Effects of a manual therapy program to reduce the evolution time of axillary web syndrome in women affected by breast cancer.

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TABLE OF CONTENTS

GENERAL INFORMATION

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ABSTRACT

Breast cancer is the most common malignant tumor in women, with more than a million new cases annually. One of the most frequent surgical and post-actinic sequelae and well known is postmastectomy lymphedema. The axillary web syndrome is another sequel that limits the functionality of the patient and delays the protocol times of application of treatments cancer, and in many cases this sequela is misdiagnosed. This surgical sequelusually disappears spontaneously after the third month of appearance, but this implies a long period of discomfort and limitations for the user, at the same time that it may delay the application of Radiotherapy within the indicated protocol deadlines (due to the need for a body posture with abduction and flexion of the affected upper limb for its application and with the lymphatic thrombus is impossible to get).

With the present quasi-experimental study, the investigator intend to show that the application of Kinesitherapy and stretching from the beginning of the appearance of the cord, in a controlled and scheduled way by the physiotherapist, it is possible to reduce the time in which the lymphatic thrombus is present, and therefore, recover functionality, mobility, reduce pain and be able to apply the patients´ treatments within of the established deadlines. The investigator intend to apply this therapy in the intervention group and compare thrombus evolution times with the control group.

QUALIFICATION

Effects of a manual therapy program to reduce the evolution time of axillary web syndrome in women affected by breast cancer.

BACKGROUND AND CURRENT STATUS OF THE STUDY TOPIC

Breast Cancer is the most common tumor in women around the world, and is one of the leading causes of death among women in developed countries (1).

It is an important Public Health problem, since according to the World Health Organization more than a million new cases are diagnosed annually, becoming almost a quarter of malignant tumors in females (2). In the West, it has been shown that one in nine to twelve women will suffer from the disease in her lifetime (3).

Most cases occur in postmenopausal women, and the main age at diagnosis is around 60 years (4).

After the diagnosis of breast cancer, the patient undergoes surgical and / or cancer treatment. Chemotherapy, radiotherapy and hormonal therapy are some of the treatment alternatives, which currently are precisely adapted to the type of tumor seeking a better response and survival (5).

Postmastectomy lymphedema is one of the best-known postsurgical and post-actinic sequelae after breast cancer, with a prevalence of around 20% of mastectomized women (6). The conservative treatment of this health problem is based on Decongestive Physical Therapy and Kinesitherapy (7,8). Pneumatic Multicompartmental Pressotherapy helps reduce the feeling of heaviness and stiffness of edema (9).

In addition to postmastectomy lymphedema, the patient undergoing surgery for breast cancer may present Axillary Web Syndrome (AWS) or superficial lymphatic thrombosis. As described by W.M. Yeung et al. In their systematic review (10), it can appear in the first eight weeks after the operation and usually resolves spontaneously within three months of its appearance (11).

The lymphatic thrombus is clinically manifested as a cord that frequently occurs in the armpit, although it can also appear along the upper limb, elbow crease even reaching the first finger (10, 12, 13). Regarding the diagnosis through imaging tests, nuclear magnetic resonance does not manage to clearly identify the axillary network syndrome, being ultrasound the most reliable method, due to the dynamism that can be applied to the patient's arm while the diagnostic test is being carried out (12, 14).

The axillary network syndrome produces pain when abducting and flexing the shoulder, with the respective loss of functionality and limitation of mobility of the affected upper limb (19).

According to the American Cancer Society, radiation therapy is applied 3-8 weeks after the operation if chemotherapy is not required. If chemotherapy is used, it is applied 3-4 weeks after completion. It is usually applied 5 days a week from Monday to Friday.

The limitation of mobility often leads to a delay in the application of this useful tool in the oncological therapeutic arsenal to prevent recurrences (20, 21, 22, 23). Hence, the need and importance of this study, where the investigator intend to demonstrate that the evolution times of the lymphatic thrombus can be reduced with assisted passive kinesitherapy and stretching.

At present, there are some publications that show possible alternatives of physiotherapy treatment for lymphatic thromb. Many are interventions with a very small sample (even on a case-by-case basis) (24, 25). Others are observational studies or even studies older than five years. There are some studies that combine manual lymphatic drainage (Vodder method) with physical therapy (strengthening, stretching, soft tissue work) with good results (26).

There is ambiguity in the relationship-association between the appearance of lymphatic thrombosis and lymphedema of the ipsilateral limb. Patients who have developed AWS are 44% more likely to develop postmastectomy lymphedema (27). There are other studies that do not find a relationship between the two (28).

The frequency of the AWS is not clear from the current posts. It depends on the type of surgical intervention, age, BMI (16), the appearance of the postoperative seroma, and even breast reconstruction (17). Thus being the frequency 30% of the operated patients (10, 18).

After reviewing the relevant literature, it should be noted that there are very few studies and therefore little evidence on the treatment of AWS. It is not possible to prescript of a clear treatment in a clinical practice guide for this postsurgical sequela. Most publications highlight the importance and need for more research to determine the etiopathogenesis and useful treatment for this health issue (10, 13).

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OBJECTIVES

GENERAL OBJECTIVES

I. Determine a preliminary exploration of the magnitude of the effect of a kinesitherapy and stretching intervention for the functional recovery of the upper limb, the recovery of the surgical scar and the improvement of the quality of life in women who have suffered from breast cancer.

II. Create a scale to objectively classify the axillary thrombus (based on its clinical manifestations).

SPECIFIC OBJECTIVES for general objective I:

- Check the intervention of assisted passive kinesitherapy and stretching for the improvement of the range of joint mobility of the affected limb in the shortest possible time.
- Analyze the reduction of pain and increase of the degree of functionality of the ipsilateral upper limb in patients with AWS after the intervention.
-Determine the impact of the physiotherapeutic intervention on the quality of life of a mastectomized woman with lymphatic thrombus.
-Analyse the physiotherapeutic intervention reduction of the time on the evolution of the Superficial Lymphatic Thrombus and the application of Radiotherapy within the terms established in the oncological protocols.

SPECIFIC OBJECTIVES for general objective II:
- Create a scale to objectively classify the axillary thrombus (based on its clinical manifestations).

METHODOLOGY
TYPE OF STUDY

Quasi-experimental, prospective study.

STUDY POPULATION

The study sample is made up of patients undergoing surgery for Breast Cancer who attend the Lymphedema Unit of the A.G.S. Campo de Gibraltar Oeste presenting Lymphatic Thrombus after the operation, the recruitment period being from December 2021 to December 2023.

CALCULATION OF SAMPLE SIZE

To calculate the sample size, the prevalence of axillary network syndrome (AWS) described in the scientific literature was taken into account. It affects 30%. The 2020 records for patients who attended the Lymphedema Unit of A.G.S. Campo de Gibraltar Oeste has also been included adding 83 new patients. With these figures, a random sample of 46 individuals in total would be enough to estimate, with a 95% confidence and a precision of +-5 percent units, a population percentage of 10%.

SELECTION CRITERIA

Patients who meet all the inclusion criteria and no exclusion criteria will be included in this study prospectively.

INCLUSION CRITERIA

- Patient over 18 years old.
- Mastectomized patients (either radical or conservative surgery).
- Patient with lymphatic thrombus in the upper limb ipsilateral to the surgical intervention.

EXCLUSION CRITERIA

- Significant psychological alterations that would prevent the retrieval of the information necessary for the investigation.
- Significant neurological alterations that would prevent the retrieval of the information necessary for the investigation.
- Patients in a situation of legal dispute that would affect their intervention in this study.
- Metastasis not treated with chemotherapy treatment.

WITHDRAWAL CRITERIA

- Withdrawal of informed consent from the patient.
- Administrative decision taken by the researchers, promoter or a regulatory authority.
- Mild adverse event.
- Serious, unexpected or clinically relevant adverse event.

VALUATION CRITERIA

Main Variables:

- Mobility of the affected shoulder, measured by goniometry.
- Functionality assessment using the Constant and DASH scale (29,30).

Secondary variables:

Sociodemographic and clinical-surgical variables

- Age
- Marital status: married or in a common-law relationship, widowed, divorced or separated, single.
- Level of completed studies: illiterate, primary studies, secondary studies, university studies.
- Type of residence: in an urban / rural area.

- Children: yes / no.
- Mother after 30 years old: yes /no.
- Smoker: yes /no.
- Type of cancer. Four categories have been assessed: ductal, infiltrating, in situ, Paget's.
- Number of lymph nodes removed.
- Type of surgery (radical-conservative).
- Breast reconstruction (yes / no).
- Radiotherapy (yes / no).
- Time from surgery to the appearance of the Lymphatic Thrombus in days.

Clinical Variables:

- Visual Analog Pain Scale.
- Goniometry of all joints of the affected upper limb.
- Record of daily performance of lymphedema prevention kinesitherapy since the operation (days per week / duration in minutes / day).
- Approximate time elapsed since breast cancer diagnosis: years. Date format dd / mm / yy will be included, if possible.
- Stage in which the cancer is found, according to the TNM scale.
- Body mass index.
- Creation of a scale to classify the type of lymphatic thrombus (based on its location, length, thickness, pain, functional limitation and whether it is palpable-visible or not).

Result Variables:

- Level of physical activity measured by the International Physical Activity Questionnaire.
-Quality of life questionnaire EORTC QLQ-BR23

Employment and leisure Variables:

- Employment situation at the time of data collection: Four categories have been assessed: Active / Retired / Unemployed / Home worker.
- Sport practice: yes / no.
- Sport and frequency.

Description of the intervention

15 sessions of Assisted Passive Kinesitherapy are carried out by the physiotherapist. Five days a week, for three weeks. If it is previously referred, the treatment will be finished earlier (the patient must achieve the same ranges of motion and strength as the contralateral limb, together with the remission of pain).

The stretches applied during the sessions will be gentle and maintained, never exceeding a pain grade 5 VAS (moderate pain), once the tension of the cord is reached between 20-30 seconds. A special effort will be made to recover flexion and abduction of the shoulder, bringing the cord to a tolerable tension on the part of the patient.

Friction will be made on the axillary scar to dislodge underlying planes and the subcutaneous tissue of the muscle fascia.

The patient will be trained in active kinesitherapy to prevent lymphedema and activate lymphatic circulation. Also with hygienic-postural measures for the same purpose.

CONTROL GROUP

All the variables and data for each patients are recorded in their clinical history. Goniometric study will be performed of the affected upper limb (shoulder, elbow, wrist). Constant scale, Quick-Dash, the Visual Analog Pain Scale and the International Scale of Physical Activity will also be performed. This assessment will be carried out the patient arrives at our unit and on day 30, 60, 90.

Axillary cord syndrome: It is a nominal qualitative variable. The presence of lymphatic cord was assessed by observation and palpitation by the assessor. Physical exam performed as suggested in previous researches: patient laying in supine position with elbow extended and the shoulder in maximum abduction. The assessor observes and palpates the beads, including the armpit, down the upper arm from the armpit to the antecubital space and through the forearm to the base of the thumb (34).

Range of motion: It is a continuous quantitative variable. For the assessment of the mobility goniometry has been used. Goniometer is the standard instrument for measuring the range of movement. The patients were asked to move thir arms in flexion, extension, abduction and external and internal rotation of the shoulder. It was considered that the maximum range of motion for the

flexion and abduction was 180º, for extension it was 45º, 100º for internal rotation and 80º for external rotation. Finally, a single index was calculated as the percentage of global movement ().
Constant Scale: According to the Spanish Society for Shoulder and Elbow Surgery (SECHC), the Constant Scale assesses pain, functionality for daily life activities, joint mobility and shoulder strength. Also, it considers the laterality and the time it takes the patient. The score ranges from 0 points to 100 points, being 100 the optimal condition for the shoulder. (35, 37).

Quick-Dash (DASH): The Disabilities of the Hand, Arm and Shoulder (DASH) questionnaire is a specific instrument for measuring the quality of life related to health problems to the upper limbs. It is validated in Spanish and it consists of 30 questions. The final score calculation is relatively complicated. In order to calculate the scores it is necessary to have answered at least 27 out of the 30 questions. The final scores is obtained by calculating the arithmetic means of the questions answered minus 1 times 25. The DASH questionnaire has excellent reproductibility and high sensitivity, being able to detect small changes. The scale ranges from 30 to 150 points. 30 points means good shoulder functionality and 150 non-functional shoulder
It has two optional subsections where sports and work functionality can be assessed (38).

Visual Analog Pain Scale (VAS): According to the National Cancer Institue (NIH), it is a tool used to help the professional assess the intensity of certain sensations and feelings, such as pain. The Visual Analog Scale for pain is composed of a straight line on which an extreme means no pain and the other extreme means the worst pain imaginable. Extreme pain corresponds to 10 points. None pain corresponds to 0 points.
The patient marks a point on the line that matches the amount of pain they feel. Also known as VAS (36).

International Scale of Physical Activity (IPAQ): The main use of the IPAQ (International Physical Activity Questionnaire) worldwide is aimed at monitoring and investigation purposes. It is an instrument designed mainly for the “monitoring” of physical activity performed by the adult population and their perception of their health. Its aim is to learn about the kind of physical activity that people do as part of their daily activities. The questions are focused on the time the patient spends being physically active during the previous 7 days. The patient should consider the activities he/she does as part of work, garden, at home, leisure, moving from one place to another during their rest, exercise or sport.

IPAQ is scored by comparing the OMS recommendations. For the group of adults from 18 to 64 years old, it is done as follows: perform at least 150 minutes per week of moderate physical activity, or 75 minutes per week of vigorous physical activity, or an equivalent combination of both, that is, between both intensities they add up to at least 150 minutes of physical activity per week. The patient must answer each question in minutes a week (39).

EORTC-QLQ-BR23 questionnaire: It consists of a validated questionnaire consisting of 30 questions. The first 28 questions are scored from 1 to 4, with the highest values being those that show greater difficulty when carrying out the activity for which they are asked or the worst state of health. 126 points is the highest score and means excellent health. 0 points means the worst health.

Finally, there are two general questions about the state of health and quality of life that score from 1 to 7, the highest value being the best state of health and quality of life. The vast majority of questions refer to the previous week (40).

Barthel Scale: The Barthel index or Barthel scale is an instrument used by social and health professionals for the functional assessment of a patient and to monitor their evolution. In the case of Social Workers, they value the independence or dependence of the person in each of the activities of daily living (ADL), obtaining as a result the level of performance of the person and carrying out a rehabilitative / compensatory intervention and / or maintenance according to the results obtained. Promoting and / or maintaining the independence of the person.

The scale measures the ability of a person to perform 10 activities of daily life, which are considered basic, in this way a quantitative estimate of their degree of independence is obtained. 100 points is the highest score and the best result in the patient's functionality. 0 points is the worst result and shows the worst functional status.

These patients will be instructed in hygienic-postural care and active assisted auto-kinesitherapy to perform daily for 30 minutes. It will be assessed every 30 days (see exercise pictures).

These exercises are explained to the patient to be executed at home.

Exercise 1.- Codman Pendulum exercises.

Exercise 2.- Standing, Affected shoulder flex sliding palm of the hand on the wall up and down. Keep maximum flex during 15 seconds.

Exercise 3.- Seated, Affected shoulder flex. Seated on a wheeled chair, leaning elbow on a table. Shoulder flex sliding chair backwards and forwards.

Lymphedema prevention exercises. (please visit our YouTube channel “Unidad Linfedema Algeciras”: https://www.youtube.com/channel/UC2usHZkrmgyDfEsKhBWKrmw

INTERVENTION GROUP

As well as the control group, all the variables and data for each patient will be collected in their medical history. Goniometric study of the affected upper limb will be performed too (shouder-elbow-wrist). Constan scale, Quick- DASH, Visual Scale will also be completed together with Analogue of Pain and the International Scale of Physical Activity. This exploration will also take place during the first session and on the 30th, 60th and 90th day.

These users will arrive at the first diagnosis of the thrombus in our unit,in order to receive manual therapy by the physical therapist. (see therapy pictures).

They will receive 15 sessions of manual therapy the physiotherapist, 5 days a week ,each session being approximately 40 minutes long.

The session will begin with pendulum exercises of the shoulder to warm up the joint and give proprioceptive stimulation to the joint capsule.

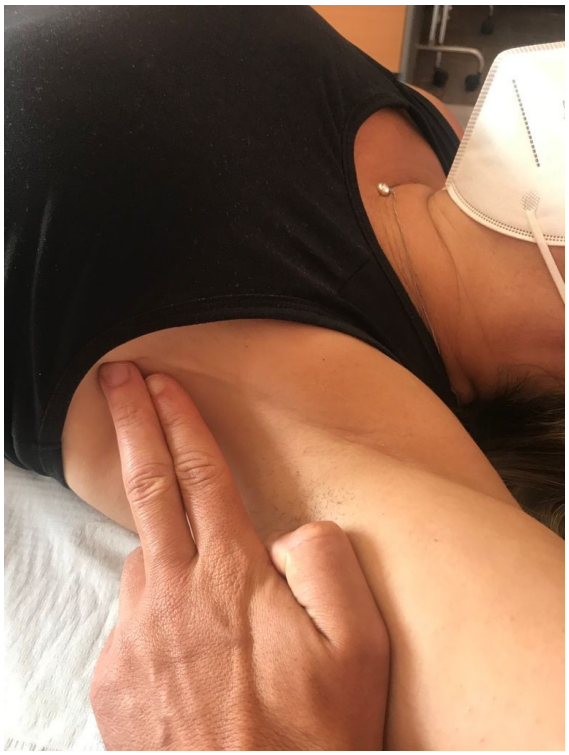
The physiotherapist will perform passive stretches looking to tensioning the lymphatic cord, never exceeding grade 6 VAS pain chart. Mainly the affected shoulder will be treated and if the cord reaches the crease of the elbow or thumb, the extension (frase sin sentido general hay que volverla a escribir).

Scar massage will be done in the area where the lymphatic cord originates at the proximal level while maintaining the tolerable tension of the lymphatic cord (during the massage also pain grade 6VAS will be exceeded).

Patients with developed lymphedema will receive Decongestive Physical Therapy (PDT) on the treated limb once the 15 day treatment described for the study is finished. Therefore, PDT does not influence on obtained contaminated results. Those patients who do not suffer from lymphedema do not receive PDT.

Manual Therapy, Scar Massage and exercises for the Intervention Group:

Exercise 4.- The Physiotherapist rests the affected limb diagonal to regular movement only if pain due to stretching is moderate.



Exercise 5.- The Physiotherapist rests the limb in shoulder flex following elbow extension.

Exercise 6.- The Physiotherapist places the limb in abduction position while patient can tolerate discomfort.

Exercise 7.- In case the cord reaches the elbow, the Physiotherapist holds the elbow extension combined with supination of the limb. The shoulder will be kept in flexed position as long as pain is moderate to keep the tension of the cord.

Exercise 8.- If the thrombus reaches the first finger, the Physiotherapist will try to reach the ulnar deviation of the wrist together with the flexion of the thumb. The shoulder will be kept in a flexed position and the elbow in an extended supination position.

ANALYSIS OF RESULTS

A descriptive analysis of all the variables included in the study will be presented at the overall level and by type of treatment in the Axillary Web Syndrome. For the qualitative variables, the relative and absolute frequencies will be presented. In the case of quantitative variables, summary statistics will be presented (mean, median, mode, minimum and maximum).

For all study objectives in which two qualitative variables are related, the non-parametric Chi-square test will be used and, if necessary, the Fisher test will be used (in cases where the absolute frequency of more than 20% of the levels is less than 5 observations). To quantify the possible predisposing factors, the relative risk measures (RR), Odds ratio (OR) and their associated confidence interval will be obtained; Likewise, the sensitivity or specificity will be presented if it is considered necessary.

All analyzes will be accompanied by graphic representations for greater detail. Missing values will be those that are not completed.

All analyzes will be carried out with free R software and the significance level for all hypothesis testing is determined at 0.05.

WORKPLAN

The study will be carried out according to the following schedule:

Development and approval of the Provincial CEIC
OCTOBER 2021
Beginning of the recruitment period and action on the intervention group
DECEMBER 2021
Drafting of results, discussion and conclusions of the project
DECEMBER 2023

According to the schedule set forth, the research project will be completed in a period of 24 months.

The researcher Jesús Baltasar González Rubiño will register the patients, whether they are in the control group or in the intervention group. The physiotherapy intervention will be applied during 12 sessions from Monday to Friday to the selected patients.

The researcher María Jesús Viñolo will be in charge of comparing the results with a double-blind system and thus comparing the results of the control group with the intervention group. The researcher Rocío Martín Valero will be the methodological advisor in this research.

Jesús Baltasar, with the help of María Jesús Viñolo and Rocío Martín Valero will write the results, discussion and conclusions of the project.

DISSEMINATION AND DISSEMINATION PLAN

1. Publication in journals indexed in the Journal Citation Report (JCR), in the field of Oncology and Rehabilitation and Physical Medicine and Physiotherapy.
2. Dissemination of results in national and international Congresses of Oncology and Rehabilitation and Physical Medicine and Physiotherapy.
3. Dissemination to the public, press releases and explanatory brochures of the project.
4. Dissemination on the website of the A.G.S. Campo de Gibraltar West.

ETHICAL ASPECTS OF THE RESEARCH

The ethical aspects of this study are included in Law 41/2002, on Patient Autonomy and Rights and Obligations Regarding Information and Clinical Documentation, as well as in Law 14/2007, on Biomedical Research. The personal data obtained during the study will be treated in accordance with the provisions of Organic Law 3/2018, of December 5, on the Protection of Personal Data and Guarantee of Digital Rights, as well as in compliance with the General Data Protection Regulation (EU) 2016/679.Before starting the data collection, the assessment and the mandatory favorable report will be requested from the Research Ethics Committee, on the methodological, ethical and judicial adequacy of the research. Sensitive data (such as NUHSA, other identifying data, etc.) will be encrypted to preserve confidentiality. Both the coding system and the databases extracted will be kept in a single device with an access key only known by the IP.

ANNEXES

Annex 1. Constant scale

OUT-PATIENT CLINIC **SHOULDER UNIT**

CONSTANT SCORE

Patient's Details

Operation/Diagnosis: **Date:**_____

Side: R L

Examination: Pre-op
3 months 6months
1 year 2 years ___ years

A.- Pain (/15): Average (1 + 2) ☐ A

1. Do you have pain in your shoulder (normal activities)?
No = 15 pts, Mild pain = 10 pts, Moderate = 5 pts, Severe or permanent = 0. ___

2. Linear scale:
If "0" means no pain and "15" is the maximum pain you can experience, please circle where is the level of pain of your shoulder. (Points given are inverse to the scale. E.g. level 5 in the scale means 10 points)

Level of pain: 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

Points: 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 ___

B.- Activities of daily living (/20) Total (1 + 2 + 3 + 4) ☐ B

1. Is your occupation or daily living limited by your shoulder?
No = 4, Moderate limitation = 2, Severe limitation = 0 ___
2. Are your leisure and recreational activities limited by your shoulder?
No = 4, Moderate limitation = 2, Severe limitation = 0 ___
3. Is your night sleep disturbed by your shoulder?
No = 2, Sometimes = 1, Yes = 0 ___
4. State to what level you can use your arm for painless, reasonably activities.
Waist = 2, Xiphoid (sternum) = 4, Neck = 6, Head = 8, Above head = 10 ___

C.- Range of movement (leave this for the doctor or physiotherapist) **(/40):** Total (1 + 2 + 3 + 4) ☐ C

1.- FWD Flexion: ___

0 - 30	0 pts
31 -60	2 pts
61 - 90	4 pts
91 - 120	6 pts
121- 150	8 pts
> 150	10 pts

2.- Abduction: ___

0 - 30	
31 - 60	
61 - 90	
91 - 120	
121 - 150	
> 150	

3.- External Rotation: ___

Hand behind head & elbow forward	2
Hand behind head & elbow back	4
Hand above head & elbow forward	6
Hand above head & elbow back	8
Full elevation of arm	10

4.- Internal Rotation: (Dorsum hand to) ___

Thigh	0
Buttock	2
SI joint	4
Waist	6
T12	8
Between shoulder blades	10

D.- Power (/25): Points: average (kg) x 2 = ☐ D

First pull: Second pull: Third pull: Fourth pull: Fifth pull:
Average pulls:

TOTAL (/100): A + B + C+ D ☐

Annex 2. DASH scale

Patient Name DOB DOS DOE DASH SCORE _____

Preop 2 week F/U 6 week F/U 12 week F/U

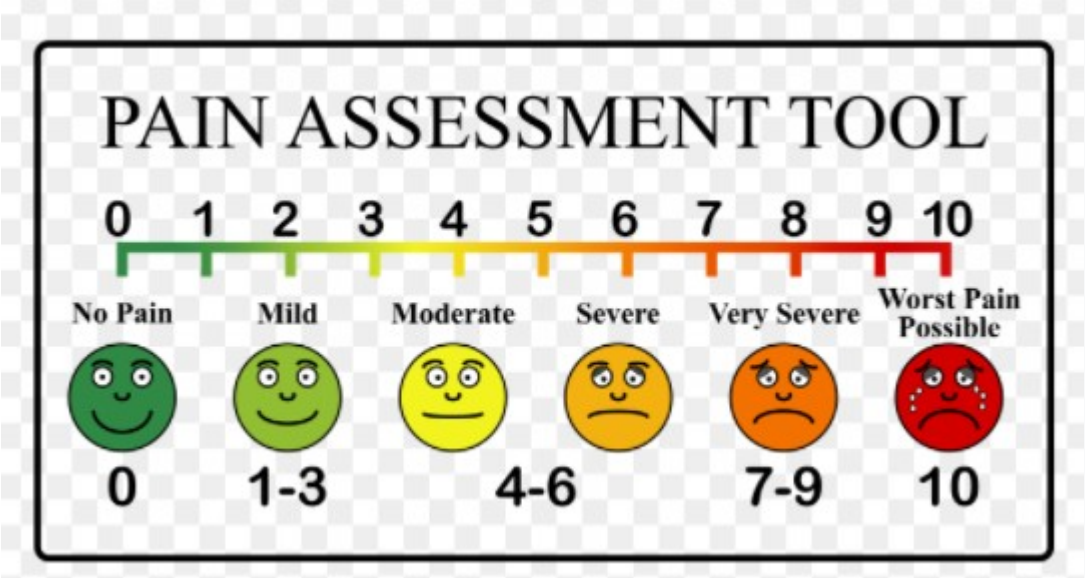
6 month F/U 12 month F/U 24 month F/U

	No difficulty	A little difficulty	Moderate difficulty	A lot of difficulty	I wasn't able to do it
1. Open a new glass jar, or one with a very tight lid	1	2	3	4	5
2. Write.	1	2	3	4	5
3. Turn a key	1	2	3	4	5
4. Prepare a meal	1	2	3	4	5
5. Open a heavy door	1	2	3	4	5
6. Put something on a shelf above head height	1	2	3	4	5
7. Do heavy domestic tasks (such as washing the floor)	1	2	3	4	5
8. Do gardening work	1	2	3	4	5
9. Make your bed	1	2	3	4	5
10. Carry a bag or a small case	1	2	3	4	5
11. Carry a heavy object (more than 5 kg).	1	2	3	4	5
12. Change a light bulb above head height	1	2	3	4	5
13. Wash or dry your hair	1	2	3	4	5
14. Wash your back	1	2	3	4	5
15. Put on a closed blouse	1	2	3	4	5
16. Use a knife to cut food	1	2	3	4	5
17. Recreational activities that require little effort (such as playing cards or knitting)	1	2	3	4	5
18. Recreational activities that require strength or impact in the arms, shoulders or hands (such as playing volleyball or hammering)	1	2	3	4	5
19. Recreational activities in which you move your arm freely (such as fishing or playing shuttlecock)	1	2	3	4	5
20. Transport from one place to another (going from one place to another)	1	2	3	4	5
21. Sexual activities	1	2	3	4	5
	It didn't affect them	**It affected them slightly**	**It affected them moderately**	**It affected them a lot**	**It affected them enormously**
22. Last week, to what extent did your arm, shoulder or hand problem affect your normal activities with your family, friends, neighbors or colleagues?	1	2	3	4	5
	It didn't limit them	**It limited them slightly**	**It limited them moderately**	**It limited them a lot**	**I wasn't able to do them**
23. Last week, were your work or normal daily activities limited because of your arm, shoulder or hand problem?	1	2	3	4	5
Rate how severe the following symptoms were last week	**None**	**A little**	**Moderate**	**A lot**	**Extreme**
24. Pain in your arm, shoulder or hand	1	2	3	4	5
25. Pain in your arm, shoulder or hand when you did specific activities	1	2	3	4	5
26. Discomfort in the skin of your arm, shoulder or hand (prickling)	1	2	3	4	5
27. Weakness in your arm, shoulder or hand	1	2	3	4	5
28. Difficulty in moving your arm, shoulder or hand	1	2	3	4	5
	No difficulty	**A little difficulty**	**Moderate difficulty**	**A lot of difficulty**	**So difficult that I wasn't able to sleep**
29. Last week, did you have any difficulty in sleeping because of pain in your arm, shoulder or hand?	1	2	3	4	5
	Totally disagree	**Disagree**	**Neither agree nor disagree**	**Agree**	**Totally agree**
30. I feel less capable, less confident and less useful because of my arm, shoulder or hand problem	1	2	3	4	5

Annex 3. TNM classification

Tumours	T0/Tis	T1	T2	T3	T4
Tumour Size	**T0**: No primary tumour. **Tis**: Tumour only in breast ducts or lobules.	0-2 cm	2-5 cm	>5 cm	Tumor of any size with extension to chest wall/skin or ulceration ****inflammatory breast cancer** is staged as T4.
Nodes	**N0**	**N1**	**N1mi**	**N2**	**N3**
	No lymph node metastases.	Cancer cells present in 1-3 axillary lymph nodes.	Lymph node tumor > 2 mm.	Cancer cells present in 4-9 axillary lymph nodes.	Cancer cells in infra or supraclavicular lymph nodes, or in >10 axillary lymph nodes.
Metastasis	**M0**	**M1**			
	No evidence of cancer metastasis.	Cancer found in other areas of body.			

Annex 4. Visual Analog Pain Scale



Annex 5. International Physical Activity Questionnaire

1a. During the last 7 days, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

Think about *only* those physical activities that you did for at least 10 minutes at a time.

_____ **days per week** ⇨

1b. How much time in total did you usually spend on one of those days doing vigorous physical activities?

_____ **hours** _____ **minutes**

or

☐ **none**

2a. Again, think *only* about those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

_____ **days per week** ⇨

2b. How much time in total did you usually spend on one of those days doing moderate physical activities?

_____ **hours** _____ **minutes**

or

☐ **none**

3a. During the last 7 days, on how many days did you **walk** for at least 10 minutes at a time? This includes walking at work and at home, walking to travel from place to place, and any other walking that you did solely for recreation, sport, exercise or leisure.

_____ **days per week** ⇨

3b. How much time in total did you usually spend walking on one of those days?

_____ **hours** _____ **minutes**

or

☐ **none**

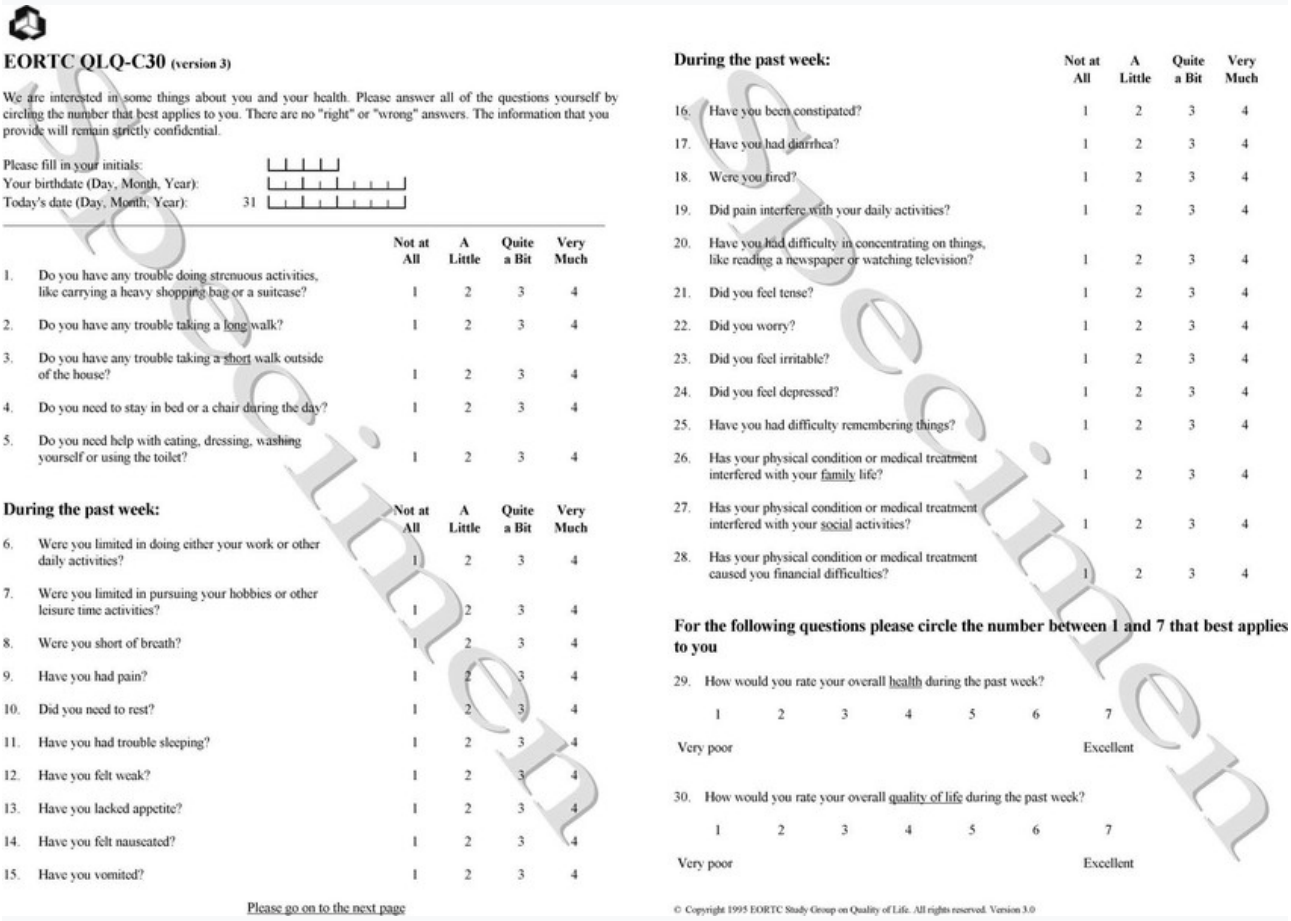
The last question is about the time you spent sitting on weekdays while at work, at home, while doing course work and during leisure time. This includes time spent sitting at a desk, visiting friends, reading traveling on a bus or sitting or lying down to watch television.

4. During the last 7 days, how much time in total did you usually spend *sitting* on a **week day?**

____ **hours** _____ **minutes**

This is the end of questionnaire, thank you for participating.

Annex 6. EORTC Questionnaire QLQ-BR23



EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials: ⌊_⌊_⌊

Your birthdate (Day, Month, Year): ⌊_⌊_⌊_⌊_⌊_⌊

Today's date (Day, Month, Year): 31 ⌊_⌊_⌊_⌊_⌊_⌊

		Not at All	A Little	Quite a Bit	Very Much
1.	Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2.	Do you have any trouble taking a long walk?	1	2	3	4
3.	Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4.	Do you need to stay in bed or a chair during the day?	1	2	3	4
5.	Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

During the past week:		Not at All	A Little	Quite a Bit	Very Much
6.	Were you limited in doing either your work or other daily activities?	1	2	3	4
7.	Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8.	Were you short of breath?	1	2	3	4
9.	Have you had pain?	1	2	3	4
10.	Did you need to rest?	1	2	3	4
11.	Have you had trouble sleeping?	1	2	3	4
12.	Have you felt weak?	1	2	3	4
13.	Have you lacked appetite?	1	2	3	4
14.	Have you felt nauseated?	1	2	3	4
15.	Have you vomited?	1	2	3	4

Please go on to the next page

During the past week:		Not at All	A Little	Quite a Bit	Very Much
16.	Have you been constipated?	1	2	3	4
17.	Have you had diarrhea?	1	2	3	4
18.	Were you tired?	1	2	3	4
19.	Did pain interfere with your daily activities?	1	2	3	4
20.	Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21.	Did you feel tense?	1	2	3	4
22.	Did you worry?	1	2	3	4
23.	Did you feel irritable?	1	2	3	4
24.	Did you feel depressed?	1	2	3	4
25.	Have you had difficulty remembering things?	1	2	3	4
26.	Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27.	Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28.	Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall health during the past week?

1 2 3 4 5 6 7

Very poor Excellent

30. How would you rate your overall quality of life during the past week?

1 2 3 4 5 6 7

Very poor Excellent

Annex 7. Patient Information Sheet

INFORMATION SHEET FOR THE PARTICIPANT IN A CLINICAL RESEARCH STUDY

Study title: Effects of a manual therapy program to reduce the evolution time of axillary network syndrome in women affected by breast cancer.

Main researcher: Jesús Baltasar González Rubiño, belonging to the Algeciras Lymphedema Unit.

Participating center: Algeciras Lymphedema Unit.

INTRODUCTION

The patients are invited to participate in a study that has been approved by the Cádiz Clinical Research Ethics Committee.

Please read this fact sheet carefully. The physiotherapist Jesús B. González Rubiño will clarify any doubts that may arise.

VOLUNTARY PARTICIPATION

The patients´ participation in this study is voluntary and the patient can override their decision and withdraw their consent at any time, without thereby altering their relationship with the doctor or damaging their treatment or the care the patients may need.

GENERAL DESCRIPTION OF THE STUDY

The objective of this study is to reduce the time of evolution of the Postmastectomy Lymphatic Thrombus.

Registration and initial clinical assessment of the patient will be made. The Upper Limb affected by the lymphatic cord will be treated with Assisted Passive Kinesitherapy and Stretching.

This lymphatic thrombus, according to the scientific literature, has a spontaneous resolution in approximately 3 months from its appearance. With this study the investigator intend that it take less time to disappear. Likewise, the investigator intend to reduce pain, improve shoulder mobility and improve the functionality of the affected arm.

46 patients / subjects will participate in this study.

BENEFITS AND RISKS DERIVED FROM PATIENTS´ PARTICIPATION IN THIS STUDY

Without the existence of any risk, the information obtained will serve to expand scientific knowledge about breast cancer recurrences. The patient will not get any health benefits from participating in this study.

ECONOMIC COMPENSATION

The patient´s participation in the study will not incur any cost to her.

CONFIDENTIALITY

The patient´s data will be treated with the utmost confidentiality in accordance with the provisions of Organic Law 3/2018, of December 5, on the Protection of Personal Data and guarantees of digital rights and the General Data Protection Regulations. According to what is established in these. Rules, the patient can exercise the rights of access, rectification, opposition, deletion, limitation of release, right to be forgotten and portability, for which the patient should contact the researcher responsible for the study, Mr. Jesús Baltasar González Rubiño.

Email: jesusb.gonzalez.sspa@juntadeandalucia.es. Telephone: 856814114.

If the results of the study are published, patient´s personal data will not be published and the patient´s identity will remain anonymous.

FINANCING

First study does not have any source of funding.

WITHDRAWAL OF CONSENT

The patient can withdraw their consent at any time without having to give explanations

If the patient no longer wish to participate in the study and the patient do, all patient´s identifiable responses will be destroyed.

The patient should also know that the patient can be excluded from the study if the study the investigators see fit.

The patient has the right to be informed of any retesting of the identifiable material withheld not provided for in this study. In that case, the researcher will have to ask the patient for a new consent that the patient could refuse.

Before signing, read the document carefully, ask all the questions the patient consider appropriate, and if the patient wish, consult it with all the people the patient consider necessary.

If in doubt, the patient should contact Jesús Baltasar González Rubiño.

SIGNATURES

Patient Company:	Investigator Company:
Name:	Name:
Date:	Date:

First document should be signed in duplicate: one copy for the participant and one for the researcher.

Annex 8. Patient Informed Consent Sheet

WRITTEN INFORMED CONSENT

Study title: Effects of a manual therapy program to reduce the evolution time of axillary network syndrome in women affected by breast cancer.

Promoter: Jesús Baltasar González Rubiño.

I (name and surname) _____

I have read and understand the information sheet provided to me.

I have been able to ask questions about the study.

I have received enough information about the study. I have spoken with:

_____

(name of researcher)

I understand that my participation is voluntary.

I understand that I can withdraw from the study:

1 When the patient wants to.

2º Without having to give explanations.

3rd Without this affecting my medical care.

I freely give my consent to participate in the study.

DATE AND SIGNATURE OF THE PARTICIPANT