Safety and efficiency of the YEARS algorithm versus computed tomography pulmonary angiography alone for suspected pulmonary embolism in patients with malignancy

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To prospectively validate the safety and efficiency of management according to the YEARS algorithm to safely rule out clinically suspected PE in patients with active malignancy to be compared with `standard' management by CTPA alone in a...

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

Summary

ID

NL-OMON52383

Source
ToetsingOnline

Brief title
Hydra study

Condition

- Embolism and thrombosis

Synonym
pulmonary embolism clotting in the lung

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: diagnosis, malignancy, pulmonary embolism

Outcome measures

Primary outcome

Safety: Recurrent venous thromboembolism during three months follow-up in patients with initially normal diagnostic tests.

Efficiency: Number of CTPA needed in each randomisation group.

Secondary outcome

To evaluate the occurrence (timing, location and severity) of recurrent symptomatic VTE during follow-up in both study arms in order to better differentiate between missed PE diagnoses and new onset VTE

To compare differences in the rate of isolated sub-segmental PE, defined as CTPA demonstrating an intraluminal filling defect in a sub-segmental artery with no filling defect visualized at more proximal artery levels, in both study arms

To assess the occurrence of incidental VTE, defined as thromboembolism that was detected by means of imaging tests performed for reasons other than clinical suspicion of venous thromboembolism[18], during follow up in both study arms

To evaluate contrast material induced complications (allergic reactions and contrast material induced nephropathy) in both study arms.

To evaluate usage and safety of antithrombotic treatment in both study groups

To evaluate practice patterns of anticoagulation therapy during end-of-life

care in terminally ill patients with cancer.

To evaluate quality of life in patients with PE at baseline or follow-up in

this study by implementing the Pulmonary Embolism Quality of Life (PEmb-QoL)

Questionnaire.

To post-hoc evaluate the performance of the 4-Level Pulmonary Embolism Clinical

Probability Score (4PEPS), in patients randomized for YEARS within the Hydra

study.

Study description

Background summary

Recently, the YEARS-algorithm was demonstrated to be a safe and efficient diagnostic strategy for patients with clinically suspected pulmonary embolism (PE). It is recognized that diagnostic algorithms for pulmonary embolism (PE) may not be as effective and safe in patients with malignancy, due to the low specificity of D-dimer test in that setting. A diagnostic algorithm that could safely rule out PE in patients with malignancy without performing computed tomography pulmonary angiography (CTPA) could nonetheless improve patient care.

Study objective

To prospectively validate the safety and efficiency of management according to the YEARS algorithm to safely rule out clinically suspected PE in patients with active malignancy to be compared with `standard' management by CTPA alone in a randomized study.

Study design

The Hydra-study will be a randomized controlled, multicenter international trial with a non-inferiority analysis for the main safety outcome (rate of 3-month VTE); if non-inferiority has been demonstrated at secondary stage a superiority analysis for the efficiency judgment criterion (rate of unnecessary CTPA) will be performed. Patients will be randomized between management according to the YEARS algorithm versus CTPA alone.

Intervention

Patients will be randomized into management by either YEARS-algorithm or direct CTPA, on a 1:1 basis and stratified by center.
The randomization process will occur directly after signing informed consent, before a D-dimer test is ordered or at least before the result of an ordered D-dimer test has become available.

Study burden and risks

Not applicable (both the YEARS algorithm as the CTPA scan are performed in daily practice).

Contacts

Public
Leids Universitair Medisch Centrum

albinusdreef 2
Leiden 2333ZA
NL
Scientific
Leids Universitair Medisch Centrum

albinusdreef 2
Leiden 2333ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

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

Inclusion criteria

- Clinically suspected PE as judged by the treating clinician
- Any type of active malignancy (other than basal-cell or squamous-cell carcinoma of the skin), defined as diagnosis within six months before the study inclusion (as confirmed histologically or high suspicion as judged by the clinician), receiving treatment for malignancy at time of inclusion or during 6 months prior to randomisation or in the presence of metastases, including recurrent or local metastatic malignancy
- Age >= 18 years
- Signed and dated informed consent, available for start of the trial procedure

Exclusion criteria

- Symptoms for more than 10 days
- Medical or psychological condition that would not permit completion of the study or signing of informed consent, including life expectancy less than 3 months, or unwillingness to sign informed consent
- Treatment with full-dose therapeutically dosed anticoagulation:
o if initiated 24 hours or more prior to eligibility assessment (prophylactic dose with Low Molecular Weight Heparin (LMWH) or direct oral anticoagulants (DOAC) is permitted), or;
o if initiation is expected prior to eligibility assessment for different indication (i.e., atrial fibrillation)
- Contraindication to CTPA
o contrast allergy
o impaired kidney function (eGFR <30 ml/min/1,73m2)
o pregnancy
- Hemodynamic instability at presentation (as a consequence of concurrent acute PE or otherwise), indicated by at least one of the following:
o systolic blood pressure (SBP) < 100 mm Hg, or heart rate >120 beats per minute (unless arrhythmia) or SBP drop by > 40 mm Hg, for > 15 min
o need for catecholamines to maintain adequate organ perfusion and a systolic blood pressure of > 100 mmHg
o need for cardiopulmonary resuscitation
- Suggestion of PE on previously performed oncologic CT scan, for which now PE-specific diagnostic testing is only performed as means of verification
- Participating in another concurrent study on thromboprophylaxis
- Prior participation in the Hydra study

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-08-2019
Enrollment:	1420
Type:	Actual

Ethics review

Approved WMO

Date:	23-07-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	08-08-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	16-10-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	19-10-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	31-10-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL68754.058.19