A randomized controlled trial comparing venous stenting with conservative treatment in patients with Deep Venous Obstruction

Published: 29-06-2016
Last updated: 07-12-2024

Primary Objective: Measure QoL (VEINES QoL/Sym) change in patients with DVO at one year after PTA and stenting compared to conventional therapy (short class II elastic compressions stockings, exercise, lymph drainage therapy and the use of (pain)…

Ethical review	Approved WMO
Status	Completed
Health condition type	Cardiac and vascular disorders congenital
Study type	Interventional

Summary

ID

NL-OMON50291

Source
ToetsingOnline

Brief title
RCT in Treatment of Deep Venous Obstruction

Condition

- Cardiac and vascular disorders congenital
- Vascular therapeutic procedures
- Vascular disorders NEC

Synonym
May-Thurner syndrome, Post thrombotic syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: subsidie van Optimed GmbH;Ettlingen;Germany

Intervention

Keyword: deep venous obstruction, May-Thurner syndrome, post thrombotic syndrome, venous stenting

Outcome measures

Primary outcome

- The primary outcome is the change in QoL in patients with DVO at one year

after PTA and stenting compared to conventional therapy (short class II elastic

compressions stockings, exercise, lymph drainage therapy and the use of (pain)

medication). based on VEINES-QOL/Sym

Secondary outcome

Secondary study parameters/endpoints

Secondary outcomes are:

- Change in QoL at 6 weeks-3months based on EuroQOL-5D, VEINES-QOL/Sym and pain

disability index

- Clinical assessment of complaints at 9-12 months, using the VCSS, the venous

claudication and the Villalta score.

ii. Other study parameters

- Complication rate in intervention group

- Patency of stents in intervention group

- Ulcer healing and recurrence

- Recurrence of DVT or pulmonary embolism especially in MTS population

Study description

Background summary

Annually about 1-2 per 1000 people in Western European countries develop deep venous thrombosis (DVT). The most frequent long-term complication of DVT is development of a Post thrombotic syndrome (PTS). (1)
PTS consists of a range of symptoms that can occur in patients following a deep vein
thrombosis. The definition of PTS is difficult to quantify but can be measured best by the Villalta score. The higher the Villalta score, the more severe complaints are. A score >15 indicates a severe PTS .
The pathological pathway of PTS is not completely understood but can be found in altered haemodynamics. Virchow*s triad consisting of hypercoagulable state, vascular wall damage and venous stasis explains the development of a deep vein thrombosis. The first two mentioned causes are encountered in standardised treatment nowadays. For the venous stasis no good treatment existed until recently percutaneous angioplasty (PTA) and dedicated venous stents became available. (2)
Patients with PTS experience symptoms related to chronic venous insufficiency caused by obstruction and valve impairment leading to venous hypertension. These symptoms may include pain, tired legs, venous claudication and cramps, oedema, pigmentation or other skin changes finally leading to ulcera.
Patients with established PTS experience a significant impact on QoL with, in several cases,
daily disabilities comparable to an impaired QoL in Chronic Obstrucive Pulmonary Disease (COPD), congestive heart disease and diabetes. (3, 4)
PTS develops in 40-50 % of all patients with a history of a DVT depending on anatomic position of deep venous thrombosis and involvement of collateral system.(5-7) Whenever DVT occurs in iliofemoral or caval veins with obstruction of collateral systems the outflow obstruction is greater than DVT*s in the calf veins. One can understand this outflow obstruction will present more clinical and invalidating symptoms. Other risk factors for severe PTS, found in a large prospective trial, are morbidity included severity of venous symptoms at 1 month, recurrent ipsilateral DVT, high body mass index and higher age. Some of these risk factors are modifiable while others are not. (8, 9)
Like mentioned before venous outflow obstruction is caused by inadequate recanalization, extravascular compression or congenital abnormalities. The most common cause of extravascular compression is called May Thurner syndrome (MTS). May Thurner is defined as compression of the left iliac common vein by the right iliac artery. Patients develop outflow obstruction and valve incompetence which can lead to impaired venous outflow of the leg. This outflow obstruction

causes venous hypertension and consequently the symptoms related to this. Patients with MTS have an increased chance of developing recurrent DVT because of anatomical variance and blood stasis.

Conventional treatment of DVO to minimalize complaints consists of the use of elastic compressions stockings, exercise, lymph drainage therapy and the use of (pain) medication. For most patients the physician selects one or a combination of the treatment modalities mentioned above in an attempt to reduce symptoms. However this is not always effective.(10)
A definitive solution for DVO patients may be a revascularisation procedure and stenting of
the affected tract. This can be achieved by endovascular or hybrid procedures in which a
PTA is performed and a dedicated venous stent is placed. This procedure is already being performed in various hospitals around the world with good results on an individual basis. The goal of PTA and stenting is to prevent PTS (whenever placed in acute settings) or recurrent DVT and associated expected decrease in quality of life. Decreased life quality during treatment of DVO may increase the socioeconomic burden and can eventually lead to loss of ability to work.
Quality of life can be measured by numerous questionnaires. General questionnaires and disease specific questionnaires have been developed.(11)
The VEINES-QoL/Sym questionnaire is a 100 point disease-specific scoring questionnaire which can be used to evaluate the psychometric properties of venous disease. It is a valid and reliable instrument which has been used to evaluate outcomes in previous literature. (12)
Improvement on QoL has been reported after venous stenting in case series. (13, 14) However a randomized trial has never been performed.

Study objective

Primary Objective:
Measure QoL (VEINES QoL/Sym) change in patients with DVO at one year after PTA and stenting compared to conventional therapy (short class II elastic compressions stockings, exercise, lymph drainage therapy and the use of (pain) medication)

Secondary Objective(s):
Measure QoL change in patients with DVO at 6 weeks-three months after PTA and stenting compared to conventional therapy (short class II elastic compressions stockings, exercise, lymph drainage therapy and the use of (pain) medication)

Measuring changes in Villalta scores and VCSS classification compared in patients after PTA and stenting compared to conventional therapy (short class II elastic compressions stockings, possible exercise, lymph drainage therapy and the use of (pain) medication) in patients with DVO

Measuring complication rates of PTA and stenting in patients with DVO

Measuring primary, primary assisted and secondary patency of stents in patients with DVO treated by PTA and stenting in patients

Measuring recurrence of DVT in patients with MTS treated with PTA and stenting or conventional treatment

Study design

We propose to conduct a prospective randomized controlled study comparing PTA and stenting to conservative therapy for patients with DVO.
May Thurner syndrome is defined as chronic compression of left common iliac vein by right common iliac artery resulting in compression of vein between artery and vertebral column.
Post thrombotic syndrome is defined as a range of clinical symptoms with venous claudication or Villalta score >5.

Patients with PTS or MTS who are referred to the department of venous surgery will be recruited. All new patients with deep venous pathology, will have imaging of the veins using duplex ultrasound (DUS) and magnetic resonance venography (MRV) or computed tomography venography (CTV). With these modalities the extent of the obstruction or occlusion of the veins will be assessed.
Eligible patients will be contacted and offered the opportunity to participate in the study. After they have signed informed consent, patients will be randomized to either conservative treatment or PTA and stenting.
Conservative treatment consists of either one or a combination of the following items: therapeutic elastic stockings short (till knee) Class II, pain medication, manual lymphatic drainage therapy and regular post thrombotic anticoagulants therapy. The necessity of each treatment modality will be evaluated on an individual basis in interaction with both the patient as well as the treating physician.
The patients in the intervention group are treated with PTA and stenting of the affected veins (for details about the procedure see section 8.c). All procedures will be performed by a team of dedicated vascular surgeons and interventional radiologists. Only percutaneous procedures will be taken into account.

On baseline and all follow up moments all patients will undergo a full clinical examination to assess the extent of complaints and clinical manifestations from DVO. The severity of complaints is being scored using the Venous Clinical Severity Score (VCSS), venous claudication score and the Villalta scale. Venous claudication is defined as experience of onset or worsening of pain during exercise, which subsides during rest, especially when sitting or lifting the leg.
To assess QoL the VEINES-QoL/Sym will be used for disease specific QoL.
In all patients blood samples are taken on first enrollment, after 6 weeks and

after 12 months for possible future examinations.
Questions about income and having a (paid) job will be asked and registered on baseline and follow up.
All patients will visit the outpatient clinic at 9-12 months after participation.
All these scorings and possible help in filling in the questionnaires will be accompanied by an independent investigator which is blinded for intervention.
The patients in the intervention group will have visits at 2 weeks, 6 weeks, 3 months, and 6 months to assess the patency of the stents by duplex ultrasound.
After 12 months all patients in the intervention group will receive a CTV to evaluate stent patency and stent position.

Intervention

After inclusion patients will be stratified for PTS/ MTS group. Patients in the intervention group will be scheduled and treated with PTA and stenting. For this treatment patients should be administered to the patient ward for at least 24 hours. Patients will be treated percutaneous by punction of the femoral vein, common femoral vein, popliteal or jugular vein. Patients with PTS will receive sedation. Patients with MTS will be treated with local anaesthesia.
After punction of the vein an introducer sheet is introduced. A wire is passed along the diseased segment. This segment is dilated with a balloon and stented.
Afterwards one or more stents will be placed into the vein and post dilatation with a balloon will follow to optimize the geometry of the stent. Patients need to lie down for at least 3 hours to optimal closure of the percutaneous punction.
Whenever necessary, creatin, haemoglobin or INR control has to be performed.
With low haemoglobin levels a packed cell should be given.
INR levels above 4 should be treated with lowering the amount of used anticoagulant tablets and can result in postpone of the procedure.
All patients will receive an infusion and the sedated patients will receive a bladder catheter.

Study burden and risks

For patients who are randomized into the intervention arm of the study a hospital stay for minimum 24 hours till 5 days is mandatory depending on the extent of intervention. Risks associated with the intervention include: bleeding, non-successful intervention, secondary thrombosis or infections of wound, urinary tract or pulmonary tract.
After the intervention patients will receive anti-coagulant treatment for at least 6 months. This is associated with an increased risk of bleeding. Most patients however already receive anticoagulant therapy for previous thrombosis.
Expected benefits for the interventional group are an expected increase in QoL, less loss of working days and thereby reducing costs for the health care and social care system.

Clinical follow up will be performed at 9-12 month for both groups with additional follow up at 2 weeks, 6 weeks, 3 and 6 months after intervention.

For patients who are randomized into the intervention arm of the study a hospital stay for at least 24 hours is mandatory. Risks associated with the intervention include: bleeding, technical or clinical non successful intervention, no relieve of complaints, secondary thrombosis and infection of wound, urinary tract or pulmonary tract.
After the intervention patients will receive anti-coagulant treatment for at least 6 months. This is associated with an increased risk of bleeding. Most patients however already receive anticoagulant therapy for previous thrombosis.
Expected benefits for the interventional group are an expected increase in HRQoL, longer walking distance and pain reduction. Resulting therefrom health and social care costs will decrease. Patients will use less frequent pain medications and will less frequent see a doctor because of unexplainable pain. The social costs will decrease because it is expected patients will have less days off work and therefore less social services will be needed.
Clinical follow up will be matching usual care and be performed at 9-12 month for both groups with usual follow up at 2 weeks, 6 weeks, 3 months and 6 months after intervention with DUS.

Contacts

Public
Medisch Universitair Ziekenhuis Maastricht

P. Debyelaan 25 P. Debyelaan 25
Maastricht 6202 AZ
NL
Scientific
Medisch Universitair Ziekenhuis Maastricht

P. Debyelaan 25 P. Debyelaan 25
Maastricht 6202 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
-- Age >18 years
- Meet criteria for PTS
- Patients with May Thurner syndrome on additional imaging
- All patients with unilateral iliofemoral obstruction on radiological work up expected to be treated solely percutaneous (without AV-fistula) based on post thrombotic changes till above the femoral/ profundal confluents
- Life expectancy of more than one year
- Deep venous thrombosis > 1 year
- Signed informed consent

Exclusion criteria

- Previous intervention of central veins (inferior vena cava, iliac veins, common femoral vein) on the affected limb
- Bilateral disease
- Known pregnancy
- Inability to answer Dutch QoL questionnaires
- Contra-indication for prolonged anticoagulant treatment
- Recent, <1 year, deep venous thrombosis or pulmonary Embolism
- Known contrast allergy
- Known dialysis
- Uncontrolled or active coagulopathy or known uncorrectable bleeding diathesis
- Hypersensitivity to nitinol or nickel
- Known to be, or suspected of being unable to comply with the study protocol (e.g. no permanent address, known to be non-compliant or presenting an unstable psychiatric history)
- Legal incapacity and/or other circumstances rendering the subject unable to understand the nature, scope and possible impact of the study
- Subjects in custody by juridical order
- Subjects who do not agree to the transmission of their pseudonymous data within the liability of documentation and notification
- Close affiliation with the investigational site: e.g. a close relative of the investigator or a possibly dependent person (e.g. employee or student of the

investigational site)

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	10-03-2017
Enrollment:	130
Type:	Actual

Medical products/devices used

Generic name:	Sinus Venous Optimed stent
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	29-06-2016
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	04-10-2017
Application type:	Amendment

Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-05-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-07-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	27-08-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
ClinicalTrials.gov	NCT03026049
CCMO	NL55641.068.15

Study results

Date completed: 07-10-2021

Summary results
Trial ended prematurely