Redistribution of pulmonary blood flow as a cause for the progression of pulmonary hypertensionin after chronic thrombo-emboli.

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Ethical review	Approved WMO
Status	Completed
Health condition type	Heart failures
Study type	Observational invasive

Summary

ID

NL-OMON31465

Source
ToetsingOnline

Brief title
Cause of progression in chronic thromboembolic pulmonary hypertension

Condition

- Heart failures
- Embolism and thrombosis

Synonym
Chronic thromboembolic pulmonary hypertension AND increased pressure in pulmonary vessels due to bloodclots

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: NWO mozaïekbeurs

Intervention

Keyword: MRI, pulmonary blood flow, pulmonary hypertension, vascular remodelling

Outcome measures

Primary outcome

Changes assessed by MRI between obstructed and non-obstructed regions

of the lungs by means of:

- Pulmonary blood volume

- Pulmonary blood flow

- Mean transit time

- Pulmonary vascular resistance

Secondary outcome

not applicable

Study description

Background summary

Chronic thromboembolic pulmonary hypertension (CTEPH) is a disease with progressive pulmonary vascular damage that develops after an episode of pulmonary embolisms.
Recent research in an animal shunt model revealed that hyperdynamic flow leads to an uncontrolled proliferation of endothelial cells in the pulmonary arterioles and pathologic vasoconstriction. In addition, it was found that the pulmonary endothelium senses the mechanical stretch and responds by enhancing collagen tissue in the vessel wall leading to a further remodeling of the pulmonary arterioles. Furthermore, there is also the clinical observation that hyperdynamic pulmonary flow in patients with a congenital atrial septal defect can lead to endothelial dysfunction and arterial remodeling, causing PH. Based

on these findings we hypothesize that in patients with CTEPH, hyperdynamic flow and increased PAP in the non-obstructed parts of the pulmonary vascular bed lead to endothelial dysfunction inducing pathologic vasoconstriction and vascular remodeling, finally inducing progressive increase in PAP.

Study objective

We aim to investigate whether this damage results from altered pulmonary blood flow patterns and related increases in shear stress and vascular remodelling. To test our hypothesis we will make use of novel techniques to quantify pulmonary perfusion in the lungs during the course of the disease by magnetic resonance perfusion imaging.

Study design

In 30 patients with CTEPH we will quantify the dynamic pulmonary blood flow using 3-dimensional contrast-enhanced MRI. After 6 months we will repeat this 3D contrast- enhanced MRI. According to our hypothesis decrease in flow and an increase in pulmonary vascular resistance in the non-obstructed parts during follow up relative to changes in flow and resistance in obstructed parts will be considered as evidence that vascular remodelling takes place in the non-obstructed vessels.

Study burden and risks

The MRI causes so far we know from literature no damage to people. Injecting of the bolus in an armvein is a routine job and will be done by a doctor, therefore no problem is expected. The contrast liquid gadolineum is not harmful for patients, unless the patient has a decreased kidney function. In that case the patient will be excluded.
In PH, independent of cause, increased pulmonary vascular pressure enhances mechanical stretch which is sensed by the pulmonary endothelium and causes endothelial injury/dysfunction. To assess whether endothelial dysfunction is the underlying cause of pulmonary vasoconstriction in CTEPH, the following markers for endothelial dysfunction will be determined:
- soluble adhesion molecules of the selectin class (soluble platelet selectin [sP-selectin], soluble endothelium
selectin [sE-selectin], soluble leukocyte selectin
[sL-selectin]) using a commercial quantitative colorimetric ELISA.
- Nitric oxide (NO, potent vasodilator) using a commercial quantitative colorimetric assay.
- endothelin-1 (potent vasoconstrictor and platelet-aggregation stimulant) using a commercial radioimmunoassay.
- urinary levels of prostacyclin metabolites (potent vasodilator and anti-platelet-aggregation).
- urinary levels of thromboxane A2 metabolites (potent vasoconstrictor and

platelet-aggregation).

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

- Mean pulmonary artery pressure (mPAP) > 25 mmHg.
- Specific features of chronic thromboembolism on pulmonary angiography as assessed by radiologist(s).
- No previous treatment of oral anticoagulation

Exclusion criteria

- Presence of systemic inflammation.
- Patients with pulmonary hypertension associated with collagen vascular disease, congenital heart disease, pulmonary venous hypertension, left heart failure, hypoxemic lung disease (COPD)
- bad kidney function (creatinin > 120)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	18-02-2008
Enrollment:	30
Type:	Actual

Medical products/devices used

Generic name:	injecting contrast bolus of gadolineum (Magnevist) in the armvein
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	14-02-2008
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
CCMO	NL20175.029.07