Pulmonary artERial hypertenSion: bonE morPHOgeNEtic protein signaling out of control (PERSEPHONE)

Published: 01-08-2017
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Assess BMP10 secretion in patients with pulmonary arterial hypertension and its effect on right ventricular adaptation to pressure overload.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac valve disorders
Study type	Observational invasive

Summary

ID

NL-OMON55717

Source
ToetsingOnline

Brief title
PERSEPHONE

Condition

- Cardiac valve disorders
- Pulmonary vascular disorders

Synonym
Pulmonary arterial hypertension

Research involving
Human

Sponsors and support

Primary sponsor: VU medisch centrum
Source(s) of monetary or material Support: CVON-Phaedra

Intervention

Keyword: Bone morphogenetic protein, Pulmonary arterial hypertension, Right heart failure

Outcome measures

Primary outcome

BMP10 levels measured in bloodsamples and conditioned medium of right atrial

cardiomyocytes

Secondary outcome

* BMP10 activity plasma vs. serum

* Importance of location of the blood sampling (right atrium vs. venous

puncture) on BMP10 activity

Study description

Background summary

Bone morphogenetic protein (BMP) signalling is essential for cardiac development. The ligand BMP10 is uniquely expressed by cardiomyocytes and steers cardiomyocyte proliferation and differentiation. In the adult heart, BMP10 is highly expressed in the right atrium, which is under high stress in patients with pulmonary arterial hypertension. Hence, the stressed right atrium may release increased amounts of BMP10, thereby disturbing the right ventricular response to pressure overload.

Study objective

Assess BMP10 secretion in patients with pulmonary arterial hypertension and its effect on right ventricular adaptation to pressure overload.

Study design

Observational study

Study burden and risks

Aim 1: BMP10 secretion by right atrial cardiomyocytes
During cardiac valve surgery or pulmonary endarterectomy, patients are placed on a cardiopulmonary bypass. Central venous cannulation for cardiopulmonary bypass is accomplished by cannulation of the right atrial appendage. For this part of the study, we want to obtain a biopsy of the right atrium during this procedure. Possible additional risk for this procedure will be bleeding and scar formation. However, as this biopsy will be performed in a setting with an experienced cardio-thoracic surgeon present, this risk is considered minimal.

Aim 2: BMP10 release as a bio-assay of right heart failure
During regular clinical follow-up patients undergo right heart catheterization and magnetic resonance imaging. During the right heart catheterization, blood samples will be withdrawn from the catheter. In addition, a venous blood sample will be withdrawn to determine if right atrial blood sampling is really essential for quantification.

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

Aim 1: BMP10 secretion by right atrial cardiomyocytes
Inclusion criteria patients:
- Patients with chronic thrombo-embolic pulmonary hypertension (CTEPH)
- Undergoing pulmonary endarterectomy, Inclusion criteria controls:
- Patients undergoing cardiac surgery and put on the heart-lung machine, Aim 2: BMP10 release as a bio-assay of right heart failure, Inclusion criteria patients:
- Idiopathic PAH (Invasively assessed mean pulmonary artery pressure >25 mmHg, pulmonary artery wedge pressure <15 mmHg)
- Right heart catheterization and magnetic resonance imaging < 1 year before participation
- Age > 18 years, Inclusion criteria controls:
- Age >18 years
- Age and sex-matched to patients
- We will include 10 subjects with a BMPR2 mutation without Pulmonary Hypertension

Exclusion criteria

Aim 1: BMP10 secretion by right atrial cardiomyocytes, Exclusion criteria patients:
- Age < 18 years, Exclusion criteria controls:
- Pulmonary hypertension (according to European Society of Cardiology guidelines: echocardiography, tricuspid regurgitation peak velocity * 2.8 m/sec, estimated systolic pulmonary artery pressure * 36 mmHg and no additional echocardiographic signs of pulmonary hypertension)(13)
- RV dysfunction (TAPSE < 16 mm)(13)
- RV (annulus) dilatation (RV end-diastolic diameter > 42 mm (base))(13)
- Tricuspid valve replacement or tricuspid annuloplasty
- Dilated right atrium or RA dysfunction (e.g. related to atrial fibrillation, congenital abnormalities; cut-off values: area > 18 cm2)
- Age < 18 years, Aim 2: BMP10 release as a bio-assay of right heart failure, Exclusion criteria patients:
- Pregnancy
- Claustrophobia
- Pacemaker, Exclusion criteria controls:
- Pulmonary hypertension (Invasively assessed mean pulmonary artery pressure > 25 mmHg)
- Increased pulmonary artery wedge pressure (>15 mmHg)
- Tricuspid valve dysfunction

- RV dysfunction
- Dilated right atrium or RA dysfunction (e.g. related to atrial fibrillation, congenital abnormalities)
- Previous cardiac surgery
- Age < 18 years

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-08-2017
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	01-08-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-02-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	18-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-11-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-01-2021
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	NL60827.029.17