.001$); the levels of

triglycerides (P < 0.001), and γ-GT (P < 0.001); and FRS (P < 0.001); and negatively associated with the level of HDL cholesterol (P < 0.001). In addition, male gender (P < 0.001), diabetes (P < 0.001), metabolic syndrome (P < 0.001), and hypertension (P < 0.001) were significantly associated with high TBRglu. The results of multiple stepwise linear regression analysis are presented in Table 2.

Table 2. Multiple stepwise regression analysis between glucose corrected FDG uptake and clinical variables

Variables	Standardized coefficient β	95% CI	P value
Fasting plasma glucose	0.375	0.003 to 0.006	<0.001
Diabetes mellitus	0.266	0.107 to 0.310	<0.001
Metabolic syndrome	0.136	0.023 to 0.138	0.006
Triglyceride	0.121	0.000 to 0.001	0.011

TBRglu, target-to-background ratio normalized with blood glucose level; CI, confidence interval.

Diabetes, metabolic syndrome, and triglyceride levels were independent determinants of high TBRglu. We compared clinical cardiovascular risk factors, and FRS data, in subjects stratified by the presence of metabolic syndrome and TBRglu (threshold 1.5) (Table 3).

Table 3. Comparison of Clinical Variables between Subjects with and without Metabolic Syndrome

Variables	without metabolic syndrome (n=197)			with metabolic syndrome (n=93)		
	TBRglu <1.5 (n=170)	TBRglu ≥1.5 (n=27)	*P* value	TBRglu <1.5 (n=55)	TBRglu ≥1.5 (n=38)	*P* value
Male/Female	84/86	21/6	0.006	28/27	25/13	NS
Age (year)	54.1 ± 8.5	54.5 ± 6.9	NS	55.1 ± 9.5	55.9 ± 9.4	NS
Body weight (kg)	63.3 ± 11.5	64.9 ± 9.0	NS	71.1 ± 12.9	74.3 ± 11.1	NS
Body mass index (kg/m^2)	23.6 ± 2.8	23.7 ± 2.5	NS	26.3 ± 2.7	27.3 ± 2.8	NS
Waist circumference (cm)	84.3 ± 7.2	84.3 ± 6.6	NS	91.7 ± 6.3	93.3 ± 6.0	NS
Systolic BP (mmHg)	114.8 ± 14.1	121.7 ± 16.8	0.023	126.9 ± 12.0	128.0 ± 14.5	NS
Diastolic BP (mmHg)	73.8 ± 10.6	78.6 ± 12.3	0.037	79.9 ± 9.8	80.9 ± 11.6	NS
Fasting glucose (mg/dl)	92.2 ± 15.0	120.7 ± 31.6	<0.001	99.0 ± 11.5	130.2 ± 30.0	<0.001
Total cholesterol (mg/dl)	190.4 ± 35.4	184.2 ± 32.4	NS	198.9 ± 39.9	203.6 ± 44.4	NS
HDL cholesterol (mg/dl)	54.1 ± 11.9	51.2 ± 15.4	NS	47.5 ± 12.6	43.3 ± 8.6	NS
LDL cholesterol (mg/dl)	115.4 ± 30.7	112.1 ± 25.5	NS	118.2 ± 32.6	112.2 ± 35.3	NS
Triglyceride (mg/dl)	104.2 ± 62.3	105.0 ± 37.8	NS	166.4 ± 72.6	240.7 ± 162.4	0.011
γ-GT (U/L)	27.6 ± 25.4	30.0 ± 17.8	NS	46.4 ± 47.1	54.0 ± 36.8	NS
hsCRP (mg/dl)	0.09 ± 0.17	0.09 ± 0.10	NS	0.14 ± 0.19	0.23 ± 0.21	0.047
Hypertension	21 (12.4%)	7 (25.9%)	NS	23 (41.8%)	21 (55.3%)	NS
Diabetes mellitus	5 (2.9%)	12 (44.4%)	<0.001	2 (3.6%)	23 (60.5%)	<0.001
Current smoking	24 (14.1%)	5 (18.5%)	NS	13 (23.6%)	12 (31.6%)	NS
Statin medication	12 (7.1%)	3 (11.1%)	NS	8 (14.5%)	5 (13.2%)	NS
Framingham risk score	8.2 ± 7.4	13.1 ± 7.0	0.001	13.5 ± 11.9	21.8 ± 16.0	0.008

TBRglu, target-to-background ratio normalized with blood glucose level; BP, blood pressure; HDL, high density lipoprotein; LDL, low density lipoprotein; hsCRP, high sensitive C-reactive protein; γ-GT, gamma; NS, not significant. Data are present as mean± SD.

Of those without metabolic syndrome, the subgroup with high TBRglu had more males (P = 0.006) and a higher frequency of diabetes (P < 0.001). Among those with metabolic syndrome, the subgroup with high TBRglu had higher fasting plasma glucose (P < 0.001), triglyceride (P = 0.011), and hsCRP (P = 0.047) levels; and diabetes was more common (P < 0.001). High uptake subjects with metabolic syndrome had significantly higher levels of hsCRP compared to low uptake subjects with the syndrome (0.23 ± 0.21 vs. 0.14 ± 0.19), whereas the hsCRP level did not differ significantly between subgroups without the syndrome (Fig 1a.).

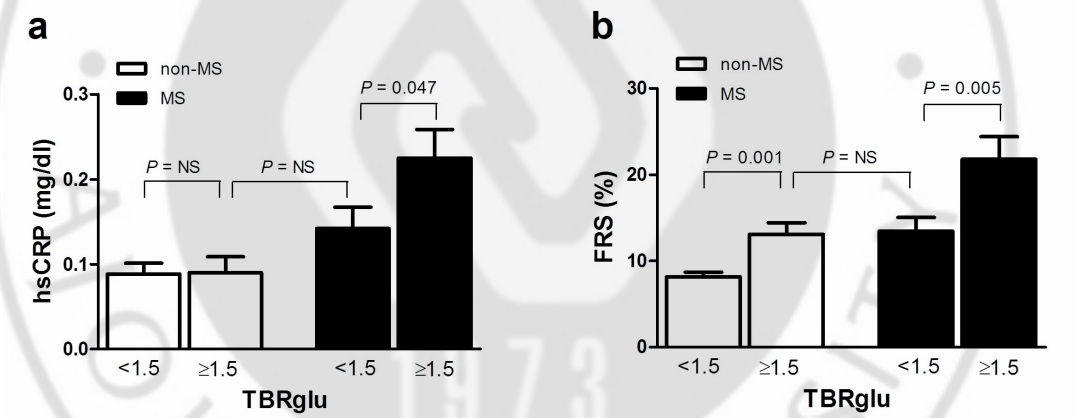

Fig 1. (a) High sensitivity C-reactive protein (hsCRP) concentrations and (b) Framingham risk scores (FRSs) in study subjects stratified by target-to-background ratio corrected for blood glucose level (TBRglu), and presence or absence of metabolic syndrome (MS). Bars: means ± standard errors.

The FRS was significantly higher in subjects with high uptake compared to both non-syndromic and syndromic subjects with low uptake (8.2 ± 7.4 vs.

13.1 ± 7.0; 13.5 ± 11.9 vs. 21.8 ± 16.0, respectively; Fig 1b.). The FRS of subjects with high uptake but no metabolic syndrome was comparable to that of subjects with low uptake and metabolic syndrome (13.1 ± 7.0 vs. 13.5 ± 11.9). Figure 2 demonstrates the representative PET images of a subject without metabolic syndrome but high carotid uptake and a subject with syndrome but low uptake.

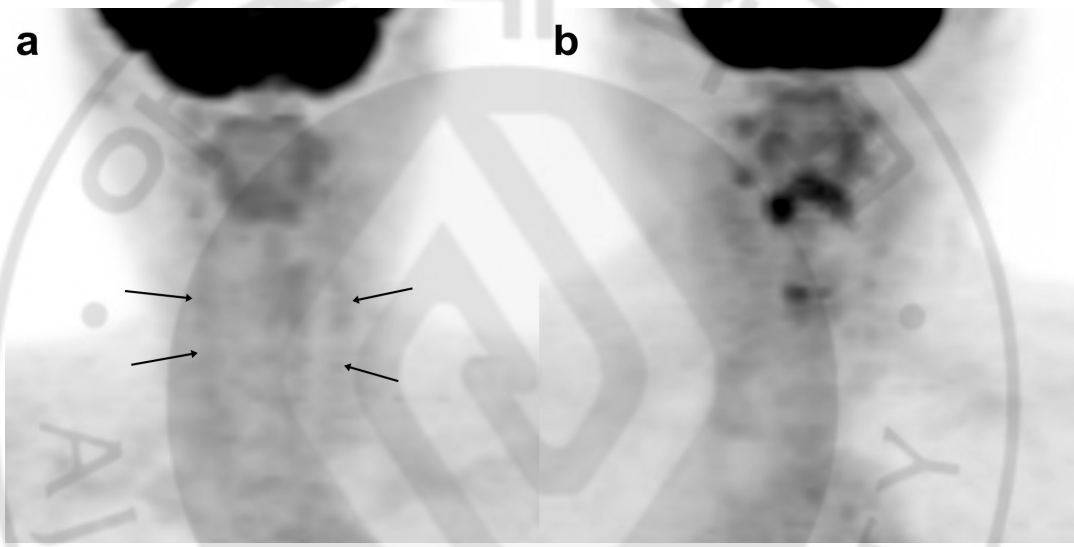

Fig 2. Representative maximum intensity of projection images of ^{18}F-FDG PET/CT. (a) A 66-year-old man without metabolic syndrome shows mildly increased FDG uptake along bilateral common carotid arteries (arrows). (b) A 63-year-old man with metabolic syndrome has no remarkable FDG uptake in bilateral carotid arteries. Framingham risk score of the subject with high uptake but no metabolic syndrome was comparable with that of subject with low uptake with metabolic syndrome (11.6 vs. 13.4).

IV. DISCUSSION

In the present study, we found that carotid artery FDG uptake was significantly associated with clinical cardiovascular risk factors, and the 10-year general cardiovascular risk (assessed using the FRS), in an asymptomatic population. As expected, both carotid artery FDG uptake and FRS were elevated in subjects with metabolic syndrome. Of such subjects, the hsCRP level was significantly higher in the high uptake than the low uptake group. Interestingly, among those with metabolic syndrome, the high uptake group had a significantly higher FRS than the low uptake group, whereas the FRS of the low uptake group with metabolic syndrome was comparable to that of the high uptake group without the syndrome.

We analyzed TBRglu along the full lengths of both common carotid arteries. Several studies have found that tumor FDG uptake is diminished during hyperglycemia (Wahl et al, 1992; Shepherd and Kahn, 1999). Although the need to apply a glucose correction to FDG uptake when noncancerous lesions are being studied is not well understood, one recent study evaluating carotid artery FDG uptake in type 2 diabetes patients observed that glucose-corrected FDG uptake parameters increased significantly as fasting blood glucose levels rose (Bucerius et al, 2012). Consistent with such findings, we noted that glucose-corrected FDG uptake values were significantly higher in hyperglycemic subjects. In addition, we found a weak ($r < 0.2$) and unexpected negative correlation between the presence of diabetes and glucose-uncorrected carotid artery FDG uptake. In addition, 60 of our subjects (20.7%) had high pre-scan glucose levels ($\geq$ 120mg/dl), and we thus used the TBRglu, a glucose-corrected FDG uptake parameter, in our work. Additionally, when we analyzed data using SUVglu, it was significantly

associated with FRS ($P < 0.001$), fasting plasma glucose ($P < 0.001$), hypertension ($P < 0.001$), diabetes ($P < 0.001$), and metabolic syndrome ($P < 0.001$). Multiple stepwise regression analysis showed that diabetes and metabolic syndrome were independent determinants of high SUVglu.

We found that high carotid FDG uptake was significantly associated with clinical cardiac risk factors including obesity, dyslipidemia, hypertension, male gender, and diabetes. This is in line with the results of previous investigations (Kaneko et al, 2013; Bucerius et al, 2012; Yun et al, 2002; Kim et al, 2010). We also found a significant association between carotid FDG accumulation, and the FRS and metabolic syndrome.

Recently, Tahara et al. described a positive association between metabolic syndrome components and FDG uptake in patients with carotid atherosclerosis (Tahara et al, 2007). Consistent with these data, we found that carotid FDG accumulation was significantly higher in those with metabolic syndrome. Moreover, the hsCRP levels of subjects with high carotid uptake and metabolic syndrome were significantly higher than those of subjects without the syndrome, and those of subjects with the syndrome but exhibiting low carotid uptake. The hsCRP level is an indicator of atherosclerotic activity during the initial stages of atherosclerosis (Hashimoto et al, 2001). Previous studies found that arterial FDG uptake increased significantly in areas of atherosclerotic plaques that were histologically macrophage-rich (Rudd et al, 2002; Tawakol et al, 2006). Thus, carotid artery FDG uptake and hsCRP concentration, both of which are inflammatory markers, reflect active inflammation during early stage carotid atherosclerosis. We thus suggest that development of atherosclerosis may accelerate more markedly in metabolic syndrome subjects with higher rather than lower uptake, as hsCRP levels rise. Interestingly, the general cardiovascular FRSs differed significantly when

metabolic syndrome subjects were stratified by carotid artery FDG activity. Those with high uptake scored significantly higher. Thus, carotid FDG uptake may help to stratify asymptomatic patients, identifying those needing active treatment such as anti-inflammatory pharmacotherapy.

The present study had several limitations. First, although we evaluated cardiovascular risk based on the FRS, our study was cross-sectional, and retrospective in nature. A longitudinal study with follow-up is needed. Second, our study population was heterogeneous. We included 42 patients with diabetes and 28 on statin medication. Among those with diabetes, 28 (9.7%) patients were taking oral hypoglycemic agents at the time of PET/CT, and 14 (4.8%) were newly diagnosed on screening. Although diabetes has been reported to significantly elevate arterial FDG uptake, we included diabetes patients in our current study because we wished to survey carotid artery FDG uptake in an asymptomatic general population. This is also why we did not exclude those taking statins which may attenuate arterial FDG uptake. Finally, we used only TBRglu for evaluation of carotid artery FDG uptake in the present study. The index may be affected by blood glucose level and the clinical significance of TBRglu has been limited. We now perform another study in a larger cohort to evaluate carotid artery FDG uptake using TBR, SUVglu and TBRglu.

V. CONCLUSION

High carotid FDG uptake in asymptomatic subjects was significantly associated with the presence of clinical cardiovascular risk factors and an elevated FRS. Of subjects with metabolic syndrome, those exhibiting high carotid uptake had significantly elevated hsCRP levels and FRSs. Therefore, carotid artery FDG activity may serve as a possible biomarker allowing cardiovascular risk stratification of asymptomatic populations.

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- 국문요약 -

심혈관 질환 증상이 없는 성인에서 목동맥 FDG 섭취와 심혈관계 질환 위험인자 간의 관계 고찰

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심혈관 질환은 동맥경화반이 염증과정의 진행에 따라 파열되어 생성된 혈색전에 의한 것으로 알려져 있다. 질환의 심각성에 대한 기존 방법인 내경의 협착 평가나 증상 분석에 비해 F-18 FDG PET/CT는 취약성 경화반의 상태를 더욱 잘 반영하는 것으로 보고되고 있다. 이에 본 연구에서는 경동맥 경화증에서의 FDG 섭취 정도와 Framingham risk score를 기반으로 한 심혈관 위험인자 사이의 관계를 분석하였고, F-18 FDG PET/CT가 향후 증상이 없는 성인을 대상으로 심혈관 질환의 예방적인 평가수단이 될 수 있는지 알아보고자 하였다. 건강검진 대상자 290명에 대해 FDG PET/CT를 시행하였다. PET/CT 영상은 양쪽 온목동맥의 Target-to-background ratio(TBR)을 공복혈당으로 보정한 TBRglu값을 얻었다. 각각의 대상자들에 대해 FRS와 대사증후군의 유무가 분석되었고, TBRglu 값과 대사증후군 상태, 임상적인 인자들 간의 통계분석이 이루어졌다. 온목동맥의 FDG 섭취 정도는 심혈관 위험인자와 유의한 관계가 있었다. 다중회귀분석 결과 중성지방, 당뇨, 대사증후군은 높은 TBRglu 값의 독립적인 결정인자였다. 대사증후군 있는 집단에서 온목동맥의 높은 FDG 섭취 정도는 높은 hsCRP값과 유의한 관계가 있었다. 대사증후군 없는 집단에서의 FRS 값은 온목동맥에서 낮은 FDG 섭취 정도를 보이는 집단에 비해 높은 FDG 섭취 정도를 보이는 집단에서 유의하게 높았으며 (13.1 ± 7.0 vs. 8.2 ± 7.4), 대사증후군 있는 집단에서도 같은 경향을 보였다 (21.8 ± 16.0 vs. 13.5 ± 11.9). 온목동맥의 높은 FDG 섭취

정도는 심혈관 위험인자와 상관관계가 있었으며 10년 후 심혈관 질환 위험도에도 높은 경향을 보였다. 대사증후군이 있는 집단에서는 온목동맥의 높은 FDG 섭취 정도가 높은 hsCRP과 FRS값과 유의한 관계를 보였다. 그러므로 온목동맥의 FDG 섭취 정도는 무증상의 일반인에서 심혈관 위험을 예측하는 하나의 생물학적 인자 역할을 할 수 있을 것이다.

핵심어: 동맥경화증, 온목동맥, 18F-FDG, 위험도 평가, 대사증후군, 심혈관계질환