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THE IMPACT OF CARDIOTOXIC CHEMOTHERAPY ON PEAK OXYGEN UPTAKE IN FEMALES

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by

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A Research Paper
Submitted in Partial Fulfillment of the Requirements for the
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RESEARCH PAPER APPROVAL

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Graduate School
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TITLE: THE IMPACT OF CARDIOTOXIC CHEMOTHERAPY ON PEAK OXYGEN UPTAKE IN FEMALES

MAJOR PROFESSOR: Dr. Juliane Wallace & Dr. Phil Anton

Individuals undergoing chemotherapy experience drug infusions that powerfully alter physiological function. Chemotherapy targets cancerous cell growth, but unfortunately it also has widespread ramifications on normal cellular function. Among chemotherapy drugs, cardiotoxic chemotherapies are particularly detrimental to patients' health. Cardiotoxic chemotherapy that damages heart muscle may negatively affect quality of life. **PURPOSE:** To assess the impact of cardiotoxic chemotherapy on peak oxygen uptake. We hypothesized that the calculated peak oxygen consumption (VO_2 peak) of the female patients who have undergone cardiotoxic chemotherapy would be lower than that of, the female caretakers in the same age range who have not undergone cardiotoxic chemotherapy. **METHODS**: We accessed patient files from the SIUC-SIH Strong Survivor program and gathered data on female cancer survivors (mean age= 55.5 yo) and caregivers (mean age= 57.8 yo). Ten female cancer survivors were randomly selected based on their cardiotoxic treatment. Ten female caregivers of similar age were randomly selected, they had not undergone any chemotherapy. Participants' VO_2 peak was calculated using data from a previously administered submaximal VO_2 assessment. Utilizing their recorded heart rate, age, treadmill walking speed and gender, an estimated VO_2peak was calculated using the Ebbeling et al. (1991) prediction equation, VO_2 peak ($ml.*kg.^{-1}*min^{-1}$) = 15.1 + (21.8 * Speed in mph) - (0.327 * HR) - (0.263 * Speed * Age) + (5 .98 * Gender) + (0.00504 * HR * Age). **RESULTS:**

An independent-samples t-test comparing the VO_2 peak of cancer survivors (M= 24.373 $ml*kg^{-1}*min^{-1}$, SD ± 4.867) and their healthy counterparts (M= 25.276 $ml*kg^{-1}*min^{-1}$, SD ±3.252) revealed no significant difference; t (18) = -.488, p=.632, p > .05. However, the Cohen's D effect size revealed a small effect of the cardiotoxic chemotherapy (d= .218). The caregiver's peak oxygen consumption is 0.218 standard deviation units above the cancer survivors VO_2 peak – this indicates a small, yet meaningful group difference. **CONCLUSION:** Although the group difference in VO_2 peak was small, these findings suggest that VO_2peak may be reduced by cardiotoxic chemotherapy. Medical and exercise professionals should implement exercise programs prior to and during chemotherapy to help strengthen heart function and to limit such harmful effects.

DEDICATION

I dedicate this research project to my parents and the faculty in the Kinesiology Department.

TABLE OF CONTENTS

LIST OF TABLES

TABLE PAGE

LIST OF FIGURES

CHAPTER 1

INTRODUCTION

As individuals undergo chemotherapy, they are subject to drug infusions that powerfully alter physiological function. Chemotherapy is designed to obstruct rapid, malignant cell division. Unfortunately, chemotherapy does not target cancerous cell growth alone and has widespread ramifications on normal cellular function. Cardiotoxic chemotherapy damages heart muscle and affects quality of life (Thomas, 2017). The purpose of our study was to evaluate the impact of cardiotoxic chemotherapy on cardiovascular output by assessing VO_2 peak. Contrasting the cardiovascular function of chemotherapy treated patients to those who undergo different treatments will illuminate the effect of cardiotoxic chemotherapy. Secondarily, understanding how a patient's cardiovascular output is impacted by chemotherapy, and how it differs from a patient who has not undergone any chemotherapy, will permit medical professionals to design patient specific exercise programs that attenuate the effects of cardiotoxic chemotherapy. Developing exercise programs that alleviate the impact of cardiotoxic chemotherapy will sustain quality of life and promote physical activity.

According to the National Cancer Institute, cancer can be defined as a, "collection of related diseases, some of the body's cells begin to divide without stopping and spread into surrounding tissues" (NCI, 2019). Cancer is a leading cause of death, worldwide; it is a genetic disease that fosters genetic deviations. The deviations negatively affect three gene types: proto-oncogenes, tumor suppressor genes, and DNA repair genes. These genes are referred to as the "drivers" of cancer. Cancer can develop in any part of the human body. In a healthy body, cells grow and divide to form new cells in a highly regulated manner. Cancer cells, on the other hand,

are characterized by abnormal, unregulated cell division and reproduction. Unchecked reproduction progresses to form cancerous tumors.

Cancer treatment depends on the type of cancer in question. Nonetheless, the most common cancer treatment is chemotherapy. Chemotherapy is used, “to stop or slow the growth of cancer cells” (NCI, 2019). Chemotherapy, radiotherapy, and surgery are among the most effective treatments. While chemotherapy is one of the most successful ways to treat cancer, it can cause serious complications. Among those is cardiotoxicity – which is known to negatively impact quality of life and survival rates of cancer patients. Toxic chemicals designed to fight cancer growth concomitantly damage the heart. The cardiac defects that arise following cardiotoxic chemotherapy infusion: include “left ventricular (LV) dysfunction, congestive heart failure (CHF), coronary vasospasm, angina, myocardial infraction, dysrhythmias, systemic hypertension, pericardial effusion, pulmonary fibrosis, and pulmonary hypertension” (Jain, Russell, Schwartz, Panjrath, & Aronow, p. 2, 2017). Cardiotoxic chemotherapy effectively treats cancerous cell growth. It is important to note that the impact of cardiotoxic chemotherapy is dependent on a host of factors. Thus, patients who undergo cardiotoxic therapy are stratified according to preexisting risk factors prior to treatment onset. Assessing risk factors helps doctors predict the corollaries of cardiotoxic treatment. According to Virizuela et al. (2018), the cardiotoxicity risk factors include - demographic characteristics (age & gender), previous cancer treatments, current anticancer treatment, hypertension, diabetes, dyslipidemia, smoking, obesity, sedentary lifestyle and prior or current heart diseases. The more risk factors a patient possesses, the greater the risk of incurring long-lasting cardiotoxic effects. As physicians document the risk factors of an individual, they can then decide which chemotherapy treatment will be best for them.

There are several types of drugs classified as cardiotoxic. The most commonly used class of cardiotoxic chemotherapy drugs are; “anthracycline agents, HER2/neu blockers, alkylating agents, antimetabolites, antimicrotubule agents, antiangiogenic antibodies, proteasome inhibitors, tyrosine kinase inhibitors (TKIs), angiogenesis inhibitors, checkpoint inhibitors, histone deacetylase inhibitors, antiandrogens, antiestrogens, and miscellaneous” (Jain et al, 2017, p. 3). The list of agents under each class is extensive, for the purposes of this study, the focus was on the commonly used for the majority types of cancer treatment; anthracyclines, trastuzumab (herceptin), tyrosine kinase inhibitors, and taxanes.

Anthracyclines agents are very effective in cancer treatment; however, cardiotoxicity is a major limitation with its usage. There are four common anthracyclines drugs utilized, “doxorubicin (DOX), daunorubicin (DNR), epirubicin (EPI), and Idarubicin (IDA)” (McGowan et al, 2017, p.64). The physiology behind how these agents affect the body has to do with anthracyclines interference with redox cycling, this interference results in a DNA damage. Anthracyclines are DNA and RNA synthesis inhibitors. These agents inhibit the activity of topoisomerase II, which is used to repair DNA. Multiple mechanisms may induce cardiotoxicity from these agents, some include, “oxidative injury from free radicals, peroxidation of membrane lipids, altered calcium handling by sarcoplasmic reticulum, and impaired protein synthesis” (Jain et al, 2017, p.2). Essentially these agents prevent DNA repair and DNA synthesis. Thus, after the cancerous cells are destroyed, there is no way the body can produce new cells due to these agents. Treatments with anthracyclines may induce many degenerative changes in the heart. According to Jain et al. (2017), these agents cause myocellular injury, left ventricle dilation, adverse remodeling of the heart, impaired contractility and chronic heart failure. Anthracyclines cardiotoxic effects can

be acute and/or chronic. Acute cardiotoxicity occurs very soon after the treatment initiation and is self-limiting. Acute effects such as, changes in patients ECG reading and dysrhythmias, can be resolved over time with assistance from family and physicians. Chronic effects are more common and present as left ventricular systolic dysfunction, which can lead to chronic heart failure. Doxorubicin, a specific anthracycline agent, is known to cause most of the chemotherapy-induced cardiotoxicity. In a study of young adults receiving a dosage of this agent resulted in, "abnormally reduced left ventricular mass and left ventricle end-diastolic posterior wall thickness… suggesting left ventricle remodeling" (Cao et al, 2017, p.97). Impact to this extent can truly limit a patient's ability to go through day-to-day activities. Left ventricular systolic dysfunction is the most common risk of anthracycline cardiotoxicity. Physicians should be monitoring changes in the systolic function periodically during treatment. Coupling other cardiotoxic agents, such as; trastuzumab, tyrosine kinase inhibitors and taxanes, with anthracycline can increase the risk for left ventricular systolic dysfunction and chronic heart failure.

Trastuzumab (Herceptin) agent, "is a humanized monoclonal antibody targeted against growth receptor protein expressed on the cell membranes" (Jain et al, 2017, p.6). This drug is mainly used with breast cancer patients because of their increased HER2 activity. HER2 is a receptor that promotes proliferation of cell growth and trastuzumab blocks these pathways, which results in cell death. Trastuzumab targets the body's immune system and acts to destroy specific cells. This agent causes left ventricular dysfunction and chronic heart failure, but these effects are reversible when treatment ceases. If the treatment does lead to chronic heart failure, then physicians work to modify the dosages. More than 50% of patients going through treatment with this agent experience left ventricular systolic dysfunction, which is an indicator for chronic heart

failure. In another study with this agent, researchers found that, “one-year mortality in this population to be 11.4% for class IV heart failure” (Moss et al, 2009, p.682). When a decrease in systolic function is found in patients, doctors will discontinue trastuzumab therapy. Even though physicians can terminate trastuzumab treatment, the decrease in systolic function will inevitably cause limitations in patients’ lifestyle and physical activity regimen.

Tyrosine kinase inhibitors (TKI), “are enzymes that activate proteins by transferring a phosphate group to the tyrosine residue of proteins in a single transduction cascade” (Jain et al, 2017, p.8). According to Jain et al (2017), these agents inhibit epidermal growth factor receptors and vascular endothelial growth factor signaling pathways, which lead to an inhibition of angiogenesis and growth. Inhibiting angiogenesis means putting an end to tumor growth, as well as, to the formation of new blood and lymphatic vessels. While TKI agents help stop the growth of cancerous tumors, they can also lead patients to develop hypertension, which eventually leads to left ventricular systolic dysfunction. In recent research, “eleven percent of patients receiving TKI agents developed CHF or a significant decrease in LVEF” (Jain et al, 2017, p.8). As shown in this study, this cardiotoxic agent does indeed decrease the hearts ability to pump blood; this severely limits what survivors can do after treatments.

Taxanes, include paclitaxel and docetaxel are commonly used to treat lung, breast, and ovarian cancer. These agents, “impair normal microtubular transport systems in cardiomyocytes, which can impair the storage and mobilization of free fatty acids from cytosolic pool to the mitochondria” (Jain et al, 2017, p.9). According to Cao et al. (2016), taxanes inhibit cell division by repressing polymerization or depolymerization of microtubules. These agents target fast growing cancerous cells and enter the cell to attach to the scaffold. As they attach themselves to

the inside of the cancer cell, it inhibits the cell from growing. These agents are effective when treating cancer, however, they do also result in chronic heart failure. Inhibiting new cell growth will inevitably lead to heart dysfunction.

All four of the cardiotoxic agents discussed, impact cardiovascular function in a negative way. As one can conclude, evidence of a significant decrease in ejection fraction and reduced left ventricular systolic dysfunction is frequently seen in patients undergoing cardiotoxic treatment. This can limit cardiovascular function in multiple ways; limit the amount and duration of exercise, fatigue levels may increase, motivation to begin a program and the energy to adhere to it may decrease. It drastically reduces the amount of physical activity a patient can participate in.

The research behind how exercise impacts cardiovascular functioning in those who are currently undergoing chemotherapy or those who have already finished their chemotherapy treatment has shown very positive results. A study in which researchers had participants perform moderate and high intensity exercise programs showed that, "combining high and moderate intensities, can reduce or minimize the cardiotoxicity of trastuzumab, increase cardiorespiratory fitness and health-related quality of life" (Jacquinot et al, 2017, p.9). Physicians should prescribe patients an exercise program and motivate them to adhere to it. Patients should participate in exercise even before they begin chemotherapy. Kirkham and colleagues (2018), had breast cancer patients participate in aerobic exercise 24 hours prior to their chemotherapy treatment. Participants demonstrated positive effects in physiological and musculoskeletal symptoms, as well as, their mood and body weight had improved. Lee et al (2018) conducted a study with high intensity interval training in patients undergoing anthracycline chemotherapy. In which, breast cancer survivors participated in an 8-week high-intensity interval training, researchers found that,

moderate to high intensity exercise revealed better cardiovascular outcomes. These researchers believe high intensity interval training is very effective with cancer patients, plus it is time efficient. High intensity exercise bouts provide more cardiac benefit than low-moderate exercise.

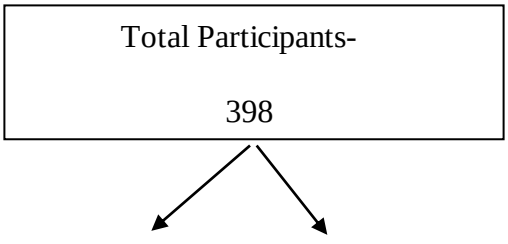
The purpose of this study was to assess the impact of cardiotoxic chemotherapy treatment on peak oxygen uptake. We hypothesized that the calculated peak oxygen consumption (VO_2 peak) of the female patients who have undergone cardiotoxic chemotherapy would be lower than that of, the female caretakers in the same age range who have not undergone cardiotoxic chemotherapy. The independent variables within the study were the caregivers, who did not undergo chemotherapy - and the participants who had gone through cardiotoxic chemotherapy treatments. The dependent variable was the calculated peak oxygen consumption (VO_2 peak) of both groups.

CHAPTER 2

METHODS

Participants

With permission from the SIU Human Subjects Committee and the Director of the SIUC-SIH Strong Survivor program, participant files were accessed from the SIUC- SIH Strong Survivor program - from which data was gathered on cancer survivors and caregivers. Out of approximately 398 patient files, 283 were females, and out of those 207 were female cancer survivors. Out of the 207 cancer survivors, 120 had undergone cardiotoxic chemotherapy. Cardiotoxic chemotherapy was operationally defined as treatment with at least one of four drugs: anthracyclines, trastuzumab (herceptin), tyrosine kinase inhibitors, and taxanes. Based on that, ten female cancer survivors were randomly selected from the 120. The cancer survivors that were included all received their last cardiotoxic chemotherapy within the last four years. Ten female caregivers were age and activity level matched to the cancer survivors. All participants had completed an exercise history and a potential contraindication questionnaire, from which their daily activity levels were recorded. All participants' heart rate, body composition, age, date of birth, and ethnicity was recorded. The type of cancer and type of cardiotoxic chemotherapy they were administered were recorded for the cancer survivors. See Figure 1.



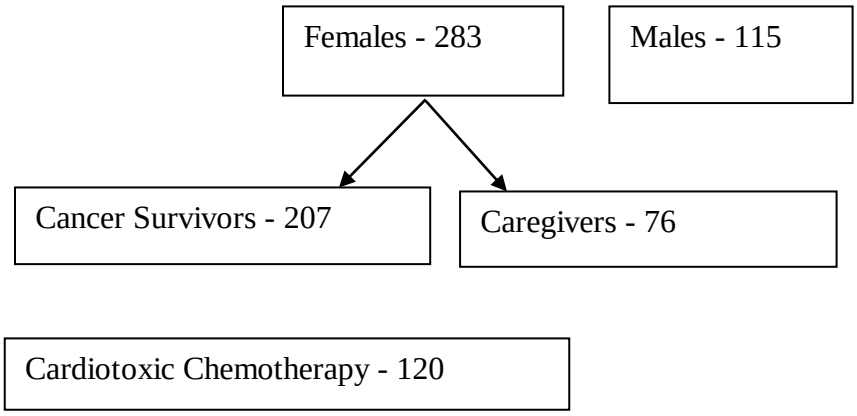


Figure 1: Participant selection

Procedures

The following participant information was recorded from each file: VO_2peak was calculated using data from a previously administered submaximal VO_2 assessment. Utilizing their recorded heart rate, age, treadmill walking speed and gender, an estimated VO_2 peak was calculated using the Ebbeling et al. (1991) prediction equation, VO_2peak ($ml*kg^{-1}*min^{-1}$) = 15.1 + (21.8 * Speed in mph) - (0.327 * HR) - (0.263 * Speed * Age) + (5 .98 * Gender) + (0.00504 * HR * Age).

Design and Analysis

IBM SPSS Statistics 25 software was used to conduct an independent t-test in order to analyze statistical differences between the VO_2 peak of the cancer survivors and caregivers. A significance level of alpha=0.05 was used for the independent t-test. Cohen's D effect size was calculated as well using SPSS.

CHAPTER 3

RESULTS

The participants in this study were ten cancer survivors and ten caregivers. The ten cancer survivors were randomly selected out of 120. The ten caregivers were age and activity level matched to the cancer survivors. Both cancer survivors and caregivers showed no difference in age, body composition, resting heart rate, level of aerobic training and level of resistance training (Table 1).

Table 1: Participant Characteristics

	Age	Body Composition (BMI)	Resting Heart Rate (RHR)	Level of Aerobic training**	Level of Resistance training**
Cancer Survivors	55.5 ± 11.03	30.4 ± 4.9	86.6 ± 10.9	2.5 ± 1.6	1.8 ± 0.79
Caregivers	56.8 ± 7.3	28.5 ± 5.7	86.7 ± 12.4	2.8 ± 0.63	2.2 ± 0.63

* $p > 0.05$
** level of activity: 1 – very low, 2- low, 3- average, and 4- high

The breakdown of participant files from the SIUC- SIH Strong Survivor lab.

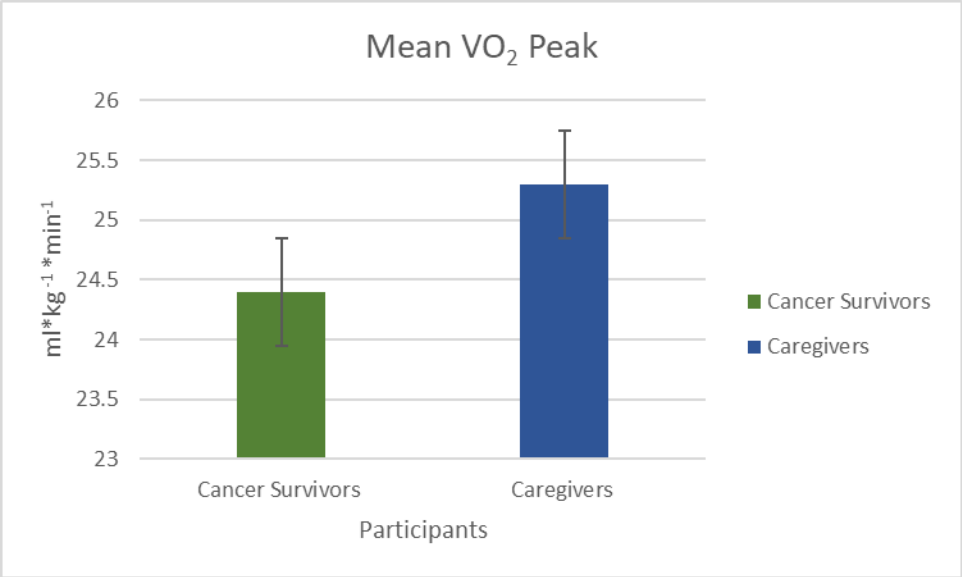


Figure 2: VO_2 Peak of Cancer Suvivors and Caregivers.

Data are mean + SD

We hypothesized that the calculated peak oxygen consumption (VO_2 peak) of the female cancer survivors who have undergone cardiotoxic chemotherapy would be lower than that of, the female caretakers in the same age range who have not undergone cardiotoxic chemotherapy. To test this hypothesis, mean values of the VO_2 peak of the cancer survivors and the caregivers were recorded and compared. An independent-samples t-test comparing the VO_2 peak of cancer survivors (M= 24.4 $ml*kg^{-1}*min^{-1}$, SD ± 4.9) and their healthy counterparts (M= 25.3 $ml*kg^{-1}*min^{-1}$, SD ± 3.3) revealed no significant difference; t (18) = -0.488, p=0.632, p > 0.05. However, the Cohen's D effect size revealed a small effect of the cardiotoxic chemotherapy (d= 0.22). The caregiver's peak oxygen consumption is 0.22 standard deviation units above the cancer survivors VO_2 peak – this indicates a small, yet meaningful group difference. Since there was no significant difference seen in the participant characteristics, it would indicate that those variables did not influence the VO_2 peak. The small effect size may have come from the cardiotoxic chemotherapy.

CHAPTER 4

DISCUSSION

The purpose of this investigation was to determine if differences in peak oxygen consumption (VO_2 peak) exist between cancer survivors who had received cardiotoxic chemotherapy and caregivers who had never been administered chemotherapy. The results revealed that there was no significant difference in the VO_2 peak between the cancer survivors and caregivers. Thus, our hypothesis was not be supported. However, there was a small effect size found from the data. The effect size indicated a lower peak oxygen uptake in the Cancer Survivors compared to the caregivers, indicating that cardiac function may be negatively impacted by cardiotoxic chemotherapy.

In previous research, chemotherapy treatment with anthracyclines, trastuzumab (herceptin), tyrosine kinase inhibitors, and taxanes have found to present patients with negative impacts on cardiac function. These four cardiotoxic agents are mostly used in cancer treatment, thus leading to a multitude of complications for patients receiving this treatment. The potential of reversing the effects is based on how long and how often the patient is getting the treatment. However, in most cases, as stated in the beginning of this paper, the effects of cardiotoxic chemotherapy are irreversible and negatively impact on cardiac function. According to Jain et al (2017), evidence of a significant decrease in ejection fraction and reduced left ventricular systolic dysfunction is frequently seen in patients undergoing cardiotoxic treatment. The results found in this study indicate that there is indeed a small change in the VO_2 peak between cancer survivors and caregivers who were age matched to the Cancer Survivors on age and activity level.

While the lower oxygen uptake noted in the cancer survivors in the current study has been

attributed to the cardiotoxic chemotherapy, there are other factors that could explain the differences. The exercise history and a potential contraindication questionnaire reported participant training levels – the activity levels for aerobic and resistance training were rated as being “low” or “very low” for the cancer patients. This could be explained by the decreased motivation and an increase in fatigue levels after treatment. The decreased levels of motivation and increased levels of fatigue could also be a reason why the present study did not show significant differences between the two groups.

There are psychological impacts of chemotherapy, a decrease in motivation may originate from the time spent being inactive during treatment. The impact of cardiotoxic chemotherapy is not only physiological but also psychological for these participants.

There were several limitations that would require more attention when reviewing the results. The biggest limitation was that the number of participants was small. Future studies should consider a larger population to work with, adding to the participant pool will likely result in significant differences. Second, undergoing chemotherapy can result in increased levels of fatigue perception, which may have affected the cancer survivors VO_2 peak. Third, the control group was not screened for any prior or current health conditions.

One way to decrease the impact of cardiotoxicity is to have patients begin an exercise protocol prior to chemotherapy treatment. There are many concerns for cardiovascular function as cancer patients start and continue going through cardiotoxic chemotherapy. However, there is little research to suggest anyone has had patients go through pre-chemotherapy exercise. This may be because of the urgency to begin treatment as soon as the diagnosis has been given. Medical professionals should suggest patients to begin exercise programs prior to beginning

chemotherapy. Rational behind this, is that, patients can potentially strengthen their systolic function, thus reducing the impact cardiotoxic drugs might have on it. Researchers have found that, “as little as 4 weeks of exercise training can significantly improve cardiac and vascular function” (Sturgeron, Ky, Libonati, & Schmitz, 2015, p. 5). If patients were to perform exercise prior to treatment, it may significantly reduce the impact of cardiotoxicity they experience. The focus of a future study should be on more of an intervention study, implementing an exercise regime with patients prior, during and after chemotherapy. While assessing their VO_2 peak levels throughout the exercise program.

Although the group difference in VO_2 peak was small, these findings suggest that VO_2 peak may be negatively impacted by cardiotoxic chemotherapy. To avoid harmful effects from cardiotoxic chemotherapy, medical and exercise professionals should recommend exercise programs prior to beginning chemotherapy. Medical professionals can implement a moderate to high intensity strength endurance workout regimen (Sturgeron, Ky, Libonati, & Schmitz, 2015). Patients who have been diagnosed can start to formulate a plan with their physician for an exercise regimen. They would construct an exercise program based on their age, fitness level, and/or fatigue perception. The program would consist of a stationary bike, treadmill walking, if not weight bearing then sitting chair exercises with light weights or simple range of motion exercises of joints to ensure movement and increase in heart rate. As patients are going through this exercise program, they will start chemotherapy, the goal is for them to continue the exercise program through treatment and post treatment. If patients feel an increase in levels of fatigue, then modifications to the program can be made as they progress. Physicians should assess left ventricle systolic function through ECG’s and biomarkers (blood tests) to track cardiotoxicity. As

stated before, the goal of this exercise program is to reduce left ventricle systolic dysfunction and help cancer patients live a long and healthy life.

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APPENDICES

APPENDIX A

Participant Characteristics

Cancer Suvivors	Age	Race	Cancer type	Type of Cardiotoxic treatment
1	58	Caucasian	Breast Cancer	Taxotere, Carboplatin – taxane
2	48	Caucasian	Breast Cancer	Taxol, Adriamycin, cytoxin – taxane
3	47	Caucasian	Breast Cancer	Herceptin
4	65	Caucasian	Breast Cancer	Afinitor - kinase inhibitor
5	35	Caucasian	Breast Cancer	Trastuzumab, decetaxel, pertuzumab
6	60	Caucasian	Breast Cancer	Taxotere, Herceptin
7	45	African American	Breast Cancer	Doxorubicin, paclitaxel
8	68	Caucasian	Breast Cancer	Taxotere, Cytoxan
9	64	African American	Uterine Cancer	Paclitaxel, carboplatin
10	65	Latin American	Overian Cancer	Taxotere, taxol, paclitaxel

Caregivers	Age	Race
1	65	Caucasian
2	59	Caucasian
3	43	Caucasian
4	57	Caucasian
5	65	Caucasian
6	60	Caucasian
7	49	Caucasian
8	62	Caucasian
9	58	Caucasian
10	50	Caucasian

APPENDIX B

Participant Information

Cancer Survivors	Current level of aerobic and resistance training	VO2 max	BMI
1	Low - Very low	21.68 ml/kg/min	27.3
2	Low - Very low	18.027 ml/kg/min	30.6
3	Low- Low	34.483 ml/kg/min	27.6
4	Low - Average	31.176 ml/kg/min	26.3
5	Low- Very low	23.094 ml/kg/min	32.7
6	Low -Low	22.136 ml/kg/min	25.5
7	Very Low- Very low	24.983 ml/kg/min	39.5
8	Low-Low	22.013 ml/kg/min	37.8
9	Average - Average	23.832 ml/kg/min	25.8
10	Very Low- Low	22.305 ml/kg/min	31.1
Mean:		24.373 ml/kg/min	30.4

Caregivers	Current level of aerobic and resistance training	VO2 max	BMI
1	Average - Low	26.916 ml/kg/min	29.2
2	Average - Low	26.865 ml/kg/min	41.1
3	Average - Average	22.509 ml/kg/min	26.4
4	Low- Average	20.916 ml/kg/min	32.4
5	Average - Low	23.176 ml/kg/min	27.4
6	Average - Low	21.693 ml/kg/min	27.5
7	Average - Low	26.097 ml/kg/min	26.4
8	Low - Very low	31.776 ml/kg/min	22.3
9	High - Average	26.957 ml/kg/min	20.8
10	Low- Low	25.85 ml/kg/min	31.9
Mean:		25.278 ml/kg/min	28.5

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Research Paper Title:
The Impact of Cardiotoxic Chemotherapy on Peak Oxygen Uptake in Females

Major Professor: Dr. Juliane Wallace and Dr. Phil Anton