Coronary calcium scoring as first-line test to detect and exclude coronary artery disease in GP patients with stable chest pain

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CONCRETE aims to: (1) evaluate whether GP access to CT calcium scoring leads to earlier CAD diagnosis and treatment, (2) assess and optimize gender-specific diagnostic stratification based on the calcium score, (3) determine which (cluster of)…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON55495

Source
ToetsingOnline

Brief title
CONCRETE

Condition

- Coronary artery disorders

Synonym
coronary artery disease, coronary heart disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: Hartstichting

Intervention

Keyword: Calcium scoring, Diagnostic strategy, Early Detection, General Practitioner

Outcome measures

Primary outcome

Main study parameters/endpoints (cluster based):

To determine the increase in detection / treatment rate of CAD in GP offices with the calcium score-based strategy, compared to GP offices with the standard of care strategy, as measured by number of patients registered for/treated by the CardioVascular Risk factor Management guideline.

Secondary outcome

Secondary study parameters and objectives (individual based):

1. To establish the diagnostic yield to diagnose obstructive CAD, for both strategies
2. To establish the effectiveness in terms of CAD diagnosis and exclusion of GP referral to the cardiologist for the calcium score cluster
3. To compare downstream diagnostic testing and treatment for both strategies as well as the time to (exclusion of) CAD diagnosis
4. To evaluate whether diagnostic stratification, in particular cut-offs for referral to the cardiologist, can be optimized for the calcium score
5. To estimate the effect of calcium scoring versus the standard of care on quality of life and cardiac complaints after 6, 12, and 24 months
6. To estimate the effect of calcium scoring on reduction of MACE (after 2

years).

7. To derive data on the costs per diagnosis of obstructive and diagnosis of non-obstructive CAD in the setting of calcium score testing versus the standard of care

8. To estimate the cost-utility of implementing the calcium score test in GP setting

9. To develop machine learning tools to evaluate big data on (combinations of) symptoms and family history/risk factors, and relationship to CAD

10. To establish and visualize relationship between (combinations of) symptoms and family history/risk factors and probability of CAD, using innovative techniques for big data analysis; these results will form the input for a risk assessment tool to be developed

Study description

Background summary

CONCRETE is an implementation study, focused on the Dutch health care system in which the GP is usually the first physician a patient consults with non-acute chest discomfort. At the moment, the impact of implementation of calcium scoring in GP setting on CAD diagnosis and treatment rate are unknown. The exercise test is the most commonly performed test in cardiology outpatient clinics in referred patients. The CT calcium score is an existing test, which is part of the cardiac CT examination as requested in outpatient clinics (scan without contrast for calcium score determination, followed by scan with contrast for evaluation of coronary stenosis). In Dutch outpatient studies, CT calcium scoring proved to have high accuracy in diagnosing or excluding CAD. A zero CS makes the probability of CAD very low, while especially from a CS of 100 the risk of relevant CAD and cardiovascular events increases. We have, based on clinical outcomes in calcium score categories of these prospective outpatient studies, prepared advice for the GP to reassure, consider drug treatment, or consider referral to a cardiologist based on the patient*s CS. The optimization of cut-off values for CT calcium score in men and women is

part of this study. It is uncertain whether the diagnostic accuracy of CT calcium scoring is the same in GP setting, although prior outpatient studies included mainly low and intermediate probability patients.
The choice of the NHG Standard Committee to have the GP refer directly to the cardiologist instead of testing in GP setting is partly due to the fact that advanced diagnostics such as CT are now not accessible in primary care. It is not certain that direct referral to the cardiologist is a better strategy for diagnosis and prognosis of CAD than an initial policy based on calcium score measurement by the GP. Recently published Dutch research has shown that the calcium score can play an important stratifying role in patients with chest pain (Rijlaarsdam-Hermsen, Neth Heart J 2019; Lo-Kioeng-Shioe, Int J Cardiol 2019). There is a situation of equipoise, where there are 2 competing strategies about which experts disagree which initial strategy can best be used in the indicated patient group.
In contrast to ischemia tests, CT calcium scoring detects also early stages of CAD. It is possible that treatment of early CAD may prevent myocardial infarction or sudden cardiac death in the future due to early treatment, although at this moment this is still unclear.
Before wide-spread implementation in GP setting can take place, we intend to perform a pragmatic cluster-randomized trial to evaluate the clinical utility of calcium scoring in terms of 1. the diagnosis/treatment rate of early CAD, and 2. referral rate, downstream testing, further treatment, quality of life, cardiac events and costs, compared to the standard of care as recommended by the NHG. The expected result of CONCRETE is cost-effective implementation of the calcium score in the GP setting that will lead to early diagnosis and treatment of CAD causing AP and subclinical atherosclerosis, and on the other hand, safe exclusion of CAD, avoiding unnecessary referrals.

Study objective

CONCRETE aims to: (1) evaluate whether GP access to CT calcium scoring leads to earlier CAD diagnosis and treatment, (2) assess and optimize gender-specific diagnostic stratification based on the calcium score, (3) determine which (cluster of) symptoms and risk factors could assist in web-based self-assessment of CAD, and (4) translate study findings to initiate a change in Dutch health care policy by providing data on cost-effectiveness.

Study design

CONCRETE is an implementation study of CT calcium scoring in GP setting. The design is a pragmatic cluster randomized trial in which direct access to CT calcium scoring is compared to the standard strategy (direct referral to the cardiologist) in patients with chest discomfort. Randomization will take place at GP level.

Intervention

Implementation of direct access to CT calcium scoring for patients with chest discomfort in GP setting. Patients in both clusters will be asked for consent to fill in questionnaires regarding complaints, and quality of life and for the researchers to gather data on work-up and follow-up.

Study burden and risks

The purpose of CONCRETE is to study the implementation of calcium scoring in GP setting, and determine the effects on GP level. In half of the GP offices, CT calcium scoring will be implemented, and compared to the standard of care as recommended by the NHG. The risk due to the implementation of CT calcium scoring in GP setting is considered negligible for the following reasons. The risk of the diagnostic test, in terms of false positives and false negatives, as well as test related risks, is expected to be no worse for CT calcium scoring compared to evaluation (with or without non-invasive diagnostic testing) in the cardiology outpatient clinic. In outpatient cardiology clinic setting, CT calcium scoring has been found to have high diagnostic accuracy to detect or exclude CAD. It is uncertain whether this is the same in GP setting, although prior outpatient studies included mainly low and intermediate probability patients. The management advice given in the CONCRETE study for the calcium score categories have been based on discussions with cardiologists, general practitioners and radiologists, and are meant for guidance, but are not obligatory. These categories are based on recent literature from important Dutch studies (Dedic, IJC 2013; Lubbers, Circ imaging 2017; Rijlaarsdam-Hermsen, Neth Heart J 2019; Lo-Kioeng-Shioe, Int J Cardiol 2019) and on the experience of physicians who have been applying the calcium score for years in practice. Based on all this, the stratification based on the CT calcium score can be considered safe. Moreover, the choice of the NHG Standard Committee to have the GP refer directly to the cardiologist instead of testing in GP setting is partly due to the fact that advanced diagnostics such as CT are now not accessible in primary care. It is not certain that direct referral to the cardiologist is a better strategy for diagnosis and prognosis of CAD than an initial policy based on calcium score measurement by the GP. Recently published Dutch research has shown that the calcium score can play an important stratifying role in patients with chest pain (Rijlaarsdam-Hermsen, Neth Heart J 2019; Lo-Kioeng-Shioe, Int J Cardiol 2019). There is a situation of equipoise, where there are 2 competing strategies about which experts disagree which initial strategy can best be used in the indicated patient group. In contrast to ischemia tests, CT calcium scoring detects also early stages of CAD. It is possible that treatment of early CAD may prevent myocardial infarction or sudden cardiac death in the future due to early treatment, although at this moment this is still unclear. The radiation dose of CT calcium scoring is very low, less than 1 mSv (below half of annual background radiation). Also, patients may benefit from detection of early stages of CAD, with subsequent early treatment. The burden for patients in the individual-level outcomes is minimal, and involves willingness to share data from GP and hospital files, and

filling in questionnaires on complaints, and quality of life.

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

Cluster:
GPs willing to be included in the trial in the collaborating GP organizations.
Individuals:
Patients with non-acute chest discomfort, either atypical AP or aspecific chest pain, with indication for further evaluation to diagnose or exclude CAD as determined by the GP

Exclusion criteria

Individuals:
Men under 40 years, women under 45 years
Unwilling to provide written informed consent for the individual level outcomes (secondary outcomes)
Pregnancy
Prior CAD (PCI/ CABG/ infarct/ stable CAD)

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-12-2018
Enrollment:	1600
Type:	Actual

Ethics review

Approved WMO Date:	12-11-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-01-2019

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-08-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-02-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-03-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-10-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-05-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-10-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL66821.042.18
Other	NL7475