Evaluation of biomarkers in VTE study: the EVA study.

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The primary objective of this study is to perform a clinical and analytical validation of novel point-of-care (POC) D-dimer assays, in particular regarding their ability to rule-out VTE using an age-adjusted D-dimer cut-of. Secondary objectives are...

Ethical review	Approved WMO
Status	Pending
Health condition type	Embolism and thrombosis
Study type	Observational invasive

Summary

ID

NL-OMON46107

Source
ToetsingOnline

Brief title
the EVA study

Condition

- Embolism and thrombosis

Synonym
venous thrombosis pulmonary embolism

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Nano-ditech corporation Cranbury NJ United States.,Nano-Ditech Corporation Cranbury NJ United States;Roche Diagnostics Nederland Almere en Radiometer Benelux Zoetermeer,Radiometer Benelux Zoetermeer,Roche Diagnostics Nederland Almere

Intervention

Keyword: biomarker, D-dimer, point-of-care, primary care

Outcome measures

Primary outcome

For our primary objective, we will quantify the diagnostic power to (safely) rule out VTE by calculating the failure rate, plus corresponding 95% CI (using Fischer*s exact test) of each POC D-dimer assay, both for using a fixed cut-of value of 500 ng/ml and for using an age-dependent cut-off. The failure rate is defined as the proportion of patients diagnosed with VTE during 3 months of follow-up in those with D-dimer below the chosen threshold in our study patients (i.e. those with a low score on the CDR).

Secondary outcome

The added diagnostic information from inflammatory or coagulation biomarkers will be quantified by using multivariable logistic regression analysis, with VTE presence as the binary outcome of the model. Various logistic models will be constructed. In a first basic model, (inflammatory - CRP, procalcitonin and/or coagulation - TAT) biomarkers will be added to a model including all items from the CDR plus the results from D-dimer testing. Next, this model will be expanded using interaction terms for biomarker results with D-dimer testing, CDR score, gender and/or age. Biomarker results will be added as continuous variables, after checking linearity assumptions.

In a limited number of study patients (100 of 750 EVA patients) a POC measurement is done in the GP's office with blood of a vingerprick additional

to the venapuncture in the laboratory.

Study description

Background summary

Venous thrombo-embolism (VTE), i.e. deep vein thrombosis (DVT) or pulmonary embolism (PE), poses a major diagnostic challenge for the general practitioner (GP) because signs and symptoms can be non-specific and even often quite minimal. The diagnostic work-up starts with scoring a clinical decision rule (CDR). If the CDR yields a low score (low VTE probability) a negative D-dimer test result can safely rule-out VTE without referral for imaging. This approach has been validated for use in primary care and is currently recommended in clinical guidelines.
However, the usability of this diagnostic approach is hampered in two clinical situations. First, D-dimer levels increase with increasing age and recently an age adjusted cut-off level for D-dimer test results was proposed to increase the diagnostic yield of D-dimer (i.e. better rule-out VTE) in elderly patients. Second, the most important differential diagnosis of VTE is a lung- (in the case of a primary suspicion of PE) or skin (in the case of a primary suspicion of DVT) infection. In these cases, due to inflammation, D-dimer levels are also increased, in the absence of VTE, again decreasing the diagnostic yield of D-dimer.
Therefore, in this study, we want to validate novel quantitative point-of-care D-dimer tests, in particular regarding their use of the age-adjusted cut-off value. In addition, we want to quantify the added diagnostic information obtained from inflammatory and coagulation biomarkers in patients suspected of VTE in primary care.

Study objective

The primary objective of this study is to perform a clinical and analytical validation of novel point-of-care (POC) D-dimer assays, in particular regarding their ability to rule-out VTE using an age-adjusted D-dimer cut-of. Secondary objectives are evaluating the added diagnostic information as obtained from inflammatory biomarkers. Finally, we want to evaluate a novel biomarker for coagulation that has recently been developed (e.g. thrombin-anti-thrombin complex; TAT). The diagnostic yield of TAT has never been tested in a clinical population of patients suspected of VTE in primary care.

Study design

Prospective cohort study with 3 months of follow-up in patients suspected of VTE in a primary care setting, in whom the general practitioner (GP) considers

ruling-out VTE.

Study burden and risks

There will be sampling of capillairy blood with a vingerprick (20 mul). This can be painfull. The risk is very low.

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

Patients are eligible for the study if:
- The general practitioner (GP) has a suspicion of deep venous thrombosis (DVT) or pulmonary embolism (PE), i.e. unexplained pain, swelling, and/or redness of the leg in case of

DVT, or unexplained shortness of breath and pain when breathing in case of PE.
- Patients have a low score on a clinical decision rule (low pre-test probability of DVT or PE), and thus the GP aims to rule-out VTE (if possible) using routine care D-dimer testing.

Exclusion criteria

Exclusion criteria are:
- Age below 18.
- Already using anticoagulant treatment with vitamin K antagonists, Non vitamin K Oral Anti Coagulants (NOAC) and/or low molecular-weight heparin (LMWH).
- With a non-low score on a clinical decision rule
- With an already determined POC D-dimer by the GP, suitable for risk stratification
- Life expectancy less than 3 months.
- Unwilling to participate with this study (opt-out procedure).

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Enrollment:	0
Type:	Anticipated

Ethics review

Approved WMO

Date:	23-08-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Approved WMO

Date:	17-11-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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: 29132
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL56475.041.16
OMON	NL-OMON29132