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Effects of supplemental behavior-oriented exercise intervention in a disease management program for breast cancer

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Objective: Breast cancer is the most common form of cancer in women. The aim of this study is to evaluate the feasibility and impact of a multimodal, behavior-oriented physical activity program on health-related quality of life (HRQoL), fatigue and endurance capacity for women undergoing adjuvant therapy for breast cancer as a supplement to standard care in a disease management program (DMP). ***Design:*** This study was designed as a classic follow-up intervention study. 68 female breast cancer patients took part in the exercise program (over 12 weeks, once a week for 90 minutes). All participants were tested twice (baseline (t_1) and at the last lesson of the program (t_2)). Data was taken at each point in time due to the SF-36 (HRQoL) and the MFI-20 (cancer-related fatigue). Furthermore, all subjects participated in a 2 km walking test to assess their endurance capacity. ***Results:*** The participants were aged 64.7±7.76, diagnosed at month 45.2±45.7 at an average BMI of 25.6±4.37. The sample showed a clearly reduced health-related quality of life at time point t_1 compared to the norm for German healthy women. We were able to detect significant improvements in the "general health state" ($p<0.01$, $d=0.34$), the "psychological well-being" ($p<0.01$, $d=0.38$) and the "vitality" ($p<0.05$, $d=0.23$) of the intervention group after a 12-week behavior-oriented physical activity program, and there was also a relevant improvement in endurance capacity ($p<0.01$, $d=0.30$). ***Conclusion****:* The effects that have been observed in this study serve as first indicators that this kind of exercise program should be standard as adjuvant therapy for women enrolled in a disease management program for breast cancer.

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Key Words: breast cancer; health-related quality of life; physical activity; disease management program

INTRODUCTION

Breast cancer is the most common form of cancer in women. Around 55,000 cases are registered and 18,000 women die as a result of this disease every year in Germany. The lifespan risk is around 9%-10% for women, which means every 10th woman will develop breast cancer during her lifetime (20). Secondly, the incidence rate seems to be clearly dependent on age. About 300 out of 100,000 women in the age group ranging between 60 and 64 years will be diagnosed with the disease, whereas the 30 to 39 age group will fall ill at a rate of 50/100,000 (27). Thirdly, the women diagnosed with breast cancer and their surroundings are often shocked by the amount of psychological strain they find themselves undergoing, not to mention the physical impairment they experience. They are often affected by a fear of death, being socially isolated, losing their autonomy and falling into depression (15, 22, 31, 35, 41).

Physical activity is related to different aspects of physical and psychological well-being (17). For instance, in the area of oncology, there are a variety of studies that verify the preventive and supportive aspects of exercise therapy intervention (28, 32, 36, 42). The positive effects of exercise have been used to treat breast cancer patients for the last 25 years. Among these studies, the research group of Thune et al. (42) determined an inverse relationship between physical activity and the development of breast cancer.

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Here, a 23% reduction in risk was associated with 4 hours of moderate exercise a week, while a reduction of as much as 47% was ascertained by completing intensive and regular physical activity.

Altogether, these findings indicate a relationship between exercise and health in premenopausal women that becomes even clearer when compared to postmenopausal women. A case in point is the MARIE-Study from Schmidt et al. (36) that showed positive results in connection with physical activity for women who develop tumors after menopause, where the probability of developing cancer is reduced significantly by about one third. The findings are based on a comparison of an active group to an inactive group (36).

Furthermore, McNeely et al. (30) concluded that physical activity represents an effective treatment for breast cancer patients, helping to improve their quality of life, cardio-respiratory fitness and physical functioning abilities while favorably influencing fatigue, in accordance with their systematic review entitled "Effects of exercise on breast cancer patients and survivors." In addition, Mutrie et al. (32) recommended that physical activity should be included in the rehabilitation stage for oncological patients, since this generates positive effects on the psychological as well as on the functional level. Even though these studies show many positive effects of physical activity in the prevention and rehabilitation in breast cancer patients, a few questions remain. Some of these unanswered questions involve the effects of various types of activities and their intensity (16, 19, 25, 40).

From the studies reviewed here, we can draw the following conclusions: (A) Regardless of strength or endurance training, physical activity has positive effects on physical, as well as psychological parameters of breast cancer patients. (B) In addition, physical activity causes no damage to physiological parameters of breast cancer patients, e.g. has no adverse effect on the development or exacerbation of lymphedema (2, 37) or on weight loss (26) and (C) evokes a high level of positive psychosocial effects (5, 34).

In view of these aspects, it would be logical to use interventions that increase physical activity as a main treatment method in the rehabilitation of breast cancer patients. Astonishingly, this knowledge has not been incorporated in any practical sense in the configuration of the disease management program (DMP) for breast cancer patients in Germany.

DMPs were established in Germany in 2002 with two main goals:

(1) From an economic perspective, DMPs have the goal of meeting the growing requirements for efficient health care for chronic illness patients. Therefore, one of the goals is supporting and coordinating therapy to reduce the current over-, under- or improper treatment of chronic diseases.

(2) From a patient perspective, DMPs have the purpose of keeping the patients apprised of their chronic disease, optional treatments, medication and special medical assistance through patient education programs. These (mostly passive) forms of intervention are supposed to increase the level of success of treatment and enhance the patients' HRQoL. Unfortunately, up to now those education programs have had an insufficient impact on patients' lifestyle (10).

To date, DMPs are indicated for coronary heart disease, diabetes mellitus type I and type II, asthma, chronic obstructive pulmonary disease and breast cancer (13). Despite the wealth of evidence regarding the positive effects of physical activity, as described above, exercise programs do not rate among the main treatment methods used in DMPs at present. Therefore this analysis deals with the feasibility and the effects of a behavior-oriented exercise intervention within the framework of a DMP for breast cancer. We hypothesized that this kind of exercise program, as a supplement to the standard care within a DMP, has positive effects on patients' HRQoL perception, cancer-related fatigue and endurance capacity.

MATERIAL AND METHODS

Subjects

68 women participated in the program. Their mean age was 64.7±7.8 and their average BMI was 25.6. 52.1% of the women were at a normal weight, 1.6% were underweight, 30.7% overweight, 14.0% obese (grade I, according to the WHO classification) and 1.6% were obese at the grade II level. The study started at an average of 45 months (standard deviation SD=54.7) after the diagnosis. Nearly all participants needed the tumor removed by surgery, 83% received irradiation treatment afterwards and 53% underwent chemotherapy (Table 1). No participant received any type of treatment during intervention. All women gave their formal consent before the intervention started.

Design of the study

The study was designed as a follow-up intervention study. A classical control group was denied on behalf of the co-operational partner, because each patient should have the possibility to instantly access the behavior-oriented intervention. All participants were tested twice: t_1 during the first meeting of the exercise program and t_2 in the 12^{th} and last meeting of the

Table 1. Sample characteristics.

	n	Mean (Min/Max)	SD
Age (in years)	66	64.7 (43/81)	7.76
Body Mass Index	64	25.6 (17.5/37.7)	4.37
Diagnosed (in month)	58	45.2 (8/324)	45.7
Surgery	67 (98.5%)		
Irradiation	57 (83.8%)		
Chemotherapy	36 (41.2%)		

Abbreviations: Min= Minimum; Max= Maximum; SD= Standard Deviation

exercise program. Data was recorded on health-related quality of life (SF-36) (12) and cancer-related fatigue (MFI-20) (39) at each time point. Personal data was also recorded. Furthermore, all the subjects participated in a 2 km walking test to assess their endurance capacity.

Intervention

A behavior-oriented exercise program was implemented as a supplement in a standard DMP for breast cancer patients with the aim of improving the HRQoL of the patients on the physical, psychological and social level (6). The exercise program was conceived for a period of time of 12 weeks, whereby the participants met once a week for 90 minutes. The content of the intervention was designed on the basis of the International Classification of Functioning, Disability and Health (ICF) (45) (WHO, 2001). Therefore it was aimed at impairments as well as physical and psychological resources. Three levels were taken into consideration: *knowledge* (e.g. dealing with the disease and learning about the positive effects of physical activity on physical and mental factors), *physical activities* (familiarizing with and performing various and adequate methods of physical activity such as endurance and resistance training) while experiencing positive *emotions* that could help to maintain an active lifestyle over time (6, 7). This combination of *physical activity*, *cognitive* and *motivational elements* can encourage patients to pursue a physically active and health-enhancing lifestyle that is more sustainable than merely an educational or exercise program (44).

Measurements

Quality of life (SF-36): HRQoL was assessed by the SF-36 (German Version) (12). The SF-36 is a common generic and internationally accepted self-administered questionnaire. The test has good construct validity and adequate internal consistency reliabilities (0.81-0.88) (8, 29, 43). The 36 items are distributed into 8 different dimensions: "physical function," "physical role function" – role limitations due to physical problems, "bodily pain," "general health," "vitality," "social function," "emotional role function" – role limitations due to emotional problems and "psychological well-being" (12). Each scale is scored separately from 0 to 100. The higher the scale value, the better the health state is.

Fatigue (MFI-20): The MFI-20 measures illness-related fatigue in cancer patients. The test is divided into five subscales assessing the following aspects: "general fatigue," "physical fatigue," "reduced activity," "mental fatigue" and "reduced motivation." Higher values demonstrate increased fatigue symptoms. The MFI was not only validated for tumor patients but also age and gender-specific categories in healthy people (39). The norm values for the group of women over the age of 60 years (n=622) (11) were used as a reference for our own statistical evaluation (Figure 2).

Endurance capacity (2 km walking test): The 2 km walking test is easy to apply and adequately assesses endurance capacity. The test was validated in a large sample size by Bös et al. (9). The test adds walking time in minutes, pulse rate after 2 km, BMI, age and gender into an algorithm to form a walk index (WI). The values of this WI were rated using groups according to five performance categories >130 "very good," 111-130 "good," 90-110 "medium," 70-89 "weak," <70 "very weak." This allows a fast and reliable estimation of the performance level (33).

Statistical analysis

Means and standard deviations were calculated for all variables. Variance analysis and t-tests for dependent samples were used for the statistics. The significance level was set to $p<0.05$. All results were subsequently checked by effect sizes for their relevance (14). According to Cohen, $0.2 < d < 0.5$ was used as a small effect size; $0.5 < d < 0.8$ as a medium effect size and $d > 0.8$ as a large effect. All statistical analyses were performed using IBM SPSS for Windows version 19.0 (IBM SPSS Inc., Chicago, IL, USA).

RESULTS AND DISCUSSION

Health-related quality of life (SF-36)

The results show that our sample deviates in almost all scale values, except for "bodily pain" (mean difference of 5.80, d=0.14), from those values for the German

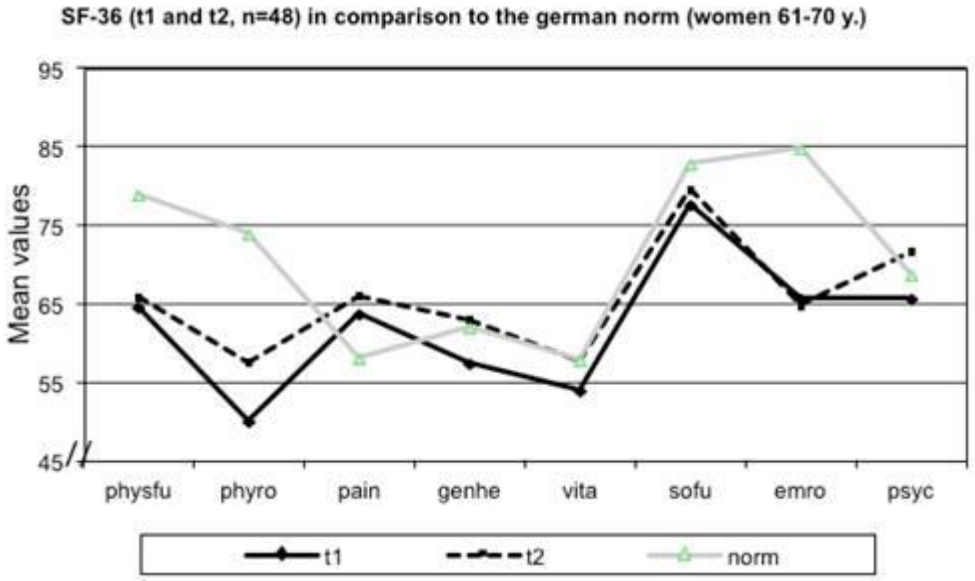

Figure 1. Mean values of the subscales SF-36 t1 and t2 in comparison to the German norm (women aged 61-70). Abbreviations: physfu=physical function; phyro=physical role function; pain= bodily pain; genhe=general health, vita=vitality; sofu=social function; emro=emotional role function; psyc=psychological well-being; y.=years.

norm for healthy women at the same age to t1. The differences predominantly exist on the scale values of the "physical role function" (md=-24.0, d=0.58) and "emotional role function" (md=-19.0, d=0.64). The effect sizes prove to have relevance under the values of the norm (Table 2). Analyzing the changes from t1 to t2, we can see that the intervention has not provided a cessation of improvement, either in the area of the "emotional role function" ($p=0.895$; $d_{emro}=-0.02$), nor for the scale values of the "physical role function" ($p=0.244$; $d_{phyro}=0.17$). Significant and relevant changes can be seen on the subscales for "general health state" ($p<0.01$; $d_{genhe}=0.34$), "psychological well-being" ($p<0.01$; $d_{psych}=0.38$) and "vitality" ($p<0.05$; $d_{vita}=0.23$).The values that have been obtained here show a significant time effect and exceed the values of the normal sample population. Further analysis proved that the effects are independent of the patient's age ($p=0.930$; $F=0.148$) and of the time point of the diagnosis ($p=0.173$; $F=1.924$). That means that the type of treatment – surgery, radiation, chemotherapy, separately or combined – did not have any impact on the SF-36 scales. Overall the improvement of psychological well-being seems to be very valuable. The literature underlines that women suffering from breast cancer are extremely stressed by the diagnosis in emotional and psychological terms and are also very challenged when facing exhausting medical treatments (3, 28). This very often results in social withdrawal and isolation. Our findings show that providing this treatment for women affected by cancer could help them to handle everyday life easier. Finally, Figure 1 shows the changes in the mean of the scale values of the SF-36 from t1 to t2 in relation to the norm.

Cancer-related fatigue (MFI-20)

A comparison of our study findings with those of Hagelin et al. (23) (which was completed for 81 cancer patients treated with curative radioactive therapy) shows a wide difference in the appearance of fatigue symptoms (see Figure 2). It is possible that this is due to the fact that the subjects in our study were not experiencing any acute therapy during the intervention. By searching for the causes of fatigue syndrome, multiple factors have to be considered. It is reasonable to posit that the necessary therapies, along with their negative side effects, are most likely to have a strong impact on the fatigue symptoms (21). Also, it is said that the general feeling of exhaustion, weakness and lack of interest is dependent on the time point of the diagnosis (38, 39). This seems to explain why the results of our evaluation are partly equivalent to the values of the German Norm (woman aged 61-70, n=622) in the MFI (9). Only two of the subscales, "mental fatigue" (mean deviation=1.0, $d_{Norm;t1}=0.2$) and "reduced motivation" (md=-1.6, $d_{Norm;t1}=0.47$), are revealed to be relevant. When checking the intervention effects in terms of the MFI (t1 to t2) they prove to have a slight effect on the "reduced motivation" scale ($d_{redmot}=0.27$; $p=0.092$).

Table 2. Mean ± standard deviation in SF-36 subscales for t1 and t2.

SF-36 Scale		Mean	SD	p	d (Norm,t1)	d (t1,t2)
Physical function n=48	T1	64.6	20.7	0.494	**0.36**	0.07
	T2	66.0	21.7			
Physical role function n=40	T1	50.0	42.4	0.244	**0.58**	0.17
	T2	57.5	44.3			
Bodily pain n=47	T1	63.8	26.4	0.532	0.14	0.09
	T2	66.1	25.4			
General health n=46	T1	57.5	14.4	**0.006**	0.17	**0.34**
	T2	63.0	17.5			
vitality n=45	T1	53.9	17.2	**0.043**	**0.37**	**0.23**
	T2	57.8	16.4			
Social function n=48	T1	77.6	19.6	0.410	**0.40**	0.11
	T2	79.7	18.9			
Emotional role function n=37	T1	65.8	41.9	0.895	**0.64**	-0.02
	T2	64.9	41.5			
Psychological well-being n=45	T1	65.7	14.5	**0.002**	**0.32**	**0.38**
	T2	71.8	17.7			

Abbreviations : SD=Standard Deviation ; d=effect size

As in the SF-36, neither the age (p=0.342; F=1.159), the time point of the diagnosis (p=0.565; F=0.340) nor the type of treatment (p=0.063; F=2.702) had any influence on these changes. All further scale values changes over the 12-week intervention time period had no statistical significance or relevance. This could be due to the relatively good starting values.

Endurance capacity (2 km walking test)

We were able to include 42 women in the data analysis. At first testing (t1), the participants scored, on average, a total of 84.3 on the walking test (SD=23.35). This is equivalent to a "weak" performance level (33). At second testing (t2), the value was, on average, 90.88 (SD=20.83) and therefore was categorized as a "medium" performance level. Having a p=0.006 and an effect size of d_{walk}=0.3, makes the improvement – independent of age (p=0.354; F=1.166), BMI (p=0.365; F=2.180) and time point of diagnosis (p=0.903; F=0.514) – not only significant but also highly relevant. This result is found to be fundamentally good considering the short duration of the intervention (12 weeks).

The findings of our study are comparable to other studies where combined intervention approaches have been used (5, 24). The study of Basen-Enquist et al. (5) proved that breast cancer survivors who took part in a lifestyle intervention that included physical activity showed a significant improvement in their endurance capacity and also positive effects on the HRQoL after 20 intervention units. Additionally, these studies showed that the positive effects of exercise helped reduce present fatigue syndromes. Adamsen et al. (1) discovered that conditioning capabilities can be highly and significantly increased, and that the presence of fatigue, loss of energy and lack of movement can be decreased, using a combined training program. Our own study, as well as the studies presented here, provide enough evidence to anchor behavior-oriented exercise intervention in DMPs for breast cancer patients.

CONCLUSIONS

In summary, our study demonstrates several strengths. It is the first one to investigate the need for a physical exercise program to supplement a disease management program for breast cancer patients. The study shows clearly that this kind of intervention is feasible for breast cancer patients within a DMP. Furthermore, the effects that have been observed serve as a motivation for creating further studies in this area. On the other hand, some limitations also have to be noted. The design of this study does not allow us to conclude a causal relationship between participating in our exercise program and the effects demonstrated here. The coming studies should have larger sample sizes and should necessarily use a control group. This would deliver further affirmation that this sort of exercise program should constitute an important element in the standard care of breast cancer patients.

Nevertheless, the results of our study make it apparent that physical activity in breast cancer follow-up care can have positive effects on patients' quality of life, fatigue and physical fitness, and should be an obligatory treatment for the care of patients with breast cancer within a DMP.

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