T1 mapping and exercise 31P-MR spectroscopy for cardiomyopathy phenotyping

Published: 02-11-2012
Last updated: 26-04-2024

The main objective of this study is to explore two novel MRI techniques to characterize myocardial properties that are expected to be useful for the diagnosis of various forms of cardiomyopathy. Furthermore, we will explore whether different stages...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Myocardial disorders
Study type	Observational invasive

Summary

ID

NL-OMON39665

Source
ToetsingOnline

Brief title
MRI for cardiomyopathy phenotyping

Condition

- Myocardial disorders

Synonym
Cardiomyopathy

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: geen financiering

Intervention

Keyword: Cardiomyopathy, Fibrosis, miRNA, MRI

Outcome measures

Primary outcome

The main study parameters are (1) T1 times as quantified by MRI, and (2) stacks of high-energy myocardial phosphate spectra as obtained by 31P-MRS at rest, during mild exercise, and during moderate exercise. For patients in category c2, response after CRT device implantation will be documented by SF36 questionnaires to quantify disease severity and quality of life, a 6 minute walking test to objectively quantify physical fitness, and by echocardiography to quantify progression or regression of left ventricular diameters and ejection fraction.

Secondary outcome

(1) miRNA signature

Study description

Background summary

This research protocol aims to explore two novel magnetic resonance imaging (MRI) techniques to visualize cardiac muscle properties and function that cannot be characterized properly with commercially available pulse sequences. MRI is the gold standard imaging modality for patients with dysfunction of the cardiac muscle, called cardiomyopathy. In many patients, the exact cause of cardiomyopathy cannot be diagnosed because current imaging modalities have important limitations. One of these limitations is the fact that mild and diffuse myocardial fibrosis cannot be visualized, even though this is an important hallmark of cardiomyopathy. A second limitation is the fact that myocardial energy metabolism cannot be quantified noninvasively during physiological exercise. Potential solutions for these limitations are a novel MRI technique called T1 mapping, and an 31P MR spectroscopy protocol (31P-MRS)

to visualize myocardial high-energy phosphate metabolism during physiological exercise using an MRI compatible ergometer, respectively.
Patients who have a clinical indication for a standard 30 min cardiomyopathy MRI protocol will be asked to participate in this research protocol, which will take an additional 30 min. The MRI data acquisition procedures will be similar to standard MRI procedures and all safety precautions will be in place. The exercise protocol consists of baseline MR spectroscopy at rest and during exercise. During the exercise protocol a stepwise increase in heart rate will be achieved until 85% of the predicted value for age and sex. The exercise test consists of cycling on the MR-compatible ergometer, while lying in the MRI scanner. The ergometer has been tested and validated with healthy volunteers in the MRI environment. The MRI protocol will consist of scout acquisitions and a reference scan for the positioning of the patient (5 min), T1 mapping (5 min), a routine clinical cardiomyopathy protocol including late gadolinium enhancement (25 min), and the exercise protocol (25 min). The total MRI procedure will be completed within 60 minutes. The research protocol does not require any additional contrast administration.
We expect to detect differences in T1 times, as well as in exercise-induced kinetic changes in high-energy phosphate dynamics during exercise between healthy volunteers and several groups of cardiomyopathy patients.
During the past decennium it has become clear that miRNAs hold great promise as a new class of biomarkers. By adding the identification of miRNA-signatures to this study protocol these signatures can be related to the different stages of cardiomyopathies which will be identified bij the new MRI techniques.

Study objective

The main objective of this study is to explore two novel MRI techniques to characterize myocardial properties that are expected to be useful for the diagnosis of various forms of cardiomyopathy. Furthermore, we will explore whether different stages of cardiomyopathies which are to be identified by the new MRI techniques, exhibit different miRNA signatures.

Study design

We will employ a novel MRI sequence called T1 mapping to quantify the extent of diffuse myocardial fibrosis, and a 31P-MRS protocol to visualize myocardial high-energy phosphate metabolism during physiological exercise using an MRI compatible ergometer. These two objectives are feasible in a 30 min research protocol that can be added to a standard clinical 30 min cardiomyopathy protocol that is clinically indicated in a range of patients with suspected or proven myocardial dysfunction. Also, MiRNA-profiling will be performed in these patients. This research protocol will be used in healthy volunteers and in a

range of patients with cardiomyopathy.

Study burden and risks

For all patients undergoing MRI, the research protocol consists of a noninvasive imaging protocol. For the majority of patients from categories a-d, the research protocol will be a 30 min extension of the clinically indicated MRI for which they were referred by their treating cardiologist. In addition, one blood sample will be taken to measure hematocrit, a parameter required to calculate extracellular matrix volume based on the T1 mapping results; this blood sample will be taken from the canula that is required for contrast administration during the routine MRI protocol. In some categories with low inclusion rates, patients will be asked to undergo an MRI which was not requested by their treating cardiologist. However, it should be noted that in these patient categories, the additional MRI does provide valuable information about cardiac function (volumes, ejection fraction, fibrosis) which may benefit the patient*s clinical follow-up. Patients from category c1 have a clinical indication for MRI before CRT device implantation. The research protocol will encompass a 30 min extension of the MRI protocol. In addition, it will include a standardized follow-up to document response to CRT. An outpatient clinic visit and echocardiography at baseline and at 1 year follow-up are routine clinical practice, but the research protocol will include two SF36 questionnaires and two 6 minute walking distance tests (one each at baseline and 1 year follow-up).
When patients wish to stop the scanning procedure and get out of the scanner they can press a *panic button*, which is standard procedure for every MRI. This *panic button* can also be used during the exercise protocol. Patients are also able to talk to the researchers in the control room at any time during the experiment. Potential hazards from high energy radiofrequency or gradient pulses are not any higher than in the manufacturer*s sequences. MRI does not require ionizing radiation, and gadolinium contrast is well tolerated with only very rare cases of gadolinium allergy reported in the literature.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Various types of cardiomyopathy due to genetic mutations, as well as acquired cardiomyopathies.

Exclusion criteria

1. Under the age of 18.
2. Have a history of claustrophobia.
3. Are anticipated not to be able be complete the exercise protocol.
4. Have renal failure (estimated glomerular filtration rate < 30 ml/min)
5. Are not able to provide written informed consent.
6. Have a contra-indication for MRI.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-12-2012
Enrollment:	320
Type:	Actual

Ethics review

Approved WMO Date:	02-11-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-03-2013
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	NL41971.018.12