CUSTODIAN: ExtracelUllar VeSicles TO Exclude Chronic CoronAry SyNdrome.

Published: 11-12-2024
Last updated: 18-01-2025

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

Summary

ID

NL-OMON57167

Source
ToetsingOnline

Brief title
CUSTODIAN

Condition

- Coronary artery disorders

Synonym
coronary artery disease, coronary artery stenoses

Research involving
Human

Sponsors and support

Primary sponsor: Persuasive dx
Source(s) of monetary or material Support: Persuasive BV

Intervention

Keyword: Angina pectoris, Biomarkers, Diagnosis, Stable Coronary artery disease

Outcome measures

Primary outcome

The main study parameter: plasma EV proteins for obstructive coronary artery disease in patients presenting with CCS-like symptoms in the cardiology outpatient department.

Secondary outcome

Secondary study parameters/endpoints are:

• To assess the added value of other plasma EV biomarkers associated with inflammation and/or coagulation and cardiovascular disease to plasma EV proteins in detection of CCS.

• To assess prediction of myocardial ischemia and revascularization with plasma EV proteins and with (addition of) other plasma EV biomarkers associated with inflammation and/or coagulation.

• To assess identification of high-risk CCS patients with plasma EV proteins and plasma (EV) biomarkers associated with inflammation and/or coagulation (plaque burden P3 or P4, or with plaque vulnerability (HRP) according to CAD-RADS 2.0).

• To compare the diagnostic and prognostic value of plasma EV proteins and plasma (EV) biomarkers associated with inflammation and/or coagulation with calcium scoring.

• Comparison with ICA/FFR.

• To compare and assess the prognostic value of plasma EV proteins and plasma

(EV) biomarkers associated with inflammation and/or coagulation during the 30 month follow up: 1) In planned revascularization procedures due to obstructive CAD; 2) In all-cause mortality; 3) in Major Adverse Cardiac Events (MACE), which comprises a) Cardiovascular mortality, b) aborted sudden cardiac death, c) Myocardial Infarction (MI); d) Unplanned hospitalization for chest pain leading to urgent revascularization; e) Stroke.

Study description

Background summary

Coronary artery disease (CAD) is a leading cause of morbidity and mortality in the Netherlands, like in other Western Countries, and can be divided in Acute Coronary Syndrome (ACS) and Chronic Coronary Syndrome (CCS). Early diagnosis of CCS is essential, because of the improvement of the prognosis following timely interventions. On the contrary, early rule out of CCS reduces costs (e.g. diagnostic procedures, hospital admissions) and patient burden. Inflammatory and coagulation protein biomarkers in Extracellular Vesicles have emerged as a highly potential diagnostic value in the early detection of CCS, as literature showed that EV protein levels were associated with future cardiovascular risk. The Myomarker study, which is the predecessor of the CUSTODIAN study, hypothesized that 5 EV proteins (CD14, Cystatin C, Serpin C1, Serpin G1 and Serpin F2) could predict chronic coronary syndrome. The results of this study could only be interpreted as a hypothesis, since it was a retrospective single centre analysis with a small sample size. Therefore, the CUSTODIAN study is set-up to address the limitations of the Myomarker study and to further study the association between the identified EV proteins and CCS via a multi-centre prospective observational cohort study.

Study objective

The objective of the study will be to analyse the diagnostic and prognostic value of circulating inflammatory and/or coagulation biomarkers in plasma, plasma Extracellular Vesicles (EV), and gene expression profiles of circulating cells for the diagnosis of CCS.

Study design

The study is a prospective and diagnostic cohort study.

Study burden and risks

No risks are associated with participation in this study, as only extra blood required for the EV isolation will be withdrawn from the intravenous access device which is already inserted as part of standard care prior to the CCTA scan. The total amount of venous blood taken is not considered harmful for any patient. No additional harm is expected to the patient as the insertion of an intravenous access device is part of standard clinical care. Furthermore, no direct benefits are expected for the participants.

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

• The subject is >= 18 years of age
• The subject is willing and able to provide informed consent and adhere to study rules and regulations and follow-up
• The subject has (recurrent) angina pectoris or an equivalent, suspected of stable coronary artery disease, based on symptoms and signs, history, clinical examination and baseline diagnostic testing (e.g., ECG recording and laboratory tests) as described in the 2019 ESC guideline on chronic coronary syndromes.
• The subject will undergo a >=64 multidetector row CCTA (with contrast) as part of usual care deemed by the treating physician.

Exclusion criteria

• The subject does not or is not able to comply with those imaging guidelines for the performance and acquisition of CCTA by the Society of Cardiac Computed Tomography (SCCT)1 established to obtain good image quality, including:
o The subject is morbidly obese (Body Mass Index (BMI) > 40).
o The subject is not able to sustain a breath-hold for 25 seconds.
• The subject is unable to remain in supine position for at least 30 minutes
• The subject is suffering from unstable angina pectoris.
• The subject is suffering from decompensated congestive cardiac failure.
• The subject is suffering from a known or suspected non-ischemic cardiomyopathy.
• The subject has a history of Percutaneous Coronary Intervention (PCI) or coronary artery bypass grafting (CABG).
• The subject currently has pacemaker- or internal defibrillator leads implanted.
• The subject has a prosthetic heart valve.
• The subject is suffering from (auto)immune disorders
• The subject is suffering from an active malignancies and/or currently receives treatment for a malignancy
• The subject is currently receiving oral, systemic or long-term cutaneous steroid therapy, or any other oral or systemic immune-suppressive medications.
• The subject is currently receiving therapeutic anticoagulants, such as direct oral anticoagulants, vitamin K antagonists, heparin or low molecular weight heparin. Patients taking thrombocyte aggregation inhibitors and prophylactic anticoagulants are allowed to participate. • The subject is suffering from a coagulation disorder
• The subject is or might be pregnant.
• The subject participates in any other clinical trial that interferes with the current study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2024
Enrollment:	1722
Type:	Anticipated

Ethics review

Approved WMO

Date:	11-12-2024
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	NL86527.100.24