Towards optimal management of Marfan Syndrome

Published: 16-09-2022
Last updated: 06-04-2024

The aim is to obtain sufficient data about aortic hemodynamics and motion in MFS patients in different disease stages (e.g. native aorta, after conventional surgery and after PEARS procedure) and while receiving different medical treatments, to...

Ethical review	Not approved
Status	Will not start
Health condition type	Cardiac and vascular disorders congenital
Study type	Interventional

Summary

ID

NL-OMON51432

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: Flexible OIO AMC

Intervention

Keyword: Advanced MRI, Exercise capacity, Marfan Syndrome, PEARS

Outcome measures

Primary outcome

There are three main study parameters end points

1. Any statistically significant differences in advanced MRI parameters between MFS patients and healthy controls.

2. Any statistically significant differences in advanced MRI parameters between MFS patients prior to compared to after PEARS procedure.

3. Any statistically significant differences in advanced MRI parameters within MFS patients using either ARB, BB or a combination of both

Secondary outcome

1. Differences in advanced MRI parameters between MFS patients who have had aortic root replacement and MFS patients with a native aorta.

2. Differences in advanced MRI parameters between MFS patients who have had aortic root replacement and MFS patients with a native aorta.

3. Differences in advanced MRI parameters between high and low risk MFS patients based on aortic sinus diameter >4.5cm and *4.5cm

4. Differences in advanced MRI parameters between MFS patients who have a HI FBN1 mutation or a DN FBN1 mutation.

5. Differences in advanced MRI parameters between genders in MFS patients.

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. Differences in exercise capacity, quantified as peak oxygen consumption

(peak VO2), within MFS patients using either ARB or BB.

10. Differences in quality of life and habitual physical activity within MFS

patients using either ARB or BB.

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 and provide optimal medication treatment. 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 in MFS after PEARS procedure as well as in MFS patients who receive different medication treatments has not previously been done. Currently, evidence for optimal medicational treatment of Marfan Syndrome is limited and the effect of medicinal treatment on exercise capacity is still incompletely understood.

Study objective

The aim is to obtain sufficient data about aortic hemodynamics and motion in MFS patients in different disease stages (e.g. native aorta, after conventional surgery and after PEARS procedure) and while receiving different medical treatments, to improve our understanding of the pathophysiology of aortic pathology in MFS.

Study design

Part observational and part interventional design with a longitudinal design for a subgroup of patients.

Intervention

Administration of Metoprolol Losartan and a combination of both.

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 1-3 subsequent MRI sessions for a subgroup of patients after surgical intervention and patients who receive different medication regimens. The nature and extent of the burden and risks associated with the additional measurements (cardiopulmonary exercise test (CPET), activity monitor and questionnaire) performed in the medication arm are negligible since these measurements are non-invasive. The risks of administering medication are no different than standard use of these medications in this patient group.

Contacts

Public
Amsterdam UMC

Meibergdreef 9
Amsterdam 1105AZ
NL
Scientific
Amsterdam UMC

Meibergdreef 9
Amsterdam 1105AZ
NL

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

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

Additional exclusion criteria for the medication sub study:
- History of aorta surgery
- More than 50mg daily Metoprolol usage at baseline
- Contra-indication for Metoprolol and/or Losartan
- Contra-indication for cardiopulmonary exercise testing (table 1)
- Patients who use antihypertensive medication for the indication hypertension.
- Patients with a baseline systolic blood pressure >140 mmHg and/or diastolic >90 mmHg.

Additional exclusion criteria healthy controls:
- History of aorta disease

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial

Masking:	Open (masking not used)

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	150
Type:	Anticipated

Ethics review

Not approved

Date:	16-09-2022
Application type:	First submission
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	NL80821.018.22