Fontan circulation: Analysis of its Impact on quality of life and Rate of deterioration (FAIR study)

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Primary Objective: - Investigating the rate of the attrition and predictors of the failing Fontan circulation, defined as decrease in functional capacity. Secondary Objective(s): - Investigating predictors of decrease in NYHA class of Fontan...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Congenital cardiac disorders
Study type	Observational non invasive

Summary

ID

NL-OMON37862

Source
ToetsingOnline

Brief title
Predictors of Fontan attrition.

Condition

- Congenital cardiac disorders
- Cardiac therapeutic procedures

Synonym
Fontan, total cavopulmonary connection

Research involving
Human

Sponsors and support

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

Intervention

Keyword: congenital heart disease, Fontan, prognosis, univentricular heart

Outcome measures

Primary outcome

Decrease of the exercise tolerance.

Secondary outcome

Decrease in NYHA class

Mortality

Quality of life

Laboratorium measurements: NTproBNP, haemoglobin level, creatinin,

endothelin-1, coagulation tests, albumin, ASAT, ALAT, γGT, creatinin.

Echocardiography: systolic, diastolic and valve function.

Magnetic Resonance Imaging: ventricular ejection fraction, pulmonary flow

patterns, hepatic flow patterns, portal hypertension, liver cirrhosis.

Holter monitoring/ECG: Arrhythmias.

Spirometry: FVC, FEV1

Study description

Background summary

The Fontan procedure is performed since 1971 in children who are born with a univentricular heart. This Fontan operation creates a unique, on-physiological circulation (the Fontan circulation) in which the systemic venous return flows passively through the lungs without passing the pumping heart. Due to this abnormal physiology there is an increased risk of short and long term complications. The short term consequences of the Fontan circulation have already been extensively investigated. Among others, due to the adjustments of pre-operative patients selection criteria and developments of the operation

technique the short term survival has increased and is now satisfactory. With increased short term survival and longer follow-up times attention has shifted towards long term survival. We are now starting to recognize an attrition or failure of the Fontan circulation after ten till fifteen years. This failure is probably related to the abnormal physiology, which results in chronic increased central venous pressures, progressive rise of the pulmonary vascular resistance, chronic decreased pre-load and increased after-load of the heart. When this attrition develops, not many treatment options are left, and the patients usually die as young adults.
The failure of the Fontan circulation can be subdivided in four mechanisms which may be responsible. First, the heart function may decrease due to the chronic abnormal circulation (decreased pre-load and increased after-load) and intrinsic myocardial abnormalities because of the congenital heart disease. Secondly, the un-physiological Fontan circulation results in a chronic increased central venous pressure. This can cause protein losing enteropathy, liver cirrhosis and other hepatic disorders. Combined with the slowed systemic venous return this can cause trombo-embolic complications. The third mechanism concerns the progressive rise of the pulmonary vascular resistance. About this mechanism there is still a lot unknown. Lastly, the autonomic nervous system and neuro-humeral axis activation are likely to contribute to the failure of the Fontan circulation.
The above mentioned mechanisms are insufficiently clarified. Besides, differences in the time and degree in which the attrition develops are major between the individual Fontan patients. It is still unknown how the attrition develops, what is the rate of de development of the attrition and which patients will development this attrition. The objective of this study is to investigate the course and rate of the attrition and the impact on the quality of life of these patients. As an important part of the qualtity of life, special attention will be given to the sexual and obstetric functioning in these patients. Despite the great probability of sexual dysfunction due to the chronic illness, unphysiological circulation, autonomic dysregulation and reduced exercise tolerance, no research has yet been done to quantify this. With increased insights in the attrition of the Fontan circulation, we might be able to increase the therapeutic options when the attrition develops or even delaying the attrition of the Fontan circulation. So we make significant improvements in the care for patients who are born with a univentricular heart.

Study objective

Primary Objective:
- Investigating the rate of the attrition and predictors of the failing Fontan circulation, defined as decrease in functional capacity.

Secondary Objective(s):
- Investigating predictors of decrease in NYHA class of Fontan patients
- Investigating predictors of mortality of Fontan patients
- Investigating the relationship between clinical parameters (i.e. heart, lung,

liver, kidney function test) and the quality of life of Fontan patients.
-Investigating the correlation between ventricle functioning on echocardiography and on magnetic resonance imaging with the NTproBNP levels in venous blood.
- Investigating the correlation between liver cirrhosis/congestion on magnetic resonance imaging and parameters for liver disease in venous blood (ASAT, ALAT, γGT).
- Investigating the correlation between ventricle functioning on echocardiography and endothelin-1 measurements.
- Investigating sexual dysfunction in Fontan patients compared to healthy subjects.

Study design

This study is a longitudinal investigation.
We will evaluate two measurements with an interval of two years (2012-2014). For both measurements we will investigate the standardized follow-up tests for heart, lung, liver, kidney function and exercise tolerance. These parameters will be evaluated with an echocardiogram, blood samples, VO2max, spirometry, Holter test, magnetic resonance imaging and heart catheterization.

For our study, we will add an once only evaluation, in the first measurement, of hepatic disorders with magnetic resonance imaging and an evaluation of the quality of life using a questionnaire. For better assessment of the perception of the patients on any sexual problems, ten patients will be randomly chosen for interviewing by a psychologist about their sexual wellbeing. These interviews are semi-structured and will take around 30-45 minutes.
In 2012 as well as in 2014 measurements in venous blood, ie endothelin-1, will be calculated. This requires an extra blood sample to be taken from the patients, which will be done during the venous puncture in context of the regular patient care. Besides that, at the second measurement the patients will be asked to fill in a questionnaire which consists of the questions about general wellbeing only.

Study burden and risks

Most of the parameters that are investigated are part of the regular follow-up of the Fontan patients.
The additional procedures for this research include the MRI liver, lab measurements and questionnaires about the quality of life. The MRI liver will be conducted simultaneously with the regular MRI for heart and lung. This does not create an extra burden for the patients.
It is possible newly developed hepatic disorders will be diagnosed. If medically relevant, the patient will be informed and referred to his/her GP.
The lab measurements will be executed as supplement to the regular venous blood samples taken in context of the regular patient care. This means one extra

blood sample has to be taken.
The questionnaires and interviews will only be taken in patients who are 16 years or older to avoid an additional load for our minor patients and because of the evaluation of sexual and obstetric function. For the patients older or equal to sixteen years it may cause an emotional burden to fill in the forms and answer the questions of the interview due to the personal questions. This is why the patients can indicate on the Informed Consentform whether they want to particate in the part of the study about sexual functioning.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

- patients who underwent a Fontan/TCPC procedure
- follow-up at UMCG
- age: 10 years or older

Exclusion criteria

No overall exclusion criteria. For the individual investigations there may be separate exclusion criteria (e.g. Pacemaker is an exclusion criterion for MRI investigation).

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-07-2012
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Date:	13-06-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL38724.042.12