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A randomized parallel-group dietary study for stages II–IV ovarian cancer survivors ☆

Raheem J. Paxton [a,*], Celia Garcia-Prieto [a], Maria Berglund [a], Mike Hernandez [b], Richard A. Hajek [a], Beverly Handy [c], Jubilee Brown [d], Lovell A. Jones [a]

[a] Dorothy I. Height Center for Health Equity and Evaluation Research, University of Houston and University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030, USA
[b] Department of Biostatistics, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030, USA
[c] Department of Laboratory Medicine, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030, USA
[d] Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030, USA

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ABSTRACT

Objective. Few studies have examined the dietary habits of ovarian cancer survivors. Therefore, we conducted a study to assess the feasibility and impact of two dietary interventions for ovarian cancer survivors.

Methods. In this randomized, parallel-group study, 51 women (mean age, 53 years) diagnosed with stages II–IV ovarian cancer were recruited and randomly assigned to a low fat, high fiber (LFHF) diet or a modified National Cancer Institute diet supplemented with a soy-based beverage and encapsulated fruit and vegetable juice concentrates (FVJCs). Changes in clinical measures, serum carotenoid and tocopherol levels, dietary intake, anthropometry, and health-related quality of life (HRQOL) were assessed with paired t-tests.

Results. The recruitment rate was 25%, and the retention rate was 75% at 6 months. At baseline, 28% and 45% of women met guidelines for intake of fiber and of fruits and vegetables, respectively. After 6 months, total serum carotenoid levels and α- and β-carotene concentrations were significantly increased in both groups ($P<0.01$); however, β-carotene concentrations were increased more in the FVJC group. Serum β-cryptoxanthin levels, fiber intake (+5.2 g/day), and daily servings of juice (+0.9 servings/day) and vegetables (+1.3 servings/day) were all significantly increased in the LFHF group (all $P<0.05$). Serum levels of albumin, lutein and zeaxanthin, retinol, and retinyl palmitate were significantly increased in the FVJC group (all $P<0.05$). No changes in cancer antigen-125, anthropometry, or HRQOL were observed.

Conclusion. Overall, this study supports the feasibility of designing dietary interventions for stages II–IV ovarian cancer survivors and provides preliminary evidence that a low fat high fiber diet and a diet supplemented with encapsulated FVJC may increase phytonutrients in ovarian cancer survivors.

Introduction

Studies investigating the role of diet in the development of ovarian cancer suggest that high-fat (i.e., total, saturated, and animal fat) and high-glycemic index diets may elevate the risk for ovarian cancer [1,2], whereas high-soy diets may lower risk [3]. Studies investigating the role of fruit, vegetable, and dairy intake and overall dietary patterns were inconclusive or revealed no relationship between these factors and ovarian cancer development [4–7]. More recently, a number of studies have examined the role of diet in the prognosis of ovarian cancer [8–13]. These studies suggest that a diet high in yellow and cruciferous vegetables may improve survival, whereas a diet high in red and processed meats may reduce overall survival [8,9].

Dietary components have been shown to play a role in the etiology of ovarian cancer and may play a role in its prognosis. To date, few dietary interventions have been conducted among ovarian cancer survivors post-diagnosis. A recent study [14] established the feasibility of developing a physical activity and dietary intervention for ovarian cancer patients during treatment. The intervention yielded statistically significant improvements in physical activity; however, minimal changes were observed in fruit and vegetable consumption. One potential strategy to increase fruit and vegetable consumption for this population is to use encapsulated fruit and vegetable juice concentrates (FVJCs). Previous studies among healthy participants showed that the use of encapsulated FVJCs was associated with improvements in serum carotenoid and tocopherol levels [15–17]. *In vitro* studies have shown that carotenoids have antioxidant activity and inhibit cell growth and malignant transformation [18,19]. Tung et al. [20] found that higher levels of β-carotene modestly reduced the risk of ovarian cancer in a case–control study. Moreover, recent

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* Corresponding author at: Dorothy I. Height Center for Health Equity and Evaluation Research, The University of Houston and University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030, USA. Fax: +1 713 745 4286.
E-mail address: rjpaxton@mdanderson.org (R.J. Paxton).

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epidemiologic studies suggest that increased carotenoid intake may be associated with improved prognosis among ovarian cancer survivors [8,9]. Although dietary supplements are frequently used by cancer survivors [21], studies are needed to investigate the feasibility of using encapsulated FVJCs and the level of adherence to recommendations for their use. FVJCs may help to close the gap between the 5 fruit and vegetable servings/day ("5-A-Day") recommended by the National Cancer Institute (NCI) and the number of servings actually being consumed.

The Ovarian Nutrition Education (ONE) Study was a randomized, comparative effectiveness dietary intervention for stages II–IV ovarian cancer survivors. The aims of the ONE Study were to (a) examine the feasibility of a telephone-based dietary intervention for stages II–IV ovarian cancer survivors who had completed treatment at least 6 months prior to the intervention; and (b) determine the differences between a low fat, high fiber (LFHF) diet and a standard National Cancer Institute (NCI) diet supplemented with a soy-based beverage and encapsulated FVJCs with respect to serum carotenoid and tocopherol levels, dietary intake, anthropometry, and health-related quality of life (HRQOL). To the best of our knowledge no previous studies have compared the effectiveness of a diet high in fruits, vegetables, and fiber versus a standard NCI diet supplemented in this way. Investigating such aims may help to elucidate the benefits associated with these supplements among high-risk cancer survivors. We hypothesized that a diet supplemented with encapsulated FVJCs and a soy-based beverage would result in significantly higher serum levels of carotenoids than women randomized to the low-fat, high fiber condition.

Subjects and methods

Study population

Ovarian cancer survivors were identified between 2003 and 2009 from The University of Texas MD Anderson Cancer Center patient database. Survivors were eligible if they (a) were 21 years of age or older; (b) were diagnosed with epithelial ovarian cancer ≥stage IIA; (c) had no evidence of recurrent or progressive disease at the time of recruitment; (d) were in their first clinical remission (cancer antigen [CA]-125 levels ≤35.0 units/mL) and computed tomography scans of the abdomen/pelvis or second-look surgery showed no evidence of ovarian cancer for the duration of the study; (e) were able to speak or read English; (f) were ambulatory/mobile and able to eat whole foods; (g) had a life expectancy of ≥6 months; (h) had a body mass index (BMI) ≥19.5; and (i) had completed treatment ≥6 months before the intervention. Women were excluded from the study if they (a) were pregnant or lactating; (b) had been diagnosed with a comorbidity that necessitated a restricted diet or medication for which a high-fiber diet was a contraindication; or (c) had evidence of bowel obstruction. Data was obtained from the tumor registry regarding ethnicity, age at diagnosis, time since diagnosis, age at randomization, and disease stage at diagnosis of the eligible participants. This study was approved by the Institutional Review Board at MD Anderson Cancer Center.

Study design and randomization

A CONSORT diagram outlining recruitment is depicted in Fig. 1. Participants in the LFHF group consumed a diet similar to the one tested in the Women's Health Eating and Living Study which consisted of 5 servings of vegetables/day (with recommendation of consumption of dark, leafy green and yellow vegetables); 16 oz of vegetable juice (primarily carrot)/day; 3 servings of fruit (high in vitamin C)/day; 30 g fiber/day; and ≤20% of energy from fat [22]. Participants in the FVJC group consumed a diet that conformed to the guidelines established by the NCI "5 A Day" program (i.e., ≥5 servings of fruits and vegetables/day and ≥25 g fiber/day) [23] with reduced fat intake (≤20% of calories from fat); 4 FVJC capsules/day (NSA, LLC, Collierville, TN); and 33 g soy-based beverage powder/day (NSA, LLC, Collierville, TN), which includes 5 g fiber.

Intervention

The intervention consisted of self-monitoring logs and telephone counseling calls. The self-monitoring logs were used to track the participants' progress toward their dietary goals. Telephone counseling based on the Social Cognitive Theory [24] was delivered by one Registered Dietitian (RD) in three phases. In phase 1, which consisted of weekly phone calls over a 2-month period (8 calls total), participants familiarized themselves with the intervention material and set short-term goals to build self-efficacy [25]; meanwhile, the RD monitored participants' dietary behaviors. In phase 2, which included semi-monthly calls over the next 2 months (4 calls total), survivors learned to navigate barriers and monitor their progress toward their dietary goals. In addition, the RD guided survivors in making structural changes (e.g., removing unhealthy foods from the home) and modifying recipes. In phase 3, the RD made monthly maintenance telephone calls (2 calls total) to ensure that participants were adhering to their dietary goals. Throughout the intervention period, participants in the LFHF group were asked to monitor their dietary behaviors, and participants in the FVJC group were asked to track their adherence to the recommendations made for the supplements and beverage and report adverse effects. On average, the telephone calls lasted 20–30 min and both groups received an equal number of calls.

Measures

Clinical measures were assessed for all survivors as a standard of care. For the purposes of this study, we focused on serum albumin and CA-125. Serum samples for clinical measures were collected during clinic visits by clinical nurses and analyzed on site. The serum levels were uploaded to a protected clinical database. These data were retrieved by a study coordinator during clinic visits at baseline and 6 months.

Serum carotenoid and α-tocopherol levels were assessed using fasting blood samples collected during clinic visits at baseline and 6 months. Samples were frozen at −80 °C and then aliquoted into a light-protected amber tube and shipped on dry ice to an independent commercial diagnostic laboratory (Kronos Science Laboratory, Phoenix, AZ), where serum levels of carotenoids and tocopherols were analyzed. Reverse-phase chromatography coupled with multi-wavelength and fluorescence detection was utilized for the simultaneous determination of serum levels of α-carotene, β-carotene, β-cryptoxanthin, lutein and zeaxanthin, retinol, lycopene, retinyl palmitate, and α-tocopherol. The method was correlated with National Institute of Standards and Technology Standard Reference Material 968c and monitored with National Institute of Standards and Technology Round Robin proficiency studies twice a year [26]. Serum levels of α-carotene, β-carotene, β-cryptoxanthin, lutein and zeaxanthin, retinol, lycopene, and retinyl palmitate were measured, as were serum levels of α-tocopherol. All assays were performed by laboratory personnel who were blinded to the intervention condition status of the samples.

Dietary intake was assessed using 3-day food records collected at baseline and 6 months. To increase the accuracy of the 3-day food records, a trained Registered Dietitian collected all food record data. Participants were asked to complete a food record for 2 weekdays and 1 weekend day within the same week. Dietary and nutrient intake was estimated using the Nutritional Data System for Research (Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN).

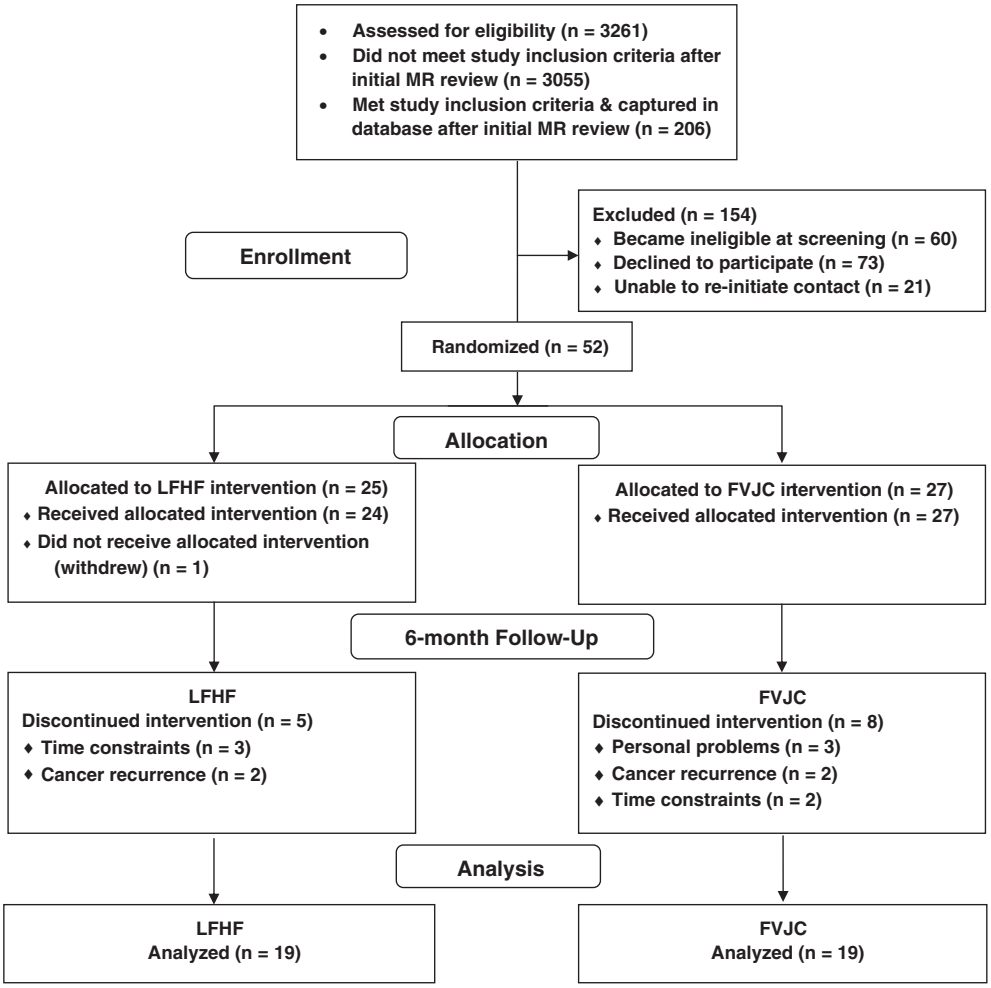

Fig. 1. CONSORT diagram.

Anthropometric indicators and medical characteristics (i.e., height, weight, and waist and hip circumferences) were assessed at baseline and 6 months by trained staff. To minimize variability in the measurements, one trained staff member measured all study participants. For the purposes of this study, we focused on weight and waist-to-hip ratios. Medical characteristics (i.e., age, stage, race, and data of diagnosis) were ascertained using the MD Anderson clinical database.

HRQOL was assessed at baseline and 6 months using the SF-36 Health Survey [27]. The SF-36 measures levels of health by asking questions pertaining to physical and mental well-being. It includes a total of four subscales each for mental (emotional well-being, vitality, role limitations due to emotional problems, and social functioning) and physical (physical functioning, general health perceptions, bodily pain, and role limitations due to physical health problems) well-being. Subscale scores range from 0 to 100, with higher scores indicating better health. The reliability and validity of the SF-36 have been established, and the instrument has been used in various populations of cancer survivors [28].

Feasibility was assessed in terms of rates of recruitment, attrition for any reason, recurrence during the study period, and adherence to the dietary intervention goals. The recruitment rate was calculated as the proportion of recruited survivors who were eligible to participate. Adherence rates were calculated as the proportion of participants in each condition who met the proposed study goals. Retention rates were calculated as the proportion of participants who remained in the intervention for the duration of the study.

Statistical analysis

Descriptive statistics of clinical and lifestyle factors were calculated for all participants. Baseline and 6-month data on serum carotenoid and tocopherol levels, anthropometric indicators, dietary variables, and HRQOL were summarized by study coordinators. Serum carotenoid and α-tocopherol levels were log transformed prior to statistical analysis. An independent sample t-test or a chi-square test of homogeneity was used to determine whether randomization improved balance. Descriptive statistics were used to summarize recruitment, retention, and adherence rates. Next, paired t-tests were used to assess within-group changes in study outcomes, and independent sample t-tests were used to determine whether changes from baseline to 6 months differed between the study groups. All statistical tests were two-sided and P values were computed using the SAS Enterprise System (version 4.1, Cary, NC).

Results

Descriptive characteristics

We identified 206 ovarian cancer survivors who were eligible to participate in the ONE Study; however, only 51 survivors opted to participate and provided written informed consent. No differences were observed between the intervention groups in terms of clinical and demographic characteristics. The majority of participants were 50–59 years old, 1.6 years out from diagnosis, diagnosed with stage

III disease, white, and overweight (60% had BMI≥25) at baseline (Table 1).

Feasibility

The recruitment rate was 25% (52/206), although one participant withdrew prior to intervention and 75% of those who were randomized completed the 6-month assessment. At baseline, few (28%) participants met current dietary guidelines for fiber intake (≥25 g/day), whereas more (45% and 57%, respectively) participants met guidelines for fruit and vegetable consumption (≥5 servings) and fat intake (≤35% of calories from fat). Retention rates did not differ by ethnicity, age at diagnosis, time since diagnosis, age at randomization, disease stage at diagnosis, or study condition (all $P>0.05$); however, four (8%) women (two in each group) had disease recurrence during the intervention and were excluded from completing the study. Participants in the FVJC group exhibited higher adherence to the recommendations of ≥5 daily servings of fruits and vegetables and ≥25 g fiber (33% and 32% adherence, respectively), whereas adherence to the recommendation of ≤20% of calories from fat was lower (21%). Participants in the LFHF group adhered most to the recommendation of ≥5 daily servings of vegetables (47%) and ≥2 daily 8-ounce servings of juice (37%) and adhered less to the recommendations of ≥30 g fiber/day (26%), ≤20% of calories from fat (16%), and ≥3 servings of fruit/day (11%). No adverse effects were reported by participants in either group.

Clinical measures

At baseline, no significant differences in serum albumin or CA-125 levels were observed between the groups (all $P>0.05$). Serum CA-125 levels remained constant from baseline (11.0 ± 5.5 U/mL) to 6 months (11.3 ± 5.5 U/mL) for all study participants ($P>0.05$). Serum albumin levels remained constant for participants in the LFHF group (4.33 ± 0.29 g/dL vs. 4.21 ± 0.30 g/dL, $P>0.05$) but were significantly increased for participants in the FVJC group (4.27 ± 0.32 g/dL vs. 4.47 ± 0.34 g/dL, $P>0.05$).

HRQOL

At baseline, no significant differences in HRQOL were observed between the groups (all $P>0.05$). After 6 months, no significant changes in HRQOL were observed among the study participants (Table 2).

Table 1
Descriptive characteristics of study participants by intervention condition.

	LFHF group (N = 24)	FVJC group (N = 27)	P-value
Age, in years			
Mean ± SD	55.7 ± 10.1	51.7 ± 9.4	0.154
30–49, n (%)	6 (25.0)	11 (40.7)	0.672
50–69	15 (62.5)	14 (51.9)	
70+	3 (12.5)	2 (7.4)	
Years since diagnosis			
Median (5%, 75%)	1.5 (1.1–3.5)	1.6 (1.1–4.5)	0.542
Stage at diagnosis			0.389
II	8 (33.3)	4 (14.8)	
III	16 (66.6)	23 (85.2)	
IV	1 (4.1)	0 (0.0)	
Race/ethnicity			
White	20 (83.3%)	24 (88.9%)	0.217
BMI (kg/m^2)			
Mean ± SD	27.1 ± 6.1	28.8 ± 7.0	0.381
Obese (>30 kg/m^2)	8 (33.3%)	8 (29.6%)	

LFHF = low fat, high fiber diet group; FVJC = fruit and vegetable juice concentrate group; SD = standard deviation, BMI = body mass index.

Table 2
Health-related quality of life among intervention participants.

	Baseline M (SD)	6 months M (SD)	Mean change	Within-group P value	Between-group P value
Physical function					0.692
LFHF	80.6 (21.0)	81.6 (22.5)	1.00	0.515	
FVJC	81.9 (25.9)	88.2 (20.3)	6.30	0.166	
Role limitations — physical					0.437
LFHF	78.1 (34.0)	80.3 (24.4)	2.20	0.465	
FVJC	69.8 (43.0)	88.2 (31.5)	18.4	0.106	
Pain					0.428
LFHF	82.0 (19.2)	80.3 (24.4)	−1.70	0.914	
FVJC	80.9 (21.8)	83.6 (20.8)	2.70	0.419	
General health					0.806
LFHF	71.3 (17.9)	70.0 (19.4)	−1.30	0.644	
FVJC	71.3 (21.9)	72.1 (20.5)	0.80	0.746	
Emotional function					0.689
LFHF	76.7 (17.7)	79.6 (17.1)	2.90	0.480	
FVJC	78.8 (17.7)	83.8 (12.3)	5.00	0.153	
Role limitations — emotional					0.134
LFHF	83.3 (35.4)	78.9 (31.8)	−4.40	0.482	
FVJC	81.9 (27.8)	91.2 (18.7)	9.30	0.096	
Social function					0.227
LFHF	87.5 (21.2)	87.5 (19.1)	0.00	0.235	
FVJC	88.5 (17.6)	90.8 (18.1)	2.30	0.331	
Fatigue					0.842
LFHF	58.8 (20.3)	57.6 (23.4)	−1.20	0.933	
FVJC	65.8 (22.1)	66.6 (19.7)	0.80	0.584	

LFHF = low fat, high fiber diet group; FVJC = fruit and vegetable juice concentrate group; M = mean; SD = standard deviation.

Dietary intake and anthropometry

At baseline, no significant differences in dietary intake or anthropometry were observed between the two groups (all $P<0.05$; Table 3). From baseline to 6 months, caloric intake was marginally, albeit insignificantly, decreased ($P=0.06$), and fat intake was decreased ($P=0.08$) in the FVJC group. From baseline to 6 months, vegetable and juice consumption and fiber intake were significantly increased in the LFHF group (all $P<0.01$). Between-group changes in dietary intake were observed only in juice consumption ($P<0.05$).

Serum carotenoid and tocopherol levels

At baseline, no significant differences in serum α-carotenoid or tocopherol levels were observed between the groups (all $P>0.05$). Total carotenoid serum levels and α- and β-carotene concentrations were significantly increased in both groups (all $P<0.01$; Table 4). Concentrations of lutein and zeaxanthin, retinol, and retinyl palmitate were significantly increased in the FVJC group (all $P<0.05$), whereas β-cryptoxanthin levels were significantly increased in the LFHF group (all $P<0.05$). Increases in β-carotene were greater in the FVJC group than in the LFHF group ($P<0.05$). A graphical depiction of changes in serum levels of carotenoids and tocopherols is included in Fig. 2.

Discussion

In this study, we found that a low fat, high fiber diet and a standard NCI diet supplemented with encapsulated FVJCs and a soy-based beverage appear to be safe for ovarian cancer survivors and are associated with significant improvements in total carotenoid serum levels and α- and β-carotene concentrations. To our knowledge, this is one of the first studies conducted among cancer survivors to demonstrate that a healthy diet supplemented with encapsulated FVJCs and a soy-based beverage is safe and feasible. Overall, these data support the feasibility of recruiting and retaining ovarian cancer survivors in a dietary intervention and offer preliminary support for

Table 3
Anthropometric and dietary variables for study participants.

	Baseline M (SD)	6-months M (SD)	Mean change	Within-group P value	Between-group P value
Waist-to-hip ratio					0.452
LFHF	0.79 (0.05)	0.79 (0.05)	0.00	0.729	
FVJC	0.79 (0.06)	0.78 (0.06)	−0.01	0.395	
Weight, in Kg					0.866
LFHF	71.3 (14.7)	71.2 (14.5)	−0.10	0.124	
FVJC	74.9 (20.0)	72.6 (19.0)	−2.30	0.275	
Energy intake, in Kcal/day					0.286
LFHF	1658 (372)	1596 (452)	−62.0	0.694	
FVJC	1754 (346)	1581 (391)	−173	0.055	
Fruit servings/day					0.889
LFHF	1.7 (2.0)	1.8 (1.2)	0.10	0.798	
FVJC	1.8 (1.4)	1.9 (1.9)	0.10	0.998	
Vegetable servings/day					0.271
LFHF	3.7 (1.5)	4.9 (1.9)	1.20	0.028	
FVJC	3.5 (2.0)	4.1 (2.0)	0.60	0.367	
Juice servings/day					0.018
LFHF	0.6 (0.9)	1.5 (1.4)	0.90	0.018	
FVJC	0.5 (0.8)	0.4 (0.7)	−0.10	0.631	
Percent fat intake/day					0.600
LFHF	32.1 (5.3)	28.2 (9.7)	−3.90	0.114	
FVJC	37.3 (7.6)	30.4 (10.7)	−6.90	0.081	
Fiber, in g/day					0.205
LFHF	20.8 (6.5)	26.0 (9.5)	5.20	0.020	
FVJC	20.5 (9.3)	23.4 (7.8)	2.90	0.352	

LFHF = low fat, high fiber diet condition; FVJC = fruit and vegetable juice concentrate group; M = mean; SD = standard deviation.

the use of encapsulated FVJCs and a soy-based beverage as a dietary supplement.

The present study is one of the first to examine the role that a healthy dietary pattern may have on clinical measures such as serum albumin and CA-125 in stages II–IV ovarian cancer survivors. Many of the women enrolled in our intervention appeared to maintain a healthy clinical state based on albumin and CA-125 levels and 4 women had disease recurrence. In a recent study, Alphs et al. [29] found that older women whose serum albumin levels exceeded 3.7 g/dL experienced a 40% reduction in mortality. Although we cannot speculate on the clinical significance of our feasibility study, previous studies have shown that dietary components are associated with improvements in ovarian cancer survival [8,9,13]. More research is needed to validate the clinical significance of a standard dietary intervention and a dietary intervention enhanced with encapsulated FVJCs in this population.

The ONE Study is among the first to report on the post-diagnosis dietary habits of ovarian cancer survivors. Our data show that few survivors met current guidelines for fiber intake and fruit and vegetable consumption at baseline, which is consistent with findings from previous studies [30–32]. Despite the baseline dietary levels, many participants made substantial improvements in their overall dietary patterns throughout the intervention. The improvements in dietary intake observed among our survivors are important in view of evidence that higher intake of both fruits and vegetables and vegetables only is associated with longer survival [8]. Although modest reductions in dietary fat intake were observed, few women were able to meet the study goal of ≤20% of calories from fat. More research is needed to identify the barriers to reducing and maintaining dietary fat goals or determine whether reducing dietary fat consumption to ≤20% of calories from fat is a realistic goal for cancer survivors.

Overall, participants in the ONE Study had significant increases in serum carotenoid levels. We believe that the significant increase in carotenoids observed among our LFHF participants was expected and reflected the increased fiber intake, servings of vegetables, and citrus juice (e.g., orange and pink grapefruit juice). However, we do not believe that the significant increase in the total carotenoid serum levels among participants in the FVJC group was due to changes in diet alone. Previous studies have shown that the use of these particular encapsulated FVJCs is associated with improvements in serum carotenoid levels [15–17]; therefore, this may serve to explain why FVJCs contributed to greater increases in β-carotene and retinyl palmitate in the FVJC group than in the LFHF group. Thus, encapsulated FVJCs may be an effective means of increasing carotenoid intake beyond what is currently being consumed. Interestingly, β-cryptoxanthin levels were significantly increased in the LFHF group compared to the FVJC group, but Lutein and zeaxanthin levels did not. It could be that LFHF women

Table 4
Serum carotenoid and tocopherol levels of study participants.

	Baseline M (SD)	6 months M (SD)	Mean change	Within-group P value	Between-group P value
α-carotene[a]					0.342
LFHF	1.78 (0.32)	2.11 (0.48)	0.33	0.004	
FVJC	1.67 (0.43)	1.87 (0.39)	0.20	0.008	
β-carotene[a]					0.007
LFHF	2.32 (0.30)	2.56 (0.42)	0.24	0.001	
FVJC	2.29 (0.38)	2.83 (0.43)	0.54	<0.001	
β-cryptoxanthin[a]					0.038
LFHF	1.82 (0.28)	1.96 (0.36)	0.14	0.019	
FVJC	1.76 (0.23)	1.77 (0.23)	−0.01	0.653	
Lutein and zeaxanthin[a]					0.916
LFHF	2.14 (0.27)	2.13 (0.24)	−0.01	0.080	
FVJC	2.25 (0.24)	2.28 (0.26)	0.03	0.027	
Lycopene (trans) [a]					0.573
LFHF	2.14 (0.27)	2.13 (0.24)	−0.01	0.518	
FVJC	2.19 (0.17)	2.24 (0.15)	0.05	0.053	
Retinol[a]					0.075
LFHF	2.75 (0.09)	2.75 (0.09)	0.00	0.919	
FVJC	1.72 (0.11)	2.76 (0.11)	0.04	0.029	
Retinyl palmitate[a]					0.022
LFHF	1.40 (0.36)	1.38 (0.31)	−0.02	0.308	
FVJC	1.21 (0.36)	1.38 (0.29)	0.17	0.049	
α-tocopherol[a]					0.292
LFHF	1.23 (0.16)	1.23 (0.14)	0.00	0.416	
FVJC	1.17 (0.15)	1.24 (0.09)	0.07	0.499	

LFHF = low fat, high fiber diet group; FVJC = fruit and vegetable juice concentrate group; M = mean; SD = standard deviation.
All units are μg/mL
[a] Estimates are log transformed.

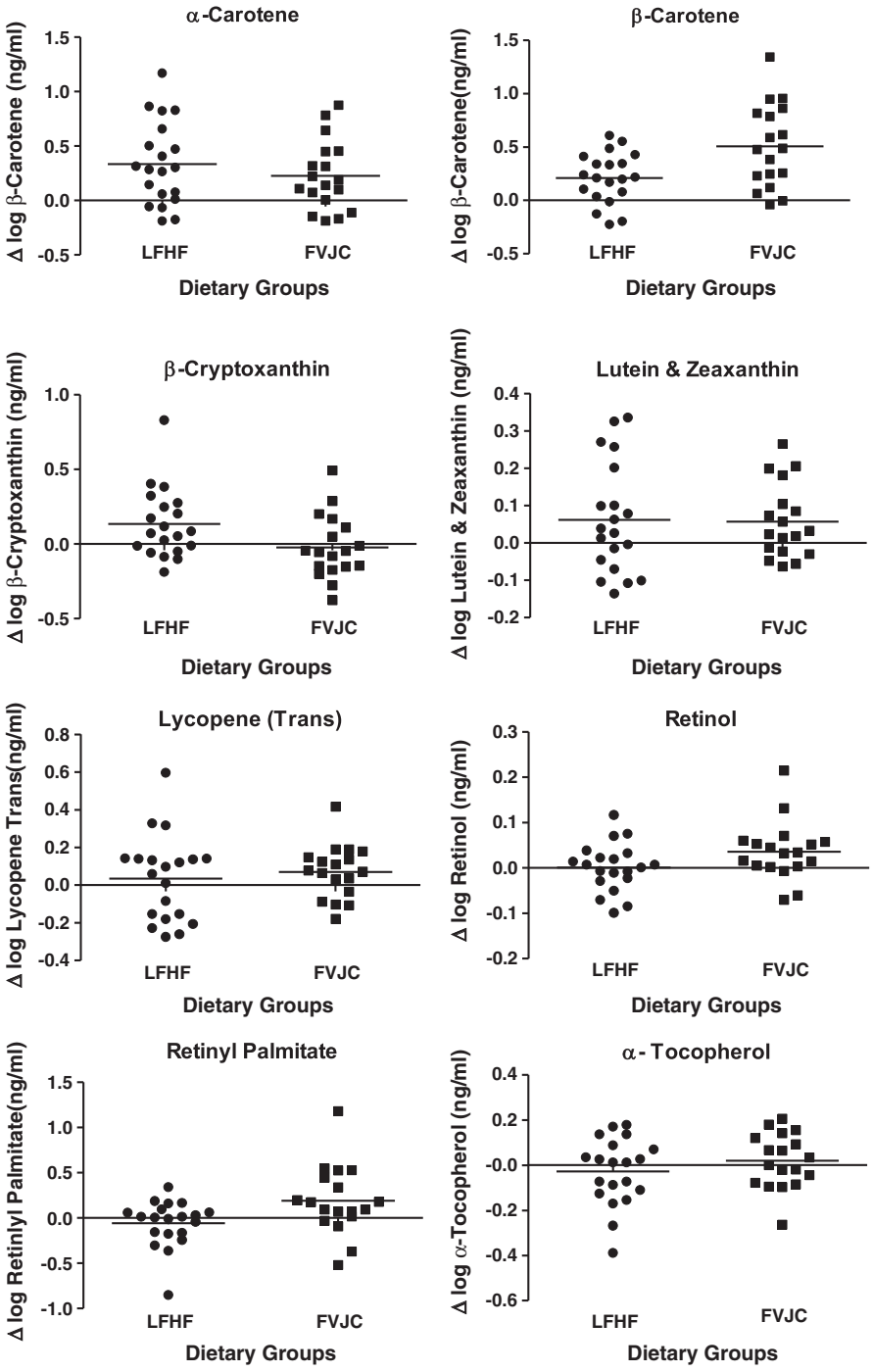

Fig. 2. One-way scatter plots were used to illustrate the range of change in serum carotenoid and α-tocopherol values for both intervention groups. Δ = change; LFHF = low fat, high fiber; FVJC = fruit and vegetable juice concentrate. All panels present data on a log-transformed scale, and dark lines represent the mean change.

consumed diets high in carrots (solids and juice), butternut squash, pumpkin and sweet or hot red peppers, while neglecting to increase green leafy vegetable intake. We are uncertain why green leafy vegetable intake was not increased among LFHF women. More research is needed to determine the factors that prevent adherence to specific dietary components.

The increase in serum carotenoid levels observed among participants in this study is important for several reasons. Previous *in vitro* studies have demonstrated that carotenoids inhibit cell growth and malignant transformation and show antioxidant activity [18,19]. Similarly, carotenoid intake may also affect estrogen metabolism by inhibiting estrogen-induced cell proliferation [33]. One study reported that higher levels of β-carotene modestly reduced the risk of ovarian cancer [20]. Recent studies of breast cancer survivors have shown that higher intake and exposure to carotenoids were associated with a reduction in second breast cancer events [34,35]. Although we are uncertain whether higher carotenoid intake is associated with improved prognosis among ovarian cancer survivors, recent epidemiological studies suggest that this relationship is probable [8,9]. To fully understand the relationship between serum carotenoid and tocopherol levels and ovarian cancer survival, more intervention and epidemiological studies are needed.

Although anthropometric and psychosocial factors have been linked to ovarian cancer prognosis [36,37], we observed no changes

in these outcomes within or between groups. We can only speculate that changes in dietary intake, without caloric restriction or changes in physical activity, will not result in weight loss; likewise, improved diet without changes in physical activity may not result in improvements in HRQOL. In a recent lifestyle intervention, von Gruenigen et al.[14] found that improvements in physical activity contributed to improved HRQOL and patients' ability to tolerate surgery and chemotherapy; such increases in physical activity may therefore affect survival. Future interventions among ovarian cancer survivors should aim to reduce weight among overweight and obese women and consider multiple behavior interventions with distal outcomes such as morbidity and mortality.

The limitations of this study are its small sample size, use of self-reported measures, and poor adherence to intake of dietary fiber and fat recommendations. Other limitations include the lack of a placebo-controlled condition or a sufficient factorial design to determine the individual effect of diet in the FVJC group. Despite these inherent limitations, this study had a number of notable strengths, including its randomized and prospective design, the use of valid and reliable measures of HRQOL, biochemical outcomes (e.g., carotenoids) that were measured by persons blinded to the experimental conditions, and multiple assessments of dietary intake.

In conclusion, this study provided evidence that a short-term dietary intervention emphasizing encapsulated FVJCs, a soy-based beverage, or a low-fat and high fiber diet is safe and feasible for stages II to IV ovarian cancer survivors. Although the use of these supplements in the context of a standard NCI diet resulted in increases in serum carotenoid levels, we advocate that encapsulated FVJCs complement fruit and vegetable consumption and do not replace it. Future double-blinded, placebo-controlled, randomized trials among cancer survivors are needed to determine the efficacy of encapsulated FVJCs. Moreover, future studies are needed to determine whether post-diagnosis dietary intake, physical activity, and serum biomarker levels are associated with ovarian cancer prognosis.

Conflicts of interest statement

- Raheem Paxton, Celia Garcia-Prieto, Maria Berglund, Mike Hernandez, Richard A. Hajek, Beverly Handy, and Jubilee Brown declare that we have no conflicts of interest.
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