Heart failure with preserved ejection fraction, early diagnosis

No registrations found.

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

Summary

ID

NL-OMON29452

Source
NTR

Health condition

he prevalence of heart failure (HF) continues to rise exponentially worldwide, solely to be attributed to an increase in HFpEF (Heart Failure with preserved Ejection Fraction). HF can be split evenly into HFpEF, formerly classified as diastolic heart failure, and HFrEF (HF with reduced ejection fraction) formerly classified as systolic heart failure. In the Netherlands, approximately 70.000 patients suffer from HFpEF. HFpEF, is characterized by an increased stiffness of the heart, and is associated with multiple comorbidities, such as diabetes, hypertension and obesity. However, HFpEF is more than just a complication of these comorbidities, and consequently requires more than just treatment of these comorbidities. Typical heart failure medications, proven to be successful in HFrEF, such as ace inhibitors and beta-blockers have failed to improve quality of life or survival in HFpEF patients. Currently, no evidence-based treatment can be offered for HFpEF, resulting in poor quality of life, enormous costs and bad outcome. Therefore, a better understanding of the underlying pathophysiology is essential in order to find a treatment for these patients.
Low-grade inflammation, caused by multiple comorbidities is suggested to play a central role in HFpEF. It is thought that low-grade inflammation causes endothelial dysfunction, which is shown to be present in these patients. Additionally, our previous research demonstrated the inability of HFpEF patients to increase myocardial oxygen delivery during exercise. We therefore hypothesize that endothelial dysfunction results in coronary microvascular dysfunction, diminished myocardial perfusion and impaired cardiac metabolism.

Sponsors and support

Primary sponsor: Academisch Ziekenhuis Maastricht (azM)
Health Foundation Limburg
Source(s) of monetary or material Support: Third Source Funding:Health Foundation Limburg

Intervention

Outcome measures

Primary outcome

-Impaired perfusion (assessed using CMR): assess if myocardial perfusion is diminished in HFpEF compared to controls assessed by CMR.

Secondary outcome

Secondary objectives are

-To assess if myocardial energy metabolism is impaired in HFpEF compared to controls

-To assess if HFpEF patients have an increase in diffuse interstitial fibrosis compared to controls (assessed using CMR-T1 mapping)

-To assess if an impairment in endothelial dysfunction is correlated to a diminished myocardial perfusion and to an impaired myocardial energy metabolism.

-To assess if a diminished myocardial perfusion is associated with degree of impairment in myocardial energy metabolism

-To evaluate whether endothelial function (assessed by flow mediated dilatation, and heat-induced skin hyperaemic response) and microvascular function (using glycocalyx thickness measurement) is impaired in HFpEF compared to controls

-To identify biomarkers associated with endothelial dysfunction, inflammation, fibrosis, impaired myocardial perfusion, hypoxia, oxidative stress and/or myocardial energy metabolism.

-To evaluate whether myocardial perfusion and myocardial metabolism is similar in DM-HFpEF compared to non DM-HFpEF

Study description

Background summary

The prevalence of heart failure (HF) continues to rise exponentially worldwide, solely to be attributed to an increase in HFpEF (Heart Failure with preserved Ejection Fraction). HF can be split evenly into HFpEF, formerly classified as diastolic heart failure, and HFrEF (HF with reduced ejection fraction) formerly classified as systolic heart failure. In the Netherlands, approximately 70.000 patients suffer from HFpEF. HFpEF, is characterized by an increased stiffness of the heart, and is associated with multiple comorbidities, such as diabetes, hypertension and obesity. However, HFpEF is more than just a complication of these comorbidities, and consequently requires more than just treatment of these comorbidities. Typical heart failure medications, proven to be successful in HFrEF, such as ace inhibitors and beta-blockers have failed to improve quality of life or survival in HFpEF patients. Currently, no evidence-based treatment can be offered for HFpEF, resulting in poor quality of life, enormous costs and bad outcome. Therefore, a better understanding of the underlying pathophysiology is essential in order to find a treatment for these patients.
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Study objective

The objective is to assess whether myocardial microvascular perfusion and myocardial energy metabolism is impaired in HFpEF patients. Additionally we will evaluate whether endothelial dysfunction is associated with diminished myocardial perfusion (e.g. coronary microvascular dysfunction) and impaired myocardial metabolism.

Study design

This case control cohort study will assess the endothelial function, myocardial perfusion and myocardial metabolism of 72 patients ;48 diagnosed with HFpEF (24 of them with Diabetes Mellitus) and 24 controls with hypertension.

Measurements will be performed based on standard study protocols (for details see methods section).

Study design: case control cohort study

Group I: HFpEF patients

Group II: controls with hypertension

Duration: 2 separate days for HFpEF patients and 3 separate days for control patients. No treatment intervention or follow-up.

HFpEF patients (these patients already had the standard HFpEF screening tests)

Day 1

-Cardiac MRI (CMR)

-Glycocalyx thickness measurement

-Heat-induced skin hyperaemic response

Day 2

-MR spectroscopy

Control patients

Day 1 Clinical assessment (standard clinical care for HFPEF patients)

-Echocardiography

-Holter

-6MWT

-Lung function test

-Exercise test

-ApneaLink

-QoL questionnaires

-Lab

Day 2

-Cardiac MRI (CMR)

-Glycocalyx thickness measurement

-Heat-induced skin hyperaemic response

Day 3

-MR spectroscopy

Intervention

1. Cradiac MRI and MR spectroscopy

-Cardiac MRI: Myocardial fibrosis, assessed using T1 mapping, appears to be linked to myocardial dysfunction in a multitude of non-ischemic cardiomyopathies. Accurate non-invasive quantitation of this extra-cellular matrix has the potential for widespread clinical benefit in both diagnosis and guiding therapeutic intervention. T1 mapping is a cardiac magnetic resonance (CMR) imaging technique, which shows early clinical promise particularly in the setting of diffuse fibrosis.

-MR spectroscopy: Cardiac MRS enables the study of in vivo changes in cardiac metabolism. Several metabolites can be measured but phosphocreatine (PCr) and adenosine triphosphate (ATP) have been shown to be altered in heart failure patients.

Phan et al. showed in a small study that patients with HFpEF have a reduced cardiac energetic reserve (creatine phosphate/adenosine triphosphate ratio) compared to controls (1.57+/-0.52 vs. 2.14+/- 0.63; p=0.003). We will try to confirm these data and analyse a correlation between energy metabolism and myocardial perfusion and endothelial dysfunction.

2.Glycocalyx thickness measurement is a
non-invasive, endothelial function measurement method. This method has no contra-indications or adverse effects.

3.Heat-induced skin hyperaemic response, is a non-invasive, endothelial function measurement method. This method has no contraindications or adverse effects. The warm electrodes (warmth until 44° C) are not painful and just a slight local warmth can be felt.

Contacts

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Eligibility criteria

Inclusion criteria

1. All patients • Age > 50 • Estimated glomerular filtration reserve (eGFR) >30 ml/min • Body weight<130kg 1.1. HFpEF group 1.1.1 All HFPEF patients •Diagnosis of HFpEF, requires three conditions to be satisfied, as stated in the ESC guidelines: (1) symptoms or signs of heart failure (2) normal or only mildly reduced LV ejection fraction in a non-dilated LV (LVEF>= 50%) (3) relevant structural heart disease (LV hypertrophy/LA enlargement) and/or diastolic dysfunction. •Current BP < 160/90 •Estimated glomerular filtration reserve (eGFR) >30 ml/min 1.1.2 HFPEF with Diabetes Mellitus •Inclusion criteria as mentioned above and Diabetes Mellitus: oDiabetes Mellitus is diagnosed as history of diabetes and use of anti-diabetic medication or fasting plasma glucose ≥ 7.0 mmol/L or 2h-post load glucose ≥ 11.1 mmol/l. 1.2 Hypertensive control patients •No coronary artery disease (CAD; coronary stenosis>70% or history of CABG) •No heart failure •Estimated glomerular filtration rate (eGFR) > 30 ml/min •Preserved left ventricular ejection fraction (LVEF) (>= 50%) on echocardiography •No left ventricular hypertrophy (lateral and septal left ventricular wall =<10mm) •No left atrium enlargement •No diastolic dysfunction type 2 or 3 •Blood pressure >140/90 mmHg or use of anti-hypertensive therapy •Normal cardiac structure and function on echocardiography

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study: - Age < 50 years - Life expectancy of <1 year (malignancy etc.) - Contraindication for CMR • ODIN protocol: • “Uitvoering van MRI onderzoek bij patiënten met een cardiaal implanteerbaar elektronisch device (CIED), waaronder een pacemaker en ICD” • ODIN protocol: • “Voorbereiding klinische patiënten voor MRI onderzoek” • Metallic implant

(vascularclip, neuro-stimulator, cochlearimplant) • Pacemaker or implantable cardiac defibrillator(ICD) • Claustrophobia • Persistent or chronic atrial fibrillation - Contraindication to adenosine: • High degree atrio-ventricular block (2nd or 3rd degree) • Severe asthma bronchial • Chronic obstructive pulmonary disease Gold ≥ III • Concomitant use of dipyridamole (Persantin) • Long QT syndrome (congenital) - Contraindication to gadolinium (Dihydroxy- hydroxymethylpropyl- tetraazacyclododecane-triacetic acid (butrol) - Gadovist ®) • Severe renal impairment (Glomerular filtration rate (GFR) < 30 ml/min/1.73m2

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-07-2017
Enrollment:	72
Type:	Actual

IPD sharing statement

Plan to share IPD: Yes

Ethics review

Positive opinion

Date:	07-08-2017
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 47584
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL6428
NTR-old	NTR6605
CCMO	NL57468.068.16
OMON	NL-OMON47584

Study results