ISRCTN72662721 https://doi.org/10.1186/ISRCTN72662721

Predictive factors in lymphedema surgery

Submission date
28/02/2022

Recruitment status
No longer recruiting

Registration date
07/03/2022

Overall study status
Ongoing

Last Edited
07/03/2022

Condition category
Surgery

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims:
Lymphedema is a condition where swelling of soft tissues occurs, either due to inherited conditions or due to trauma or cancer therapy where the lymphatic system sustains an injury. The lymphatic system plays a large role in transporting fluid around the body, as well as a role in fighting infections. If the system doesn´t function well enough, swelling of a body part can occur due to insufficient draining of fluid. This can also lead to an increased risk of infection. Patients often experience distress due to the increased volume, recurrent infections, the distorted appearance of the body part, decreased range of motion, pain, heaviness, and discomfort. Most often the arms or legs are affected, but also other parts of the body. The symptoms tend to get worse over time, and without treatment, the tissues often develop irreversible changes in form abnormal fat formation and scarry tissues. The most important treatment is compression therapy, where the patient wears a garment that gives pressure to the affected area to reduce how much fluid goes from the bloodstream into the soft surrounding tissues. The pressure also gives support to the venous system, which also transports fluids in the blood circulation and this helps to fight the formation of swelling. In recent years it has become possible to do operations that aim to improve the function of the lymphatic system. Two main types of operations are currently available; One is moving lymph nodes or lymphatic tissue from an unaffected part of the body into the affected area, connecting the tissue to the local blood circulation. How this works is still unclear, but it is believed that this stimulates the growth of new lymphatic vessels and/or that the lymphatic tissue has a suction mechanism that accumulates the excess fluid and moves it into the venous system which it is linked to. The other type of operation is called lymphaticovenous anastomosis (LVA) surgery, which aims to redirect the flow of the lymphatic system into the blood circulation, before the area where the lymphatic system is damaged and leaks into the surrounding tissues. Otherwise, the lymphatic fluid is normally drained into the bloodstream closer to the heart, but by creating a shortcut already out on the arm or leg, one can help the drainage of the lymphatic system, improve the removal of lymph fluid and reduce swelling. A lymphatic vessel is thus connected directly to a small blood vessel so that the lymphatic fluid can be emptied into the bloodstream. These are called microsurgical operations because a microscope is used during the operation to sow very small structures. The surgical wound that is formed is only a few centimeters in size and in many cases, the procedure can be performed under local anesthesia. There are still many questions unanswered regarding what factors before and during surgery can predict a good outcome for LVA-surgery. such as the importance of how far along in the disease progress the patient is (disease stage), what patients are best suited for surgery, which lymphatic vessels are best suited to use, such as the quality

and size of the lymphatic vessels and receiving blood vessels, level of fibrosis/scar tissue in the lymphatic vessel, pressure-differences between the lymphatic- and blood vessel, and the number and site of anastomosis. This study aims to systematically map these factors in patients that undergo LVA-surgery for lymphedema, and see if some of these factors correlate to either better or worse outcomes after surgery in form of volume measurements and quality of life.

Who can participate?
Patients with lymphedema, where the diagnosis has been established with an examination where the lymphatic system and its transport is seen in real-time with an infrared camera, and have prerequisites for a lymphaticovenous anastomosis surgery (identifiable lymphatic vessels that seem to stop working properly, and the lymphatic fluid leaks into the surrounding soft tissue, causing swelling).

What does the study involve?
This study evaluates patients before and on two occasions after their LVA surgery at 6-12 months and 12-24 months after surgery. The authors will collect information about factors before and during the surgery, using patient records and a standardized form that the surgeon fills out straight after the surgery. Outcome measures will then be registered in form of volume measurements carried out with tape measurements by lymph-therapists, the number of infections, the effect of surgery on compression garment use, amount of fluid in the tissues (bioimpedance), and quality of life surveys, specially designed for lymphedema that the patient.

What are the possible benefits and risks of participating?
The possible benefit is an improvement of the patient's lymphedema, with a reduction in volume, decreased number of infections, decreased need or discontinuation of compression therapy, and increased quality of life. The possible risks are that the patient doesn´t gain any benefit from the surgery, but risks of making the lymphedema worse related to LVA-surgery is not described in the literature. As with all surgery, there is a risk for infections, but this particular surgical wound is only a few cm long, and the surgery is performed in superficial areas of the tissues, posing no risk to deeper structures, such as bigger vessels and nerves. If the patient does not receive alleviation of some sort from the lymphedema, the patient will have undergone surgery in local anesthesia in vain and will have a few cm long scar, which is however in most cases very discrete.

Where is the study run from?
Uppsala University Hospital (Sweden)
Maastricht University Medical Center+ (the Netherlands)
Nijmegen Radboud UMC, Holland (the Netherlands)

When is the study starting and how long is it expected to run for?
January 2019 to August 2029

Who is the main contact
Dr. Maria Rydevik Mani, maria.mani@surgsci.uu.se

Contact information

Type(s)
Principal investigator

Contact name

Dr Maria Rydevik Mani

Contact details
Department of Plastic and Reconstructive Surgery
Uppsala University Hospital
Uppsala
Sweden
751 85
+46 709628260
maria.mani@surgsci.uu.se

Type(s)
Scientific

Contact name
Ms Anna Nilsson

Contact details
Department of Plastic and Reconstructive Surgery
Uppsala University Hospital
Uppsala
Sweden
75185
+46 731419841
anna.nilsson@surgsci.uu.se

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
DNr 2019-03033

Study information

Scientific Title
The ppLVA study = perioperative predictive (factor) LVA study

Acronym
ppLVA

Study objectives
To better evaluate LVA surgery, a form has been developed for the surgeon to fill in perioperative regarding number of LVA´s and the estimated quality of each LVA (fibrosis, leakage, backflow)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/08/2017, Swedish Ethical Review Authority (Etikprövningsmyndigheten, Box 2110, 750 02, Uppsala, Sweden; +46 10-475 08 00; registrator@etikprovning.se), ref: DNr 2019-03033, amendment 09/07/2019

Study design
Observational cohort study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Lymphaticovenous anastomosis surgery on lymphedema patients

Interventions
Patients with lymphedema that are eligible for Lymphaticovenous anastomosis-surgery (LVA surgery) are recruited for the study, which is a retrospective observational study with a prospectively maintained database. Prior to their first visit to the lymphedema clinic, they have to have their lymphedema diagnosis confirmed with a lymphoscintigraphy and other causes for edema excluded. To be accepted for LVA-surgery, the patients undergo an assessment with indocyanine green lymphography (ICG-L) to see if they meet prerequisites for LVA-surgery. Before surgery, ultrasound of the veins is carried out to exclude venous insufficiency. At the first visit information on demographics is filled out and the patients fill out QoL questionnaires, both specific and non-specific to lymphedema (LyQLI and EQ-5D). The patients will meet a lymph therapist which evaluates their compression therapy and measures the volume of the lymphedematous body part with tape-measurements. Furthermore bioimpedance measurements are taken, 2D and 3D photos, and the patients are asked to answer questions about their level of activity and lymphedema treatment thus far.

The patients eligible for surgery will then be operated on in day surgery under local anaesthesia, and the surgeon will fill out a structured perioperative evaluation form directly after surgery, describing the perioperative findings, e.g. the location and size of the vessels, level of fibrosis, whether lymphatic fluid leaked out of the lymphatic vessel when cut, backflow of blood from vein to lymphatic vessel after anastomosis, size-match of anastomosis and the number of anastomosis performed. The patient will then have a wound control one and two weeks after the operation with a nurse, with suture removal at the latter visit. Two weeks post operatively the patient is asked to not use their compression garments, but can continue as usual after that. One month after surgery, the patient sees a doctor for clinical evaluation and a lymph therapist who performs volume measurements. Impedance measurements are taken as well as 2D and 3D photos, and the patient fills out QoL questionnaires and questions about their current activity level. This is all repeated at 6, 12 and 24 months post-operatively to assess the results of surgery, apart from clinical assessment at 6 months. Additionally, an evaluation of compression garment usage and lymphoscintigraphy is done at 12 months post operatively, as well as a repeated ICG-L is, to assess the level of lymphedema and the patency of the anastomosis.

The patients undergoing LVA-surgery accept to follow this protocol for assessment and follow-up, as part of ongoing lymphedema research at the clinic. This particular study will not have any further impact on the patients, other than additional structured registration of peri-operative findings, and analysis of the data to see if positive correlations can be found between some of the perioperative factors and post-operative outcomes in form of change in volume, QoL, compression therapy or number of infections.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Clinical assessment is done by a physician and a lymph therapist pre- and post-operatively at 1, 6, 12 and 24 months to assess invalidity due to lymphedema, weight, nikotin status, number of infections, range of motion, skin problems, swelling, heaviness, pressure sensation, numbness, pitting edema and stage of lymphedema, and whether this is better, worse or unchanged after surgery. This is done through interview and clinical assessment. The lymph therapist will evaluate and take history of compression therapy and measure the volume outcome with tape measurements.

Key secondary outcome(s))
1. Bio-impedance is measured with a non-invasive measurement tool, and 2D and 3D photos will be taken at 1, 6, 12 and 24 months
2. An assessment with ICG-L is made by injecting a small amount of fluorescent dye into the dermal skin after local anesthesia pre-operatively and 12 months post-operatively.
3. Lymphoscintigraphy is done pre-operatively and at 12 months post-operatively, by injecting a small amount of radioactive substance into the dermis to assess the level of lymphedema at the nuclear medicine department.
4. Quality of life (EQ-5D and LyQLI), level of activity, and previous treatment of lymphedema questionnaires are completed at 1, 6, 12 and 24 months
The data collected peri-operatively is registered by the surgeon directly after surgery, by filling out a peri-operative evaluation form for LVA-surgery, developed at the Uppsala University Hospital.

Completion date
16/08/2029

Eligibility

Key inclusion criteria
Patients with ICG confirmed primary or secondary lymphedema assessed suitable for LVA surgery.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Edema caused by other dysfunction.
2. Advanced Lymphedema with no visual lymph vessels on ICG imaging.

Date of first enrolment
16/08/2019

Date of final enrolment
01/01/2025

Locations

Countries of recruitment
United Kingdom

Netherlands

Sweden

Study participating centre
Uppsala University Hospital
Department of Plastic and Reconstructive Surgery
Uppsala
Sweden
75185

Sponsor information

Organisation
Uppsala University Hospital

ROR
https://ror.org/01apvbh93

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes