# Right ventricle remodeling after pulmonary valve replacement and percutaneous pulmonary valve insertion, a functional and histopathological assessment.

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Primary objectives: to investigate functional and histopathological changes of the right ventricle before and after PVR and PPVI. To investigate if non-invasive assessment of RV-remodeling using CMR T1 mapping and T1rho mapping is possible and to...

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

## Summary

### ID

NL-OMON43787

**Source**
ToetsingOnline

**Brief title**
RV-REPAIR

### Condition

- Congenital cardiac disorders

**Synonym**
congenital heart disease, pulmonary valve dysfunction

**Research involving**
Human

## Sponsors and support

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

## Intervention

**Keyword:** grown up congenital heart disease, pulmonary valve replacement, remodeling, right ventricle

## Outcome measures

### Primary outcome

Cardiac magnetic resonance parameters including T1, T1 rho relaxation time and

LGE (late gadolinium enhancement) for fibrosis.

Histopathologiy: percentage of of fibrosis.

### Secondary outcome

Echocardiograpic parameters including strain and strainrate.

Cardiopulmonary excercise testing.

Electrocardiograpy and Holter testing.

Laboratory tests (BNP, ANP, hs-troponine, hs-CRP, cystatine C, PICP, TIMP-1).

Quality of life questionnaires (SF-36 and TAAQOL).

# Study description

### Background summary

Pulmonary regurgitation and (re-)stenosis are a common problem after initial surgical repair for pulmonary stenosis in patients with congenital heart disease such as Fallot*s tetralogy and isolated pulmonary valve stenosis. Re-intervention is indicated in symptomatic patients with severe PR/PS as well as in asymptomatic patients with progressive loss of RV-function. The timing of re-intervention however is unclear, preferably re-intervention should take place before irreversible RV-damage (fibrosis), due to pressure- and volume overload, occurs. In the past emphasis was paid to the onset of symptoms

instead of preventing right ventricular damage. Because symptoms in right ventricular failure are linked to the 'poin-of-no-return' (when the right ventricle doesn't fully recover after pulmonary valve replacement), most likely a better strategy is to intervene before symptoms arise. To be able to make reliable criteria for valve replacement we need to better understand the anatomical and functional impairments of the right ventricle and link this to histopathological changes. We believe myocardial fibrosis is correlated to this 'point-of-no-return'. In the last decades knowledge concerning RV volumes and function, and changes in electrocardiographic parameters and exercise parameters has grown. But, the relation between volums, funcion and histopathology is missing.

## Study objective

Primary objectives: to investigate functional and histopathological changes of the right ventricle before and after PVR and PPVI.
To investigate if non-invasive assessment of RV-remodeling using CMR T1 mapping and T1rho mapping is possible and to validate this with the golden standard of histopathology. -To investigate RV fibrosis with CMR T1 mapping and T1*-mapping (T1* relaxation time) and compare with LGE (occurrence of late enhancement) in patients receiving conservative treatment.
Secondary objectives: to investigate changes in echocardiographic parameters, electrocardiographic parameters, laboratory parameters (biomarkers), exercise capacity and quality of life in patients undergoing PVR or PPVI. To assess and compare the abovementioned parameters (except endomyocardial biopsies) in patients with RV-overloading not undergoing PVR or PPVI.

## Study design

Single center, prospective, observational trial with patients undergoing PVR or PPVI.

## Study burden and risks

Included patients will have extra outpatient clinic visits for post-interventional CMR, excercise testing, QoL questionnaires, ECG, Holter monitoring and echocardiography. Endomyocardial biopsies are performed during PPVI or PVR procedure. Risks of reaction to MR contrast are estimated as very low. The endomyocardial biopsy performed during valve replacement has a small risk of serious complications. According to the risk classification advise of the Federation of University Medical centers (hulplijst risicoclassificatie uit NFU advies kwaliteitsborging mensgebonden onderzoek) the study has to be graded as moderate risk.
Patients not undergoing valve replacement will undergo the same studies except for the endomyocardial biopsy and the echocardography performed

post-intervention and after 1 month follow-up.

## Contacts

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

### Inclusion criteria

Grown-up congenital heart disease patients with pulmonary insufficiency and/or stenosis and an indication for pulmonary valve replacement or percutaneous pulmonary valve insertion according to local GUCH team advise (based on current ESC GUCH guidelines). Also subjects who do not meet the indication criteria for valve replacement are eligible to participate in the study. They will form a conservative cohort.

## Exclusion criteria

- Individual is younger than 18 years of age.
- Individual has an estimated glomerular filtration rate (eGFR) of <30mL/min/1.73m2, using the MDRD calculation.
- Individual has any serious medical condition, which in the opinion of the investigator, may adversely affect the safety and/or effectiveness of the participant or the study (i.e., patients with clinically significant peripheral vascular disease, abdominal aortic aneurysm, bleeding disorders such as thrombocytopenia, haemophilia, significant anaemia).
- Individual is pregnant, nursing or planning to be pregnant.
- Individual has a known, unresolved history of drug use or alcohol dependency, lacks the ability to comprehend or follow instructions, or would be unlikely or unable to comply with study follow-up requirements.
- Individual is currently enrolled in an investigational drug or device trial.
- Individual with any contraindications for MRI:
a. The presence of implanted non-MRI-compatible cardiac pacemaker or implanted cardioverter defibrillator.
b. Implanted electronic devices like cochlear implants and nerve stimulators.
c. Patients who are unable to fit into the bore of the magnet.
d. Claustrophobia

# Study design

## Design

**Study type:** Observational invasive

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| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Diagnostic |

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 08-02-2016 |
| Enrollment: | 40 |
| Type: | Actual |

# Ethics review

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| Approved WMO Date: | 21-10-2015 |
| Application type: | First submission |
| Review commission: | METC NedMec |
| Approved WMO Date: | 05-02-2016 |
| Application type: | Amendment |
| Review commission: | METC NedMec |
| Approved WMO Date: | 19-04-2017 |
| Application type: | Amendment |
| Review commission: | METC NedMec |

# 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 | NL53771.041.15 |