Assessment of myocardial function, metabolism, and perFUSION in early and advanced disease stages of Hypertrophic CardioMyopathy: FUSION-HCM

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In different stages of HCM:- To measure myocardial fatty acid oxidation, uptake and esterification- To measure myocardial glucose uptake en oxidation- To measure myocardial perfusion- To measure myocardial function- To measure volume parameters of...

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

Summary

ID

NL-OMON49221

Source
ToetsingOnline

Brief title
FUSION-HCM

Condition

- Myocardial disorders
- Cardiac and vascular disorders congenital

Synonym
Enlarged heart muscle disease

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: NWO VICI Jolanda van der Velden

Intervention

Keyword: Cardiomyopathy, Hypertrophic, metabolism

Outcome measures

Primary outcome

myocardial fatty acid oxidation, uptake and esterification, glucose uptake en

oxidation, perfusion, function and volume parameters of the heart

Secondary outcome

biomarker analysis

Study description

Background summary

Hypertrophic cardiomyopathy (HCM) is a genetic disorder characterized by asymmetric hypertrophy of the heart in absence of loading conditions like hypertension. The genetic mutation underlying HCM sets in motion a cascade of functional and metabolic changes ultimately leading to disease. The theory of energy deficiency currently is the leading theory of the pathomechanism of HCM. Based on inefficient contraction of the heart, heart muscle cells become energy deficient and cannot regulate their metabolism properly. To find evidence to support this theory, this study will measure cardiac metabolism in vivo by measuring which ratio of substrates (free fatty acids/glucose) the heart uses to generate energy. As the pathomechanism of HCM is thought to be a cascade of changes, cardiac substrate metabolism and perfusion will be measured in different stages of disease: no symptoms, mild symptoms, and advanced HCM

Study objective

In different stages of HCM:
- To measure myocardial fatty acid oxidation, uptake and esterification
- To measure myocardial glucose uptake en oxidation
- To measure myocardial perfusion

- To measure myocardial function
- To measure volume parameters of the heart
- biomarker analysis

Study design

Observational with invasive measurements

Study burden and risks

Participants will have to spend two full days in the hospital and lie still for long periods in scanners. Intravenous lines will be inserted which can be painful and unpleasant. Averse reaction of dotarem are rare. The side-effects of docutamine and adenosine can be unpleasant. A doctor will always be present to terminate the test if necessary. The radiation exposure is 7,1 mSv, which falls in category IIb and is associated with low risk. It corresponds with a maximum risk om 1 in 10.000 and is comparable to the average background radiation in some parts of the world (Dutch Committe for Radiation Dosimetry, 6 september 2015). Performing this research in this population is justified because this research will thoroughly examine the sequence of events leading to HCM and aims to find ways to better predict progression of disease in mutation carriers and/or find targets for preventative therapy.
This study with capacitated adults will yield a tremendous amount of knowledge about the sequence of events driving HCM. This study is the first to do extensive measurements of function and metabolism in HCM in different stages of disease. The implications of this study involve predictive and prognostic strategies for HCM which currently do not exist. Additionally, findings of this study may lead to new therapeutic targets for HCM or verification of therapeutic strategies that are currently being researched.
For this study it is essential to involve both MYBPC3 and MYH7 mutation carriers because these two groups form the vast majority of HCM-causing mutations. The risks can be considered negligible because the VU has much experience with the procedures performed in this study and specialists (cardiologists, internists, nuclear radiologists) are involved in all aspects of the study. All procedures except the 11C-palmitate PET/CT scan are routinely performed in the VUmc for clinical and/or research purposes.

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

MYBPC3 mutation carrier
MYH7 mutation carrier
Genotype-negative first degree relative of a MYBPC3 or MYH7 mutation carriers

Exclusion criteria

>=65 years old
Diabetes mellitus
Pregnancy
Claustrophobia
Pacemaker/ICD
Renal insufficiency <60 GFR
Hypertension
Aortic valve disease
BMI >30 kg/m2
Left bundle branch block
Obstructive coronary artery disease
Atrial fibrillation

Hormone replacement therapy

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-12-2019
Enrollment:	105
Type:	Anticipated

Ethics review

Approved WMO

Date:	24-08-2020
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	NL69153.029.19