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Prevalence of Diet Change and Micronutrient Supplementation in Breast Cancer Survivors – A Cross-sectional Study

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Abstract

Background: Breast cancer (BC) is the most commonly diagnosed cancer in women and alternative methods (intake of dietary supplements and diet change) are commonly used in BC patients. The aim of this study was to investigate breast cancer or treatment-related adverse symptoms, dietary changes and micronutrient intake.

Methods: 153 BC survivors with prospectively recorded data were surveyed by a self-developed questionnaire. Data concerning tumor characteristics and treatment were obtained from the breast department's registry.

Results: The most prevalent symptoms (> 50% of patients) during and after oncological therapy were chronic fatigue and pain. 42.5% (n=65) BC patients took micronutrients during and 48.4% (n=74) after therapy. There was a significant correlation between women taking micronutrients before diagnosis and cancer-related use after diagnosis (p <0.001). Furthermore, the percentage of women taking micronutrients increased with increasing tumor stages. Micronutrients most frequently (>25%) applied were vitamin C, D, zinc and calcium. The vast majority of applications were administered orally and were more often based on self-information (n=65, 42.5%) than on information received from the oncologist (n=29, 19%). Most patients would be willing to take micronutrients during (n=55, 75.4%) or after therapy (n=44, 67.8%), even if the expected adverse symptom relief was minor (<50%). About one third of BC patients (n=55, 35.9%) confirmed diet adjustments after BC diagnosis. They were on average 4.5 years younger than the remaining (p=0.015). Diet changes (p=0.011) occurred significantly more often in the last decade.

Conclusion: There is an increased demand for functional nutritional medicine in BC patients. Most applications occur without medical recommendation and prescription. Further data is needed to provide evidence-based recommendations.

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Keywords: Breast cancer • Micronutrient • Diet change • Adverse symptom

Abbreviations: BC: Breast Cancer • CF: Chronic Fatigue • ER: Estrogen Receptor • FNM: Functional Nutritional Medicine • HER2: Human Epidermal Growth Factor Receptor 2 • HR: Hormone Receptor • MN: Micronutrient • PR: Progesterone Receptor

Introduction

Breast cancer (BC) is the most common malignancy in women and main cause of cancer deaths worldwide [1]. Standard BC treatment comprises surgery, radiation therapy and pharmacotherapy (chemotherapy, antiestrogens, biologicals), respectively [2]. Although treatment efficacy and thus recurrence-free and overall survival have tremendously improved during the past decades [3], BC survivors still suffer from a variety of short-, mid- and long-term treatment-induced and cancer-related side effects and adverse symptoms [4-6].

To overcome these symptoms, BC patients often seek for help in other medical fields than conventional oncology [7,8]. Dietary supplements are widely used among BC patients [9]. Furthermore, there is evidence that some BC survivors change their diet after diagnosis (e.g. increased intake of fruits and vegetables) [10]. Obviously, conventional, alternative and complementary medical care should work together to potentiate cancer treatment efficacy and tolerability but also to avoid interference. Thus, the aim of this cross-sectional cohort study was to assess type and frequency of cancer resp. treatment-related adverse symptoms, applied diet changes, knowledge about and supplementation of micronutrients (MNs).

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Materials and Methods

Study design

We performed a single-center, cross-sectional cohort study. Since 2011, data from all BC patients treated at the BC center of the Department of Obstetrics and Gynecology, Inselspital Bern, have been prospectively recorded in a local registry (software ODSeasy, comp. Asthenis (GER)). Registered BC patients from 2011-2018 above age 18 (n=669) were contacted by mail and asked to participate in this study. Subjects were excluded if they did not live in Switzerland, had no internet access, or did not speak German, respectively. Written informed consent was obtained from each participant. The study protocol was approved by the cantonal ethics committee (ref.-No. KEK-BE: 2019-01952). The study was carried out from February, 24th till May, 8th 2020.

Questionnaire

The questionnaire was developed in German in three steps. First, by literature search, the main symptoms in BC patients and MNs frequently used in functional nutritional medicine (FNM) were recorded [11]. Then, the applicability of the questionnaire was tested in five BC survivors of different age groups. Thereafter, the adjusted questionnaire was tested for statistical applicability and finally implemented as an online version in the data collection software RedCap™ (Research Electronic Data Capture) [12]. Overall, the questionnaire consists of 15 questions (Q) covering four domains: 1) subject's characteristics (Q10-Q15), 2) prevalence and intensity of adverse symptoms during (Q8) and after (Q9) oncological therapy (n=19 symptoms, VAS for symptom intensity (0=none to 10=worst imaginable; intensity categories: none=VAS 0, low=VAS 1-3, moderate=VAS 4-6, severe=VAS 7-9, very severe=VAS 10)), 3) diet change (Q7) and 4) MN supplementation (Q1-Q6) (supplementary file 1). Completing the questionnaire was estimated to take 20-30 minutes. By mail, participants received a personal hyperlink with login for individual access to the online questionnaire. In case of non-response, the patient was reminded to complete the questionnaire two weeks prior to study closure. Data were continuously collected and stored in REDCap™.

Statistical analysis

Statistical analysis was performed with R version 3.6.1. Cohort characteristics and main data were summarized by descriptive statistics, such as mean, standard deviation and correlation. To test the statistical significance of differences in mean of continuous variables between subgroups the two samples T-test was performed. Similarly, the Fisher's exact test was used to test the statistical significance of differences in the distribution of binary variables between subgroups. Statistical significance was considered at p-value of 0.05 or lower. Missing data were not imputed, nor were observations with missing entries deleted from the dataset. As a result, the number of observations varied between different questions and thus between different analyses.

Results

174 out of 669 BC patients agreed to participate in the study. 153 finally filled out the questionnaire (n=149 complete and n=4 incomplete questionnaires). The remaining women either did not respond to the study invitation letter (n=329), refused participation (n=74), had died (n=9), or could not be reached by mail (return to sender) (n=83), respectively.

Characteristics of the study cohort are presented in Table 1. At the time of the survey, mean age of participants was 59.4 ± 10.9 years. Mean time since BC diagnosis was 4.5 ± 2.3 years. 10 out of 153 women had bilateral BC or ipsilateral recurrence before the inclusion in the study.

Distribution of tumor stages (according to the TNM classification) varied as follows: Tis: 15 (9.2%), T0: 9 (5.5%), T1: 75 (46.0%), T2: 47 (28.8%), T3: 16 (9.8%), T4: 1 (0.6%). 34.4% had nodal-positive disease (N1: 41 (25.2%), N2: 11 (6.7%), N3: 4 (2.5%), Nx: 15 (9.2%)). In three patients (1.8%) distant metastasis were present at diagnosis. Most tumors were hormone-receptor (HR) positive (ER+: 136 (83.4%), PR+: 127 (77.9%)) and HER2 receptor negative (124 (76.1%)). Tumor grade was distributed as follows: G1: 22 (13.5%), G2: 71 (43.6%), G3: 67 (41.1%), Gx: 3 (1.8%). BC treatment consisted in surgery: breast-conserving surgery: 111 (68.1%), mastectomy: 51 (31.3%), not specified surgery: 1 (0.6%); irradiation 142 (87.1%), chemotherapy 92 (56.4%) and endocrine therapy 132 (81.0%). Some women refused systemic treatment (chemotherapy: 5 (3.1%), endocrine therapy: 1 (0.6%)).

Adverse symptoms during and after oncological therapy

Participants were asked to retrospectively record adverse symptoms and their intensity during and after oncological therapy (Table 2). During oncological therapy, at least half of BC patients reported one of the following symptoms: ageusia, alopecia, appetite change, chronic fatigue (CF), dysesthesia, nausea, pain, body weight change, wounds, xerophthalmia and xerostomia. Patients perceived alopecia (n=46, 32.2%), ageusia (n=18, 13.1%) and CF (n=14, 10.1%) as the most compromising. After oncological therapy, the most prevalent symptoms (in > 50% of patients) were CF and pain.

Prevalence of MN supplementation

About one third of BC patients (n=53, 34.6%) took MNs before BC diagnosis. This number increased to 42.5% (n=65) during and 48.4% (n=74) after oncological therapy. We found a significant correlation between women taking MNs before and after cancer diagnosis ($p < 0.001$): Of the women who already took MNs before being diagnosed with BC, 94.3% (n=50) continued afterward in relation to cancer, while only 49.5% (n=46) of the study participants who had not previously taken MNs, started after the BC diagnosis. We further asked about sources of information on cancer-related MN use and tests carried out for MN deficiency. A large proportion of the patients informed themselves about the use of MN (n=65, 42.5%) while only 29 (19%) were informed by

Table 1. Characteristics of the cohort.

Characteristic	Mean (SD) or n (%)
Age at diagnosis	54.4 (10.75)
Menopausal status at diagnosis (n=163)	
Premenopausal	68 (41.7)
Perimenopausal	7 (4.3)
Postmenopausal	88 (54.0)
Level of education (n=147)	
Primary school leaving certificate	12 (8.2)
Secondary school leaving certificate	6 (4.1)
Completed apprenticeship	74 (50.3)
College of higher education leaving certificate	25 (17.0)
Bachelor's degree	6 (4.1)
Master's degree	17 (11.6)
Doctorate	4 (2.7)
Professorship	2 (1.4)
No school leaving certificate	1 (0.7)
Professional activity (n=134)	
1-41 hours per week	55 (41.0)
More than 42 hours per week	16 (11.9)
Unemployed	13 (9.7)
Retired	48 (35.8)
Unable to work	2 (1.5)
Monthly salary (n=145)	
< 5'000 CHF	71 (49.0)
5'000 - 10'000 CHF	41 (28.3)
> 10'000 CHF	9 (6.2)
No own income	24 (16.6)
Alcohol consumption (n=148)	
Never	24 (16.2)
Max. once a month	33 (22.3)
2-4 times a month	45 (30.4)
2-3 times a week	33 (22.3)
4 times a week	7 (4.7)
> 4 times a week	6 (4.1)
Nicotine consumption (n=144)	
Non-smoker	105 (72.9)
Ex-smoker	18 (12.5)
Less than 7 units[a] per week	12 (8.3)
1-10 units[a] per day	3 (2.1)
11-20 units[a] per day	6 (4.2)
Physical activity (n=148)	
Never	3 (2.0)
Rarely	12 (8.1)
Less than once a week	9 (6.1)
1-2 times a week	46 (31.1)
More than 2 times a week	78 (52.7)

a) one unit equals 1 cigarette, 1 cigar, 1 cigarillo, 1 pipe or 1 bong;
b) physical exercise as doing sports

their oncologist. 40 BC patients (26.1%) were tested for MN deficiency. Of those, the majority was tested after oncological therapy (n=32); one out of two presented a MN deficiency (n=18, 56.2%).

Study participants were asked about the intake of 21 MNs. 13 MNs was taken by at least 10% of micronutrient users for cancer-related reasons. Table 3 summarizes type of MNs, mean duration of use and the prescriber. During oncological therapy the most frequently (>25%) applied MNs for cancer-related causes were vitamin C, D, zinc and calcium, whereas after oncological therapy only calcium (32.4%) and vitamin D (45.9%) were taken by a high percentage of BC survivors.

The vast majority of applications were administered orally, only very few applications of calcium, iron, vitamin B12, vitamin C and selenium were

Table 2. Prevalence and intensity of adverse symptoms during and after oncological therapy.

Adverse symptom	(n)	Prevalence n (%)	Intensity Low n (%)	Moderate n (%)	Severe n (%)	Very severe n (%)
During oncological therapy						
Ageusia	(137)	74 (54.0)	14 (10.2)	15 (10.9)	27 (19.7)	18 (13.1)
Alopecia	(143)	99 (69.2)	16 (11.2)	18 (12.6)	19 (13.3)	46 (32.2)
Appetite change	(142)	103 (72.5)	40 (28.2)	29 (20.4)	24 (16.9)	10 (7.0)
CF	(139)	111 (79.9)	33 (23.7)	32 (23.0)	32 (23.0)	14 (10.1)
Dermatitis	(137)	63 (46.0)	26 (19.0)	16 (11.7)	13 (9.5)	8 (5.8)
Diarrhoea	(136)	60 (44.1)	28 (20.6)	25 (18.4)	4 (2.9)	3 (2.2)
Dysesthesia	(134)	81 (60.4)	17 (12.7)	26 (19.4)	27 (20.1)	11 (8.2)
Dysosmia	(136)	55 (40.4)	16 (11.7)	13 (9.6)	17 (12.5)	9 (6.6)
Dysphagia	(136)	36 (26.5)	18 (13.2)	12 (8.8)	4 (2.9)	2 (1.5)
Mucositis	(136)	42 (30.9)	24 (17.6)	10 (7.4)	6 (4.4)	2 (1.5)
Nausea	(140)	91 (65.0)	40 (28.6)	25 (17.9)	22 (15.7)	4 (2.9)
Pain	(138)	103 (74.6)	39 (28.3)	38 (27.5)	21 (15.2)	5 (3.6)
Vomiting	(140)	48 (34.3)	34 (24.3)	10 (7.1)	2 (1.4)	2 (1.4)
Weight change	(143)	103 (72.0)	36 (25.2)	28 (19.6)	29 (20.3)	10 (7.0)
Wounds	(134)	69 (51.5)	32 (23.9)	18 (13.4)	15 (11.2)	4 (3.0)
Xerophtalmia	(139)	80 (57.6)	29 (20.9)	2 (1.4)	20 (14.4)	5 (3.6)
Xerostomia	(140)	86 (61.4)	34 (24.3)	25 (17.9)	22 (15.7)	5 (3.6)
After oncological therapy						
CF	(135)	91 (67.4)	34 (25.2)	28 (20.7)	24 (17.8)	5 (3.7)
Pain	(127)	79 (62.2)	33 (26.0)	29 (22.8)	15 (11.8)	2 (1.6)
Secondary tumor or tumor recurrence	(112)	11 (9.8)	2 (1.8)	0 (0)	1 (0.9)	8 (7.1)
Weight loss	(18)	20 (16.9)	9 (7.6)	7 (5.9)	2 (1.7)	2 (1.7)
Other	(81)	24 (29.6)	8 (9.9)	6 (7.4)	5 (6.2)	5 (6.2)

a) Subjects who either did not provide any information or no longer remember their suffering make up the difference to the total number of study participants (n=153).

Table 3. Cancer-related use of micronutrients during and after oncological therapy.

Micronutrient	During oncological therapy			After oncological therapy		
	Prevalence of use n (%)	Median duration of use (months)	Prescribing Person n (%)	Prevalence of use n (%)	Median duration of use (months)	Prescribing person n (%)
Vitamins, water-soluble						
Vitamin B6	6 (9.2)	3.5	p: 2 (33.3) h: 1 (16.7) n: 3 (50)	9 (12.2)	12	p: 4 (44.4) h: 4 (44.4) n: 1 (11.1)
Vitamin B9	7 (10.8)	3.5	p: 2 (28.6) h: 1 (14.3) n: 4 (57.1)	5 (6.8)	12	p: 3 (60) n: 2 (40)
Vitamin B12	10 (15.4)	6	p: 5 (50) h: 1 (10) n: 4 (40)	6 (8.1)	9	p: 3 (50) h: 2 (33.3) n: 1 (16.7)
Vitamin C	17 (26.2)	9	p: 2 (11.8) h: 5 (29.4) n: 10 (58.8)	8 (10.8)	18	p: 1 (12.5) h: 4 (50) n: 3 (37.5)
Vitamins, fat-soluble						
Vitamin A	7 (10.8)	3.5	p: 2 (28.6) h: 1 (14.3) n: 4 (57.1)	5 (6.8)	42	p: 3 (60) h: 1 (20) n: 1 (20)
Vitamin D3	22 (33.8)	42	p: 16 (72.7) h: 1 (4.5) n: 5 (22.7)	34 (45.9)	42	p: 27 (79.4) h: 3 (8.8) n: 4 (11.8)
Vitamin E	9 (13.8)	42	p: 3 (33.3) h: 1 (11.1) n: 5 (55.6)	5 (6.8)	42	p: 3 (60) h: 1 (20) n: 1 (20)

Trace elements						
Iron	7 (10.8)	3.5	p: 4 (57.1) h: 1 (14.3) n: 2 (28.6)	3 (4.1)	3.5	p: 2 (66.7) n: 1 (33.3)
Selenium	15 (23.1)	3.5	p: 5 (33.3) h: 3 (20) n: 6 (40) x: 1 (6.7)	11 (14.9)	24	p: 3 (27.3) h: 4 (36.4) n: 3 (27.3) x: 1 (9.1)
Zinc	18 (27.7)	6	p: 10 (55.6) h: 1 (5.6) n: 7 (38.9)	10 (13.5)	18	p: 5 (50) h: 3 (30) n: 2 (20)
Minerals						
Calcium	24 (36.9)	24	p: 18 (75) h: 2 (8.3) n: 4 (16.7)	24 (32.4)	42	p: 19 (79.2) h: 3 (12.5) n: 2 (8.3)
Magnesium	10 (15.4)	42	p: 3 (30) h: 1 (10) n: 6 (60)	8 (10.8)	42	p: 5 (62.5) h: 2 (25) n: 1 (12.5)
other MNs	9 (13.8)	18	p: 2 (22.2) h: 3 (33.3) n: 4 (44.4)	11 (14.9)	18	p: 2 (18.2) h: 6 (54.5) n: 3 (27.3)

p: prescribed by a physician; h: prescribed by a "healer"; n: no prescription/self-prescribed x: no statement

administered intravenously. It is noticeable that during oncological therapy patients mainly applied water-soluble vitamins without prescription (n= 21, 52.5%) and after oncological therapy with prescription from a physician (n=11, 39.3%).

BC patients were also asked about cost coverage. Overall, health insurances only covered cost for few patients during (n=10, 15.4%) and after (n=13, 17.6%) oncological therapy. About one fifth of patients spent more than 100 Swiss Francs per month for MN supplementation during and after oncological therapy, respectively.

BC patients not applying MNs during and/or after oncological therapy were asked if there were certain thresholds in efficacy for considering MN supplementation and if yes, if they were ready to cover the cost (Figure 1). It stands out that the vast majority of women were willing to take MNs during (n=55, 75.4%) or after therapy (n=44, 67.8%) even if it reduced their symptoms only by less than 50%. And still 33 (45.8%) and 21 (32.3%) women would take FNM during and after therapy respectively if a symptom relief of only 10% could be expected. The greatest proportion of these women were willing to pay (part of) the costs for MNs during therapy (n= 42, 76.4%) or after therapy (n=31, 70.5%).

Table 4 shows the correlation between tumor stage and application of FNM. In non-metastatic BC patients, the percentage of women taking MNs increased with increasing tumor stages. We could not observe an association between participants age and the use of MNs.

Diet change

Participants were asked if they had changed their diet after BC diagnosis. About one third of BC patients (n=55, 35.9%) confirmed diet adjustments. Modifications were specified as follows: reduced consumption of red meat in 41 (74.5%), total carbohydrates in 36 (65.5%), complex carbohydrates in 6 (10.9%), salt in 16 (29.1%) and phytoestrogen-containing food in 4 (7.3%) participants. 37 (67.3%) women reported about increased consumption of complex carbohydrates and 40 (72.7%) of fruits and vegetables. After BC diagnosis the intake of phytoestrogen-containing food was (further) increased by almost half of subjects (n=26, 47.3%).

In contrast, about two thirds of BC patients (n=94, 61.4%) had not changed their diet after BC diagnosis. The main reasons for not changing the diet were lack of information about possible benefits (n=36, 38.3%), lack of belief in the role of nutrition in cancer (n=5, 5.3%) and perceived lack of mental strength for changes (n=3, 3.2%), respectively. Interestingly, one quarter of subjects was convinced that their diet was already optimal (n=24, 25.5%).

The women who had changed their diet after cancer diagnosis were on average 4.5 years younger than those who had not (p=0.015).

Use of FNM over time

Diet change after diagnosis and cancer-related use of MN during therapy have increased since 2011 (diet change: 3 (27.3%), MN during therapy: 2 (18.2%)) to 2018 (diet change: 16 (55.2%), MN during therapy: 11 (37.9%)). We found a statistically significant increase of diet changes (p=0.011) in the period 2015-2018 (40 (44.4%)) compared to the period 2011-2014 (15 (23.8%)). However, regarding the percentage of BC patients using MN after therapy, we could not find an increase from 2011-2018.

Discussion

The major finding of our study was that a high proportion of BC patients, 48% in our study cohort, used MNs and that the number had increased in the last decade. The cancer-related application was more frequent in BC patients who already applied MNs before diagnosis and those with higher tumor stages. However there seemed to be a lack of information and supplementation was often performed without prescription. Furthermore, the frequency of diet changes following the diagnosis of BC increased over the last decade. One third of our study population changed nutritional habits, mainly by reducing consumption of red meat and total carbohydrates and increasing the intake of complex carbohydrates, vegetables and fruits.

Accordingly, to the literature more than half of the patients suffered during and after systemic therapy from compromising side effects.

CF presents one of the most common and most disturbing side effects in BC patients [13]. Supplementation of MNs and diet adjustments may attenuate the impact of CF on quality of life. A randomized controlled trial found that oral supplementation of zinc during chemotherapy (2 × 35 mg/day for 16 weeks, starting 45 days before the first chemotherapy cycle) decreased fatigue in colorectal cancer patients [14].

In a 3-month randomized, pilot trial Zick SM, et al. showed that a diet rich in fruits, vegetables, whole grain products and omega-3 fatty acids-enriched food significantly improved fatigue in BC survivors [15].

In contrast to these findings, in our cohort 111 (72.5%) patients reported CF during therapy but only 18 (11.8%) supplemented zinc. Solely a quarter of all participants stated to consume more complex carbohydrates (n=37, 24.2%) and more fruits and vegetables (n=40, 26.1%) after BC diagnosis.

The vitamins most widely used by our participants in relation to BC diagnosis were vitamin C and D.

A metanalysis of 30 prospective studies analyzed the association between vitamin D status (vitamin D intake, blood 25(OH)D levels) and BC risk and

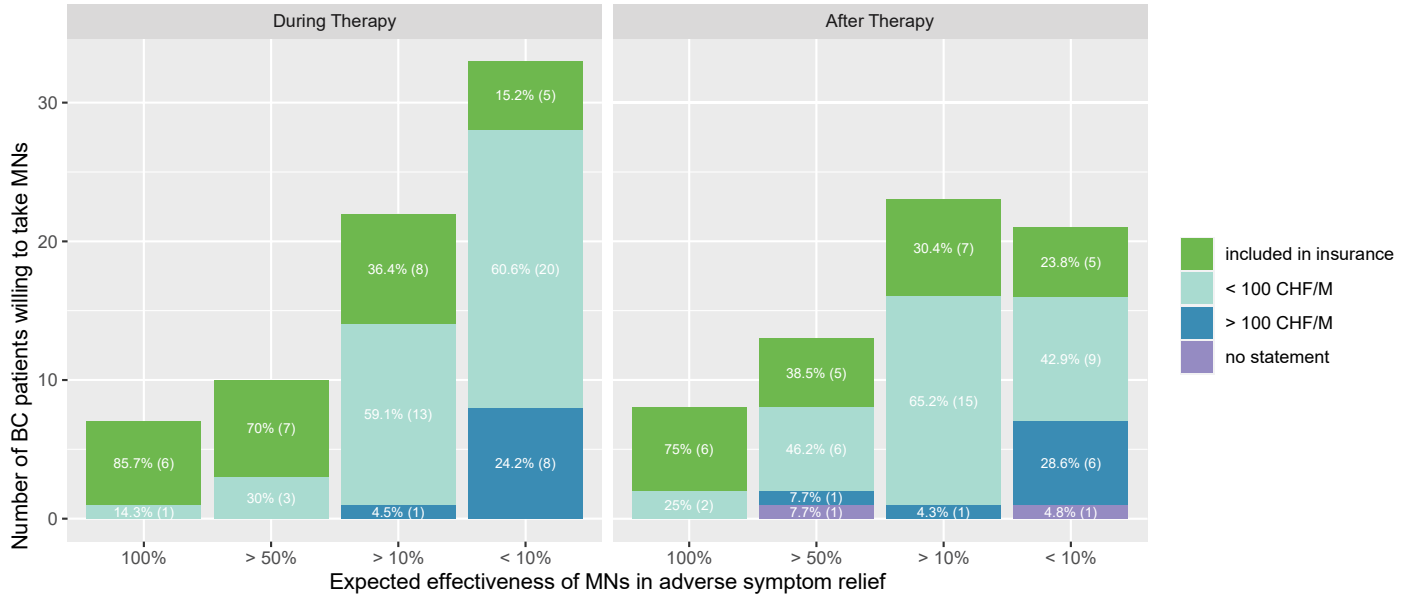

Figure 1. Assumed willingness to apply and pay for micronutrients according to a threshold of expected effectiveness in adverse symptom relief.

Table 4. Frequency distributions between tumor stage and applications of FNM.

Tumor Stage TNM n (%)	Cancer-related use of MN during therapy		Cancer-related use of MN after therapy		Diet change after Diagnosis	
	Yes	No	Yes	No	Yes	No
Stage T						
T0	1 (11.1)	8 (88.9)	4 (44.4)	5 (55.6)	4 (44.4)	5 (55.6)
Tis	4 (30.8)	9 (69.2)	7 (50)	7 (50)	4 (30.8)	9 (69.2)
T1	27 (45)	33 (55)	31 (57.4)	23 (42.6)	22 (35.5)	40 (64.5)
T2	19 (50)	19 (50)	19 (59.4)	13 (40.6)	12 (30.8)	27 (69.2)
T3	8 (50)	8 (50)	8 (66.7)	4 (33.3)	9 (60)	6 (40)
T4	0 (0)	1 (100)	-	-	0 (0)	1 (100)
Stage N						
N0	32 (42.1)	44 (57.9)	36 (54.5)	30 (45.5)	27 (35.1)	50 (64.9)
N1	14 (42.4)	19 (57.6)	20 (66.7)	10 (33.3)	12 (35.3)	22 (64.7)
N2	5 (50)	5 (50)	5 (62.5)	3 (37.5)	4 (40)	6 (60)
N3	5 (50)	5 (50)	1 (33.3)	2 (66.7)	3 (75)	1 (25)
Stage M						
M0	55 (43.7)	71 (56.3)	62 (55.9)	49 (44.1)	45 (35.4)	82 (64.6)
M1	1 (33.3)	2 (66.7)	1 (33.3)	2 (66.7)	2 (66.7)	1 (33.3)

mortality. The authors found that high vitamin D status is weakly associated with low BC risk but strongly associated with better BC survival [16]. Based on these data from observational studies supplementation of vitamin D may be recommended in BC patients with low levels (≤ 25nmol/l), which is also suggested for postmenopausal osteoprotection unrelated to cancer. But in our cohort only 26% of BC patients were tested for MN deficiency.

Just recently, Codini M, et al. summarized a number of positive effects of intravenous vitamin C supplementation in BC patients. Vitamin C may have dose-dependent, anticancer effects e.g. the neutralization of reactive oxygen species and the reduction of inflammation and cell proliferation. In vitro experiments showed that vitamin C can induce apoptosis in BC cell lines, without having a significant impact on normal cells and selectively inhibits proliferation in chemotherapy-resistant cells. Intravenous vitamin C treatment in vivo has shown reduced side effects of standard oncological therapy, improved quality of life and transient stabilization of the disease compared to control groups. Furthermore, several studies proofed no interference of high dosed vitamin C with the standard therapy [17]. Despite these findings, in our study only few patients received intravenous administrations of vitamin C.

Our analysis showed that applications of MNs increased with higher non-metastatic tumor stages. This may reflect a higher level of physical and psychological distress in patients with advanced tumor stages, but probably also the hope for cure by alternative methods.

Overall only 19% of all participants stated that they had been informed about the possible use of micronutrients for cancer-related issues. Even if robust data are still rare we believe that BC patients interested in MN supplementation should be informed about the current evidence.

The World Cancer Research Fund/American Institute for Cancer Research (WCRF) recommends to consume complex carbohydrates, fruits and vegetables and to limit the of red meat and total amount of carbohydrates for the prevention of cancer [18]. The results of our survey shown that most dietary changes corresponded to these recommendations. The association between fat-reduced diet and tumor recurrence was the subject of two randomized controlled trials, which reported divergent results: The Women's Healthy Eating and Living (WHEL) Randomized Trial reported that low-fat dietary change had no effect on prognosis, whereas the Women's Intervention Nutrition Study (WINS) reported a positive effect of fat change [19,20].

However, for phytoestrogen-containing foods, both increased and decreased intakes were reported. The possible effects of phytoestrogens on BC are controversially discussed: While isoflavones may via their estrogenic and proliferative effects possibly raise BC incidence, other data concluded that high soy intake (20-50 mg isoflavones/day) may be protective against BC and BC recurrence [21]. A prospective cohort study with median follow-up of 113 month found out that higher intake of isoflavones was associated with decreased all-cause mortality in woman with HR negative cancer and

women without endocrine therapy. With regard to HR positive tumors, it remained unclear if phytoestrogens interfere with anti-hormonal therapy [22]. As NAMS stated in the isoflavone report from 2011, the effect of isoflavones on breast cancer depends on numerous factors, such as: type of food containing isoflavones respectively pure supplementation, exposed subject (human subjects, cell lines or rodents) time of ingestion and isoflavone concentrations. They summarised that the intake of soy products had a protective effect on breast cancer, while data on breast cancer survivors were still too weak and further studies were needed [23]. In our cohort the majority of women who changed their phytoestrogen containing food intake after BC diagnosis did increase it. Whether this was done intentionally or accidentally, by increasing vegetable consumption, remains unknown.

We also found out that patients who had changed their diet after diagnosis were significantly younger than those who maintained their eating habits (4.5 years, p=0.015). We assume that younger people find it easier to adopt new eating habits and to follow the emerging trend of an environmentally conscious, meat-reduced diet.

The majority of patients (n=36, 38.3%) who had not made any dietary change stated that they had not received any information about possible benefits of diet change. It should be considered that professionally supervised dietary changes and lifestyle adjustments can have positive effects, as the patient is actively involved in the therapy process and can mobilize the body's own resources.

Our study provides detailed information on how BC patients use FNM and how they think about it. To the best of our knowledge our study is the first to link the applications of FNM to both tumor characteristics and the characteristics and attitude of patients, yet several limitations should be considered. Due to the study design, the drop-out rate was relatively high and the number of participants may have been affected by recalls of participation. Furthermore, it can be assumed that especially BC patients already interested in FNM were willing to participate at the survey which could lead to selection bias.

Nevertheless, our study reflects an increasing demand for FNM among BC patients. Thus, the majority of patients are willing to take micronutrients even at low levels of efficacy and tend to cover the costs themselves. Furthermore, our study indicates that many supplementations are preceded without a prescription by a physician and/or without a prior testing for deficiency. Currently, the WCRF recommends against the use of high-dose micronutrients because randomized controlled trials have failed to demonstrate a protective effect and some have shown the potential for unexpected adverse symptoms [18]. By evaluating the individual demands of BC patients, our study emphasizes on the need of evidence-based recommendations regarding FNM application in oncological patients.

Conclusion

We have found an increased need for use of FNM in BC patients. Many uses occur without a medical prescription. As there is currently a lack of evidence-based data, it is of great importance to collect such data in order to be able to provide evidence-based recommendations.

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Conflict of Interest

Not applicable.

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