# Examination of (handgrip) exercise to triggers coronary vasoconstriction in patients who are referred for a coronary function test

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Main research question: Does (handgrip) exercise provoke vasoconstrictive responses of the coronary arteries in patients with suspected ANOCA with clinically indicated coronary function test including acetylcholine provocation test?Secondary...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Coronary artery disorders
Study type	Observational non invasive

# Summary

### ID

NL-OMON51571

**Source** ToetsingOnline

#### **Brief title**

(handgrip) exercise to triggers coronary vasoconstriction

# Condition

• Coronary artery disorders

**Synonym** epicardiaal spasm / spasm of the coronairarteries

#### **Research involving**

Human

### **Sponsors and support**

#### Primary sponsor: Radboud Universitair Medisch Centrum

#### Source(s) of monetary or material Support: n.v.t.

### Intervention

Keyword: coronary fynction test, coronary vasoconstriction, exercise, handgriptest

### **Outcome measures**

#### **Primary outcome**

The observation of epicardal and/or microvascular spasm

#### Secondary outcome

nvt

# **Study description**

#### **Background summary**

Patients with angina symptoms and no obstructive coronary artery disease (ANOCA) pose a diagnostic and therapeutic challenge.

Up to 40% of patients undergoing a coronary angiogram for symptoms/signs of ischemia (such as angina/chest pain) do not have obstructive atherosclerotic coronary artery disease (CAD). However, angiography only concentrates on fixed atherosclerotic disease in the epicardial vessels. In about half of the 40% of patients without obstructive CAD, the mechanism underlying cardiac ischemia is coronary vasomotor dysfunction. In coronary vasomotor dysfunction, ischemia is caused by impaired coronary blood flow because of impaired endothelial and/or non-endothelial coronary vasoreactivity resulting in the coronary epicardial or microvasculature not dilating properly or even becoming vasospastic. We have previously shown that the majority of patients with coronary vasomotor dysfunction have vasospastic (epicardial and/or microvascular vasospasm) angina, while a smaller part have co-existing or isolated microvascular dysfunction. Furthermore, we have shown that vasospastic angina is associated with underlying atherosclerotic disease as assessed by intracoronary imaging (submitted).

Patients with vasomotor dysfunction often have episodes of chest pain leading to frequent first aid visits and hospital admissions with associated high health care costs. Moreover, it is associated with a worsened cardiovascular prognosis. Patients are at an increased risk for long-term coronary ischemic events. Therefore, in order to reduce complaints and health care costs, and improve prognosis; and increased understanding of the underlying pathophysiology, and subsequent adequate diagnosis and treatment are of paramount importance.

With regards to coronary artery vasospasm, including the vasomotor dysfunction endotypes epicardial and microvascular spasm, the abnormal coronary artery responses, including increase of coronary vasomotor tone. This may occur either in response to drugs, toxins or through (patho)physiological stimuli including exercise.

During exercise sympathetic activity is increased which causes dilatation of coronary vessels and thus an increase in myocardial blood flow. In this process cardiac efferent adrenergic signals and release of various hormones play an pivotal role. How the activation occurs exactly is not determined yet. In patients with (partial) denudation of the endothelial layer coronary spasm might occur. Accordingly, patients with suspected ANOCA may demonstrate abnormal, vasoconstrictive responses of the coronary arteries to exercise stimuli. Sueda et al. demonstrated that a third of patients with coronary spastic angina had a positive treadmill exercise test. This might alternatively be explained by non-spasm microvascular dysfunction, requiring different treatment. This indicates that exercise might induce coronary spasm. However in these patients only electrocardiogram and complaints were monitored. Also local handgrip exercise, when performed at high intensity, is capable of activating the sympathetic nervous system. Accordingly, also intensive local handgrip exercise may provoke abnormal coronary artery responses. To our knowledge no study yet have demonstrated epicardial spasm on angiography due to handgrip exercise.

Hypothesis: We expect that high intensity handgrip exercise is a trigger for epicardial and microvascular spasm in patients who have epicardial or microvascular spasm during acetylcholine provocation test.

#### **Study objective**

Main research question:

Does (handgrip) exercise provoke vasoconstrictive responses of the coronary arteries in patients with suspected ANOCA with clinically indicated coronary function test including acetylcholine provocation test?

Secondary objective, to explore whether handgrip exercise provokes coronary spasm in patients with a normal acetylcholine response.

### Study design

This is a prospective pilot study aiming to determine whether handgrip exercise has coronary vasoconstrictive response in patients with proven coronary epicardial spasm, as assessed by intracoronary acetylcholine provocation testing.

The study protocol will add 5 minutes handgrip exercise to a standard invasive investigation as described below.

Thirty patients will be included who have been planned for clinically indicated invasive coronary vasoreactivity testing. This includes coronary angiography (including 6 to 10 angiograms), acetylcholine spasm provocation testing (including 5 angiograms), and thermodilution based assessment of coronary microvascular dysfunction.

First, angiography will be performed to evaluate whether coronary obstruction is present, if not, acetylcholine provocation testing and coronary physiology measurements will be performed. Then the patients will perform 5 minute handgrip exercise to evaluate exercise induced coronary spasm with two additional angiograms (1 after the exercise and 1 after nitroglycerine if spasm occurs).

Each week the Radboud university medical center performs 3 to 4 coronary function tests CRT procedures. Considering a consent rate of 75% 3 study procedures can be performed each week. Indicating an approximate study duration of 10 weeks. There is no follow up connected to the study.

Number of subjects - This is a pilot study aiming to give a first indication of the effect of exercise on coronary vasospasm. There is no sample size calculation possible at this stage. We expect a maximum of 3 patients to drop out during the assessments, based on a 90% completion rate.

Variables - The primary outcome is the presence of epicardial vasoconstriction after handgrip test, as determined by angiography / electrocardiogram and complaints.

### Study burden and risks

There are no major risks associated with participation in the study for patients in the short or long term. Patients will only be exposed to additional X-rays due to one or two additional recordings of the left coronary artery, depending on whether nitroglycerin will be administered. Furthermore, the hospital visit will be extended by five minutes for the patients, which will not give a drastic change to their day.

# Contacts

### Public

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# **Trial sites**

# **Listed location countries**

Netherlands

# **Eligibility criteria**

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

# **Inclusion criteria**

patients will be included who have been planned for clinically indicated invasive coronary vasoreactivity testing.

# **Exclusion criteria**

below 18 years of age incapacitated

# Study design

# Design

Study type: Observational non invasiveMasking:Open (masking not used)Control:Uncontrolled

Primary purpose:

Diagnostic

### Recruitment

NL	
Recruitment status:	Recruiting
Start date (anticipated):	13-02-2023
Enrollment:	30
Type:	Actual

# **Ethics review**

Approved WMO	
Date:	07-06-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	
Date:	06-10-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

# **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 CCMO **ID** NL80584.091.22