Nutritional Training Increases Long-term Fruit and Vegetable Consumption in Women with Early Breast Cancer – A Randomized Controlled Trial

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Key words
- breast neoplasms
- rehabilitation
- Mediterranean diet
- health promotion
- patient participation

Abstract

After primary treatment of early breast cancer many women want to change their dietary habits and this may influence disease recurrence. The aim of the study was to increase fruit and vegetable (FV) intake for at least 6 months in women with early breast cancer by a short modular nutritional training program and offering refresher sessions. Design: Single-centre randomized controlled study in women attending an in-hospital cancer rehabilitation program. Subjects in the intervention group (INT) participated in a 2-week structured nutritional training program and were invited to visit brief refresher courses after 3 and 6 months. Women in the control group (CON) were offered standard nutritional advice. All subjects completed 4-day food records before arrival (baseline), and 1, 3 and 6 months after the start of the study. Of 152 women included in the study complete follow-up was available for 118. Consumption of FV (mean ± SD) was similar at baseline (INT 483 ± 235, CON 460 ± 177 g/d) but only increased in the intervention group and at all follow-up times (1 month: 743 ± 287 vs. 526 ± 177; 3 months: 673 ± 246 vs. 485 ± 169; 6 months: 631 ± 222 vs. 505 ± 172 g/d; $p < 0.001$). There was no discernible effect of the refresher courses on FV intake. There was no relevant effect of intervention on energy and fat intake. A short modular nutritional training program increases FV intake in breast cancer survivors for at least 6 months. This program can be easily implemented and may be combined with other training programs to comprehensively modulate lifestyle.

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Abbreviations

INT	intervention group
CON	control group
FV	intake of fruits and vegetables
TFV	intake of fruits and vegetables including juices and jams
T1–T4	study time points 1 to 4

Introduction

Breast cancer is still a formidable disease with high incidence and recurrence rates after primary treatment of above 20 % [1]. Cancer prevention as well as prevention of recurrence after primary treatment, therefore, ranges high in priority of anti-cancer strategies. Data accumulating during the last decade increasingly outline the relevance of lifestyle factors for cancer incidence [2]. Thus, specific components of lifestyle have been associated with a decreased incidence of breast cancer and of breast cancer recurrence [3–7], while deranged energy metabolism and the metabolic syndrome may well be major contributors to cancer progression [8,9].

The most important protective factors for several types of cancer appear to be regular muscular activity, a preference for plant foods and the avoidance of high-energy foods and these have been suggested to be incorporated into worldwide teaching and training programs [2]. The evidence for an impact of nutritional factors on breast cancer is inhomogeneous [8,10,11]. Analysis of the EPIC study data showed no effect of vegetable and fruit intake on breast cancer risk [12]; however, more recent studies observed a protective effect of consumption of plant foods on breast cancer recurrence [7,13,14]. Similarly, an association has been shown between a diet rich in plant foods and a lower risk of metabolic syndrome [15,16]. In addition, many women with early breast cancer want to modify their lifestyle after cancer diagnosis including changing their dietary habits to improve health and quality of life [17,18]. A recent German survey

found that the dietary intake in women with early breast cancer deviates far from most recent recommendations for a protective dietary composition [19].

Since there is a lack of structured educational programs for breast cancer patients in Germany, we designed in a modular approach separate programs for exercise and nutrition training in women with early breast cancer. We report here on the development and the effects of a 2-week intensive nutritional training program aimed primarily at strengthening nutritional preferences for plant foods.

Subjects and Methods

Study design and recruitment

The study was designed as a randomized controlled trial to test the effect of a 2-week nutritional training program (INT, intervention) on the long-term intake of plant foods. The training program was offered to women with early breast cancer during a 3–4 week in-hospital rehabilitation program. The training program was followed by 2 half-day refresher seminars 3 and 6 months after inclusion into the study. The effect of the intervention was compared to the standard of care, including nutritional advice, offered to all patients during the rehabilitation program. The randomization procedure was arrival of participants at Tumor Biology Center during even- or odd-numbered weeks. The study was reviewed by and the procedures followed were found to be in accordance with the ethical standards of the responsible institutional committee on human experimentation.

The primary objective was to increase the intake of fruit and vegetables in women with early breast cancer for at least 6 months by the 2-week training program. The secondary objectives were A) to increase for 6 months the percentage of patients who reach a fruit and vegetable intake of 650 g/d as recommended by the German Nutrition Society (DGE) to reduce primary cancer risk [20]; and B) to judge the effect of the refresher seminars on the long-term effect of the training program. Quantification of dietary intake was done by analysis of 4-day food records at baseline and 1, 3 and 6 months later.

Earlier data had shown that the intake of fruit and vegetables as measured in patients at our institution varies with a standard deviation of 250 g/d and increases by about 50 g/d during the normal 3–4-week rehabilitation program. We aimed for an increase in the fruit and vegetable intake in the intervention group of 200 g/d. The sample size needed to detect this difference at the level of $\alpha = 0.01$ and to allow for a power of $(1-\beta) = 0.90$ was 47 subjects per group. Since we expected a drop-out rate of 33 % until the end of the study, we aimed at including a total of at least 141 patients.

An invitation letter to participate in the study was sent to all women who had finished primary breast cancer treatment and who were waiting to participate in our in-hospital rehabilitation program within the following 4 weeks. The invitation was accompanied by a specially designed protocol booklet and we asked the women to keep a self-administered 4-day food record within the 2 weeks before arrival at our hospital.

Study requirements for all patients were: arriving at our center with a complete 4-day food record; completing a questionnaire on nutritional habits and social situation at entry and after 1 month; and preparing complete 4-day food records for follow-up at 1, 3 and 6 months after entering the study. Additionally it was required for subjects in the intervention group to participate in the 2-week nutrition training course;

After admittance to the Tumor Biology Center all patients were interviewed, underwent a routine medical examination and the body weight was measured with a calibrated scale. After giving informed consent patients were included according to inclusion and exclusion criteria. Inclusion criteria were: female sex, age 18–70 years, early breast cancer after curative treatment, willingness to participate in the 6-months program. Exclusion criteria: breast cancer recurrence, presence of active secondary cancer, relevant food allergies, smoking, presence of severe disease that would impair participation in the program, inability to comprehend or appraise the implications of participation. After entering the study, further exclusion criteria were: participation in less than 7 out of 8 units of the 2-week training course, and presenting less than the required 4 complete 4-day food records. The random assignment to the intervention (INT) or to the control group (CON) was performed according to the calendar week. Patients arriving in odd calendar weeks were automatically assigned to the INT and patients arriving in even calendar weeks were assigned to the control group (CON). The nutritional training program was presented during the first 2.5 weeks of the usual 3–4 week duration of the rehabilitation program. On the last day of the rehab-program body weight was measured again.

Nutritional training program and standard nutritional advice

The nutritional training program was developed as a structured program at our institution for groups of 5–10 women and was tested on 2 pilot groups. The program consisted of six 90-min units of theory and two 3½-h cookery classes; both types of components were designed with an emphasis on motivation and practical advice for the individual patients' situation at home. The methodical elements of the units included hand-out material, workshops, sensory tests, short lectures, and discussion forums as well as exercises to practice the acquired knowledge. The program focused on increasing the intake of fruit and vegetables but also focused on increasing whole meal products and reducing fats and meat consumption. Weight reduction, although expected due to modification of dietary habits, was not an objective of this study.

The Department of Nutrition and Metabolism at Tumor Biology Center Freiburg offers a range of voluntary counseling services to all patients including weekly lectures, open workshops, discussion groups, cookery classes and according to medical needs individual nutritional counseling. Patients of both INT and CON groups were free to benefit from this standard program.

Refresher courses

Additional components of the intervention program were 2 half-day refresher courses 3 and 6 months after entering the study. These courses were designed to re-motivate the participants and to discuss possible problems of implementing new habits in the domestic environment. All participants in the intervention group were offered to attend any of 2 scheduled half-day refresher courses, with travel costs and accommodation covered by Tumor Biology Center. Patients who had participated together in the same training group were invited together as a group to the refresher courses. These courses were scheduled to take place 13 (refresher course 1) and 25 (course 2) weeks after the initial program. Participants in the refresher courses were required to keep the food records T3 and T4 within the week after the date of the respective refresher course.

Dietary assessment

Self-administered food records are recognized as the gold standard for measuring individual dietary habits due to high precision in quantifying the ingested amount of various foods [21]. However, due to the time requirements for the patient and the researcher this instrument is mainly used in smaller study populations. Food frequency questionnaires and repeated 24 h-recalls are more common, particularly in larger samples. These latter instruments show similar but relevant measurement errors due to various reasons, e. g. intentional or unconscious underreporting (regarding fat consumption), over reporting, compliance [22]. We chose the more laborious but also more accurate method of 4-day food records for assessing dietary intake, since we did not obtain additional parameters of nutritional intake, e. g. plasma carotenoid concentrations.

4 separate and complete 4-day food records had to be prepared by all study participants: 1) within 2 weeks before arrival at Tumor Biology Center (t1 = baseline), 2) within the 2 weeks after rehabilitation (t2 = 1 month), 3) 3 months after entering the study (t3 = 3 months/within 1 week of refresher course 1) and 4) 6 months after entering the study (t4 = 6 months/within 1 week after refresher course 2).

All participants received special 4-day food record booklets including a detailed manual with an example of a food record as well as examples of portion sizes and weights for most of the common foods and beverages. Foods and drinks were counted in common measures, e. g. spoons, cups, glasses, handful etc. Mixed dishes had to be divided into single components and measured separately. Brands of ready to eat manufactured foods had to be listed in the record. The food records covered 3 consecutive weekdays and 1 weekend day (i. e., either from Sunday to Wednesday or from Wednesday to Saturday). All food intake data presented in this paper represent means of the 4 recorded days.

Food data analysis

The data were analyzed by trained nutritionists blinded to the study arm of the patients (INT or CON) with PRODI 4.5 compact, a nutritional computing and counseling program based on the German Federal Food Database ("Bundeslebensmittelschluessel") version II.3 extract, which contains complete data sets of 30 nutrients in 1 600 single foods, food compositions and recipes [23]. The database is able to calculate single nutrients as well as amounts of a food group (e. g. fruit, vegetables, potato products, meat, meat products, etc.). The values of the food records were entered by a skilled dietician. With PRODI imprecise portion descriptions in the patient's food record can be replaced by weighted mean portion sizes to prevent missing data.

It is important to note, that in PRODI 4.5 within the food group "fruit" not only raw and cooked fruit and juices but also jams are included. However, since the ingested amounts of jams were generally small, it is unlikely that they influenced the value of total fruit significantly. Similarly the food group "vegetables" includes raw and cooked vegetables as well as vegetable juices. We used calculations of raw and cooked fruit and vegetables (= FV) to estimate "fruit and vegetable intake" as presented in the primary study objective. In addition we calculated and presented total intake of fruit and vegetables including juices and jams (= TFV).

Statistics

Descriptive statistics were calculated for all relevant variables. If not mentioned otherwise data are displayed as means ± SD. The graphical time course of intake of FV and TFV is shown as means ± SEM. The major study objective was to increase FV intake. Two-way repeated measures ANOVA with one factor repetition was used to test for differences in FV intake and post hoc pairwise comparisons were performed according to the Holm-Sidak method. All further statistical testing was exploratory:

Differences in TFV, total energy and fat intake were analyzed with ANOVA as described above; Student's t-test was used to test for differences in FV intake in participants attending or not attending a refresher course; and Wilcoxon´s test was used to test for differences between the groups regarding the percentages of patients reporting to consume more than the recommended amount of 650 g/d of FV. All statistical analyses were performed using the software "Statistical Package for Social Sciences" (SPSS), version 11.5.1 [24].

Results

Of the 222 patients invited by mail to participate in the study, 32 declined to prepare a food record, 3 presented inadequate food records and 35 did not meet the inclusion criteria when arriving at Tumor Biology Center. Of the remaining 152 patients 81 arrived in odd-numbered weeks and 71 arrived in even-numbered weeks. 5 patients in each group declined participation in the study when confronted with the study protocol. Thus we included 76 patients in the intervention group and 66 patients in the control group (**Fig. 1**). Recruitment was stopped when more than 140 patients had been included into the program. In the intervention group during follow-up 15 patients did not prepare all required food records and dropped out before the end of the study. In the control group 9 patients dropped out. 45 and 29 patients of the intervention group attended the refresher courses at 3 and 6 months, respectively. Final analysis was on 61 patients in the intervention group and 57 control patients.

Patient characteristics

All patients included had completed primary treatment of their breast cancer and had no residual or recurrent disease. Patients in both groups did not differ with respect to age, height or weight (**Table 1**). Time since cancer diagnosis ranged from less than 3 to more than 12 months with the median at 6–12 months; the distribution of the intervals was similar in both groups. More than 80 % of subjects had undergone adjuvant radiotherapy and two thirds of subjects in both groups had received adjuvant chemotherapy. Drop-outs had no distorting effect on these parameters. Both groups also were similar with respect to all social characteristics obtained at study entry (**Table 2**). After 1 month (T2) a larger fraction of patients in the intervention group reported a change in eating habits. BMI was similar in both groups at baseline and after 1 month, while data on body weight at 3 and 6 months were not available.

Fruit and vegetable (FV) intake

The primary objective of intervention aim was an increase in FV intake at 1, 3 and 6 months. **Table 3** shows that mean daily intakes of FV in the intervention group increased at all time points when compared to the baseline level, while there was no significant change in the control group. At T2, T3 and T4 the FV intake in the intervention group was large than in the control group. Reported FV intake was highest directly after the training program at T2 and declined significantly again at T3 without fur-

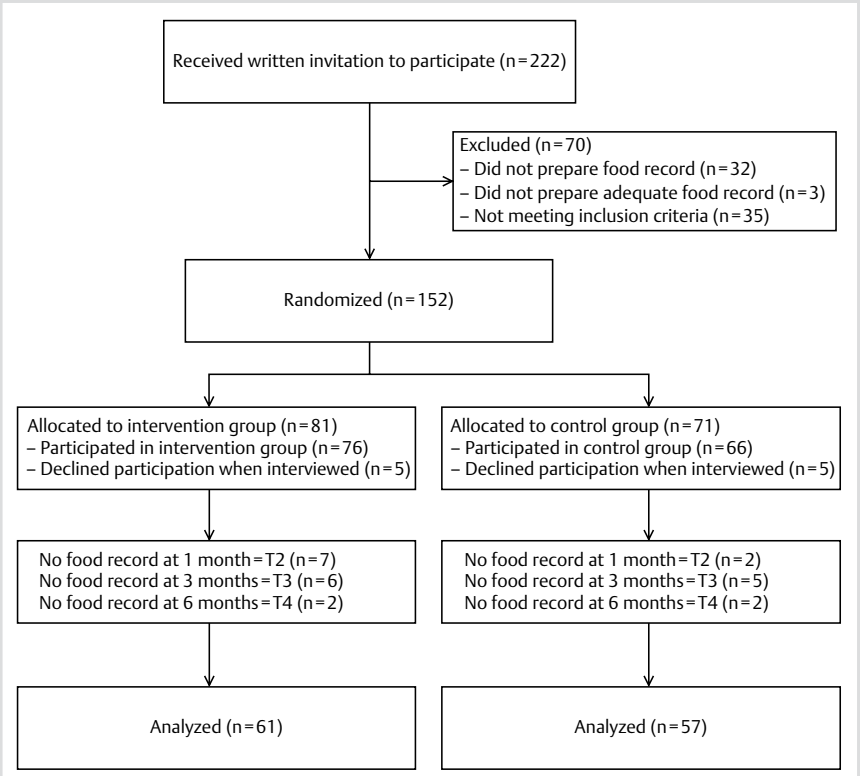

Fig. 1 Flow diagram. "Food record" refers to 4-day food records.

Table 1 Patient characteristics and pre-treatment.

	Intervention group * [n=61]	Control group * [n=57]
age [years]	51.4±10.2	54.6±9.0
height [m]	1.66±0.06	1.64±0.06
BMI at T1 [kg/m²]	24.3±4.1	24.4±4.3
BMI at T2 [kg/m²]	24.3±4.0	24.0±3.8
time since diagnosis		
<3 months (n)	2	2
3–6 months (n)	17	20
6–12 months (n)	28	28
>12 months (n)	14	7
previous adjuvant radiotherapy	n=52 (85%)	n=52 (91%)
previous adjuvant chemotherapy	n=39 (64%)	n=38 (67%)

* all data variations are given as means±SD

Table 2 Social aspects.

	Intervention group n=61	Control group n=57
marital status		
married	62%	60%
unmarried partnership	12%	12%
divorced	13%	11%
education		
9-year elementary school	30%	30%
middle school	28%	28%
high school	23%	25%
highest professional education		
apprenticeship	38%	41%
technical school	20%	16%
university degree	17%	13%
employment at diagnosis		
full time	28%	25%
at least half time	16%	25%
housewife	13%	18%
retired	21%	18%
reporting change in eating habits		
at baseline, T1	48%	42%
after rehab treatment, T2	88%	64%

ther change at T4 and without reaching the baseline level. The maximal increase in FV intake at T2 was 260 g/d (+54%) in the intervention group, while FV intake at T2 increased not significantly by 66 g/d in the control group, similar to the value projected at study conception. The mean FV intake in the intervention group reached the recommended level (≥650 g/d) at 1 month and 3 months but not at 6 months, while the mean control values always remained below this level.

Total fruit and vegetable intake

Fruit and vegetable juices contribute to the total amount of fruit and vegetable intake. They are sometimes recommended as a first step to increase the intake of plant foods, although juices usually contain less bioactive ingredients and fiber than the foods from whole plants. The parameter TFV includes FV as defined above, but also includes fruit and vegetable juices (100% juice) as well as jam intake (minimum fruit content: 50%).

Fig. 2 demonstrates that the behavior of this parameter is very similar to FV: TFV intake is similar for both groups at baseline and in the intervention group increases rapidly at T2 with small decrements at T3 and T4 without returning to the baseline. TFV in the control group does not change over time. Analysis by ANOVA (as for FV above) yields results identical to those reported for FV intake.

Table 3 Mean intake of fruit and vegetables [g/day].

	Intervention group * n = 61	Control group n = 57
T1 = baseline	483 ± 235	460 ± 177
T2 = 1 month	743 ± 287 *	526 ± 177§
T3 = 3 months	673 ± 246 * #	485 ± 169§
T4 = 6 months	631 ± 222 * #	505 ± 172§

§ Data between groups were significantly different by ANOVA
* Data differ significantly from T1 = baseline
# Data differ significantly from T2
§ Data differ significantly from the resp. value of the intervention group

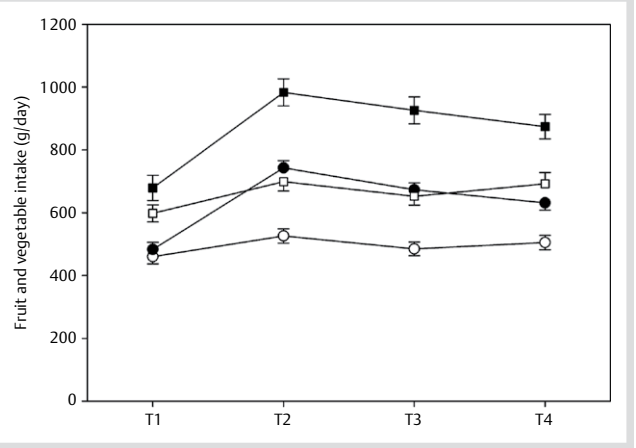

Fig. 2 Intake of fruit and vegetables without juices or jams (circles) and total fruit and vegetables (squares) in control subjects (open symbols) and in participants in the intervention group (filled symbols) as reported in the 4-day food records at T1 = before, T2 = 4 weeks after, T3 = 3 months after, and T4 = 6 months after the begin of the study. Data are given as means ± SEM.

Percentage of patients who met the aim of >650 g/d FV

The percentage of patients consuming more than 650 g/d of FV was low and similar in both groups at baseline (CON 18 %, INT 25 %). While there was an increase in this percentage in the control group at T2 (30 %), at T3 and T4 the baseline situation was reached again. In the intervention group a significantly higher percentage of patients consumed > 650 g/d of FV at all follow-up time points T2–T4 with values between 49 and 54 %, i. e., twice the values at baseline (**Table 4**).

Total energy and fat intake

Total energy intake did not change significantly within the groups between T1 and T4. Analysis by ANOVA reported a significantly higher energy intake in the intervention group, but post-hoc testing identified only a difference between groups at T3, thus marginalizing the relevance of this finding (**Table 5**). Fat intake did not differ between groups; however, in the intervention group all follow-up data were lower than at baseline, while in the control group only fat intake at T3 was lower than at baseline (**Table 5**).

Refresher courses

Refresher courses after 3 and 6 months were attended by 41 and 29 patients, respectively. 27 patients visited both, 43 at least one and 18 patients attended no refresher course. FV intake at T4 = 6 months for patients attending at least one (661 ± 205 g/d) or no refresher course (607 ± 236 g/d) did not differ significantly.

Table 4 Percentage of patients consuming > 650 g fruit and vegetables per day.

	Intervention group n = 61	Control group n = 57
T1 = baseline	24.6	17.5
T2 = 1 month	54.1 *	29.8
T3 = 3 months	52.5 *	14.0
T4 = 6 months	49.2 *	17.5

* indicates significant difference ($p < 0.01$) from baseline value within the respective group

Table 5 Energy and fat intake.

	Energy intake [kcal/d]		Fat intake [% of total energy]	
	Intervention n = 61	Control n = 57	Intervention n = 61	Control n = 57
T1 = baseline	2002 ± 440	1868 ± 492	36 ± 6	36 ± 6
T2 = 1 month	1941 ± 474	1788 ± 429	31 ± 5#	34 ± 6
T3 = 3 months	2022 ± 520 *	1792 ± 395	33 ± 6#§	33 ± 5#
T4 = 6 months	1993 ± 553	1852 ± 438	33 ± 6#§	35 ± 5

* Significant difference between intervention and control groups
# Significantly different from T1 of same group
§ Significantly different from T2 of same group

Discussion

Insulin sensitivity may be one of the major factors modulating cancer development and progression [25] and it is influenced by body weight and physical activity. Plant foods have been shown to reduce the risk of metabolic syndrome [15, 16] and the risk of breast cancer recurrence [7, 13, 14]. Our structured 2-week nutritional training program was aimed at increasing the consumption of plant foods in women with early breast cancer and it successfully raised the intake of fruits and vegetables to the recommended level [20] for a follow-up period of 6 months.

Our data appear to be representative of the effect in women with early breast cancer. Subjects were invited without previous screening to participate in the study, some 68 % of the invited subjects could be randomized with exclusions mainly due to subjects declining or failing the inclusion criteria, and 78 % of the randomized subjects entered the final analysis. The drop-out rate was slightly higher in the intervention group (20 %) than in the control group (14 %), and this may have increased the effect size.

Major intervention trials aimed at changing eating habits have arrived at similar or smaller effect sizes as those observed in the present study. Pierce and co-workers in the large randomized WHEL trial used in a multimodal approach telephone counseling in combination with cooking classes and newsletters to increase the intake of vegetables and fruit from about 7 to 11 servings per day [26]. Assuming a serving size of about 80 g, this corresponds to an intake of some 880 g, very similar to the average of 874 g of total fruit and vegetables reached at 6 months in our intervention group. As reported for the Women's Health Initiative Randomized Controlled Dietary Modification Trial group-based nutritional training including 18 sessions per year increased the intake of fruit and vegetables from 3.6 to 5.1 servings per day (equivalent to some 400 g/d) [27]. Our compact 2 week program invested 17 h of training in groups of 5–10 women or some 2.5 h

per participant. This compares well with similar time requirements in the WHEL trial (18 phone calls per year) [28] and in the Women's Health Initiative (18 group sessions of 8–15 participants per year) [27]. The WINS trial aiming at reducing dietary fat intake invested much more time including 8 h of individual counseling [29]. Recently, a nutrition education program to promote a Mediterranean diet was presented requiring 15 weeks of intensive training and 100 weeks of consolidation [30].

The study was not designed to monitor outcome parameters but nutritional intake. Thus, the aim was to prove the effectivity of the training program to reliably change the eating behavior of the participants. While this was achieved, it remains to be shown that the induced dietary changes are associated with a relevant clinical benefit.

The refresher courses in our study were offered on a voluntary basis and did not significantly change mean fruit and vegetable consumption when comparing patients participating or not participating in these courses. Still, since this was not a primary objective of the study, it cannot be ruled out that the refresher courses contributed to stabilizing vegetable and fruit intake at a high level. However, the initial intensive training during rehabilitation appears to be the key factor in changing eating habits. This corresponds to the observations of others, who also observed long-term adherence to initial counseling in studies aiming at low-fat and/or high-FV eating patterns [22, 26, 31–33].

The training program was designed to be easily implementable in different health care settings. The theoretical units were developed including written material to clearly present relevant nutrition facts, to engage and involve the participants to envision their situations at home and to creatively evaluate potential paths to change their and their families eating behavior lastingly. To increase motivation was a major aim in each unit.

Cookery classes similarly were aimed at demonstrating the feasibility of the projected changes and to support the elements of pleasure in following the proposed eating patterns. Implementing the program at several institutions would be a prerequisite for a multicenter study to test for the clinical relevance of this nutritional training.

Since the 17 h of the complete program are divided into small individual modules, the program can be spread over a 2 week period and leave enough time to be combined with a similar training aimed at increasing physical exercise or stress control.

We are well aware that the reported fruit and vegetable intake was not controlled using biomarkers (e.g. serum concentrations of carotenoids) and we therefore had to rely on the data the patients noted in the 4-day food records. However, comparable studies found a direct and strong association between the amount of self-reported fruit and vegetable intake and serum levels of carotenoids [34–37]. In breast cancer survivors there is a 2-fold risk of underreporting energy intake by women with a body mass index > 30 kg/m² [38]. However, this risk of bias was similar in both study groups with 6 and 5 participants having a BMI > 30 kg/m² in the intervention and control group, respectively. To our knowledge there are also no data suggesting an overreporting of fruit and vegetable intake in breast cancer patients with intensive dietary support. Therefore, we feel it was justified to use the food record data to estimate actual dietary intake.

In conclusion, this short modular training program has been shown to successfully modulate dietary habits of cancer patients in the intended direction. The program is easy to teach and might be implemented without major difficulties in other institutions. The program is intended to be combined with other training modules aiming at physical exercise and stress reduction to modulate typical Western lifestyle patterns more comprehensively.

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