

AEROBIC AND RESISTANCE EXERCISES IN POST-OPERATIVE BREAST
CANCER PARTICIPANTS AT RISK OF LYMPHEDEMA: AN EXPLORATORY
STUDY

by

NOR SAHIRA BT MOHD SALIM

Thesis submitted in fulfilment of the requirements
for the degree of
Masters of Science (Sports Science)

April 2018

ACKNOWLEDGEMENT

First and foremost, my greatest thanks to God the Almighty for giving me patience, strength, ability and ideas for completing my research project for my master of degree. Special gratitude to my parents and family members who have always support me and give me motivation until the end of my study.

I would like to express my greatest gratitude towards my supervisor Dr. Vina Tan Phei Sean, my co-supervisor Dr Maya Mazuwin bt Yahya, Dr Juharfa Bt Haron, and Pn Roslaini Bt Che Romli for her guidance, encouragement, helps, gracious support and continuous advice in planning and execution this research project. Special thanks are also extended to all my classmates Noor Fatin Nazieffa, Azzaizirawati, Siti Nur Syafiqah, Wan Nabila, Maziana, Amirah and Amrun for all the opinions and suggestion given regarding this study and their utmost support during conducting this study.

Greatest appreciation to all the staffs of the Sports Science Unit, University Sains Malaysia, and Breast Cancer Awareness & The Research Unit (Bestari) of Hospital Universiti Sains Malaysia (HUSM), especially for helping with the laboratory work and for their support especially during the process of data collection.

I would like to grap this opportunity to dedicate my specials thanks to my family and my beloved colleague and friends especially Siti Najwani and Muhammad Umairul, for their help, encouragement and moral support in

completing this study. Last but not least, I am hoping that this research will give benefits especially to mankind.

TABLE OF CONTENT

Acknowledgement	ii
Table of Content	v
List of Tables	ix
List of Figures.....	iv
ABSTRAK	xii
ABSTRACT	14j
CHAPTER 1: INTRODUCTION.....	1
1.1 Introduction.....	1
1.2 Problem Statement	5
1.3 Purpose of Study	5
1.4 Objectives of Study.....	5
1.4.1 General objective:	5
1.4.2 Specific Objective:	5
1.5 Hypotheses.....	5
1.6 Significance of Study	7
CHAPTER 2: LITERATURE REVIEW.....	8
2.1 Breast Cancer	8
2.2 Lymphedema	9
2.3 Exercise for Cancer Patients	11
2.3.1 Exercise for lymphedema.....	13

2.3.2 Aerobic exercise for lymphedema	16
2.3.3 Resistance exercise.....	18
2.3.4 Overall effect of exercise on lymphedema of breast cancer related patients	20
CHAPTER 3: METHODOLOGY	23
3.1 Study design.....	23
3.2 Sample size calculation.....	23
3.3 Study participants & recruitment	24
3.4 Experimental Design.....	25
3.4 Exercise prescription.....	25
3.4.1 Aerobic training	26
3.4.2 Resistance training	27
3.5 Study measurements	29
3.5.1 General information	29
3.5.2 Arm circumference measurement	29
3.5.3 Lymphedema relative volume (LRV)	30
3.5.4 Ultrasound	31
3.5.5 Hand grip strength test	32
3.3.6 Perceived exertion and pain scale	33
3.7 Data analysis	35
CHAPTER 4: RESULTS	36
4.1 Characteristic of participants	36

4.2 Arm circumference measurements.	37
4.3 Arm fluid volume measurements.....	41
4.4 Skin and tissue thickness measurements by ultrasound.....	42
Table 4.9: Measurement of skin thickness in upper arm	<u>42</u>
Table 4.10: Measurement of Tissue Thickness in upper arm	44
Table 4.11: Measurement of Skin Thickness in forearm	45
Table 4.12: Measurement of Tissue Thickness in forearm	46
4.5 Handgrip strength test measurements.	47
Table 4.13: Measurement of handgrip strength test before and after six week of exercise intervention within affected and unaffected arm.....	48
4.6 Visual Analog Scale (VAS).....	48
CHAPTER 5: DISCUSSION	51
5.1 Introduction.....	51
5.2 Arm circumference	51
5.3 Arm fluid volume.....	52
5.4 Hand grip strength test.....	53
5.5 Skin and tissue thickness	54
5.6 Pain score.....	55
CHAPTER 6: CONCLUSION AND RECOMMENDATION.....	57
6.1 Conclusion	57
6.2 Recommendations.....	57
REFERENCES	59

APPENDICES	60
Appendix 1: Ethical Approval Letter.....	61
Appendix 2: Consent Forms – English and Bahasa Malaysia.....	65
Appendix 3: Data Collection Sheet	82
Appendix 4:.....	85

LIST OF TABLES

TABLE	TITLE	PAGE
Table 4.1	Characteristic of the participants	39
Table 4.2	Table 4.2 Measurements of axillary arm circumference at baseline and after six weeks of exercise	40
Table 4.3	Measurement of mid upper arm circumference before and after six week of exercise intervention	41
Table 4.4	Measurement of elbow arm circumference at baseline and after six weeks of exercise intervention	41
Table 4.5	Measurement of mid forearm circumference before and after six week of exercise intervention	42
Table 4.6	Measurement of wrist circumference at baseline and after six week of exercise intervention	42
Table 4.7	Measurement of middle palm circumference in axillary at baseline and after six week of exercise intervention	43
Table 4.8	Measurements of lymphedema relative volume (LRV) at baseline and after 6 weeks	44
Table 4.9	Measurement of skin thickness in upper arm	44
Table 4.10	Measurement of tissue thickness in upper arm	46
Table 4.11	Measurement of skin thickness in forearm	47
Table 4.12	Measurement of tissue thickness in forearm	47
Table 4.13	Measurement of handgrip strength test before and after six week of exercise intervention within affected and unaffected arm.	49
Table 4.14	Comparison of Visual Analog Scale between 3 participants before and after six week of intervention	50

LIST OF FIGURE

FIGURE	TITLE	PAGE
Figure 1.1	Arm lymphedema in the right arm compared to non-swollen left arm	3
Figure 2.1	Sentinel lymph node biopsy of the breast.	9
Figure 2.2	Graphical image between a normal hand and hand affected by lymphedema.	11
Figure 3.1	Seated row using elastic band	27
Figure 3.2	Triceps extension using elastic bands	28
Figure 3.3	Biceps curl using elastic band	28
Figure 3.4	Arm abduction and adduction using weight	29
Figure 3.5	Arm circumference measurement	31
Figure 3.6	Example of arm fluid volume measurement	32
Figure 3.7	Participant and the technician during ultrasound test.	33
Figure 3.8	Ultrasound image showing the skin and tissue on the ventral aspect of the forearm. The skin forms a distinct white band as the tissue is less echogenic.	33
Figure 3.9	Hand grip test during pre-test.	34
Figure 3.10	Borg rating of perceived exertion scale	35
Figure 3.11	Visual analogue scale for pain	36
Figure 4.1	Comparison between upper arm skin thickness of the three participants across the time within unaffected arm and affected arm	44
Figure 4.2	Comparison between upper arm tissue thickness of the three participants across the time within unaffected arm and affected	

	arm	
Figure 4.3	Comparison between forearm skin thickness of the three participants across the time within unaffected arm and affected arm	45
Figure 4.4	Comparison between forearm arm tissue thickness of the three participants across the time within unaffected arm and affected arm	47
Figure 4.5	Comparison between three participants of VAS across 8 weeks, 2weeks after surgery and during 6 weeks of exercise intervention.	50

Senaman Jenis Aerobik dan Rintangan Di Kalangan Wanita dengan Kanser Payudara yang Berisiko Mendapati Lymphaedema Selepas Menjalani Pembedahan: Kajian Tinjauan

ABSTRAK

Pengenalan: Kanser payudara adalah kanser utama yang sering dihadapi wanita dan penyebab kedua kematian di kalangan wanita. Penyakit kanser payudara mempunyai peratusan yang tinggi untuk mendapatkan lymphedema. Lymphedema adalah salah satu daripada komplikasi kepada pesakit kanser payudara, kerana ia boleh memburukkan lagi fizikal dan emosi pesakit kanser payudara. Latihan senaman membantu mengurangkan kesan sampingan selepas pembedahan dan membantu para pesakit untuk kembali kepada aktiviti harian mereka. **Objektif:** Tujuan kajian ini adalah untuk menentukan kebolegunaan latihan jenis aerobik dan rintangan yang ditetapkan untuk mengawal lymphedema kepada pesakit kanser payudara selepas pembedahan. **Kaedah:** Tiga pesakit yang menjalani pembedahan membuang noda limfa selepas dua minggu telah direkrut. Kumpulan rawatan ($n = 2$) disediakan dengan menggabungkan latihan aerobik (Berjalan, 40% -60% HRreserve) dan lima jenis latihan rintangan (8-15 repetisi, 2-3 set) termasuk pemanasan dan menyejukkan badan selama enam minggu. Kumpulan kawalan ($n = 1$) hanya meneruskan senaman kekuatan pasif yang disediakan oleh fisioterapi Hospital Universiti Sains Malaysia (HUSM). Lilitan lengan, isipadu cecair lengan, ketebalan kulit dan tisu, ujian kekuatan lengan, dan skor rasa sakit telah diuji sebelum dan selepas enam minggu membuat latihan untuk kedua-dua kumpulan. Untuk kumpulan rawatan untuk mengakses intensiti senaman skala Borg-rating dan skala sakit telah digunakan. **Keputusan:** Keputusan tidak menunjukkan perbezaan yang ketara dalam setiap pengukuran. Walau bagaimanapun, setiap pengukuran menunjukkan perubahan yang baik. **Perbincangan:** Kesakitan yang dialami oleh pesakit kanser payudara selepas pembedahan boleh dikurangkan dengan aktiviti fizikal. Intensiti aktiviti fizikal mempengaruhi masa

penyembuhan. Menggabungkan latihan aerobik dan rintangan membantu dalam melambatkan atau mengawal lymphedema Kesimpulan: Kajian ini menyediakan maklumat berharga mengenai latihan aerobik dan rintangan yang dalam mengawal perkembangan lymphedema kepada pesakit kanser payudara selepas pembedahan. Dalam kajian penerokaan ini, kami mendapati bahawa menggabungkan latihan aerobik dan rintangan membantu dalam mengawal lymphedema lengan, meningkatkan kekuatan lengan dan mengurangkan kesakitan selepas pembedahan membuang limfa nodal.

Aerobic and Resistance Exercises in Post-Operative Breast Cancer Participants at Risk of Lymphedema: An Exploratory Study

ABSTRACT

Introduction: Breast cancer is the most common cancers affecting women and the second leading cause of death among women. Breast cancer survivor have high percentage to get arm lymphedema. Lymphedema is one of the most troubling complications to in breast cancer survivors, because it can worsen the physical and emotional strain in breast cancer survivors. Exercises help to decrease side effects after surgery and help participants get back to their daily activities. Objective: The purpose of this study is to determine the applicability of prescribed aerobic and resistance exercises to control the development of lymphedema in post-operative breast cancer participants. Method: Three patients with two weeks of post left axillary clearance surgery were recruited. Treatment group (n=2) was provided with combine aerobic training (Walking, 40%-60% HR_{reserve}) and five type of resistance exercise (8-15 reps, 2-3 sets) include warm-ups and cool down for six weeks. While control group (n=1) only continue with passive strength exercise that provided by physiotherapy of Hospital University Sains Malaysia (HUSM). Arm circumference, arm fluid volume, skin and tissue thickness, arm strength test, and pain score was tested before and after six weeks of exercise intervention for both group. For treatment group to access the exercise intensity Borg-rating scale and pain scale were used. Results: Result showed no significant differences in each of the measurement. However, each of the measurement showed good trend. Discussion: Pain level on post-operative breast cancer survivor can be reduces by physical activity. Intensity of the physical activity influences the timing of the pain to reduce.

Combine aerobic and resistance training do help in slow down or managing the arm lymphedema compare to passive strength exercise only. Conclusion: Current study provides valuable information regarding the prescribed aerobic and resistance exercises to control the development of lymphedema in post-operative breast cancer participants. In this current exploratory study, we found that combine aerobic and resistance training do help in delay arm lymphedema, improve arm strength and reduce pain after post-operative unilateral axillary clearance surgery.

CHAPTER 1: INTRODUCTION

1.1 Introduction

Normally, human cells grow and divide to form new cells as the body needs them. When cells grow old or become damaged, they die, and new cells take their place. **Cancer** develops when cells failed to fulfil normal controls of cell division and multiply abnormally and have the potential to invade or spread to other parts of the body (Marrieb *et al.*, 2012). It can start almost anywhere in the human body, which is made up of trillions of cells. Cancer cells can induce nearby normal cells to form blood vessels that supply tumors with oxygen and nutrients, which they need to grow (Marrieb *et al.*, 2012). These blood vessels also remove waste products from tumors. Cancer cells are also often able to evade the immune system, a network of organs, tissues, and specialized cells that protect the body from infections and other conditions. Although the immune system normally removes damaged or abnormal cells from the body, some cancer cells are able to “hide” from the immune system.

Cancer is not a single condition based on a single organ system; on the contrary, there are over 200 different type of cancer (National Cancer Institute, retrieved 2017). From Cancer Index Malaysia (2017), about 21,700 people died from cancer in 2012 and breast cancer is the top cancer type affecting both men and women in Malaysia. Breast cancer is a major global health problem and the leading cause of death among women of all ethnic backgrounds (Breast Cancer Index, 2017). Each year, an estimated 1.6 million new participants are diagnosed worldwide and in 2015, 560,000 women will die of breast cancer each year (2005-2007) (World Health Organisation & National Cancer Registry of Malaysia 2005-

2007). Malaysian Oncology Society (2017) stated that in 2012, breast cancer was the most common form of cancer affecting women in Malaysia. About one in 19 women in this country are at risk, compared to one in eight in Europe and the United States (Malaysian Oncology Society, 2017). Hence, it is important for the health care professional to provide the best treatment for breast cancer patients. Hence, it is important for the health care professional to provide the best treatment for breast cancer patients.

Treatment of most cancers requires several approaches depending on the type and stage of the cancer. It is different for each person. Treatment depends on the type of cancer, location, drugs and dose, and patient's general health (Nokhandani *et al.*, 2015). Treatments for breast cancer vary and include drug therapy, radiation, hormonal therapy, chemotherapy and surgery (Nokhandani *et al.*, 2015). Surgery may be done for different reasons, such as to 1) remove as much of the cancer as possible (breast-conserving surgery or mastectomy), 2) restore the breast's shape after the cancer is removed (breast reconstruction), 3) relieve symptoms of advanced cancer or to find out whether the cancer has spread to the lymph nodes under the arm (sentinel lymph node biopsy or axillary lymph node dissection) (American Cancer Society, 2017).

Surgical dissection of lymph nodes and vessels challenges the remaining lymphatic system. In some participants, although the participant underwent limited axillary surgical removal, as in a lumpectomy, participants will also develop lymphedema (Kelly, 2002). People with breast cancer have at least two or three lymph nodes removed from under each arm. If the cancer has spread, the most likely area to be infected first would be the underarm lymph nodes because they drain lymphatic fluid from the breast (Kelly, 2002). Surgery will cut off or damage some

of the nodes and vessels through which lymphatic fluid drain, thus stemming the spread of cancer. Over time, the flow of lymphatic fluid can overwhelm the remaining pathways, resulting in a backup of fluid into the body's tissues, which result in lymphedema (Figure 1).



Figure 1.1: Arm lymphedema in the right arm compared to non-swollen left arm

Lymphedema is an abnormal accumulation of lymph fluid caused by excess of tissue fluid and poor centripetal lymph drainage due to damages at the lymphatic collector wall (Olszewski, 2008). In simpler terms, lymphedema is an accumulation of excess fluid in any body part that has experienced damage to the lymphatic system.

Left untreated, lymphedema leads to chronic inflammation, infection and hardening of the skin that results in further lymph vessel damage and distortion of the shape of affected body parts (Foldi *et al.*, 2005; Olszewski, 2010). Lymphedema complications can be long-lasting with no known cure (Cheifetz & Haley, 2010). Therefore, treatment of lymphedema is very crucial for a person's well-being.

Following surgery for breast cancer patients, not only are they faced with possible issues of lymphedema, they also experience long-term problems at the arm

on the side affected by cancer. Symptoms include discomfort and pain, shoulder stiffness and reduced range of movement, weakness of shoulder muscles, and swelling of the arm (Cheifetz, 2010). These impairments can impact on daily functional activities and health-related quality of life (Cheifetz & Haley, 2010). Report of lymphedema was as high as 80% in two years after breast cancer diagnosis (Norman *et al.*, 2009). With the high probability of lymphedema occurrence, strategies to prevent, reduce or control lymphedema are required to maintain quality of life and normal function. Therefore, a professional health care team may be required to assist the breast cancer patient's post-surgery.

One potential health care service to counteract lymphedema and post-surgery arm issues is exercise. A supervised exercise program for lymphedema patients may control swelling, reduce the arm fluid volume, increase muscle strength, restore range of motion (ROM) (Cheifetz 2010). Exercise has the potential to facilitate lymphedema control by resetting the sympathetic tone of the lymphatic vessels and activate the lymph flow (Johansson *et al.*, 2013, Roddie, 1990, Olszewski and Engeset, 1980).

Exercises help to decrease side effects of the surgery and help participants get back to their daily activities (American Cancer Society, 2017). Researchers have found that aerobic exercises enhanced cardiovascular fitness, provided effective weight management, and improved overall health and wellbeing, all of which are very beneficial to people with lymphedema from all causes (Kwan *et al.*, 2011). Resistance exercises were also related to reduced lymphedema, with improvements in self-esteem, physical fitness, body composition, and quality of life (Cheifetz, 2010). These studies suggest that progressive resistance exercise could be safely conducted at any time interval following surgery for breast cancer patients

(Kilbreath *et al.*, 2006). Although, exercise regimens combining aerobic and resistance exercises appear safe, larger and more rigorous studies are required (Kwan *et al.*, 2011). Furthermore, exercises can be safe for cancer survivors when it is prescribed appropriately (Cramp & Daniel, 2008, Holmes *et al.*, 1997, Newton *et al.*, 2015). With this study, we aim to investigate the potential of combined aerobic and resistance exercises as a treatment to prevent and control lymphedema at the unilateral post-operative arm in breast cancer patients.

1.2 Problem Statement

Studies on exercise for breast cancer patients are beneficial to improve morbidity outcomes and to enhance quality of life. However, prescribed exercises are not part of the breast cancer professional medical team's services. Also lacking are studies of prescribed exercises in early post-operative breast cancer patients. Therefore, we may be omitting a very efficient and beneficial treatment from breast cancer patients by not prescribing individual exercises. With this study, we are able to debunk myths regarding benefits/harm of early exercises in post-operative breast cancer patients.

1.3 Purpose of Study

The main aim of this research is to determine the benefits and tolerance of early prescribed, combined aerobics and resistance exercises in post-operative breast cancer patients.

1.4 Objectives of Study

1.4.1 General objective:

To determine the applicability of prescribed aerobic and resistance exercises to control the development of lymphedema in post-operative breast cancer participants.

1.4.2 Specific Objective:

1. To compare bilateral **arm circumference** changes in post-operative breast cancer patients before and after prescribed exercises and with the control group.
2. To compare bilateral **arm fluid volume** changes in post-operative breast cancer patients before and after prescribed exercises and with the control group.
3. To compare the bilateral **handgrip strength** in post-operative breast cancer patients before and after prescribed exercises and with the control group.
4. To assess **arm tissue** development in post-operative breast cancer patients' operated arm after prescribed exercises and with the control group.
5. To assess the **difficulty and pain score** related to the prescribed exercises in post-operative breast cancer patients and with the control group.

1.5 Hypotheses

H_{01} : There are no significant arm circumference changes in post-operative breast cancer patients with prescribed exercise.

H_{A1} : There are significant arm circumference changes in post-operative breast cancer patients with prescribed exercise.

H_{02} : There are significant fluid volume changes in post-operative breast cancer patients with prescribed exercise.

H_{A2} : There are no significant fluid volume changes in post-operative breast cancer patients with prescribed exercise.

H_{03} : There are significant differences on handgrip strength in post-operative breast cancer patients before and after prescribed exercises.

H_{A3}: There are no significant differences on handgrip strength in post-operative breast cancer patients before and after prescribed exercises.

H₀₄: There are significant differences on arm scar tissue development in post-operative breast cancer patients' operated arm after prescribed exercises.

H_{A4}: There are no significant differences on arm scar tissue development in post-operative breast cancer patients' operated arm after prescribed exercises.

H₀₅: There are significant differences on difficulty and pain score related to the prescribed exercises in post-operative breast cancer patients.

H₀₅ There are significant differences on difficulty and pain score related to the prescribed exercises in post-operative breast cancer patients.

1.6 Significance of Study

The present study adds to the limited knowledge in the field of exercise science by examining a combination of prescribed aerobic and resistance exercises to control lymphedema development in post-operative breast cancer patients. The outcomes of this study will inform on the possible application of exercise to help reduce and manage lymphedema symptoms and possibly prevent severe lymphedema occurrence in the short-term period post-operation. Overall, this study will help inform on the possible exercise guidelines to treat or delay lymphedema and improve physical health of breast cancer patients after surgery.

CHAPTER 2: LITERATURE REVIEW

2.1 Breast Cancer

Breast cancer is the most common cancers affecting women (Boer *et al.*, 2017), around 1 in 8 women in developed countries (Saunders and Jassal, 2009; Hong and Dong, 2014; Attard *et al.*, 2016) and the second leading cause of death among women (Ferley *et al.*, 2010; Stewart and Bill, 2014 Rahib *et al.*, 2014). Each year, an estimated 1.6 million new participants are diagnosed with breast cancer worldwide (World Health Organisation & National Cancer Registry of Malaysia 2005-2007) and this results in an increase in frequency of death caused by breast cancer (Al Hakk *et al.*, 2002). In the United States, women account for more than 40,000 deaths each year because of breast cancer (Al-Hajj *et al.*, 2002; Saunders and Jassal, 2009; Attard *et al.*, 2016). Whilst it is predominantly a disease of older women, it can be occurring in women under 30s years of age (Al-Hajj *et al.*, 2002; Albert, 2016).

Cancers are believed to involve a series of sequential mutations of cell growth that occur as a result of genetic instability and or environmental factors with the potential to invade or spread any part of the human body (Aubele, 1999; Golub, 2001). Breast cancer most often involves glandular breast cells in the ducts or lobules (Kossir, 1999, Kelly, 2002). Breast cancer symptoms include swelling of all or part of a breast (even if no distinct lump is felt), skin irritation or dimpling, breast or nipple pain, nipple retraction (turning inward), redness, scaliness, or thickening of the nipple or breast skin, nipple discharge (Senkus *et al.*, 2013). The most common symptom of breast cancer is a new painless lump (Holmes *et al.*, 2005). A tissue mass that is hard and has irregular edges is more likely to be cancerous, but breast cancers can be tender, soft, or rounded (Melody *et al.*, 1999). They can even be painful. Sometimes cancer at the breast can spread to lymph nodes under the arm or around the collar bone and cause a lump or swelling there, even before the original

tumor in the breast tissue is large enough to be felt. Swollen lymph nodes should also be checked by a health care provider to eliminate the possibility of breast cancer (Cordoso *et al.*, 2012)

Treatment of most cancers requires several approaches depending on the type and stage of the cancer. It is different for each person. Treatment depends on the type of cancer, location, drugs and dose, and patient's general health (Al-Hajj *et al.*, 2013). Treatments for breast cancer vary and include drug therapy, radiation, hormonal therapy, chemotherapy and surgery (Nokhandani *et al.*, 2015). Surgery may be done for different reasons. However, surgery is a must to remove as much of the cancer cell from the infected organ and lymph node (American Cancer Society, 2017). Early and timely treatment can lead to better survival and delays in treatment may lead to death (Hong and Dong, 2014).

2.2 Lymphedema

People who have breast cancer, they need to undergo a surgery especially in stage 3 and 4. During surgery they will likely have one or more lymph nodes removed from under their arm (Kelly, 2002; Mehrara, 2017). This will result with secondary **lymphedema** (Armer, 2005; Armer and Stewart, 2010; Mehrara, 2017). **Lymph nodes** are part of the immune system, which protects your body against infection and disease (Kelly, 2002). There are small rounded organs that are clustered in many areas of the body. They are connected to one another by lymph vessels, which carry a colourless fluid, called lymph (Kelly, 2002; Saunders & Jassal, 2009). The lymphatic system is part of the immune system (Saunders & Jassal, 2009). It helps protect and maintain the body fluid by filtering and draining lymph and waste products away from each body region. The lymphatic system also