Evaluation of the clinical impact of ventricular dyssynchrony in patients with corrected tetralogy of Fallot

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Congenital cardiac disorders
Study type	Observational invasive

Summary

ID

NL-OMON31427

Source
ToetsingOnline

Brief title
Cardiac dyssynchrony in corrected tetralogy of Fallot patients

Condition

- Congenital cardiac disorders
- Cardiac and vascular disorders congenital

Synonym
dyssynchronie, tetralogy of Fallot

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Willem Alexander Kinder-en Jeugd Fonds

Intervention

Keyword: Cardiac MRI, Dyssynchrony, Echocardiography, tetralogy of Fallot

Outcome measures

Primary outcome

Primary study parameters are:

-time to peak systolic myocardial velocity assessed with echocardiography

(tissue doppler imaging) and MRI at different sites within the left and right

ventricle.

-Comparison of time to peak systolic myocardial velocity between corrected

tetralogy of Fallot patients and healthy subjects.

Secondary outcome

Not applicable

Study description

Background summary

Cardiac resynchronization therapy (CRT) has emerged as a valuable tool in the management of patients with left ventricular (LV) dysfunction and QRS prolongation. Left ventricular (LV) dyssynchrony, as effect of intraventricular conduction defects or bundle branch block causes nonsynchronous LV contractions and places the failing heart at a further mechanical disadvantage.
Atrial-synchronized biventricular pacing or CRT aims to resynchronize the failing heart improving myocardial contraction without increased energetics.
In patients with congenital heart disease, heart failure is one of the major causes of late mortality. The right ventricle (RV) sustaining either the systemic or pulmonary circulation is of special notice in these patients as, in contrast to ischemic heart disease, the RV is often the failing ventricle. The possible negative effects of RV dyssynchrony, as result of right bundle branch block, on the failing RV are unclear .
CRT has been reported to improve cardiac function as well as quality of life and life expectancy in the majority of selected patients. Inclusion criteria for CRT used in large clinical trials are NYHA-class III to IV, QRS-duration

>=120-130 ms and depressed left ventricular ejection fraction <= 35%. However, 20% to 30% of the patients who meet these criteria do not respond to CRT. To better predict the success of CRT inter-and intraventricular dyssynchrony was evaluated and recent studies pointed out that the severity of left ventricular (LV)-dyssynchrony is a good predictor for response to CRT. Furthermore, studies comparing inter-and LV-dyssynchrony to QRS-duration revealed that mechanical dyssynchrony may be present in the absence of QRS-prolongation and that QRS prolongation is more related to interventricular dyssynchrony as compared to intraventricular dyssynchrony. Therefore, evaluation of LV dyssynchrony is getting increasingly important in the selection of adult patients for CRT. Tissue Doppler Imaging (TDI) is the most widely used tool to assess cardiac dyssynchrony and proved to be a better predictor for response to CRT as compared to strain-analysis. Recently, Cardiac Magnetic Resonance imaging (CMR) was used to assess cardiac dyssynchrony and it was concluded that CMR and TDI provided comparable information on LV dyssynchrony.

Over the past decades the survival and life expectancy of patients with congenital heart disease has increased dramatically. In patients with a corrected congenital heart defect, heart failure is one of the major causes of late mortality. Failure of the right ventricle is poorly understood, especially with regard to therapeutical intervention and until recently no evidence-based therapy for RV failure is available. Data on the role of CRT in the management of heart failure in patients with a congenital heart defect are scarce. CRT has been used in the immediate post-operative period after correction of a congenital heart defect and improved cardiac output and narrowed QRS-duration was observed. Furthermore, Dubin et al. evaluated the acute effect of CRT in chronic right ventricular (RV) failure and demonstrated the feasibility of RV-CRT in improving RV function and decreasing QRS-duration during a clinically indicated cardiac catheterization.

Reports on the beneficial effects of CRT as treatment for chronic heart failure in children and adults with a congenital heart defect are limited. Recently, a retrospective international multicenter study evaluated the use of CRT in pediatric patients with acquired or congenital heart disease.

One-hundred-and-three pediatric patients in whom CRT was initiated were included and CRT induced increase in ejection fraction and decreased QRS-duration. However, inclusion criteria were heterogeneous and only 54% of the patients met the criteria for CRT in adults.

A substantial part of the study populations of the above mentioned studies included patients after correction of a tetralogy of Fallot. This well defined group is of special interest because these patients often develop RV failure in the presence of right bundle branch block (RBBB) and RV volume overload due to pulmonary or tricuspid insufficiency. After surgical correction, QRS-duration is related to right ventricular dilatation as well as increased left ventricular dimensions. Furthermore, Gatzoulis et al. reported that QRS >= 180 ms is the most sensitive predictor for malignant ventricular arrhythmias and sudden death. Pulmonary valve replacement (PVR) can be performed to restore pulmonary valve function and cancel the deleterious effects of pulmonary

insufficiency on cardiac function. After pulmonary valve replacement cardiac function improves in the majority of patients with a reduction of QRS duration. Whether this corresponds with improved intraventricular synchronization of the right ventricle has not been studied. Until now, optimal timing for pulmonary valve replacement still remains unclear.
RV failure and QRS prolongation (RBBB) remains a common problem long term after correction of tetralogy of Fallot and other congenital heart defects, but the indication and the role of CRT remains uncertain. CRT has been reported to improve ejection fraction and reduce QRS-duration in patients with tetralogy of Fallot. However, inclusion criteria for initiation of CRT as therapy of heart failure are not known. Until now, data are lacking on the degree of intra- and interventricular dyssynchrony and its relation to ventricular size and function and QRS duration. Currently, in adult patients with ischemic heart disease, these parameters have become important predictors of success of CRT After correction of tetralogy of Fallot, long-term follow-up is needed and repeated evaluation of pulmonary insufficiency and biventricular function is essential. CMR is nowadays regarded as the optimal tool in the follow-up of this patient group. Recently, Westenberg et al. reported a new application of CMR. Velocity encoded MRI was used to assess left ventricular dyssynchrony and it was concluded that CMR and TDI provided comparable information on LV dyssynchrony.

Study objective

1. To compare velocity encoded MRI and tissue Doppler echocardiography in the assessment of cardiac dyssynchrony
2.To define the presence and degree of RV mechanical dyssynchrony in patients with corrected tetralogy of Fallot with RV dysfunction using velocity encoded MRI and tissue Doppler imaging
3.To define the effects of pulmonary valve replacement on the degree of mechanical dyssynchrony of the RV in patients with corrected tetralogy of Fallot .
Secondary objectives
4.To select possible candidates for CRT in patients with corrected tetralogy of Fallot and RV failure

Study design

prospective patient based study

Study burden and risks

Echocardiography is a non-invasive and safe imaging tool and poses no risks of any damage. The burden is minimal as the patient/healthy controls is examined in the supine position during 30 minutes.
MRI is a non-invasive, safe imaging tool and poses no risks of any damage. The burden is little: the patient/healthy subject is postioned in the supine

position in the MRI scanner with a narow MRI tunnel during 60-90 minutes. During this time the subjects favourite music can be played. If there is any doubt whether or not the subject can undergo the MRI examination, a dummy MRI scanner (MRI-machine without magnetic field) is available, to test the subjects ability to undergo the MRI examination.

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 with corrected tetralogy of fallot aged > 8yr

healthy subjects with no signs ans syptoms of cardiac disease aged >8 yr

Exclusion criteria

Contraindications for MRI examination, such as pacemaker dependency and claustrofobia.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-07-2008
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	NL18572.058.08