The LYMPH Trial - Surgical versus Conservative Complex Physical Decongestion Therapy for Chronic Breast Cancer-Related Lymphedema: A Pragmatic, Randomized, Multicenter Superiority Trial

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Primary Objective:The primary objective of this trial is to test whether lymphatic surgery provides better QoL (assessed with the Lymph-ICF-UL, upper limb, questionnaire) 15 months after randomization (and therefore about one year after surgery)...

Ethical review	Approved WMO
Status	Pending
Health condition type	Spleen, lymphatic and reticuloendothelial system disorders
Study type	Interventional

Summary

ID

NL-OMON57192

Source
ToetsingOnline

Brief title
Surgical vs "non-surgical" treatment of chronic lymphedema

Condition

- Spleen, lymphatic and reticuloendothelial system disorders
- Haematological and lymphoid tissue therapeutic procedures

Synonym
accumulation of lymphatic fluid, Lymphedema

Research involving
Human

Sponsors and support

Primary sponsor: University Hospital Basel
Source(s) of monetary or material Support: Ministerie van OC&W,Rising Tide Foundation and Stiftung Krebsforschung Schweiz

Intervention

Keyword: Breast cancer related lymphedema, Conservative complex physical decongestion therapy, Lymphatic surgery

Outcome measures

Primary outcome

The primary endpoint of this trial is the patient reported QoL outcome

lymphedema-specific QoL, which will be assessed 15 months after randomization

(and therefore about 12 months after surgery) measured by the Lymph-ICF-UL

questionnaire.

Secondary outcome

Safety Endpoints:

- Adverse Events

- Complications of surgery (applicable in surgery group only)

- Lymphangitic events (erysipelas)

Patient reported outcomes (PROs):

- QoL: Lymph-ICF-UL

- QoL: LYMPH-Q

- QoL: EuroQol EQ-5D-5L

- Pain score (visual analogue scale)

Study description

Background summary

Chronic breast cancer related lymphedema (BCRL) is caused by lymphatic system failure after sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND) and/or radiotherapy. It is a debilitating condition resulting in physical and psychological morbidity, i.e. an affected arm which may become swollen, heavy and deformed, and it is, tense, painful and/or prone to infections. Further, BCRL can also result in a significant financial burden to patients and society.

To date, conservative complex physical decongestion therapy (CDT) is the gold standard for BCRL and includes manual lymphatic drainage, local compression with bandages and garments, physical exercises and meticulous skin care. It is, however, too often ineffective to prevent stage progression in curing BCRL and purely symptomatic.

Lymphovenous anastomosis (LVA) and vascularized lymph node transfer (VLNT) are two surgical techniques that, in contrast to CDT, are able to actually address the underlying causes and eventually restore the lymphatic drainage. LVA achieves this by creating numerous bypasses between lymphatic vessels and venules allowing the drainage of excessive fluid within the subcutaneous tissues into the venous system, while VLNT usually brings functioning lymph nodes to an area devoid of lymph nodes or with dysfunctional lymph nodes, thus enabling the spontaneous development of new lymphatic basin pathways. Both techniques have shown very promising results with low complication rates and improved Quality of Life (QoL) for the patients. However, no multicentric randomized controlled trial (RCT) has yet prospectively evaluated the superiority of these surgical techniques over CDT alone, limiting patient*s access to most effective treatment available. Requests for cost reimbursement must still be submitted to insurance companies in most countries and are often rejected, thus delaying surgical treatment and resulting in prolonged suffering of affected patients. This is untenable seeing as affected patients suffer from a heavy physical, psychological and financial burden. This pragmatic, randomized, multicenter trial aims to establish a solid scientific basis assessing the superiority of surgical treatment over CDT alone.

Study objective

Primary Objective:
The primary objective of this trial is to test whether lymphatic surgery

provides better QoL (assessed with the Lymph-ICF-UL, upper limb, questionnaire) 15 months after randomization (and therefore about one year after surgery) compared to conservative treatment only for patients with chronic lymphedema (LE).

Secondary Objectives:
Secondary objectives will compare lymphatic surgery versus conservative treatment only in terms of further QoL aspects, arm volume, safety, burden on patients and pain.

Study design

Pragmatic, randomized, international, multicenter superiority trial

Intervention

Patients randomized to the control arm will receive the standard of care treatment CDT. A treatment example/suggestion is described in detail in protocol section 3.4.2, but according to the pragmatic study design, CDT will not be standardized.

Patients randomized to the interventional arm should undergo surgical treatment (LVA or VLNT with or without liposuction) as soon as possible but latest 3 months after randomization.

According to the pragmatic study design, the intervention will not be standardized to assure that some flexibility is allowed that offers surgeons considerable leeway how to perform lymphatic surgery, which resembles the flexibility in usual care. However, the key aspects of the preoperative workup will be documented and the intervention including the surgical technique, number of LVAs, time of surgery, and practical details.
Patients randomized to the interventional arm will also receive CDT as SOC as described in protocol chapter 3.4.1.

Due to the nature of the study, patients and surgical teams cannot be blinded to allocation and surgical procedure.
Examples of the possible surgical interventions are described in detail in protocol section 3.4.1.

Study burden and risks

Burden/risks:
- Very common side effects are, as with (almost) all operations, pain, bleeding/bruising and swelling.
- Common side effects are, as with (almost) all operations, delayed wound healing and wound infections.

- A rare side effect in patients with lymph node transplantation from the thigh is lymphedema at the donor site. No other side-effects are currently known.
- Quality of life and pain questionnaires: You will probably need about 10 minutes to fill in the questionnaires. You can usually do this while waiting for the appointment in the waiting room. If you do not want to or cannot answer individual questions, this is fine.
- Measurement of arm circumference: For the uniform recording of (changes in) arm circumference, the study team will carry out the appropriate measurement on you. This should take about 5 minutes.
- Photographs of the arms: For further assessment of lymphedema, we will take photographs of your arms at the beginning and after 15 months, which takes about 2 minutes.
- Assessment of lymphedema: Your investigator and you should also independently rate the aesthetics of the arm using the following 4 options: excellent, good, normal and poor. This should take no more than 3 minutes.

Expected benefit:
- It may be that by participating in the study, conservative therapy will be carried out more consistently and successfully, which could lead to an improvement in your lymphedema.
- Through the regular recording of your quality of life and the consistent, uniform measurement of lymphedema, it may be possible to react more quickly in the event of a deterioration of your condition.
- Should you receive surgery, the causes of your lymphedema could be addressed, which could lead to an improvement in your lymphedema.
- The results of the study could provide patients with an appropriate therapy recommendation in the future and simplify the reimbursement of costs by health insurance companies.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Written informed consent.
- Patients >= 18 years of age.
- Previous diagnosis of breast cancer.
- Clinical diagnosis of chronic BCRL as defined by the international society of lymphology (ISL; inter-limb difference of >10% in volume or excess volume between the affected and non-affected arm present for more than 3 months).
- Minimum of 3 months CDT.
- Ability to complete the QoL questionnaires.

Exclusion criteria

- No indication for lymphatic surgery according to clinical judgment of the treating surgeon (individual reasons will be specifically documented).
- Primary congenital LE or non-BCRL.
- Previous surgical BCRL treatment.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	16-12-2024
Enrollment:	10
Type:	Anticipated

Ethics review

Approved WMO Date:	19-12-2024
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT05890677,SNCTP,BASECproject-ID:2023-00733
CCMO	NL86116.068.24