Differences in body fat distribution and antioxidant status in Korean men with cardiovascular disease with or without diabetes[1–3]

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ABSTRACT

Background: Abnormal body fat distribution and reduced antioxidant status have been shown to be effective markers of risk of cardiovascular disease (CVD).

Objective: The objective of this study was to determine the differences in body fat distribution and antioxidant status in healthy men (control subjects) and in men with CVD with or without diabetes.

Design: An oral-glucose-tolerance test was performed and CVD patients were subdivided into groups according to the presence or absence of diabetes. Adipose tissue areas were calculated from computed tomography scans made at the L1 and L4 vertebrae. Fasting serum concentrations of lipids, testosterone, insulin-like growth factor I, antioxidants, and plasma homocysteine were determined.

Results: There were no significant differences in mean age, body mass index (in kg/m^2), or blood pressure between the groups. The visceral fat area at the L1 vertebra was nonsignificantly greater in CVD patients without diabetes than in control subjects, whereas it was significantly greater in CVD patients with diabetes than in control subjects at both the L1 and L4 vertebrae. Both groups of CVD patients had higher plasma concentrations of homocysteine and lower serum insulin-like growth factor I concentrations and superoxide dismutase activities than did control subjects. Serum β-carotene and lycopene concentrations were lowest in the CVD patients with diabetes.

Conclusion: The concurrent presence of CVD and diabetes is associated with a greater negative effect on the risk factors typically associated with significant declines in health status. *Am J Clin Nutr* 2001;73:68–74.

KEY WORDS Visceral fat, antioxidants, diabetes, cardiovascular disease, Korean men

INTRODUCTION

In addition to the traditional risk factors for cardiovascular disease (CVD) (hypertension, diabetes, smoking, and hypercholesterolemia), abdominal obesity, impaired antioxidant status, and hyperinsulinemia have been reported to be risk factors (1). An elevated fasting insulin concentration is associated with insulin resistance, which increases an individual's risk of CVD (2–4). Insulin resistance has also been reported to be closely associated with visceral fat accumulation (5). Therefore, central body fat distribution appears to be a greater risk factor for CVD than does obesity itself (6). Men with angiographically confirmed CVD had a higher waist-to-hip ratio (WHR) and a higher serum insulin concentration than did healthy men of similar ages and body mass indexes (BMI; in kg/m^2) (7, 8).

The serum α-tocopherol concentration was inversely correlated with WHR ($r = -0.23$, $P = 0.0001$) in healthy Swedish adults (9). Carotenoids, glutathione peroxidase, superoxide dismutase, and α-tocopherol are known to protect serum lipoproteins and vascular endothelium against oxidative stress and lipid peroxidation, which lead to atherosclerosis (10–12). Previous studies indicated that the concentrations of antioxidants in plasma and tissue were lower in patients with CVD than in a healthy control group and that the β-carotene concentration in adipose tissue was significantly lower in patients with myocardial infarction than in the control group (13).

It is well accepted that a poor antioxidant status promotes free radical production and that such an increase in free radicals correlates with increases in total homocysteine (tHcy) concentrations. An elevated tHcy concentration is thought to be a risk factor for CVD and may accelerate the progression and the initial incidence of arteriosclerosis via direct cytotoxic effects on endothelial cells or via LDL oxidation due to free radical generation (14–16). Moderate hyperhomocysteinemia is defined as plasma concentrations of tHcy >15–16 μmol/L and has been identified in 20–40% of patients with atherosclerotic vascular disease (14, 17).

The risk of CVD is 2–3 times greater in men with diabetes than in men without diabetes (13). It was observed that risk fac-

tors such as hypertension, dyslipidemia, abdominal obesity, and insulin resistance occur frequently in persons with diabetes. In addition, the antioxidant defense system of such persons may be damaged by oxidative stress after glycosylation (13). CVD patients with abdominal obesity and insulin resistance may have a higher prevalence of type 2 diabetes mellitus.

An increase in morbidity and mortality rates as a result of CVD was observed in 1996 (18). However, little has been reported about the effects of central visceral fat accumulation, hyperinsulinemia, compromised antioxidant status, and elevated plasma tHcy on the incidence and progression of CVD in Korean men. We investigated whether there are differences in body fat distribution and antioxidant status among 3 groups: healthy men, CVD patients without diabetes, and CVD patients with diabetes.

SUBJECTS AND METHODS

Subjects

Fifty-six men with CVD (aged 30–69 y) were referred by the Division of Cardiology, Yonsei Cardiovascular Center, Yonsei Severance Hospital, Seoul, Korea. The inclusion criteria required angiographic evidence with ≥50% occlusion of one or more major coronary arteries, previous myocardial infarction, or angina pectoris. The CVD patients were taking drugs such as blood pressure–lowering agents, aspirin, and antithrombosis agents, but none were taking drugs known to influence lipid concentrations. Just one diabetic patient was already taking an oral hypoglycemic agent.

Sixty-four healthy men were selected for the control group from volunteers who responded to advertisements for a nutrition study conducted by the Clinical Nutrition Research Team at Yonsei University in 1998. All control subjects had normal glucose tolerance and normal results on electrocardiograms and none had a diagnosis of any type of CVD (including coronary heart disease, stroke, and peripheral vascular disease) or cancer. All subjects gave their informed consent before participating in the study. After completing an oral-glucose-tolerance test, the CVD patients were subdivided into 2 groups: subjects with (n = 26) and without (n = 30) diabetes. The Institutional Review Board for Clinical Research of the Yonsei University (Severance Hospital) approved the study protocol and all subjects gave their informed consent.

Alcohol consumption, smoking status, dietary supplement intake, and anthropometry

Alcohol consumption was calculated as the grams of ethanol ingested per day and cigarette smoking data were reported as the number of cigarettes smoked per day. The body heights and weights of subjects in light clothing were measured and BMI was computed. Waist and hip circumferences were measured and the WHR was computed as an indication of the index of body fat distribution. A survey was used to determine the use of dietary supplements.

Computed tomography of the fat areas at the L1 and L4 vertebrae

To quantify fat area, all subjects underwent computed tomography (CT) scanning with a High Speed Advantage 9800 Scanner (General Electric, Milwaukee). Cross-sectional images were made of the abdomen at the L1 and L4 vertebrae. Each slice was analyzed for the cross-sectional area of fat by using a density contour program available with the CT scanner. The parameters

for total abdominal fat density at the L1 and L4 vertebrae were between −150 and −50 Hounsfield units. Total abdominal fat area was divided into visceral and subcutaneous fat areas.

Blood collection and blood pressure measurement

Venous blood specimens were collected after a 12-h fast into plain (for serum glucose, lipid, antioxidant, and hormone analyses) or EDTA-treated (for tHcy analysis) tubes. The tubes for antioxidant analysis were immediately covered with aluminum foil and placed on ice in the dark until they arrived at the laboratory. Blood pressure was read from the left arm while subjects remained seated. An average of 3 measurements was recorded for each subject.

Serum lipids and lipoproteins

Serum total cholesterol, LDL cholesterol, and triacylglycerol were measured with commercially available kits on a Hitachi 7150 Autoanalyzer (Hitachi Ltd, Tokyo). After precipitation of serum chylomicrons, LDL, and VLDL with a precipitating agent, the HDL cholesterol left in the supernate was measured with an enzymatic method.

Oral-glucose-tolerance test

All subjects ingested a 75-g glucose solution after an overnight fast. Serum samples were collected before and 30, 60, 90, and 120 min after the glucose load. The criteria developed by the World Health Organization Expert Committee on Diabetes Mellitus was used to determine whether subjects had diabetes [a fasting glucose concentration >7.7 mmol/L (140 mg/dL) and a 2-h glucose concentration >11.1 mmol/L (200 mg/dL)]. Glucose was measured with a glucose oxidase method by using a glucose analyzer (Beckman Instruments, Irvine, CA). Insulin was measured by using an immunoradiometric assay (Dainabot, Tokyo) and C-peptide was measured by using a radioimmunoassay with commercial kits from Immuno Nucleo Corporation (Stillwater, MN). Each glucose, insulin, and C-peptide response was calculated as the area under the response curve.

Hormones

Serum testosterone was measured with a kit from Immuchem (Diagnostics Product Corp, Los Angeles). Serum insulin-like growth factor I (IGF-I) was measured with an immunoradiometric assay kit from Diagnostic System Laboratories (Webster, TX).

Serum sex hormone binding globulin and plasma total homocysteine

Radioimmunoassays were used to measure serum sex hormone binding globulin (SHBG). The free androgen index was the ratio of the percentage of testosterone to moles of SHBG (19). Plasma tHcy was analyzed with a Bio20 Autoloader Amino Acid Analyzer (Pharmacia Biotech, Cambridge, United Kingdom) with a postcolumn ninhydrin reaction system according to the modified method of Anderson et al (20) and Ueland et al (21).

Serum retinol, carotenoids, and tocopherols

Reversed-phase HPLC was used to determine retinol, carotenoids, and tocopherols in serum simultaneously as described by Yeum et al (22), Bankson et al (23), and McCrehan (24). The HPLC system consisted of an Alliance Waters 2690 separation module, a Waters 996 photodiode array detector, a Waters 474 scanning fluorescence detector, a C_{18} Symmetry 3.9 × 15 cm

TABLE 1
Age, anthropometric measures, and fat areas at different sites of the body in healthy men and in CVD patients with or without diabetes[1]

	Control subjects ($n = 64$)	Nondiabetic CVD patients ($n = 30$)	Diabetic CVD patients ($n = 26$)
Age (y)	52.9 ± 0.93	53.2 ± 1.37	55.0 ± 1.50
BMI (kg/m^2)	24.3 ± 0.37	24.8 ± 0.46	25.1 ± 0.40
WHR	0.92 ± 0.01	0.93 ± 0.01	0.95 ± 0.01[2]
Systolic BP (mm Hg)	126.8 ± 2.66	132.8 ± 2.43	134.4 ± 2.82
Diastolic BP (mm Hg)	86.2 ± 2.71	82.6 ± 2.38	84.5 ± 2.03
L1 vertebra			
Total fat (cm^2)	216.1 ± 10.6	241.6 ± 12.0	243.7 ± 12.0
Subcutaneous fat (cm^2)	76.8 ± 4.20	77.0 ± 4.43	74.1 ± 4.10
L4 vertebra			
Total fat (cm^2)	252.0 ± 9.25	257.4 ± 9.80	271.4 ± 11.1
Subcutaneous fat (cm^2)	131.4 ± 5.30	137.3 ± 7.40	133.5 ± 6.10

[1] $\overline{x}$ ± SEM. WHR, waist-to-hip ratio; CVD, cardiovascular disease; BP, blood pressure.

[2] Significantly different from control subjects, $P < 0.05$ (ANOVA followed by the Bonferroni test).

column, and a PDA Millennium for version 2.15 DATA STATION (Waters, Milford, MA). The 474 scanning fluorescence detector was set at 294 nm for the detection of tocopherols. Retinol, carotenoids, and tocopherols were reported as serum concentrations uncorrected or corrected for the sum of serum cholesterol (mmol/L) and serum triacylglycerol (mmol/L) as suggested by Thurnham et al (25).

Serum antioxidant enzymes and malondialdehyde

Glutathione peroxidase activity was determined by using the coupled enzyme procedure at 340 nm, with hydrogen peroxide as substrate, according to Paglia and Valentine (26) and Deagen et al (27). Superoxide dismutase activity was estimated by the method of Marklund and Marklund (28) and Sheri et al (29). Malondialdehyde was assayed according to the fluorometric method described by Buckingham (30).

Statistical analysis

Statistical analyses were conducted with SPSS/PC+ (version 7.0; SPSS Inc, Chicago). For descriptive purposes, values are presented as means ± SEMs. To determine differences in body fat distribution and in antioxidant status between the 3 groups, the sample sizes were selected on the basis of the following assumptions: the present study would have 80% power to detect a 20% relative difference in tHcy concentrations between the healthy men and the 2 CVD patient groups ($\alpha = 0.05$, two-tailed). Because these variables were reportedly 20% higher in a group of CVD patients than in a healthy group (31), differences between groups were evaluated by performing an analysis of variance followed by the Bonferroni test. A P value <0.05 was considered to indicate statistical significance.

RESULTS

Alcohol consumption, cigarette smoking, and vitamin supplementation

Twenty-eight percent of the control subjects, 33% of the CVD patients without diabetes, and 15% of the CVD patients with dia-

betes were current smokers. Fifty-eight percent of the control subjects, 47% of the CVD patients without diabetes, and 38% of the CVD patients with diabetes typically consumed >5 g ethanol/d. Fifty-six percent of the control subjects, 30% of the CVD patients without diabetes, and 46% of the CVD patients with diabetes supplemented their diet with a multivitamin (B complex and vitamin C) preparation; however, none had taken any supplement for 1 mo before blood collection.

Age, BMI, blood pressure, and body fat distribution

There were no significant differences in age, BMI, or systolic or diastolic blood pressure between the 3 groups (**Table 1**). CVD patients with diabetes showed the highest mean WHR values. Visceral fat area at the L1 vertebra tended to be greater in the CVD patients without diabetes than in the control group. CVD patients with diabetes had a significantly greatest visceral fat area at the L1 and L4 vertebrae than did the control subjects (**Figure 1**).

Serum lipid, glucose, insulin, and C-peptide concentrations

Serum HDL-cholesterol concentrations were lowest in the CVD patients with diabetes (**Table 2**). Of the 3 groups, CVD patients with diabetes had the highest atherogenic index, fasting
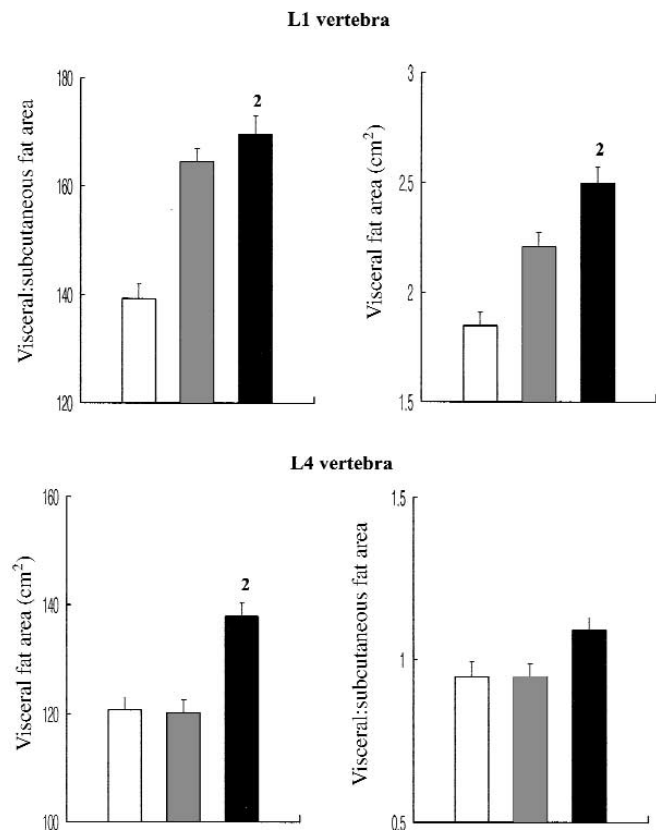
FIGURE 1. Mean (±SEM) visceral fat area and the ratio of visceral to subcutaneous fat area at the L1 and L4 vertebrae in healthy men (□, control subjects; $n = 64$) and in CVD patients with (■; $n = 26$) or without (■; $n = 30$) diabetes. [2] Significantly different from control subjects, $P < 0.05$ (ANOVA followed by the Bonferroni test).

TABLE 2
Serum lipids, glucose, insulin, and C-peptide and responses to a 75-g oral-glucose-tolerance test in healthy men and in CVD patients with or without diabetes[1]

	Control subjects ($n = 64$)	Nondiabetic CVD patients ($n = 30$)	Diabetic CVD patients ($n = 26$)
Triacylglycerol (mmol/L)	1.67 ± 0.1	1.78 ± 0.16	1.79 ± 0.24
Total cholesterol (mmol/L)	5.14 ± 0.12	4.90 ± 0.17	4.80 ± 0.18
HDL cholesterol (mmol/L)	1.29 ± 0.04	1.10 ± 0.05	1.00 ± 0.05^2
LDL cholesterol (mmol/L)	3.09 ± 0.10	2.98 ± 0.16	2.98 ± 0.18
Atherogenic index[3]	3.16 ± 0.13	3.63 ± 0.20	4.05 ± 0.26^2
Total:HDL cholesterol	4.16 ± 0.13	4.63 ± 0.20	5.05 ± 0.26^2
LDL:HDL cholesterol	2.52 ± 0.11	2.81 ± 0.16	3.12 ± 0.22^2
Fasting concentration			
Glucose (mmol/L)	5.44 ± 0.09	5.49 ± 0.17	$6.90 \pm 0.33^{2,4}$
Insulin (pmol/L)	59.3 ± 4.36	61.4 ± 5.49	77.4 ± 13.4
C-peptide (μg/L)	0.85 ± 0.04	0.97 ± 0.08	1.03 ± 0.11
Response area			
Glucose (mmol·h/L)	16.2 ± 3.78	17.1 ± 0.49	23.1 ± 0.97^2
Insulin (pmol·h/L)	607.1 ± 31.7	949.6 ± 161.2^2	643.4 ± 73.2
C-peptide (μg·h/L)	3.24 ± 0.25	4.58 ± 0.60^2	3.69 ± 0.63

[1] $\overline{x} \pm$ SEM. CVD, cardiovascular disease.
[2] Significantly different from control subjects, $P < 0.05$ (ANOVA followed by the Bonferroni test).
[3] (Total cholesterol $-$ HDL cholesterol)/HDL cholesterol.
[4] Significantly different from nondiabetic CVD patients, $P < 0.05$.

glucose concentration, and glucose response area. Response areas of insulin and C-peptide were significantly greater in the CVD patients without diabetes than in the control group.

SHBG, antioxidant enzyme activity, and plasma total homocysteine

The mean testosterone concentration was lower in the 2 groups of CVD patients than in the control group, but not significantly so (**Table 3**). Serum IGF-I concentrations were significantly lower in the 2 groups of CVD patients than in the control subjects. Serum SHBG, glutathione peroxidase, the free androgen index, and malondialdehyde were not significantly different between the 3 groups. Serum superoxide dismutase activities were significantly lower in the 2 groups of CVD patients than in the control subjects. tHcy concentrations were significantly higher in the 2 groups of CVD patients than in the control group (**Figure 2**).

Serum retinol, carotenoids, and tocopherols

There were no significant differences in uncorrected and lipid-corrected serum concentrations of α-carotene, retinol, and α- or γ-tocopherol between the 3 groups (**Table 4**). The corrected and uncorrected serum cryptoxanthin concentrations were lower in the CVD patients with diabetes than in the control subjects, but not significantly so. The CVD patients with diabetes had the lowest uncorrected and lipid-corrected lycopene concentrations, and uncorrected β-carotene concentrations in this group were lower (NS) than in the control group (**Figure 3**).

DISCUSSION

The results indicate that visceral fat accumulation is higher in CVD patients than in healthy men of similar ages and BMIs and that excessive visceral fat accumulation may accelerate the pro-

gression of type 2 diabetes mellitus. Visceral fat accumulation induces insulin resistance, which encourages pancreatic β-cells to secrete more insulin to maintain normal glucose metabolism. Thus, hyperinsulinemia results, which exacerbates insulin resistance and further increases the accumulation of upper body fat (4). Excessive accumulation of visceral fat may result in a relative deficiency of insulin, the secretion of which is insufficient to regulate insulin resistance and leads to impaired glucose tolerance and potentially to type 2 diabetes mellitus (32, 33).

Compared with the healthy control group with normal glucose tolerance, the CVD patients with diabetes showed severe insulin resistance, resulting in hyperglycemia when insulin concentrations were not maintained. The similar response areas of C-peptide and insulin in the control subjects and the CVD patients with diabetes indicate that further visceral fat accumulation and a relative deficiency of insulin may lead to a greater incidence of type 2 diabetes mellitus in CVD patients. This suggests that further visceral fat accumulation and a relative deficiency of insulin in those with CVD may lead to a greater incidence of type 2 diabetes mellitus.

Insulin resistance has been reported to influence lipoprotein lipase activity, lipoprotein metabolism, and glucose metabolism (4). Decreased lipoprotein lipase activity due to insulin resistance may delay triacylglycerol-rich lipoprotein uptake and decrease HDL-cholesterol formation. Another study reported that insulin resistance accelerated HDL-cholesterol catabolism, which led to a decrease in serum HDL-cholesterol concentrations (34). In addition to insulin resistance, serum testosterone concentrations in men were positively related to serum HDL cholesterol and were presumably related to the regulation of hepatic lipase activity (35).

An elevated serum testosterone concentration in men increases the number of β-receptors in visceral fat cells and the activity of hormone-sensitive lipase, leading to fat mobilization (36). Growth hormone activity is also more apparent in visceral than in subcutaneous fat and it accelerates the lipolysis of visceral fat in the presence of testosterone. In the present study, IGF-I and testosterone concentrations were significantly different between the control subjects and the CVD patients with and without diabetes. These differences in hormone concentrations may partly reflect the difference in visceral fat area between the CVD patients with or without diabetes.

TABLE 3
Sex hormones and antioxidant enzyme activities in healthy men and in CVD patients with or without diabetes[1]

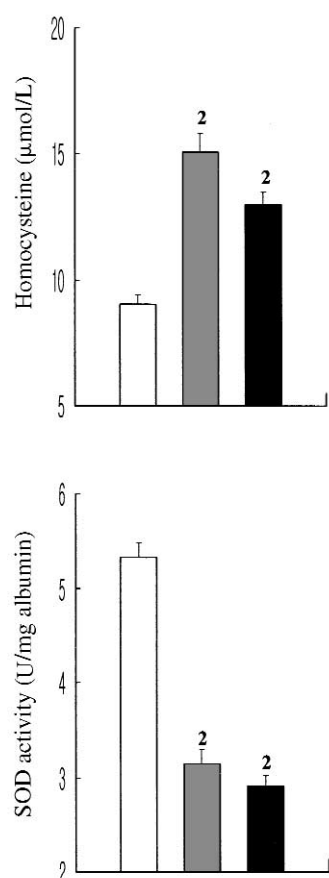|	Control subjects ($n = 64$)	Nondiabetic CVD patients ($n = 30$)	Diabetic CVD patients ($n = 26$)
Testosterone (nmol/L)	18.4 ± 0.66	17.3 ± 1.12	15.5 ± 1.22
SHBG (nmol/L)	52.8 ± 2.60	55.7 ± 5.38	48.1 ± 3.88
Free androgen index[2]	39.7 ± 2.74	35.3 ± 2.40	34.0 ± 2.42
IGF-I (μg/L)	142.4 ± 7.68	72.3 ± 15.5^3	77.4 ± 17.1^3
Glutathione peroxidase (nmol NADPH/mg albumin)	38.9 ± 1.23	38.9 ± 1.49	35.9 ± 1.59
Malondialdehyde (nmol/mL)	4.32 ± 0.19	4.45 ± 0.41	4.56 ± 0.45

[1] $\overline{x} \pm$ SEM. CVD, cardiovascular disease; SHBG, sex hormone binding globulin; IGF-I, insulin-like growth factor I.
[2] Ratio of the percentage of testosterone to moles of SHBG.
[3] Significantly different from control subjects, $P < 0.05$ (ANOVA followed by the Bonferroni test).

FIGURE 2. Mean (±SEM) plasma homocysteine concentrations and serum total superoxide dismutase (SOD) activity in healthy men (□, control subjects; $n = 64$) and in CVD patients with (■; $n = 26$) or without (■; $n = 30$) diabetes. [2]Significantly different from control subjects, $P < 0.05$ (ANOVA followed by the Bonferroni test).

The CVD patients without diabetes had moderate hyperhomocysteinemia (mean tHcy concentration: 15.1 μmol/L), whereas the CVD patients with diabetes had mild hyperhomocysteinemia (mean tHcy concentration: 13.1 μmol/L). It has been suggested that tHcy may have direct cytotoxic effects or produce free radicals that can result in endothelial damage and dysfunction (14). An increase in free radical production contributes to oxidative stress and exhausts the antioxidant system. Therefore, a high tHcy concentration may be associated with low antioxidant capacity (12, 14). In the present study, hyperhomocysteinemic CVD patients with or without diabetes had lower superoxide dismutase activity than did the control subjects. Superoxide dismutase, a major antioxidant enzyme, catalyzes the dismutation of superoxide anions to hydrogen peroxide and oxygen. The antioxidant defense system includes enzymatic and nonenzymatic antioxidants. The most prominent nonenzymatic antioxidants are vitamins E and C and carotenoids in the cytoplasm and lipid membranes of cells (37).

β-Carotene is a fat-soluble carotenoid and antioxidant that is well known for its relation to atherosclerosis. β-Carotene is concentrated in lipoprotein fractions such as HDL and LDL and accumulates in atherosclerotic plaques (38, 39). It is well established that high serum β-carotene concentrations may protect against endothelial damage by decreasing cholesterol uptake into those cells and that β-carotene inhibits atherosclerotic lesion formation (39, 40).

In the present study, serum β-carotene concentrations were associated with physiologic and lifestyle factors, including carotenoid intake, sex, age, BMI, and smoking status (41, 42). The lower serum β-carotene concentration in CVD patients without diabetes than in the control group may have been related not only to CVD itself, but also to this group's lower carotenoid intakes and current smoking status. The lower serum concentrations of β-carotene and lycopene in the CVD patients with diabetes than in the other 2 groups may have resulted from the increased oxidative stress due to diabetes rather than to behavioral or dietary choices. Persons with diabetes appear to be more susceptible to ambient oxidative stress and might be under greater oxidative stress than are persons without diabetes because of glycosylation followed by oxidation processes (13).

Oxidative stress affects the peroxidation of polyunsaturated fatty acids in LDL and exhausts ubiquinone-10 as well as vitamin E and carotenoids, including lycopene, cryptoxanthin, and lutein (44). Each of these compounds, singly, contributes little to the resistance to LDL oxidation, but collectively may contribute a great deal. Therefore, ingestion of a combination of different antioxidants rather than of a single micronutrient may have a better effect against LDL oxidation (43).

In summary, the male CVD patients in the present study had greater visceral fat accumulation and insulin and tHcy concentrations and lower IGF-I, superoxide dismutase, and β-carotene concentrations than did the control subjects, who were healthy men matched for age and BMI. In addition, the CVD patients with diabetes had the greatest visceral fat areas and tHcy concentrations and the lowest serum concentrations of HDL cholesterol and carotenoids of the 3 groups. Given the significant differences observed between the 3 groups, lifestyle modifications such as smoking cessation, reductions in abdominal fat, and consumption

TABLE 4
Serum concentrations of carotenoids, retinol, and tocopherol in healthy men and in CVD pateints with or without diabetes[1]

	Control subjects ($n = 64$)	Nondiabetic CVD patients ($n = 30$)	Diabetic CVD patients ($n = 26$)
Uncorrected concentrations			
α-Carotene (μmol/L)	0.06 ± 0.01	0.06 ± 0.01	0.05 ± 0.01
Retinol (μmol/L)	4.53 ± 1.50	4.90 ± 1.31	4.12 ± 0.97
Cryptoxanthin (μmol/L)	1.50 ± 0.16	1.31 ± 0.19	0.97 ± 0.13
α-Tocopherol (μmol/L)	24.7 ± 1.87	25.7 ± 2.83	29.9 ± 3.14
γ-Tocopherol (μmol/L)	2.95 ± 0.30	3.24 ± 0.57	2.84 ± 0.47
Lipid-corrected concentrations			
α-Carotene (μmol/mmol)	0.01 ± 0.001	0.01 ± 0.001	0.01 ± 0.001
β-Carotene (μmol/mmol)	0.19 ± 0.02	0.14 ± 0.02	0.12 ± 0.02
Retinol (μmol/mmol)	0.72 ± 0.08	0.76 ± 0.07	0.64 ± 0.07
Cryptoxanthin (μmol/mmol)	2.34 ± 0.25	2.01 ± 0.24	1.55 ± 0.25
Lycopene (μmol/mmol)	1.14 ± 0.12	0.93 ± 0.17	0.65 ± 0.13[3]
α-Tocopherol (μmol/mmol)	3.91 ± 0.33	4.07 ± 0.51	4.72 ± 0.55
γ-Tocopherol (μmol/mmol)	0.47 ± 0.05	0.51 ± 0.09	0.43 ± 0.07

[1]$\bar{x}$ ± SEM. CVD, cardiovascular disease.
[2]Each concentration of vitamins and carotenoids was divided by the sum of cholesterol and triacylglycerol (mmol/L).
[3]Significantly different from control subjects, $P < 0.05$ (ANOVA followed by the Bonferroni test).
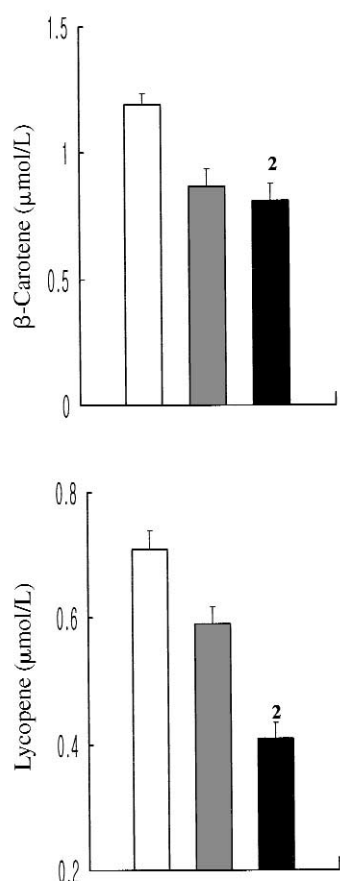
FIGURE 3. Mean ($\pm$SEM) serum β-carotene and lycopene concentrations in healthy men ($\square$, control subjects; $n = 64$) and in CVD patients with ($\blacksquare$; $n = 26$) or without ($\blacksquare$; $n = 30$) diabetes. [2]Significantly different from control subjects, $P < 0.05$ (ANOVA followed by the Bonferroni test).

of antioxidant-rich foods are recommended to delay the progression of CVD and to maintain a healthy life. In addition, given the significantly lower serum antioxidant concentrations in the CVD patients than in the control subjects, it may be prudent for patients with CVD to supplement their diet with antioxidants such as ubiquinone-10, vitamins E and C, and mixed carotenoids, including β-carotene, lycopene, cryptoxanthin, and lutein.

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