Risk factor assessment for future arterial cardiovascular events in patients with unprovoked pulmonary embolism.

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON23577

Source
NTR

Brief title
The Pythia Study

Health condition

Pulmonary embolism
Arterial cardiovascular events
Risk factors

Sponsors and support

Primary sponsor: Leiden University Medical Center
Source(s) of monetary or material Support: Leiden University Medical Center

Intervention

Outcome measures

Primary outcome

The primary endpoint of this study is the incidence of arterial cardiovascular events and

deaths during the follow-up period.

Arterial cardiovascular events are defined as:

1. (Fatal) acute coronary syndrome with or without PCI; Non-fatal AMI is defined as the presence of at least two of the following criteria:

A. Typical ischemic chest pain;

B. Elevation of creatinine kinase (CK) enzyme or its MB fraction or troponin;

C. New EKG changes which include new or persistent ST/T changes, new BBB or new Q-waves in at least two consecutive leads.

2. (Fatal) stroke; Ischemic stroke is defined as the presence of a new focal neurological deficit, lasting for more than 24 hours. CT scans or MR images are required to exclude a non-ischemic origin of the neurological event;

3. Carotid endarterectomy;

4. Coronary artery bypass grafting;

5. Symptomatic peripheral arterial disease.

Secondary outcome

The secondary endpoints are the contributable arterial cardiovascular risk factors at baseline that may predict future arterial cardiovascular events.

The cardiovascular risk factors measured at baseline are:

1. Medical and familial history;

2. Smoking status;

3. Medication use;

4. SCORE-score (lipids, blood pressure);

5. EKG;

6. Radiological imaging: Carotid ultrasound IMT and presence of plaque, Agatston¡¯s Calcium score;

7. D-dimer, Factor VIII, Mean platelet values, soluble P-selectin;

8. hs-CRP.

Study description

Background summary

Acute pulmonary embolism (PE) is a frequent problem occurring in around 0.7 – 1.0 per 1000 inhabitants per year in the Netherlands. Several studies have observed an increased risk of arterial cardiovascular events occurring during follow-up after PE. One prospective study demonstrated a higher incidence of arterial cardiovascular events in patients with unprovoked pulmonary embolism (PE) than in those with PE associated with transient risk factors (e.g. post surgery, immobilization, pregnancy, etcetera; relative risk [RR] 7.2; 95%CI, 1.71-30.45). In a second study, the incidence of fatal and non-fatal arterial cardiovascular events was 15% in patients with unprovoked VTE and 8.5% in patients with provoked VTE (adjusted hazard ratio [HR] 1.6; 95%CI, 1.2–2.0). Importantly, in neither of the studies individualised patient data explaining the increased risk for arterial cardiovascular events were available. Identification of patients at high risk for arterial cardiovascular events is very relevant since these patients may benefit from modified treatment regimens including preventive use of antiplatelet and cholesterol synthesis inhibiting treatment. Thus, the identification of risk factors that predict the occurrence of arterial cardiovascular events would be an important step forward in the prevention of arterial cardiovascular events.

Several common, well established risk factors for both venous thromboembolism and arterial cardiovascular events which could contribute to the association between both disease entities have been identified. These include thrombogenic factors (platelet function and markers of thrombogenesis); atherogenic risk factors (classical atherogenic risk factors, inflammation and vessel wall abnormalities). These risk factors can be assessed by blood tests (thrombogenic and atherogenic risk factors), determination of the Systematic Coronary Risk Evaluation -score (SCORE-score), and radiologic examination for atherosclerotic vessel wall changes (Agatston calcium score by CT scan and intima media thickness- plaque assessment of the carotid artery by ultrasonography).

In a recent study we have shown that 20% of patients with unprovoked PE developed arterial cardiovascular events during 4 years of follow-up; patients with provoked PE and patients without PE were shown to have a risk of 5.0-7.0% (HR 2.18; 95% CI 1.1-4.5) .

In the proposed study we hypothesize that: a) there is a wide variability in thrombogenic and atherogenic risk factors, SCORE-score and degree of atherosclerosis assessed by calcium

score and IMT/plaque in patients with unprovoked PE; and b) patients with unprovoked PE who develop an arterial cardiovascular event during follow-up had more thrombogenic risk factors, a higher SCORE-score and higher levels of atherosclerotic vessel wall changes at baseline, compared to the patients without an arterial event during follow-up.

Study objective

1. There is wide variability in thrombogenic and atherogenic risk factors, SCORE-score and degree of atherosclerosis assessed by calcium score and IMT/plaque in patients with unprovoked PE;

2. Patients with unprovoked PE who develop an arterial cardiovascular event during follow-up had increased levels of thrombogenic and atherogenic risk factors, a higher SCORE-score and higher levels of atherosclerotic vessel wall changes at baseline, compared to the patients without an arterial event during follow-up.

Study design

1. <24 hours: Study inclusion;

2. <1 week: Coronary calcium score and IMT measurement and arterial risk factors analysis;

3. 7 months: Thrombotic risk factors analysis;

4. 1 year till end of study: Yearly follow-up visit.

Intervention

Baseline patient assessment:

Patients are asked for inclusion in the study ¡Ü 24h hours after diagnosis of PE. All arterial cardiovascular events that occur after inclusion will be scored. At baseline, patients are assessed for previous cardiovascular history, smoking status, use of medication and family history of arterial cardiovascular events. During physical examination, body weight, body length and blood pressure will be measured and a standard screening for the presence of malignancy is carried out (rectal exam, palpation of mammae in females and further analysis in case of any red flags, like smoking, weightloss and rectal blood loss). Blood is drawn to assess glucose, total cholesterol, HDL-cholesterol, HDL/Cholesterol ratio and triglycerides. The Systematic Coronary Risk Evaluation ¨Cscore (SCORE-score) corrected for the Dutch population is assessed and recalculated for every patient to the age of 60.8 Baseline EKG¡¯s are obtained. Coronary calcium assessment by CT scan9 and intima media thickness and presence of atherosclerotic plaque by carotid ultrasonography is performed6 as soon as feasible after inclusion within a week after diagnosis of PE. After 7 months (6 months VKA and wash-out period of 1 month) factor VIII, D-dimer, hs-CRP, soluble P-selectin and mean platelet volume are measured.

Follow-up assessment:

Patients are instructed to contact study personnel if they develop symptoms of arterial cardiovascular events. Participants are withdrawn and their data censored if they withdraw consent or start anticoagulant therapy (reasons for starting anticoagulants are documented).Six follow up outpatient study visits are planned (within one week, one month after anticoagulant treatment (7 months) and at 12, 24, 36 months and end of follow-up period. (See figure 1.).

Contacts

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Eligibility criteria

Inclusion criteria

Consecutive patients presenting with an episode of unprovoked acute PE are potentially eligible for study inclusion. Acute PE is confirmed by at least one filling defect in the pulmonary arteries on CT scan or a high probability ventilation-perfusion (V/Q) lung scan.

Unprovoked PE is defined as PE in absence of temporary risk factors (malignancy now or in previous 5 years, immobility > 3 days, recent long flight (< 7
days), recent surgery (< 4 weeks), plaster cast of extremity, pregnancy/post partum period, hormone replacement therapy or oral contraceptive use at time of diagnosis or patients with known thrombophilia (Factor V Leiden, Protein C or S deficiency)). Patients > 18 years having given written informed consent are eligible for study inclusion. Patients may present as follows:

1. Presenting with suspected PE without clinical DVT;

2. Presenting with suspected PE and clinical symptoms of DVT: An ultrasound of the symptomatic leg is performed at baseline for proper comparison, should these patients at follow-up present with recurrent leg complaints;

3. Presenting with ultrasound proven DVT and concomitant clinical complains of PE: PE should be objectively proven before study inclusion.

Exclusion criteria

1. Acute onset of PE for more than 14 days;

2. Provoked PE (see criteria mentioned above);

3. Pregnancy;

4. Age less than 18 years;

5. Likelihood of non-compliance (e.g. no fixed address);

6. Life expectancy less than 3 months;

7. Failure to sign informed consent;

8. Diagnosis of PE during anticoagulant treatment;

9. Continuation of anticoagulation after the 6 months treatment period;

10. Participation in this study during a previous episode of acute PE.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2010
Enrollment:	250
Type:	Anticipated

Ethics review

Positive opinion

Date:	06-07-2010
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	NL2281

Register	ID
NTR-old	NTR2408
Other	METC LUMC : P10.141
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A