Biobehavioral Intervention Improves Dietary Patterns and Biomarkers of Carotenoid and Fatty Acid Intakes in Overweight Cancer Survivors

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Abstract

Cancer survivors are at risk for suboptimal nutrition due to therapy, inadequate dietary patterns, and susceptibility to unproven dietary advice. Effective biobehavioral interventions aimed at increasing adherence to evidence-based survivorship recommendations are key in reducing cancer recurrence, comorbidities, and all-cause mortality. Data from a six-month phase II non-randomized trial were analyzed to determine pre- to post- changes in: (1) dietary patterns; (2) skin and plasma carotenoids; and (3) red blood cell fatty acid (RBC FA) composition. Overweight cancer survivors (N=29) were provided weekly produce harvesting, semi-monthly group education, remote motivational interviewing, and access to a secure web portal. Data were collected at baseline and post-intervention. Dietary patterns were assessed via 30-day food frequency questionnaires (FFQs) and Healthy Eating Index 2010 (HEI-2010) scores. Skin carotenoids were measured by resonance Raman spectroscopy, plasma carotenoids by high performance liquid chromatography, and RBC FAs by gas chromatography. Increases were documented in HEI-2010 total diet (p=0.006), total fruit (p=0.003), and fatty acids (p=0.007) scores. HEI-2010 scores for total vegetables also trended positively (p=0.054). As assessed by FFQ, survivors increased total dietary intakes of carotenoids by 66% (p<0.001) including increased individual intakes of all five carotenoids analyzed. Mean total dietary fat intakes decreased by 12.37 g (p=0.010), with survivors decreasing intakes of saturated, unsaturated, and *trans* fats. Plasma concentrations of total carotenoids increased by 35% (p<0.001), as did plasma α-carotene, β-carotene, and lycopene (p<0.001, p<0.001, p=0.017, respectively). Total skin carotenoids increased (p=0.015) and were highly correlated with total plasma carotenoids (r=0.728, p<0.001). Despite changes in dietary intakes of FAs, RBC FA composition was largely unchanged. However, relative abundance of omega-3 FAs decreased by 6% as compared to baseline (p=0.001). Results warrant larger randomized controlled trials to establish efficacy.

Introduction

There is a growing number of cancer survivors in the United States, with the population expected to increase to over 20 million by the year 2026.[1] The increased prevalence is due to improved and earlier screening, more effective therapies, and more successful amelioration of disease.[1,2] Despite these advances, cancer remains an ongoing public health challenge. In the United States, it is the second most common cause of death.[2] This is in part due to survivors' increased risk of comorbidities, such as cardiovascular disease (CVD) and type 2 diabetes (T2DM), even after completion of active cancer therapy.[3] Additionally, a large number of cancer survivors are considered overweight or obese, which further adds to their increased risk of developing comorbid conditions.[4] Cancer, which was once described as an acute condition, now must be managed chronically.

Inherited genetic mutations account for only five to ten percent of all new US cancer cases; rather, it is primarily environmental factors that drive cancer development and progression.[2] Fortunately, evidence-based guidelines for cancer prevention and survivorship have been developed by a number of expert committees to provide guidance for appropriate lifestyle behaviors to reduce cancer risk.[5–7] These recommendations are based on convincing evidence that healthy lifestyle behaviors can reduce the risk of many chronic conditions, including cancer.[5]

Research has demonstrated that adherence to these recommendations for cancer prevention and survivorship does in fact reduce cancer-specific mortality.[8] Despite this evidence, however, most cancer survivors are not meeting the recommendations. This may be due to lack of reimbursement for lifestyle modification programs, poor coordination among healthcare providers, and/or limited resources.[9] To increase adherence to these guidelines, many lifestyle interventions have been developed. Investigation of these lifestyle interventions suggests improved adherence to guidelines, resulting in positive effects on not only modifiable behaviors, but also on health outcomes and quality of life of cancer survivors.[10–12]

The evidence-based guidelines, which are built upon the foundation of a primarily plant-based diet, incorporate recommendations for dietary patterns high in fruits, vegetables, and whole grains. Diets rich in fruits and vegetables have been associated with decreased risk for a number of conditions, including cancer.[13,14] Plant-based diets are high in many nutrients and phytochemicals that may reduce disease. Carotenoids, which are phytochemicals that may exert protective effects in the body, are abundant in fruits and vegetables.[15,16] Because carotenoids are not endogenously produced, they must be consumed in the diet.[17] Furthermore, they are easily deposited in human tissue, including blood and adipose tissue, which gets its yellow hue from these deposited carotenoids.[18] Because of this, their possible influence on cancer risk as well as their use as biomarkers of produce intake have been studied.[19–23]

Despite potential benefits, research has not confirmed that carotenoids are required by our body and they are therefore not yet deemed essential to human health.[24] However, the carotenoid compounds exert biological activities that are important for the normal growth, development, and function of many body systems. For example, the provitamin A carotenoids (α-carotene, β-carotene, and β-cryptoxanthin) are important for both immune system function and vision.[24] While the functions of non-provitamin A carotenoids are yet to be established, other proposed mechanisms include regulation of genes associated with cell growth, apoptosis, and cell signaling by bioactive metabolites.[15]

As mentioned above, large epidemiological studies have described a reduction in cancer risk with the consumption of carotenoid-containing produce, including specific carotenoids such as lycopene and β-carotene.[19–21,25,26] However, consumption of whole foods, rather than these carotenoids in isolation, is preferred. Indeed, *in vivo* studies have demonstrated the preferential effects of whole food diets when compared to isolated supplements in halting cancer progression. In one study, male rats induced to develop prostate cancer were fed diets containing either whole tomato powder, isolated lycopene beadlets, or control beadlets. Results demonstrated that consumption of the tomato powder, but not the lycopene beadlets, inhibited carcinogenesis.[27] Authors suggested that the whole tomato powder may contain additional phytochemicals or other active ingredients in addition to lycopene that confer this beneficial effect.

Due to their chemical structure, carotenoids are lipid-soluble and therefore must be incorporated into micelles for absorption.[24] As such, they must be consumed with dietary fat. The amount of dietary fat ingested influences the bioaccessibility of carotenoids. Greater amounts of dietary fat seem to improve bioaccessibility, however an exact recommendation has yet to be determined.[15]The type of dietary fat may also impact this absorption.[24] For example, research has demonstrated that some carotenoids are more readily absorbed in the presence of saturated fatty acids (SFAs) than when in the presence polyunsaturated fatty acids (PUFAs) and monounsaturated fatty acids (MUFAs).[28] Other studies find that other carotenoids are better absorbed in opposite conditions.[15] The chain length of the FAs, too, plays a role in bioaccessibility of carotenoids. For example, research has demonstrated that carotene micellarization is more efficient in the presence of long-chain compared to medium-chain triglycerides.[29,30]

The purpose of the Growing Hope intervention was to assess the impact of a comprehensive, garden-based lifestyle intervention on cancer survivor adherence to evidence-based guidelines. Data were analyzed to determine if the biobehavioral intervention improved overall diet quality and individual dietary components. Additionally, markers of carotenoid status in the skin and plasma along with RBC FA composition were assessed to discover if these biomarkers were correlated with self-reported dietary patterns in the cancer survivor population.

Methods

Participants

Overweight and obese adult cancer survivors were recruited from The James Cancer Hospital and Solove Research Institute, associated Ohio State University Comprehensive Cancer Center oncology clinics, and the James*Care* for *Life* survivorship outreach program. Recruitment fliers and study brochures were distributed in person and via email. Interested participants were asked to complete a 15-item screener in person or by emailing study personnel to confirm eligibility.

Inclusion criteria were as follows: 1) voluntary agreement to participate and sign an informed consent document; 2) English-speaking; 3) ≥18 years of age); 4) completion of active cancer treatment (chemotherapy, radiation therapy, and/or surgery) within the previous 48 months; 5) body mass index (BMI) ≥25 kg/m^2; and 6) access to Internet, basic computer skills, and an active email account.

Potential participants were excluded if 1) cognitively unable to consent; 2) having physical or mental limitations that would prevent full participation in the program; 3) having participated in the previous feasibility study;[10] 4) receiving active cancer treatment (including surgery, neoadjuvant hormonal chemotherapy, or radiation); 5) having pre-existing medical conditions that would prevent unsupervised physical activity (e.g., severe orthopedic conditions, unstable angina, recent history of myocardial infarction, hospitalization within six months); 6) taking medications that did not allow for increased intake of fruits and vegetables (e.g., pharmacologic doses of warfarin); 7) involved in another clinical trial; 8) planning to begin medications during the course of the intervention or using some non-prescription substances (such as herbal or botanical products); or 9) having active metabolic or digestive illnesses (e.g., Crohn’s, Celiac, IBS), renal or hepatic insufficiency, cachexia, short bowel syndrome, or pregnancy.

Upon confirmation of eligibility, participants completed informed consent forms, HIPAA Authorization Forms, were scheduled for a study orientation, and were registered with the Clinical Trials Office. All study procedures were approved by The Ohio State University Institutional Review Board.

Intervention

The 2015 pilot study was conducted to assess efficacy of an established comprehensive lifestyle program, Growing Hope.[10] Growing Hope is a single-arm multifaceted biobehavioral intervention in which each participant serves as his or her own control. Through participation in this six-month intervention, participants had access to: 1) weekly harvesting of free, fresh fruits, vegetables, and herbs at an urban cancer survivors’ garden supported by an NIH-aligned Comprehensive Cancer Center; 2) semi-monthly evidence-based group education sessions led by experts in oncology, nutrition, and physical activity and supplemented with an online web portal for additional survivor-specific resources and information on evidence-based recommendations; and 3) remote motivational interviewing coaching (tele-MIC) with a Registered Dietitian Nutritionist (RDN) trained in oncology and sports nutrition, behavior change, and motivational interviewing techniques.

Each week throughout the course of the intervention, participants were encouraged to harvest fresh produce up to two times per week. A wide variety of fruits, vegetables, and herbs were available throughout the growing season (May-October). Participants were educated on the evidence-based guidelines for cancer prevention and survivorship at semi-monthly group sessions.[5,31,32] Experts in each of the subject areas were brought in to lead the group education sessions on topics aligning with the evidence-based recommendations. Most relevant to this study was the recommendation to eat carotenoid-containing fruits and vegetables with lipid to enhance absorption. At the end of each education session, a cooking demonstration was presented by The Ohio State University Medical Center chef or a RDN to teach participants how to prepare healthy recipes utilizing produce harvested from the garden to maximize nutrient and phytochemical intake.

To supplement in-person education sessions, a secure online web portal was provided for participant use. Participants could sign on to the web portal using a uniquely-assigned study ID to access group education presentations, handouts, and in-class recipes, as well as additional study-related materials. Other resources, such recent research publications, information and support from the tele-MIC, additional recipes, and links to survivor-specific websites were also available through the web portal for continued reference throughout the study.

The final component of the intervention was tele-MIC provided by a RDN. The tele-MIC provided individualized coaching to participants over the course of the intervention. Each week, the tele-MIC reached out to participants to reinforce class concepts, help them set goals, provide additional resources, and answer relevant questions. Interactions were thoroughly documented.

Data Collection

At baseline (month 0), participants completed clinical, anthropometric, lifestyle, and dietary assessments. Data were collected via secure online surveys to assess lifestyle behaviors, including dietary patterns, as well as demographic and health history information. Clinical indicators of health, including carotenoid and FA status, were assessed objectively at laboratory visits. At the end of the intervention (month 6), these assessments were repeated. Study data were collected and stored through use of REDCap (Research Electronic Data Capture) data capture tools hosted at The Ohio State University.[33]

Dietary Intakes. Dietary intakes were assessed via the VioScreen (Viocare, Inc., Princeton, NJ) 30-day food frequency questionnaire (FFQ). This validated FFQ utilizes computer software to graphically depict foods and portion sizes for more accurate estimates of food and beverage consumption patterns.[34] This algorithm-driven, computer-delivered FFQ is based on paper FFQs developed at the Fred Hutchinson Cancer Research Center and employs the food and nutrient information database, Nutrition Data System for Research (NDSR-V44), developed by the Nutrition Coordinating Center (NCC) located at the University of Minnesota, for dietary analysis.[35]

Clinical Measures. Skin and plasma carotenoid concentrations and RBC FA composition were analyzed to serve as biochemical indicators of health. These data were collected at laboratory visits by trained professionals. Prior to their scheduled lab visits, participants were instructed to fast overnight for a minimum of 12 hours, hydrate, and abstain from vigorous physical activity and alcohol consumption for 72 hours. All fasting samples were collected between 7:00am-10:00am to control for diurnal variation.

Utilizing standardized sterile techniques, trained phlebotomists collected approximately 20 mL venous blood samples from each participant. Blood was collected into Vacutainer™ tubes (Becton, Dickinson and Co., Franklin Lakes, NJ) with appropriate additives for specific tests. Tubes containing whole blood samples were immediately covered with foil to protect from light and maintained on ice. They were then centrifuged at 1,100 rpm for 20 minutes. Serum, RBCs, and plasma were removed, aliquoted into 6 x 1 mL vials, and stored at -80 °C.

Skin carotenoids were measured on the palm of the hand noninvasively via resonance Raman spectroscopy (RRS) using a Pharmanex Nu Skin Biophotonic Scanner (Nu Skin, Provo, UT). Participants were asked to use the same hand for a total of three measurements. These measures were then averaged, and the mean was used for each time point. For plasma carotenoid analysis, samples were prepared utilizing methods previously described and analyzed by HPLC-DAD.[36] Compounds were separated using YMC C30 column (150 x 4.6 mm, 3.5 mm ID) with guard column and eluted with MeOH:MTBE:Water (96:2:2 v/v) at a flow rate of 1.0 mL/min. Compounds of interest were identified by retention time and spectral analysis and compared to standard curves of authentic standards to confirm identification and for quantification, respectfully. Analytes were monitored by DAD at 450nm. Data were reported as concentrations in μmol/L.

For RBC FA analysis, lipids were extracted and methylated from RBCs and analyzed by gas chromatography using methods previously described.[37] Retention times were compared to authentic standards for FA methyl esters for identification and quantification.[37] Data are reported as percent FA/total detected FAs.

Data Analysis

Data analysis was conducted in collaboration with a biostatistician at The Ohio State University Center for Biostatistics. Descriptive statistics were generated for all demographic and outcome measurements using SAS v9.4 (SAS Institute, Cary, NC). Additionally, statistical analyses for the effect of the intervention on dietary and clinical measures were conducted by comparing pre- and post-intervention scores. The hypothesis of no change in these variables was tested using a paired t-test. Significance was established a priori $\alpha=0.05$. Some variables were log-transformed prior to analysis due to heteroscedasticity.

Results

Twenty-nine (N=29) overweight adult cancer survivors completed the intervention. The majority were white and female (86.2% and 82.8%, respectively, Table 1). The average BMI at baseline was 31.85 kg/m^2. The mean age was 58 years, and the mean age of initial cancer diagnosis was 52.9 years for females and 65.2 years for males. Breast (44.8% of total, 54.2% of females) and prostate (17.2% of total, 100% of males) cancers were the most prevalent primary cancers reported in this cohort.

Based on FFQ data, participant adherence to the evidence-based dietary guidelines improved from pre- to post-intervention. Participants reported overall increases in diet quality, with significant improvements of HEI-2010 scores (Table 2). Total diet scores improved by 7.5% (p=0.006). Individual scores for the subcategories of interest improved as well. Indeed, total fruit and whole fruit scores increased by 22.6% and 13.6% (p=0.003, p=0.009, respectively). Similarly, scores for total vegetables increased by 8.2%, but this trend did not reach significance (p=0.054). Fatty acid scores also increased by 32.1% (p=0.007).

Dietary intakes of fruits and vegetables increased by 0.41 and 1.05 servings/day from pre- to post-intervention (p<0.001 and p=0.022, respectively). Other food intake patterns changed in concordance with suggested dietary recommendations, with mean total energy, added sugar, and red and processed meat intakes decreasing over the course of the intervention (p=0.012, p=0.036, p=0.012, and p=0.004, respectively).

As with produce consumption, increased intakes of dietary carotenoids were documented. Total carotenoid intakes increased by 66% from pre- to post-intervention (p<0.001, Figure 1). Additionally, individual intakes of all five major carotenoids increased. The major contributing carotenoid at both time points was β-carotene, which comprised 39% of total carotenoid intakes post-intervention. However, the largest change from pre- to post-intervention was seen in α-carotene, which increased by 126% (p<0.001). The smallest of these changes was observed for lycopene, which increased by 43% (p=0.012).

While consumption of plant-based foods increased, intakes of fats from all sources decreased. Indeed, mean total dietary fat decreased by 12.37 grams from pre- to post-intervention (p=0.010, Figure 2). Similarly, decreased intakes of saturated, *trans*, and unsaturated FAs were noted. Mean intakes decreased by 5.47 grams, 0.71 grams, and 5.82 grams, respectively (p=0.004, p=0.009, and p=0.031). Investigating changes in unsaturated fat intakes, significant decreases were only seen in MUFAs, with participants decreasing mean intake by 4.51 grams (p=0.017). Significant changes were not documented in PUFAs. However, as reflected in improved HEI-2010 score, the ratio of dietary intakes of MUFA + PUFA to SFA increased from 1.91 to 2.17 (p=0.007).

Carotenoid status, which served as a surrogate biomarker for fruit and vegetable intake, was also improved from pre- to post-intervention. Total plasma carotenoid concentrations increased by 35% ($p<0.001$), and increases were also documented in plasma α-carotene, β-carotene, and lycopene ($p<0.001$, $p<0.001$, $p=0.017$, respectively, Table 3). Similar to dietary intake data, plasma β-carotene was the largest contributor of total plasma carotenoids both at baseline and post-intervention. Lycopene was the second greatest carotenoid in abundance. However, again, α-carotene increased most substantially of the carotenoids from pre- to post-intervention, increasing by 91%.

Total skin carotenoids also increased over the course of the intervention ($p=0.015$). Further, total skin and total plasma carotenoids were highly positively correlated with one another ($r=0.728$, $p<0.001$, Figure 3). Similarly, plasma carotenoids were correlated with dietary carotenoids, though this relationship was much weaker ($r=0.266$, $p=0.047$). There was no significant relationship between skin and dietary carotenoids.

Changes in RBC FA composition were slight. No changes were noted in saturated, *trans*, or total unsaturated FAs from pre- to post-intervention (Table 4). However, significant decreases in relative abundance of omega-3 PUFAs were apparent; these FAs decreased by 6% relative to baseline ($p=0.001$). No significant changes were seen in relative abundance of MUFAs. Similarly, no changes were demonstrated in ratio of MUFA + PUFA to SFA. Lastly, each of the examined groups of FAs were assessed for correlation between RBC composition and recorded dietary intakes, yet none were significant.

Discussion

Compared to the cancer survivor population in the US, the participants in this study were similar in age, as 86% of all cancers develop after age 50.[38] Other key demographics, such as race, were also comparable to US prevalence data.[39] However, in this study, females were overrepresented, as only 53% of those with cancer in the US population are estimated to be women.[39] Lastly, lifestyle interventions for cancer survivors tend to be biased toward whites who are highly educated, which is similarly reflected in the Growing Hope participants.[40]

Despite the small sample size of this pilot study, efficacy of the intervention was demonstrated. While underpowered for subgroup analysis to assess individual differences, significant changes for several key variables were documented as discussed below.

Diet Quality

HEI-2010 scores for the survivors in the Growing Hope study were, on average, much higher than those seen in the general US population.[41] Research suggests that cancer survivors exhibit poor diet quality, with an average total HEI-2010 score of 47.2 reported in one recent analysis of NHANES data.[42] Indeed, cancer survivors' health behaviors appear to be quite similar to those observed in the US population.[40] Comparatively, Growing Hope participants had better diet quality at baseline, with mean HEI-2010 scores of 69.6. This may be in part due to the "healthy volunteer effect" whereby participants in research trials are often healthier than the general population. This phenomenon has been seen in the control arms of many large trials.[43]

The increase in diet quality is therefore quite impressive, as participants began the Growing Hope intervention with relatively high diet quality, yet still improved significantly from pre- to post-intervention. This may be explained by study participants' inherent likelihood to make health changes. Indeed, previous work has identified that cancer survivors express high levels of interest in lifestyle interventions.[40] Further, those who take the initiative to voluntarily participate are in an action stage of behavior change and are therefore more likely to make additional behavior changes than those who do not participate.[44] Similarly, this study was based on social cognitive theory, which describes self-efficacy as an important construct for understanding why people make and maintain health behaviors.[45] Other lifestyle interventions based on this model have demonstrated improvements in diet quality, possibly in part due to increases in self-efficacy.[46] While the Growing Hope intervention included components to increase self-efficacy, it is possible that participants who joined the study had greater baseline self-efficacy than those who did not.

Compared to other comprehensive interventions for cancer survivors, the participants in the Growing Hope study achieved similar results related to improved diet quality. For example, those in the Lifestyle, Exercise, and Nutrition (LEAN) randomized controlled weight loss trial for overweight and obese breast cancer survivors began the study with a mean baseline HEI-2010 score of 70.2, and improved by 9.7%, over the course of the intervention.[47] Similar to the Growing Hope study, survivors participating in other lifestyle interventions also decreased intakes of dietary fat and increased intakes of fruits and vegetables in an effort to reduce weight and improve health.[47,48] Results demonstrate the efficacy of the biobehavioral intervention regarding these lifestyle changes and support a multifaceted approach to achieving behavior change.[47,49]

Carotenoids as Biomarkers

Many fruits and vegetables contain carotenoids. Participants in the Growing Hope study were given access to free, fresh produce for the duration of the study, including high-carotenoid foods such as melons, berries, peppers, squash, tomatoes, leafy greens, cabbage, broccoli, and others. Therefore, an increase in consumption of produce and corresponding increase in intakes of dietary carotenoids is expected. In this study, the intakes of individual carotenoids that were seen in greatest quantities were β-carotene and lycopene. This is not surprising, as both are among the carotenoids most prevalent in the US diet.[16] The largest change in individual carotenoid intakes, though not the greatest absolute amount, was demonstrated in α-carotene. During the last month of the study, participants consumed primarily fall produce, including winter squash, which is high in α-carotene.[50] Therefore, dietary intake data may show different carotenoid intakes if assessed during the early spring or peak summer months, when other types of produce are bountiful.

There is no recommended dietary allowance (RDA) for carotenoids as they have no confirmed function outside of their provitamin A activity. However, recommendations for increased consumption of carotenoid-rich produce have long been supported.[51] Despite this, a clinically meaningful change in total carotenoid intake is difficult to determine. In the β-carotene supplementation trials, 20 or 30 mg was given to participants.[52,53] Therefore, based on the reported increased consumption of fruit and vegetables, the reported increase in dietary intakes of total carotenoids by approximately 10 mg/day is reasonable. However, FFQ data were not highly correlated with either skin or plasma carotenoid measures. Previous work suggests that the use of FFQs requires correction factors to adjust for measurement error, and therefore may not be the most appropriate method of measuring carotenoid intake.[54]

To validate self-report data of increased produce intake, multiple studies have utilized either plasma or skin carotenoid measures.[17,22,55,56] Indeed, the Institute of Medicine (IOM), now part of the Health and Medicine Division of the National Academies, states that blood concentrations are the best biological markers for consumption of produce, and higher concentrations are associated with a lower risk of many chronic diseases, including cancer.[51] However, because carotenoids are present in produce with a number of other compounds, it is difficult to disentangle the health benefits that may be attributable to carotenoids alone, as additive or synergistic effects are likely.[51,57] Therefore, no recommended reference for plasma carotenoids currently exists.[17,51] Because of this, increases in plasma and skin carotenoid concentrations were reflective of positive changes in produce intake, but a threshold for "adequate" intake could not be determined.

In the plasma, carotenoid levels reach peak concentrations 24 to 48 hours after ingestion and return to baseline levels within two to three weeks.[17,51] Changes in skin carotenoid concentrations can be observed as quickly as two weeks after changes in consumption of carotenoids, however, return to baseline takes approximately one month.[17] Therefore, measurement of carotenoid status post-intervention was likely only reflective of the two to four weeks previous to data collection. Measuring these values at multiple time points throughout the intervention would be useful in tracking participants' changes in dietary intakes and should be considered for future study.

Based on the results of this intervention, increases in dietary carotenoids were not well-correlated with skin or plasma measures. However, skin and plasma measures were highly correlated, suggesting that the use of Raman spectroscopy is valid in the cancer survivor population. Variability in plasma carotenoids may be partially attributed to genetic variants, particularly those coding for proteins involved in uptake, transport, and metabolism.[24,58] A natural level of variability in skin carotenoids has also been observed. This may be explained by genetics, seasonal differences, skin pigmentation, BMI, or even smoking.[17] In this study, seasonal differences may have impacted results, as sun exposure throughout the summer may have caused the destruction of some carotenoids in the skin due to ultraviolet light. Similarly, participants lost, on average, approximately 4.67% of body weight over the course of the intervention. Because adipose tissue is a depot for carotenoids, this may have impacted results. However, significant increases in carotenoids were still observed, so the magnitude of these effects was likely small, if any. All participants had BMI >25 kg/m^2, none were smokers, and the majority were non-Hispanic white, so these potential factors likely did not impact results from this cohort.

Due to the natural variations among individuals in both plasma and skin carotenoids, analysis of these values allows for their use as measurements of changes in carotenoid status rather than as references for absolute intakes. Indeed, researchers have found that the slope of increase for skin carotenoid values is approximately equal among individuals with equal increases in dietary intakes of fruits and vegetables, despite differing baseline levels.[17] This demonstrates that skin carotenoid measures are reflective of changes in dietary intakes regardless of high or low baseline status.[17]

Fatty Acids as Biomarkers

Again, similar to results of the LEAN study, participants in Growing Hope decreased total fat intake from pre- to post-intervention.[47] While reduction in fat was not expressly proposed as a part of the intervention nor do recommendations for cancer survivorship pertain directly to fat intake, the participants were urged to follow a primarily plant-based diet that was high in fruits and vegetables and low in red and processed meats. The survivors, who were overweight at study baseline, were also encouraged to lose weight throughout the intervention. Because fat is higher in calories per gram than other macronutrients, it is not surprising that when trying to reduce calorie intake, survivors may have chosen foods higher in fat to reduce or eliminate from their diets, leading to decreased intake of all types of fat.

While a reduction in dietary fat intake was seen, participants still consumed approximately 60 g of fat on average at study end. When looking at the composition of the diet, fat contributed about 36% of calories pre-intervention and 35% of calories post-intervention. Therefore, the energy contribution of fat to the diet remained relatively stable. The types of fat consumed were improved, however, as the HEI-2010 score for FAs increased significantly and calculated ratios for reported dietary intakes of MUFA + PUFA to SFA improved as well. Yet this amount of fat is still considered to be relatively high based on the range of 20-35% of calories recommended by the US Dietary Guidelines for Americans and the Academy of Nutrition and Dietetics (AND).[59,60] As such, participants in future studies may need additional guidance on both appropriate types and amounts of dietary fats.

Analyzing changes in dietary fat intake by saturation level, participants decreased consumption of saturated, unsaturated, and *trans* fats. However, when looking more closely at changes in unsaturated fat intake, only significant decreases in MUFAs were documented. This is not typically a recommended change, as participants on low-fat diets are often encouraged to replace SFA intake with a combination of PUFAs and MUFAs.[59,60] However, participants reported decreased intakes of both red and processed meats, and total protein HEI-2010 scores trended down. Therefore, it is not surprising that MUFA intakes decreased, as a large contributor of MUFA in the American diet is meat.[61] Despite this, approximately 15% of calories were provided by MUFAs both at baseline and post-intervention, which falls within the recommended range suggested by the AND.[60]

Despite these decreases in intake, increases in carotenoid status were seen. Because as little as 3-5 g of dietary fat is hypothesized to be required for efficient absorption of carotenoids, it appears that any decreases in fat intake were not substantial enough to impact carotenoid status in this study.[62,63]

Like FFQ data for carotenoids, FFQ results for dietary fat intake did not correlate with objective biomarkers of RBC FAs. This may be explained by the methodology used, as RBC FAs were analyzed based on relative abundance, and decreases in individual concentrations of FAs were not measured. Because reported intakes of all types of dietary fat decreased, it is not surprising that the composition of RBC FAs was relatively unchanged from pre- to post-intervention and therefore not significantly associated with FFQ measures of consumption.

Because RBC FAs have the longest half-life of the blood fractions, these measures best reflect long-term dietary intake over the past months and are less impacted by recent intake compared to measures in plasma, which reflect intake over weeks.[64,65] However, there is no validated biomarker for total fat intake.[66] Nevertheless, previous studies have demonstrated a dose-response relationship between FA consumption and RBC composition, particularly for omega-3 PUFA supplementation.[67,68] This was not demonstrated in the Growing Hope study.

Indeed, RBC FA composition was relatively unchanged over the course of the intervention. Similar to results from the Women's Health Initiative (WHI), participants in this study had RBC SFA composition of approximately 43% of total, MUFA approximately 14-15%, and PUFA approximately 41%.[69] The only significant change documented in Growing Hope participants was in omega-3 PUFA composition, with a decrease of 6% relative to baseline. Decreases in SFA and MUFA may not have been observed because these fatty acids can be endogenously produced, and therefore dietary intake is not the sole contributor to RBC composition.[69]

As mentioned above, correlation between dietary fat intake and RBC FA composition was not significant. Again, these results were similar to those found in analysis of WHI data.[69]

However, other studies have demonstrated positive associations between RBC FA composition and estimated FA intakes by dietary questionnaires.[65]

Also important to consider when assessing RBC FA composition is the natural variability seen between individuals. Though less of an issue in RBCs than plasma, genetic variants are estimated to explain up to 30% of the variability in blood levels of some FAs among individuals.[69,70] Therefore, a larger sample size may be needed to account for this variability in order to see differences.

Limitations

Due to the small sample size of this pilot study, results may not be generalizable to the cancer survivor population. While some demographics were similar to the general population, the participants in the Growing Hope study were relatively homogenous, with the majority being white, female, breast cancer survivors. Thus, findings should be replicated in a broader, more diverse population for generalizability. Similarly, without the inclusion of a control group for comparison, investigators relied on pre-post changes in individual participants. While many significant changes in both dietary intakes and objective clinical variables were documented, this study design introduces some error not seen in randomized controlled trials, and thus, findings may lack external validity.

Regarding the nature of the intervention, which was not a controlled feeding study, it may be difficult to elucidate small changes in dietary intakes. While analysis of diet quality data demonstrates positive results, it is important to recognize limitations to dietary recall methods. Consumption data was collected by self-report, which has inherent limitations, such as recall bias.

Additionally, because the primary objective was to examine overall dietary patterns, FFQs rather than food records or 24-hour recalls were utilized. This “big picture” analysis impedes the ability to gather detail regarding individual intakes of nutrients and phytochemicals. Further, while FFQs impose less of a burden on respondents than diet records, this burden is not completely diminished and may explain some of the changes seen. Participants utilizing food-based FFQs often experience response error, as well as underestimate dietary intakes.[71] Collection of objective measures of dietary intake, such as those pertaining to carotenoid status, however, diminished these biases.

Finally, the duration of the Growing Hope study was approximately six months. While similar to many other lifestyle interventions, this does not allow for examination of maintenance of behavior change. Therefore, a follow-up period would increase the ability to confirm the results of the intervention are maintainable in the long-term. Longer follow-up would also allow for the ability to determine the impact of diet quality on cancer recurrence and survival.

Conclusion

A multifaceted biobehavioral intervention for cancer survivors improves adherence to the evidence-based guidelines for cancer survivorship. The use of several components, including an urban garden harvesting experience and one-on-one motivational interviewing with a RDN health coach, encouraged participants to make positive behavior changes. The use of a multidisciplinary team and several factors to influence behavior has been shown in other studies to impact lifestyle changes better than the use of any one in isolation. Results of this intervention, too, confirm efficacy of this approach.

Indeed, this study demonstrates an improvement in produce consumption and FA intakes to better align with a higher quality dietary pattern. Results also show that carotenoid status serves as a biomarker of produce intake in the overweight cancer survivor population. Participants increased carotenoid status despite decreases in FA intakes, demonstrating a meaningful change in dietary choices.

While a low-fat dietary pattern was not promoted through this intervention, participants increased consumption of plant-based products such as fruits and vegetables and decreased consumption of animal-based products such as red and processed meats, which are often higher in fat. Of note, while dietary intakes of all FAs decreased from pre- to post-intervention, the ratio of PUFAs + MUFAs to SFAs improved, demonstrating higher diet quality for these measures.

Implications for Future Research

Results of this study indicate a need for continued research into the impact of multifaceted biobehavioral interventions on lifestyle changes and associated health outcomes in cancer survivors. Indeed, based on the promising outcomes reported in this study, randomized controlled trials to determine efficacy and maintenance of behavior change are warranted to further define impact. Sustained changes to dietary patterns and their influence on key health measures, particularly in overweight and obese cancer survivors, should be the focus of future study.

Literature supporting the utilization of carotenoids as markers of produce consumption is convincing, but much about the mechanism of carotenoids in the body outside of their provitamin A activity has yet to be elucidated. There is great interest in understanding the metabolism of carotenoids for investigation of their downstream metabolites, as the function of these compounds may explain the potential cancer-protective effects seen with carotenoid consumption. The Growing Hope study resulted in decreased intakes of all types of fatty acids yet an increase in carotenoid status, demonstrating that, while some amount of fat is important to carotenoid absorption, FA intakes above certain levels may not further influence carotenoid status.

Tables and Figures

Table 1. Baseline Participant Characteristics (N=29)

Participant Characteristics		**% (n)**
Age (years)		58
BMI (kg/m^2)		31.85 ± 5.11
Sex	Male	17.2 (5)
	Female	82.8 (24)
Race/Ethnicity	Black/African American	10.3 (3)
	White/Caucasian	86.2 (25)
	Asian	3.4 (1)
Marital Status	Married	62.1 (18)
	Divorced	13.8 (4)
	Never Married	13.8 (4)
	Other[a]	10.3 (3)
Education	Less than grade 12/Grade 12 equivalent	10.3 (3)
	College 1 to 3 years	10.3 (3)
	College 4 years or more	44.8 (13)
	Professional or Graduate	34.5 (10)
Employment	Employed or Self-Employed	51.7 (15)
	Retired	44.8 (13)
	Out of work < 1 year	3.4 (1)
Household Income	Prefer not to answer/Don't know	20.7 (6)
	$10,000-$49,000	27.6 (8)
	>$50,000	51.7 (15)
Primary Cancer Diagnosis (age, years)	Male	65.2
	Female	52.9
Primary Cancer	Breast	44.8 (13)
	Prostate	17.2 (5)
	Ovarian/Uterine	13.8 (4)
	Colorectal	6.9 (2)
	Other[b]	17.3 (5)

[a] Widowed; Prefer Not to Answer [b] Lymphoma, Brain, Pancreatic

Table 2. Healthy Eating Index 2010 Scores

HEI-2010 Component	**Max Score**	**Baseline Mean (SD)**	**Post-Intervention Mean (SD)**	**Mean Difference (95% CI)**	**P-value**
Total Diet	100	69.58 (12.29)	74.78 (9.79)	+5.21 (1.59, 8.83)	0.006*
Adequacy (higher score indicates higher consumption)					
Total Fruit	5	3.59 (1.48)	4.40 (1.06)	+0.81 (0.29, 1.33)	0.003*
Whole Fruit	5	4.20 (1.29)	4.77 (0.69)	+0.57 (0.15, 0.98)	0.009*
Total Vegetables	5	4.49 (0.86)	4.86 (0.41)	+0.37 (-0.01, 0.74)	0.054
Greens and Beans	5	4.34 (1.16)	4.59 (1.04)	+0.24 (-0.23, 0.72)	0.307
Whole Grains	10	5.90 (3.58)	5.67 (3.49)	-0.23 (-1.16, 0.69)	0.607
Dairy	10	7.51 (2.34)	6.77 (2.86)	-0.74 (-1.59, 0.10)	0.082
Total Protein Foods	5	4.66 (0.53)	4.42 (0.96)	-0.24 (-0.58, 0.11)	0.170
Seafood and Plant Proteins	5	4.33 (1.01)	4.55 (0.90)	+0.21 (-0.08, 0.51)	0.148
Fatty Acids	10	4.71 (2.95)	6.22 (3.15)	+1.51 (0.45, 2.57)	0.007*
Moderation (higher score indicates lower consumption)					
Refined Grains	10	8.66 (2.22)	9.76 (0.73)	+1.10 (0.25, 1.96)	0.013*
Sodium	10	2.75 (2.80)	2.28 (2.89)	-0.47 (-1.71, 0.78)	0.449
Empty Calories	20	14.43 (4.27)	16.51 (3.85)	+2.07 (0.57, 3.57)	0.008*

Figure 1. Changes in Dietary Carotenoid Intakes

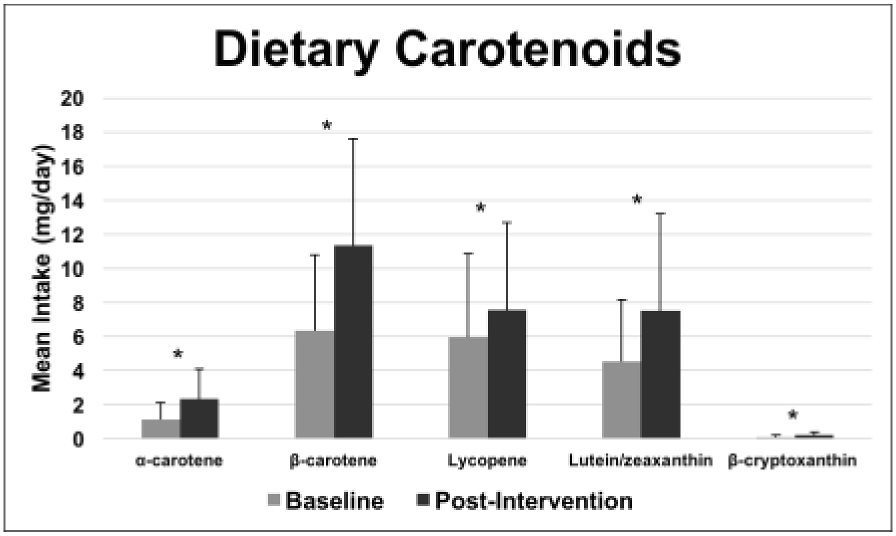

Figure 2. Changes in Dietary Fatty Acid Intakes

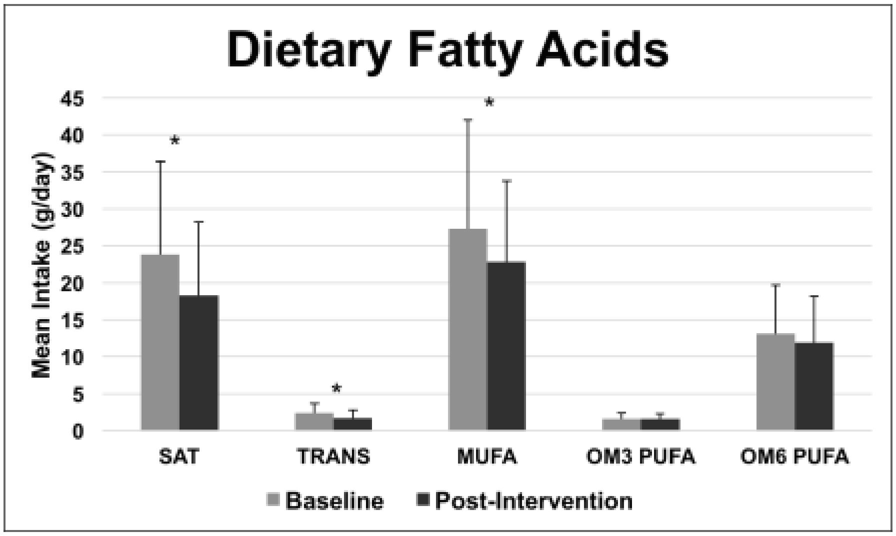

Table 3. Plasma Carotenoid Concentrations

Plasma Carotenoid (μmoL/L)[a]	**Pre Mean (SD)**	**Post Mean (SD)**	**Fold-change (95% CI)**	**P-value**
Total plasma carotenoids	1.75 (0.87)	2.33 (1.22)	1.35 (1.15, 1.58)	<0.001*
α-carotene	0.14 (0.01)	0.29 (0.26)	1.91 (1.52, 2.40)	<0.001*
Total β-carotene	0.67 (0.54)	0.96 (0.71)	1.50 (1.21, 1.86)	<0.001*
β-carotene all-trans	0.60 (0.51)	0.88 (0.68)	1.56 (1.22, 2.01)	0.001*
β-carotene -cis	0.07 (0.04)	0.08 (0.04)	1.29 (1.03, 1.62)	0.028*
Total lycopene	0.72 (0.36)	0.85 (0.34)	1.26 (1.05, 1.53)	0.017*
Lycopene all-trans	0.53 (0.26)	0.60 (0.24)	1.20 (0.99, 1.44)	0.060
Lycopene -cis	0.19 (0.12)	0.25 (0.11)	1.46 (1.12, 1.89)	0.006*
Lutein	0.10 (0.06)	0.13 (0.08)	1.27 (0.98, 1.64)	0.066
β-cryptoxanthin	0.14 (0.16)	0.12 (0.08)	1.02 (0.82, 1.27)	0.840

[a] Data log-transformed prior to analysis

Figure 3. Correlation between Skin and Plasma Carotenoids

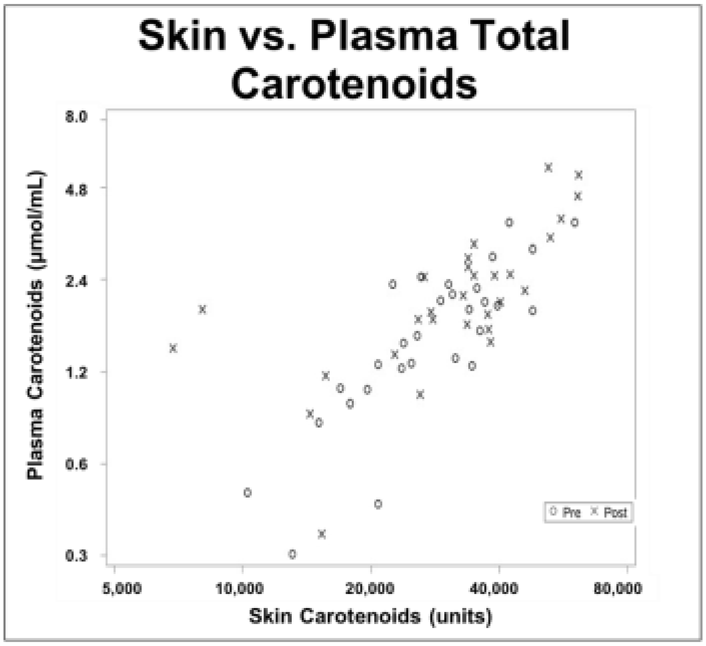

Table 4. Red Blood Cell Fatty Acid Composition

RBC FA (% AUC)	**Pre Mean (SD)**	**Post Mean (SD)**	**Fold-change (95% CI)**	**P-value**
Saturated fat[a]	42.94 (1.77)	43.21 (1.61)	1.006 (0.992, 1.021)	0.380
Trans fat[a]	1.62 (0.17)	1.66 (0.19)	1.020 (0.976, 1.065)	0.374
Total unsaturated fat[a]	54.97 (1.69)	54.70 (1.61)	0.995 (0.984, 1.006)	0.351
MUFA[a]	14.28 (1.40)	14.46 (1.35)	1.013 (0.977, 1.050)	0.481
PUFA[a]	40.69 (1.63)	40.24 (1.86)	0.989 (0.973, 1.004)	0.142
Omega-3 PUFA[a]	6.22 (0.97)	5.83 (0.93)	0.935 (0.900, 0.971)	0.001*
Omega-6 PUFA[a]	34.47 (1.46)	34.41 (1.64)	0.998 (0.982, 1.015)	0.822
MUFA + PUFA: SFA	1.28 (0.09)	1.26 (0.08)	0.991 (0.965, 1.016)	0.348

[a]Data log-transformed prior to analysis

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