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Cyanoacrylate glue in breast surgery. Can cyanoacrylate glue reduce seroma after axillary dissection?

Submission date
19/08/2024

Recruitment status
No longer recruiting

Registration date
19/08/2024

Overall study status
Completed

Last Edited
19/08/2024

Condition category
Surgery

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[X] Individual participant data

Plain English summary of protocol

Background and study aims
The incidence of seroma and lymphorrhoea after axillary dissection remains the most frequent complication in breast surgery. The prolonged use of drains and the numerous evacuative punctures cause considerable discomfort for cancer patients and the prolonged seroma delays the start of adjuvant treatments. There have been numerous attempts to reduce this complication with mechanical or pharmacological aids with poor results. Cyanoacrylate glue already used in abdominal and gynecological surgery has shown excellent results in reducing lymphorrhoea after pelvic lymphadenectomies. The literature is scant about the effect of cyanoacrylate glue in breast surgery. This study aims to evaluate the effects of cyanoacrylate glue in reducing seroma formation in patients undergoing breast surgery and complete axillary dissection.

Who can participate?
Women over 18 years old with breast cancer undergoing radical mastectomy or breast-conserving surgery and axillary dissection

What does the study involve?
Each patient who meets the inclusion criteria and signs a specific informed consent can be enrolled in the study. Allocation within two study Arms will be randomly assigned. Experimental Arm will receive breast and axillary surgery (radical mastectomy or breast conserciving surgery with axillary dissection), 1 ml of cyanoacrylate glue distributed to the axillary cavity using a nebulizer and a suction drain at the end of the surgery. The Control Arm will receive breast and axillary surgery (radical mastectomy or breast-conserving surgery with axillary dissection) and a suction drain will be placed at the end of the surgery.
The quantity of seroma will be measured during the outpatient visits on day 7 and day 15. The volume of seroma was reported in ml on specific eCRF along with surgical complications and possible side effects. On day 15 the drain will be removed in both Arms. From day 21, the seroma will be drained by fine needle aspiration and reported in ml on the eCRF. Patients will be followed up till day 90 after surgery.

What are the possible benefits and risks of participating?
The benefit of participating in the study was a probable reduction of postoperative seroma. The risks are possible side effects of cyanocrylate glue although neither mild nor severe side effects have been reported.

Where is the study run from?
Breast Surgery Unit at National Cancer Institute, IRCCS, Fondazione Pascale, Italy

When is the study starting and how long is it expected to run for?
November 2017 to August 2022

Who is funding the study?
Italian Ministry of Health

Who is the main contact?
Raimondo di Giacomo, MD, Head of Breast Surgery Unit at National Cancer Institute, IRCCS, Fondazione Pascale, Italy, r.digiacomo@istitutotumori.na.it

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
GLUBreast Trial

Acronym
GLUBreast

Study objectives
Preventing the incidence of post-surgical seroma can reduce the number of post-operative outpatient visits and avoid the delay of adjuvant therapies.
Glubran® 2 (Butyl-2-CyanoAcrylate+Metacryloxysulfolane [NBCA+ MS] is a biodegradable synthetic glue.
The hypothesis is that the application of the glue after axillary dissection for breast cancer can reduce the formation of seroma.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 10/04/2018, Comitato Etico Fondazione Pascale (Via Mariano Semmola, 53, Naples, 80131, Italy; +39 08117770132; comitatoetico@istitutotumori.na.it), ref: 12/18

Study design
Prospective randomized single-center study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital, Medical and other records

Study type(s)
Prevention, Treatment, Efficacy

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Prevention of post-operative seroma after axillary dissection in patients with breast cancer

Interventions
The study is a prospective randomized single-center study enrolling patients who meet inclusion criteria. Patients will be assigned either an Experimental Arm or a Control Arm by a random allocation program. The Experimental Arm will be treated with breast and axillary surgery (mastectomy or breast conserving with axillary dissection). 1 ml of cyanoacrylate glue will be applied to the axillary cavity and a suction drain will be placed at the end of the procedure. The Control arm received breast and axillary surgery (mastectomy or breast conserving with axillary dissection) and a suction drain will be placed. The seroma will be measured in ml on day 7 and day 15. On day 15 the drain will be removed in both Arms. From day 21 seroma, if present, will be treated and measured by fine needle aspiration.

A multivariable mixed-effect model for repeated measures was performed including the following covariates: age, tumor size, Body Mass Index (BMI), time to visit, type of surgery, and surgical complications. Differences between study arms were evaluated through Pearson's Chi-squared test or Fisher’s exact test (if an exact test was needed) for categorical variables and the Mann–Whitney test for continuous variables. Volume drained as volume (ml/day) mean in all visits. To investigate the independent contribution of predictors on the presence/absence of liquid (expressed as the risk of seroma formation) and volume drained (expressed as daily drained seroma volume), the significance of each coefficient was evaluated through t-statistics using Satterthwaite's method. Regression stratified by type of surgery was also performed. Statistical significance was set at $p < 0.05$. Analyses were performed using R software 4.2.3.

Intervention Type
Procedure/Surgery

Primary outcome measure
Efficacy of cyanoacrylate glue to prevent post-operative seroma in breast surgery measured using the total volume of fluid drained at days 7, 15 and 21

Secondary outcome measures
The following secondary outcome measures were assessed using covariate data obtained from patient medical records:
1. Total volume of seroma drained (ml) correlation to BMI (Kg/m2) in all visits at days 7, 15, and 21 till complete healing
2. Total volume of seroma drained (ml) correlation to breast-conserving surgery or total mastectomy in both arms in all visits at days 7, 15, and 21 till complete healing
3. Adverse events were reported as an occurrence at least one visit per patient and were measured as the presence or absence of fever (> 37.2 C), pain (measured using the visual analogue score (VAS) 0 to 10 at baseline, and in all visits during 90 days of follow up), skin dehiscence, skin redness.
4. The rate of infection was measured using the presence or absence of fever and the need for post-operative antibiotics during 90 days of follow-up; hospital re-admission rate and re-operation were measured in numbers and percentages.

Overall study start date
06/11/2017

Completion date
02/08/2022

Eligibility

Key inclusion criteria
1. Female gender
2. 18 years of age or older
3. New diagnosis of invasive breast cancer confirmed by core needle biopsy
4. Palpable and positive axillary lymph nodes requiring axillary dissection
5. Patients suitable for breast-conserving surgery (BCS) or modified radical mastectomy (MRM) without reconstruction
6. Ability of understanding and sign the informed consent

Participant type(s)
Patient

Age group
Mixed

Lower age limit
18 Years

Upper age limit
90 Years

Sex
Female

Target number of participants
200

Total final enrolment
180

Key exclusion criteria
1. Male gender
2. Treated with neo-adjuvant chemotherapy
3. Scheduled for breast reconstruction
4. Previously treated with radiation therapy to the chest wall for lymphoma
5. Inability to understand and sign the informed consent

Date of first enrolment
24/04/2018

Date of final enrolment
01/06/2022

Locations

Countries of recruitment
Italy

Study participating centre
Istituto Nazionale Tumori Napoli IRCCS Fondazione G. Pascale
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Sponsor information

Organisation
Istituto Nazionale Tumori IRCCS "Fondazione G. Pascale"

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Sponsor type
Hospital/treatment centre

Website
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ROR
https://ror.org/0506y2b23

Funder(s)

Funder type
Government

Funder Name
Ministero della Salute

Alternative Name(s)
Italian Ministry of Health, Italy Ministry of Health, Ministry of Health of Italy, Ministry of Health - Italy, Ministry of Health, Italy

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Italy

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed journal

Intention to publish date
01/10/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a publically available repository (https://zenodo.org/records/13150809).

The type of data stored includes breast anamnestic data, demographic data, complications, outpatient visits and follow-up, inclusion and exclusion criteria, hospitalisation data, intervention data, premature study discontinuation data, randomisation data, surgical treatment data. Data are available from 01/08/2024. Consent from participants was required and obtained. Data are anonymised
• Any ethical or legal restrictions: We act in respect of Law No. 675 of 31 December 1996) and regulated subsequently by the Personal Data Protection Code (Legislative Decree No. 196 of 30 June 2003) as amended by Legislative Decree No. 101 of 10 August 2018, which also established that the Italian DPA is the supervisory authority responsible for monitoring application of the General Data Protection Regulation (pursuant to Article 51 of Regulation No. 2016/679).

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Dataset		01/08/2024	19/08/2024	No	No
Interim results article		10/09/2019	19/08/2024	Yes	No
Other files			19/08/2024	No	No
Other unpublished results		01/08/2024	19/08/2024	No	No
Participant information sheet			19/08/2024	No	Yes
Participant information sheet	Informed consent		19/08/2024	No	Yes