Amsterdam/Aarhus Chronic Thromboembolic Pulmonary Hypertension / Chronic Thromboembolic Disease (CTEPH/CTED) Cohort (2A3C) Study

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Describe long-term changes in cardiorespiratory function and structure in a cohort of CTEPH and CTED patients treated with PEA and/or BPA in Denmark and the Netherlands.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Pulmonary vascular disorders
Study type	Observational invasive

Summary

ID

NL-OMON47632

Source
ToetsingOnline

Brief title
2A3C Study

Condition

- Pulmonary vascular disorders

Synonym
Chronic Thromboembolic Pulmonary Hypertension

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Chronic Thromboembolic Pulmonary Hypertension, Hemodynamics, Magnetic Resonance Imaging

Outcome measures

Primary outcome

Main study parameters/endpoints: This is an observational study evaluating determinants of a persistent response to BPA or PEA. Main study parameter/endpoint is change in extracellular volume fraction after unloading of the RV after PEA or BPA. This is measured calculated from pre and post contrast T1 relaxation times measured by MR imaging.

Secondary outcome

- Change in RV function and volumes after PEA or BPA. This is measured by MR imaging (RV ejection fraction, end diastolic volume, end systolic volume) and right heart catheterization (end systolic elastance, RV-Arterial coupling)
- Change in lung perfusion defects before and after PEA measured by MR perfusion
- Change in serum levels of biomarkers of fibrosis and extracellular matrix
- Change in platelet transcriptomes
- Change in exercise capacity (peak oxygen uptake during cardiopulmonary exercise testing, or CPET, and distance walked in 6 minutes) and gas exchange during CPET (ventilatory efficiency, pulse oximetry)
- Change in quality of life

- Change in diffusion capacity

Study description

Background summary

Rationale: In chronic thromboembolic disease (CTED) and chronic thromboembolic pulmonary hypertension (CTEPH), persistent thrombi after acute pulmonary embolism occlude the pulmonary vasculature and cause persistent perfusion defects in the lungs. Patients become symptomatic due to gas exchange abnormalities and pressure overload of the right ventricle (RV), either at rest or on exertion. A secondary pulmonary vasculopathy induced by high shear stress in non-obstructed vessels can contribute to further cardiorespiratory compromise. A diagnosis of CTEPH is a clear indication for interventional treatment, consisting of pulmonary endarterectomy (PEA) or balloon pulmonary angioplasty (BPA), or pharmacological treatment when PEA and BPA are not possible or insufficient. Occluded vessels are opened by PEA and BPA and these interventions are also believed to lead to (partial) reverse remodelling of the lung vasculature and the RV. PEA and BPA can also be indicated for symptomatic CTED patients, who have persistent emboli but no signs of pulmonary hypertension. The early cardiorespiratory effects of BPA and PEA have been well described and it has become clear that residual pressure overload, RV dysfunction and gas exchange abnormalities are quite common. Little is known about the subsequent clinical course of residual pulmonary vascular and RV maladaptation after PEA and BPA. We have observed in our clinic both late reversal of pulmonary vascular and RV remodelling and recurrent adverse remodelling. We hypothesize that late reverse or adverse remodeling of the lung vasculature and RV are critical determinants of long-term clinical outcome in CTEPH and CTED. We also hypothesize that advanced imaging and biomarker analysis will allow for a better understanding of determinants of treatment success of PEA and BPA and that application of these methods will aid in recognition of those patients requiring additional (pharmacological) treatment.

Study objective

Describe long-term changes in cardiorespiratory function and structure in a cohort of CTEPH and CTED patients treated with PEA and/or BPA in Denmark and the Netherlands.

Study design

Study design: Prospective cohort study. CTEPH/CTED patients who are evaluated for invasive treatment with PEA or BPA will undergo structured follow up using right heart catheterization, MR imaging, quality of life questionnaire,

spirometry test, exercise testing and blood sampling before PEA or BPA, and again six and eighteen months after the last BPA session or day of surgery.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: The study relies on information and results from procedures that are part of the clinical routine for CTEPH and CTED patients. This routine consists of the initial medical evaluation after referral and two follow-up visits six and eighteen months after PEA surgery or the last BPA procedure. Patients participating in the study will undergo an extended MR imaging protocol to assess RV function and lung perfusion, which includes administration of 0.3 mmol/kg of gadoterate meglumine contrast media. In rare cases, gadoterate meglumine may induce an allergic reaction. The patients will be informed about these risks and closely observed during the administration of the contrast agent. Milder, rare side effects of gadoterate meglumine are nausea, paraesthesias, skin irritation and headache. While a right heart catheterization is routinely done 3-6 months after PEA or BPA to assess the effects of the intervention, the 18 months* right heart catheterization is currently only done in symptomatic patients (approximately one third of patients). In the last 15 years we have performed about 250 right heart catheterizations each year, with no significant complications. Occasionally, patients experience a local hematoma at the site of venous access in the internal jugular vein.

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

- Diagnosis of CTEPH or CTED (according to ESC/ERS guidelines (11))
- Scheduled for evaluation to determine possibility of PEA or BPA
- Age > 18

Exclusion criteria

- Pacemaker or other metal objects in the body
- Severe claustrophobia
- Severe renal insufficiency (eGFR < 30 mL/min)
- Allergy to gadolinium contrast
- Inability to provide informed consent

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-09-2017

Enrollment:	200
Type:	Actual

Ethics review

Approved WMO Date:	13-06-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-05-2018
Application type:	Amendment
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	NL60598.029.17