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Mechanical debulking to eliminate thrombolysis and/or open surgery from initial therapy of acute and subacute ischaemia of lower limbs

Submission date
03/05/2017

Recruitment status
No longer recruiting

Registration date
11/05/2017

Overall study status
Completed

Last Edited
15/04/2019

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
Peripheral arterial disease (PAD) is a common condition in which the blood flow to the legs is restricted. This happens because of the buildup of a fatty substance (plaque) on the walls of arteries. Over time this can cause the main arteries in the legs to become narrowed (stenosed) or blocked (occluded). As the arteries become narrower, patients begin the feel pain even when at rest and are at severe risk of developing ulcers or gangrene (acute lower limb ischaemia), which in severe cases can lead to amputation. Many patients are treated with blood thinning medication or surgery to restore blood flow to the leg (revascularisation), however these treatments are not always successful. Today, the most popular and frequently used treatments are surgery and/or thrombolysis. Thrombolysis is a treatment which involves breaking down blood clots which may be blocking the arteries using a type of medication called thrombolytics. They are administered through catheter (tube) inserted into the major artery in the groin. Both therapies are associated with high death rate and serious complications. Catheter therapy itself is less invasive than surgical treatment and therefore, different catheters have been developed that can break up the clot mechanically (mechanical debulking). However, mechanical removal has not replaced the traditional treatment so far, mainly due to limited experience with the new techniques as well as low efficacy of those approaches alone which often requires a combination with thrombolysis. The aim of this study is to find out whether mechanical debulking can be successfully and safely used without having to use thrombolysis and/or open surgery.

Who can participate?
Adults with symptomatic acute lower limb ischaemia.

What does the study involve?
All participants undergo treatment using the mechanical debulking method. This involves a catheter (thin, flexible tube) being inserted into the main artery in the affected leg via the groin and used to mechanically break down the blood clot. Participants are monitored closely for any complications until they are discharged from hospital. In addition, they undergo blood vessel

scans to see if the arteries have become successfully unblocked at discharge and after 30 days and 12 months. In addition, the number of patients who require further treatment, such as amputation or thrombolysis, are recorded for one year.

What are the possible benefits and risks of participating?
Participants may benefit from a better chance of survival and lower complication rate. In addition, patients who are unable to have traditional treatment for medical reasons benefit from being able to receive treatment. There is a small risk of a blockage to blood flow or blood vessel perforation (piercing).

Where is the study run from?
University Hospital and 3rd Medical Faculty of Charles University (Czech Republic)

When is the study starting and how long is it expected to run for?
January 2009 to December 2016

Who is funding the study?
Investigator initiated and funded (Czech Republic)

Who is the main contact?
Professor Miroslav Bulvas
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Prospective, single-arm and non-sponsored trial to evaluate potential of selected mechanical debulking techniques to eliminate thrombolysis and/or open surgery from initial therapy of acute and subacute ischaemia of lower limbs

Study objectives
The aim of this study is to establish whether the initial treatment of patients with acute and subacute lower limb ischaemia can be done successfully and safely by mechanical debulking of target vessels with a catheter combining thrombectomy and atherectomy, without having to use catheter-directed thrombolysis and/or open surgery.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Board of University Hospital Kralovske Vinohrady and Charles University 3rd Medical School, 01/04/2009, ref: EK /IV-2/2009

Study design
Prospective single-arm single-centre non randomised study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Acute and subacute ischeamia of lower limbs

Interventions
After recruitment, all patients undergo digital subtraction angiography and endovascular treatment. The procedure starts with local anesthesia of the groin tissue and insertion of percutaneous sheath. Significant stenosis proximal to target occlusion is dilated before

mechanical debulking to allow sufficient inflow to Rotarex head during its action. Endovascular therapy is based on target vessel mechanical debulking with the Rotarex catheter. Intraluminal passage of guide wire through occlusion is a condition for usage of the technique together with the vessel diameter of 4 mm or more. Control angiography is performed after Rotarex passage. Running (activation) time and number of catheter passages are documented. Percutaneous aspiration thromboembolectomy (PAT) or clot extraction with endomyocardial biopsy device are performed to remove residual clot, if necessary. Percutaneous transluminal angioplasty (PTA) or stenting are used as adjunctive techniques to treat underlying residual stenoses and/or vessel wall irregularities, if angiographically relevant. Additional significant infrapopliteal lesions (acute, subacute or chronic) are managed by PAT, PTA and/or stenting. Catheter-directed thrombolysis and/or open surgical revascularization are immediately considered in patients where mechanical treatment is not successful. Number of patent calf vessels is registered before and after treatment. After the intervention, low molecular weight heparin or unfractioned heparin is administered subcutaneously in preventive doses for 24 hours. Clopidogrel is administered orally in a dose of 75 mg/24 hours for next three months and Oral administration of acetylsalicylic acid (100mg/24 hours) is started after three months and maintained for life. Long-term oral anticoagulation with warfarin is started, if necessary. Individual antithrombotic measures are adopted in selected cases.

Major and minor complications are monitored. After discharge, the patients are followed on ambulantory basis including duplex sonography and ankle-brachial index measurements.

The criteria for reintervention during follow-up are based on clinical symptoms (clinically driven intervention). Repeat percutaneous or surgical interventions are planned only in case of the presence of rest pain, ischaemic lesions (primary ulcer or nonhealing ulcer), or disabling intermittent claudication, while partial or complete reocclusions of previously treated arterial segment which do not present with these symptoms are managed conservatively.

Intervention Type
Procedure/Surgery

Primary outcome measure
1. Number of thrombolytic and surgical revascularization procedures, deaths and amputations is registered at discharge, 30 days and 12 months
2. Amputation-free survival (percentage of patients who survived with both limbs) is evaluated at 30 days and 12 months

Secondary outcome measures
1. Clinical success is defined as technical success of the procedure and relief of acute ischemic symptoms at discharge and at 30 days
2. Overall clinical success is defined as relief of acute ischemic symptoms and the patient´s return to at least his/her pre-occlusive clinical baseline level after the therapy - including adjunctive therapeutic procedures
3. Technical success is defined as restoration of antegrade flow and residual diameter stenosis of 30% or less
4. Hemodynamic success is defined by increase of ABI (ankle-brachial index) for more than 0.10 after the intervention. It reflects overall effect of all recanalization techniques used. ABI is established by doppler as a dimensionless ratio of distal systolic blood pressure and arm systolic blood pressure
5. Primary patency refers to continued flow through treated target vessel without intervention at given time interval (30 days, 12 months), established on the basis of symptoms, physical

examination, ultrasound examination or angiography
6. Secondary patency refers to continued flow through treated target vessel that was restored after reocclusion (durability of second intervention).
7. Number of infrapopliteal interventions is registered immediately after the intervention on angiography
8. Difference in observed parameters between thrombotic and embolic subgroups is assessed by statistical evaluation.
9. Difference in observed parameters between patients with acute and subacute ischaemia is assessed by statistical evaluation
10. Adverse events are registered during intervention, at 30 days and 12 months
10.1. Hemorrhagic and nonhemorrhagic complications are monitored and recorded in patient´s hospital documentation, hospital database, intervention protocol, hospital ambulatory care database and database of laboratory examinations
10.2. Major bleeding is defined as an intracranial bleed, bleeding resulting in death, or bleeding requiring transfusion, surgery, or cessation of endovascular treatment
10.3. Minor bleeding is defined as less severe bleeding managed by local compression, increases in vascular sheath size, or decreases in dose of the lytic, anticoagulant, or antiplatelet drug
10.4. Non-bleeding complications include puncture-related injury, local arterial injury (perforation, dissection, occlusion), embolization requiring intervention, rethrombosis, pericatheter thrombosis requiring unexpected additional intervention, reperfusion injury, compartment syndrome, renal failure, acute myocardial infarction, etc.
10.5. An unexpected amputation (ie, caused by distal emboli) or an increase in the level of amputation as a direct result of the revascularization procedure is regarded as a major complication. Any adverse effect occurring during the time period beginning with the diagnostic arteriogram to 24 hours after revascularization is defined as a procedure-related complication
10.6. Other adverse events that are detected more than 24 hours after revascularization may also be procedure-related (acute renal failure, delayed embolization, or hematoma from the intervention or access site)

Overall study start date
01/01/2009

Completion date
31/12/2016

Eligibility

Key inclusion criteria
1. Symptomatic lower limb(s) ischaemia: acute, categories IIA or IIB (the Rutherford classification of acute limb ischaemia), onset of symptoms: 14 days or less
2. Symptomatic subacute lower limb ischemia: categories 3-6 (the Rutherford classification for chronic limb ischaemia), severe claudication, critical limb ischemia, ischemic tissue defect, rest ischemic pain, symptoms duration: from 15 days to 3 months
3. Aged 18 years and over
4. Written informed consent given prior to study entry (or court agreement in unconscious patient)
5. Occluded graft and/or native artery supplying lower limb (supratibial location, lumen diameter 4 mm or more at the site of occlusion, stented or non-stented, with or without calcifications, with or without additional infrapopliteal occlusions/stenoses)

6. Diagnosis of vascular occlusion on digital subtraction angiogram after informed consent is obtained
7. Ability to traverse the occlusion intraluminally with guidewire

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
300

Total final enrolment
316

Key exclusion criteria
1. Serious hemodynamic circulatory incompetence contraindicating application of x-ray contrast material
2. Anatomy excluding endovascular approach and treatment
3. Category III acute lower limb ischemia (irreversible)
4. Occluded vessel diameter less 4 mm, arterial spasm resistant to nitroglycerine
5. Written informed consent or court agreement were not obtained
6. Situation when primary surgical approach is necessary

Date of first enrolment
01/04/2009

Date of final enrolment
30/04/2015

Locations

Countries of recruitment
Czech Republic

Study participating centre
University Hospital and 3rd Medical Faculty of Charles University
Cardiovascular Centre
Srobarova 50
Prague
Czech Republic
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Sponsor information

Organisation
Charles University

Sponsor details
Charles University Research Program Q38
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Sponsor type
University/education

Website
http://www.lf3.cuni.cz

ROR
https://ror.org/024d6js02

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

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

Intention to publish date
31/03/2019

Individual participant data (IPD) sharing plan

The study protocol, study report and datasets generated during and/or analysed during the current study are available upon request from miroslav.bulvas@fnkv.cz

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		08/05/2017	11/05/2017	No	Yes
Results article	results	01/06/2019	15/04/2019	Yes	No