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Metabolism Clinical and Experimental 60 (2011) 537 – 543
Metabolism
Clinical and Experimental
www.metabolismjournal.com

Association of serum lycopene and brachial-ankle pulse wave velocity with metabolic syndrome

Hyun Yang Yeo[a,b,c,1], Oh Yoen Kim[a,b,1], Hyo Hee Lim[b], Ji Young Kim[a,b], Jong Ho Lee[a,b,c,*]

[a]Yonsei University Research Institute of Science for Aging, Yonsei University, Seoul, South Korea
[b]National Research Laboratory for Clinical Nutrigenetics/Nutrigenomics, Department of Food and Nutrition, Yonsei University, Seoul, South Korea
[c]Interdisciplinary Course of Science for Aging, Graduate School, Yonsei University, Seoul, South Korea

Received 19 January 2010; accepted 4 May 2010

Abstract

Metabolic syndrome (MetS) is known to inversely correlate with antioxidant status. Recently, it has been reported that MetS is associated with arterial stiffness, a composite risk factor for early atherosclerosis. In addition, our recent study for healthy women showed an inverse relationship between arterial stiffness and circulating lycopene. Therefore, this study aimed to investigate the interrelationship between arterial stiffness, antioxidant status, and the risk of MetS. Korean men (N = 299) were subgrouped according to the number of MetS risk factors (RF 0, RF 1-2, RF ≥3). Anthropometric parameters, brachial-ankle pulse wave velocity (baPWV; a marker of arterial stiffness), antioxidants (lycopene, β-carotene, α-tocopherol), lipid profiles, glucose, insulin, and oxidative stress (low-density lipoprotein [LDL] particle size, oxidized LDL) were measured. Corresponding to the number of MetS RF, baPWV (1306 ± 17, 1364 ± 16, and 1420 ± 33 cm/s; $P < .001$) and insulin resistance (1.5 ± 0.1, 1.9 ± 0.1, and 2.7 ± 0.2; $P < .001$) gradually increased after adjustment for age, body mass index, smoking, and drinking, whereas serum lycopene among antioxidants and LDL particle size gradually decreased (0.036 ± 0.001, 0.031 ± 0.001, and 0.028 ± 0.001 mmol/L; $P = .004$ and 23.9 ± 0.1, 23.7 ± 0.1, and 23.3 ± 0.1 nm; $P < .001$, respectively). Brachial-ankle pulse wave velocity inversely correlated with serum lycopene after adjustment for the above confounders, blood pressure, insulin resistance, and oxidative stress ($r = -0.136$, $P < .05$). Oxidative stress markers also significantly correlated with baPWV as well as serum lycopene. Study subjects were divided into 2 groups by the median level of serum lycopene. When serum lycopene was lower than median level (≤0.0294 mmol/L), baPWV was significantly higher in MetS subjects than non-MetS subjects (1436 ± 41 vs 1367 ± 23 cm/s) after adjustment for age, body mass index, smoking, drinking, and oxidative stress ($P = .041$). However, when serum lycopene levels were high, no statistically significant difference was observed between the 2 subject groups (1386 ± 36 vs 1326 ± 13 cm/s). In conclusion, our result shows the interrelationship between circulating lycopene, baPWV, and MetS. In addition, much enhanced baPWV in MetS may be associated with lower lycopene concentration.

1. Introduction

Metabolic syndrome (MetS) is a cluster of metabolic abnormalities including central obesity, hypertension, dyslipidemia (ie, hypertriglyceridemia and low concentration of high-density lipoprotein [HDL] cholesterol), glucose intolerance, and insulin resistance (IR), which further increase the risk of type 2 diabetes mellitus (DM) and cardiovascular disease (CVD) [1-3]. Some recent studies have shown the inverse association of diet rich in fruits and vegetables and serum antioxidants status with MetS [4-7]. Low intake or low serum concentrations of vitamins and carotenoids were associated with the increased risk of MetS [6,7]. Among carotenoids, lycopene has been the most powerful antioxidant detected in human biological specimens [8,9]. Low concentration of plasma lycopene was associated with early carotid atherosclerotic lesions and increased intima-media thickness of the carotid artery wall [10-12]. Dietary intervention with either lycopene-containing foods or supplementation showed potential short-term improvement in low-density lipoprotein (LDL) oxidation [13,14]. Lycopene may enhance LDL degradation by

There is no conflict of interest on this study.

* Corresponding author. Department of Food and Nutrition, Yonsei University, Seoul 120-749, South Korea. Tel.: +82 2 2123 3122; fax: +82 2 364 9605.
E-mail address: jhleeb@yonsei.ac.kr (J.H. Lee).

[1] These 2 authors equally contributed to the work.

0026-0495/$ – see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.metabol.2010.05.003

inhibiting cholesterol synthesis [14,15] and effectively suppress adhesion molecule and monocyte adhesion to endothelial cells [11,16,17].

In addition, emerging evidences have demonstrated the association of MetS with arterial stiffness. Arterial stiffness is a predictor for cardiovascular morbidity and mortality [18] as well as a composite risk factor for early atherosclerosis [19,20]. It has been reported that a persistent MetS status exacerbated the severity of arterial stiffness [21,22] and that the improvement of MetS status could attenuate the progression of vascular damage [23]. Brachial-ankle pulse wave velocity (baPWV) has been commonly measured because it is a simple and noninvasive index for the severity of arterial stiffness and reflects the early atherosclerotic change [18,19,24-26].

A recent study of our groups shows an inverse correlation between circulating lycopene and arterial stiffness in healthy women [24]. However, to our knowledge, there has been no study for the investigation of the interrelationship between arterial stiffness, serum antioxidant concentration, and the risk of MetS. Therefore, this study aimed to investigate the association between baPWV, serum lycopene levels, and MetS risk. In addition, we examined other related markers such as oxidative stress and IR.

2. Subjects and methods

2.1. Study subjects

Study participants were recruited from the Health Service Center in the course of a routine checkup visit or by a newspaper announcement for health examination (January 2007∼March 2008). Subjects were excluded if they have orthopedic limitations, weight loss/gain over the previous 6 months, or any diagnosis of vascular disease, DM, cancer (clinically or by anamnesis), renal disease, liver disease, thyroid disease, and acute or chronic inflammatory diseases. Definition of MetS followed a modification of the National Cholesterol Education program–Adult Treatment Panel III guideline, Asian-Pacific guideline, and American Diabetes Association guideline. This definition includes at least 3 of the following components: (1) waist circumference greater than 90 cm (men), (2) triglyceride (TG) at least 150 mg/dL, (3) HDL cholesterol less than 40 mg/dL (men), (4) blood pressure at least 130/at least 85 mm Hg, and (5) fasting glucose at least 100 mg/dL (but fasting glucose ≥126 mg/mL was classified as DM). *Non-Mets healthy subjects* were defined as no history or diagnosis of MetS, impaired glucose tolerance, DM, and the diseases mentioned above. None of the subjects were taking any medications (antihypertensive, antidyslipidemic, antithrombotic, and antidiabetic drugs). During the recruitment period, about 65% of total people who visited the Center were found to be healthy without MetS or any other disease; and about 25% of total people were found to have MetS. Among them, those who satisfied the study criteria were recommended to participate in this study for further biochemical measurement. Finally, 80% of subjects who got the recommendation (genetically unrelated Korean men) consented to participate in the study (N = 299). Written informed consent was obtained from all subjects, and the protocol was approved by the Institute of Review Board of Yonsei University.

2.2. Anthropometric parameters and blood collection

Body weight and height were measured unclothed and without shoes in the morning. Body mass index (BMI) was calculated as body weight in kilograms divided by height in square meters. Blood pressure was obtained from the left arm of seated patients with an automatic blood pressure monitor (TM-2654; A&D, Tokyo, Japan) after 20 minutes of rest. Study subjects were interviewed for their smoking and drinking behavior at their visit. Smoking habit was categorized as "current smoker" and "nonsmoker," and drinking habit was also categorized as "current drinker (current alcohol consumption)" and "nondrinker." Nonsmoker or nondrinker included both never- and ex-consumer. *Ex-smoker* and *ex-drinker* were defined as subjects who stopped their smoking or drinking habit at least 1 year before participating in this study. In addition, the number of cigarette smoked per day was examined. Regarding alcohol consumption, the kind and the amount of alcohol were also examined; and then the amount of alcohol (in grams) per day was calculated. After overnight fast, venous blood specimens were collected in EDTA-treated and plain tubes. The tubes for antioxidant analysis were immediately covered with aluminum foil and placed on ice in the dark until they arrived at the analytical laboratory (within 1-3 hours). Afterward, the blood specimens were separated into plasma or serum, and stored at −70°C until analysis.

2.3. Serum lycopene, β-carotene, and α-tocopherol

Ultraperformance liquid chromatography (UPLC; Waters, Milford, MA) was used to determine α-tocopherol, lycopene, and β-carotene in serum. The UPLC system was composed of a Waters Acquity UPLC, Waters tunable UV detector, sample manager module (autosampler), and column compartment/heater, both enabling temperature control. Data were collected and processed by Empower chromatographic software (Waters, Milford, MA, USA). Waters tunable UV detector was set at 294 nm for α-tocopherol and 450 nm for lycopene and β-carotene. Concentrations of α-tocopherol, lycopene, and β-carotene in serum were reported as uncorrected or corrected concentrations, expressed as the sum of the serum total cholesterol and triglycerides (in millimoles per liter).

2.4. Brachial-ankle pulse wave velocity

Brachial-ankle pulse wave velocity was measured using an automatic waveform analyzer (model VP-1000; Nippon Colin, Komaki, Japan). Subjects were examined

in the supine position after 5 minutes of bed rest. Electrocardiogram electrodes were placed on both wrists, and a microphone for the phonogram was placed on the left edge of the sternum. Pneumonic cuffs were wrapped around both upper arms and ankles and connected to a plethysmographic sensor to determine the volume pulse waveform. Waveforms for the upper arm (brachial artery) and ankle (tibial artery) were stored for 10-second sample times with automatic gain analysis and quality adjustment. An oscillometric pressure sensor was attached to the cuffs to measure blood pressure at the 4 extremities. The baPWVs were recorded using a semiconductor pressure sensor (1200 Hz sample acquisition frequency) and calculated using the equation (La − Lb)/ΔTba. *La* and *Lb* were defined as the distance from the aortic valve to the elbow and to the ankle, respectively. The distance from the suprasternal notch to the elbow (La) and that from the suprasternal notch to the ankle (Lb) were expressed by La = [0.2195 × height of subject (in centimeters)] − 2.0734 and Lb = [0.8129 × height of subject (in centimeters)] + 12.328. The time interval between arm and ankle distance (*ΔTba*) was defined as the pulse transit time between brachial and tibial arterial pressure waveforms. The average baPWVs from both the left and right sides were used for the analysis (correlation between the right and left baPWVs: r^2 = 0.925, P = .000). The coefficients of variation for inter- and intraobserver variability were 1.54% and 1.73%, respectively.

2.5. Serum lipid profile

Serum total cholesterol and triglycerides were measured using commercially available kits on a Hitachi 7150 Autoanalyzer (Hitachi, Tokyo, Japan). High-density lipoprotein cholesterol was measured by an enzymatic method, and LDL cholesterol was indirectly estimated in subjects with triglyceride less than 400 mg/mL using the Friedewald formula.

2.6. Glucose, insulin, and IR

Serum glucose was measured by a glucose oxidase method using a Glucose Analyzer (Beckman Instruments, Irvine, CA). The measurement of insulin was performed using radioimmunoassays with commercial kits (Immuno Nucleo, Stillwater, MN). Insulin resistance was calculated with the homeostasis model assessment (HOMA) using the following equation: HOMA-IR = [fasting insulin (in micro–international units per milliliter) × fasting insulin (in millimoles per liter)]/22.5.

2.7. Plasma LDL particle size and oxidized LDL

Particle size distribution of LDL (1.019-1.063 g/mL) isolated by sequential flotation ultracentrifugation was examined by a pore-gradient lipoprotein system (CBS Scientific, Del Mar, CA) using commercially available nondenaturing polyacrylamide slab gels (Alamo Gels, San Antonio, TX). Standards of latex beads (34 nm), thyroglobulin (17 nm), apoferritin (12.2 nm), and catalase (10.4 nm) were used to estimate the relative migration (Rf) rates of each band. The gels were scanned by a GS-800 Calibrated Imaging Densitometer (Bio-Rad Laboratories, Graz, Austria). The LDL particle size was calculated with reference to the Rf value of the standards. Plasma oxidized LDL (oxLDL) was measured by using an enzyme immunoassay (Mercodia, Uppsala, Sweden). The resultant color reaction was read at 450 nm with a Wallac Victor^2 multilabel counter (Perkin Elmer Life Sciences, Turku, Finland).

2.8. Data analysis

Statistical analyses were performed with SPSS version 12.0 for Windows (Statistical Package for the Social Science, Chicago, IL). Subjects (men and women, separately) were subgrouped according to the number of MetS risk factors (RF 0, RF 1-2, and RF ≥3) or according to serum lycopene concentration (low or high: split by median level). The differences were tested by 1-way analysis of variance (ANOVA) with Bonferroni method or general linear model (GLM) with adjustment for confounders. Results were expressed at mean ± standard error (SE). The noncontinuous variables were tested by χ^2 test and expressed as percentage. Pearson and partial correlation coefficients were used for better understanding of the relationship between baPWV, serum lycopene, and the components of MetS risk. A 2-tailed value of $P < .05$ was considered statistically significant.

3. Results

3.1. Clinical and biochemical parameters according to the number of MetS risk factors

Table 1 and Fig. 1 present clinical and biochemical parameters according to the number of MetS risk factor (RF 0, RF 1-2, and RF ≥3). The levels of each MetS component gradually increased (waist circumferences, blood pressures, triglyceride, and glucose) or decreased (HDL cholesterol) corresponding to the number of MetS RF (Table 1). Brachial-ankle pulse wave velocity, LDL particle size, serum lycopene concentration (lipid corrected), and HOMA-IR were also significantly altered corresponding to the number of MetS RF (Fig. 1). These patterns were maintained after adjustment for age, BMI, smoking, and drinking. On the other hand, the levels of total cholesterol and oxLDL and the lipid-corrected levels of α-tocopherol and β-carotene were not significantly different according to the number of MetS RF after the adjustment.

3.2. Correlation of baPWV and serum lycopene with MetS components

Table 2 presents correlations of MetS components with baPWV or serum lycopene. Brachial-ankle pulse wave velocity was positively correlated with systolic and diastolic

Table 1
General and biochemical parameters of Korean men according to the number of MetS risk factor

	Total (N = 299)	RF 0 (n = 83)	RF 1-2 (n = 161)	RF ≥3 (n = 55)	P_0	P_1
Age (y)	49.3 ± 0.4	50.0 ± 0.8	48.8 ± 0.6	49.7 ± 1.0	.482	–
BMI (kg/m^2)	24.4 ± 0.2	22.9 ± 0.3	24.4 ± 0.2	26.7 ± 0.4	<.001	–
Waist (cm)	86.0 ± 0.4	81.7 ± 0.6	85.8 ± 0.5	93.3 ± 1.0	<.001	<.001
Current smoker (%)	39.5	32.5	41.6	43.6	.304	–
Current drinker (%)	84.3	83.1	85.1	83.6	.914	–
Systolic blood pressure (mm Hg)	121.8 ± 0.8	113.8 ± 1.1	122.6 ± 1.1	131.5 ± 1.4	<.001	<.001
Diastolic blood pressure (mm Hg)	75.3 ± 0.6	69.8 ± 1.0	75.6 ± 0.8	82.7 ± 1.2	<.001	<.001
Triglyceride (mg/dL)[a]	129.5 ± 3.9	87.5 ± 3.7	130.3 ± 4.6	190.5 ± 10.9	<.001	<.001
Total cholesterol (mg/dL)[a]	193.6 ± 1.8	188.1 ± 3.2	196.6 ± 2.6	193.4 ± 4.2	.172	.174
HDL cholesterol (mg/dL)[a]	52.5 ± 0.8	56.2 ± 1.5	52.7 ± 1.2	46.2 ± 1.9	<.001	.022
Glucose (mg/dL)[a]	94.1 ± 0.6	89.2 ± 0.8	93.7 ± 0.9	102.9 ± 1.3	<.001	<.001
Insulin (μU/mL)[a]	8.2 ± 0.2	7.0 ± 0.3	8.0 ± 0.3	10.7 ± 0.8	<.001	.004
OxLDL (U/L)[a]	66.3 ± 1.6	64.2 ± 2.8	66.1 ± 2.2	70.0 ± 3.7	.475	.886
α-Tocopherol (mmol/L)[a,b]	1.574 ± 0.029	1.690 ± 0.061	1.537 ± 0.039	1.510 ± 0.061	.057	.346
β-Carotene (mmol/L)[a,b]	0.062 ± 0.002	0.073 ± 0.005	0.059 ± 0.003	0.052 ± 0.004	.013	.367

Data are mean ± SE. Tested by 1-way ANOVA or by GLM with adjustment. P_0: unadjusted; P_1: adjustment for age, BMI, smoking, and drinking.
[a] Log transformed.
[b] Lipid-corrected concentrations.

blood pressures and triglyceride, and the relation was maintained after adjustment for age, BMI, smoking, and drinking. It also positively correlated with fasting glucose, but the significance disappeared after the adjustment. Serum lycopene was negatively correlated with waist circumference, blood pressure, triglyceride, glucose, and HOMA-IR. After the adjustment, the significances were still maintained for waist circumference, triglyceride, and HOMA-IR. On the other hand, HDL cholesterol levels were not significantly correlated with either baPWV or serum lycopene.

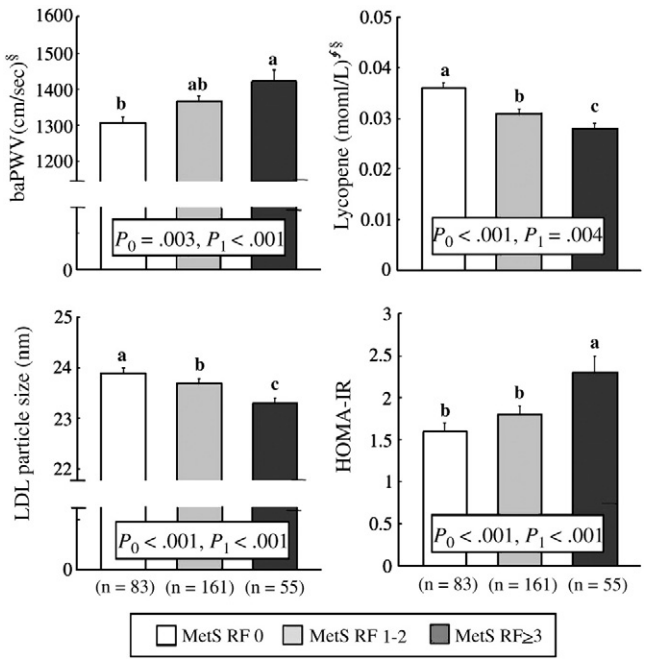

Fig. 1. Brachial-ankle PWV, serum lycopene, LDL particle size, and HOMA-IR according to the number of MetS risk factor. Mean ± SE. §Tested by log-transformed, ¶lipid-corrected concentrations. Tested by 1-way ANOVA with Bonferroni method (P_0) and GLM univariate procedure (P_1). Sharing the same letter indicates no significant difference between 2 groups. P_0: unadjusted; P_1: adjusted for age, BMI, smoking, and drinking.

3.3. Association of baPWV and serum lycopene

Fig. 2 shows the correlation between baPWV and serum lycopene (lipid corrected). Negative correlation was observed between the 2 variables after adjustment for age, BMI, smoking, and drinking ($r_1 = -0.160$, $P_1 < .01$). Further adjustment for blood pressure alone or with HOMA-IR, respectively, maintained the significances ($r_2 = -0.142$, $P_2 < .05$, $r_3 = -0.139$, $P_3 < .05$). When all the above variables including oxidative stress (oxLDL, LDL particle size) were adjusted, the correlation between baPWV and serum lycopene still remained significant ($r_4 = -0.136$, $P_4 < .05$). In addition, negative correlations were observed between oxLDL and LDL particle size ($r_1 = -0.161$, $P_1 = .001$), between lycopene and oxLDL ($r_1 = -0.259$, $P_1 < .001$), and between baPWV and LDL particle size ($r_1 = -0.221$, $P_1 < .001$). Positive correlations were observed between lycopene and LDL particle size ($r_1 = 0.180$, $P_1 = .002$) and between baPWV and oxLDL ($r_1 = 0.143$, $P_1 = .031$). These patterns were significant after adjustment for age, BMI, smoking, and drinking.

As baPWV significantly correlated with serum lycopene, study subjects were subdivided into 2 groups according to serum lycopene concentration split by median level (≤0.0294 mmol/L, n = 149 vs >0.0294 mmol/L, n = 150). When serum lycopene levels were low (≤0.0294 mmol/L), baPWVs were significantly enhanced in MetS subjects than non-MetS healthy subjects (original value: 1436 ± 41 vs 1367 ± 23 cm/s, $P_0 = .025$). These patterns were maintained after adjustment for age, BMI, smoking, and drinking ($P_1 = .006$) and after further adjustment for oxidative stress ($P_2 = .041$)

Table 2
Correlations of baPWV and serum lycopene with components of MetS in study subjects

	Waist	Systolic blood pressure	Diastolic blood pressure	Triglyceride[a]	HDL cholesterol[a]	Fasting glucose[a]	HOMA-IR[a]
Unadjusted							
baPWV[a]	0.068	0.445[§]	0.336[§]	0.175[§]	−0.048	0.119[†]	0.085
Lycopene[a]	−0.346[§]	−0.119[†]	−0.147[†]	−0.645[§]	0.111	−0.125[†]	−0.230[‡]
Adjusted[b]							
baPWV[a]	0.044	0.380[§]	0.470[§]	0.187[‡]	−0.023	0.092	0.082
Lycopene[a]	−0.192[‡]	−0.073	−0.014*	−0.589[§]	0.026	−0.108*	−0.163[‡]

Numbers indicate Pearson or partial correlation coefficient.
[a] Tested by log transformation.
[b] Adjusted for age, BMI, smoking, and drinking.
* $P < .1$.
[†] $P < .05$.
[‡] $P < .01$.
[§] $P < .001$.

(estimated value after the adjustment: 1449 ± 31 vs 1367 ± 17 cm/s). On the other hand, when serum lycopene levels were high (>0.0294 mmol/L), baPWVs were not statistically significantly different between the 2 groups (original value: 1386 ± 36 vs 1326 ± 13 cm/s, estimated value: 1371 ± 44 vs 1323 ± 17 cm/s). In addition, a significant interaction was found between serum lycopene levels and MetS status for baPWV after adjustment for age, BMI, smoking, drinking, and oxidative stress ($P = .046$).

4. Discussion

This present study shows the following: (1) Brachial-ankle pulse wave velocity, a marker of arterial stiffness, increased and serum lycopene decreased significantly with the increasing number of MetS components. (2) Brachial-ankle pulse wave velocity was inversely associated with serum lycopene concentration; and this association was maintained after the adjustment for age, BMI, smoking, drinking, IR, and oxidative stress. (3) Subjects with MetS had much enhanced baPWV compared with non-MetS healthy subjects, particularly when serum lycopene levels were low. Therefore, our new finding demonstrated that circulating lycopene levels may play an important role in MetS status and are closely associated with baPWV. In addition, increased oxidative modification of LDL (ie, high oxLDL and small LDL particle size) may be one of mechanisms how the low circulating lycopene could further enhance arterial stiffness in MetS status.

Our results are in accordance with several emerging evidence. According to Lin et al [27], baPWV was strongly

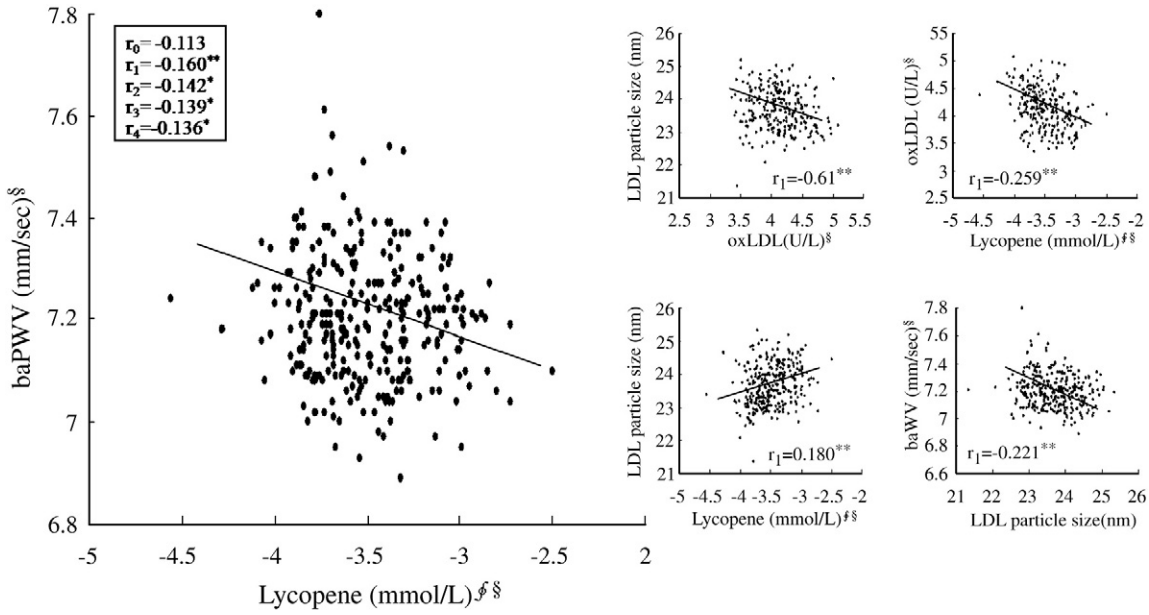

Fig. 2. Correlation between baPWV, serum lycopene, and oxidative stress. r: Pearson (r_0) or partial (r_1~r_4) correlation coefficient. r_0: unadjusted; r_1: adjusted for age, BMI, smoking, and drinking; r_2: adjusted for confounders used in r_1 and systolic and diastolic blood pressure; r_3: adjusted for confounders used in r_2 and IR; r_4: adjusted for confounders used in r_3 and oxidative stress (oxLDL, LDL particle size). *$P < .05$, **$P < .01$, and ***$P < .001$.

related to MetS as well as MetS components in middle-aged Taiwan Chinese; and this relationship was still significant after adjusting for age, BMI, HOMA-IR, smoking, alcohol drinking, physical activity, etc. Tomiyama et al [23] also showed that persistent MetS was associated with acceleration of arterial stiffening in middle-aged Japanese men, and the resolution of MetS may be associated with attenuation of the progression of arterial damage. In addition, we could find the inverse relation between serum antioxidant levels particularly lycopene and the increased risk of MetS as shown in the reports of Sugiura et al [6] and Sluijs et al [7]. *Metabolic syndrome* is defined as a clustering of metabolic abnormalities such as excess body weight, hyperglycemia, IR, elevated blood pressure, low HDL cholesterol, and hypertriglyceridemia, which increase the risk for developing CVD and type 2 DM [1-3]. In addition, oxidative stress that occurs by an imbalance between prooxidants and antioxidants is more frequently observed in MetS subjects than in non-MetS subjects [28,29]. The increment of oxidative stress is known to accelerate IR and the metabolic abnormality, which bring about CVD, type 2 DM, or the complication of the diseases [28,29]. Oxidative modification of LDL particles has been suggested to play a role in the formation of foam cells, atherosclerotic lesions, and coronary artery disease [30].

Antioxidant carotenoids are known to inhibit the oxidation of LDL by quenching singlet oxygen, a potential initiator of lipid peroxidation, and to retard atherosclerotic progression [13,15-17,31]. In particular, lycopene is suggested to exhibit the highest physical quenching rate [3,4]; and the intervention studies with lycopene-containing foods or supplementation showed improvement in LDL oxidation [13,14]. Riccioni et al [10,11] reported that early carotid atherosclerotic lesions and the increased carotid intima thickness were associated with low concentration of plasma lycopene. In our study, serum lycopene levels rather than other antioxidants (ie, α-tocopherol, β-carotene) significantly decreased corresponding to the number of MetS RF after the adjustment for age, BMI, smoking, and drinking. The significance still remained after further adjustment for IR and oxidative stress such as oxLDL and LDL particle size. The significantly enhanced baPWV in MetS subjects compared with non-MetS healthy subjects was observed in low lycopene status. Serum lycopene is also inversely associated with baPWV; and interestingly, the inverse relationship was still significant after adjustment for age, BMI, smoking, drinking, blood pressure, IR, and oxidative stress. It is in line with previous reports for both in vitro and humans that lycopene has superior antioxidant capability; thus, it may reduce atherosclerotic risk [30,32]. Our study also showed negative correlations between oxLDL and LDL particle size and between baPWV and LDL particle size, and positive correlations between lycopene and LDL particle size and between baPWV and oxLDL. It is consistent with the our previous report and other reports showing the association of oxLDL with small dense LDL particle [32,33] as well as the ankle-brachial index, a reliable marker of generalized atherosclerosis determined by a Doppler probe [34]. These results additionally suggest a possibility that increased oxidative modification of LDL may be one of the mechanisms how low circulating lycopene reduces arterial stiffness, particularly in MetS status, the clustering of metabolic abnormalities.

The present investigation has several limitations. First, study subjects were all Korean men; thus, the results may not be applicable to women, other ethnic groups, or patients with the cardiometablic syndrome whose lycopene intake, prevalence of altered vascular stiffness, or biochemical characteristics may differ from those in our subjects. Second, this cross-sectional study is not designed for assessing the time sequential associations because the exposure and outcomes are collected at one point in time. Third, serum lycopene levels may be related with dietary intake. Therefore, if dietary intakes were also assessed in study subjects, it would be better and more informative to explain the association of serum lycopene with baPWV and Mets. Fourth, the associations of MetS, baPWV, and serum carotenoids with inflammatory response were not evaluated in our subjects. Enhanced inflammatory responses are commonly observed in MetS status than non-MetS status and are closely associated with oxidative stress and antioxidant status [28,35-37]. Therefore, it would be needed to measure circulating inflammatory markers.

Despite these limitations, the present study for the first time showed the interrelationship between circulating lycopene, baPWV, and the risk of MetS. It also suggested that much enhanced baPWV in MetS status may be associated with low serum lycopene levels. Therefore, our finding suggests that circulating lycopene levels may play an important role in baPWV, a composite risk factor for early atherosclerosis [19,20] particularly in MetS status. In addition, the increased oxidative modification of LDL such as high oxLDL and small LDL particle size may be suggested as one of the mechanisms how lower circulating lycopene could further enhance arterial stiffness in MetS status.

Acknowledgment

This study was supported by the National Research Foundation , Ministry of Education, Science and Technology (Mid-career Researcher Program: 2010-0015017, and M10642120002-06N4212-00210), and Korea Health 21 R&D Projects, Ministry of Health & Welfare (A080348), Seoul, Korea.

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