Cardiac Imaging in congenital aortic stenosis: unravelling risk factors and predicting clinical outcome

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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-OMON52322

Source
ToetsingOnline

Brief title
CAS

Condition

- Cardiac and vascular disorders congenital

Synonym
bicuspid aortic valve, Congenital aortic stenosis

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Nederlandse Hartstichting

Intervention

Keyword: Cardiac imaging, Congenital aortic stenosis, Left ventricular function, Myocardial characteristics

Outcome measures

Primary outcome

The main study parameters are the prevalence and patterns of myocardial

fibrosis.

Secondary outcome

Secondary study parameters that will be determined at baseline include:

• Left ventricular function and dimensions, measured by echocardiography

(speckle tracking echocardiography with strain and strain rate measurements as

strain volume loops) and CMR (SSFP cine images for ejection fraction and strain

measurements)

• Shear wave velocity, measured using high frame rate echocardiography.

• Flow patterns, measured by 4D flow MRI

• Physical activity in daily life, measured by questionnaires (TSK-NL Heart and

SQUASH)

• Blood biomarkers

• Conduction abnormalities and arrhythmias, measured by Holter ECG and ECG

• Supraventricular and ventricular arrhythmias measured by Holter ECG and ECG

• Quality of life, assessed by using a questionnaire (SF-36)

Additionally, patients will be followed clinically for the duration of 3 years.

Clinical outcome will be assessed with all-cause mortality, incident heart

failure, arrhythmias, endocarditis, aortopathy, (re-) interventions and

operations of the aortic valve and/or ascending aorta and hospitalization for

other cardiac reasons as endpoints.

Study description

Background summary

Congenital aortic stenosis (ConAoS) accounts for 4-8% of all congenital cardiac diagnoses. It is often caused by a bicuspid aortic valve (BAV), which has an estimated prevalence of 0.5-2% in the general population. Patients with ConAoS may remain asymptomatic, but gradual deterioration of the stenosis and the strong association of BAV with aortic dilatation contributes to important morbidity and mortality. The prevalent nature of this heart defect implies an important health problem resulting in hospitalization and (re-) interventions. As it is still largely unknown which markers predict adverse outcome, the aim of this study is to evaluate trends in imaging and biomarkers in this patient population and their relation with clinical outcome.

It is increasingly acknowledged that aortic stenosis is not only a disease of the valve, but also of the left ventricle (LV) and the aorta. In the course of disease progression, pressure overload and ventricular wall stress lead to remodeling of the LV, which eventually leads to left ventricular hypertrophy (LVH) and myocardial fibrosis. Although these processes have been described in patients with aortic stenosis, little is known about the prevalence and prognostic relevance of LVH and myocardial fibrosis in patients with ConAoS, who are often relatively young. Applying upcoming innovative imaging modalities such as high frame rate echocardiography and T1-mapping in patients with ConAoS will increase our knowledge on tissue characterization, which in turn will facilitate identifying patients at high risk for complications and rapid disease progression.

The CAS study is a clinical observational study investigating the effects of ConAoS on the left ventricular function and the prevalence, pattern and expanse of LVH, myocardial stiffness and myocardial fibrosis. Moreover, we will assess the prognostic capacity of the presence of these pathological processes, correlating our findings at baseline to clinical outcome by assessing the occurrence of cardiovascular events and all-cause mortality during 3-year clinical follow-up. We will unravel biomarker and imaging predictors for myocardial dysfunction (systolic and diastolic) with specific attention for male-female differences.
This newly gained knowledge will enable us to improve and individualize current

treatment protocols and derive novel therapeutic strategies for adult patients with ConAoS.

Study objective

The general aim of this study is to gain knowledge on the impact of ConAoS in adult patients, studying the aortic valve itself, the left ventricle and the aorta.

The following primary objective is conducted: to describe the prevalence and pattern of myocardial fibrosis in patients with ConAoS.

Study design

Prospective observational cohort study with 3-year clinical follow-up, conducted at the Erasmus MC.

Study burden and risks

The burden of participation is limited because of the non-invasive nature of the investigations and because the majority of the investigations are part of routine care. Additional burden for participants is mostly attributed to the more extensive nature of the CMR and echocardiography, leading to a greater time investment for the participants. Generally, CMR and echocardiography examinations are tolerated well. Adverse events are rare, but can occur due to the use of contrast agents during the investigations. To minimize the burden for patients, all examinations will be planned at one day.
There are no benefits for participants, besides the contribution to new knowledge and insights on ConAoS, which will in the future hopefully lead to better diagnostic methods and treatments.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

The study population consists of 100 adult ConAoS patients, who are visiting the outpatient clinic of the Erasmus MC.
In order to be eligible to participate in this study, a subject must meet the following criteria:
• Aged >= 18 years
• Capable of understanding and signing informed consent.

Inclusion criteria for the CAS study are patients diagnosed with a valvular congenital aortic stenosis. Two groups of patients will be included:
• Patients with a prior aortic valve replacement (AVR)
• Patients without a prior AVR and with an aortic jet velocity >= 2.5 m/s.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• Patients with severe aortic regurgitation
• Presence of any of the following contra-indications for MRI
o Contra-indication to gadolinium based contrast media (eGFR <30 ml/min or contrast allergy)
o Other contra-indications such as presence of pacemaker/ICD, severe claustrophobia or pregnancy
• Patients known with or previously treated because of significant aortic coarctation.
• Patients known with genetic syndromes or connective tissue disorders

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):	13-01-2022
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	22-11-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-01-2023
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
ClinicalTrials.gov	NCT05252351
CCMO	NL77550.078.21