Dutch randomized trial comparing standard catheter-directed thrombolysis versus ultrasound-accelerated thrombolysis for thrombo-embolic infra-inguinal disease.

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Te demonstrate that the use of US-accelerated catheter-derived thrombolysis in patients with recently (between 1 and 7 weeks) thrombosed infra-inguinal bypass grafts or native arteries will significantly reduce (at least 12 hours) therapy time...

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

Summary

ID

NL-OMON35325

Source
ToetsingOnline

Brief title
DUET 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: De behandeling met trombolyse is een standaardbehandeling en wordt verder niet gefinancierd. Alleen het EKOS Endo Wave System wordt voor deze trial met korting door de industrie geleverd.

Intervention

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

Outcome measures

Primary outcome

1. Technical success defined as complete lysis of thrombus of the target vessel

or bypass without distal thrombo-embolic complications.

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

the thrombosed native infra-inguinal artery or infra-inguinal bypass graft with

outflow via at least one crural artery.

3. Number of units urokinasis needed for uninterrupted flow mentioned at point

1.

Secondary outcome

1. Thrombolysis induced hemorrhagic complications

2. 30-day mortality

3. Duration of hospital admission

4. Costs of hospital admission

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

Resonance Angiography (MRA)

6. Drop of serum fibrinogen concentration to below 1.0 g/L during procedure

7. Conversion to open surgery

8. 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 high rate of limb loss and significant morbidity and mortality. Traditional therapy consisted of thrombectomy and graft revision, whereas currently catheter-directed thrombolysis is often used. Major advantages of catheter-dericted thrombolysis as compared to surgery are: less-invasive character, gentler clot removal, clearing out and visualizing the distal runoff vessels and the involved segment, thereby revealing the underlying lesion, easy combination with additional endovascular intervention to treat stenosis of the inflow or outflow arteries. 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 would 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. However, no randomized trials have been performed in the arterial system so far.

Study objective

Te demonstrate that the use of US-accelerated catheter-derived thrombolysis in patients with recently (between 1 and 7 weeks) thrombosed infra-inguinal bypass grafts or native arteries will significantly reduce (at least 12 hours) therapy time compared to standard thrombolysis alone without increasing complication rate.

Study design

Multi centre randomized trial.

Intervention

Group A (standard thrombolysis): During angiography a thrombolysis delivery catheter will be navigated proximally into the thrombus, followed by a control angiography at standardized intervals. During each control angiography the tip of the thrombolysis catheter will be repositioned proximally in the remaining

thrombus.

Group B (US-accelerated thrombolysis): During angiography a thrombolysis delivery catheter will be navigated into the thrombosed segment with a guide wire in such a way that the treatment zone traverses the entire clot and the tip lies distal to the thrombus. 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 at standardized intervals.

Study burden and risks

The EKOS endowave system has been extensively used for the treatment of venous thrombosis. Furthermore, the EKOS endowave system has been used for the treatment of arterial thrombosis. However, until now no randomized trials have been performed. So far, no serious adverse events of the EKOS system itself have been published. It is believed that the risks of US-accelerated thrombolysis will be similar or less compared to those associated with standard thrombolysis. If not participating in this trial, patients would be eligible for standard thrombolysis therapy.

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

17. Patients < 18 years or >85 years old.
18. Severe co-morbid condition with life expectancy < 1 month
19. Contra-indication for MRI

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-11-2009
Enrollment:	60
Type:	Actual

Medical products/devices used

Generic name:	EKOS Endo Wave System
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	13-10-2009
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-05-2010

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-05-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-06-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-01-2011
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

No registrations found.

In other registers

Register	ID
CCMO	NL28737.100.09