Towards optimal management of Marfan Syndrome

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The aim is to investigate the value of novel MRI parameters for aortic hemodynamics and aortic motion and pressure waveforms in MFS patients as potential new biomarkers for guiding surgical and medical treatment of MFS, by analysing these parameters...

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

Summary

ID

NL-OMON56008

Source
ToetsingOnline

Brief title
TOWER

Condition

- Cardiac and vascular disorders congenital

Synonym
Marfan Syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: NWO VIDI uitgereikt aan dr. ir. P. van Ooij

Intervention

Keyword: Advanced MRI, Marfan Syndrome, PEARS

Outcome measures

Primary outcome

There are two main study parameters end points:

1. The difference in 3D aortic displacement expressed in mm, OSI (dimensionless) and PWV (m/s) between MFS patient and healthy control aortas.

2. Change in 3D aortic displacement expressed in mm, OSI (dimensionless) and PWV (m/s) between MFS patient aortas prior to compared to after PEARS procedure or conventional aortic surgery.

Secondary outcome

1. Differences in advanced MRI parameters (displacement, OSI and PWV) between MFS patients who have had aortic root replacement and MFS patients with a native aorta.

2. Differences in advanced MRI parameters(displacement, OSI and PWV) between high and low risk MFS patients based on aortic sinus diameter >4.5cm and <=4.5cm

3. Differences in advanced MRI parameters (displacement, OSI and PWV) between MFS patients who have a HI FBN1 mutation or a DN FBN1 mutation.

4. Differences in advanced MRI parameters (displacement, OSI and PWV) between genders in MFS patients.

5. Differences in advanced MRI parameters (displacement, OSI and PWV) between MFS patients who use different cardiac medication.

6. The correlation between regional WSS and elastic fibre thickness in resected aorta tissue of MFS patients.

7. The correlation between biomechanical tissue stiffness and elastic fibre

thickness

8. Differences in the extracellular matrix of cultured Marfan muscle cells

based on mutation type.

9. The correlation between pressure and flow waveform morphologies and aortic

root geometry in MFS patients with a native aortic root.

Study description

Background summary

Better understanding of aortic hemodynamics and motion in Marfan syndrome (MFS) is required to ultimately improve indication criteria for surgical intervention. In-house developed cardiac magnetic resonance imaging protocols allow us to acquire advanced and detailed functional vascular parameters. The Personalised External Aortic Root Support (PEARS) procedure is an emerging alternative for early surgical intervention on the aorta root, with major benefits, mainly concerning perioperative risks. To our knowledge evaluation of advanced MRI parameters and pressure waveforms in MFS after PEARS procedure has not previously been done.

Study objective

The aim is to investigate the value of novel MRI parameters for aortic hemodynamics and aortic motion and pressure waveforms in MFS patients as potential new biomarkers for guiding surgical and medical treatment of MFS, by analysing these parameters in MFS patients in different disease stages (e.g. native aorta, after conventional aorta surgery and after PEARS procedure) and comparing the acquired values with healthy controls.

Study design

Observational design with a longitudinal design for a subgroup of patients.

Study burden and risks

Most procedures are part of standard clinical care. Added burden of current study is the addition of study sequences to the MRI investigation, which will result in an increase of scan time of twenty to thirty minutes and a subsequent

MRI sessions for a subgroup of patients after aortic surgery. The pressure waveform analysis will take an additional 15 minutes.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Marfan Syndrome patients with a known Fibrilline-1 mutation
- Between 18-50 years of age

Inclusion criteria for participation in the surgery substudy:
- Marfan Syndrome patients with a known Fibrilline-1 mutation
- Planned elective thoracic aorta surgery (aortic (root) replacement, or PEARS procedure)

Healthy controls:
- Between 18-50 years of age

Exclusion criteria

A potential subject who meets any of the following criteria (both patients and healthy controls) will be excluded from participation in this study:
- Contraindication for MR imaging
- Mental retardation
- Pregnancy, or planned pregnancy during study period

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-02-2023
Enrollment:	150
Type:	Actual

Ethics review

Approved WMO

Date:	05-12-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	15-05-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-10-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL82669.018.22