Characterizing the myocardium of Systemic Sclerosis patients with pulmonary hypertension using CMR parametric mapping

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To evaluate the presence and extent of myocardial inflammation, fibrosis and myocardial perfusion in SSc patients with either PH-LHD or PAHPAH and/or PH-LHD, in comparison to patients with idiopathic pulmonary arterial hypertension (IPAH) by means...

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

Summary

ID

NL-OMON48562

Source
ToetsingOnline

Brief title
CMR parametric mapping of SSc patients with PH

Condition

- Heart failures
- Autoimmune disorders

Synonym
Scleroderma, Systemic sclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: MRI, pulmonary hypertension, systemic sclerosis, tissue characterization

Outcome measures

Primary outcome

In this study we will explore parametric mapping to characterize the myocardium. Native T1 mapping is able to detect local and diffuse necrosis and fibrosis, whereas T2 mapping detects the extent of edema, which is used to assess activity of (subclinical) myocardial inflammation. Stress and rest perfusion CMR using adenosine will be used to assess focal perfusion defects and exclude relevant epicardial coronary stenosis, and additional T1-mapping will assess global myocardial (microvascular) perfusion. The presence and extent of myocardial inflammation, fibrosis and myocardial perfusion will be compared with the control group of IPAH patients. Additionally, the relation between disease severity and clinical status will be explored, and compared with the traditional late gadolinium enhanced images for the detection of focal disease.

The established ShMOLLI (Shortened Modified Look-Locker Inversion Recovery) sequence will be used for T1 mapping. Although T1-relaxation using ShMolli is a reproducible and consistent sequence to distinguish normal from diseased myocardium, the normal value needs to be determined for each MRI-scanner, since

the normal value is scanner (i.e. vendor, field strength, location) dependent.

In order to validate the T1-relaxation times in healthy individuals in this CMR, 20 patients without myocardial disease scheduled for a non-myocardial CMR scan (e.g. for the follow-up of aortic dilatation) will be asked to participate. Patients will be asked to give written informed consent to acquire this additional sequence and to use the results for scientific purposes.

Secondary outcome

To compare SSc-patients with PH and IPAH-patients in regards to features on electrocardiogram (such as right axis deviation, right ventricular strain pattern, right atrial dilatation), and echocardiography parameters (estimated pulmonary arterial pressures by tricuspid valve- and pulmonary valve regurgitation velocity, right atrial area, right ventricle (RV) fractional area change, TAPSE, global longitudinal RV strain, the RV- and left ventricle (LV)-end diastolic and systolic volume, the LV ejection fraction and diastolic function). Besides high-sensitive troponin-T, NT-proBNP and CRP, differences in blood result analyses will include characterization of T-cells subset and pro-inflammatory and pro-fibrotic mediators in peripheral blood mononuclear cells.

Study description

Background summary

Systemic sclerosis (SSc) is a systemic immune-mediated disease that is characterized by vasculopathy and fibrosis of the skin and internal organs. Pulmonary hypertension due to left heart disease (PH-LHD) and pulmonary arterial hypertension (PAH) are frequent and severe complications of SSc.

Despite recent advances in the treatment armamentarium, SSc-PAH survival is still poor with a median survival of 4 years. There is growing evidence this may be due to intrinsic right ventricular dysfunction caused by primary cardiac involvement of SSc, which results in earlier right ventricle failure, but the mechanism of action is still unknown. Since systemic sclerosis in the skin (and other internal organs) is characterized by fibrosis, inflammation and vasculopathy, it is speculated that the same process takes place in the myocardium. Parametric mapping in cardiovascular magnetic resonance imaging (CMR) is evolving as a new technique, which provides a non-invasive tool for quantifying tissue alterations in myocardial disease, such as diffuse, more subtle edema, necrosis and fibrosis. The myocardial microvasculature can be determined by adenosine stress perfusion CMR imaging and stress T1 mapping. Thesehis techniques haves the potential to detect cardiac involvement in this patient group and could therefore be of additional value in monitoring therapy or early recognition of PH in SSc patients, as well as gaining insight in the underlying pathophysiology.

Study objective

To evaluate the presence and extent of myocardial inflammation, fibrosis and myocardial perfusion in SSc patients with either PH-LHD or PAHPAH and/or PH-LHD, in comparison to patients with idiopathic pulmonary arterial hypertension (IPAH) by means of CMR parametric mapping and adenosine stress perfusion CMR imaging.

Study design

Feasibility study, with prospective enrollment of consecutive patients.

Study burden and risks

There are minimal risks for subjects included in this feasibility study. CMR bears only minimal risks and is largely part of their regular clinical treatment. During a stress perfusion CMR, adenosine is administrated. Patients might suffer from side effects of adenosine administration, such as headache, nausea, chest pain, and flushing. Serious side effects, such as high degree AV-block, are relatively rare, and almost all reverse quickly when adenosine infusion is terminated. Discomfort may be caused since the subject has to stay in a fixed position in the CMR. Peripheral blood samples will be taken once, which may also cause some discomfort. Possible side effect from blood drawing include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. There is also a slight possibility of infection.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Age >=18
- Diagnosis of SSc according to the 2013 ACR-EULAR classification criteria
- Diagnosed with pulmonary hypertension WHO group 1 (PAH) and (in combination with)/or WHO group 2 (PH due to LHD) according to ESC[6]/ERS guidelines.
- Written informed consent

Exclusion criteria

- Severe lung diseases (severe interstitial lung disease with a forced vital capacity <40%, COPD GOLD stadium III-IV), history of pulmonary embolisms.
- History of myocardial infarction, ischemic heart failure, moderate to severe valve stenosis or

regurgitations (with or without heart failure).
- Patients with WHO group 3 PH (due to lung disease), defined as a pulmonary capillary wedge <15mmHg in combination with a forced vital capacity <60% (of 65%?) and/or moderate to severe interstitial lung disease on a high resolution computed tomography.
- Known contra-indications for CMR (e.g.: severe claustrophobia, metal implants, severe renal failure, severe astma, high degree AV-block)
- Known GFR < 30 ml/min

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-09-2019
Enrollment:	25
Type:	Actual

Ethics review

Approved WMO Date:	02-08-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-04-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	09-03-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL66117.091.18