Reduced Microvascular Blood Volume as a Driver of Coronary Microvascular Disease in Patients with Non-Obstructive Coronary Artery Disease: The MICORDIS-study

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON23861

Source
NTR

Brief title
MICORDIS

Health condition

Non-obstructive coronary artery disease
Coronary microvascular dysfunction
Capillary recruitment
Capillary rarefaction

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: Netherlands Heart Institute

Intervention

Outcome measures

Primary outcome

The primary endpoint is the difference in myocardial blood volume (MBV) between non-obstructive coronary artery disease patients and healthy controls. We compare MBV between groups at baseline, during hyperinsulinemia and during increased cardiac contraction. MBV is measured using myocardial contrast echocardiography. Hyperinsulinemia is induced by a two hour hyperinsulinemic euglymic-clamp and cardiac contraction is increased via the infusion of dobutamine.

Secondary outcome

1. MBV, MBF, ÄMBV, baseline characteristics, cardiovascular risk factors, questionnaire results, blood parameters and measurement indexes compared between males and females from the patient and control group.

2. Differences in MBV between baseline and after HE-clamp of the patient and control group. Differences in MBV between baseline and after dobutamine stress of the patient and control group.

3. Baseline characteristics, cardiovascular risk factors, questionnaire results and measurement indexes compared between the patient and control group.

4. MBV, MBF and ÄMBV compared between insulin resistant subjects and non-insulin resistant subjects.

5. Correlation between MBV measured with MCE and MBV measured with CMR.

6. Protein expression and phosphorylation of microvascular endothelial cells compared between the patient and control group.

Study description

Background summary

Rationale: About 21-46% of patients (i.e. 65% of female patients and 35% of male patients) with signs and symptoms of ischemia have non-obstructive coronary artery disease (NOCAD). Patients with NOCAD are at increased risk of major adverse cardiac events and have a worse prognosis compared to healthy subjects. The pathophysiology of NOCAD remains unresolved, but is considered to involve coronary microvascular endothelial independent dysfunction, endothelial dependent coronary dysfunction (spasm) and impaired effects of insulin. The coronary flow reserve (CFR) is currently determined to assess coronary microvascular dysfunction, but this technique does not detect all types of coronary microvascular

dysfunction because it hampers evaluation of myocardial blood volume (MBV). Studies have shown that adenosine infusion increases myocardial blood flow (MBF) without a significant increase in MBV, but that increased myocardial oxygen consumption and hyperinsulinemia increases both MBF and MBV. We hypothesize that dysregulation of MBV because of a reduced capillary recruitment contributes to coronary microvascular dysfunction in NOCAD patients with signs and symptoms of ischemic heart disease.
Objective: To investigate whether MBV is reduced in patients with NOCAD and signs and symptoms of ischemia, relative to healthy controls, and to investigate the underlying mechanisms. The specific aims are to investigate 1) if MBV is reduced in NOCAD patients at baseline, 2) if MBV is reduced in NOCAD patients during hyperinsulinemia and 3) if MBV is reduced in NOCAD patients during increased myocardial contraction.
Study population: The study will be conducted in NOCAD patients with signs and symptoms of ischemia. NOCAD is defined as no or less than 50% obstruction of the coronary arteries and/or a fractional flow reserve higher than 0.80 in every epicardial coronary artery. The control group will consist of healthy controls matched on age and sex.
Study design: The study is an observational cross-sectional cohort study. The patient group will undergo CFR measurement and coronary reactivity testing during coronary angiography. Both groups will undergo myocardial contrast echocardiography with hyperinsulinemic euglycemic-clamp to induce hyperinsulinemia and admission of dobutamine to increase myocardial contractility, cardiac magnetic resonance with T1-mapping to evaluate volume changes and needle biopsy of the leg muscle to look at the microcirculation on cellular level.

Main study parameters/endpoints: The primary endpoint is the difference in MBV between NOCAD patients and healthy controls. We compare MBV between groups at baseline, during hyperinsulinemia and during increased cardiac contraction.

Study objective

To investigate whether myocardial blood volume (MBV) is reduced in patients with non-obstructive coronary artery disease and signs and symptoms of ischemia, relative to healthy controls. The specific aims are to investigate 1) if MBV is reduced in NOCAD patients at baseline, 2) if MBV is reduced in NOCAD patients during hyperinsulinemia and 3) if MBV is reduced in NOCAD patients during increased myocardial contraction.

Study design

2 visits in 30 days

Intervention

None

Contacts

Public

Scientific

Eligibility criteria

Inclusion criteria

Patient group:

- Age > 40 years

- Stable and chronic symptoms suggesting ischemic heart disease

- NOCAD on coronary angiography: coronary artery stenosis < 50% and/or FFR > 0.80

- Prior TTE assessment

Control group:

- Age > 40 years

Exclusion criteria

- age > 80 years

- Obstructive coronary artery disease, defined as 50% or more obstruction of any coronary artery

- FFR < 0.80

- Pregnancy

- (History of) coronary revascularization (e.g. percutaneous coronary intervention or coronary artery bypass grafting)

- (History of) coronary artery disease, or acute coronary syndrome (e.g. myocardial infarction and unstable angina pectoris)

- (History of) stroke

- (History of) cardiac arrhythmia’s

- (History of) heart valve disease

- Left ventricular dysfunction (i.e. left ventricular ejection fraction < 35%)

- Congenital heart disease

- Insulin-dependent diabetes mellitus

- Extensive comorbidities (i.e. cancer, other chronic diseases)

- Impaired renal function, defined as creatinine > 100 and eGFR < 30.

- Symptomatic asthma or chronic obstructive pulmonary disease

- Known allergic reaction to contrast agent

- Insufficient echocardiographic imaging quality

- Contra-indications for CMR (e.g. severe claustrophobia, metal implants, severe renal failure, severe asthma and known hypersensitivity for gadolinium)

- Contra-indications for microbubble usage (e.g. right-to-left shunt, severe pulmonary hypertension, uncontrolled hypertension and adult respiratory distress syndrome)

- Contra-indications for adenosine usage (e.g. hypersensitivity to active substances, second or third degree atrio-ventricular block, sick sinus syndrome, long QT syndrome, severe hypertension, concomitant use of dipyridamole)

- Contra-indications for dobutamine usage (e.g. hypersensitivity to dobutamine, severe heart failure, acute pericarditis, myocarditis or endocarditis, aortic dissection or aneurysm, inadequately controlled arterial hypertension or hypotension, hypovolemia)

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-08-2018
Enrollment:	56
Type:	Anticipated

Ethics review

Positive opinion

Date:	25-09-2018
Application type:	First submission

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
NTR-new	NL7282
NTR-old	NTR7515
Other	METC : 2018.176

Study results