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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?

Submission date
19/10/2017

Recruitment status
No longer recruiting

Registration date
30/10/2017

Overall study status
Completed

Last Edited
21/11/2023

Condition category
Circulatory System

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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 defections 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 then 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 Linkoping (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?
Linkoping University (Sweden)

Who is the main contact?
Mrs Aleksandra Trzebiatowska-Krzynska

Contact information

Type(s)
Scientific

Contact name
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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 group 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 patienst 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 increase 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 group 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 increase 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 begans their day with CMR, the second with cardiopulmonary exercise test and the third one with echocardiography examination. Three patients were rotating between three examination within about four hour. 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 till all patients some time before the examinations 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 sign written consent and went through brief examination including ECG and control of blood pressure.
As it is 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 future the some examinations (eg.CMR and CPET will be repeated but at the moment the study is finished from 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 end 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 a 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 then 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 Linkoping
Garnisonsvagen 1
Linkoping
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Sponsor information

Organisation
Linkoping University

Sponsor details
Department of Medical and Health Sciences
Department of Cardiology
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/05ynxx418

Funder(s)

Funder type
University/education

Funder Name
Linkoping 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?
Results article		27/09/2018	21/11/2023	Yes	No