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Absorption estimates improve the validity of the relationship between dietary and serum lycopene

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Abstract

Objective: Studies show low correlations between dietary intake and serum concentrations of lycopene, which make it difficult to assess the effectiveness of dietary interventions with this phytonutrient. We hypothesized that 1) combining food-frequency questionnaires (FFQs) and 3-d diet records (3D-DRs) by the triads method would improve the validity of this relation and 2) correcting dietary information for differences in lycopene absorption from food matrices would further improve validity.

Methods: We measured dietary intakes of lycopene from 49 adults by 3D-DR and FFQ. Serum lycopene was measured by high-performance liquid chromatography with diode array detection. Cholesterol and triacylglycerol concentrations were measured spectrophotometrically. Lycopene-containing foods were given absorption factors based on literature and laboratory values. Associations between dietary and serum lycopene were modeled using multiple regression. The triads method was used for validation of relations among FFQ, 3D-DR, and serum lycopene.

Results: Raw data showed low correlations between dietary and serum lycopene ($r = +0.15$ for 3D-DR, $+0.35$ for FFQ). Mathematical modeling showed that the 3D-DR and FFQ methods must be used to collect accurate dietary information for lycopene. Validity coefficients calculated by the triads method were $+0.34$ for 3D-DR and $+0.78$ for FFQ. Correcting for absorption increased the validity coefficient to $+0.72$ for 3D-DR and from $+0.45$ to $+0.66$ for serum lycopene.

Conclusion: The relation between dietary intake and serum concentrations of lycopene and other carotenoids can be improved by collecting 3D-DR and FFQ data and by adjusting dietary information for nutrient absorption. Published by Elsevier Inc.

Keywords: Lycopene; Absorption; Bioaccessibility; Food frequency; Food record; Human; Mathematical model

Introduction

Lycopene is an abundant carotenoid in human blood [1,2] that is associated with antioxidant status, gap-junction formation, and apoptosis [3–6]. Experimental and epidemiologic studies have suggested that high lycopene intakes are associated with decreased risks for atherosclerosis [7] and cancer, with an especially strong association with decreased prostate cancer [8,9] (but see Kavanaugh et al. [10]).

Rich dietary sources of lycopene are limited to tomatoes, red peppers, pink grapefruit, pink guava, and watermelon [11]. Hypothetically, the fact that lycopene-rich foods are limited to a few brightly colored fruits and vegetables should improve dietary intake estimates of this carotenoid, because these estimates rely on recording or recalling the foods that one eats. Furthermore, serum concentrations of lycopene appear to decrease and increase proportionally to the amount of lycopene in the diet [12]. Because lycopene intake should be relatively simple to recall and its serum concentrations are proportional to intake, one would expect that serum concentrations of lycopene would correlate well with dietary intake. However, most studies have shown low correlations between dietary intakes and serum concentrations of lycopene ($r = -0.09$ to $+0.3$) [13–16]. This makes assessing the impact of dietary interventions with lycopene difficult.

We hypothesized that the major reason for low correlations between dietary and serum lycopene is the difficulty of estimating dietary intakes. Common instruments for dietary record

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collection (24-h recalls, 3-d diet records [3D-DRs] or 7-d diet records, and food-frequency questionnaires [FFQs]) have well-known limitations [17,18]. For example, 3- and 7-d diet records cover a very limited time and thus may over- or underestimate infrequently consumed foods and nutrients. FFQs, in contrast, are usually designed to provide dietary data for 6–12 mo but are limited by lapses of memory and by the small number of foods that can be listed on a questionnaire.

In a previous study, we found that averaging DRs and FFQ increased correlations between β-carotene intake estimates and serum concentrations [19]. Research in other laboratories has led to the development of the triads method for validating relations between diet and serum nutrient concentrations [20–25]. The triads method uses at least two types of dietary information (FFQ and a food record or recall) and serum concentrations of a nutrient biomarker to determine validity coefficients for nutrient concentrations. We hypothesized that using the triads method and other rigorous statistical models would improve the validity of the relation between dietary intake estimates and serum lycopene.

We hypothesized that a second major reason for the low correlations between dietary and serum lycopene is the variability in lycopene absorption from its major food sources. Carotenoid absorption is known to depend on its food matrix [26–34]. For example, lycopene from tomatoes mixed with fat is better absorbed, and thus more bioaccessible, than lycopene provided as tomato juice or in low-fat salads [29–31]. Several studies have provided information allowing bioaccessibility ratios to be estimated for lycopene from tomato juice or puree, raw tomatoes [32,33], tomato oleoresin [32,34], or raw versus processed tomatoes [35]. Thus, transforming dietary intake estimates of lycopene by their ''bioaccessibility'' ratios should improve correlations between dietary intake estimates and serum lycopene.

Materials and methods

Chemicals

All solvents used were high-performance liquid chromatographic or reagent grade. Chemicals were purchased from Sigma-Aldrich Chemical Company (St. Louis, MO, USA), Fisher Scientific (Pittsburgh, PA, USA) and J. T. Baker Chemical Company (Phillipsburg, NJ, USA). Chromatographic standards were from Sigma-Aldrich. Purities for lycopene, β-carotene, and retinyl acetate standards were >90%, >97%, and >97%, respectively.

Subjects

The sample size needed to attain significance was calculated based on previous publications using the triads method [20–25], because there are no reports specifically for lycopene. We enrolled 54 subjects from Yolo and Sacramento counties in California through advertisements, postings, and word-of-mouth. We collected complete data on 49 subjects (25 men and 24 women). Most subjects (68%) were Caucasian, with the remainder approximately equally distributed among Asian, Hispanic, and those who declined to state a racial background. Subjects were normal weight (body mass index [BMI] 24.2 ± 5.4 kg/m^2), non-smokers, and 39.7 ± 12.3 y of age. Subjects were healthy, with no current illness or histories of diabetes, cancer, heart disease, or chronic digestive disorders. Cholesterols, insulin, and triacylglycerols (TAGs; Table 1) were within normal clinical ranges, as were blood pressure and heart rate (data not shown). Subjects took no medications known to influence carotenoid, retinoid, or fat metabolism.

Four subjects did not complete the study because they did not send in the 3D-DR, and one left because of illness unrelated to the study. The characteristics of the subjects who completed the study were not different from subjects who did not complete the study.

The human subjects institutional review committees of the University of California at Davis and the United States Department of Agriculture approved the study, and each subject signed an informed consent. Volunteers were enrolled into the study year-round, with approximately equal numbers of volunteers enrolling in the spring/summer and the autumn/winter.

Blood collections

Fifteen milliliters of blood was collected from an antecubital vein into 7.5-mL serum tubes after an overnight fast. Blood collection tubes were immediately placed into

Table 1
Serum concentrations of cholesterol, triacylglycerol, insulin, and lycopene

Parameter	Mean ± SD	Normal ranges (US)		References
		Clinical reference range	Mean	
Total cholesterol (mmol/L)	5.06 ± 1.03	<5.18	5.2	[46,36]
HDL cholesterol (mmol/L)	1.34 ± 0.32	0.77–2.05		[46]
LDL cholesterol (mmol/L)	3.29 ± 1.10	1.53–4.62		[46]
Triacylglycerol (g/L)	1.24 ± 0.77	0.4–1.5	1.4	[36,46]
Insulin (pmol/L)	62 ± 51	36–179		[46]
Lycopene (μmol/L)	0.51 ± 0.26	0.42–0.47		[1,3,36]

HDL, high-density lipoprotein; LDL, low-density lipoprotein.

a covered ice bucket to protect them from heat and light. Serum was harvested within 3 h by centrifuging for 15 min at 3000 × *g* on an RP5 Sorvall Centrifuge (Newtown, CT, USA) at 4 °C in an HP4 rotor and then stored in tightly capped 2-mL plastic Cryovials at −70 °C until use. Samples were thawed at room temperature under plastic sleeve-covered fluorescent lights to minimize sample degradation from exposure to ultraviolet light. Blood was used for lycopene, cholesterol, TAG, and insulin analysis. Samples were batched and analyzed within 4 mo of collection.

Anthropometry and blood chemistries

Height and weight were measured (to the nearest 0.1 inch and 0.1 lb, respectively) on standard hospital scales and used to calculate BMI. Large population studies typically have shown that serum lycopene concentrations are correlated with total cholesterol and TAG [1,2,36]. Furthermore, lycopene supplementation decreased total cholesterol, low-density lipoprotein (LDL), and TAG in rabbits fed a high-fat atherosclerotic diet [7]. The relations among cholesterols, TAG, and lycopene are not well understood, but most lycopene appears to be circulated with LDL and there appears to be a positive association of serum lycopene with LDL and an inverse association with TAG under fasting conditions [37–39]. Therefore, we measured TAG and total, high-density lipoprotein (HDL), and LDL cholesterol concentrations in our population and investigated the relation of dietary lycopene and serum lycopene before and after correcting for differences in TAG and cholesterol. Cholesterols and TAGs were measured at the University of California–Davis Medical Center Pathology Laboratory on a Beckman Coulter Synchron LX (Beckman Coulter Inc., Brea, CA). Serum insulin was measured at University of California–Davis Medical Center Pathology Laboratory by chemiluminescence.

Chromatography

Samples were thawed at room temperature under plastic sleeve-covered fluorescent lights to minimize sample degradation. Serum *cis*- and *trans*-lycopene were analyzed by a reversed-phase high-performance liquid chromatographic method developed in our laboratory and described in detail elsewhere [40]. Liquid chromatography of lycopene was run on an Agilent 1100 gradient chromatograph (Hewlett-Packard GmbH, Chemical Analysis Group, Waldbronn, Germany) with a binary pump, degasser, refrigerated autosampler, column heater, and diode array detection. Chromatographic analysis was run and interpreted using a Chemstation for LC 3D version A.08.03 (847) for Agilent Technologies. Chromatography was run on Prodigy 5-mm C18 ODS 250- × 4.6-mm reversed-phase column (Phenomenex, Torrance, CA, USA). Retinyl acetate measured at 325 nm was the internal standard for these measurements. This method does not separate individual *cis*-lycopene isomers, which migrate as one peak. All-*trans*-lycopene was identified and measured in comparison with an authentic all-*trans*-lycopene standard. Total-*cis*-lycopene was identified by its proximity to *trans*-lycopene on our chromatograms and by its spectrophotometric profile. It was measured by comparison with the *trans*-lycopene standard. Chromatographic reproducibility was good, with coefficients of variation <3% ($n = 14$). We added *cis*- and all-*trans*-lycopene concentrations to obtain total serum lycopene concentrations, which were used for mathematical modeling and calculations.

Diet analysis

Dietary intakes for each subject were estimated with an FFQ developed from US national dietary intake surveys, validated for carotenoids [41], and updated for ease of use and with newer dietary information (HHHQ 98.2, Block Dietary Data Systems, Berkeley, CA, USA). Subjects were asked to estimate their typical dietary intakes for the 6 mo before the study. Data was entered onto the Scantron form by the subject and then evaluated for completeness and internal consistency by dietary staff who were trained to look for common reporting errors on this test. For example, FFQs where >20% of the foods were marked as never eaten or 85% of the portion sizes were marked ''medium'' were flagged, and the subject was questioned by the dietary staff. Subjects were provided food models and pictures of foods as aids to estimate portion size. FFQs were completed the day that the subjects came in to donate blood for lycopene analysis. Data were analyzed by Block Dietary Data Systems.

Each subject also completed one 3D-DR consisting of 2 non-consecutive weekdays and 1 weekend day. Subjects were provided pictures of foods to aid in estimating portions of food and were instructed to eat their typical diets and to write down the type, amount, and brand names of all foods and to provide recipes of the meals they prepared. The 3D-DRs were checked for completeness and accuracy and entered into our diet analysis system by a dietitian. The 3D-DR data were analyzed with Nutrition Data System for Research (NDS-R) 4.02 (Nutrition Coordinating Center, University of Minnesota, MN, USA), which uses food composition data provided mainly by the US Department of Agriculture Nutrient database (www.ncc.umn.edu/products/database.html). Subjects were provided with booklets for collecting 3D-RD data on the day they provided their blood sample and were asked to complete their records within 3 wk.

Approximately 88% of our volunteers completed their 3D-DRs within 3 wk of providing their blood samples and FFQs. Thus, the FFQ, 3D-DR, and serum lycopene data were collected at comparable times. The 3D-DRs were not distributed equally throughout the week, as could be expected based on the request for 2 weekdays and 1 weekend day, but all days were well represented. Specifically, Saturdays and Mondays were somewhat over-represented, forming 18% and 16% of the records, respectively. Thursday was somewhat under-represented, at 11% of the records.

Before the study we had set criteria for 3D-DR data, so that any subject who reported energy intakes >5000 or

<900 kcal/d or reported consuming <10 items per day would be interviewed by the study dietitian to determine whether their 3D-DR accurately reflected their typical intake. However, none of the 3D-DRs exceeded these ranges.

Estimating nutrient absorption

There is as yet no single comparison of lycopene absorption from its major food sources, and no ''gold standard'' for selecting nutrient absorption or bioaccessibility data. However, tomatoes are the major source of dietary lycopene in the United States and Europe [36]. Several studies have attempted to compare lycopene absorption, or bioaccessibility, from different tomato preparations [26–35]. Although these estimates vary from reference to reference, they share commonalities. For example, all reports have shown that lycopene is better absorbed (and thus more bioaccessible) from puree than from whole fruit, and that fat increases bioaccessibility. Thus, we were able to select bioaccessibility estimates for lycopene-containing foods from literature values [26–35]. The values we selected were 0.1 (fresh tomatoes), 0.35 (watermelon), and 1.6 (tomato juice or puree).

We supplemented these literature values with data from our own experiments. We estimated lycopene bioaccessibility for tomato-based foods containing cheese or meat as 4.0 based on our laboratory results feeding tomato-based chili containing 30% fat [42]. We estimated bioaccessibility for pink grapefruit as 0.35 from our results with canned pink grapefruit slices (data not published). Other lycopene-containing foods (pink guava, apricots, red papaya, red peppers) are not consumed very often in typical Western diets and were uncommon in the diets of our subjects. Because our laboratory results for pink grapefruit were similar to literature reports for watermelon, we set our bioaccessibility estimate from these uncommonly eaten fruits and vegetables as 0.35. We transformed each lycopene-containing food by its bioaccessibility estimate and added the transformed data to calculate the amount of bioaccessibility-transformed lycopene eaten by each subject.

Data analysis

Data analysis was performed using SAS and R software (SAS Institute, Cary, NC, USA). To investigate the association among serum lycopene concentrations, food intakes, and other covariates (e.g. sex, age, BMI, total cholesterol, HDL cholesterol, LDL cholesterol, insulin, and TAGs [36]), we modeled the data using multiple regression with a forward selection procedure. Forward selection procedures begin by determining which variable provides the most information about an interaction and retains this variable in all future models. Then the remaining variables are considered to determine which, in combination with the first, provides the most additional information. The forward selection process then continues on to generating the minimum number of factors required to describe the interaction [43]. We correlated non-transformed 3D-DRs and FFQ records and bioaccessibility-transformed data to serum lycopene concentrations. Data were evaluated by simple statistics (mean ± standard deviation) and by correlation coefficients analyzed with the SAS CORR procedure to obtain Spearman's rank correlations among the three assessment methods (3D-DR, FFQ, and serum lycopene).

The relation between dietary and serum lycopene was also validated using the triads method [20–25]. Briefly, validity coefficients compare intakes calculated by the dietary assessment method with ''true'' long-term dietary intake [20–25]. The triads method is a triangulation method that does not assume normal distribution of dietary intakes or serum biomarker concentrations; instead its major assumptions are that all three methods (3D-DR, FFQ, and serum lycopene) are linearly correlated with the true (t) dietary intake and that errors are independent. The triads equation for estimating the validity coefficient for FFQ is:

$$PQt = (rQB \times [rQR/rRB])^{1/2}$$

The triads equation for estimating the validity coefficient for the 3D-DR is:

$$PRt = (rRB \times [rQR/rQB])^{1/2}$$

The triads equation for estimating the validity coefficient for serum lycopene is:

$$PBt = (rQR \times [rRB/rQB])^{1/2}$$

where *PQt* is the validity coefficient for FFQ, *PRt* the validity coefficient for 3D-DR, *PBt* the validity coefficient for serum lycopene, *rQB* the correlation between FFQ and serum lycopene, *rRB* the correlation between 3D-DR and serum lycopene, and *rQR* the correlation between FFQ and 3D-DR.

For the triads method we first calculated Spearman's correlation coefficients pairwise among serum lycopene, FFQ, and 3D-DR. We then calculated the coefficients of serum lycopene and dietary lycopene adjusted for bioaccessibility, energy (kilojoules) in the diet, and percentage of fat in the diet. We used these correlation coefficients to calculate validity coefficients. We used bootstrap techniques (a general-purpose approach to statistical inference that estimates properties of a population by measuring the properties of its approximate distributions) to construct 95% confidence intervals for the validity coefficients [44]. The number of bootstrap samplings was 1000 samples for each validity coefficient [20–25].

Results

Dietary intakes of lycopene, total and LDL cholesterol, total TAG, and insulin are listed in Table 2. Our volunteers had a wide range of lycopene intakes, similar to other reports of carotenoid intake [24,45]. Approximately 6% of these volunteers reported no lycopene intake on their 3D-DR, but all

Table 2
Dietary intakes of subjects

Parameter	3D-DR (mean ± SD)	FFQ (mean ± SD)	Mean US intake	References
Energy intake (kJ)	7.2 ± 2.0	8.2 ± 3.6	9.0 (2146 kcal)	[47]
Total fat (g)	67.9 ± 31.3	92.0 ± 52.6	87.6	[36]
Cholesterol (mg)	227 ± 142	227 ± 158	265	[47]
Lycopene (μg)	5054 ± 5875	6656 ± 7671	3505–7658*	[45]
			5612–6762†	[45]
Fat (%)	34 ± 8	38 ± 8	33 ± 0.3	[47]

3D-DR, 3-d dietary record; FFQ, food-frequency questionnaire.
* Mean intake for women (first entry) and men (second entry) from 24-h recall.
† Mean intake for women (first entry) and men (second entry) from the FFQ.

reported lycopene intakes in their FFQ, and all had measurable amounts of lycopene in their serum. Two subjects who reported no lycopene on their 3D-DR also reported low lycopene intakes on their FFQ, and the third reported a moderately high intake. Although the mean dietary intake of lycopene estimated by the 3D-DR is close to the mean intake estimated by the FFQ, these methods did not correlate well with each other ($r = +0.26$), as is often the case [17,18]. Excluding the data of the two subjects who reported no lycopene intake in their 3D-DRs did not improve this correlation ($r = +0.27$). Dietary intake estimates of lycopene were not correlated with age or BMI (data not shown).

Serum concentrations of lycopene, cholesterol, TAG, and insulin are listed in Table 1. Serum lycopene concentrations ranged from 0.06 to 1.35 μmol/L (mean 0.51 μmol/L). These concentrations were well within the normal range for the US adult population [1,2,36]. Lycopene serum concentrations did not correlate with age or BMI and were not correlated with cholesterol, LDL cholesterol, or TAG (data not shown), although these are covariants of lycopene in larger studies [36].

We modeled the relation between dietary intake estimates and serum concentrations of lycopene with a forward procedure designed to find the minimum number of variables that would accurately describe this relation. First, we modeled the effect of covariants (age, sex, BMI, TAG, cholesterols) on the association of serum with dietary lycopene. None of these covariates had significant effects. Second, we log-transformed these covariates because they did not have a linear relation with serum lycopene. Even after log-transformation none of the covariants were significant. Third, we modeled the association of serum lycopene and FFQ lycopene after adjusting for lycopene bioaccessibility, energy (kilojoules) in the diet, and percentage of fat in the diet. The FFQ lycopene corrected for energy and bioaccessibility was associated with serum lycopene, although the impact of these corrections was small (parameter estimate 0.0089, $P = 0.043$, for energy; 0.0027, $P = 0.0001$, for bioaccessibility). Fourth, we modeled the association of serum lycopene with the 3D-DR lycopene after adjusting for bioaccessibility, energy (kilojoules), and percentage of fat in the diet. The results indicate that unadjusted 3D-DR lycopene and 3D-DR lycopene adjusted for bioaccessibility were significantly associated with serum lycopene. However, as with the FFQ, these corrections seemed to have only a small impact (parameter estimate −0.0072 for energy and 0.0098 for bioaccessibility, $P = 0.0001$ for both).

We included all parameters in the model. The results indicate that lycopene intakes estimated by 3D-DR, 3D-DR lycopene adjusted for bioaccessibility, and FFQ lycopene adjusted for bioaccessibility were significantly associated with serum lycopene concentrations ($P = 0.001$), whereas the relation between FFQ corrected for energy and serum lycopene approached significance ($P = 0.053$). The 3D-DR lycopene adjusted for bioaccessibility had the largest impact on serum lycopene concentrations, followed by unadjusted 3D-DR lycopene and FFQ adjusted for bioaccessibility (Table 3). Despite the relatively low impact of FFQ, the mathematical model showed that FFQ and 3D-DR estimates of dietary intake are needed to correctly predict serum lycopene concentrations.

This motivated us to use the triads method to further explore the validity of the relations between dietary intake estimates and serum lycopene concentrations. Results from the triads calculations are presented in Table 4. The results indicated a significant correlation between serum lycopene and dietary lycopene estimated by the FFQ. Furthermore, FFQ and 3D-DR estimates of lycopene adjusted for bioaccessibility were correlated with serum lycopene and with each other. Interestingly, the triads model suggested that FFQ adjusted for bioaccessibility was the most important parameter for estimating serum lycopene concentrations. Unadjusted FFQ was the second most important parameter, and the

Table 3
Model of the influence of bioavailability and energy on correlations of FFQ and 3D-DR data and serum concentrations of lycopene

Variable	Parameter estimate	SE	*t* Statistic	Pr > |*t*|
Intercept	23.4	7.8	3.0	0.0045
FFQ				
Corrected for energy	0.0068	0.0034	2.0	0.053
Bioaccessible	0.0016	0.00040	4.0	0.0002
3D-DR	−0.0051	0.0012	−4.4	<0.0001
Bioaccessible	0.0071	0.00132	5.4	<0.0001

3D-DR, 3-d dietary record; FFQ, food-frequency questionnaire; Pr, probability; *t*, Student's *t* test.

Table 4
Validity coefficients

	Correlation coefficients			Validity coefficients*						Range for validity coefficients†			
				FFQ lycopene		3D-DR lycopene		Serum lycopene					
	r_{QB}	r_{RB}	r_{QR}	ρ_{QT}	95% CI‡	ρ_{RT}	95% CI	ρ_{BT}	95% CI	FFQ $r_{QB} - \rho_{QT}$	Serum lycopene $r_{QB} - \rho_{BT}$	Serum lycopene $r_{RB} - \rho_{BT}$	3D-DR $r_{RB} - \rho_{RT}$
Lycopene (raw data)	0.35	0.15	0.26	0.78	0.21–1.0	0.34	0.08–0.70	0.45	0.12–1.0	0.35–0.78	0.35–0.45	0.15–0.45	0.15–0.34
Lycopene (bioaccessible)	0.33	0.48	0.36	0.49	0.09–1.0	0.72	0.02–0.73	0.66	0.11–1.0	0.33–0.49	0.33–0.66	0.48–0.66	0.48–0.72
Energy (J)	0.12	−0.01	−0.07	0.78	0.05–1.0	0.08	0.05–1.0	0.15	0.04–0.96	0.12–0.78	−0.01–0.15	−0.01–0.15	−0.01–0.08

3D-DR, 3-d dietary record; CI, confidence interval; FFQ, food-frequency questionnaire; r_{QB}, correlation between FFQ lycopene and serum lycopene; r_{QR}, correlation between FFQ and 3D-DR; r_{RB}, correlation between 3D-DR and serum lycopene; ρ_{BT}, validity coefficient of biomarker; ρ_{QT}, validity coefficient of questionnaire; ρ_{RT}, validity coefficient of 3D-DR.

* All CI values >1.00 were truncated as 1.00 is the largest possible value.

† Lower limits are appropriate correlation coefficients and upper limits are appropriate validity coefficients calculated by the method of triads.

‡ $P < 0.05$.

validity coefficient of 3D-DR lycopene adjusted for bioaccessibility was the third most important parameter for estimating changes in serum lycopene. Thus, mathematical modeling and the triads method concluded that FFQ and 3D-DR data are needed to estimate serum concentrations of lycopene accurately, but mathematical modeling suggest that the most important dietary information is bioaccessibility-adjusted 3D-DRs, whereas the triads method suggests that bioaccessibility-adjusted FFQ is most predictive.

Discussion

Subjects in this study were representative of healthy well-fed US and European populations (Tables 1 and 2). Dietary intakes and serum concentrations of lycopene were somewhat higher than mean US values [1,36,45], but this was expected because Davis, California, is in a major tomato-producing area. Although large population studies have suggested that age, sex, BMI, cholesterol, and TAG are associated with serum lycopene concentrations [1,2,36], none of these covariates were significant in this much smaller population. Although lycopene appears to be transported on LDL [37,38], LDL was also not a significant covariant in this study, presumably because of its size. Dietary intakes of lycopene were also not correlated with age or BMI, perhaps because the range for these parameters in our study was not great. Subjects were recruited for our study year-round, but there was no statistical difference between lycopene intake or serum concentrations in the volunteers recruited in the autumn/winter versus the spring/summer months.

Lycopene intake estimates obtained with the FFQ were higher than estimates obtained with the 3D-DR (Table 2). This is a common finding that may be related to the respective weaknesses in the FFQ and 3D-DR methods for estimating dietary intakes [17,18]. Serum lycopene was not highly correlated with dietary intake estimated by the FFQ or 3D-DR, which is also a common finding for lycopene [13–16].

Mathematical modeling showed that 3D-DR and FFQ records contributed independently to the relation between serum and dietary lycopene, and that FFQ and 3D-DR estimates of dietary intake were needed to correctly derive the association with serum lycopene (Table 3). This result may be due to the fact that FFQ and 3D-DR estimates have weak relations to serum lycopene; however, it suggests that the triads method, which uses FFQ and 3D-DR data, would be more predictive of serum lycopene concentrations than the FFQ or 3D-DR alone. This appears to be the case: correlations between dietary and serum lycopene were +0.15 for the 3D-DR and +0.35 for the FFQ, whereas validity coefficients were +0.34 for the 3D-DR and +0.78 for the FFQ (Table 4). These validity coefficients are similar to results shown for an Australian population [24] and somewhat higher than seen in an American study that included smokers [45].

Correcting dietary lycopene by estimating its bioaccessibility from foods improved our mathematical model and

tended to increase the validity of the relation between dietary and serum lycopene (Tables 3 and 4). Correcting for bioaccessibility increased the validity coefficient for the 3D-DR from +0.34 to +0.72 and that for serum lycopene from +0.45 to +0.66. Although adjusting FFQ data for bioaccessibility did not improve its validity coefficient, it was already high at +0.78. This is an important finding, because it suggests that serum concentrations of lycopene depend not only on the amount of the lycopene in the diet but also on the bioaccessibility of lycopene in the diet.

Our subjects were healthy, non-smoking adults from Davis, California, who appeared to be representative of a well-fed US population, so caution should be used when extending our results to larger studies, especially those that include smokers or people with higher than average risks for diseases such as prostate cancer. Even so, it is likely that revising estimated dietary intakes of lycopene by incorporating information on bioaccessibility would improve the validity of the relation between dietary and serum lycopene in these populations.

Although there have been numerous studies of lycopene bioaccessibility and bioavailability [26–35], to our knowledge this is the first study to investigate the impact of bioaccessibility on the relation between dietary intake estimates and serum concentrations of lycopene or, for that matter, any other carotenoid. It is possible that better and more complete data on bioaccessibility would result in even stronger relations between dietary intake (adjusted for bioaccessibility) and serum concentrations of lycopene. Furthermore, it appears that adjusting dietary intake estimates of other carotenoids by bioaccessibility estimates might improve their validity for predicting serum carotenoid concentrations. Recent enhancements in computing power should make it possible to test this hypothesis for lycopene and other phytonutrients.

Conclusion

Our results suggest that the relation between dietary intakes and serum concentrations of lycopene, and probably other carotenoids, can be improved by collecting DRs and FFQ and using the triads method. Furthermore, our data suggest that correcting dietary information for differences in lycopene bioaccessibility may improve the validity of dietary intake estimates for this phytonutrient.

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