Endothelial Colony Forming Cells, Endothelial Progenitor Cells and Bicuspid Aortic Valves: in vitro culture of peripheral blood cells to study biomarkers and pathogenesis in BAV?

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

Summary

ID

NL-OMON46125

Source
ToetsingOnline

Brief title
In vitro endothelial cell modelling of patients with bicuspid aortic valves

Condition

- Cardiac valve disorders
- Cardiac and vascular disorders congenital
- Aneurysms and artery dissections

Synonym
Bicuspid aortic valves, two aortic valves

Research involving

Human

Sponsors and support

Primary sponsor: Anatomie
Source(s) of monetary or material Support: de Nederlandse Hartstichting

Intervention

Keyword: Bicuspid aortic valve (BAV), Biomarker, Endothelial colony forming cells (ECFCs)

Outcome measures

Primary outcome

The parameters studied are endothelial cell communication and endothelial cell function. -

- The cell communication will be primarily studied in the ECFCs. The response of smooth muscle cells to the presence of ECFC secreted factors will determine what the focus will be of the study. There are 4 likely candidates: inflammatory factors, growth factors, nitric oxide regulation and extracellular matrix remodelling.

- Endothelial cell function will be studied in the EMT response, migration and calcification.

- The results from the ECFCs will then be studied in the EPC*s to look for potential biomarkers

Secondary outcome

The results obtained with the ECFC*s will studied for potential links to valvular development. This might elucidate the pathogenesis of bicuspid aortic valves.

Study description

Background summary

Rationale: Bicuspid aortic valve (BAV), a heart valve with only two leaflets instead of three, is the most common congenital heart malformation. In a significant proportion of patients stenosis or insufficiency of the aortic valves and/or ascending aortic aneurysm contribute to important morbidity and mortality. Turner patients are more prone to the development of cardiovascular diseases, amongst which BAV and dilation. Endothelial dysfunction has been reported in BAV patients, possibly indicating a role for the endothelium in the development of stenosis, regurgitation and/or development of aortic aneurysms. To investigate the endothelial cell functioning and potential biomarkers, endothelial progenitor cells (EPCs) and endothelial colony forming cells (ECFCs) can be isolated from peripheral blood and can be cultured for in vitro experiments. Cell function can be investigated by measuring parameters as migration and response to different signals.
This study is an in vitro cell functioning study to unravel biomarkers of adverse outcome and to explore the pathogenic basis of bicuspid aortic valves and its associated pathologies. This will help to individualize treatment protocols and develop novel therapeutic strategies.

Hypothesis: (1) Cell function will correlate with aortic valve stenosis/regurgitation and aortic root diameter in patients with BAV disease. (2) Cell functional profiles will differ between patients with stenosis or regurgitation of the valves and aortic root dilation and may identify high-risk patients and low risk patients.

Study objective

The main objective of this study is to find biomarkers for the prognosis of the BAV patients by investigating ECFC and EPC functioning, and to gain knowledge on physiological and pathological processes in patients by investigating molecular signalling in these cells.

Objectives:
• To describe the functional characteristics of ECFCs and EPCs of BAV patients;
• To identify cell characteristics associated with the valve stenosis/regurgitation and/or root dilation;
• To associate patient follow-up data to cell characteristics to define potential biomarkers;
• To identify differences in cell functioning of BAV patients with and without Turner Syndrome;
• To identify molecular signalling pathways that are disturbed in

stenosis/regurgitation and/or root dilation.

Study design

In vitro study.

Duration: 3 years inclusion, 15 years follow-up

Setting: Outpatient clinic of an academic hospital.

Study burden and risks

The burden to the patient is one time venous blood sampling. Venous blood sampling of 80 ml has a very low risk. The time consumption for the patient is estimated to be less than 15 minutes.

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

• aged >= 18 years;
• capable of understanding and signing informed consent.
• echocardiogram at most 1 year and 2 months before blood drawing
• for the patient population: Bicuspid aortic valves

Exclusion criteria

• Consuming more than 3 units of alcohol the evening before drawing blood
For the control population:
• Valvular stenosis
• Regurgitation
• Aortic dilation

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:	Recruiting
Start date (anticipated):	02-06-2017
Enrollment:	400
Type:	Actual

Ethics review

Approved WMO Date:	02-06-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	11-07-2017
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

No registrations found.

In other registers

Register	ID
CCMO	NL55229.058.15