

Rivaroxaban versus low-molecular weight heparin prior to scheduled Ultrasound evaluationN in patients with suspected Deep Vein Thrombosis

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24892

Source

Nationaal Trial Register

Brief title

RUN-DVT

Health condition

Deep vein thrombosis

Sponsors and support

Primary sponsor: Zuyderland MC

Source(s) of monetary or material Support: Almost all staff costs are covered by Zuyderland Medical Centre and in kind donations of the physicians themselves by waiving remuneration. This covers >50% of the costs. Additionally, a grant has been requested to a pharmaceutical company to partly cover the salary of the PhD student.

Intervention

Outcome measures

Primary outcome

Primary study outcomes will be patients' and physicians satisfaction, including patient reported outcome measures (PROMs) and patient reported experience measures (PREMs).

Secondary outcome

A subgroup-analysis will be performed in patients with active malignancy. Moreover, cost-effectiveness analyses will be done on the difference between the use of dalteparin and rivaroxaban (including drug and pharmacy costs as well as time needed for a health care provider to initiate treatment). In additional analyses, data on number of patients, time to treatment, and duration of stay in the outpatient clinic will be compared to other hospitals in the region to estimate the impact on peak load in emergency departments and waiting times. Safety outcomes will be clinically relevant bleeding within 72 hours after administration of anticoagulant drug. Definitions are derived from the EINSTEIN study (N Engl J Med 2010;363:2499-2510): Major bleeding is defined as a clinically overt bleeding that is associated with a fall in the haemoglobin level of 20 g per liter (1.24 mmol/L) or more, or if it led to transfusion of two or more units of red cells, or if it was retroperitoneal, intracranial, occurred in a critical site, or contributed to death. Clinically relevant non-major bleeding is defined as overt spontaneous bleeding not meeting the criteria for major bleeding but associated with medical intervention, unscheduled contact with a physician, or associated with impairment of activities of daily life. Examples of these bleedings are spontaneous epistaxis or gingival bleeding lasting more than 5 minutes, macroscopic haematuria, macroscopic gastro-intestinal haemorrhage or haemoptysis (more than a few spots), intramuscular hematoma, or subcutaneous hematoma larger than 25 cm². In addition, we will also register the occurrence of symptomatic pulmonary embolism within 72 hours after administration of anticoagulant drug, requiring evaluation by a physician or hospital admission.

Study description

Background summary

In patients with deep vein thrombosis (DVT) of the lower extremity, urgent diagnostics and treatment are needed. During the time between clinical suspicion and definite ultrasound diagnosis patients go untreated, with risk for embolization of the thrombus, which could lead to severe morbidity and even death. In almost all hospitals, patients with suspected DVT are therefore referred to the emergency department for further diagnostics and treatment. However, this system poses a large burden on health care services, very often resulting in overtime work by physicians and several hours of waiting time for the patients. Therefore, Zuyderland MC uses a more directive approach (to the best of our knowledge as the only hospital in the Netherlands), by performing DVT diagnostics during a scheduled appointment

at a specialized DVT clinic the next day, instead of referring patients to the emergency department. In order to prevent embolization of the DVT, all patients receive one dose of an anticoagulant from their general practitioner, awaiting further testing. This transition from emergency care to elective care for patients suspected for DVT has several potential benefits: reducing peak load in emergency departments, reducing waiting times, improving patients and physicians' satisfaction, and enabling deployment of dedicated care givers specialized in thrombosis instead of general emergency department staff. However, 'real world' data on these benefits are lacking, hampering the implementation of such system in other hospitals. Therefore, the first goal of this study is to evaluate these potential benefits, including patients' and physicians' satisfaction by means of questionnaires.

Secondly, the preferred type of anticoagulant drug will be evaluated. Currently, Zuyderland Medical Centre uses low-molecular weight heparin (LMWH) as the preferred type of pre-emptive anticoagulation. However, as LMWHs have to be dosed on body weight, have to be stored under controlled circumstances, and have to be administrated parenterally which requires some training, this results in several logistic disadvantages. Therefore, general practitioners asked Zuyderland Medical Centre to explore alternative approaches such as the use of direct oral anticoagulants (DOACs) instead of LMWHs as this could take away many of these inconveniences: all patients can use the same dose, patients can take the pill without help, and the general practitioner could keep a small stock at his/her practice which make urgent pharmacy visits no longer necessary.

Current guidelines support the use of DOACs in case diagnostic studies are deferred and from a pharmacokinetic/dynamic point of view there are no reasons to believe that DOACs are inferior to LMWH. Therefore, in 2021 the regional protocol will be changed from LMWH to DOAC as the preferred type of pre-emptive anticoagulation. However, in our opinion studies on the use of DOACs in this setting are scarce and evidence on potential benefits such as patients' and physicians satisfaction of DOACs over LMWH are lacking. Therefore, we will evaluate the change in protocol from LMWH to DOAC in a regular clinical setting of pre-emptive anticoagulation (even though guidelines support the use of DOACs in this setting), in order to provide 'real world data' and to evaluate if all assumptions on potential benefits including patients' and physicians' satisfaction are true.

Study objective

Primary:

- 1) Prospective evaluation of scheduled/elective care for patients suspected for DVT in terms of patients' and physicians satisfaction (PROMs and PREMs) and waiting hours for the patients.
- 2) To evaluate whether oral administration of rivaroxaban would be preferred over the currently used injection of dalteparin in terms of patients' and physicians satisfaction, non-major bleedings and cost-effectiveness.

Secondary:

- 3) To evaluate whether this approach is also feasible for patients with active malignancy.
- 4) To explore if PROMS, either alone or in combination with standard laboratory tests (D-dimer, complete blood count, C-reactive protein etc.), may help in differentiating between different causes of a swollen leg (such as deep vein thrombosis, bacterial infection, ruptured Baker's cyst, venous insufficiency etc.).

Study design

- Clinically relevant bleeding within 72 hours after administration of anticoagulant drug (definitions see secondary outcome section).
- Symptomatic pulmonary embolism within 72 hours after administration of anticoagulant drug, requiring evaluation by a physician or hospital admission.

Intervention

Questionnaires

Contacts

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Eligibility criteria

Inclusion criteria

We will include patients > 18 years in whom acute DVT of the lower extremity is suspected by their general practitioner based on either a high Wells score or positive D-dimer testing who were referred to Zuyderland MC for further evaluation and whom received pre-emptive anticoagulation (DOAC or LMWH) from their general practitioner.

Exclusion criteria

- Patients suspected for symptomatic pulmonary embolism or DVT of the upper extremity (in these patients urgent evaluation is indicated, which should not be deferred to the next day).
- Patients not receiving pre-emptive anticoagulation either due to violation of the clinical protocol or because of a contra-indication according to the currently used clinical protocol, for

example because of:

- Current use of anticoagulant drugs (DOACs, LMWHs, or vitamin-K antagonists). The use of antiplatelet drugs (aspirin, clopidogrel etc.) is allowed.
- Patients with a very high bleeding risk (as judged by the general practitioner or internist) which is considered to be a contra-indication for pre-emptive use of anticoagulation. For example in case of active major bleeding (e.g. 2 units of more blood or blood products transfused in 24 hours), recent clinically significant bleeding (within the last 7 days); thrombocytopenia (platelets less than $20 \times 10^9/L$), surgical procedure with high bleeding risk within in the last two weeks (e.g. head and neck surgery, neurosurgery or eye surgery), uncontrolled systolic hypertension (230/120 mmHg or higher). Exclusion is always allowed if bleeding risk is considered to be unacceptably high for other, unmentioned reasons.
- Pregnancy or breast feeding.
- Clinically significant liver disease (acute hepatitis, cirrhosis etc.).
- Concomitant use of strong cytochrome P-450 3A4 inhibitors (e.g., human immunodeficiency virus protease inhibitors or systemic ketoconazole) or inducers (e.g., rifampicin, carbamazepine, or phenytoin).
- Hypersensitivity to the active substance or to any of the excipients

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL	
Recruitment status:	Recruiting
Start date (anticipated):	01-06-2021
Enrollment:	1000
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date: 15-10-2021

Application type: First submission

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
NTR-new	NL9842
Other	METC Zuyderland : METCZ20200210

Study results