Exercise tolerance in breast cancer patients during radiotherapy after aerobic training

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Introduction

Physical activity (PA) can have a beneficial effect on both physical and mental health in cancer patients. However, evidence from cross-sectional and retrospective research suggests that cancer treatment can be associated with both short- and long-term reductions in PA [1-4]. While the benefit of postoperative radiotherapy (RT) for breast cancer is well documented [5, 6], there are a number of side effects associated with this treatment that might affect the patients’ quality of life (QoL) and even possibly survival [7–9]. Among the long-term RT complications there is heart and lung damage, impaired shoulder mobility, and chronic pain [7, 8]. Many complications occur simultaneously during RT for breast cancer; therefore research on the impact of exercises and their effects is needed.

The purpose of this study was to examine whether moderate-intensity endurance training would have a positive effect on aerobic capacity (oxygen saturation, heart rate, blood pressure, dyspnea, walk distance) in comparison with those women who were not taking any PA during postoperative RT of breast cancer.

Material and methods

Patients

Forty-six patients with breast cancer from 37 to 65 years old were included in the study. The participants with breast cancer were recruited from the Outpatient Department of Radiotherapy of the Greater Poland Cancer Centre in Poznan. All study procedures were reviewed and approved by the Bioethics Committee at Poznan University of Medical Sciences, and participation in the study was conditional upon obtaining voluntary informed consent. All patients were recruited and randomly assigned to either an exercise or a control group. Some patients (group A) were simultaneously treated in the Rehabilitation Ward and received (for 6 weeks) AT. The rest of the patients, without rehabilitation (group B), took irregular PA on their own. Criteria for inclusion were: female gender, age between 20 and 65 years, histologically established breast cancer (AJCC stage I to stage IIIIC), and good general health (ECOG performance status 0–1). The exclusion criteria included concurrent major health problems that could affect the patient’s participation in an exercise program, including uncontrolled hypertension, cardiovascular diseases resulting in circulation failure (above stage II of heart failure according to the New York Heart Association), abnormal levels in blood tests, acute or chronic respiratory disease, and cognitive dysfunction as well as neuromuscular, musculoskeletal impairment or disease (except breast cancer) affecting motion pat-
tern or postural control. The baseline characteristics of both groups (A and B) are presented in Table 1.

**Interventions**

**Radiotherapy**

All participants in this study underwent breast surgery and then received external beam radiation treatments 7 days per week for 5 weeks. The affected breast and regional lymph nodes were treated to a total dose of 50 Gy in a daily fraction of 2 Gy after 4–5 weeks following surgical treatment [10]. Radiotherapy planning was performed using computed tomography to reduce radiation dose to the heart and lungs according to the dose constraints which were applied in each case. For patients after total mastectomy, chest wall and axillary lymph nodes were irradiated, and for women after breast-conserving surgery the entire breast was irradiated. Because of some differences in radiotherapy techniques, patients were stratified between arms with the aim of proper allocation.

**Exercise program**

Patients assigned to the exercise group attended a supervised exercise program 5 times per week for 6 weeks in the Rehabilitation Ward of the Greater Poland Cancer Centre in Poznan. Participation in the exercise group was voluntary, based on a referral from a radiation oncologist. The basic method of physiotherapy was endurance training by cycling. The 40–45-minute exercises consisted of a 2-minute warm-up, 40 minutes of cycling, and a 3-minute relaxation period. The PA was moderate with the maximal heart rate of 65–70% of the maximum (220-age). After cycling, group breathing exercises were introduced. They included respiratory muscle training, especially abdominal and diaphragm muscle workout, relaxation exercises and breathing exercises to increase respiratory motion in lower ribs and to teach diaphragmatic breathing. One or more physiotherapists assisted with all the exercises. The physical training was conducted before a radiotherapy session (after 23 hours following the previous radiotherapy dose).

**Outcome measures**

Testing was performed 1 week before (baseline) and 1 week after completion of RT.

**Six-minute walk test (6MWT)**

The 6MWT is a useful measure of functional capacity, targeted at people with at least moderately severe impairment. It has been widely used for measuring the response to therapeutic interventions for pulmonary and cardiac disease. The American Thoracic Society guidelines provide a standardized approach for performing the test [11, 12]. The walk test was performed in an indoor corridor 30 m long. Patients were instructed to walk the corridor from one end to the other as many times as possible within the permitted time. The par-
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Participants were instructed to come to the testing sessions wearing exercise clothing and comfortable shoes and to abstain from food and caffeine. The test was performed under the control of a physician who encouraged the patients with remarks such as “you are doing well”. At the beginning and after 6 minutes the physician measured $\text{SO}_2$, heart rate (HR), arterial blood pressure including systolic blood pressure (SBP) and diastolic blood pressure (DBP) as well as the total distance walked (6-minute walk distance – 6MWD) by the patient. Arterial $\text{SO}_2$ and HR can also be measured via pulse oximetry with a VM-2101-Finger Oximeter – Viamed, United Kingdom. Arterial blood pressure was measured on the arm on the side opposite to the breast cancer site. Secondary measures can include dyspnea measured with a modified Borg scale (0–10) [13, 14].

Statistical analysis

Data analyses were conducted using STATISTICA version 10.0, StatSoft Poland. The results of anthropometric parameter measures and 6MWT parameters were subjected to analysis. The quantitative data were described through mean, standard deviation, minimum and maximum. The Shapiro-Wilk test was used to assess the normal distribution compatibility. The differences between the results for $\text{SO}_2$, HR, SBP, DBP, 6MWD and speed were analyzed using the t-test for connected variables. To evaluate the subjective assessment concerning dyspnea, Wilcoxon’s tests were used. The results with $p < 0.05$ were regarded as statistically significant.

Results

Table 2 presents the list of mean and standard deviation values of 6MWT parameters and the $p$ value before RT in the study groups. There were no significant differences in the 6MWT parameters before the beginning of RT between the groups.

In group A falls in HR were found both before (1.3%) and after (1.7%) 6MWT (statistically insignificant), while a significant decrease in DBP before exercise was observed. After the end of the therapy in group A 6MWD ($p = 0.00$) significantly increased and hence so did walking speed. This group showed lower values than at the beginning of the assessment concerning dyspnea after RT but they were statistically insignificant.

In group B after RT a statistically significant rise in HR was observed both before and after 6MWT. Systolic blood pressure was found to decrease by 1.9%, including statistically significantly (6.7%) after the test, and a small decrease in 6MWD (by 2.2%) was observed. After RT the patients in group B reported greater dyspnea (by 29.5%) than in group A – the differences were statistically significant.

Table 3 summarizes the parameters of 6MWT before and after RT and their statistical evaluation in the study groups.

Discussion

Many clinical data have confirmed the benefit in survival for postoperative RT in breast cancer patients [5–7]. However, there are a number of complications associated with this type of treatment. A common problem after RT for breast cancer is fatigue, depression, loss of physical functioning, and increased risk for side effects from heart, lung, skin, muscles and joints [8, 15, 16]. Physical activity during RT has a positive effect on most parameters in quality of life, dyspnea, and fitness (e.g. an increase in motion range in the shoulder) [17–22]. In the present study we performed a trial to determine whether moderate-intensity aerobic exercise would offer some benefit to breast cancer patients during the course of RT by improving exercise capacity. We used the 6MWT, which is the most common test for the objective assessment of exercise capacity in patients with cardiopulmonary disease [23]. This is a simple and widely used exercise tolerance measure in chronic respiratory diseases, heart failure as well as in cancer patients [23–26]. Miller et al. [25] found that the 6MWT might provide prognostic information beyond pulmonary function tests and dosimetric parameters in predicting RT-induced lung injury (RTLI). Rawat and co-authors [26] also confirmed the value of this test in assessing the risk of radiation-induced lung dysfunction in patients with cancer of the esophagus.

In the present study it was found that RT without regular PA changed 6MWT parameters. Especially a statistically significant increase in HR and SBP was noted. However, we did not find any significant effect of RT on 6MWD changes.

Table 2 List of mean and standard deviation values (SD) of 6MWT parameters and $p$ values before radiotherapy in study groups

| Parameters | Group A | Group B | $p$  | Group A | Group B | $p$  |
|------------|---------|---------|------|---------|---------|------|
|            | before 6MWT | after 6MWT |      | before 6MWT | after 6MWT |      |
| $\text{SO}_2$ [%] | 98.37 (0.9) | 98.45 (0.7) | 0.583 | 98.05 (1.1) | 98.15 (0.8) | 0.717 |
| HR [1/minute] | 81.04 (10.3) | 78.75 (6.9) | 0.183 | 105.08 (16.5) | 97.85 (11.2) | 0.102 |
| SBP [mm Hg] | 125.95 (17.2) | 126.2 (19.3) | 0.919 | 135.56 (23.3) | 133.65 (17.8) | 0.764 |
| DBP [mm Hg] | 81.57 (10.4) | 80.65 (9.6) | 0.583 | 82.56 (9.0) | 82.25 (9.9) | 0.913 |
| 6MWD [m] | – | – | 423.37 (66.6) | 426.40 (53.0) | 0.571 |
| MET | – | – | 3.01 (0.3) | 3.03 (0.2) | 0.571 |
| dyspnea | – | – | 3.48 (1.4) | 3.05 (1.9) | 0.305 |

$p$ = p values, 6MWT – 6-minute walk test, $\text{SO}_2$ – oxygen saturation, HR – heart rate, SBP – systolic blood pressure, DBP – diastolic blood pressure, 6MWD – 6 minute walk distance, MET – metabolic equivalent of task.
The authors declare no conflicts of interest.

Table 3. Summary of parameters of 6MWT before and after RT and their statistical evaluation

| Parameters         | Group A |       |       |       | Group B |       |       |       |
|--------------------|---------|-------|-------|-------|---------|-------|-------|-------|
|                    | Before RT | After RT | Difference | p   | Before RT | After RT | Difference | p   |
| before 6MWT         |         |        |        |      |         |        |        |      |
| $SO_2$ [%]         | 98.37 (0.8) | 98.22 (0.9) | –0.15 (0.8) | 0.212 | 98.45 (0.7) | 98.15 (1.0) | –0.30 (1.1) | 0.229 |
| HR [1/min]         | 81.04 (10.3) | 80.00 (11.2) | –1.04 (10.1) | 0.494 | 78.75 (6.9) | 83.35 (11.1) | 4.60 (8.6) | 0.012 |
| SBP [mm Hg]        | 125.95 (17.2) | 123.62 (15.8) | –2.33 (10.7) | 0.152 | 126.2 (19.3) | 124.91 (17.5) | –1.35 (11.2) | 0.598 |
| DBP [mm Hg]        | 81.57 (9.9) | 78.88 (9.6) | –2.68 (7.1) | 0.044 | 80.65 (9.6) | 78.25 (10.3) | –2.40 (6.7) | 0.126 |
| after 6MWT          |         |        |        |      |         |        |        |      |
| $SO_2$ [%]         | 98.08 (1.0) | 98.11 (1.0) | 0.02 (1.0) | 0.885 | 98.15 (0.8) | 98.75 (1.0) | –0.3 (1.1) | 0.229 |
| HR [1/min]         | 101.86 (14.7) | 100.17 (14.1) | –1.68 (12.8) | 0.381 | 97.85 (11.2) | 105.80 (12.8) | 7.95 (10.1) | 0.700 |
| SBP [mm Hg]        | 134.71 (20.9) | 126.24 (16.8) | –8.46 (13.2) | 0.000 | 133.65 (17.8) | 126.90 (18.1) | –6.75 (12.6) | 0.026 |
| DBP [mm Hg]        | 82.42 (9.3) | 81.68 (10.6) | –0.73 (9.4) | 0.602 | 82.2 (9.8) | 83.20 (13.2) | 0.95 (10.9) | 0.701 |
| 6MWD [m]           | 423.37 (66.6) | 447.33 (65.3) | 23.95 (36.1) | 0.000 | 426.40 (53.0) | 417.00 (57.6) | –9.40 (32.6) | 0.213 |
| Speed [km/h]       | 4.23 (0.6) | 4.45 (0.6) | 0.24 (0.3) | 0.000 | 4.26 (0.5) | 4.17 (0.6) | –0.09 (0.3) | 0.213 |
| MET                | 3.01 (0.3) | 3.13 (0.3) | 0.12 (0.2) | 0.000 | 3.03 (0.2) | 2.98 (0.3) | –0.04 (0.1) | 0.213 |
| dyspnea            | 3.48 (1.4) | 2.96 (1.3) | –0.51 (0.7) | 0.764 | 3.05 (1.9) | 3.95 (1.5) | 0.91 (0.7) | 0.018 |

RT – radiotherapy; p – p values; 6MWT – 6-minute walk test; $SO_2$ – oxygen saturation; HR – heart rate; SBP – systolic blood pressure; DBP – diastolic blood pressure; 6MWD – 6-minute walk distance; MET – metabolic equivalent of task

As Rawat [26] showed, the changes in the distance correlate with those in pulmonary function tests (PFTs). In the group without regular PA a decrease in the distance was found in 6MWT but it was not substantial. In the aerobic exercise group during RT, after the end of the therapy, there were found improvements of HR (both resting and post-activity), SBP as well as 6MWD. The study found that the women who performed moderate-intensity aerobic exercise during RT of breast cancer were able to prevent declines in aerobic capacity. The results of our study are consistent with those presented by Mustian et al. [21]. This improvement of aerobic capacity may be due to the changes in erythrocyte levels in the aerobic exercise group during radiation treatment of breast cancer, as observed by Drouin and co-authors [22]. As far as the fatigue intensification assessment after RT is concerned, our results confirm other authors’ observations [19, 21]. The moderate-intensity aerobic training caused dyspnea to decrease, which emphasizes the significant physiotherapy value during RT in this group of patients. The study results support the potential for PA to be a safe, effective, and economical method for improving aerobic fitness in females undergoing radiation treatment of breast cancer. However, any factors could play an additional role in maintaining proper psycho-physical status of patients who undergo oncological therapy [27].

The results of the study suggest that moderate-intensity aerobic exercise performed during radiation treatment may preserve or maintain capacity tolerance parameters with a substantial change in dyspnea in females being treated for breast cancer compared with declines observed in non-training peers.
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