High intensity interval training in patients with a right ventricle to pulmonary artery conduit

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Primary Objective: To assess the efficacy, expressed by change in peak oxygen consumption obtained with cardiopulmonary exercise testing (CPET), of a HIIT program in patients with an RV-PA conduit.Secondary Objective(s): To determine predictors for…

Ethical review	Approved WMO
Status	Pending
Health condition type	Congenital cardiac disorders
Study type	Interventional

Summary

ID

NL-OMON56579

Source
ToetsingOnline

Brief title
Right HIIT

Condition

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

Synonym
Congenital Heart Disease; Congenital absence of an unobstructed connection between the right ventricle and pulmonary artery (Truncus arteriosus, Other forms of pulmonary atresia with biventricular correction), Pulmonary atresia with ventricular septum defect, Severe tetralogy of Fallot

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Nederlandse Hartstichting

Intervention

Keyword: Cardiorespiratory fitness, Congenital heart disease, Exercise training, Predictors for response

Outcome measures

Primary outcome

Change in peak oxygen consumption measured by CPET.

Secondary outcome

• Other measures of exercise capacity: measured by CPET (including maximum

wattage, ventilatory efficiency slope, heart rate recovery, ventilatory

thresholds)

• Cardiovascular dimensions and function:

o Echocardiographic parameters

* Standard echocardiographic parameters indicating ventricular and valvular

size and function (as described in echocardiography guidelines)

o MRI parameters

* Ventricular size, mass, mass-volume ratio, function (ejection fraction),

flow measurements in the aorta and main pulmonary artery (2D and 4D), pulmonary

regurgitation fraction, right and left ventricular and systemic and pulmonary

vascular kinetic energy

• Blood biomarkers

o Commonly used biomarkers in CHD such as NT-proBNP, proteomics (including

GDF-15) and non-coding RNA for identification of predictors of response to

exercise training

• Gut microbiome composition

• Anthropometric measurements: changes in weight (and derivatives such as BMI, BSA)

• Daily physical activity (measured using accelerometry with wearables, provided on each visit and worn for the following seven days)

• Quality of life: measured by age-appropriate questionnaires (CHQ-CF45 and CHQ-PF28 for participants aged under 18 years, SF-36 for participants aged over 18 years and PedsQL MFS for all participants)

Study description

Background summary

Congenital heart disease (CHD) is the most common birth defect and represents a collection of relatively common and rare disorders characterized by abnormal anatomy of the heart. One group of patients suffers from imperfect connection of the right ventricle to the pulmonary artery, limiting blood supply to the lungs. CHD in this group of rare disorders includes truncus arteriosus, pulmonary atresia and tetralogy of Fallot with severe right ventricular outflow obstruction. To ensure blood flow to the pulmonary vasculature, a surgically implanted connection of the right ventricle to the pulmonary arteries, a right ventricle to pulmonary artery (RV-PA) conduit, is required.
In general, survival of patients with CHD, including the mentioned types, has increased over the past decades, leading to an increased prevalence of long-term sequelae. Heart failure is one of the critical long-term sequelae of CHD, affecting life expectancy and quality of life, with a current lack of effective therapy. Especially patients with diseases of the right ventricle, as in the mentioned group, have a serious risk of heart failure at a young age, with over 45% having heart failure at an average age of 30 years.
Hence, there is a need for preventive strategies. Exercise training may be such a preventive strategy. In patients with cardiovascular disease in general, a higher exercise capacity reduces the risk for adverse events. In patients with CHD, several studies suggest that specific types of exercise training may improve exercise capacity. Unfortunately, patients with rare forms of CHD, e.g.

patients with truncus arteriosus are understudied. It is unknown whether results obtained from other disease groups are applicable to this type of CHD. Also, patients with other rare forms of CHD characterized by an RV-PA conduit are less well studied. The presence of such a conduit increases the risk of residual lesions, which may have reduced inclusion in previous studies.
We hypothesize that an exercise training program in patients with an RV-PA conduit will elicit similar responses in exercise capacity as has been demonstrated by previous studies in patients with other types of CHD. We will test this hypothesis in the proposed intervention study. With growing evidence for similar or superior results of high-intensity interval training (HIIT) compared to aerobic training in a more time-efficient fashion, we will use a HIIT program.
Yet, previous studies testing the response to exercise training in patients with CHD yielded an average increase, albeit the groups are composed of responders and non-responders. The profile of (non-)responders has not been identified yet. If there is a biomarker predicting response to therapy, this may be useful to select patients for exercise therapy, which requires a large amount of patient commitment. Therefore, our secondary aim is to identify predictors for response to exercise training.

Study objective

Primary Objective:
To assess the efficacy, expressed by change in peak oxygen consumption obtained with cardiopulmonary exercise testing (CPET), of a HIIT program in patients with an RV-PA conduit.

Secondary Objective(s):
To determine predictors for response to exercise training, obtained using CPET, echocardiography, magnetic resonance imaging (MRI), gut microbiome analysis and blood biomarker profile.

Study design

The study is a randomized controlled trial with a modified cross-over design. Participants will be randomized into two groups, one intervention and one control group. The intervention and control period will last 12 weeks, in which the intervention group will receive a standardized HIIT program, and the control group will continue exercise as usual. Before and after this time period there will be a study visit with measurements, including CPET, echocardiography, MRI, gut microbiome analysis, collection of blood and questionnaires on quality of life and daily physical activity level. After 12 weeks, the control group will receive the same intervention as participants from the intervention group, with a third study visit after this period. At the regular outpatient clinic visit one year after completion of the study, participants will be provided questionnaires of quality of life and daily

physical activity.

Intervention

12-week high intensity interval training program, semi-supervised (online), three times a week.

Study burden and risks

The burden associated with participation mainly consists of a time investment. Participants will exercise three times a week and will attend two or three study visits at the hospital. The amount of time spent for exercise training is also part of the general recommendations of the World Health Organization. Procedures performed during study visits are part of standard follow-up in these patients (except for gut microbiome analysis), with one or two additional visits due to participation in the study.
Included participants will have no restrictions in their level of physical exercise. In daily life, they can be subject to peak physical exercise levels. In our previous experience no untoward effects have been observed in exercise testing or training. Heart rhythm disturbances may occur during CPET. CPET is performed with close monitoring of vital parameters and under supervision of a medical doctor. No (serious) adverse events have been reported with exercise training in patients with CHD.
Participants may benefit from the proposed positive effects of exercise training, based on the current literature. We will include patients with an RV-PA conduit, because this is an understudied population in which long-term complications such as heart failure are a major issue. The study population will include children and young adults, in order to obtain a group that has been treated according to current surgical strategies and to be able to study exercise training as a preventive strategy, so before overt heart failure is present.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr. Molewaterplein 40
Rotterdam 3015 GD
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr. Molewaterplein 40

Rotterdam 3015 GD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)

Inclusion criteria

1. Congenital absence of an unobstructed connection between the right ventricle and pulmonary artery, requiring surgical implantation of an RV-PA conduit, including patients with:
a. Truncus arteriosus
b. Pulmonary atresia with ventricular septum defect
c. Severe tetralogy of Fallot
d. Other forms of pulmonary atresia with biventricular correction
2. Age 12 to 45 years.
3. Current follow-up in ACAHA.
4. Signed informed consent.

Exclusion criteria

1. Ventricular arrhythmias and/or channelopathy.
2. ICD implanted due to inherited arrhythmia syndromes
3. Left ventricular ejection fraction (LV EF) and/or right ventricular ejection fraction
(RV EF) <30%
4. Elite athletes (i.e. national team, Olympians, professional athletes, exercising >=10 h/week, according to definition in 2020 ESC Guidelines for Sports Cardiology and Exercise in Patients with Cardiovascular Disease).(37)
5. Cardiovascular lesions requiring intervention (according to international guidelines)

6. Cardiovascular intervention (surgery or catheterization) less than 6 months ago.
7. Cardiovascular medication changes less than 3 months ago.
8. Hospitalization for treatment of cardiovascular events less than 6 months ago.
9. Comorbidities or developmental delay impeding exercise training (e.g. neuromuscular disease, symptomatic myocardial ischemia, syndromic diagnoses such as trisomy 21).
10. Inability to provide informed consent.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2024
Enrollment:	49
Type:	Anticipated

Ethics review

Approved WMO

Date:	29-02-2024
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	07-05-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-09-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-12-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL85656.078.23