# Atrioventricular septal defect: longterm follow-up after correction

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In patients long-term after AVSD correction the objectives are:1) To evaluate myocardial function using novel echocardiographic techniques.2) To study atrial en ventricular size and function in relation to quantification of AVV function with the use...

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

## Summary

### ID

NL-OMON37347

**Source**
ToetsingOnline

**Brief title**
the AVSD-study

### Condition

- Congenital cardiac disorders
- Cardiac and vascular disorders congenital

**Synonym**
atrioventricular septal defect, hole in wall between atria and ventricles

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Leids Universitair Medisch Centrum
**Source(s) of monetary or material Support:** Willem Alexander Kinderfonds

## Intervention

**Keyword:** Atrioventricualr septal defect, Echocardiography, Exercise capacity, Magnetic resonance imaging

## Outcome measures

### Primary outcome

Main study parameter

Echocardiography: peak systolic strain

MRI: AVV-function, percentage of AVV regurgitation.

### Secondary outcome

Clinical status, peak oxygen uptake. Dimensions and function of left and right

atria en ventricles.

# Study description

### Background summary

Congenital heart defects are the most frequent congenital defects with an incidence of 0.8% per year. Patients with an atrioventricular septal defect (AVSD) constitute 5% of all congenital heart defects. The key features of AVSD are the absence of a common atrioventricular valvular orifice with 2 bridging leaflets, classically believed the result of nonfusion of the endocardial cushions, thus preventing proper formation of the AV septum and closure of the ostium primum. AVSD can present as an isolated defect or in the setting of complex cardiac malformations. After birth, humans with an AVSD become symptomatic within the first year of life and repair is nowadays undertaken within the first 6 months of life1 with excellent long-term survival.1, 2 However, reoperation rate after AVSD correction is up to 15%, with predominantly reintervention because of hemodynamically significant left atrio-ventricular valve (AVV) regurgitation.3 In pregnant woman with corrected AVSDs, the presence of left AVV regurgitation was related to more interventions during delivery and after pregnancy AVV regurgitation showed deterioration in over 10% of the woman.4 Furthermore, moderate to severe left AVV regurgitation at latest follow-up in patients after AVSD correction is a risk factor for mortality, stressing the need of careful follow-up of AVV function after AVSD correction.

Left AVV regurgitation leads to a volume-overloaded atrium and ventricle, which can lead to left ventricular myocardial failure.3 Numerous studies on long-term follow-up in patients after AVSD correction have been published mainly evaluating re-intervention rate. Few studies have evaluated clinical status, exercise capacity and myocardial function after AVSD correction. Reduced exercise capacity has been described in patients after correction of congenital heart disease, including patients after AVSD correction.

Novel echocardiographic techniques have been introduced to assess global as well as regional myocardial function. Tissue Doppler imaging and speckle tracking strain imaging are echocardiographic techniques allowing detailed evaluation of myocardial function.5-7

As stated above, evaluation of AVV regurgitation is important after AVSD correction. Interestingly, evaluation of regurgitation of the AVVs in all follow-up studies of patients after AVSD correction is performed with echocardiography. Using echocardiography, AVV regurgitation can only be assessed semi-quantitatively, using a grading system based on the width of the vena contracta of the regurgitant jet.3 Direct quantification of AVV regurgitation using 3D velocity encoded magnetic resonance imaging (3D-VE-MRI) has been recently developed by Westenberg et al. from the department of Radiology of the LUMC.8 Using this technique AVV regurgitation was directly quantified in adult patients with ischemic heart disease.9 Recently, we reported the use of 3D-VE MRI to assess AVV function in healthy children and in children with corrected tetralogy of Fallot.10 No reports on the application of 3D-VE-MRI to assess AVV regurgitation after AVSD correction are available.

Indications for AVV surgery are well defined in adults. However, in the pediatric patient population indications are less clear. Because of the unpredictable need for AVV replacement and its concomitant problems of size limitations and anticoagulation requirements.3 The use of recently introduced imaging techniques such as TDI, speckle tracking strain imaging and 3D-VE-MRI be aid in the decision making and timing of AVV surgery.

Reference List

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9. Roes,S.D. et al. Flow assessment through four heart valves simultaneously using 3-dimensional 3-directional velocity-encoded magnetic resonance imaging with retrospective valve tracking in healthy volunteers and patients with valvular regurgitation. Invest Radiol. 44, 669-675 (2009).
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11. Hoohenkerk,G.J. et al. More than 30 years' experience with surgical correction of atrioventricular septal defects. Ann. Thorac. Surg. 90, 1554-1561 (2010).

## Study objective

In patients long-term after AVSD correction the objectives are:
1) To evaluate myocardial function using novel echocardiographic techniques.
2) To study atrial en ventricular size and function in relation to quantification of AVV function with the use 3D VE MRI.
3) To study clinical status and exercise capacity after AVSD correction in relation to cardiac dysfunction.
4) To assess the use of comprehensive evaluation of cardiac function, including AVV function, using echocardiography and MRI in the decision-making and timing of AVV surgery.

## Study design

Study design: prospective cohort-study
A surgical database including all AVSD patients corrected at the LUMC/AMC is available.11 This database includes 312 patients, 162 patients with AVSD and Down syndrome and 150 patients with AVSD without Down syndrome. Patient over 8 years of age and without any contrinidcatiosn for exercise testing or MRI examination will be invited to undergo a symptom-limited exercise test including peak oxygen uptake (VO2-max), echocardiographic examination and MRI examination. Echocardiographic examination includes semi-quantitative assessment of AVV regurgitation and tissue Doppler imaging and speckle tracking strain imaging of myocardial function. MRI examination includes 3D VE-MRI of the AVV for the quantification of AVV regurgitation.

The patients will be asked to visit the LUMC two times. During 1 visit a short physical examination will be performed and a ECG will be made. Length and weight will be measured. An echocardiographic examination will be performed with a duration of 30 minutes, during which the patients will be asked to turn to their left side and with the use of echogel and a transducer a echocardiographic examination will be carried out, which poses a minimal burden to the patient.
During the same visit a MRI examination will take place with a duration of approx. 75 minutes. Prior to the MRI examination a intravenous canula will be placed, which is needed for the administration of a contrast agent to allow detection of scar tissue in the atria and/or ventricles of the patients. From this IV canula, blood will be taken to assess proBNP, a blood marker for cardiac stress, and therefore no additional puncture is needed. During the MRI examination the subjects will be placed within the MRI scanner. A dummy MRI-scanner is available to test if the subjects are feeling comfortable within the MRI scanner. During the MRI examination, subjects own music can be played and the parents are allowed to be close to the subject. The subjects are monitored by ECG, microphone and camera monitoring.
During a second visit a symptom limited peak exercise test will be carried out on a bicycle ergometer. The patient will be asked to sit a bicycle ergometer and to exercise until exhaustion with a mask through which in and expired gas will be analysed to assess peak oxygen uptake, a marker for exercise validity.

After collection of the data, the data will be analyzed. The obtained data on myocardial performance obtained with echocardiography will be compared to normal data from healthy subjects. Furthermore the atrial and ventricular size obtained with MRI, will be compared to normal subjects and the relation between size and function and the amount of AVV regurgitation will be analyzed. Subsequently the parameters of myocardial and AVV-function will be related to clinical status and exercise capacity in the patients. Finally, the obtained parameters will be related to the indication for reintervention based on standard examination and to the surgical records on correction and reinterventions available in the AVSD-database, available through the research of Dr Hoohenkerk, from the department of thoracic surgery of the LUMC.

**Study burden and risks**

The patients will be asked to visit the LUMC two times. During 1 visit a short physical examination will be performed and a ECG will be made. Length and weight will be measured. An echocardiographic examination will be performed with a duration of 30 minutes, during which the patients will be asked to turn to their left side and with the use of echogel and a transducer a echocardiographic examination will be carried out, which poses a minimal burden to the patient.
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During a second visit a symptom limited peak exercise test will be carried out on a bicycle ergometer. The patient will be asked to sit a bicycle ergometer and to exercise until exhaustion with a mask through which in and expired gas will be analysed to assess peak oxygen uptake, a marker for exercise validity.
Subjects over 8 years of age will be asked to participate and therefore also minors will be included in this study. As a consequence parents of children from 8 to 12 years old will be asked to participate and sign the informed consent document. For participants from 12 years to 16 years of age both the participant him/herself and the parents are asked to sign the informed consent document. Subjects over 16 years of age will sign their own informed consent document.
Within the information letter the information provided to children will be described in an age-specific way, to optimise the discussion making whether or not to participate.
Minors over the age of 8 years will be included and if any verbal, physical sign of resistance is observed by the researchers or the parents of the subject the examinations will be terminated. During the echocardiographic examinations the echocardiographist is in close contact with the subject and parents to detect any resistance. During the MRI examination, microphones and camera*s are used to detect any sign of resistance.

Benefits and risks assessment, group relatedness
The influence of possible sequella, due to correction of an AVSD, most-commonly within the first year of life, start immediately after the operation. In case of a regurgitant valve causing volume overload to the atrium and ventricle, the period during which this volume overload occurs is essential to assess the effects and meaning of the regurgitation. Therefore it is essential that patients with different timeframes after correction are included in this study. Better understanding of the influence of atrioventricular valve regurgitation will lead to better patients managemnet. Furthermore, the need for reintervention because of valve regurgitation sometimes is present already at young age. If only adults were included in this study, the younger patients will probably not benefit from the findings of this study. Finally, healthy minors are included in this study because the findings in pediatric patients can only be interpreted correctly if compared to subject with similar age and body composition. Therefore a matched control group, also including minors, is essential.

# 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

Living patients after AVSD correction performed at the LUMC/AMC
>8years of age
No chromosomal abnormalities
No contra-indications for exercise test: severe aortic stenosis, inability to cycle.
No contra-indications for MRI examination: PM dependency, claustrofobia
Age-matched healthy controls

### Exclusion criteria

<8years of age
Chromosomal abnormalities
Contra-indications for exercise test: severe aortic stenosis, inability to cycle.
Contra-indications for MRI examination: PM dependency, claustrofobia

## Study design

### Design

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

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 25-10-2012 |
| Enrollment: | 70 |
| Type: | Actual |

## Ethics review

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| Approved WMO Date: | 26-03-2012 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br><br>metc-ldd@lumc.nl |

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| Approved WMO Date: | 29-11-2012 |

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|---|---|
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br><br>metc-ldd@lumc.nl |

# 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 | NL38510.058.11 |