Biomarker activity in adult patients with pulmonary hypertension.

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The aim of this project is to evaluate the clinical value of biomarkers in adult patients with pulmonary hypertension, in particular:1) To quantify biomarkers of neurohormonal activity as NTproBNP, endotheline-1 and of immunological activity as CRP...

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

Summary

ID

NL-OMON45066

Source
ToetsingOnline

Brief title
BioPulse

Condition

- Pulmonary vascular disorders

Synonym
Pulmonary hypertension

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Eerste geldstroom (geld van Ministerie van OC&W aan universiteiten)

Intervention

- No intervention

Keyword: Biomarkers, Morbidity, Mortality, Pulmonary hypertension

Explanation

N.a.

Outcome measures

Primary outcome

All cause mortality

Secondary outcome

heart failure, hospitalization

Study description

Background summary

Pulmonary hypertension (PH) is a rare progressive disease characterized by elevated pulmonary arterial pressure and increased pulmonary vascular resistance which ultimately leads to right ventricular failure and premature death (1). PH can be idiopathic, heritable or associated with multiple other clinical conditions. However, the aetiology of PH is still incompletely understood; multiple factors are involved in the pathogenesis of PH, including genetic predisposition, thrombo-embolic, fibrotic and inflammatory mediators (2-4).

The presenting symptoms of PH are nonspecific and therefore the diagnosis is often delayed by on average 2 years (5). An early diagnosis is crucial as without treatment PH has a median survival of 2.8 years and an estimated 5-year survival of 34% (6). The definitive diagnosis can only be set after right heart catheterization. Nevertheless, to monitor the patients* clinical condition less invasive methods are preferred. Currently the six-minute walking test, NYHA classification and echocardiography, all diagnostic tests which have proven to correlate with disease severity and prognosis (7), are used to evaluate the clinical condition of the patient. However, these diagnostic tools have significant limitations and fail to identify early changes in cardiac function.

Because of the frequent delay in diagnosis and limitations of current diagnostic tools, there is a great need to identify additional measures. These new measures, like biomarkers, can be combined with existing tools to detect and monitor subtle molecular changes in the heart and lungs that reflect and possibly prelude early deteriorations in cardiac function before they become clinically visible. Currently, biomarkers play a role in management of patients with heart failure from other origins like ischemic and hypertrophic heart disease, but the specific role of biomarker measurement in diagnosing and monitoring patients with pulmonary hypertension and associated right ventricular failure has not been investigated yet.

Small biomarker studies have shown that well-established biomarkers for acquired heart failure like BNP and NT-proBNP may also be relevant for various classes of PH (8-9). However, the role of natriuretic peptides in monitoring these patients longitudinally and in predicting outcome remains unclear. Another hormone, endothelin-1, is elevated in the plasma of PH patients and correlates with pulmonary arterial pressure (10). The marker for cardiac necrosis, troponin T, is assumed to be associated with a poor prognosis for patients with pulmonary arterial hypertension (PAH) (11).

In patients with acquired heart failure there is evident involvement of the immunologic system, where cytokines contribute to sustained myocardial dysfunction. The same phenomenon is described in PH patients. The exact pathway to higher circulating cytokines is not exactly known. The intramyocardial cytokine synthesis is probably brought up by increased wall stress and hypoxia. Pro-inflammatory cytokine IL-6 is related to disease severity in idiopathic PAH patients (12).

Despite recent improvements in medical treatment options, inevitable complications as right heart failure and eventually premature death are a major concern in patient with PH. Heart failure appears to result not only from cardiac overload but also from a complex interplay among genetic, neurohormonal, inflammatory and biochemical changes acting on the cardiac myocytes, the
cardiac interstitium or both(13).

Therefore, the main goal of this project is to evaluate trends in biomarkers and their relation with decreased ventricular function in adult patients with pulmonary hypertension.
Thereby, this proposal aims to identify and validate new, potentially important biomarkers, which can be implemented in the clinical management of patients with PH. Finally, the goal is to establish the role of biomarkers as a clinical tool for decision-making and outcome prediction.

Study objective

The aim of this project is to evaluate the clinical value of biomarkers in

adult patients with pulmonary hypertension, in particular:
1) To quantify biomarkers of neurohormonal activity as NTproBNP, endotheline-1 and of immunological activity as CRP, IL-1, IL-6 and cardiac necrosis (troponin T) in blood samples, using high density antibody arrays and ELISAs, obtained in approximately 100 adult patients with pulmonary hypertension.
2) To asses the actual cardiac function (dimensions and function of the right and left ventricle, measured with echocardiography) and the clinical condition (measured with a 6-min walking test and NYHA classification) in these PH patients.
3) To correlate circulating levels of identified biomarkers with cardiac and systemic parameters.
4) To identify new biomarkers as a diagnostic and prognostic tool in patients with PH.

By storing the blood samples of these pulmonary hypertension patients during a period of 4 years, we will create a longitudinal database to study the predictive value of biomarkers for mortality and morbidity. We expect new biomarkers will be detected in the upcoming years, which can be studied then.

Study design

This will be a prospective and observational single center study.

Intervention

N/A

Study burden and risks

not applicable

Contacts

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Trial sites

Trial sites in the Netherlands

Erasmus MC, Universitair Medisch Centrum Rotterdam
Target size: 200

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients to be included must meet the following criteria:
1. Men and women, aged 18 years or older, capable of understanding and signing informed consent.
2. Patients with pulmonary hypertension.

Exclusion criteria

Patients living abroad or who do not speak dutch or english

Study design

Design

Study phase: N/A

Study type:	Observational invasive
Intervention model:	Single
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment started
Start date (anticipated):	15-05-2012
Enrollment:	300
Duration:	240 months (per patient)
Type:	Actual

Medical products/devices used

Product type:	N.a.

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N.a.

Ethics review

Approved WMO

Date:	22-12-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	01-09-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	09-11-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-04-2025
Application type:	Amendment
Review commission:	METC Erasmus MC

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	NL38088.078.11
Research portal	NL-008237