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Cardiopulmonary function in breast cancer patients versus healthy control women

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Tetiana Odynets[1], Yuriy Briskin[2], Oksana Ikkert[3], Valentina Todorova[4], Anzhelika Yefremova[5]

[1] Department of Physical Rehabilitation, Khortytsia National Academy, Zaporizhzhya, Ukraine
[2] Department of Theory of Sport and Physical Culture, Lviv State University of Physical Culture, Lviv, Ukraine
[3] Department of Human and Animals Physiology, Ivan Franko National University of Lviv, Lviv, Ukraine
[4] Department of Gymnastics and Martial Arts, South Ukrainian National Pedagogical University named after K.D. Ushynsky, Odessa, Ukraine
[5] Department of Physical Education and Sport, Ukrainian State University of Railway Transport, Kharkiv, Ukraine

Abstract

Introduction. The study investigated cardiopulmonary function in breast cancer patients versus healthy control women.
Methods. Overall, 115 women after breast cancer surgery and 50 healthy controls were included. The outcome measures were spirographic and hemodynamic parameters.
Results. Most of the investigated parameters in breast cancer patients were significantly lower than in healthy women. The actual vital capacity (VC) was significantly lower by 0.34 l ($p < 0.001$), forced vital capacity (FVC) by 0.25 l ($p < 0.001$), forced expiratory volume in 1 second (FEV1) by 0.26 l ($p < 0.001$), peak expiratory flow (PEF) by 0.95 l/s ($p < 0.001$), maximum expiratory flow25 (MEF25) by 0.98 l/s ($p < 0.001$), maximum expiratory flow50 (MEF50) by 0.65 l/s ($p < 0.001$), expiratory reserve volume by 0.48 l ($p < 0.001$), maximal voluntary ventilation by 22.73 l/min ($p < 0.001$). The percentage of predicted values of VC, FVC, FEV1, PEF, MEF25, and MEF50 was lower by 9.93% ($p < 0.001$), 7.39% ($p < 0.001$), 8.87% ($p < 0.001$), 15.7% ($p < 0.001$), 18.09% ($p < 0.001$), and 15.96% ($p < 0.001$), respectively. As for the cardiovascular system, the actual stroke volume was higher in the control group compared with the main group by 12.20 ml/beat ($p < 0.001$), stroke index by 8.85 ml/beat/m2 ($p < 0.001$), cardiac output by 0.87 l/min ($p < 0.001$), left ventricular work by 0.96 g · m/beat ($p < 0.001$), LVP by 0.26 W ($p < 0.001$).
Conclusions. Cancer treatment negatively affected most cardiorespiratory parameters. The results support the need for physiotherapy intervention in breast cancer patients after treatment.
Key words: hemodynamics, spirography, cardiorespiratory system, breast cancer

Introduction

There is a growing body of research that emphasizes that breast cancer is a common pathology of women throughout the world [1, 2]. Patients who underwent breast cancer surgery and adjuvant cancer therapies are associated with several physical health problems, decrease in upper limb strength, lymphedema, shoulder pain, fatigue, cardiotoxicity, and issues related to peak oxygen uptake, cardiovascular endurance, and respiratory function [3–6].

Recent studies have shown high prevalence of cardiovascular side effects being important targets for interventions in breast cancer survivors [7–11]. It has been reported that breast cancer survivors often experience activity-related dyspnoea, radiation pneumonitis, deconditioning, respiratory muscle weakness, impaired lung diffusion, and exercise intolerance [12–19]. Considering the high frequency of cardiovascular risk factors, radiation pneumonitis, and respiratory muscle weakness, it is necessary to provide management of women after breast cancer surgery for implementing rehabilitation programmes.

The hypothesis of this study is that women with breast cancer have reduced cardiopulmonary function compared with age-matched healthy controls. Consequently, the aim of the study was to investigate features of cardiopulmonary function in breast cancer patients versus healthy control women.

Subjects and methods

A total of 115 women after breast cancer surgery (main group) and 50 age-matched healthy women (control group) were involved in the study.

Inclusion criteria for breast cancer patients were: women aged 50–60 years, I–II cancer stage, radical mastectomy by Madden, presence of lymphedema, impairment of active range of motion in the shoulder joint, decrease in upper limb strength, time after surgery up to 6 months. The focus was on women aged 50–60 years because the incidence of breast cancer was the highest in this age category. All the patients underwent radiation therapy. Women were excluded if they had chronic nonspecific lung disease, metastatic disease, congestive heart failure, III–IV cancer stages, period after surgery of more than 6 months.

The following respiratory parameters were measured: vital capacity (VC, l), forced vital capacity (FVC, l), forced expiratory volume in 1 second (FEV_1, l), peak expiratory flow (PEF, l/s), maximum expiratory $flow_{25}$ (MEF_{25}, l/s), maximum expiratory $flow_{50}$ (MEF_{50}, l/s), maximal voluntary ventilation (MVV, l/min), inspiratory reserve volume (IRV, l), expiratory reserve volume (ERV, l). Obstructive disorders were identified only with FEV_1 < 80% predicted and FEV_1/FVC < 70%. Restrictive disorders were identified only with FEV_1 reduced (< 80% of predicted normal), FVC reduced (< 80% of predicted normal), and FEV_1/

Correspondence address: Tetiana Odynets, Department of Physical Rehabilitation, Khortytsia National Academy, 59 Naukove Mistechko Str., 69017, Zaporizhzhya, Ukraine, e-mail: tatyana01121985@gmail.com

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FVC ratio normal (> 70%) [20, 21]. Spirometry was carried out by using an SMP-21/01 RD spirometer (Monitor Ltd. Co., Rostov-on-Don, Russia).

The following hemodynamic indicators were assessed: stroke volume (SV, ml/beat) – amount of blood pumped by the left ventricle at each heartbeat, cardiac output (CO, l/min) – amount of blood pumped by the left ventricle each minute, stroke index (SI, ml/beat/m^2) – stroke volume normalized for body surface area, systemic vascular resistance (SVR, dyn · s/cm^5) – the resistance to the flow of blood in the vasculature, left ventricular work (LVW, g · m/beat) – an indicator of the amount of work the left ventricle must perform to pump blood each minute, left ventricular power (LWP, W) – left ventricle work performed per time unit [22]. Hemodynamic indicators were assessed with the KARDIOLAB electrocardiographic complex (Scientific and Technological Centre of Radio-Electronic Medical Equipment and Technologies XAI-Medica of the National Aerospace University, Kharkiv, Ukraine, registration certificate number 6037/2007, conformity certificate number UA-MI/2p-2765–2009).

The measurements of respiratory and hemodynamic parameters were established as absolute volumes and percentages of the predicted values. The independent researcher who assessed the spirographic and hemodynamic parameters was blinded to the group assignment of the participants.

Statistical analysis

The analysis of respiratory and hemodynamic parameters of breast cancer patients and age-matched healthy controls was performed by using the Statistica for Windows (version 8.00) software. The distribution of the data recorded was tested with the Shapiro-Wilk test. This analysis was performed as a preliminary measure before parametric calculations of the analysis of difference. Independent *t*-tests served to analyse the cardiopulmonary parameters between groups.

Ethical approval

The research related to human use has complied with all the relevant national regulations and institutional policies, has followed the tenets of the Declaration of Helsinki, and has been approved by the Ethics Committee of Khortytsia National Academy (number 2017/12–11).

Informed consent

Informed consent has been obtained from all individuals included in this study.

Results

Demographic and treatment-related characteristics of the studied women are given in Table 1. A comparison of respiratory function parameters between the main group and the control group is presented in Table 2. The results presented in Table 2 show that most indicators of lung function in women with breast cancer were significantly lower as compared with healthy controls.

In the breast cancer patients, the actual VC was significantly lower by 0.34 l ($p < 0.001$), FVC by 0.25 l ($p < 0.001$), FEV_1 by 0.26 l ($p < 0.001$), PEF by 0.95 l/s ($p < 0.001$), MEF_{25} by 0.98 l/s ($p < 0.001$), MEF_{50} by 0.65 l/s ($p < 0.001$), ERV by 0.48 l ($p < 0.001$), MVV by 22.73 l/min ($p < 0.001$). The percentage of predicted values of VC, FVC, FEV_1, PEF, MEF_{25}, and MEF_{50} was lower by 9.93% ($p < 0.001$), 7.39% ($p < 0.001$), 8.87% ($p < 0.001$), 15.7% ($p < 0.001$), 18.09% ($p < 0.001$), and 15.96% ($p < 0.001$), respectively.

The comparison of IRV did not show a statistically significant difference between women with breast cancer and

Table 1. Demographic and treatment-related characteristics of the participants

Characteristics	Main group (n = 115)	Control group (n = 50)	p
Age ($M \pm m$)	57.44 ± 2.16	57.69 ± 2.34	> 0.05
Race			
White, *n* (%)	113 (98%)	49 (98%)	> 0.05
Black, *n* (%)	2 (2%)	1 (2%)	> 0.05
Married/committed relationship, *n* (%)	88 (77%)	37 (74%)	> 0.05
High school graduate, *n* (%)	73 (64%)	31 (62%)	> 0.05
College graduate, *n* (%)	29 (25%)	14 (28%)	> 0.05
Post-graduate, *n* (%)	13 (11%)	5 (10%)	> 0.05
Body mass index, kg/m^2 ($M \pm m$)	25.92 ± 0.42	26.01 ± 0.81	> 0.05
Treatment			
Radiotherapy, *n* (%)	98 (85%)	–	–
Chemotherapy, *n* (%)	17 (15%)	–	–
Surgery type (Madden mastectomy), *n* (%)	115 (100%)	–	–
Time after surgery (months)	5.23 ± 0.32	–	–
Cancer stage			
Stage 1, *n* (%)	33 (29%)	–	–
Stage 2, *n* (%)	82 (71%)	–	–

M – mean, *m* – error of mean

Table 2. Comparison of spirometry parameters ($M \pm m$) between the groups

Indicator		Groups		*p*
		Main group (n = 115)	Control group (*n* = 50)	
Vital capacity (l)	Actual	2.45 ± 0.02	2.79 ± 0.07	< 0.001
	% of predicted	78.33 ± 0.94	88.26 ± 2.30	< 0.001
Forced vital capacity (l)	Actual	2.36 ± 0.02	2.61 ± 0.05	< 0.001
	% of predicted	79.97 ± 0.88	87.36 ± 1.69	< 0.001
Forced expiratory volume in 1 second (l)	Actual	2.03 ± 0.02	2.29 ± 0.06	< 0.001
	% of predicted	83.35 ± 1.29	92.22 ± 2.64	< 0.001
Peak expiratory flow (l/s)	Actual	3.23 ± 0.09	4.18 ± 0.19	< 0.001
	% of predicted	55.66 ± 1.61	71.36 ± 3.28	< 0.001
Maximum expiratory $flow_{25}$ (l/s)	Actual	2.88 ± 0.08	3.86 ± 0.17	< 0.001
	% of predicted	56.17 ± 1.58	74.26 ± 3.43	< 0.001
Maximum expiratory $flow_{50}$ (l/s)	Actual	2.82 ± 0.07	3.47 ± 0.16	< 0.001
	% of predicted	79.00 ± 2.25	94.96 ± 4.33	< 0.001
Inspiratory reserve volume (l)		1.11 ± 0.03	1.24 ± 0.07	> 0.05
Expiratory reserve volume (l)		0.70 ± 0.03	1.18 ± 0.09	< 0.001
Maximal voluntary ventilation (l/min)		58.86 ± 1.52	81.59 ± 3.94	< 0.001

M – mean, *m* – error of mean

Table 3. Comparison of hemodynamic parameters ($M \pm m$) between the groups

Indicator		Groups		*p*
		Main group (n = 115)	Control group (*n* = 50)	
Stroke volume (ml/beat)	Actual	46.25 ± 0.87	58.45 ± 2.05	< 0.001
	% of predicted	72.87 ± 1.22	94.98 ± 3.27	< 0.001
Stroke index (ml/beat/m^2)		26.05 ± 0.48	34.90 ± 1.29	< 0.001
Cardiac output (l/min)		3.39 ± 0.05	4.26 ± 0.13	< 0.001
Systemic vascular resistance (dyn · s/cm^5)	Actual	2116.43 ± 34.93	1692.140 ± 55.94	< 0.001
	% of predicted	133.63 ± 2.19	103.16 ± 3.32	< 0.001
Left ventricular work (g · m/beat)	Actual	4.14 ± 0.07	5.10 ± 0.15	< 0.001
	% of predicted	75.31 ± 1.20	97.20 ± 3.17	< 0.001
Left ventricular power (W)	Actual	2.11 ± 0.04	2.37 ± 0.08	< 0.01
	% of predicted	78.65 ± 1.55	92.42 ± 3.30	< 0.001

M – mean, *m* – error of mean

age-matched healthy controls. A detailed analysis of VC revealed normal values only in 20% of breast cancer patients. FVC was normal in 28% of breast cancer patients, FEV_1 in 22%, PEF in 9%, MEF_{25} in 30%, and MEF_{50} in 35%.

A comparison of hemodynamic parameters between the main group and the control group is presented in Table 3. It was found that the actual value of SV was higher in women of the control group compared with the main group by 12.20 ml/beat ($p < 0.001$), SI by 8.85 ml/beat/m^2 ($p < 0.001$), CO by 0.87 l/min ($p < 0.001$), LVW by 0.96 g · m/beat ($p < 0.001$), LVP by 0.26 W ($p < 0.01$). The percentage of predicted values of SV, LVW, and LVP was lower by 22.11% ($p < 0.001$), 21.89% ($p < 0.001$), and 13.77% ($p < 0.001$), respectively. Women with breast cancer had higher results for SVR by 424.29 dyn · s/cm^5 and its percentage of predicted value by 30.47% ($p < 0.001$) compared with the controls. It was an unfavourable prognostic factor for raising blood pressure in breast cancer patients.

With the consideration of the baseline values of cardiac index and SVR, the following types of blood flow regulation were identified among the breast cancer women: hypokinetic in 80% of the patients, normokinetic in 16%, and eukinetic only in 4%. At the same time, the hypokinetic type of regulation was observed only in 22% of the age-matched healthy control women, normokinetic in 72%, and hyperkinetic in 6%.

Discussion

It was identified that women after breast cancer surgery and adjuvant therapy had impaired cardiopulmonary function compared with controls. A great deal of research [2–4, 23, 24] indicates that women who underwent breast surgery and adjuvant therapy are more likely to present a higher risk of cardiotoxicity, reduced peak oxygen consumption, and impaired cardiopulmonary parameters. The importance of the problem is underlined by the presence of numerous physical exercise interventions [8–11, 25–28] for improving life quality and functional state of the cardiovascular system in breast cancer survivors.

On the basis of an analysis of the cardiovascular system functional state carried out by rheography, it was found that most indicators of central hemodynamics were reduced with the exception of SVR, which was significantly higher than the normal values. Most breast cancer patients (80%) had the hypokinetic type of blood flow regulation, while the healthy controls (72%) were normokinetic.

All of the obtained respiratory parameters turned out to be decreased in breast cancer patients. Restrictive and obstructive types of respiratory dysfunction were revealed. These findings are supported by studies that confirm that mastectomy leads to a decrease in PEF and forced expiratory flow.

Our observations complement the research [4, 11, 24] on pulmonary function, which was characterized by a decrease in the relative values of VC, FEV_1, MEF_{25}, MEF_{50}, MVV, and ERV, indicating the presence of obstructive disorders of the respiratory system and its reduced functionality in breast cancer patients.

Limitations

This study has important limitations. Our findings are based on a small sample and the obtained results may not be generalizable to all women population suffering from breast cancer.

Conclusions

In conclusion, we confirm that the performed breast cancer treatment negatively affects most parameters of the cardiorespiratory system in women. The results of the present study support the continued need and feasibility of physiotherapy intervention in breast cancer patients after completion of treatment.

Prospects for further study will be directed at determining the effectiveness of individualized physical interventions in breast cancer patients with cardiopulmonary function disorders.

Disclosure statement

No author has any financial interest or received any financial benefit from this research.

Conflict of interest

The authors state no conflict of interest.

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