Cardiac mitochondrial function; Comparison of in and ex vivo measurements

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Observational invasive

Summary

ID

NL-OMON47816

Source
ToetsingOnline

Brief title
31P-MRS study

Condition

- Heart failures
- Diabetic complications

Synonym
diabetic cardiomyopathy

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: heart, mitochondrial function, MRS

Outcome measures

Primary outcome

The primary goal is to compare in vivo with ex vivo measurements of mitochondrial function through regression analysis.

Secondary outcome

Furthermore markers of PPAR-expression will be examined and statistical analysis will be done to assess differences between groups (diabetic/lean/obese) where $P<0.05$ will be considered statistically significant different. Also liver fat accumulation will be determined with MRI in order to asses the relationships between liver fat accumulation and cardiac metabolism.

Study description

Background summary

It has been suggested that mitochondrial dysfunction, through down-regulation of nuclear ligands (PPARs), might play a role in the development of diabetic cardiomyopathy. Also, mitochondrial dysfunction has been associated with other cardiac diseases like for example chronic heart failure. However, human data on this topic is scarce. This is due to the fact that there is no validated measurement for assessing cardiac mitochondrial function non-invasively in vivo. It has been suggested that measuring PCr/ATP ratio*s with 31P-MRS in the heart, might reflect cardiac mitochondrial function. However, so far no direct validation of this method has been performed.

Study objective

The primary objective of this study is to validate 31P-MRS as a non-invasive in vivo measure of mitochondrial function. Secondary objectives are to determine whether there is mitochondrial dysfunction in the heart of type 2 diabetic patients and to determine the role of cardiac PPAR-expression in the

development of cardiac dysfunction in type 2 diabetes.

Study design

Here it concerns an observational study, where in vivo and ex vivo measurements of mitochondrial function in type 2 diabetic, normo-glycemic obese and lean participants are compared.

Study burden and risks

Patients will visit the University once. Total participation time in the study will be about 5 hours. At this visit characterisation of the subject will take place; body composition will be measured with a Bodpod measurement and basal energy expenditure will be measured with indirect calometry. During this measurement blood samples (4x10ml) will be drawn. Thereafter a MRS measurement of the heart will be performed. Patients will have to lie still during 60 minutes in an MRI-scanner. Hereafter they will go to a different MRI scanner for additional functional measurements of the heart (cardiac function measurements and T1 mapping, this also takes about 60 minutes, contrast agents will be used during these measurements) and liver fat accumulation will be determined. These measurements will be performed 1 week before surgery.

Patients will undergo their regularly planned surgery, without modification. The only addition to the procedure is the sampling of a small amount of atrial appendage tissue. As the atrial appendage will be used to obtain access to the heart for the heart-lung machine for extra-corporal ventilation during surgery, the atrial appendage will be handled any way. The removal of a small amount of tissue of the atrial appendage is quite harmless, seen that it will be opened and incised during this procedure anyway. The cardiothoracic surgeons in the university hospital Maastricht are experienced with this technique and are skilled to perform this small additional procedure. Additional risks of this study include the risk of causing bruises during the blood sampling. MRI is a modern diagnostic tool, which does not imply significant risks (no ionizing radiation). The use of contrast agents in the MRI is contra-indicated in patients with poor renal function. In rare cases, contrast agents can cause allergic reactions, therefore a medical specialist (radiologist) will always be present during the procedure. Furthermore the measurement and contrast injection will be given by experienced trained personnel. There are no direct benefits for subjects participating in the study.

Contacts

Public
Maastricht Universitair Medisch Centrum +

Universiteitssingel 50
Maastricht 6221XS
NL
Scientific
Maastricht Universitair Medisch Centrum +

Universiteitssingel 50
Maastricht 6221XS
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Patients undergoing elective valve replacement or cardiopulmonal bypass surgery
- Gender: male or male
- The patients should be aged 40-75 years
- The type 2 diabetic patients should be obese (BMI > 27 kg/m2) and non-insulin dependent
- The obese controls should be BMI matched with the diabetic patients (BMI > 27 kg/m2)
- The lean subjects should have a normal BMI (20-25 kg/m2)

Exclusion criteria

- Insulin dependent diabetic subjects.
- Patients with instable angina or heamodynamically instable patients
- Use of Thiazolidines (glitazone/rosiglitazone/pioglitazone/troglitazone)
- Weight gain/loss > 3 kg in the last 6 months or signs of cachexia
- Contraindications for MRI scans.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-03-2017
Enrollment:	45
Type:	Actual

Ethics review

Approved WMO Date:	15-04-2015
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	10-02-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	07-06-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO	

Date:	26-07-2017
Application type:	Amendment
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
ClinicalTrials.gov	NCT03049228
CCMO	NL48376.068.14