Thirty years arterial switch operation for transposition of the great arteries; a follow-up study.

Published: 20-12-2010
Last updated: 04-05-2024

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

Summary

ID

NL-OMON39105

Source
ToetsingOnline

Brief title
TGA - 30

Condition

- Congenital cardiac disorders
- Cardiac and vascular disorders congenital
- Cardiac therapeutic procedures

Synonym
Ventriculo-arterial discordance; transposition of the great arteries

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: congenital, heart, switch, transposition

Outcome measures

Primary outcome

For the 1st objective, endpoints will be occurrence of an adverse outcome (e.g. late mortility, reoperation, diminished LV function, arrhythmia, signs of myocardial ischemia) and the operation related factors that are independently associated with these outcomes.

For the 2nd objective, the extent and incidence of wall irregularities in the coronary arteries and the calcium score will be determined in ASO patients. To gain more insight in the pathophysiology behind this, both details of the anatomy of the coronary arteries, endothelial function and the presence of endothelial and immunological markers will be investigated.

Secondary outcome

The predictive value of several serum markers to assess poor left ventricular function in patients after ASO will be evaluated, with echocardiography and Magnetic Resonance Imaging (MRI) as reference. The predictive value of serum endothelial damage markers to determine presence of atherosclerosis will be assessed with Carotid Intima-Media Thickness (CIMT) and Computed Tomography (CT) scan as reference. Also, the serum endothelial markers will be correlated to endothelial dysfunction as established by flow mediated dilation (FMD).

Study description

Background summary

The Wilhelmina children*s hospital (WKZ) was one of the first centres in the world were the arterial switch operation (ASO) was used as first choice of treatment for transposition of the great arteries (TGA). Therefore the WKZ has one of the longest follow-up periods for this group of patients. As after introduction of any new surgical technique, long-term follow-up studies are mandatory to provide patients and physicians with data about morbidity and mortality; what to expect when patients are adolescent and adult. Early and intermediate follow-up studies, with a maximum of 15 years follow-up, have shown a favourable survival compared with the atrial switch operation, with less morbidity. Only a limited number of follow-up studies have been performed that focused on myocardial blood flow and left ventricular function. These showed decreased myocardial blood flow, decreased coronary flow reserve and overall slightly depressed left ventricular (LV) function in a substantial proportion of patients studied (long) before they reached adult age. Based on these observations and the theoretical consideration that manipulation and reimplantation (in the neo-aorta) of the coronary arteries at neonatal age, without an anatomic sinus of Valsava, may lead to altered coronary blood flow throughout life, it is of great interest to investigate alterations of LV function and coronary capacity in patients long after ASO. If factors associated with these outcomes are identified, the therapeutic regimen at neonatal age might be adjusted, in order to improve outcome.
Little is known about the long term effects of use of cardiopulmonary bypass (CPB) at a neonatal age. Short-term effects of increased oxidative stress and a persisting pro-inflammatory state have been reported. Whether these abnormalities persist is unknown, because no studies have been performed to investigate this. Possible CPB- related immunological effects on endothelial function, a major determinant of atherosclerosis in the normal population, will be scrutinized in this study.

Study objective

The main objectives are 1) is to evaluate the prevalence of cardiac complications long-term after ASO by investigation of cardiac function as well as clinical outcome and to determine which factors (associated with life style or operative techniques) are associated with occurrence of late problems;
2) to investigate the coronary anatomy and presence of wall irregularities in the coronary arteries and - if present - to determine the etiological determinants for these wall irregularities (e.g. abnormal blood flow pattern or endothelial dysfunction).
With all this information we hope to provide more evidence for future guidelines for patients after ASO;
3) to investigate the immunological consequences of neonatal thymectomy on the

developing immune system and to evaluate the role of thymic regrowth.

Study design

Observational, cross-sectional cohort study

Study burden and risks

Most of the investigations that are part of the study protocol are also implemented in the regular follow-up after ASO. Based on the new American Heart Association (AHA) guidelines and Canadian guidelines, extensive echocardiography, physical examination, electrocardiogram (ECG), saturation measurement and ergometry should be routinely performed. Secondly these guidelines recommend cardiac MR and/or CT imaging be performed if any doubt remains on anatomy or hemodynamic status. The new European Society of Cardiology (ESC) guidelines also recommend a new, more extensive work-up as part of standard follow-up after ASO for TGA.
Additional to the normal 2D echocardiography protocol, the Ventripoint system will be used. This is a 2-dimensional method that localizes different anatomic landmarks in magnetic 3D space and reconstructs RV volumes and EF using a database consisting of many MR datasets of patients with different pathologies. It will add approximately 5 minutes to the echoprotocol.
If not already clinically indicated, patients will be asked to undergo FMD, CIMT, CT imaging of the coronary arteries, cardiac MR imaging including the administration of gadolinium contrast and blood withdrawal in addition to the routine check-up.
There are some risks associated with these additional investigations. The risk for insertion of an intravenous (i.v.) catheter (for gadolinium infusion and blood withdrawal) is considered very low and the risk of FMD and CIMT, which both use high resolution ultrasonography, is even nonexistent.
The administration of gadolinium contrast, as part of the MR imaging, can give side effects in a small portion of patients (<0.1%), most of these are minor, but seldom (<0.01%) an anaphylactic reaction will occur.16 In case of any doubt about kidney function, serum creatinin and glomerular filtration rate (GFR) will be determined before planning a patient for the cardiac MR imaging. Patients with a GFR < 30 ml/min will not receive gadolinium contrast. CT scan uses X-ray beams; this radiation can lead to the development of malignancies in a small portion of patients. However different dose minimizing strategies, such as prospective ECG gated scanning, can reduce the radiation to a maximum of 2-3 mSv, which is equivalent to the average background radiation a person annually receives. As part of the coronary CT-scan, contrast will also be administered. For the CT-scan low osmolar iodinated contrast will be used, Ultravist, Bayer B.V., Mijdrecht. Patients will be screened for contra-indications (e.g. previous reactions) for use of iodinated contrast and for elevated risk of contrast nephropathy (page 22 of protocol). A severe reaction to iodinated contrast occurs rarely (< 1/1000), but all general precautions will be taken. A

minor reaction occurs more often but is self limiting and subsides quickly. Patients with a history of reactions to iodinated contrast or with renal problems will not undergo CT-scan. In contrast to the standard coronary CT protocol, neither nitrolglycerine nor beta-blockade will be given, since this is not necessary for answering the research question.

The major burden for participants will be the extra time that the study related investigations will take. MR imaging is a long investigation which can also be burdensome. Furthermore insertion of an i.v. catheter can be painful. To reduce the burden for the patients all investigations will be planned consecutively if possible, in a maximum of two days.

The benefit for the participating patients is little. However, there is a possible benefit for the entire group of patients undergoing ASO in the future: with all the information gathered in this study, a more appropriate follow-up regime might be developed. Also the information about complications later in life and possible predictors thereof can provide better insight for patient and their parent(s) on what to expect long term after ASO for TGA.

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)
Elderly (65 years and older)

Inclusion criteria

transposition of the great arteries
arterial switch operation in WKZ
12 years of age or older
wiritten informed consent

Exclusion criteria

For MRI: pacemaker, claustrophobia, decreased renal function (the latter only for use of Gadolinium late enhancement)

Study design

Design

Study type:	Observational non 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):	11-08-2011
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	20-12-2010
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	10-08-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-11-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL33476.041.10