Detection Of Latent Pulmonary Hypertension In Genetically Susceptible Individuals.

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We hypothesize that the development of a follow-up program of unaffected mutation carriers will lead to early identification of disease and in the development of strategies to prevent the development of disease and successful treatment.

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

Summary

ID

NL-OMON53083

Source
ToetsingOnline

Brief title
DOLPHIN-GENESIS

Condition

- Heart failures
- Chromosomal abnormalities, gene alterations and gene variants
- Pulmonary vascular disorders

Synonym
early disease, pulmonary hypertension

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: hartstichting

Intervention

Keyword: biomarkers, early detection, genetics, pulmonary hypertension

Outcome measures

Primary outcome

-Platelet markers (RNA profiles)

-Metabolites and cytokines markers

-Exosome markers

-Change in mean pulmonary artery pressure (mPAP)

-Change in cardiac output (CO)

-Change in right atrial pressure (RAP)

-Change in right ventricular ejection fraction (RVEF) (%)

-Change in right ventricular end diastolic volume (RVEDV) (ml)

-Change in right ventricular end systolic volume (RVESV) (ml)

-Change in CPET markers: maximal work (VE), peak oxygen consumption (VO2),

maximal oxygen pulse (O2-pulse), VO2 max, anaerobic threshold (AT), ventilation

for a given volume of carbon dioxide production (VE/VCO2-slope) and the

end-tidal CO2 tension (PET-CO2).

-Change in 6 minute walking distance

- Changes in pulmonary vasculature

Density and abscence of pulmonary vasculature

Abnormal or abberant morphology of pulmonary vasculature

Secondary outcome

non

Study description

Background summary

Idiopathic and heritable forms of PAH (IPAH and HPAH, respectively) are rare diseases that severely limit life expectancy. In recent years, the role of BMPR2 signaling in vascular function and biology has become much better defined. The abnormal pressure response to exercise in BMPR2 mutation carriers suggests that the pulmonary circulation is abnormal even in the subclinical stage. Because of the large vascular reserve capacity of the lung, pulmonary hypertension at rest is thought to develop only after destruction of at least two thirds of the total vascular bed.

Study objective

We hypothesize that the development of a follow-up program of unaffected mutation carriers will lead to early identification of disease and in the development of strategies to prevent the development of disease and successful treatment.

Study design

Prospective observational cohort study

Study burden and risks

-RHC (right heart catherization)
Because RHC are part of our routine clinical assessment protocol a baseline and during regular one-year follow-up assessment, the present study requires one RHC measurement per patient and unaffected carrier at baseline. RHC performed in experienced centres has low morbidity (1.1%) and mortality rates (0.055%) [21]. We consider that the additional measurements are justified by an expected improvement of patients clinical symptoms, quality of life and survival by our goal oriented therapeutic approach in order to preserve/improve RV function during long term follow-up. Furthermore, the results of the present study could be of great value in order to improve the treatment strategy for PAH patients worldwide.

-Liquid biopsy
Venous punction will be done by highly qualified medical doctors of the Department of Pulmonology VUmc. Occasionally punction can cause a hematoma. The total amount of blood withdrawn will be 80 ml per patient for the complete study. The time taken for the procedure will take 10 min.
Drawing of blood by venous punction is a regular diagnostic technique and will be conducted in compliance with the safety guidelines of the department

regarding the procedure.

-Cardiac MRI and cardiac echo are safe procedure with risk associated with participation

-Cardio Pulmonary exercise testing (CPET) is safe and routinely used at our department for patients with PAH and unaffected carriers. There is a small risk of cardiac ischemia during exercise. Therefore we will use ECG-monitoring during exercise and subjects obtained permission for the CPET after approval by a pulmonologist.

- Contrast CT thorax
The risks associated with contrast fluid are allergic reaction or anaphylaxis in severe cases. Both are very rare and can be treated medicamentally by our expertised research group withouth permanent damage, even in cases of anaphylaxis.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (16-17 years)
Adults (18-64 years)

Inclusion criteria

1. Diagnosis of idiopathic PAH, according to ESC/ERS guidelines (ref: Galie ERJ 2015)
Or
Unaffected BMPR2 or other mutation carrier or other mutations associated with PAH
Or
Healthy relative of heritable PAH patient not carrying the disease causing mutation
2. Age >18 and <80 years
3. Able to understand and willing to sign the Informed Consent Form

Exclusion criteria

- Pregnant subjects
- Claustrophobia
- Inability to provide informed consent
- In case of PAH patients: TLC < 70%pred or radiographic evidence of interstitial lung disease
- In case of BMPR2 mutation carriers and family control subjects, one or more of the following: abnormal spirometry, TLC < 70%, echocardiographic evidence of pulmonary hypertension

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-09-2017
Enrollment:	140
Type:	Actual

Ethics review

Approved WMO Date:	06-09-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-02-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-06-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-08-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-06-2022
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	NL61732.029.17