NOSTRADAMUS: Testing for thrombophilia in patients with a first episode of venous thromboembolism: a randomized controlled trial to assess effects on clinical outcomes, quality of life, and costs

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To compare the clinical outcome after a first episode of VTE in patients with well-defined thrombophilia who have been identified and treated for a longer duration with anticoagulants with patients with VTE who have not been routinely tested.

Ethical review	Approved WMO
Status	Pending
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Interventional

Summary

ID

NL-OMON29979

Source
ToetsingOnline

Brief title
NOSTRADAMUS

Condition

- Chromosomal abnormalities, gene alterations and gene variants
- Embolism and thrombosis

Synonym
blood clots, venous thrombosis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ZonMW;Nederlandse Hartstichting (NHS)

Intervention

Keyword: anticoagulants, pulmonary embolism, thrombophilia, venous thrombosis

Outcome measures

Primary outcome

The primary efficacy outcome consists of:

*recurrent VTE 18 months after the acute episode of VTE.

Secondary outcome

Secondary efficacy outcomes are:

* recurrent VTE at the end of the study.

* a composite endpoint of recurrent VTE and bleeding at the end of the study

* quality of life

* costs of testing and subsequent predefined prolongation of anticoagulant

therapy

Study description

Background summary

The last two decades genetic epidemiological studies have identified several hereditary risk factors associated with venous thromboembolism (VTE), often interacting with classical environmental risk factors. In 50-60% of patients with a first episode of VTE such a thrombophilic defect can be detected in blood. This has resulted in widespread testing, also in patients with a first episode, but whether this is effective is unknown. One of the potential

implications of detecting thrombophilia would be to prolong the duration of anticoagulant treatment after the acute episode of VTE, as is suggested in for instance the guidelines of the American College of Chest Physicians 2004 (grade 2 level of evidence). Whether this is justified is intensely debated and depends on the balance between potentially beneficial and harmful effects, besides costs.

Study objective

To compare the clinical outcome after a first episode of VTE in patients with well-defined thrombophilia who have been identified and treated for a longer duration with anticoagulants with patients with VTE who have not been routinely tested.

Study design

A randomized controlled trial of testing and no testing for thrombophilia in patients with a first episode of VTE will be performed. Subsequent additional anticoagulant treatment for a predefined period will be installed in those in whom thrombophilia is detected in the testing group, while others will receive a standard predefined duration of treatment. In addition, the impact on quality of life of thrombophilia testing will be measured. Efficacy and safety outcomes are risk for recurrent VTE and clinically important bleeding (also as a composite outcome). Other outcomes are overall quality of life and costs associated with the outcome measures 18 months after the initial episode of VTE. Outcomes will be compared between thrombophilic patients allocated to the testing group and to the no testing group. A total of 1336 patients will have to be included to detect a benefit of 90% by prolonging anticoagulant treatment in patients with thrombophilia while on treatment, and no reduction in the 6 months after cessation of treatment (overall RRR 55%) [power 80%, confidence level 95%].

Intervention

Randomization into a testing and a non-testing group.
In the testing group, anticoagulant treatment will be prolonged (doubled in duration) in those who tested positive for thrombophilia.

Study burden and risks

Patients will undergo 2 additional venapunctures for thrombophilia tests and other predictive coagulation parameters.
Patients will be asked to fill out 3 quality of life questionnaires, 3 times; each will take approximately 30 minutes to fill out.

The results of this study will answer the dilemma whether testing for

thrombophilia is beneficial (endpoints recurrent VTE after prolonged anticoagulation) or is outweighed by an increase in bleeding and/or diminished quality of life (besides costs).

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
1105 AZ AMSTERDAM
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
1105 AZ AMSTERDAM
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1) Subjects must be willing and able to give written informed consent
2) Confirmed symptomatic DVT, i.e., proximal vein or extensive calf-vein thrombosis, involving at least the upper third part of the deep calf veins (trifurcation, AND/OR confirmed symptomatic PE, no longer than 2 months prior to randomization
3) age 18 years or older

Exclusion criteria

1. Previous episodes of DVT or PE
2. Active bleeding or high risk for bleeding contraindicating treatment with LMWH, fondaparinux or VKA
3. Insertion of a caval filter to treat the episode of VTE
4. Active cancer or anti-cancer treatment in the 6 months prior to the acute episode of VTE
5. Life expectancy < 18 months
6. Arterial thrombotic events in the context of a confirmed antiphospholipid antibody syndrome
7. Indications for VKA other than DVT

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2006
Enrollment:	1336
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	vitamin K antagonist (coumadin derivate)
Generic name:	acenocoumarol
Registration:	Yes - NL intended use

Ethics review

Approved WMO
Application type: First submission

Review commission: METC Amsterdam UMC

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
EudraCT	EUCTR2006-004199-11-NL
CCMO	NL13891.018.06