Mechanistic insights in mitral valve prolapse and associated left ventricular remodelling: Barlow*s Disease versus Fibroelastic Deficiency

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Primary Objective:1) Assess different LV loading mechanisms in Barlow's Disease (BD) versus Fibroelastic deficiency (FED), including transvalvular mitral regurgitant and prolapse volume, both with echocardiography and cardiac magnetic resonance...

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

Summary

ID

NL-OMON52184

Source
ToetsingOnline

Brief title
Mitral valve prolapse and left ventricular remodelling

Condition

- Cardiac valve disorders
- Cardiac and vascular disorders congenital

Synonym
bulging mitral valve, mitral valve prolapse

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Ziekenhuis Antwerpen - Universiteit Antwerpen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Cardiomyopathy, Cardiovascular imaging, Genetics, Mitral valve prolapse

Outcome measures

Primary outcome

Difference in left ventricular volume and function, prolapse volume and mitral regurgitant volume in patients with Barlow's Disease versus Fibroelastic Deficiency, measured by echocardiography and cardiac magnetic resonance imaging.

Secondary outcome

1) Difference in genetic variants (incl. cardiomyopathy and mitral valve prolapse genes genes) in patients with Barlow's Disease versus Fibroelastic Deficiency

2) Difference in ventricular arrhythmias (incl. ventricular ectopy, (non)sustained ventricular tachycardia, ventricular fibrillation and sudden cardiac death) in patients with Barlow's Disease versus Fibroelastic Deficiency and association with left ventricular fibrosis (detected by cardiac magnetic resonance late gadolinium enhancement)

Study description

Background summary

Mitral valve prolapse (MVP) is a frequent valvular disorder which can be

associated with mitral regurgitation, heart failure, ventricular arrhythmias and sudden cardiac death. Barlow's Disease (BD) and fibroelastic deficiency (FED) present the 2 most common MVP subtypes and currently the same assessment and treatment is recommended for both entities. Interestingly, recent evidence points to the existence of a concomitant cardiomyopathy in BD, regardless of mitral regurgitation severity, which could be caused by mutations in cardiomyopathy genes. Furthermore risk at ventricular arrhythmias and sudden cardiac death has been observed to be higher in patients with BD. We hypothesize that mechanisms of left ventricular remodelling in BD include a larger prolapse volume and underlying genetic substrate, beyond volume overload related to mitral regurgitation. These will result in more severe left ventricular remodelling and dysfunction in patients with BD compared to FED.

Study objective

Primary Objective:
1) Assess different LV loading mechanisms in Barlow's Disease (BD) versus Fibroelastic deficiency (FED), including transvalvular mitral regurgitant and prolapse volume, both with echocardiography and cardiac magnetic resonance imaging.

Secondary Objective(s):
2) Assess the prevalence of titin (and other) genetic variants and its impact on left ventricular remodelling in BD versus FED.
3) Assess the arrhythmogenic potential of BD versus FED, and its relationship with the severity of mitral regurgitation, the degree of left ventricular remodelling and the presence of myocardial fibrosis.

Study design

This study is designed to be a multicentre, international prospective cohort study in which we aim to enrol a total of 200 mitral valve prolapse patients, 100 with Barlow's Disease and 100 with fibroelastic deficiency.
To achieve an adequately powered cohort, patients will be recruited at the Departments of Cardiology of 2 large volume centres, namely the Antwerp University Hospital (UZA, Belgium) and the Maastricht University Medical Center + (MUMC+, The Netherlands), who already have an ongoing collaboration.

Study burden and risks

Participation in this study has a very low burden since several of the investigations are frequently performed in clinical routine, such as echocardiography, cardiac magnetic resonance imaging and 24h-holter. The investigations are performed in an ambulatory setting.
* An in-dept 3D-echocardiography has a duration of 20-30 minutes, is non-invasive and part of the routine cardiac follow-up.

* A cardiac magnetic resonance (CMR) scan has a duration of 30-40 minutes, is non-invasive and uses no radiation. Exclusion criteria for CMR will be checked to minimize the risk (e.g. pregnancy, severe chronic kidney disease, devices*). A potential burden of claustrofobia, venous puncture and admission of a contrast agent will be mentioned.
* For 24h-holter monitoring, the patient is asked to wear a small monitor which is connected to chest electrodes for a duration of 24 hours. This is not painful and has a low patient burden with potentially irritation from skin electrodes and discomfort.
* Finally, after genetic counseling one blood sample is taken for genetic testing. The inherent risk of genetic testing includes that certain variants of unknown significance can be detected, but this risk will be limited since we will focus on a specific set of cardiac genes. In case a potentially significant genetic variant is detected, an appointment with a genetic counselor will be scheduled.
Patients could benefit from this study based on the extensive risk assessment regarding severity of mitral regurgitation, fibrosis, arrhythmias and genetic burden. To conclude, participation in this observational study is associated with a very low burden and very few risks and potential benefits can be significant.

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

* Non syndromal mitral valve prolapse
* Age 18-80 years old
* Legally and mentally competent to sign informed consent

Exclusion criteria

* History of cardiac surgery
* Concomitant valve disease (moderate - severe)
* Ischaemic heart disease
* Hypertrophic cardiomyopathy
* Intra-cardiac device
* History of myocarditis
* Left bundle branch block
* Chronic kidney disease stage 4-5
* Pregnancy

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):	01-03-2024

Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	17-01-2023
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL78276.068.22
Other	NTR ID NL9677