TREAT study: Improving the interpretation of TRoponin concentrations following Exercise And Their clinical significance

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Primary aim: To establish reference values for exercise-induced elevations of cTn concentrations following walking, cycling and running exercise. Secondary aim: Assess the prevalence of (sub)clinical coronary artery disease in individuals with high…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON51559

Source
ToetsingOnline

Brief title
TREAT study

Condition

- Other condition
- Coronary artery disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
cardiovascular diseases, coronary atherosclerosis

Health condition

hart- en vaatziekten

Research involving
Human

Sponsors and support

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

Intervention

Keyword: biomarker, computed tomography (CT) scan, exercise, troponin

Outcome measures

Primary outcome

Baseline and post-exercise concentrations of high-sensitivity cTn I (hs-cTnI) and T (hs-cTnT) will be established for our primary aim.

Secondary outcome

Subsequently, the prevalence and magnitude of coronary artery calcification (i.e. Agatston score) and atherosclerotic plaque characteristics (density, phenotype (calcified/partially calcified/non-calcified), degree of stenosis, CT-derived fractional flow reserve), will be assessed in a subgroup of n=100 individuals with high versus n=50 with low post-exercise hs-cTnI concentrations. Finally, we will assess the incidence of major adverse cardiovascular events yearly and (cardiovascular and all-cause) mortality at 5-, 10-, 15-, and 20-years of follow-up.

Study description

Background summary

Cardiac troponins (cTn) have a key role in the diagnosis of a myocardial injury[1, 2].

Intriguingly, exercise produces transient elevations of cTn concentrations[3], mimicking the cTn kinetics of a myocardial infarction[4]. The clinical relevance of exercise-induced elevations remains unclear. We recently showed that the magnitude of post-exercise cTn concentrations is associated with an increased risk for mortality and major adverse cardiovascular events in long-distance walkers[5]. Furthermore, exercise-induced cTn responses were different in recreational cyclists with occult obstructive coronary artery disease compared to healthy controls[6, 7]. Hence, post-exercise elevations of cTn concentrations could represent: 1) an acute coronary event, 2) (sub)clinical myocardial injury, or 3) a physiological response. The interpretation of cTn concentrations following exercise is, therefore, challenging and causes clinical confusion[8]. Therefore, more insight into physiological versus pathological post-exercise cTn concentrations is needed.

Study objective

Primary aim: To establish reference values for exercise-induced elevations of cTn concentrations following walking, cycling and running exercise.
Secondary aim: Assess the prevalence of (sub)clinical coronary artery disease in individuals with high versus low post-exercise cTn concentrations.
Tertiary aim: To determine the association between post-exercise cTn concentrations and major adverse cardiovascular events and mortality during long-term follow-up.

Study design

Observational cohort study.

Study burden and risks

Overall, the risks of this study are low, and all efforts will be made to further minimize these risks. Visits 1 to 3 include a venous blood draw at baseline (V1), within 6 hours post-exercise (V2) and after 24 - 48 hours post-exercise (V3). All blood draws (3x30mL) are performed by an experienced researcher/nurse/physician, but a hematoma may occur in ± 5% of the participants. This will typically disappear within 2 weeks and is not associated with any (functional) limitations. Participants may experience transient pallor, dizziness, weakness or sweating following the blood draw of 30 ml per time point (90 ml in total). These symptoms generally disappear rapidly.
A subgroup of 150 athletes will be invited for visit 4 to determine the presence of (sub)clinical coronary artery disease using a contrast enhanced coronary CT angiography. The occurrence of contrast nephropathy is extremely rare in athletes with an estimated GFR >30 ml/min[9]. Mean radiation dose is estimated at 4.5 mSv , while a recent study observed no evidence of DNA damage in patients undergoing CT angiography with <7.5 mSv of radiation dose[10].

Incidental findings in the scan field may lead to additional diagnostic tests with extra costs and risks not covered by this study. Incidental findings (i.e. pulmonary nodules, pulmonary embolism and liver abnormalities) will be reported to the general practitioner of the participant. For subjects with heart rates >60 bpm, metoprolol will be administered iv. to lower heart rate and all subjects will receive 2 puffs of nitro-glycerine (0,8mg) sublingually directly before scanning to dilate the coronary arteries in concordance with clinical routine protocol. This may temporarily lower blood pressure.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

• Participant of a mass-participation exercise event with a:
o Walking distance >=30 km
o Cycling distance >=120 km
o Running distance >=15 km
• Age: >= 40 and <70 years old
• Able to understand and perform study related procedures

For Phase 2 of the study (i.e. assessment of (sub)clinical coronary artery disease), the following additional criteria are present:
• Free from (known) cardiovascular diseases

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in phase 2 of this study (CT scans):
• Renal transplantation in the past
• Contrast nephropathy in the past
• eGFR < 30 ml/min
• Atrial fibrillation (heart rhythm disorder)
• Previous allergic reaction to iodine contrast
• Participation in other studies involving radiation
• Not willing to be informed about potential incidental findings from the CT-scan

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-06-2022
Enrollment:	1500
Type:	Actual

Ethics review

Approved WMO Date:	09-05-2022
Application type:	First submission
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	ID
CCMO	NL79864.091.22