Prevention of PostAmputation Pain with Targeted Muscle Reinnervation (PreventPAP trial): A national, multicenter, randomized, sham-controlled superiority trial, comparing standard neurectomy with targeted muscle reinnervation in amputations of the lower extremities.

Published: 28-11-2024
Last updated: 08-02-2025

To compare postamputation pain (phantom limb pain and residual limb pain) one year postoperatively in patients receiving a lower extremity amputation with standard neurectomy versus those who received targeted muscle reinnervation.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Vascular therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON57141

Source
ToetsingOnline

Brief title
PreventPAP trial

Condition

- Vascular therapeutic procedures
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Amputation, postamputation pain

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Zorginstituut Nederland en ZonMW

Intervention

Keyword: Amputation, Neuroma, Phantom pain, TMR

Outcome measures

Primary outcome

1. The mean difference in pain scores for phantom limb pain and residual limb pain one year postoperatively. Pain is measured for 30 consecutive days on the 11-point (0-10) numerical rating scale (NRS)

2. Pain behaviour and interference one year postoperatively according to the Patient-Reported Outcomes Measurement Information System (PROMIS) Pain Behavior and Interference Questionnaire Short-Forms (7a and 8a respectively).

Secondary outcome

- Phantom pain and residual limb pain, measured with the NRS at one timepoint at 3, 6, and 9 months.

- PROMIS pain behaviour and interference (7a and 8a respectively) at 3, 6, and 9 months.

- Quality of life measured with the EuroQol-5D-5L at 2 weeks, and 3, 6, 9, and 12 months

- Neuropathic pain measured with the PainDetect questionnaire at 12 months

- Type of pain (local, diffuse, radiating) measured using the localizing map from the Interdisciplinary Care for Amputees Network (ICAN) at 3,6,9 and 12 months.

- Hospital Anxiety and Depression (HADS) questionnaire, at 12 months

- Global perceived treatment effect measured with the Global perceived effect (GPE-DV) score at 12 months

- Prosthetic rehabilitation measured with the Prosthetic Limb Users Survey of Mobility (PLUS-M, seven items short form) at 12 months

- Societal/healthcare costs with a trial-based cost-utility analysis (i.e., costs per QALY). The Medical Consumption Questionnaire (iMCQ) and Productivity Costs Questionnaire (iPCQ) will be used for the measurement at 3,6,9, and 12 months.

- Budget impact analysis (BIA) at 12 months

- Surgery duration and length of hospital stay

- Adverse events (infection, rebleed, etc. with Clavien-Dindo scores) until 30 days postoperative

Study description

Background summary

In the Netherlands, every year approximately 3300 lower extremity amputations (sacroiliac to forefoot) are performed. In current amputation practice the nerves are cut, without employing any nerve surgical techniques to prevent the development of chronic pain due to neuroma formation. Around 61% of the patients with a transtibial or transfemoral amputation develop postamputation pain (PAP). PAP is a severe lifelong disabling condition profoundly affecting

quality of life.
Microsurgical nerve handling can prevent formation of a painful neuroma and its sequelae. The last years Targeted Muscle Reinnervation (TMR) is the most frequently studied technique for patients with amputation pain with promising results. TMR involves the rerouting of a cut mixed nerve end to a functional motor nerve, with this preventing neuroma formation.
The expected benefit of implementing TMR during amputation surgery is a significant reduction of the incidence of PAP. Prevention of this chronic pain syndrome will lead to a significant improvement in quality of life, participation in family life and society and reduction of health-related costs for thousands of amputation patients every year. To achieve this, a transformation of nerve handling during amputation is needed. With the proposed study we can make this happen.

Study objective

To compare postamputation pain (phantom limb pain and residual limb pain) one year postoperatively in patients receiving a lower extremity amputation with standard neurectomy versus those who received targeted muscle reinnervation.

Study design

A national, multicenter, randomized, sham-controlled superiority trial

Intervention

Patients with a lower extremity amputation are randomized in either standard neurectomy or targeted muscle reinnervation (TMR). With TMR each transected nerve is identified after amputation and is dissected proximally for length. A nerve stimulator is used to identify functional motor nerve branches. Near the point where the motor branch enters the muscle, the motor nerve branch is transected and an end-to-end coaptation is performed with a nearby amputated nerve.

Study burden and risks

The additional risks of performing TMR during amputation are negligible. TMR can be performed at any level of the lower extremities with a standardized technique. For TMR to be possible, in upper leg amputations, an additional incision (ca 10 centimeters) has to be made on the dorsal side of the leg, medial tot the sartorius muscle. To properly blind study participants a superficial incision for upper leg amputations must also be performed in the control group. In our experience this will not result in more postoperative pain or difficulty in sitting. Another factor that will differ from current standards is that the procedure will take 30 to 90 minutes longer. The extra time investment will depend on technical aspects related to the level of

amputation and surgeon experience. Although an increase in surgical time of this length is associated with a slightly higher risk of infection, studies have not found more complications in patients undergoing acute TMR compared to those receiving standard care. The burden of the study is minimal, as participation only requires patients to fill out multiple online questionnaires at five evaluation moments (at 2 weeks, and at 3, 6, 9, and 12 months). Prophylactic TMR results in a reduction of the chance to develop PAP. The risks and the burden for patients are negligible.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Age between 18 and 75 years old
Scheduled for a lower extremity amputation (transfemoral to transtibial), as a

primary or secondary sequela of vascular disease.

Exclusion criteria

- Less than 18 years of age
- Over 75 years of age
- Other reason for amputation besides a primary or secondary sequela of vascular disease
- Insensate limbs at the level of amputation
- CRPS (Complex Regional Pain Syndrome)
- Existing neuroma or prior neuroma surgery in the affected limb
- Physiologically unstable patients at the time of amputation
- Cognitive impairment, delirium
- Undergoing radiotherapy on the affected limb
- Unfit for general anesthesia

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	31-12-2024
Enrollment:	203
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	28-11-2024
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	27-01-2025
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
CCMO	NL87196.058.24