Biomarker activity and chronic heart failure in adult patients with congenital heart disease.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Cardiac and vascular disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON44822

Source
ToetsingOnline

Brief title
BioCon

Condition

- Cardiac and vascular disorders congenital

Synonym
congenital heart disease, heart failure

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Biomarkers, Congenital heart disease, morbidity, mortality

Outcome measures

Primary outcome

Cardiovascular death or complications as heartfailure, hospitalization,

reoperation, arrhythmias and thormboembolic events.

Secondary outcome

Not applicable

Study description

Background summary

Congenital heart disease (ConHD) with an incidence of around 8 cases per 1000 live births is the most prevalent form of congenital abnormality1. The number of adults with congenital heart disease is steadily increasing due to the success of paediatric cardiology and open-heart surgery. This nascent demographic phenomenon is creating major issues concerning the optimal management of adults with ConHD. It is estimated that now ± 30.000 adult patients with ConHD are alive in the Netherlands. Total correction of congenital heart disease is rare and most patients have residual lesions and sequels 2-4. Observational studies in ConHD have taught us that at some point a patient with a cardiac malformation will experience a decline in cardiac function or complications 5.
Late complications such as heart failure, arrhythmias, residual lesions and thromboembolic complications are common, and patients require pharmacological treatment, reoperation, or catheter intervention. It is of great important to deliver adequate interventions to patients with
ConHD and to detect complications as right and left ventricular dysfunction as early as possible 6. Current clinical diagnostic tools such as echocardiography and MRI fail to identify early changes that prelude adverse cardiac remodelling and heart failure. Therefore, there is a great need to identify additional measures that can be combined with existing tools to monitor subtle molecular changes in the heart that reflect and possibly predict adverse changes before they become clinically apparent. Currently biomarkers play a role in management of patients with heart failure from other origin as ischemic and hypertrophic heart disease, but the specific role of biomarker measurement in monitoring

patients with ConHD has not been investigated. Previous small studies of biomarkers in ConHD patients have shown that well-established biomarkers for acquired heart failure like NT-proBNP and BNP may also be relevant for ConHD patients. However, the role of biomarkers in monitoring these patients longitudinally and in predicting outcome remains unclear. Another measureable hormone in ConHD patients is the vasoconstrictive peptide endothelin-1. High levels of endothelin-1 are associated with worse NYHA class and more ventricular impairment 7-9.
Also there is evident involvement of the immunologic system, where cytokines contribute to sustained myocardial dysfunction in patients with acquired heart failure. This phenomenon is also described in patients with ConHD. 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 cytokines IL-1 and IL-6 as well as anti-inflammatory cytokines are elevated and especially more pronounced in the cyanotic ConHD patients group 10-11.
Heart failure is a growing problem in patient with ConHD and it appears to result not only from cardiac overload or injury but also from a complex interplay among genetic, neurohormonal, inflammatory and biochemical changes acting on the cardiac myocytes, the cardiac interstitium or both 12.
The main goal of this project is therefore to evaluate trends in biomarkers and their relation with decreased functional capacity and ventricular function in adult patients with ConHD. Thereby, this proposal aims to identify and validate new potentially important biomarkers, which can be implemented in the clinical management of patients with ConHD. 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 congenital heart disease, in particular:
1) 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 602 adult patients with ConHD.
2) assess the actual cardiac function (dimensions and function of the right and left ventricle,
measured with echocardiography and/or MRI and the clinical condition measured with an
extensive exercise protocol or NYHA classification) in these patients
3) correlate circulating levels of identified biomarkers with cardiac and systemic parameters.
4) identify potential new biomarkers as diagnostic and prognostic tools.
5) repeat measurements of these biomarkers every year for 4 years, once after 8 to 10 years and follow the patient for 15 years.

By storing the blood samples of these well-defined ConHD patients, who will be

followed for 15 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 coming years, which can be studied then. Additional financial resources will be sought for future studies.

Study design

This will be a prospective and observational single-center study.

Study burden and risks

Not applicable

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

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 is known with a congenital heart disease. Cardiac diagnoses are atrial septal defect, ventricular septal defect, pulmonal stenoses, Tetralogy of Fallot, Transposition of the great arteries, eisenmenger syndrome, aortic pathology and Fontan circulation.

Exclusion criteria

Patients living abroad or who were not Dutch speaking.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-05-2011
Enrollment:	602
Type:	Actual

Ethics review

Approved WMO

Date:	10-08-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	23-06-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-12-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL31894.078.10