

RESEARCH ARTICLE

BENTHAM
SCIENCE

Effects of an Integrative Mind-Body-Medicine Group Program on Breast Cancer Patients During Chemotherapy: An Observational Study



Heidemarie Haller¹, Kyung-Eun Choi², Silke Lange¹, Sherko Kümmel³, Anna Paul¹, Holger Cramer¹, Gustav Dobos¹ and Petra Voiss^{1,3,*}

¹Department of Internal and Integrative Medicine, Evang. Kliniken Essen-Mitte, Faculty of Medicine, University of Duisburg-Essen, Essen, Germany; ²Institute for Medical Sociology, Health Services Research, and Rehabilitation Science (IMVR) at the Faculty of Human Sciences and the Faculty of Medicine of the University of Cologne, Germany; ³Breast Unit, Evang. Kliniken Essen-Mitte, Germany

Abstract: Background: Breast cancer is one of the leading cancers in women in the Western world. Cancer treatment, especially chemotherapy, is often associated with physical and psychosocial side effects.

Objective: To improve the quality of life and manage side effects, a new integrative mind-body-medicine group concept for breast cancer patients receiving chemotherapy was developed and pilot tested.

Methods: Breast cancer patients participated in a 66 hours mind-body-medicine group program tailored to the needs of cancer patients during chemotherapy. The program was integrated into standard care encompassing mindfulness training, yoga, moderate exercise, nutrition, complementary self-help strategies, cognitive restructuring, and acupuncture. Quality of life (EORTC QLQ-C30), depression and anxiety (HADS), stress (PSS-10), and fatigue (BFI) were assessed before and after the program, as well as satisfaction and safety. Analyses were carried out on exploratory basis with paired samples t-tests.

Results: Fifty-seven female patients, aged 51.3±10.5 years, with breast cancer diagnoses were enrolled. After completing the program, global EORTC quality of life was improved (D=9.5; 95%-CI=[2.9|16.1]; p=.005), although the EORTC-symptom scales assessing fatigue (D=9.9; 95%-CI=[1|18.8]; p=.030), nausea (D=7.1; 95%-CI=[0.6|13.6]; p=.031), and dyspnea (D=12.5; 95%-CI=[2.9|22.1]; p=.011) were found to be increased. Stress (D=-3.5; 95%-CI=[-5|-2.1]; p=.000), anxiety (D=-3.8; 95%-CI=[-4.9|-2.7]; p=.000) and depression (D=-3.9; 95%-CI=[-4.9|-2.8]; p=.000) were also found to be significantly reduced. Regarding the severity of (D=0.2; 95%-CI=[-0.8|0.5]; p=.644) and the impairment due to fatigue (D=0.1; 95%-CI=[-0.8|0.6]; p=.696), no significant worsening was observed. Patients were satisfied with the program. No serious adverse events were reported.

Conclusion: Breast cancer patients benefit from an integrative mind-body-medicine group program during chemotherapy regarding the quality of life and psychological symptoms. Randomized controlled trials are warranted.

ARTICLE HISTORY

Received: June 16, 2020
Accepted: October 31, 2020

DOI:
10.2174/138161282666620121111122



This is an Open Access article published under CC BY 4.0
<https://creativecommons.org/licenses/by/4.0/legalcode>

Keywords: Breast cancer, chemotherapy, mind-body therapies, mindfulness-based stress reduction, acupuncture, quality of life, anxiety, depression.

1. INTRODUCTION

In 2012, the worldwide incidence of mortality from 27 major cancers combined was estimated to account for 14.1 million new cases and 8.2 million deaths [1]. Breast cancer has increased in prevalence since 1990-2015 [2]. Every year, 1.7 million women are newly diagnosed with the most incidences reported from high-income countries [1]. In Germany, about 71,600 women and nearly 700 men were diagnosed with breast cancer in 2013 [3]. The relative 5-year survival rate in Germany was 88% for women [3]. While the average number of years of living with a disability has improved over the last decades [4], patients' health-related quality of life (HQoL), including physical, psychosocial, and social dimensions, continues to be affected by psychosocial symptoms and side effects of cancer treatment [5]. In particular, cancer-related fatigue was found to significantly decrease HQoL [6, 7], while sleep disturbances, stressful life events, and psychological distress contribute to even higher levels of breast-cancer mortality [8-11].

Several complementary therapies have been proven to ameliorate psychological well-being and the HQoL of patients with breast cancer [12, 13]. The Clinical Practice Guideline of the Society for Integrative Oncology (SIO), which is endorsed by the American Society of Clinical Oncology (ASCO) [14], recommends meditation with a grade A evidence to improve anxiety/stress reduction and quality of life and Mindfulness Based Stress Reduction (MBSR) to enhance depression/mood disturbances. With a Grade A evidence, the modality should be offered because there is high certainty that the net benefit is substantial [14]. However, hardly any hospital in Germany offers the recommended therapies during cancer treatment. Despite the fact that about 75% of German patients with breast cancer are interested in complementary medicine (CAM) [15].

A core construct of several complementary therapies is mindfulness [16]. It involves two components: self-regulation of attention and adopting a particular orientation toward one's experience in the present moment [17]. The most commonly used mindfulness-based interventions are mindfulness-based stress reduction (MBSR) and mindfulness-based cognitive therapy (MBCT) [17, 18]. MBSR is a structured 8-week group program of weekly sessions lasting an average of 2.5 h with an additional silent day retreat. Key components of MBSR comprise sitting and walking

*Address correspondence to this author at the Department of Internal and Integrative Medicine, Evang. Kliniken Essen-Mitte, Faculty of Medicine, University of Duisburg-Essen, Am Deimelsberg 34a, 45276 Essen, Germany; Tel: +49 (0)201 174-33024; Fax: +49 (0)201 174-33000; E-mail: p.voiss@kem-med.com

meditation, yogic exercises and mindful relaxation techniques. To incorporate mindfulness into everyday life, daily home practice is recommended and monitored [19]. MBCT combines MBSR techniques with cognitive-behavioral methods such as psychoeducation, cognitive restructuring, and developing pleasant activities [20, 21]. In 2017, an updated systematic review and meta-analysis for the effectiveness of MBSR and MBCT in women with breast cancer were conducted [22], revealing small but significant post-intervention effects on HQoL, fatigue, sleep, stress, anxiety, and depression.

Usually, MBSR and comparable mind-body programs are offered to breast cancer patients after completing chemotherapy [23-25]. In other trials, only some of the patients were on chemotherapy while participating in the program and subgroup analyses were not reported. A reduction of anxiety and depression in breast cancer patients and survivors is observed after taking part in these interventions [26-28]. Other mind-body therapies like Yoga, Tai Chi, and physical exercise are examined during chemotherapy. In a recent trial, a yoga program once a week for 12 weeks during chemotherapy failed to demonstrate a significant beneficial effect on fatigue [29]. Two other recently published studies failed to show an effect of yoga on CRF in women with breast cancer during (neo)adjuvant treatment [30, 31]. These findings are in contrast to the conclusions of a Cochrane Review [12] that “yoga, specifically, complex yoga interventions incorporating breath control and/or meditation beyond physical yoga postures, can be considered a supportive intervention for improving short term health-related quality of life, depression, anxiety, fatigue and sleep disturbances in women with recently diagnosed non-metastatic breast cancer who are currently undergoing chemotherapy or radiotherapy or have completed curative cancer treatment”.

So far, no mindfulness program exclusively for cancer patients during chemotherapy has been developed. Based on 10 years of experience with different integrative mind-body-medicine group programs [32, 33], the Department of Complementary and Integrative Medicine and the Breast Unit at the Evang. Kliniken Essen-Mitte, Germany, have established an innovative, integrative concept that is specially tailored to the particular needs of breast cancer patients during chemotherapy. The focus of the mind-body-medicine group program lies in enhancing the coping abilities as well as the treatment of side effects caused by chemotherapy. For the latter, acupuncture treatments are implemented within the group sessions. The SIO guideline [13] recommends acupuncture for selected patients with a Grade C evidence for the reduction of hot flushes, pain, fatigue, anxiety, and depression. Grade C evidence recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences [14]. Acupressure and electroacupuncture can also be considered as an addition to antiemetic drugs to control nausea and/or vomiting during chemotherapy (Strength of Evidence Grade B: high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial).

The best time to offer psychological/behavioral interventions is when stress is high, that is at the time of initial diagnosis and treatment [34, 35]. Thus, this observational study aims to examine the pilot effects of the developed integrative mind-body-medicine group program.

2. METHODS

2.1. Design

This was a single-arm observational study conducted in 2012 to 2015 at the Department of Integrative Oncology, Evang. Kliniken Essen-Mitte. The study was approved retrospectively by the Ethics Committee of the University of Duisburg-Essen (approval number 17-7909-BO) and registered retrospectively at ClinicalTrials.gov (NCT03868865). The trial was conducted in accordance with the declaration of Helsinki and good clinical practice guide-

lines. The writing was supported by Karl und Veronica Carstens-Stiftung.

2.2. Patients

Patients receiving chemotherapy at the Evang. Kliniken Essen-Mitte were offered to participate in an integrative mind-body-medicine group program. Patients were included if they had curative malignancy (breast cancer of TNM staging I-III), received chemotherapy, were at least 18 years old, gave their written informed consent and were willing and physically/mentally able to participate in a six hours program eleven times during chemotherapy. Exclusion criteria included insufficient knowledge of the German language, physical or mental disabilities resulting in ineligibility for participation in the program or filling out the questionnaires.

2.3. Outcome Measures

Outcome measures were assessed before (T0) and after the intervention (T1). They encompassed standardized questionnaires for quality of life, depression and anxiety, fatigue, perceived stress, satisfaction, and adverse events.

The European Organization for Research and Treatment of Cancer (EORTC) quality of life questionnaire (QLQ-C30) based on 30 core items is a cancer-specific multidimensional self-reporting instrument, which is well validated and used worldwide [36, 37]. Besides the global quality of life subscale, this instrument assesses five functional domains of quality of life: physical, role, emotional, cognitive, and social function. Symptom scales further assess fatigue, pain, nausea and vomiting, dyspnea, insomnia, loss of appetite, constipation, diarrhea, and financial difficulties. Scores of all subscales range from 0 to 100, while a higher score represents a better level of functioning or a worse amount of symptoms. Psychological distress was assessed by the Hospital Anxiety and Depression Scale (HADS) to measure the two dimensions, anxiety and depression. Scores ranging from 0 to 21 with higher values indicate higher distress. Values of ≥ 8 indicate potential subclinical anxiety or depressive disorders [38]. The Brief Fatigue Inventory (BFI) has been validated as a short and comprehensive instrument to assess the severity of fatigue and fatigue-related impairment in cancer patients [39] with a 9-item, 11-point rating scale. Higher scores on the BFI correspond to greater severity of fatigue/impairment due to fatigue over the past 24 hours [40].

Perceived stress was assessed by the 10-item version of the Perceived Stress Scale (PSS) [34, 41], rated for the past month on a 5-point rating scale. The scale ranged from 0 to 40; a higher total score indicated greater stress.

Satisfaction was assessed at T1 by 5 questions regarding fulfilled expectations about the program contents, relevance for coping with cancer, social support of the group setting, transferring into everyday life, and recommendation of the program. Each question could be scored from 1=totally agree to 6=totally disagree.

All adverse events that occurred during the study period were recorded by the study physician during each integrative mind-body-medicine group program visit, regardless of their potential relation to the study intervention. At T1, patients were also asked to report adverse events not previously mentioned.

2.4. Intervention

The integrative mind-body-medicine group program focuses on support in coping with the disease, on lifestyle modification [42] and on the reduction of chemotherapy-induced side effects. The self-contained modules of the program can be followed in an individual order to allow the adoption of different chemotherapy regimens. Continued access is possible. Patients can join the program eleven times for six hours each visit. They participate in each of the eleven modules once (Fig. 1). Usually, the patients join the program one or two days ahead of the next chemotherapy cycle.

Schedule	Module										
	1	2	3	4	5	6	7	8	9	10	11
9:00-9:30	Arrival, Meet, Course of The Program, Retrospection										
9:30-10:45	Management of side effects with CM	Exercise during and after treatment	Stress-management	Nutrition during chemotherapy	CM self-care strategies	Coping with cancer, self-care	Social support	Relaxation techniques	Management of side effects with CM	Mindfulness	Cognitive restructuring
10:45-11:45	Yoga										
11:45-13:45	Lunch (Mediterranean Wholefood Diet) / Physician Group Consultations with Acupuncture										
13:45-14:30	Exercise										
14:30-15:00	PME	Body scan	Breathing-meditation	Body scan	PME	Imagination	Body scan	Breathing-meditation	PME	Breathing-meditation	Imagination

Fig. (1). Timetable of the integrative mind-body-medicine group program. Progressive Muscle Relaxation (PME); Complementary Medicine (CM).

For example, if patients receive treatment with epirubicin and cyclophosphamide every two weeks, they participate every two weeks in the program.

The conceptual framework of the program was developed in 2000 at the Department of Integrative Medicine at Evang. Kliniken Essen-Mitte and was published in 2013 [42]. On the one hand, the program is based on the MBSR Program developed by Kabat-Zinn at the University of Massachusetts [19, 43]. On the other hand, elements of the mind-body-medicine cancer program of the Benson-Henry Mind/Body Medical Institute at Harvard Medical School are taken into account, which is rooted in psychoneuroendocrinology and focuses on relaxation techniques, exercise, cognitive restructuring, diet, and social support [44].

Mindfulness-based interventions not only include training in the formal practice of mindfulness through meditation and/or mindful exercise but also training in the informal practice of mindfulness by retaining a mindful state of consciousness during routine activities in everyday life [19, 45]. The integrative mind-body-medicine group program is held by health professionals specially trained in MBSR, nutrition, physical exercise and psychosocial counseling.

In addition to elements of the MBSR and Benson programs, complementary methods (phytotherapy, compresses and poultices, massages, and hydrotherapy) of self-regulation and self-care are incorporated that focus on reducing side effects of chemotherapy and improving quality of life. During every program visit, a 120 minutes group medical round with acupuncture treatment provided through an integrative oncologist is part of the program. Patients can discuss their current medical status, their bothering symptoms and adverse events. Individualized recommendations are given and targeted acupuncture is provided depending on the reported symptoms of each patient. At every visit, blood is drawn first to rule out an increased risk of infection through acupuncture treatment in case of neutropenia (absolute neutrophil count less than 1000/ μ L). Every patient joining the program receives a sea-band at the first visit to do acupressure of pericardium 6 in case of nausea and vomiting [13], a compact disc with diverse relaxation techniques (for example, progressive muscle relaxation as prescribed by Jacobson, body scan, breathing exercise, imagination, etc.) and a manual.

Each session is complemented by mindful exercise, yoga, or qi gong; aerobic exercise, mindful meditation or body scan; and/or education on nutrition. Patients are encouraged to practice formal mindfulness (with the use of additional material such as manuals and compact disc) as well as informal mindfulness at home by ensuring a mindful state of consciousness during routine activities and to practice aerobic and resistance exercise [46].

2.5. Statistical Analysis

All analyses were carried out on exploratory basis. Thus, an alpha of 0.05 was assumed for all comparisons. Missing values were excluded pairwise. The effects were analyzed by paired samples t-tests and displayed as mean post-pre differences (Δ) with 95% confidence intervals (CI). All analyses were performed using SPSS software (release 22.0, IBM).

3. RESULTS

3.1. Patient Flow and Characteristics at Baseline

From November 2012 to April 2015, a total of 57 patients received the mind-body-medicine program in parallel with their adjuvant or neoadjuvant chemotherapy. The patients were female, 51.1 ± 10.4 years old, and treated for breast cancer stage TNM I (29.8%), TNM II (57.9%), and TNM III (12.3%). None of the 57 patients dropped out during the observation period.

3.2. Study Effects

The results of the analyses are shown in Table 1. After completion of the program, the patients reported improved global EORTC quality of life ($\Delta=6.9$; 95%-CI=[0.8|12.9]; $p=.027$), while the EORTC symptom scales evaluating fatigue ($\Delta=10.3$; 95%-CI=[1.2|19.4]; $p=.027$), nausea ($\Delta=7.7$; 95%-CI=[0.7|14.1], $p=.031$), and dyspnea ($\Delta=12.3$; 95%-CI=[2.5|22.2]; $p=.015$) significantly increased and the cognitive functioning scale significantly decreased ($\Delta=9.7$; 95%-CI=[1.8|17.6]; $p=.017$) (Fig. 2). Regarding the other EORTC-QLQ-C30 subscales and the intensity of impairment due to fatigue, measured with the BFI, no significant changes were observed.

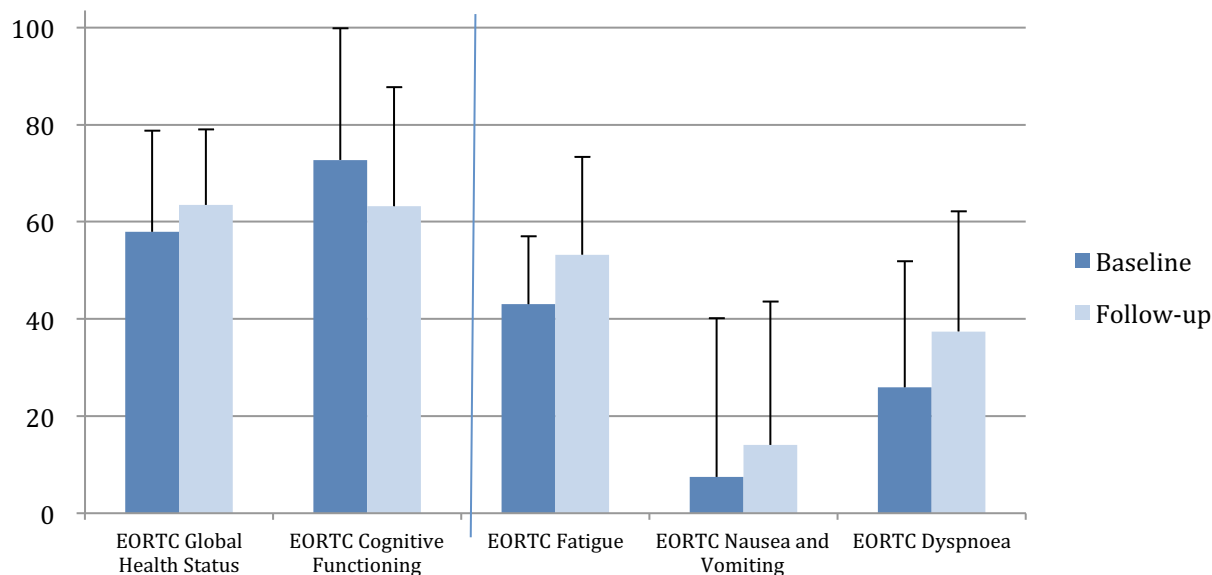


Fig. (2). Significant effects measured with the EORTC quality of life questionnaire (QLQ-C30). European Organization for Research and Treatment of Cancer (EORTC); Higher scores represent a better level of functioning in Global Health Status and Cognitive Functioning and a worse amount of symptoms in Fatigue, Nausea and Vomiting, and Dyspnoea. (A higher resolution/colour version of this figure is available in the electronic copy of the article).

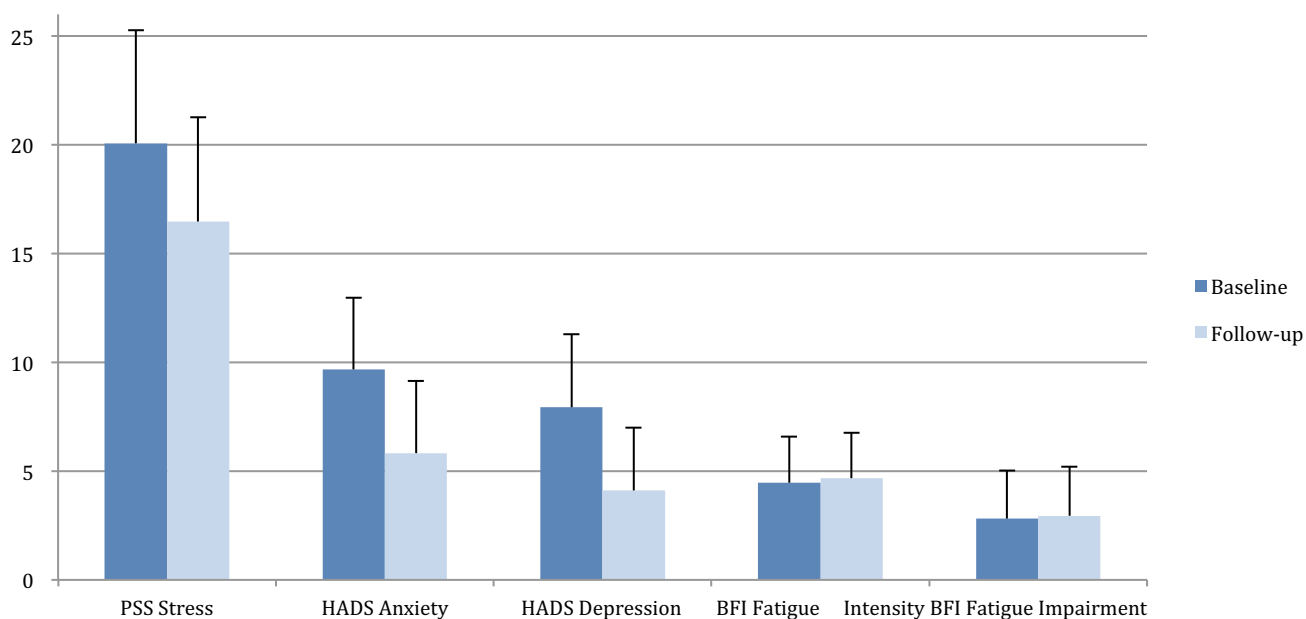


Fig. (3). Effects on the PSS, HADS, and BFI. Perceived Stress Scale (PSS)*; Hospital Anxiety and Depression Scale (HADS)*; Brief Fatigue Inventory (BFI). Higher values indicate higher stress, anxiety and depression; higher scores on the BFI correspond to greater intensity of fatigue / impairment due to fatigue. * means “significant effect”. (A higher resolution/colour version of this figure is available in the electronic copy of the article).

The perceived stress level ($\Delta=-3.6$; 95%-CI=[-5.2|-2.1]; $p=.000$), anxiety ($\Delta=-3.8$; 95%-CI=[-4.9|-2.6], $p=.000$), and depression ($\Delta=-3.8$; 95%-CI=[-4.8|-2.8]; $p=.000$) were significantly observed to be reduced after the program (Fig. 3).

3.3. Satisfaction

Out of the 57 patients, 96.5% rated that their expectations about the program were fulfilled or totally fulfilled, that the topics

of the program were relevant to cope with cancer, and that the group setting was supporting. 91.2% of the patients rated that they were able to easily transfer the program contents into everyday life. 96.5% of the patients would recommend the program to other patients. Two patients (3.5%) disagreed with all of the statements. In addition, three patients who received more than 11 cycles of chemotherapy requested a longer program that goes along with every chemotherapy cycle.

Table 1. Results of the paired samples t-tests.

-	Paired Differences						Significance (2-Tailed)
	N	Baseline Mean	Post Mean	Mean Difference	95% Confidence Interval of the Difference		
					Lower	Upper	
EORTC-QL	51	57.0	63.9	6.9	0.8	12.9	.027
EORTC-PF	54	79.7	75.8	-3.9	-10.3	2.6	.235
EORTC-RF	54	55.9	55.6	-0.3	-10.7	10.1	.953
EORTC-EF	54	55.3	61.6	6.3	-2.6	15.2	.160
EORTC-CF	55	72.7	63.0	-9.7	-17.6	-1.8	.017
EORTC-SF	52	63.5	62.2	-1.3	-10.6	8.1	.785
EORTC-FA	54	43.0	53.3	10.3	1.2	19.4	.027
EORTC-NV	54	7.4	14.8	7.4	0.7	14.1	.031
EORTC-PA	54	29.0	25.0	-4.0	-14.6	6.6	.450
EORTC-DY	54	25.9	38.3	12.3	2.5	22.2	.015
EORTC-SL	54	42.0	46.3	4.3	-7.4	16.1	.463
EORTC-AP	53	13.2	16.3	3.1	-6.6	12.9	.520
EORTC-CO	54	13.6	10.5	-3.1	-14.0	7.8	.574
EORTC-DI	54	7.4	13.6	6.2	-1.1	13.5	.096
EORTC-FI	52	17.3	21.1	3.8	-2.2	9.8	.204
PSS	53	20.1	16.5	-3.6	-5.2	-2.1	.000
HADS-A	52	9.7	5.9	-3.8	-5.0	-2.6	.000
HADS-D	52	7.9	4.1	-3.8	-4.8	-2.8	.000
BFI-INT	50	4.5	4.7	0.2	-0.5	0.8	.557
BFI-IMP	49	2.8	3.0	0.2	-0.6	0.9	.654

European Organization for Research and Treatment of Cancer (EORTC); global quality of life (QL); physical function (PF), role function (RF), emotional function (EF), cognitive function (CF), and social function (SF); fatigue (FA), nausea and vomiting (NV), pain (PA), dyspnea (DY), insomnia (SL), loss of appetite (AP), constipation (CO), diarrhea (DI), and financial difficulties (FI); Perceived Stress Scale (PSS); Hospital Anxiety and Depression Scale (HADS), anxiety (A), depression (D); Brief Fatigue Inventory (BFI), intensity of fatigue (INT), fatigue-related impairment (IMP).

3.4. Safety

Minor side effects like bruises through acupuncture were reported, but no serious side effects and no infection through the acupuncture needle occurred. One patient developed a disk prolapse, which was unrelated to the integrative mind-body-medicine group program.

4. DISCUSSION

We evaluated the concept of a new integrative mind-body-medicine group program for breast cancer patients receiving chemotherapy regarding HQoL, fatigue, perceived stress, anxiety, and depression. The global quality of life, perceived stress, anxiety and depression significantly improved during the participation in the program even though the symptoms of nausea, dyspnea and fatigue increased significantly. Regarding the severity of and the impairment due to fatigue, measured with the BFI, no significant changes were observed. The cognitive function decreased significantly during chemotherapy, while other functions like physical and social rarely changed and emotional function improved.

During ongoing chemotherapy, HQoL and functional scales usually decrease and symptoms like fatigue, insomnia, dyspnea, sleep problems, and nausea increase [47-52]. The overall worsening of physical symptoms correlates with the decrease of the overall HQoL [53, 54]. These preliminary findings suggest that participation in the program might improve HQoL, stress, anxiety and depression during ongoing chemotherapy. The HQoL after neoadjuvant chemotherapy might affect prognosis, so that it seems to be

highly important to enhance it [53]. Perceived stress shortly after diagnosis probably influences the prospective HQoL (especially pain and fatigue) one to two years after diagnosis [55, 56]. Therefore, concepts that address stress early during treatment need to be implemented. However, not only stress but also anxiety during chemotherapy correlate with the HQoL of women with breast cancer. A recent study [54] reported that 44 % of breast cancer patients after the first cycle of chemotherapy suffered from serious or/and intense anxiety with the need to optimize their conventional and supportive healthcare. At the end of chemotherapy, an association between anxiety and depression and CRF was described by another study [57]. In further publications, depression has also been found as one of the strongest factors related to CRF [58-61]. Patients experience CRF as the most distressing symptom with the greatest negative impact on HQoL, with its peak during and shortly after chemotherapy [57]. The mind-body therapies assimilated in this program are recommended in guidelines to reduce depression, anxiety and stress [13]. Additionally, evidence supports the participation of breast cancer survivors in Mindfulness Based Stress Reduction to reduce CRF [22, 24, 62]. Patients in this trial reported a significant increase in CRF after chemotherapy (mean difference of 10.3 in the EORTC, effect size 0.38) but the severity of and the impairment due to fatigue did not increase significantly (mean difference of 0.2 in the BFI each). EORTC and BFI measure different time frames and the clinical relevance remains unclear. In addition, the effects might be a result of the reduction of anxiety and depression, as associations with CRF are likely. CRF during treatment is hypothesized to be caused by the activation of pro-

inflammatory cytokines [24, 57, 63]. Among breast cancer patients undergoing chemotherapy, changes in Interleukin 6 were associated with changes in fatigue over the course of treatment [64]. Interestingly, mind-body therapies seem to reduce inflammatory markers and might be a treatment option for CRF [24, 65, 66].

In an exercise trial from 2018 [50], the effects of resistance and high-intensity interval training to moderate-intensity aerobic and high-intensity interval training on usual care in women with breast cancer undergoing chemotherapy were compared. The 16 weeks of resistance and high-intensity interval training were effective in preventing increases in CRF and in reducing symptoms burden for patients during chemotherapy. Interestingly, the participants with the highest levels of CRF and symptoms and the lowest HQoL were those who gained the greatest benefits from the exercise training. Maybe in our program, the exercise part needs to be strengthened to achieve a better effect concerning CRF during chemotherapy.

No conclusion can be drawn concerning the effects of the acupuncture treatment and complementary self-help strategies in our integrative mind-body-medicine group program with regard to symptom management. The patients appreciated the acupuncture and the self-help recommendations in particular. No serious side effects and no infection through acupuncture needles were reported. So far, no reliable data is available concerning the safety of acupuncture during neutropenia. In one study, neutropenia was an exclusion criterion [67]. In another small feasibility study on ovarian cancer patients during chemotherapy, no serious adverse events occurred, but neutropenia was not reported [68].

Our findings are only preliminary due to the observational design of the study. We are not able to attribute to causation, nor are we able to detect which contents of the program led to the elevated HQoL and the decreases in anxiety and depression. Also, we did not evaluate the adherence to the recommended exercise and relaxation training at home. A further limitation is the small sample size.

Future research needs to focus on the efficacy and comparative effectiveness of the integrative mind-body-medicine group program. In a randomized controlled trial, the program could be compared to usual care and to resistance and high-intensity interval training or to standard Mindfulness-based Stress Reduction.

In the future, we need to implement cost-effective interventions that address the physical and psychological symptoms burden during chemotherapy and early in the treatment to improve HQoL and maybe even survival in breast cancer patients.

CONCLUSION

Breast cancer patients seem to benefit from an integrative mind-body-medicine group program during chemotherapy concerning HQoL and psychological symptoms. Further randomized controlled trials are warranted.

LIST OF ABBREVIATIONS

ASCO	= American Society of Clinical Oncology
BFI	= Brief Fatigue Inventory
CAM	= Complementary and Alternative Medicine
CI	= Confidence Intervals
CRF	= Cancer Related Fatigue
EORTC	= European Organization for Research and Treatment of Cancer
HADS	= Hospital Anxiety and Depression Scale
HQoL	= Health Related Quality of Life
MBCT	= Mindfulness-based Cognitive Therapy

MBSR	= Mindfulness Based Stress Reduction
PSS	= Perceived Stress Scale
QLQ-C30	= Quality of Life Questionnaire
SIO	= Society for Integrative Oncology
Δ	= Post-pre Differences

AUTHORS' CONTRIBUTIONS

HH analyzed and interpreted the patient data and was a major contributor in writing the manuscript.

KEC was involved in designing the study and accessing the data.

SL was involved in designing the study and developing the integrative mind-body-medicine group program.

SK was involved in recruiting the patients and critically revising the manuscript.

AP was involved in developing the integrative mind-body-medicine group program and critically revising the manuscript.

HC analyzed and interpreted the patient data and critically revised the manuscript.

GD critically revised the manuscript.

PV was involved in designing the study and developing the integrative mind-body-medicine group program, and was a major contributor in writing the manuscript.

All the authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved retrospectively by the Ethics Committee of the University of Duisburg-Essen (approval number 17-7909-BO), Germany.

HUMAN AND ANIMAL RIGHTS

No animals were used in this study. Reported experiments on humans were in accordance with the ethical standards of the committee responsible for human experimentation (institutional national), and with the Helsinki Declaration of 1975, as revised in 2008 (<http://www.wma.net/en/20activities/10ethics/10helsinki/>).

CONSENT FOR PUBLICATION

Written and informed consent was obtained from all the patients.

AVAILABILITY OF DATA AND MATERIALS

The raw-datasets generated and analysed during the current study are not publicly available but are available from the corresponding author (Petra Voiss) on reasonable request.

FUNDING

The funding for this study was supported by the Karl und Veronika Carstens-Stiftung (KVC 0/100/2018). No other funding source was given.

CONFLICT OF INTEREST

Petra Voiss reports personal fees for lectures from Novartis, Mundipharma, Celgene und Roche outside the submitted work.

Sherko Kueimmel reports personal fees from Roche/Genentech, Genomic Health, Novartis, Amgen, Celgene, Daiichi Sankyo, Astra Zeneca, Somatex, MSD, Pfizer, PFM medical, Lilly, Sonoscape, non-financial support from Roche, Daiichi Sankyo, Sonoscape, outside the submitted work.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

- [1] Ferlay J, Soerjomataram I, Dikshit R, *et al.* Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer* 2015; 136(5): E359-86. <http://dx.doi.org/10.1002/ijc.29210> PMID: 25220842
- [2] Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015; 386(9995): 743-800. [http://dx.doi.org/10.1016/S0140-6736\(15\)60692-4](http://dx.doi.org/10.1016/S0140-6736(15)60692-4) PMID: 26063472
- [3] Barnes B. Bericht zum Krebsgeschehen in Deutschland 2016. Berlin: Robert Koch-Institut 2016. Available at: <https://edoc.rki.de/handle/176904/3264>
- [4] GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016; 388(10053): 1545-602. [http://dx.doi.org/10.1016/S0140-6736\(16\)31678-6](http://dx.doi.org/10.1016/S0140-6736(16)31678-6) PMID: 27733282
- [5] Brandão T, Schulz MS, Matos PM. Psychological adjustment after breast cancer: a systematic review of longitudinal studies. *Psychooncology* 2017; 26(7): 917-26. <http://dx.doi.org/10.1002/pon.4230> PMID: 27440317
- [6] Abrahams HJG, Gielissen MFM, Schmits IC, Verhagen CAHHVM, Rovers MM, Knoop H. Risk factors, prevalence, and course of severe fatigue after breast cancer treatment: a meta-analysis involving 12 327 breast cancer survivors. *Ann Oncol* 2016; 27(6): 965-74. <http://dx.doi.org/10.1093/annonc/mdw099> PMID: 26940687
- [7] Alcântara-Silva TR, Freitas-Junior R, Freitas NM, Machado GD. Fatigue related to radiotherapy for breast and/or gynaecological cancer: a systematic review. *J Clin Nurs* 2013; 22(19-20): 2679-86. <http://dx.doi.org/10.1111/jocn.12236> PMID: 23651041
- [8] Trudel-Fitzgerald C, Zhou ES, Poole EM, *et al.* Sleep and survival among women with breast cancer: 30 years of follow-up within the Nurses' Health Study. *Br J Cancer* 2017; 116(9): 1239-46. <http://dx.doi.org/10.1038/bjc.2017.85> PMID: 28359077
- [9] Chida Y, Hamer M, Wardle J, Steptoe A. Do stress-related psychosocial factors contribute to cancer incidence and survival? *Nat Clin Pract Oncol* 2008; 5(8): 466-75. <http://dx.doi.org/10.1038/nponc1134> PMID: 18493231
- [10] Lin X, Chen W, Wei F, Ying M, Wei W, Xie X. Night-shift work increases morbidity of breast cancer and all-cause mortality: a meta-analysis of 16 prospective cohort studies. *Sleep Med* 2015; 16(11): 1381-7. <http://dx.doi.org/10.1016/j.sleep.2015.02.543> PMID: 26498240
- [11] Suppli NP, Johansen C, Kessing LV, *et al.* Survival After Early-Stage Breast Cancer of Women Previously Treated for Depression: A Nationwide Danish Cohort Study. *J Clin Oncol* 2017; 35(3): 334-42. <http://dx.doi.org/10.1200/JCO.2016.68.8358> PMID: 28095267
- [12] Cramer H, Lauche R, Klose P, Lange S, Langhorst J, Dobos GJ. Yoga for improving health-related quality of life, mental health and cancer-related symptoms in women diagnosed with breast cancer. *Cochrane Database Syst Rev* 2017; 1: CD010802. <http://dx.doi.org/10.1002/14651858.CD010802.pub2> PMID: 28045199
- [13] Greenlee H, DuPont-Reyes MJ, Balneaves LG, *et al.* Clinical practice guidelines on the evidence-based use of integrative therapies during and after breast cancer treatment. *CA Cancer J Clin* 2017; 67(3): 194-232. <http://dx.doi.org/10.3322/caac.21397> PMID: 28436999
- [14] Lyman GH, Greenlee H, Bohlke K, *et al.* Integrative Therapies During and After Breast Cancer Treatment: ASCO Endorsement of the SIO Clinical Practice Guideline. *J Clin Oncol* 2018; 36(25): 2647-55. <http://dx.doi.org/10.1200/JCO.2018.79.2721> PMID: 29889605
- [15] Fremd C, Hack CC, Schneeweiss A, *et al.* Use of complementary and integrative medicine among German breast cancer patients: predictors and implications for patient care within the PRAE-GNANT study network. *Arch Gynecol Obstet* 2017; 295(5): 1239-45. <http://dx.doi.org/10.1007/s00404-017-4348-2> PMID: 28331996
- [16] Ludwig DS, Kabat-Zinn J. Mindfulness in medicine. *JAMA* 2008; 300(11): 1350-2. <http://dx.doi.org/10.1001/jama.300.11.1350> PMID: 18799450
- [17] Bishop SR. Mindfulness: a proposed operational definition. *Clin Psychol Sci Pract* 2004; 11: 230-41. <http://dx.doi.org/10.1093/clipsy.bph077>
- [18] Baer RA. Mindfulness training as a clinical intervention: A conceptual and empirical review. *Clin Psychol Sci Pract* 2003; 10: 125-43. <http://dx.doi.org/10.1093/clipsy.bpg015>
- [19] Kabat-Zinn J. Full catastrophe living: using the wisdom of your body and mind to face stress, pain, and illness. New York: Delta Trade Paperback/Bantam Dell 1990.
- [20] Teasdale JD, Segal ZV, Williams JM, Ridgeway VA, Soulsby JM, Lau MA. Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. *J Consult Clin Psychol* 2000; 68(4): 615-23. <http://dx.doi.org/10.1037/0022-006X.68.4.615> PMID: 10965637
- [21] Crane R. Mindfulness-based cognitive therapy: distinctive features. New York, NY: Routledge/Taylor & Francis Group 2009.
- [22] Haller H, Winkler MM, Klose P, Dobos G, Kümmel S, Cramer H. Mindfulness-based interventions for women with breast cancer: an updated systematic review and meta-analysis. *Acta Oncol* 2017; 56(12): 1665-76. <http://dx.doi.org/10.1080/0284186X.2017.1342862> PMID: 28686520
- [23] Hoffman CJ, Ersser SJ, Hopkinson JB, Nicholls PG, Harrington JE, Thomas PW. Effectiveness of mindfulness-based stress reduction in mood, breast- and endocrine-related quality of life, and well-being in stage 0 to III breast cancer: a randomized, controlled trial. *J Clin Oncol* 2012; 30(12): 1335-42. <http://dx.doi.org/10.1200/JCO.2010.34.0331> PMID: 22430268
- [24] Lengacher CA. A Large Randomized Trial: Effects of Mindfulness-Based Stress Reduction (MBSR) for Breast Cancer (BC) Survivors on Salivary Cortisol and IL-6. *Biol Res Nurs* 2019; 21(1): 39-49. PMID: 30079756
- [25] Reich RR, Lengacher CA, Alinat CB, *et al.* Mindfulness-Based Stress Reduction in Post-treatment Breast Cancer Patients: Immediate and Sustained Effects Across Multiple Symptom Clusters. *J Pain Symptom Manage* 2017; 53(1): 85-95. <http://dx.doi.org/10.1016/j.jpainsymman.2016.08.005> PMID: 27720794
- [26] Henderson VP, Clemow L, Massion AO, Hurley TG, Druker S, Hébert JR. The effects of mindfulness-based stress reduction on psychosocial outcomes and quality of life in early-stage breast cancer patients: a randomized trial. *Breast Cancer Res Treat* 2012; 131(1): 99-109. <http://dx.doi.org/10.1007/s10549-011-1738-1> PMID: 21901389
- [27] Würtzen H, Dalton SO, Elsass P, *et al.* Mindfulness significantly reduces self-reported levels of anxiety and depression: results of a randomised controlled trial among 336 Danish women treated for stage I-III breast cancer. *Eur J Cancer* 2013; 49(6): 1365-73. <http://dx.doi.org/10.1016/j.ejca.2012.10.030> PMID: 23265707
- [28] Jeitler M, Jaspers J, von Scheidt C, *et al.* Mind-body medicine and lifestyle modification in supportive cancer care: A cohort study on a day care clinic program for cancer patients. *Psychooncology* 2017; 26(12): 2127-34. <http://dx.doi.org/10.1002/pon.4433> PMID: 28370730
- [29] Jong MC, Boers I, Schouten van der Velden AP, *et al.* A Randomized Study of Yoga for Fatigue and Quality of Life in Women with Breast Cancer Undergoing (Neo) Adjuvant Chemotherapy. *J Altern Complement Med* 2018; 24(9-10): 942-53. <http://dx.doi.org/10.1089/acm.2018.0191> PMID: 30247961
- [30] Lötze D, Wiedemann F, Rodrigues Recchia D, *et al.* Iyengar-Yoga Compared to Exercise as a Therapeutic Intervention during (Neo)adjuvant Therapy in Women with Stage I-III Breast Cancer: Health-Related Quality of Life, Mindfulness, Spirituality, Life Satisfaction, and Cancer-Related Fatigue. *Evid Based Complement Alternat Med* 2016; 2016: 5931816.

- <http://dx.doi.org/10.1155/2016/5931816> PMID: 27019663
- [31] Chaoul A, Milbury K, Spelman A, *et al.* Randomized trial of Tibetan yoga in patients with breast cancer undergoing chemotherapy. *Cancer* 2018; 124(1): 36-45.
<http://dx.doi.org/10.1002/ncr.30938> PMID: 28940301
- [32] Spahn G, Choi KE, Kennemann C, *et al.* Can a multimodal mind-body program enhance the treatment effects of physical activity in breast cancer survivors with chronic tumor-associated fatigue? A randomized controlled trial. *Integr Cancer Ther* 2013; 12(4): 291-300.
<http://dx.doi.org/10.1177/1534735413492727> PMID: 23766391
- [33] Dobos G, Overhamm T, Büssing A, *et al.* Integrating mindfulness in supportive cancer care: a cohort study on a mindfulness-based day care clinic for cancer survivors. *Support Care Cancer* 2015; 23(10): 2945-55.
<http://dx.doi.org/10.1007/s00520-015-2660-6> PMID: 25711654
- [34] Golden-Kreutz DM, Browne MW, Frierson GM, Andersen BL. Assessing stress in cancer patients: a second-order factor analysis model for the Perceived Stress Scale. *Assessment* 2004; 11(3): 216-23.
<http://dx.doi.org/10.1177/1073191104267398> PMID: 15358877
- [35] Golden-Kreutz DM, Thornton LM, Wells-Di Gregorio S, *et al.* Traumatic stress, perceived global stress, and life events: prospectively predicting quality of life in breast cancer patients. *Health Psychol* 2005; 24(3): 288-96.
<http://dx.doi.org/10.1037/0278-6133.24.3.288> PMID: 15898865
- [36] Montazeri A. Health-related quality of life in breast cancer patients: a bibliographic review of the literature from 1974 to 2007. *J Exp Clin Cancer Res* 2008; 27: 32.
<http://dx.doi.org/10.1186/1756-9966-27-32> PMID: 18759983
- [37] Aaronson NK, Ahmedzai S, Bergman B, *et al.* The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993; 85(5): 365-76.
<http://dx.doi.org/10.1093/jnci/85.5.365> PMID: 8433390
- [38] Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; 67(6): 361-70.
<http://dx.doi.org/10.1111/j.1600-0447.1983.tb09716.x> PMID: 6880820
- [39] Radbruch L, Sabatowski R, Elsner F, Everts J, Mendoza T, Cleeland C. Validation of the German version of the brief fatigue inventory. *J Pain Symptom Manage* 2003; 25(5): 449-58.
[http://dx.doi.org/10.1016/S0885-3924\(03\)00073-3](http://dx.doi.org/10.1016/S0885-3924(03)00073-3) PMID: 12727043
- [40] Mendoza TR, Wang XS, Cleeland CS, *et al.* The rapid assessment of fatigue severity in cancer patients: use of the Brief Fatigue Inventory. *Cancer* 1999; 85(5): 1186-96.
[http://dx.doi.org/10.1002/\(SICI\)1097-0142\(19990301\)85:5<1186::AID-CNCR24>3.0.CO;2-N](http://dx.doi.org/10.1002/(SICI)1097-0142(19990301)85:5<1186::AID-CNCR24>3.0.CO;2-N) PMID: 10091805
- [41] Cohen S, Janicki-Deverts D. Who's Stressed? Distributions of Psychological Stress in the United States in Probability Samples from 1983, 2006, and 2009. *J Appl Soc Psychol* 2012; 42(6): 1320-34.
<http://dx.doi.org/10.1111/j.1559-1816.2012.00900.x>
- [42] Paul A, Cramer H, Lauche R, Altner N, Langhorst J, Dobos GJ. An oncology mind-body medicine day care clinic: concept and case presentation. *Integr Cancer Ther* 2013; 12(6): 503-7.
<http://dx.doi.org/10.1177/1534735412473639> PMID: 23329568
- [43] Kabat-Zinn J. An outpatient program in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: theoretical considerations and preliminary results. *Gen Hosp Psychiatry* 1982; 4(1): 33-47.
[http://dx.doi.org/10.1016/0163-8343\(82\)90026-3](http://dx.doi.org/10.1016/0163-8343(82)90026-3) PMID: 7042457
- [44] Benson H, Stuart M. The wellness book Mind-body medicine. New York, NY: Fireside 1999.
- [45] Shapiro SL, Carlson LE, Astin JA, Freedman B. Mechanisms of mindfulness. *J Clin Psychol* 2006; 62(3): 373-86.
<http://dx.doi.org/10.1002/jclp.20237> PMID: 16385481
- [46] Cormie P, Atkinson M, Bucci L, *et al.* Clinical Oncology Society of Australia position statement on exercise in cancer care. *Med J Aust* 2018; 209(4): 184-7.
<http://dx.doi.org/10.5694/mja18.00199> PMID: 29719196
- [47] Ancoli-Israel S, Liu L, Rissling M, *et al.* Sleep, fatigue, depression, and circadian activity rhythms in women with breast cancer before and after treatment: a 1-year longitudinal study. *Support Care Cancer* 2014; 22(9): 2535-45.
<http://dx.doi.org/10.1007/s00520-014-2204-5> PMID: 24733634
- [48] Grassi L, Berardi MA, Ruffilli F, *et al.* IOR-IRST Psycho-Oncology and UniFE Psychiatry Co-Authors. Role of psychosocial variables on chemotherapy-induced nausea and vomiting and health-related quality of life among cancer patients: a European study. *Psychother Psychosom* 2015; 84(6): 339-47.
<http://dx.doi.org/10.1159/000431256> PMID: 26402426
- [49] Alawadi SA, Ohaeri JU. Health - related quality of life of Kuwaiti women with breast cancer: a comparative study using the EORTC Quality of Life Questionnaire. *BMC Cancer* 2009; 9: 222.
<http://dx.doi.org/10.1186/1471-2407-9-222> PMID: 19586536
- [50] Mijwel S, Backman M, Bolam KA, *et al.* Adding high-intensity interval training to conventional training modalities: optimizing health-related outcomes during chemotherapy for breast cancer: the OptiTrain randomized controlled trial. *Breast Cancer Res Treat* 2018; 168(1): 79-93.
<http://dx.doi.org/10.1007/s10549-017-4571-3> PMID: 29139007
- [51] Sultan A, Choudhary V, Parganiha A. Worsening of rest-activity circadian rhythm and quality of life in female breast cancer patients along progression of chemotherapy cycles. *Chronobiol Int* 2017; 34(5): 609-23.
<http://dx.doi.org/10.1080/07420528.2017.1286501> PMID: 28276853
- [52] Groenvold M. Health-related quality of life in early breast cancer. *Dan Med Bull* 2010; 57(9): B4184. PMID: 20816024
- [53] Takada K, Kashiwagi S, Goto W, *et al.* Novel evaluation scale for QOL (QOL-ACD-BP) in preoperative chemotherapy for breast cancer. *J Cancer Res Clin Oncol* 2018; 144(8): 1547-59.
<http://dx.doi.org/10.1007/s00432-018-2670-0> PMID: 29779135
- [54] Charalambous A, Kaita CP, Charalambous M, Tistis T, Kouta C. The effects on anxiety and quality of life of breast cancer patients following completion of the first cycle of chemotherapy. *SAGE Open Med* 2017; 5: 2050312117717507.
<http://dx.doi.org/10.1177/2050312117717507> PMID: 28694967
- [55] Härtl K, Engel J, Herschbach P, Reinecker H, Sommer H, Friese K. Personality traits and psychosocial stress: quality of life over 2 years following breast cancer diagnosis and psychological impact factors. *Psychooncology* 2010; 19(2): 160-9.
<http://dx.doi.org/10.1002/pon.1536> PMID: 19189279
- [56] Harris LN, Bauer MR, Wiley JF, *et al.* Chronic and episodic stress predict physical symptom bother following breast cancer diagnosis. *J Behav Med* 2017; 40(6): 875-85.
<http://dx.doi.org/10.1007/s10865-017-9855-x> PMID: 28528393
- [57] Fabi A, Falcicchio C, Giannarelli D, Maggi G, Cognetti F, Pugliese P. The course of cancer related fatigue up to ten years in early breast cancer patients: What impact in clinical practice? *Breast* 2017; 34: 44-52.
<http://dx.doi.org/10.1016/j.breast.2017.04.012> PMID: 28500901
- [58] Servaes P, Gielissen MF, Verhagen S, Bleijenberg G. The course of severe fatigue in disease-free breast cancer patients: a longitudinal study. *Psychooncology* 2007; 16(9): 787-95.
<http://dx.doi.org/10.1002/pon.1120> PMID: 17086555
- [59] Servaes P, Verhagen CA, Bleijenberg G. Relations between fatigue, neuropsychological functioning, and physical activity after treatment for breast carcinoma: daily self-report and objective behavior. *Cancer* 2002; 95(9): 2017-26.
<http://dx.doi.org/10.1002/ncr.10891> PMID: 12404297
- [60] Nieboer P, Buijs C, Rodenhuis S, *et al.* Fatigue and relating factors in high-risk breast cancer patients treated with adjuvant standard or high-dose chemotherapy: a longitudinal study. *J Clin Oncol* 2005; 23(33): 8296-304.
<http://dx.doi.org/10.1200/JCO.2005.10.167> PMID: 16219926
- [61] Bower JE, Wiley J, Petersen L, Irwin MR, Cole SW, Ganz PA. Fatigue after breast cancer treatment: Biobehavioral predictors of fatigue trajectories. *Health Psychol* 2018; 37(11): 1025-34.
<http://dx.doi.org/10.1037/hea0000652> PMID: 30321021
- [62] Zhang Q, Zhao H, Zheng Y. Effectiveness of mindfulness-based stress reduction (MBSR) on symptom variables and health-related

- quality of life in breast cancer patients-a systematic review and meta-analysis. *Support Care Cancer* 2018.
<http://dx.doi.org/10.1111/ecc.12632> PMID: 30488223
- [63] Bower JE, Ganz PA, Irwin MR, Kwan L, Breen EC, Cole SW. Inflammation and behavioral symptoms after breast cancer treatment: do fatigue, depression, and sleep disturbance share a common underlying mechanism? *J Clin Oncol* 2011; 29(26): 3517-22.
<http://dx.doi.org/10.1200/JCO.2011.36.1154> PMID: 21825266
- [64] Liu L, Mills PJ, Rissling M, *et al.* Fatigue and sleep quality are associated with changes in inflammatory markers in breast cancer patients undergoing chemotherapy. *Brain Behav Immun* 2012; 26(5): 706-13.
<http://dx.doi.org/10.1016/j.bbi.2012.02.001> PMID: 22406004
- [65] Bower JE, Irwin MR. Mind-body therapies and control of inflammatory biology: A descriptive review. *Brain Behav Immun* 2016; 51: 1-11.
<http://dx.doi.org/10.1016/j.bbi.2015.06.012> PMID: 26116436
- [66] Bower JE. Cancer-related fatigue-mechanisms, risk factors, and treatments. *Nat Rev Clin Oncol* 2014; 11(10): 597-609.
<http://dx.doi.org/10.1038/nrclinonc.2014.127> PMID: 25113839
- [67] Pais I, Correia N, Pimentel I, *et al.* Effects of acupuncture on leucopenia, neutropenia, NK, and B cells in cancer patients: a randomized pilot study. *Evid Based Complement Alternat Med* 2014; 2014: 217397.
<http://dx.doi.org/10.1155/2014/217397> PMID: 25152759
- [68] Lu W, Matulonis UA, Dunn JE, *et al.* The Feasibility and Effects of Acupuncture on Quality of Life Scores During Chemotherapy in Ovarian Cancer: Results from a Pilot, Randomized Sham-Controlled Trial. *Med Acupunct* 2012; 24(4): 233-40.
<http://dx.doi.org/10.1089/acu.2012.0904> PMID: 24761165