Vascular reactivity in patients with heart failure, ex- and in vivo vasoresponsiveness

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Primary objective is to analyse vasoreactivity of the vascular system of patients with and without heart failure, in and ex vivo. Secondary objectives are to identify signal transduction pathways associated with the altered vasoreactivity in this...

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

Summary

ID

NL-OMON55621

Source
ToetsingOnline

Brief title
VASOR

Condition

- Heart failures

Synonym
Heart failure, vasoplegia

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Bontius stichting

Intervention

Keyword: Heart failure, Vascular reactivity, Vasoplegia, Vasoplegic syndrome

Outcome measures

Primary outcome

- Change in SVR after phenylephrine administration (phase 1).

Secondary outcome

In vivo (phase 1):

- Systemic arterial pressure waveform morphology.

- Pulse transit time.

- Change in MAP, systemic arterial pressure waveform morphology and pulse transit time after phenylephrine administration.

- Change in MAP, cardiac index and SVR after nitroglycerin administration.

- Vasoplegia: the continuous need of vasopressors (norepinephrine *0.2 µg/kg/min for at least 12 consecutive hours, terlipressin or methylene blue) in combination a state with a cardiac index *2,2 l/min/m2 for at least 12 consecutive hours, starting within the first 3 days postoperatively.

- Copeptin, norepinephrine, epinephrine, atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), N-terminal prohormone of BNP (NTproBNP), angiotensin II, cortisol, aldosterone, renin and vanillylmandelic acid (VMA) levels.

Ex vivo (phase 1 and 2):

- Change in vessel diameter in response to vasoactive drugs.

- Activated signalling proteins which are associated with vasoresponsiveness.

- Receptors (quantity and function) which are associated with

vasoresponsiveness.

Study description

Background summary

Vasoplegia is a state defined by hypotension, a high cardiac index and the continuous need of vasopressors. It occurs in 5-25% of the patients undergoing cardiac surgery on cardiopulmonary bypass (CPB) and is associated with an increased morbidity and mortality. Vasoplegia is a result of activation of several vasodilator pathways, inactivation of vasoconstrictor pathways and the resistance to vasopressors, but the precise aetiology remains unclear. Important risk factors for the development of vasoplegia after cardiac surgery are a left ventricular ejection fraction <30%, CPB and CPB duration. We hypothesize that in patients with chronic heart failure, the responsiveness of the vascular system is permanently altered due to chronic endogenous adrenergic stimulation, resulting in down regulation and/or desensitization of vascular *1-adrenoreceptors. The vascular system of patients with heart failure is easily pushed out of balance by the systemic inflammatory reaction caused by the CPB and surgical trauma, making these patients more prone for developing vasoplegia. Also activation of inducible nitric oxide synthase, activation of adenosine triphosphate dependent potassium channels and deficiency of arginine vasopressin may play an important role.

Study objective

Primary objective is to analyse vasoreactivity of the vascular system of patients with and without heart failure, in and ex vivo. Secondary objectives are to identify signal transduction pathways associated with the altered vasoreactivity in this patient group and to analyse vasoreactivity of the vascular system of patients with and without vasoplegia, in and ex vivo.

Study design

Prospective, cross-sectional study.

Intervention

Not applicable

Study burden and risks

During phase 1, the protocol follows standard care, except for 5 phenylephrine challenges, 1 biopsy from the incision area, 5 blood samples (20 ml each, 100 ml total), 1 urine sample and 2 vasodilation tests. During phase 2 only a biopsy from the incision area is taken. Patients included in the study will not have a direct benefit from the study, but understanding the difference in vascular responsiveness between patients with and without heart failure in detail, might yield therapeutic options or preventive strategies for vasoplegia, leading to safer surgical interventions and improvement in outcome. The measurements necessary to assess the defined study parameters are not expected to negatively influence the result of treatment.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Group 1:

- Diagnosed with heart failure in line with the European Society of Cardiology guidelines;
- Left ventricular ejection fraction <=<35%;
- Undergoing cardiac surgery on CPB., Group 2:
- Not diagnosed with heart failure;
- Left ventricular ejection fraction >50%;
- Undergoing cardiac surgery on CPB.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in the phase 1 of this study:
- Age <18 years;
- Incapacitated adults;
- Emergency operation;
- Patients in need of moderate of high dosages of intravenous inotropic support (>4 gamma dobutamine or dopamine), vasopression and/or mechanical support;
- Patients with aortic valve insufficiency > grade 1;
- Patients using a daily dosage of nitroglycerine or isosorbide dinitrate;
- Patients using alpha blockers.

For phase 2, patients that meet any of the following criteria will be excluded from the study:
- Age <18 years;
- Incapacitated adults;
- Emergency operation;
- Patients in need of moderate or high dosages of intravenous inotropic support (>4 gamma dobutamine or dopamine) and/or vasopression;
- Patients using a daily dosage of nitroglycerine or isosorbide dinitrate;
- Patients using alpha blockers.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-02-2016
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	22-05-2015
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	26-01-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	23-06-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	11-10-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	21-02-2020

Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	04-03-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	25-05-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	10-09-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 22119
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL51125.058.14
OMON	NL-OMON22119