Dutch randomized trial comparing Ultrasound-accElerated Thrombolysis with standard dose Urokinase versus half dose Urokinase for thrombo-embolic infra-inguinal arterial disease (DUET II)

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To demonstrate that the use of US-accelerated catheter-derived thrombolysis in patients with recently (less than 7 weeks) thrombosed infra-inguinal bypass grafts or native arteries with half the dose urokinase (50.000 IU/h) will significantly reduce...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Embolism and thrombosis
Study type	Interventional

Summary

ID

NL-OMON44501

Source
ToetsingOnline

Brief title
DUET II study

Condition

- Embolism and thrombosis

Synonym
thrombo-embolic infra-inguinal arterial occlusion/ thrombosed leg artery

Research involving
Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: periferal arterial occlusion, thrombo-embolic, thrombolysis, ultrasound-accelerated

Outcome measures

Primary outcome

Occurrence of hemorrhagic complications.

Secondary outcome

1. Technical success defined as >95% lysis of thrombus within 48 hours

2. Duration of catheter-derived thrombolysis needed for uninterrupted flow in

the thrombosed infra-inguinal bypass graft or native artery with outflow via at

least one crural artery

3. Amount of Urokinase (in IU) needed for uninterrupted flow.

4. 30-day mortality

5. 30-day patency of the target artery or bypass, as evidenced by Colour Flow

Doppler Ultrasound (Duplex)

6. Conversion to open surgery

7. Distal thrombo-embolic complications

Study description

Background summary

Thrombosis of an infra-inguinal bypass graft or the native lower leg arteries has been associated with a substantial need for amputations and significant

morbidity and mortality. Traditional therapy consisted of surgical interventions like thrombectomy and bypass revision, whereas currently catheter-directed thrombolysis is preferred. Advantages of catheter-directed thrombolysis as compared to surgery are: less-invasive character, gentler clot removal, clearing out and visualizing the small distal runoff vessels and eventual collaterals. Moreover the underlying lesion can be treated by endovascular means and inflow and outflow arteries can be optimized. Drawbacks might be: higher costs, longer time needed to revascularization compared to surgery, thrombolysis induced hemorrhagic complications, a small but significant incidence of stroke, and renal dysfunction related to repeated angiography.
To reduce these limitations reduction of thrombolytic therapy time will be necessary. Based on available literature US-accelerated thrombolysis has been shown to reduce therapy time of patients with deep vein thombosis by increasing clot permeability to the thrombolytic agent. A similar result was seen in a recent recies of patients with an acute obstruction of the native lower limb arteries.
Recently, the Dutch multicentre DUET I trial has been published. In this trial US-enhanced thrombolysis was compared to standard catheter directed thrombolysis for patients with lower limb arterial thrombus}.
Major conclusions of the DUET I trial are: 1.US-accelerated thrombolysis significantly reduces the duration of thrombolysis time compared to standard catheter directed thrombolysis, 2.US-enhanced thrombolysis significantly decreases the amount of urokinase without increase of complications. However, still the amount of adverse events including bleeding complications was around 28%.

Study objective

To demonstrate that the use of US-accelerated catheter-derived thrombolysis in patients with recently (less than 7 weeks) thrombosed infra-inguinal bypass grafts or native arteries with half the dose urokinase (50.000 IU/h) will significantly reduce hemorrhagic complication rate compared with US-accelerated catheter-derived thrombolysis with the standard dose urokinase (100.000 IU /h) with comparable technical success rates.

Study design

multicentre randomized controlled trial

Intervention

Group A (US-accelerated thrombolysis with 100.000 IU urokinase/h):
During angiography an US-enhanced thrombolysis delivery catheter will be navigated into the thrombosed arterial segment over a guide wire in such a way that the treatment zone traverses the entire clot and the tip lies distal to

the thrombus in a run off artery.
After final positioning, the guide wire will be exchanged for a matching US core wire and thrombolytic therapy will be started. Likewise a control angiography will be performed every 6 hours by day, or whenever clinically needed.
Group B (US-accelerated thrombolysis with 50.000 IU urokinase/h):
Intervention will be similar to group A, but US-accelerated thrombolysis will be performed with 50.000 IU urokinase/h.

Study burden and risks

Urokinase in combination with the EKOS endowave system (EKOS corporation, Bothell, WA, USA) has been extensively used previously for the treatment of venous thrombosis as well as arterial thrombosis.
The only difference between the two groups is the dose Urokinase used. It is expected that the use of half the dose of Urokinase will bring no extra risks for the patients in that group.
If not participating in this trial, patients will be treated with US-accelerated thrombolysis therapy with the common dose of 100.000 IU urokinase/h.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Patients with recently (less than 7 weeks) thrombosed femoro-popliteal or femoro-crural native arteries with ischemic complaints.
2. Patients with recently (less than 7 weeks) thrombosed femoro-popliteal or femoro-crural venous or prosthetic bypass grafts with ischemic complaints.
3. Limb ischemia class I and IIa according to the acute Rutherford classification.
4. Patients >18 years and < 85 years old.
5. Patients understand the nature of the procedure and provide written informed consent, prior to enrolment in the study

Exclusion criteria

1. Patients with isolated common femoral artery thrombosis including the origin of the superficial femoral artery and profunda femoral artery.
2. Patients with clinical complaints of lower limb ischemia due to thrombosis of femoro-popliteal or femoro-crural native arteries or femoro-popliteal and femoro-crural bypass grafts >7 weeks.
3. Patients with acute lower limb ischemia class IIb and III according to the acute Rutherford classification (see below).
4. Patients for whom antiplatelet therapy, anticoagulants or thrombolytic drugs are contraindicated
5. Recent (< 6 weeks) ischemic stroke or cerebral bleeding
6. Patients with recent (<6 weeks) surgery
7. Severe hypertension (diastolic blood pressure >110 mmHg, systolic blood pressure >200 mmHg)
8. Current malignancy
9. Patients with a history of prior life-threatening contrast medium reaction
10. Patients with uncorrected bleeding disorders (GI ulcera, mennorrhagia, liver failure)
11. Female patients of child bearing age not taking adequate contraceptives or currently breastfeeding.
12. Pregnancy
13. Any patient considered to be hemodynamically unstable at onset of procedure
14. Patients refusing treatment.
15. Patients currently participating in another investigational drug or device study that have not completed the entire follow up period.
16. Patients < 18 years or >85 years old.

17. Severe co-morbid condition with life expectancy < 1 month

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-10-2016
Enrollment:	124
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Urokinase
Generic name:	Medacinase
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	23-02-2016
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	15-04-2016
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-07-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 19905
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2015-002161-27-NL
CCMO	NL49466.100.15
OMON	NL-OMON19905