

Null Results in Brief

Associations of Serum Carotenoid Levels with Serum Insulin-like Growth Factor-I and Insulin-like Growth Factor Binding Protein-3 Levels in Black Men and White Men

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Introduction

Carotenoids in tomatoes are hypothesized to play a chemopreventive role in prostate cancer (1); lycopene, in particular, has received considerable attention as a potent antioxidant because it seems to be the most effective quencher of singlet oxygen and free radicals (2). In addition, epidemiologic, animal, and *in vitro* studies suggest that lycopene might exert an anticarcinogenic role via the modulation of components of the insulin-like growth factor (IGF) system (3-9). Dietary intake of lycopene is negatively associated with serum IGF-I and positively associated with IGF-binding protein (IGFBP)-3 (10). IGF-I has important mitogenic properties whereas IGFBP-3 reduces IGF-I availability and has IGF-independent tumor suppressor activity (11-14). Several epidemiological studies also showed associations of serum IGF-I and IGFBP-3 levels with prostate cancer risk (13). In this analysis, we evaluated the relation of serum carotenoid concentrations with serum IGF-I and IGFBP-3 concentrations in Black men and White men.

Materials and Methods

Coronary Artery Risk Development in Young Adults (CARDIA) is a prospective, multicenter epidemiologic study of the evolution of cardiovascular disease risk factors in 5,115 young Black and White, male and female adults. A detailed description of the design, recruitment,

and methods of the CARDIA Study is published elsewhere (15). The Young Adult Longitudinal Trends in Antioxidants (YALTA) study measured carotenoid concentrations in sera collected from most CARDIA participants in 1985-1986 (the baseline examination) and 1992-1993 (year 7; ref. 16). The CARDIA Male Hormone Study (CMHS) measured concentrations of sex hormones, IGF-I, and IGFBP-3 in sera in 1987-1988 (year 2), 1992-1993 (year 7), and 1995-1996 (year 10). The present study examined associations of serum IGF-I and IGFBP-3 with serum carotenoids using data collected at the year 7 examination. There were 470 Black men and 656 White men who completed the year 7 examination (ages 25-37 years) and had measurements of serum hormone and carotenoid concentrations.

Serum IGF-I and IGFBP-3, carotenoid, and cholesterol concentrations were measured using an immunoradiometric assay, a modified liquid chromatography-based assay, and an enzymatic method, respectively. Detailed descriptions of the measurements including alcohol intake (milliliters per day), body mass index (BMI; kilograms per square meter), smoking status (cigarettes per day), and the quality control procedures are published elsewhere (17-22).

In preliminary analysis, age-adjusted differences in sociodemographic and lifestyle characteristics and serum measurements between Black men and White men were assessed by ANOVA. Because serum IGF and carotenoid levels differed between Black and White men, subsequent analyses were conducted within each race group. Race-specific, age- and multivariable-adjusted Pearson partial correlation coefficients were computed for serum measurements. Multivariable linear regression analysis was used to assess the associations of serum lycopene, the sum of four other carotenoids (α -carotene, β -carotene, lutein plus zeaxanthin, and β -cryptoxanthin), and the sum of all five serum carotenoids with serum IGF-I, IGFBP-3, and IGF-I/IGFBP-3 molar ratio. Covariates included in the model were age, BMI, alcohol intake, cigarette smoking, and serum total cholesterol concentration (23). Analyses were carried out using SAS software, version 8.2 (SAS Institute, Inc.).

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Table 1. Year 7 age-adjusted characteristics of men by race in the CMHS and the YALTA study (1992-1993)

	Black men (n = 470), mean* (SE)	White men (n = 656), mean* (SE)	P
Age (y)	31.4 (0.2)	32.4 (0.1)	<0.0001
BMI (kg/m ²)	27.3 (0.2)	25.9 (0.2)	<0.0001
Alcohol intake (mL/d)	18.3 (1.4)	15.7 (1.2)	0.17
Cigarette smoking (cigarettes/d)	3.7 (0.4)	4.0 (0.3)	0.49
Total cholesterol level (mg/dL)	180.8 (1.7)	179.5 (1.4)	0.57
IGF-I level (ng/mL)	163.8 (4.4)	186.0 (3.7)	0.0001
IGFBP-3 level (ng/mL)	3,074.0 (41.9)	3,436.2 (35.4)	<0.0001
Lycopene level (µg/dL)	33.8 (0.7)	34.5 (0.6)	0.48
Sum of four other carotenoid levels (µg/dL)	45.4 (1.2)	48.9 (1.0)	0.03
Sum of all five carotenoid levels (µg/dL)	79.2 (1.5)	83.3 (1.3)	0.04

*Means were adjusted for age.

Results

Black men were younger and had a higher BMI than White men (Table 1). Mean serum IGF-I, IGFBP-3, and the sum of four and all five carotenoid concentrations were significantly lower in Black men than in White men. There were no differences between Black and White men in alcohol intake, cigarette smoking, serum total cholesterol, or serum lycopene concentration. Pearson partial correlation coefficients of serum total cholesterol with lycopene, the sum of four other carotenoids, and the sum of all five carotenoids were 0.33, 0.21, and 0.33 in Black men and 0.45, 0.08, and 0.26 in White men, respectively ($P < 0.05$), suggesting the need for adjustment of total cholesterol in the multivariable analysis (24).

In multivariable analyses, lycopene level was not associated with IGF-I, IGFBP-3, and IGF-I/IGFBP-3 molar ratio in either Black men or White men (Table 2). Similarly, there were no significant associations of the sum of four carotenoids or all five carotenoids with any of the serum IGFs measured.

Discussion

Although other studies have examined the relationship between dietary carotenoids and serum IGF levels, to our knowledge this is the first to examine associations between serum IGF and carotenoid levels in Black and White men. In this study, after adjustment for age, BMI, alcohol intake, cigarette smoking, and serum total cholesterol level, there were no meaningful associations between lycopene, the sum of four carotenoids, or the sum of all five carotenoids and IGF-I, IGFBP-3, or the molar ratio of IGF-I/IGFBP-3.

Results of two studies suggest an inverse association between dietary intake of cooked tomatoes or lycopene supplementation with serum IGF-I level (5, 6), whereas data from other studies showed no associations of intake of tomato products or lycopene with IGF-I in women (7) or in men (25, 26). Similarly, there is also inconsistent evidence of a positive association between dietary intake of lycopene and serum IGFBP-3 levels (26, 27). In our study, we observed no significant associations between serum carotenoids and IGF levels in either Black or White men. Reasons for the variation in results across studies are unclear. It is possible that other dietary or lifestyle factors associated with dietary intake of carotenoids could explain findings from other studies. Alternatively, it is possible that unmeasured confounding factors that are metabolically determined could mask associations between serum carotenoids and IGF levels.

A primary strength of this study is the large number of Black and White men, which allowed the assessment of the associations of IGF levels with serum carotenoid concentrations by race. Based on samples sizes of 470 Black men and 656 White men, we had 90% power to observe a Pearson partial correlation of ≥ 0.15 , assuming a two-sided test at the 5% level and adjusting for five covariates for each ethnic group. In our study, the partial correlations ranged from -0.002 to 0.08 , supporting the absence of any meaningful association between serum carotenoid and IGF levels. Adjustment for serum cholesterol, which may be associated with carotenoid concentrations either through a link with healthy lifestyle or by equilibration of fat-soluble carotenoids across adipose and blood lipids, is an additional strength of this analysis. A limitation of this study is that other components of the IGF system such as IGF-2, IGFBP-1,

Table 2. Multivariate regression coefficients for cross-sectional associations of serum IGF-I, IGFBP-3 levels, and IGF-I/IGFBP-3 molar ratio with serum lycopene, sum of four other serum carotenoid, and sum of all five serum carotenoid concentrations

	IGF-I		IGFBP-3		IGF-I/IGFBP-3							
	Black men		White men		Black men		White men					
	β (ng/mL)	P										
Lycopene ($\Delta 1$ µg/dL)	0.15	0.63	0.12	0.66	4.01	0.16	-1.63	0.55	-0.000015	0.97	0.000176	0.52
Sum of four other carotenoids ($\Delta 1$ µg/dL)	0.33	0.08	0.10	0.47	2.05	0.24	-0.64	0.65	0.000400	0.06	0.000116	0.41
Sum of all five carotenoids ($\Delta 1$ µg/dL)	0.26	0.09	0.10	0.42	2.41	0.09	-0.77	0.52	0.000268	0.13	0.000116	0.33

NOTE: Data were adjusted for age, BMI, alcohol intake, cigarette smoking, and serum total cholesterol concentration.

or IGFBP-2 were not measured because of the limited volume of serum available. Another limitation is the cross-sectional design, which cannot exclude the possibility of reverse causality.

In conclusion, we found no evidence of associations of serum carotenoids with serum IGF-I, IGFBP-3 levels, and the molar ratio. These results do not support the hypothesis that these components of the IGF system are associated with carotenoid levels.

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