

# Right ventricular myocardial deformation parameters in patients with congenital heart defect comparison between patients with transposition of the great arteries and patients with Fallot anomaly: Can myocardial deformation parameters predict patients exercise capacity?

<b>Submission date</b> 19/10/2017	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 30/10/2017	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 21/11/2023	<b>Condition category</b> Circulatory System	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Congenital heart defects are heart problems that people are born with. Due to excellent results of childhood heart surgery, the number of adult patients with corrected congenital heart defects is growing. They all need follow-up at specific outpatient facilities, also known as Grown-Ups with Congenital Heart disease, GUCH, or in North America as Adults with Congenital Heart Disease, ACH. This group is facing repeat cardiac surgery with potential complications (such as arrhythmia (heart rhythm problems) and heart failure), thus follow up and regular examinations are needed. The knowledge about treatment options, and, especially optimal (best) time for it, is growing. New modalities (treatment and diagnosing methods), such as myocardial deformation imaging, also known as strain imaging (a type of imaging that measures deformations in the heart muscle based on colours and speckle tracking), enables an increase in our understanding of what happens in the myocardium after heart surgery. Better understanding allows better timed treatments. By studying new modalities in various situations, the aim of this study is to find predictors of exercise capacity and based on this knowledge, to optimize treatment and decrease morbidity in this patient group.

### Who can participate?

Adults aged 18 and older who have a congenital heart deflections in the great arteries or a Fallot anomaly.

### What does the study involve?

36 patients with Fallot and without pressure overload are enrolled in one group and eight

patients in the pressure overload population. No gender differences were found in the background data. Recruitment began Oct 2013 and closed on March 2015. The patients underwent cardiac MRI (CMRI) on a 1.5T scanner. Cine-images in the short-axis view of the left and right ventricle were used for volumetric analysis using "Segment". Global, regional longitudinal, circumferential and radial strain was calculated using a feature tracking software. Reproducibility was analyzed for volumetric and longitudinal strain measurements. In addition, all participants underwent cardiopulmonary exercise testing with measurement of oxygen uptake and their anaerobic threshold. Furthermore, all patients underwent a complete echocardiographic investigation including 3D volume acquisitions and measurements of longitudinal LV and RV strain. Resting ECG was acquired for the measurement of QRS-duration. Standard blood chemistry was taken at the outpatient visit, and also included measurement of NT-pro-BNP.

What are the possible benefits and risks of participating?

Participants may benefit from undergoing a more detailed assessment than it was planned. Echocardiography and cardiopulmonary exercise tests are included in yearly follow up but CMR is performed in occasion of any specific clinical problem or, in patients with Fallot anomaly, every 2 to 5 years. There are no expected risks for participants related to this study.

Where is the study run from?

University Hospital Linköping (Sweden)

When is the study starting and how long is it expected to run for?

January 2011 to December 2018

Who is funding the study?

Linköping University (Sweden)

Who is the main contact?

Mrs Aleksandra Trzebiatowska-Krzynska

## Contact information

**Type(s)**

Scientific

**Contact name**

Mrs Aleksandra Trzebiatowska-Krzynska

**ORCID ID**

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**Contact details**

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# Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

Version 1\_26/11/2012

## Study information

### Scientific Title

Cardiac Magnetic Resonance derived right ventricular myocardial deformation parameters in patients with the systemic pressure loaded right ventricle, comparison between patients with Transposition of the Great Arteries and patients with Fallot anomaly: Is it possible to predict patients ventricular exercise capacity based on myocardial deformation parameters and does it differ depending on the right ventricular pressure load?

### Acronym

TIMING

### Study objectives

The aim of this study is to investigate differences in the physiological adaptation to different loading conditions of the left and the right ventricle.

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

The Regional Ethical Review Board in Linkoping, 14/11/2012, ref: 2012/334-31

### Study design

Single centre observational study

### Primary study design

Observational

### Secondary study design

Case series

### Study setting(s)

Hospital

### Study type(s)

Diagnostic

Participant information sheet

Please contact Aleksandra.Trzebiatowska-Krzynska@liu.se to request a participant information sheet in details.

### **Health condition(s) or problem(s) studied**

Two groups of patients with congenital heart disease are included in the study. Patients with the D-transposition of the great arteries (D-TGA) and patients with Fallot anomaly. The main difference between patients is the pressure load of the right ventricle. In patients with the D-TGA, the right ventricle is situated in the systemic position which means that it is exposed to systemic pressure. In patients with the Fallot anomaly, volume overload is the most common type of overload in this group but the mixed type with some degree of pressure load can be present. The increased pressure load increases wall stress and causes hypertrophy of the myocardium. Thus it can be expected that, in response, the deformation pattern of the myocardium will change.

### **Interventions**

Two groups of patients with congenital heart disease are included in the study: participants with the D-transposition of the great arteries (D-TGA) and participants with Fallot anomaly. The main difference between patients is the pressure load of the right ventricle. In patients with the D-TGA, the right ventricle is situated in the systemic position which means that it is exposed to systemic pressure. In patients with the Fallot anomaly, volume overload is the most common type of overload in this group but the mixed type with some degree of pressure load can be present. The increased pressure load increases wall stress and causes hypertrophy of the myocardium. Thus it can be expected that, in response, the deformation pattern of the myocardium will change.

Participants receive three CMR examinations, three Cardiopulmonary exercise test and three echocardiography examinations. One patient begins their day with CMR, the second with cardiopulmonary exercise test and the third one with echocardiography examination. Three patients were rotating between three examinations within about four hours. In that way totally nine examinations were performed (each patient three examinations). This way of arrangement allows comparable loading conditions and we can exclude the differences between methods related to change in patients' clinical status (volume load, heart rhythm etc).

The information about the study was given to all patients some time before the examination day (by phone or in relation to the previous visit) and all patients received written information by mail. On the day of examination, between 07.30 – 08.15 each patient had signed written consent and went through a brief examination including ECG and control of blood pressure.

As it is an observational study, comparison between two groups, any kind of follow-up is not planned (except routine control). Depending on the results of the study it is possible that in the future some examinations (eg. CMR and CPET) will be repeated but at the moment the study is finished from the patients' perspective.

Cardiac Magnetic Resonance (CMR) is performed on a 1.5T scanner (Achieva Nova Dual, Philips Healthcare, Best, The Netherlands) equipped with a cardiac phased array receiver coil. Cine images are obtained using a breath-hold segmented-k-space balanced fast-field echo sequence (SSFP) employing retrospective ECG gating in the long axis planes (2- and 4-chamber views and the apical long-axis view) of the LV as well as a stack of short axis slices (2mm gap) covering both ventricles from the base to the apex. Volumes and ejection fraction for both ventricles are acquired from short axis slices after manually tracing the endocardial borders excluding the papillary muscles. End-diastole and end-systole are defined as the frames with the largest and the smallest ventricular slice area in relation to the ECG and the opening and closure of the

aortic and atrioventricular valves. In case of discrepancies (e.g. long QRS duration in case of RBBB or LBBB morphology) the size of the ventricular area was the determining factor.

Maximal, graded exercise testing was performed seated on an upright electrically braked ergometer. The test starts with the patient pedaling against minimal resistance, with gradual increments of resistance of 15-25 watts every two minutes. The goal is to reach the anaerobic threshold and a long test duration as possible (8-12 minutes). The test was symptom limited. Maximal workload in Watt, oxygen uptake, carbon dioxide production and ventilator flow is measured. Peak oxygen consumption is measured during the last stage of maximal exercise. Patients are continuously monitored by a 12-lead electrocardiogram. Heart rate and cuff blood pressure is measured close to the final minute of each exercise stage.

## **Intervention Type**

Device

## **Pharmaceutical study type(s)**

Not Applicable

## **Phase**

Not Applicable

## **Drug/device/biological/vaccine name(s)**

Cardiac Magnetic Resonance

## **Primary outcome measure**

1. Strain (longitudinal and radial) is measured using a feature tracking software (2D-Cardiac Performance Analysis version 1.2 Tom Tec Imaging Systems Germany). Global longitudinal strain provided by the software was calculated as the average value of 6 segments in the left ventricle and 6 segments in the right ventricle, from the 4-chamber view.
2. End diastolic and end systolic volume of the left and right ventricle is performed on a workstation equipped with a semiautomatic software for cardiac analysis, "Segment", designed for volumetric analysis. CMR collected volumes and for both ventricles were derived from short axis slices after manually tracing the endocardial borders excluding the papillary muscles. End diastole and end-systole were defined as the frames with the largest and the smallest ventricular slice area in relation to the ECG and the opening and closure of the aortic and atrioventricular valves. In case of discrepancies (e.g. long QRS duration in case of RBBB or LBBB morphology) the size of the ventricular area was the determining factor. Ejection fraction was then calculated by the program based on the measured volumes.
3. Maximal workload in Watt, peak oxygen uptake, ventilatory gas value (oxygen and carbon dioxide) and maximal heart rate are measured using an electrically braked stationary cycle ergometer Yaeger Oxycon.
4. End diastolic, end systolic volume and longitudinal strain of both left and right ventricle are measured off line using TomTec Imaging system for 4D RV volume calculations

## **Secondary outcome measures**

There are no secondary outcomes.

## **Overall study start date**

02/01/2011

## **Completion date**

30/12/2018

## Eligibility

### Key inclusion criteria

1. Congenital heart defect in form of transposition of the great arteries or Fallot anomaly
2. Older than 18 years

### Participant type(s)

Patient

### Age group

Adult

### Lower age limit

18 Years

### Sex

Both

### Target number of participants

44

### Total final enrolment

44

### Key exclusion criteria

1. Claustrophobia
2. Implanted pace-maker
3. Arrhythmia interfering with image acquisition on CMR

### Date of first enrolment

02/10/2013

### Date of final enrolment

30/03/2015

## Locations

### Countries of recruitment

Sweden

### Study participating centre

University Hospital Linköping

Garnisonsvagen 1

Linköping

Sweden

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# Sponsor information

## Organisation

Linköping University

## Sponsor details

Department of Medical and Health Sciences  
Department of Cardiology  
Garnisonvagen 1  
Linköping  
Sweden  
581 85

## Sponsor type

Hospital/treatment centre

## ROR

<https://ror.org/05ynxx418>

# Funder(s)

## Funder type

University/education

## Funder Name

Linköping University

# Results and Publications

## Publication and dissemination plan

2 manuscripts are in preparation and should be published during 2018. Study protocol and other documents concerning performing of the study were left to the Regional Ethical Review Board in Linköping before start of the study. Documents are available on request. The protocol is not published and is not available online.

## Intention to publish date

31/07/2019

## Individual participant data (IPD) sharing plan

The current data sharing plans for the current study are unknown and will be made available at a later date.

## IPD sharing plan summary

Data sharing statement to be made available at a later date

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		27/09/2018	21/11/2023	Yes	No