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Perineural local anaesthetic catheter after major lower limb amputation trial (PLACEMENT)

Submission date
23/12/2022

Recruitment status
Recruiting

Registration date
12/09/2023

Overall study status
Ongoing

Last Edited
16/07/2025

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
Leg amputations are painful and life-changing events. About 10000 people have a leg amputation in the UK every year. Pain may be felt in the stump straight after surgery and in the longer term. Pain may also be felt in the foot which is no longer there. This is called 'phantom pain' and may interfere with fitting and using an artificial leg. Long term pain may also delay recovery and limit what people can do for the rest of their lives. Morphine is often used to help with pain. However, morphine has major side effects, including sickness, confusion, and breathing problems. Reducing pain after amputation is an important topic. A 2014 review showed that only 1 out of every 3 patients in the UK had the 'best' pain relief after amputation.

Who can participate?
This research will take place in 20 NHS hospitals. 650 patients having an amputation because of blocked arteries and/or diabetes will take part.

What does the study involve?
This research will test a method for managing pain after leg amputation. It involves the surgeon placing a tiny tube, called a 'perineural catheter,' next to the main nerve which is cut during surgery. Local anaesthetic is slowly pumped into the tube for up to the first 5 days after surgery. Putting the tube in and taking it out is simple and problems are rare. The tube can replace some (or all) of the morphine often needed. The tube may also reduce phantom pain.
The research will be a 'randomised' trial. This means patients having amputation surgery will be randomly chosen by a computer to either have the tube or not. Everything else will be the same. All patients will have the best anaesthetic and pain control medication. The amount of pain will then be compared between those who did and those who did not have the tube. The amount of pain, morphine used, painkiller side effects, and surgery complications will be recorded for up to 5 days after the amputation surgery. We will ask patients about their pain and if they are walking on an artificial leg 3 and 6 months after their amputation.

What are the possible benefits and risks of participating?
Benefits:
This research is aiming to find out if the placement of a tiny tube (catheter) during amputation surgery, and delivery of a local anaesthetic through the tube for five days after surgery, will

affect the amount of short- and long-term pain experienced by participants, compared with those who do not receive the tube and local anaesthetic. If pain is reduced, this may lead to lower morphine use and fewer side effects, which could help to improve recovery after amputation surgery. Participants will be helping to answer questions about the treatment of lower limb amputation that may result in improved pain management for patients undergoing lower limb amputation in the future.
Risks:
The major burden on participants is the time taken to complete pain and quality of life questionnaires for the first 5 days following their amputation surgery, and 3 and 6 months after their operation. While there are also theoretical risks associated with placement of a perineural nerve catheter (PNC), this procedure is performed routinely and does not seem to be associated with more than very rare complications. This has not been formally studied previously, however, so it is possible that complications simply have not been previously noticed. We will minimise the risks associated with this by routine review by a trial steering committee, which will look at complication rates while the study is running and can call a halt to the study if unexpected complications arise.

Where is the study run from?
Cardiff University (UK)

When is the study starting and how long is it expected to run for?
September 2022 to February 2027

Who is funding the study?
NIHR Health Technology Assessment (HTA) (UK)

Who is the main contact?
placement-trial@cardiff.ac.uk

Study website
https://www.placement-trial.co.uk/sites.html

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1006695

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
1854-21, IRAS 1006695, CPMS 55264

Study information

Scientific Title
Perineural Local Anaesthetic Catheter aftEr Major lowEr limb amputatioN Trial (PLACEMENT)

Acronym
PLACEMENT

Study objectives
Primary objective:
To compare 'freedom from pain' in participants following major lower limb amputation (MLLA) randomised to receive perineural catheter (PNC) placement with participants following MLLA randomised not to receive PNC placement. Freedom from pain is defined as the proportion of pain scores with self-reported pain ≤3 on a 0 to 10 Numeric Rating Scale (NRS). Pain scores will be assessed twice daily for the first five days following amputation surgery.

Secondary objectives include assessing the effect of PNC placement on:
1. Participant satisfaction of pain management, total opioid use and opioid side effects for the first five days after surgery
2. The rate and severity of postoperative complications rate at discharge
3. Surgical site infection at 30 days

4. Hospital stays, including re-admissions after discharge at 90 days
5. Phantom limb pain, chronic stump pain, residual limb surgery, delayed wound healing, health-related quality of life, depression, time to achieve prosthesis fitting (if applicable), level of independence, MLLA of contralateral limb (for unilateral amputees), healthcare resource use, cost-effectiveness, and mortality at 3 and 6 months.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 31/07/2023, East Midlands - Leicester Central Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8284; leicestercentral.rec@hra.nhs.uk), ref: 23/EM/0020

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Major lower limb amputation, including above- below- and through knee amputation, for complications of chronic diseases, including peripheral arterial disease and diabetes.

Interventions
All participants recruited into the trial are scheduled to undergo either an above knee, below knee, or through knee amputation for complications of peripheral vascular disease or diabetes. The intervention arm will receive a perineural catheter (PNC), placed adjacent to the sciatic nerve for above knee amputations or adjacent to the tibial nerve for below knee amputations. Local anaesthetic (Levobupivacaine hydrochloride 0.125 to 0.25%, 1 to 15mg/hr, maximum 400mg per 24 hours OR Ropivacaine hydrochloride 0.2%, 10 to 20mg/hr, maximum 800mg per 24 hours OR Bupivacaine hydrochloride 0.1 to 0.25%, maximum 400mg per 24 hours) will be infused via the PNC for the first five postoperative days. Additional postoperative pain will be managed with standard analgesics, including morphine, as required.

The control arm will not receive a PNC during amputation. Postoperative pain will be managed with standard analgesics, including morphine, as required.

Follow-up activity for both trial arms: Participants' pain scores will be assessed twice daily for the first five postoperative days. Participants will be followed up for additional short and long-term pain and health-related quality of life outcomes at three and six months postoperatively.

Randomisation process will primarily use an online tool with a telephone backup.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Levobupivacaine hydrochloride, ropivacaine hydrochloride monohydrate, bupivacaine hydrochloride anhydrous

Primary outcome measure
Freedom from pain, defined as the proportion of time points with self-reported pain ≤3 using an 11-point Numeric Rating Scale (NRS, range 0 to 10) assessed twice daily for the first five postoperative days.

Secondary outcome measures
(Up to 5 days)
1. Participant satisfaction related to pain management during the preceding 24 h, assessed pre-operatively and once daily postoperatively for up to five days using a 4-point Likert scale
2. Opioid use assessed once daily postoperatively for five days, converted to morphine equivalents using the University of Alberta Multidisciplinary Pain Centre Opioid Conversion Guide
3. Opioid side effects (frequency and severity of symptoms) assessed once daily postoperatively for five days
(At discharge)
4. Morbidity, assessed using Clavien-Dindo grading at discharge
5. Length of hospital stay
(At 30 days)
6. Surgical site infection rates classified as per the 2008 CDC/NHSN document assessed at 30 days
(At 90 days)
7. Days alive and out of hospital assessed at 90 days (DAOH-90)
(At 3 to 6 months)
8. Chronic residual limb pain assessed at 3 and 6 months
9. Phantom limb pain assessed at 3 and 6 months
10. Length of hospital stay assessed at 3 and 6 months
11. Residual limb surgery assessed at 30 days, 3 months, and 6 months
12. Health-related QoL assessed using EQ-5D-5L at 3 months and 6 months
13. Participant reported anxiety and depression assessed using HADS at 3 months and 6 months
14. Prosthesis fitting assessed as rate and time to fitting using SIGAM at 3 and 6 months
15. Assessment of health care resource usage during the first 6 months postoperatively
16. Mortality assessed at 6 months.

Overall study start date
01/09/2022

Completion date
28/02/2027

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 02/07/2024:
1. Aged 18 years or older
2. Undergoing elective or emergency MLLA (BKA, TKA, or AKA) for complications of PAD, diabetes, or acute or chronic infection
3. Able to assess pain using NRS
4. Life expectancy of greater than two weeks
5. (For people of childbearing potential) Willing to undergo a preoperative pregnancy test and agree to either use a highly effective method of contraception or abstain from sexual intercourse for 7 days after MLLA.
6. (For male participants with female sexual partners who are considered to be of childbearing potential)* Willing to agree to use a condom or abstain from sexual intercourse for seven days after MLLA

Previous participant inclusion criteria:
1. Aged 18 years or older
2. Undergoing elective or emergency MLLA (BKA, TKA, or AKA) for complications of PAD and/or diabetes
3. Able to assess pain using NRS
4. Life expectancy of greater than two weeks
5. (For people of childbearing potential) Willing to undergo a preoperative pregnancy test and agree to either use a highly effective method of contraception or abstain from sexual intercourse for 7 days after MLLA.
6. (For male participants with female sexual partners who are considered to be of childbearing potential)* Willing to agree to use a condom or abstain from sexual intercourse for seven days after MLLA

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
650

Key exclusion criteria
Current participant exclusion criteria as of 02/07/2024:
1. Undergoing MLLA for trauma or cancer

2. Undergoing digital, metatarsal, tarsal amputation, disarticulation of the hip or hindquarter amputation
3. Undergoing simultaneous bilateral amputations
4. Undergoing MLLA revision (excluding previous guillotine amputation)
5. Allergy or intolerance to the PNC or local anaesthetic agents, or chronically taking class 1B anti-arrhythmic agents or local anaesthetic agents, for example in the form of transdermal patches.
6. Expected to be sedated for more than 24 hours postoperatively
7. Unable to provide consent due to incapacity (as defined by the Mental Capacity Act 2005)
8. Vulnerable or protected adults.
9. People who are currently pregnant or breastfeeding
10. Previously enrolled in PLACEMENT (excluding PLACEMENT feasibility trial) for a prior MLLA

Previous participant exclusion criteria:
1. Undergoing MLLA for trauma or cancer
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8. Vulnerable or protected adults.
9. People who are currently pregnant or breastfeeding
10. Previously enrolled in PLACEMENT (excluding PLACEMENT feasibility trial) for a prior MLLA

Date of first enrolment
01/09/2023

Date of final enrolment
31/08/2026

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
University Hospital of Wales
Heath Park
Cardiff
United Kingdom
CF14 4XW

Study participating centre
Southmead Hospital
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Study participating centre
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Sponsor type
University/education

Website
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ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Internal report
Conference presentation
Publication on website
Other publication
Other
The findings will be presented at medical conferences, published in free to access medical journals, and shared with people who write amputation surgery guidelines and policies. We will share results via the national press, amputation charities and social media.

Intention to publish date
31/03/2027

Individual participant data (IPD) sharing plan

The current data sharing plans for this study are unknown and will be 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?
Protocol file	version 1.1	14/07/2023	26/09/2023	No	No