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

By

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Last but not least, to my family who had all been giving me so much love, sacrifice and understanding, keeping my feet on the ground when at times I drifted away, and lifted me up high when I was down and lost. This, is for each and every single one of you.

ABSTRAK

Latar belakang dan objektif:

Limfadenopati akibat kanser payudara adalah sangat memberi kesan terhadap pesakit baik dari segi aktiviti harian, keyakinan diri dan kualiti kehidupan (Ahmed, 2006). Ia merupakan satu komplikasi yang menganggu sebahagian besar pesakit yang telah menjalani mastektomi dan pembuangan kelenjar lifa ketiak (ACS, 2006). Penelitian eksperimentasi prospektif ini bertujuan mengkaji adakah latihan senaman erobik dan ketahanan ini sesuai dan mampu mengurangkan kejadian limfedema.

Kaedah Kajian:

Ini merupakan penelitian pilot, 16 pesakit yang memenuhi kriteria telah di bahagikan secara rawak kepada dua kumpulan. 10 di kumpulan intervensi senaman, dan 6 di kumpulan kontrol. Kumpulan senaan diberikan latihan senaman erobik dan ketahanan selama enam minggu sehingga parameter berkenaan diukur semula.

Keputusan:

Hasil yang signifikan telah didapatkan dalam kumpulan intervensi, peratusan RLV ketiak pada kumpulan intervensi (0.56 (2.34)) adalah lebih rendah berbanding kumpulan kontrol (5.03 (2.84)) ($p = 0.009$) dan peratusan RLV bahgian tengah lengan atas pada kumpulan intervensi (0.93 (1.84)) lebih rendah berbanding kontrol (5.66 (10.85)) ($p = 0.005$). isipadu air lengan dalam kumpulan intervensi (3.79 (5.92)) juga lebih rendah secera signifikan berbanding kumpulan kontrol (22.36 (9.49)) ($p = 0.001$).

Kesimpulan:

Kami membuat kesimpulan bahawa kajian ini memberikan kuputusan positive berbading kumpulan kontrol dan adalah sesuai untuk diamalkan oleh pesakit.

Keywords: limfadenopati akibat kanser payudara, senaman erobik dan ketahanan

ABSTRACT

Background and Objectives:

Breast cancer related lymphadenopathy (BCL) is a serious problem that affects the activity of daily living, self-esteem and quality of life (Ahmed, 2006). BCL affects a high percentage of post mastectomy and axillary clearance patients.(ACS, 2006) This experimental exploratory study is aimed to see whether a tailored resistance and aerobic exercise applied as early as to weeks post-surgery may prevent the development of upper limb edema and whether it is feasible from the aspect of safety and applicability.

Methodology:

This is a pilot study, 16 patients fits the inclusion criteria were randomized into two arms. 10 were enrolled in the exercise groups, and 6 designate to the routine physiotherapy group. Subjects in the exercise group were prescribed resistance and aerobic exercise two weeks post-surgery and were required to comply to the regime for six weeks where the parameters were measured again.

Results:

Significant outcomes were found in the interventional group, the percentage of RLV of Axilla in intervention group (0.56 (2.34)) was significantly lower than percentage of RLV of Axilla in control group (5.03 (2.84)) ($p = 0.009$) and the percentage of RLV of Middle Upper Arm in intervention group (0.93 (1.84)) was significantly lower than percentage of RLV of Middle Upper Arm in control group (5.66 (10.85)) ($p = 0.005$). The Arm Fluid Volume in intervention group (3.79 (5.92)) was also significantly lower than the Arm Fluid Volume in control group (22.36 (9.49)) ($p = 0.001$).

Conclusions:

We conclude that this study provide positive outcomes as compared to the control group results and it is feasible to be carried out by the patients.

Keywords: Breast cancer related lymphadenopathy, aerobic and resistance exercise

Chapter One: Study Protocol

1.1 LITERATURE REVIEW

Mastectomy and axillary dissection

Breast cancer is one of the most common cancer in women and it occurs at any age with most of the cases are in the childbearing age women. Treatment for breast cancer varies and depends on its time of presentation, stage and overall patient's condition. They include pharmacological therapy, hormonal therapy, radiation therapy and surgery (1).

Mastectomy is by far the definitive standard treatment for operable breast cancer and when breast conservation surgery is not applicable. (2)

Axillary clearance or dissection is indicated in positive axillary lymph nodes involvement. It is confirmed clinically and supported with either a needle biopsy or an imaging, or both. (3). It is carefully carried out in the same setting after mastectomy of the involved breast is done.

Advancement in the approach to breast cancer surgical management has made it became less insulting to both breast and axilla. The option for sentinel lymph node biopsy has reduced the number of unnecessary axillary clearance therefore reducing the complications carried by the dissection (4).

Lymphedema

Breast cancer related lymphedema is a well-known complication of mastectomy and axillary dissection. Incidence varies and may come up to 80% within 2 years after the breast cancer diagnosis. (1) Lymphedema is an abnormal fluid collection in the limbs as a result from, either obstruction, stasis, injury to the lymphatic vessels or any disturbances to the body fluid osmotic pressure (5).

Specifically in breast cancer, the spread of cancer cells to the axillary lymph nodes may cause obstruction to the lymphatic drainage of the ipsilateral upper limb (4) even the surgery itself can cut and damage the lymphatic vessels causing disturbances in the lymphatic flow due to the direct injury or the inflammatory reaction in the surrounding tissue.

It is very important to address such complication, as it surely will affect the patient's quality of life. Patients with breast cancer related lymphedema patients reported sense of heaviness, weakness, tightness and even pain. The latter is reported up to 50% experienced and is commonly described as burning, aching, hypersensitive scars and tenderness. Lymphedema will in time, lead to chronic inflammation, infection, scleroderma and permanent distortion of the limb if it is left untreated (6). Apart from pain and discomfort, symptoms include reduce range of movement due to weakness and arm swelling (7).

These complications very much affect the quality of life of these cancer patients. Hence it is very important and crucial for the doctors and health care workers to address this matter, providing relief and solutions to this breast cancer related lymphedema.

Exercise in breast cancer related lymphedema patients.

In the yesteryears, complete rest and restriction of movement was practiced on cancer patients who underwent intensive treatment (8-10). However, this practice changed in the past 20 years with the introduction of ERAS (Early Recovery After Surgery) protocols. Patients are encouraged for early ambulation and more studies were done to prove that exercise is feasible, safe and may be included as part of recovery measures for cancer patients (8, 9, 11).

Exercise may improve one's immune system thus reducing the risk of infection (12, 13). It also helps in terms of improving the range of movement and mobility hence getting back the patients to their normal daily activities much earlier. Exercise also improves strength, particularly in the upper body, in post-surgery breast cancer patients. American Cancer Society (ACS) advocates to start stretching exercise as early as day three to day seven post-surgery day. They recommended some resistance and stretching exercise (14).

Mobility and arm strengthening are suggested to be initiated as soon as the drains are removed. This is to avoid frozen shoulder, increase strength, mobility and range of movement as well as improving posture (15, 16).

Any movements that involve large muscle groups and increase oxygen intake are known as aerobic exercise (10). Swimming, cycling, jogging and even walking are examples of aerobic exercises (17). Studies demonstrated that patients on regular aerobic exercise experience less fatigue , feels better and have higher oxygen uptake while undergoing chemo and radiotherapy (18). Aerobic exercise can improve cancer patient's quality of life (10). It also improves cardiovascular fitness, overall health and wellbeing, which is without a doubt, beneficial to patients with lymphedema (19).

Upon other benefits of exercise, specifically aerobic exercise, is the weight reduction and increase in muscle mass which in turn will improve blood and lymph circulation hence reducing the risk of developing lymphedema (11, 20).

Prescription of aerobic exercise in cancer patients is aimed to improve cardiovascular function (10) hence improving lymphatic flow and protein reabsorption where both play important roles in the management of lymphedema (11, 15).

Apart from aerobic exercise, another form of exercise recommended by the American Cancer Society is resistance exercise (19). These groups of exercises are aimed to improve strength and mobility of the upper limbs especially in post-operative breast cancer patients. It is suggested that these exercises should be initiated as early as possible as t is safe and beneficial to the patients. Combination of passive stretching with resistance exercise will reduce morbidity in breast cancer patients (16) (21).

A study on effects of resistance exercise on breast cancer patients reported that it did not increase the risk of developing lymphedema over the group which was not prescribed with the exercise regime (9). These exercises also showed no harmful effects and improved overall health and wellbeing of the cancer survivors (22

Prescribed exercise has shown benefits for breast cancer related lymphedema patients. It improves shoulder range of movement, helps in weight management, and improves muscle strength (9). It works by resetting the sympathetic tone of the lymphatic vessels, thus improving the lymphedema control (11).

A study was conducted on 14 subjects with unilateral upper limb lymphedema who completed six months breast cancer treatment (23). These 14 patients were divided into two arms, one with prescribed exercise regime (n=7) for eight weeks and showed no differences in the arms circumference measurement between these two groups. However, the exercise group reported better quality of life as compared to the non-prescribed group.

Another study conducted on eight patients with breast cancer related lymphedema who were subjected to a weekly exercise class for eight weeks showed reduction in affected arm volume with significant improvement in the quality of life (24). The duration of exercise suggested for the best results is between six to eight weeks (25).

Even though these studies gave different results for the lymphedema control, they were homogenous on the improvement in the quality of life for all subjects. Starting the exercises early can give better control and prevent the development of lymphedema after mastectomy and axillary dissection (16).

1.2 OBJECTIVES OF STUDY

General objective:

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

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 the difficulty and pain score related to the prescribed exercises in post-operative breast cancer patients and with the control group.

Significance of Study

This pilot study will add information on the role of prescribed exercise in lowering the risk of developing lymphedema in post-surgery breast cancer patients. It may also be a platform or a base for further research on the feasibility and effect of prescribed exercise in post-surgery cancer patients.

1.3 METHODOLOGY

Exploratory study design

This Pilot Study was designed to assess the feasibility of prescribed resistance and aerobic exercise as part of post-surgery lymphedema prevention and. This research is in collaboration with Breast Cancer Awareness & Research Unit (BESTARI) of Hospital Universiti Sains Malaysia (HUSM). BESTARI is a center, focused on focused on breast cancer education, awareness and consultation. Any cases related to breast cancer either from HUSM or other district hospitals will be directed to BESTARI. All post breast surgery patient is subjected to upper limb physiotherapy session. This study is aimed to find out, whether the prescribed exercise regime can produce better outcome, or at least at par with current practice.

Recruitment

Patient recruitment will be carried out with utmost sensitivity to ensure that patients do not feel forced into participating in the study or violated during treatment.

Actual recruitment will be conducted in a neutral environment space to ensure the patient is not pressured to join the research with undue stress will identify the appropriate patients based on the criteria listed in Appendix B.

Patients will be briefed regarding the aims, methods and key outcomes of the proposed study. This briefing will take place about a week prior to surgery after the potential patient has met up with their surgeon. Should the patient agree to participate in the study, she will have to sign an informed consent form. The exercise regime will start after two week of post-operation and will be carried out for six weeks.

Sampling design

Sample size calculation is not required in an Exploratory Study (26). Therefore, purposive sampling will be conducted based on the research participant criteria. A study sample of 10 patients would be enough to explore the research objectives.

Study participants

About **20** female breast cancer patients will be recruited after being identified by the surgeon as requiring unilateral mastectomy and axillary lymph node dissection. **Patients then will be randomized into exercise group (N=10) and control group (N=10).** Inclusion and exclusion criteria for the study patients are listed below.

Inclusion criteria:

1. Stage 1 - 3 breast cancer patients.
2. Age between 21 and < 60 years old.
3. Candidates for unilateral axillary clearance.
4. No other chronic diseases (example diabetes).
5. Physically able to be independently mobile and to conduct physical activity.
6. Mentally sound, able to make independent decisions and not on any psychiatric medication.
7. Medical clearance by treating physician/surgeon to participate in this study.

Exclusion criteria:

1. Have bilateral disease or bilateral axillary.
2. Undergone any other surgery of the upper limbs.
3. Undergone breast reconstruction surgery.
4. Having any neurological deficit or other injury.
5. Taking medications that affect fluid retention or excretion from the body, e.g. diuretics.

Study protocol and analysis

Baseline

During the first meeting, through medical and personal history will be documented. Age, weight, height, will be measured before surgery, after surgery and six weeks after exercise training. All the procedure will be carried out at BESTARI.

Exercise Familiarisation

Patients will be taught on how the exercise regime is carried out, what should be documented and how to report on their experience during the study. They will also be assessed on their strength and the suitable weight that they can carry. Reassessment of their ability after surgery will be conducted with the pre-exercise strength and load as a guideline. They will also be given pictograms on the exercise steps. All the meetings will take place at BESTARI.

Arm circumference measurement

Participants were asked to remove any clothing around their arms. Both arms were measured post-surgery and after 6 weeks of exercise intervention. Participants were seated with arms fully extended, pronated and supported on a table.

Circumference measurements were taken in centimeter. We started with measuring the metacarpal (palm), a point marked 2cm above the ulnar styloid (wrist), at the lateral epicondyle (elbow), 10cm distal and proximal to it (mid forearm and mid upper arm), and at the acromion (axilla). These were modified from (20).

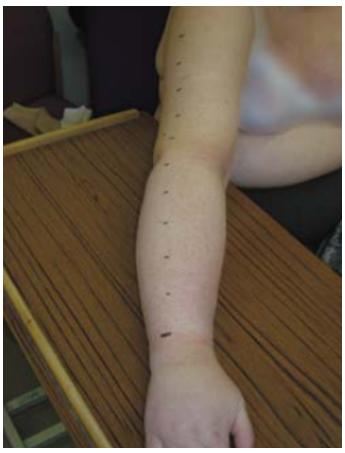


Figure 1 Arm circumference measurement for lymphedema

Arm fluid volume test

The arm volume will be measured using the water-displacement method (WDM) (22). Each arm of the patient will be submerged in a relaxed, straight position with the fist and proximal phalanges extended. A cylindrical container with a soft drainpipe 45cm above the bottom will be filled with water. Each arm needs to be submerged in the water in a straight position with the fist and the proximal phalanges resting at the bottom (Figure 3). The water displaced will be collected in a container and weighed in grams. Then contralateral arm also be measured and used as a control. Measurement will be repeated three times and averages will be calculated to the nearest 0.1 g.

The lymphedema absolute volume (27) will be obtained by calculating the difference in volume between the arm with surgery and the contralateral arm. The relative lymphedema volume (RLV), which takes the patient's body size into account, will be defined as an increase in volume of at least 5% in the post-operative surgical arm compared with the contralateral arm using the below formula (22):-

$$\frac{\text{Volume post-operative arm- volume contralateral arm}(cm^3)}{\text{Volume contralateral arm } (cm^3)} \quad X\ 100$$

Figure 2 Example of arm fluid volume measurement

Handgrip strength test

Handgrip strength test will be assessed by using a handheld dynamometer (Lafayette, USA), three times - during familiarization, after surgery, and after six weeks of exercise training. Patients were comfortably seated with arms flexed at the elbow at a 90-degree position (Figure 3). Participants were asked to squeeze the dynamometer as hard as possible with verbal encouragement. After a test, the dynamometer changed hands and the same test is repeated on the other arm. This procedure will be repeated for a total of three sets for each arm. The highest value from the three tests represented the arm strength of the patient.

Figure 3 Hand grip measurement with arm flex

Patient's self-report

Patients will be handed out the Borg-rating of perceived exertion scale and visual analog pain scale before, during and after exercise.

Borg- rating scale

Borg Scale is used to assign numbers to how patients and as a self-monitoring how hard body is working. This will help to adjust the intensity of the activity by speeding up or slowing down movements or adjust the exercise load (22).

- The exercise intensity will be assessed using Borg-rating scale
- The scale star with 6 'no exertion at all to 20 'maximal exertion'
- During exercise, for every 3-minute researcher will ask the patient about the perceived intensity of the exercise. The patient is required to mark along the line to match the level of pain that she perceives.
- If the level is above the 13 to 14 patients will be asked to reduce their pace/speed/repetition/load of the exercise. If the level is below the 12 mark, patients will be asked to increase their pace/speed/repetition/load. Adjustments will be made to ensure that the patients will exercise according to their ability.
- If there is any worsening or onset of symptoms, the exercise thought to be associated with the symptoms is skipped, or a lighter weight is used, until the symptoms cleared up.

Rating	Perceived Exertion
6	No exertion
7	Extremely light
8	
9	Very light
10	
11	Light
12	
13	Somewhat hard
14	
15	Hard
16	
17	Very hard
18	
19	Extremely hard
20	Maximal exertion

Figure 4 Borg Rating of Perceived Exertion Scale

Pain Index

- The level of pain will be assessed using the Visual Analogue Scale
- The scale is 10 cm long with 'no pain' at one end, and 'the most pain imaginable' at the other end.
- The patient is required to mark with a pen along the line to match the level of pain that he or she perceived.

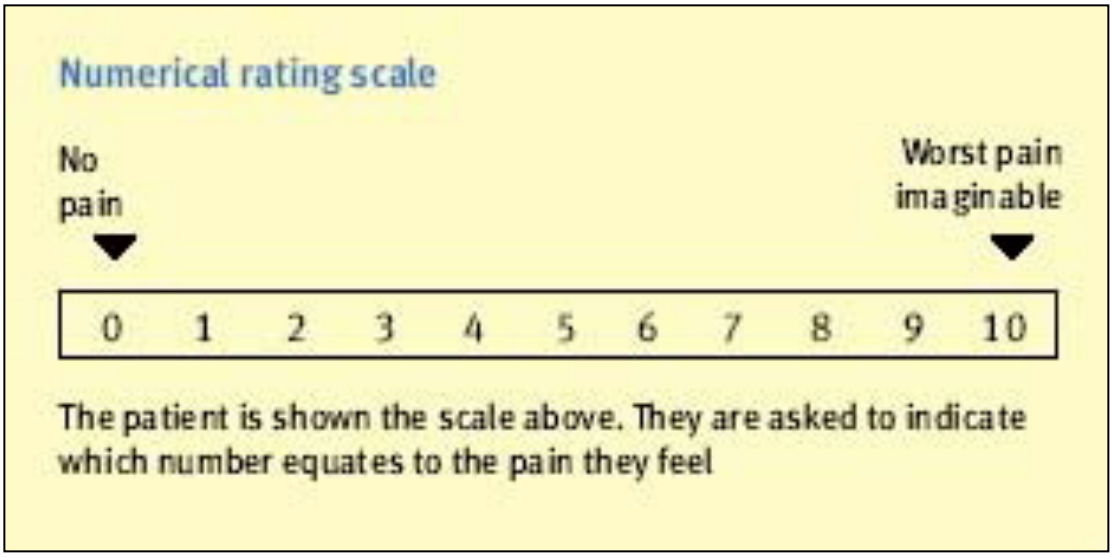


Figure 5 Visual Analog Scale

Exercise prescription

The prescribed exercise program will start after 2 weeks post-operation. At the first 2 weeks of our exercise program, subjects will be guided and monitored in our exercise and sports science laboratory, three to four times a week. Warm-ups, cool-downs steps will be taught. Then, from week 3 onwards, patients are encouraged to carry out the same exercises at their own home with self-reports and adjustments as necessary.

Progression of exercises will be conducted at the fourth week with another visit to our exercise and sports science laboratory. The researcher will also visit the homes of patients, if allowed and possible, to monitor their exercises. Patients who want to be in USM for their exercises for the whole 6 weeks are highly encouraged to ensure careful exercise monitoring. Family members of the patients who are interested to join the exercises are also encouraged. All self-reports and self-monitoring of exercise at home will be collected after 6 weeks of the program.

Aerobic training

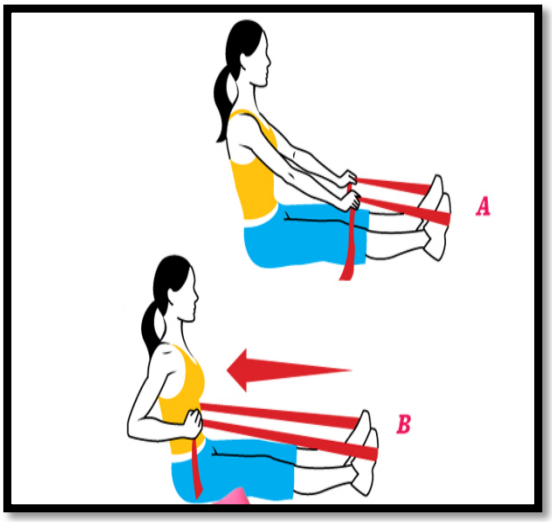
Subjects will be required to conduct low to moderate intensity activity (e.g. walking) for 5 to 30 minutes three times per week. Aerobic session starts with 5 min, then progress to 40 min by the end of 6 weeks. Low to moderate intensity is monitored at 40-60 % $HR_{reserve}$.
($HR_{reserve}$ = (HR_{max} - $HR_{rest)}$ x %intensity + HR_{rest}). Subject's exertion will also be recorded on the Borg scale (8-12 consider low to moderate, 13- 14 consider moderate to hard) and if patients experience any discomfort during the exercise, adjustment will be made accordingly during the visit session.

Resistance training

Resistance exercise will be carried out using exercise resistance bands and free weights. Subjects will be required to perform of 5-15 repetitions for 2-3 sets per day on alternate days with aerobic training for 6 weeks. The activities are repeated with reassessment of load every two weeks to maintain a participant's rating of minimal 14 (between somewhat hard and hard) on the Borg scale for the exercise. Exercises will be stopped when there is acute, sharp pain or causing major discomfort to the subjects.

The types of resistance band exercise in the 5 stations are as follow:

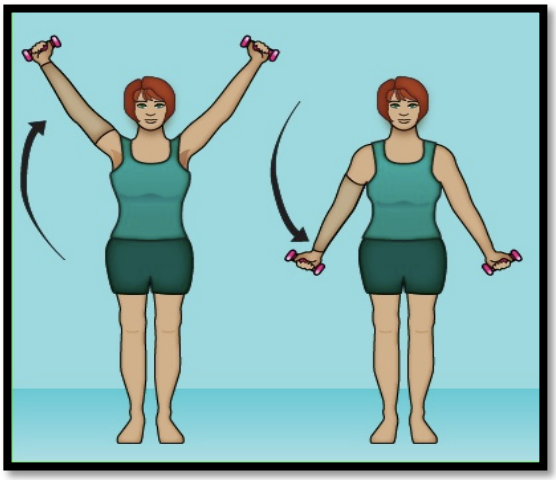
1) seated row
2) triceps extension
3) bicep curl
4) shoulder abduction
5) shoulder adduction (Johansson and Piller, 2007).



1. Seated row using elastic band

2. Triceps extension using elastic bands

3. Biceps curl using elastic band



4. Arm abduction and adduction using weight

Statistical analysis

Descriptive data of participants will be reported as means and standard deviation. All data were stored in a common database and analysed using Statistical Package for Social Science (SPSS) Version 22.0. Data will be assessed for normality of distribution. In determining the differences in lymphedema parameters pre- and post-exercise, we will use paired t-test for post-operative arm changes across time (within groups) and between the experimental group and control group (between group). We will use equivalent non-parametric tests if the data distribution is not normal. Statistical significance is set at p-value less than 0.05. Nonparametric tests will be performed, two will be used which were the Mann-Whitney U test, and Wilcoxon's test. The former is to compare the changes between the interventional and control groups and the later is to compare before and after the intervention.

Potential Risk to Patients

This exercise program is used as a guide and will be adjusted according to subjects' self-report of pain or discomfort in their affected arm. Should the patients report any worsening or onset of lymphedema symptoms, adjustments will be made on the regime until the symptoms improve and resolve.. As patients will have follow-up visits post-operation, their participation in this study will be made known to their treating physician/surgeon that will provide a neutral and unbiased assessment if the patient is advised to continue/discontinue their participation in the study. There are no reported risk to spouse or partner or close family member following participation in this study. The research team involved with experts from related fields such as clinical exercise expertise (Dr Vina Tan Phei Sean), Senior Lecture and surgeon of breast cancer (Dr Maya Mazuwin Bt Yahya), and Senior staff nurse of Breast Cancer Awareness & Research Unit of HUSM (Pn. Roslaini bt Che Romli).

Vulnerability

Patients will be reassured that at any time, should they choose to quit the program, they would still have the same quality and professional care that they are entitled to without any bias or prejudice. This statement will also be pointed out in the informed consent form that is required for their participation.

Benefits

Apart from the fitness, health and experimental values expected from this program, the process of gathering, recruiting and experiencing the same routine will help them improve their well-being and social interaction by knowing that there are others in the same tribulations as they are. Confident level is expected to be boosted and patients may improve in their daily activities.

Community sensitivities

The diagnosis of breast cancer and the treatment that follows are life-changing events that affect not only the patient but their families as well. The word cancer itself is somewhat a taboo to be freely said and must be explained to patients meticulously. Signing up for this study may not be the priority and this study may be an intrusion rather than a positive action to be doing something to contribute to the understanding of lymphedema development post-operation. Thus, we will always emphasize that their participation is entirely voluntary and the purpose of our interest to conduct this study. The data collection will be conducted in a closed laboratory and only by the designated researchers.. Furthermore, we understand the discomfort and stigma that may be attached to breast cancer patients and the patients' medical condition will be kept confidential to avoid unnecessary stress and anxiety. In addition, patients' privacy will be respected at all times throughout the study and even after the conclusion of the study.

Confidentiality and Privacy

Patients will be identified by a patient number. No identifiable data will be shared publicly. The information will be used for research purpose only and will be encrypted in a password protected medium. The data will be retained by the researchers for knowledge purposes only. Neither the name nor any identifying information will be used in any publication or presentation resulting from this study. Permission from patients will be obtained before any videos or photographs are taken.

Ethical considerations

1. Research will be conducted upon approval by Jawatankuasa Etika Penyelidikan Manusia (JEPeM) USM and National Medical Research Register (NMRR)

2. Permission for data collection after NMRR approval.

3.Confidentiality of the data will be maintained at highest level as possible.

4.Only researcher will have the access to the data

Conflict of interest

There is no conflict of interest pertaining to this study.

Gantt chart and research activities

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Proposal preparation, presentation, ethical approval																		
Data collection																		
Data analysis																		
Report writing																		
Submission																		

1.4 REFERENCES

1. Norman SA, Localio AR, Potashnik SL, Torpey HAS, Kallan MJ, Weber AL, et al. Lymphedema in breast cancer survivors: incidence, degree, time course, treatment, and symptoms. Journal of Clinical Oncology. 2009;27(3):390.
2. Armer JM, Stewart BR. Post-breast cancer lymphedema: incidence increases from 12 to 30 to 60 months. Lymphology. 2010;43(3):118-27.
3. Noguchi M, Katev N, Miyazaki I. Diagnosis of axillary lymph node metastases in patients with breast cancer. Breast cancer research and treatment. 1996;40(3):283-93.
4. Giuliano AE, Hunt KK, Ballman KV, Beitsch PD, Whitworth PW, Blumencranz PW, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. JAMA. 2011;305(6):569-75.
5. Olszewski WL, Jain P, Ambujam G, Zaleska M, Cakala M, Gradalski T. Tissue fluid pressure and flow in the subcutaneous tissue in lymphedema - hints for manual and pneumatic compression therapy. Phlebolymphology. 2010;17:144-50.
6. The International Lyphoedema Framework. Compression Therapy: A position document on compression bandaging 2005 [Available from: https://www.lympho.org/wp-content/uploads/2016/03/Compression-bandaging-final.pdf
7. Hayes S, Janda M, Cornish B, Battistutta D, Newman B. Lymphedema secondary to breast cancer: how choice of measure influences diagnosis, prevalence, and identifiable risk factors. Lymphology. 2008;41(1):18-28.
8. Letellier M-E, Towers A, Shimony A, Tidhar D. Breast Cancer-Related Lymphedema: A Randomized Controlled Pilot and Feasibility Study. American Journal of Physical Medicine & Rehabilitation. 2014;93(9).
9. Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, GalvÃO DA, Pinto BM, et al. American College of Sports Medicine Roundtable on Exercise Guidelines for Cancer Survivors. Medicine & Science in Sports & Exercise. 2010;42(7).
10. Courneya KS, Jones LW, Peddle CJ, Sellar CM, Reiman T, Joy AA, et al. Effects of aerobic exercise training in anemic cancer patients receiving darbepoetin alfa: a randomized controlled trial. The oncologist. 2008;13(9):1012-20.
11. Kwan ML, Cohn JC, Armer JM, Stewart BR, Cormier JN. Exercise in patients with lymphedema: a systematic review of the contemporary literature. Journal of cancer survivorship : research and practice. 2011;5(4):320-36.
12. Scheffer DdL, Latini A. Exercise-induced immune system response: Anti-inflammatory status on peripheral and central organs. Biochim Biophys Acta Mol Basis Dis. 2020;1866(10):165823-.
13. Fairey AS, Courneya KS, Field CJ, Bell GJ, Jones LW, Mackey JR. Randomized controlled trial of exercise and blood immune function in postmenopausal breast cancer survivors. Journal of applied physiology (Bethesda, Md : 1985). 2005;98(4):1534-40.

14. American Cancer Society. Physical Activity and the Cancer Patient 2014 [Available from: https://www.cancer.org/treatment/survivorship-during-and-after-treatment/staying-active/physical-activity-and-the-cancer-patient.html
15. Cheema BS, Gaul CA. Full-body exercise training improves fitness and quality of life in survivors of breast cancer. Journal of strength and conditioning research. 2006;20(1):14-21.
16. Kilbreath SL, Refshauge KM, Beith JM, Ward LC, Simpson JM, Hansen RD. Progressive resistance training and stretching following surgery for breast cancer: study protocol for a randomised controlled trial. BMC Cancer. 2006;6:273-.
17. Jönsson C, Johansson K. The effects of pole walking on arm lymphedema and cardiovascular fitness in women treated for breast cancer: a pilot and feasibility study. Physiotherapy Theory and Practice. 2014;30(4):236-42.
18. Galvão DA, Taaffe DR, Spry N, Joseph D, Newton RU. Combined resistance and aerobic exercise program reverses muscle loss in men undergoing androgen suppression therapy for prostate cancer without bone metastases: a randomized controlled trial. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2010;28(2):340-7.
19. American College of Sports Medicine Position Stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. Medicine and science in sports and exercise. 1998;30(6):975-91.
20. Ahmed RL, Thomas W, Yee D, Schmitz KH. Randomized controlled trial of weight training and lymphedema in breast cancer survivors. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2006;24(18):2765-72.
21. Kilbreath SL, Refshauge KM, Beith JM, Ward LC, Lee M, Simpson JM, et al. Upper limb progressive resistance training and stretching exercises following surgery for early breast cancer: a randomized controlled trial. Breast Cancer Research and Treatment. 2012;133(2):667-76.
22. Johansson K, Piller N. Weight-bearing exercise and its impact on arm lymphoedema. Journal of Lymphoedema. 2007;2(1):15-22.
23. McKenzie DC, Kalda AL. Effect of upper extremity exercise on secondary lymphedema in breast cancer patients: a pilot study. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2003;21(3):463-6.
24. Bracha J, Jacob T. Using exercise classes to reduce arm lymphoedema. Journal of Lymphoedema. 2010;5(1):46-55.
25. Hornsby WE, Douglas PS, West MJ, Kenjale AA, Lane AR, Schwitzer ER, et al. Safety and efficacy of aerobic training in operable breast cancer patients receiving neoadjuvant chemotherapy: a phase II randomized trial. Acta oncologica (Stockholm, Sweden). 2014;53(1):65-74.
26. Whitehead AL, Julious SA, Cooper CL, Campbell MJ. Estimating the sample size for a pilot randomised trial to minimise the overall trial sample size for the external pilot and main trial for a continuous outcome variable. Stat Methods Med Res. 2016;25(3):1057-73.
27. Warren AG, Janz BA, Slavin SA, Borud LJ. The Use of Bioimpedance Analysis to Evaluate Lymphedema. Annals of Plastic Surgery. 2007;58(5).

Appendix 1. Data collection sheet 1

PARTICIPANT'S I.D: _____ : _____
Cancer side.: _____ AGE: _____

1. Arm Circumference measurements

Location	Pre (date)	Post (date)
Axillary		
Mid upper arm		
Elbow		
Mid forearm		
Wrist		
Palm		

2. Arm fluid volume measurement

	Pre	Post
Valume of Water dripping from cylindrical container		

3. Hand grip strength test

Hand grip strength test	1	2	3	average
Pre				
Post				

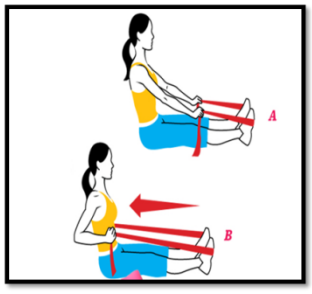
Appendix 2. Data collection sheet 2

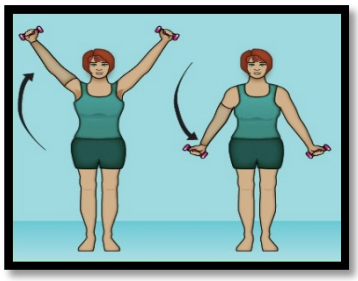
PARTICIPANT'S I.D: _____ GENDER: _____

Cancer stage.: _____ AGE: _____

DATE: _____

TIME:_____

WEEK1						
EXERXISE	**VOLUME/REPETITION/WEIGHT**			**HEART RATE (after)**	**Perceived exertion**	**Pain score**
Aerobic						
Seated row using elastic band 						

Triceps extension 						
Biceps curl using elastic band 						
Arm abduction and adduction using weight 						
WEEK2						
EXERXISE	**VOLUME/REPETITION/WEIGHT**			**HEART RATE (after)**	**Perceived exertion**	**Pain score**