Biological Antioxidant Potential Negatively Correlates With Carotid Artery Intima-Media Thickness

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SUMMARY

Oxidative stress is a crucial factor in the pathogenesis and development of cardiovascular disease. Recently, simplified methods for the detection of reactive oxygen species (ROS) using the derivatives of reactive oxygen metabolites (d-ROMs) test as an index of ROS products and the biological antioxidant potential (BAP) test as an index of antioxidant potential have been utilized. These methods are easy to perform, quick, inexpensive since they use small equipment, and provide reliable results compared with established oxidative stress and antioxidant markers. Because oxidative stress has been shown to represent the balance of production of ROS and antioxidant capacity, it is more appropriate to evaluate ROS and antioxidant capacity simultaneously. However, no study has examined the associations among d-ROMs, BAP values, and carotid artery intima-media thickness (IMT) concurrently. Therefore, we studied the associations among d-ROMs, BAP values, and the carotid artery IMT. Carotid artery IMT, blood pressure (BP), fasting circulating d-ROMs, BAP, glucose metabolism, lipid, and C-reactive protein levels were measured in 95 subjects (age: 49.5 ± 13.8 years; men: 41; women: 54), including 42 healthy subjects and 53 patients with hypertension, dyslipidemia, and diabetes mellitus who were not on medication. The results of multiple regression analysis revealed that dependent carotid artery IMT determinants remained significantly associated with age, systolic BP, total cholesterol, and BAP, whereas dependent BAP determinants remained significantly associated with body mass index and carotid artery IMT. BAP was strongly correlated with carotid artery IMT in our cohort. Our results suggest that BAP may be a useful risk marker for carotid atherosclerosis. (Int Heart J 2016; 57: 220-225)

Key words: Antioxidant markers, Carotid atherosclerosis, Oxidative stress

Oxidative stress is involved as a crucial factor in the pathogenesis and development of a variety of chronic and degenerative diseases, including aging, cancer, and cardiovascular disease. An enhanced oxidative stress status, defined as an imbalance between oxidants and antioxidants in favor of the former, plays a significant role in the onset and progression of atherosclerosis.¹⁻³⁾ Levels of oxidative stress markers, such as thiobarbituric acid-reactive substances (TBARSs),⁴⁾ 8-iso-prostaglandin (PG) F₂ α ,⁵⁾ oxidized low-density lipoprotein (LDL) (oxLDL),⁶⁾ and myeloperoxidase (MPO),^{7,8)} independently predict an increased risk for coronary artery disease (CAD). In contrast, glutathione peroxidase (GPx), superoxide dismutase (SOD), catalase enzymes, and total antioxidant status (TAS) are antioxidant markers that constitute the first line of defense against oxidative stress by removing key reactive oxygen species (ROS).⁹⁾ Meta-analyses of observational studies have identified inverse associations of circulating SOD, GPx, and catalase activity levels with CAD.¹⁰⁾ Furthermore, another study has demonstrated that a low GPx1

activity level was independently associated with an increased risk of cardiovascular events in patients with CAD.¹¹⁾

An increased carotid artery intima-media thickness (IMT) measured noninvasively by B-mode ultrasonography is considered a good surrogate marker for early atherosclerosis. It is reportedly associated with cardiovascular risk¹²⁾ and the severity of coronary atherosclerosis¹³⁾ and can predict cardiovascular events, such as myocardial infarction and stroke, in several populations.¹⁴⁾ Progression of carotid artery IMT is prevented by intensive lipid-lowering therapy.^{15,16)} With regard to the relationship between oxidative stress markers and carotid artery IMT, several clinical studies have reported that circulating levels of TBARS in chronic hemodialysis¹⁷⁾ and type 2 diabetic patients,¹⁸⁾ oxLDL in asymptomatic familial combined hyperlipidemia families,¹⁹⁾ and MPO in hemodialysis patients²⁰⁾ were positively correlated with carotid artery IMT. Furthermore, increased urinary excretion of 8-iso-PG F₂ α was also associated with increased carotid artery IMT.²¹⁾ In contrast, several clinical studies have demonstrated correlations between antioxidant

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markers and carotid artery IMT: SOD activity in diabetic patients,¹⁸⁾ catalase activity in chronic hemodialysis¹⁷⁾ and type 2 diabetic patients,¹⁸⁾ and serum TAS in workers occupationally exposed to mercury vapor²²⁾ were negatively correlated with carotid artery IMT.

Nonetheless, assays used for determination of the above-mentioned oxidative stress and antioxidant markers are complicated. Recently, several studies utilizing simplified methods for the detection of ROS using the derivatives of reactive oxygen metabolites (d-ROMs) test and the biological antioxidant potential (BAP) test have been published.²³⁻²⁵⁾ These methods are easy to perform, quick, inexpensive, utilize small equipment, and provide reliable results compared with established oxidative stress and antioxidant markers.^{26,27)}

Because oxidative stress has been shown to represent the balance of production of ROS and antioxidant capacity, it is more appropriate to evaluate ROS and antioxidant capacity simultaneously. However, only one study has reported an association between d-ROMs and carotid artery IMT in patients with hypercholesterolemia,²⁸⁾ and, thus far, no study has examined the associations among d-ROMs, BAP values, and carotid artery IMT concurrently. Therefore, we measured d-ROMs and BAP values as indices for ROS production and antioxidant potential, respectively, and carotid artery IMT within the same subjects to investigate the association between carotid artery IMT and clinical parameters values, including d-ROMs and BAP.

METHODS

Subjects: A total of 195 consecutive Japanese subjects who visited our department for assessment of cardiovascular risk or disease participated in this study. Medical and familial histories were obtained from all subjects. Subjects with the following conditions that could potentially significantly influence carotid artery IMT, blood pressure (BP), circulating lipids, and glucose metabolism were excluded from the study: those with a history of cardiovascular disease, including stroke, CAD, thromboembolic disease, or congestive heart failure; peripheral arterial disease; malignancy; infectious disease; liver or renal disease; overt endocrine disease; and current smokers and those currently on medication. Subjects with hypertension, dyslipidemia, and diabetes mellitus (DM), as defined by the established diagnostic criteria,²⁹⁻³¹⁾ were included. Written informed consent was obtained from each subject, and the study was approved by the institutional review board of Gunma University Hospital.

We performed physical examinations and carotid artery IMT measurements in the morning (after a 12-hour fast) and simultaneously obtained blood samples from the antecubital vein for serum and plasma analyses.

Physical examination: The height and weight of subjects were measured, and the body mass index (BMI) was calculated (weight in kilograms divided by height in meters squared). BP was measured in the morning (after a 12-hour overnight fast) by the same investigator with a sphygmomanometer on the right arm of the subject after a 10-minute rest in the supine position.

Laboratory analyses: Serum total cholesterol, triglyceride, high-density lipoprotein (HDL) cholesterol, and LDL chole-

sterol concentrations were measured by enzymatic methods, and C-reactive protein concentrations were measured by latex immunoassay, respectively, using an automatic analyzer (LA-BOSPECT 008; Hitachi, Tokyo). Serum insulin concentrations were measured by chemiluminescence immunoassay using an automatic analyzer (AIA-2000 LA; Tosoh, Tokyo). Plasma glucose concentrations were measured by a hexokinase method, and hemoglobin A1c (HbA1c) levels were measured by high-performance liquid chromatography, using automatic analyzers (ADAMS Glucose GA-1170 and ADAMS A1c HA-8180, respectively; Arkray, Tokyo).

Measurement of d-ROMs and BAP: Based on the recommendation from the manufacturer (Diacron International, Grosseto, Italy), all analyses were performed within 48 hours of venous blood collection to avoid false high or false low results. To analyze serum levels of ROS and serum antioxidant potential, d-ROMs and BAP tests were performed, respectively.

The d-ROMs were measured using a free radical elective evaluator (FREE Carpe Diem; Diacron International) that included a spectrophotometric device reader, and measurement kits (d-ROMs test) (Wismerll Co. Ltd., Tokyo) were optimized to the FREE Carpe Diem System according to the manufacturer's protocol. Briefly, a 20 μ L serum sample and 1 mL buffered solution (R2 kit reagent, pH 4.8) were gently mixed in a cuvette, and 20 μ L of chromogenic substrate (R1 kit reagent) was then added to the cuvette. After mixing well, the cuvette was immediately incubated in the thermostatic block of the analyzer for 5 minutes at 37°C, and absorbance at 505 nm was recorded.²³⁻²⁵⁾ The results are expressed in arbitrary units (U. CARR), one unit of which corresponds to 0.8 mg/L of hydrogen peroxide.²³⁻²⁵⁾

The BAP was measured using a free radical elective evaluator (FREE Carpe Diem) that included a spectrophotometric device reader, and measurement kits (BAP test) (Wismerll Co. Ltd.) were optimized to the FREE Carpe Diem System according to the manufacturer's protocol. Briefly, 50 μ L of chromogenic substrate (R2 kit reagent) and 1 mL of reactive solution (R1 kit reagent) were gently mixed in a cuvette, and absorbance at 505 nm was recorded. A 10 μ L serum sample was then immediately added to the cuvette. After mixing well, the cuvette was immediately incubated in the thermostatic block of the analyzer for 5 minutes at 37°C, and absorbance at 505 nm was recorded.²³⁻²⁵⁾ The results are expressed in mmol/L of reduced ferric ions.

Carotid artery IMT measurement: The wall thickness of the carotid artery was evaluated bilaterally by ultrasonography (LOGIQ 9; GE Healthcare Japan Corporation) using a 7.5-MHz linear type B-mode probe.³²⁻³⁴⁾ After the subject had rested for at least 10 minutes in the supine position with the neck in slight hyperextension, visualization of the bilateral common carotid arteries was optimized, and three measurements of end-diastolic IMT of the far wall of each artery were averaged: one at the thickest site and the other two measurements from 1 cm upstream and 1 cm downstream from the thickest site. A physician who was blinded to the clinical characteristics of the subjects evaluated all scans. The variability of the ultrasonographic measurements was assessed by performing 5 measurements over a 1-month period in 12 volunteers. The intraobserver coefficient of variation for the IMT measurement was 5.5% $\pm$ 0.8%.

Statistical analyses: Data are expressed as the mean $\pm$ stand-

ard deviation. Pearson's correlation coefficient analysis was used to examine the relationships between carotid artery IMT values and clinical parameters values, including d-ROMs, BAP, and other clinical variables, and between BAP values and clinical parameters values, including carotid artery IMT and other clinical variables. We chose the clinical parameters of significant correlation with carotid artery IMT by Pearson's correlation coefficient analysis as candidate confounding factors. Multiple regression analysis for correlation between carotid artery IMT as a dependent variable and these clinical parameters values as independent variables was then performed. In addition, we chose clinical parameters of significant correlation with BAP values by Pearson's correlation coefficient analysis as candidate confounding factors. Multiple regression analysis for correlation between BAP values as a dependent variable and these clinical parameters values as independent variables was then performed. All the probability values were two tailed. $P < 0.05$ was considered statistically significant for all analyses performed. All statistical analyses were performed using IBM SPSS software (version 21.0).

RESULTS

Clinical characteristics and complications: Of the 195 subjects available during the study period, 95 met the inclusion criteria. The average age was 49.5 ± 13.8 years (range, 23–77 years), and the cohort consisted of 41 men (age: 52.3 ± 14.8 years; range, 24–77 years) and 54 women (age: 47.3 ± 12.8 years; range, 23–68 years). We included 42 healthy subjects, 23 subjects with essential hypertension, 44 with dyslipidemia, and 8 with type 2 diabetes mellitus. The characteristics of the subjects are summarized in Table I.

Univariate and multivariate analyses for correlations with carotid artery IMT: The results of the univariate regression analysis revealed that carotid artery IMT was positively correlated with age ($r = 0.730$, $P < 0.001$), systolic BP ($r = 0.586$, $P < 0.001$), diastolic BP ($r = 0.536$, $P < 0.001$), fasting plasma

glucose ($r = 0.254$, $P = 0.013$), HbA1c ($r = 0.287$, $P = 0.005$), total cholesterol ($r = 0.474$, $P < 0.001$), triglycerides ($r = 0.281$, $P = 0.006$), and LDL cholesterol ($r = 0.506$, $P < 0.001$) and negatively correlated with HDL cholesterol ($r = -0.205$, $P = 0.047$) and BAP ($r = -0.484$, $P < 0.001$; Figure 1). There were no significant associations between carotid artery IMT and clinical parameters, including d-ROMs (Figure 2) and other clinical variables (Table II). In addition, the results of the multiple regression analysis, including age, systolic BP, diastolic

Table I. Subject Characteristics

Variable	Subjects
Number	95
Age (years)	49.5 ± 13.8
Sex (M/F)	41/54
Body mass index (kg/m^2)	22.4 ± 3.4
Normal healthy participants [n (%)]	42 (44)
Hypertension [n (%)]	23 (24)
Dyslipidemia [n (%)]	44 (46)
Diabetes mellitus [n (%)]	8 (8)
Systolic BP (mmHg)	121.4 ± 15.4
Diastolic BP (mmHg)	78.3 ± 10.8
Fasting plasma glucose (mg/dL)	100.0 ± 25.1
HbA1c (%)	5.8 ± 1.2
Insulin ($\mu\text{U}/\text{mL}$)	5.7 ± 4.5
eGFR ($\text{mL}/\text{minute}/1.73 \text{ m}^2$)	87.0 ± 15.7
C-reactive protein (mg/dL)	0.09 ± 0.15
Total cholesterol (mg/dL)	213.0 ± 41.7
HDL cholesterol (mg/dL)	59.3 ± 13.9
Triglycerides (mg/dL)	106.0 ± 54.4
LDL cholesterol (mg/dL)	125.2 ± 36.7
d-ROMs (U.CARR)	377.2 ± 82.1
BAP ($\mu\text{mol}/\text{L}$)	2395.4 ± 359.9
Carotid artery IMT (mm)	0.66 ± 0.14

The results are presented as the mean $\pm$ SD. BAP indicates biological antioxidant potential; BP, blood pressure; d-ROMs, derivatives of reactive oxygen metabolites; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; IMT, intima-media thickness; and LDL, low-density lipoprotein.

Figure 1. Correlation between carotid artery intima-media thickness (IMT) and biological antioxidant potential (BAP) in subjects. The results of the univariate regression analysis revealed a negative correlation between carotid artery IMT and BAP ($r = -0.484$, $P < 0.001$).

Figure 2. Correlation between carotid artery intima-media thickness (IMT) and derivatives of reactive oxygen metabolites (d-ROMs) in subjects. The results of the univariate regression analysis revealed no correlation between carotid artery IMT and d-ROMs ($r = 0.005$, $P = 0.962$).

Table II. Pearson's Correlation Coefficients Between Carotid Artery Intima-Media Thickness Values and Clinical Parameters Values, Including Derivatives of Reactive Oxygen Metabolites, Biological Antioxidant Potential, and Other Clinical Variables

Variable	<i>r</i>	<i>P</i>
Age (years)	0.730	< 0.001
Body mass index (kg/m ²)	0.193	0.061
Systolic BP (mmHg)	0.586	< 0.001
Diastolic BP (mmHg)	0.536	< 0.001
Fasting plasma glucose (mg/dL)	0.254	0.013
HbA1c (%)	0.287	0.005
Insulin (μ U/mL)	-0.037	0.723
C-reactive protein (mg/dL)	0.078	0.452
Total cholesterol (mg/dL)	0.474	< 0.001
HDL cholesterol (mg/dL)	-0.205	0.047
Triglycerides (mg/dL)	0.281	0.006
LDL cholesterol (mg/dL)	0.506	< 0.001
d-ROMs (U.CARR)	0.005	0.962
BAP (μ mol/L)	-0.484	< 0.001

BAP indicates biological antioxidant potential; BP, blood pressure; d-ROMs, derivatives of reactive oxygen metabolites; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; and LDL, low-density lipoprotein.

Table III. Independent Predictors of Carotid Artery Intima-Media Thickness by Multiple Regression Analysis

Variable	β	<i>P</i>
Age (years)	0.481	< 0.001
Systolic BP (mmHg)	0.441	< 0.001
Diastolic BP (mmHg)	-0.190	0.127
Fasting plasma glucose (mg/dL)	-0.019	0.894
HbA1c (%)	0.012	0.933
Total cholesterol (mg/dL)	0.151	0.041
BAP (μ mol/L)	-0.176	0.015

BAP indicates biological antioxidant potential; BP, blood pressure; and HbA1c, hemoglobin A1c.

BP, fasting plasma glucose, HbA1c, total cholesterol, and BAP revealed that dependent carotid artery IMT determinants remained significantly associated with age, systolic BP, total cholesterol, and BAP (Table III).

Univariate and multivariate analyses for correlations with BAP: Accordingly, we performed univariate and multivariate analyses for correlations between BAP and clinical parameters, including carotid artery IMT and other clinical variables. The results of the univariate regression analysis revealed that BAP was positively correlated with HDL cholesterol ($r = 0.216$, $P = 0.035$) and negatively correlated with age ($r = -0.416$, $P < 0.001$), BMI ($r = -0.305$, $P = 0.003$), systolic BP ($r = -0.247$, $P = 0.016$), diastolic BP ($r = -0.297$, $P = 0.004$), fasting plasma glucose ($r = -0.211$, $P = 0.040$), total cholesterol ($r = -0.382$, $P < 0.001$), triglycerides ($r = -0.392$, $P < 0.001$), LDL cholesterol ($r = -0.356$, $P < 0.001$), and carotid artery IMT ($r = -0.484$, $P < 0.001$; Figure 1). BAP did not significantly correlate with HbA1c, insulin, or C-reactive protein (Table IV). Furthermore, the results of the multiple regression analysis, including age, BMI, systolic BP, diastolic BP, fasting plasma glucose, total cholesterol, and carotid artery IMT revealed that dependent BAP determinants remained significantly associated with BMI and carotid artery IMT (Table V).

Table IV. Pearson's Correlation Coefficients Between Biological Antioxidant Potential Values and Clinical Parameters Values, Including Carotid Artery Intima-Media Thickness and Other Clinical Variables

Variable	<i>r</i>	<i>P</i>
Age (years)	-0.416	< 0.001
Body mass index (kg/m ²)	-0.305	0.003
Systolic BP (mmHg)	-0.247	0.016
Diastolic BP (mmHg)	-0.297	0.004
Fasting plasma glucose (mg/dL)	-0.211	0.040
HbA1c (%)	-0.197	0.056
Insulin (μ U/mL)	-0.112	0.280
Total cholesterol (mg/dL)	-0.382	< 0.001
HDL cholesterol (mg/dL)	0.216	0.035
Triglycerides (mg/dL)	-0.392	< 0.001
LDL cholesterol (mg/dL)	-0.356	< 0.001
C-reactive protein (mg/dL)	-0.098	0.344
Carotid artery IMT (mm)	-0.484	< 0.001

BP indicates blood pressure; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; IMT, intima-media thickness; and LDL, low-density lipoprotein.

Table V. Independent Predictors of Biological Antioxidant Potential by Multiple Regression Analysis

Variable	β	<i>P</i>
Age (years)	-0.094	0.510
Body mass index (kg/m ²)	-0.252	0.013
Systolic BP (mmHg)	0.146	0.395
Diastolic BP (mmHg)	0.000	0.999
Fasting plasma glucose (mg/dL)	-0.060	0.522
Total cholesterol (mg/dL)	-0.172	0.101
Carotid artery IMT (mm)	-0.356	0.017

BP indicates blood pressure; and IMT, intima-media thickness.

DISCUSSION

In the present study, we have demonstrated, for the first time, that carotid artery IMT was positively correlated with age, systolic BP, and total cholesterol, negatively correlated with BAP, and did not correlate with d-ROMs, and that BAP was negatively correlated with BMI and carotid artery IMT. BAP was strongly correlated with carotid artery IMT. The advantages of usage of BAP are that the method is easy to perform, quick, inexpensive, utilizes small equipment, and provides reliable results compared with established antioxidant markers.^{26,27)}

Dursun, *et al* reported that catalase activity was inversely correlated with carotid artery IMT in uremic and hemodialysis patients¹⁷⁾ and that erythrocyte Cu/Zn SOD and catalase activities were negatively correlated with carotid artery IMT in type 2 diabetic patients undergoing hemodialysis and those with normal renal function.¹⁸⁾ Skoczyńska, *et al* also demonstrated a negative linear correlation between serum TAS and carotid artery IMT in workers occupationally exposed to mercury vapor.²²⁾ These findings that have reported an inverse association between antioxidant markers and carotid artery IMT are compatible with the results of the present study.

In addition, Demirbag, *et al* found a negative correlation

between plasma TAS and thoracic aortic IMT in patients without a history of atherosclerotic cardiovascular disease.³⁵⁾ Since there is a strong and statistically significant positive correlation between the assays for BAP and TAS,³⁶⁾ BAP may potentially be negatively correlated with thoracic aortic IMT. In the present study, subjects with dyslipidemia, diabetes mellitus, and hypertension were included. Although there were differences in both the study populations and the methods used to assess antioxidant markers and IMT between the aforementioned studies and the present study, the findings of the aforementioned studies support the results of our study. Hence, BAP negatively correlated with carotid artery IMT in our subjects.

Conversely, Kotani, *et al* reported that d-ROMs were positively correlated with carotid artery IMT in patients with hypercholesterolemia.²⁸⁾ However, our findings showed that d-ROMs were not correlated with carotid artery IMT in our cohort. Forty-four percent of the subjects in our cohort were either healthy participants or subjects with mild disease conditions, which is likely reflected in the relatively narrow range of carotid artery IMT values between 0.44 and 1.12 mm in our cohort and may be responsible for the lack of significant associations between d-ROMs and carotid artery IMT.

The mechanisms underlying the negative correlation between BAP and carotid artery IMT in subjects in this study are not fully understood. However, several credible mechanisms linking antioxidant markers with atherogenic processes should be considered. Among antioxidant enzymes, SOD, GPx, and catalase constitute the first line of defense against oxidative stress by removing the key ROS.⁹⁾ Several observational studies have demonstrated that low SOD, GPx, and catalase activity levels were associated with high risk of CAD.¹⁰⁾ Conversely, high GPx and SOD activity levels may confer protection against ROS production. Overexpression of GPx³⁷⁾ or intracellular SOD³⁸⁾ in transgenic mouse models of reperfusion injury prevents postischemic free radical injury and inhibits LDL oxidation in endothelial cells. Furthermore, overexpression of SOD³⁹⁾ or administration of exogenous SOD⁴⁰⁾ or catalase^{40,41)} has been shown to attenuate leukocyte adhesion to endothelial cells, while SOD or catalase administration has been shown to suppress vascular smooth muscle cell proliferation induced by oxLDL.^{42,43)} Thus, the levels of antioxidant markers may inversely correlate with the development of carotid atherosclerosis and, consequently, may underlie the strong inverse relationship between BAP levels and carotid artery IMT.

With regard to the relationship between carotid artery IMT and pro-atherosclerotic factors, such as BMI and HbA1c, Wang, *et al* demonstrated that carotid artery IMT had a positive correlation with age, gender, having DM, BMI, and HbA1c in middle-aged and elderly Chinese people and that BMI, HbA1c, and having DM predicted carotid artery IMT thickening remained significant after adjusting for age and gender.⁴⁴⁾ However, the present study showed that HbA1c and BMI did not correlate with carotid artery IMT. The subjects of the present study had lower mean HbA1c (5.8% versus 7.4%) and mean BMI levels (22.4 kg/m² versus 25.6 kg/m²) and a lower prevalence of DM (8% versus 68.8%) than the subjects of the aforementioned study. Therefore, the differences in the background of the subjects may have contributed to the difference between the results of the present study and the results of the aforementioned study.

This is the first study that investigated the relationship be-

tween BAP and pro-atherosclerotic factors, such as BMI, total cholesterol, fasting plasma glucose, and blood pressure. The results of multiple regression analysis revealed that BAP significantly correlated with BMI and carotid artery IMT, but did not significantly correlate with blood pressure and fasting plasma glucose. Total cholesterol was slightly correlated with BAP ($P = 0.101$), however, the correlation was not significant.

The d-ROMs and BAP as oxidative stress and antioxidant markers have advantages and disadvantages compared with other oxidative stress and antioxidant markers, respectively.^{26,27)} The advantages of these oxidative stress, and antioxidant markers are that the methods are easy to perform (they do not require skilled operators or complex instrumentation), quick, inexpensive, utilize small equipment, and provide reliable results compared with established oxidative stress and antioxidant markers.^{26,27)} In contrast, the disadvantages of these markers are that the specificity is not established and they are probably not suitable for samples stored for prolonged periods compared with established ones.^{26,27)} In the present study, we used simpler methods such as d-ROMs as an indicator of ROS production and BAP as a readout for antioxidant potential. However, BAP alone was significantly correlated with carotid artery IMT. Thus, the measurements of BAP may be superior to the measurements of GPx, SOD, catalase, and TAS for the assessment of antioxidant potential due to their simplicity, quickness, convenience, and reproducibility.

The present study has several limitations. First, the number of subjects was relatively small, and a larger cohort will be necessary to confirm our findings. Second, the study may have had a bias in the enrollment of study subjects. Finally, as a cross-sectional study, it was not possible to determine a cause-and-effect relationship between BAP and carotid artery IMT.

In conclusion, BAP was strongly correlated with carotid artery IMT. Our results suggest that BAP may be a useful risk marker for carotid artery atherosclerosis. Further studies are needed to determine whether the correlation between BAP and carotid artery IMT exists not only in subjects with coronary risk factors or CAD, but also in subjects with no health issues.

DISCLOSURE

There are no conflicts of interest to declare.

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