Inclusive Invasive Physiological Assessment in Angina Syndromes - Angina with No Obstructive Coronary Artery Disease

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6.2.1 Primary objective The primary objective is to assess the effectiveness of a stepwise medical therapy approach guided by coronary function testing in reducing angina burden of patients with angina pectoris and no obstructive epicardial coronary…

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

Summary

ID

NL-OMON52005

Source
ToetsingOnline

Brief title
ILIAS ANOCA

Condition

- Coronary artery disorders

Synonym
Microvascular dysfunction, non-obstructive coronary artery disease

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: AMC Medical Research

Intervention

Keyword: Coronary angiography, Microvascular dysfunction, Non-obstructive Coronary Artery Disease, Vasospasm

Outcome measures

Primary outcome

1.Health status based on Seattle Angina Score (SAQ)[12]

Health status and symptoms will be assessed at baseline and again at 6 months using the Seattle Angina Questionnaire. The primary endpoint is the difference in within-subject change in overall SAQ score at 6 months from baseline between the standard care and ICFT-guided treatment arms

Secondary outcome

1. Health status (Seattle Angina Score) over time.

Health status and symptoms will be assessed at baseline and again at 6 months, 12 months, 24 months using the Seattle Angina Questionnaire. The key secondary outcome is the difference in within-subject change in SAQ score over time between the standard care arm and ICFT-guided arm.

2. Prevalence of endotypes

Diagnosis of endotypes: obstructive CAD, abnormal vasoconstriction, abnormal vasodilatation, combined abnormal vasoconstriction and abnormal vasodilatation, functional chest pain, and non-cardiac chest pain.

3. Endothelial dysfunction

The presence of endothelial dysfunction will be assessed by the Amsterdam UMC Core Laboratory. The relationship of endothelial dysfunction with the occurrence of abnormal vasoconstriction and abnormal vasodilatation will be assessed. Additionally, the impact of medical therapy on health status will be assessed for patients with and without endothelial dysfunction.

4. Robustness of criteria for abnormal vasoconstriction

Evaluation of the impact of coronary function testing-guided medical therapy versus standard care on the 6-, 12-, and 24-month within-subject change in SAQ score in patients whom have recognizable angina during coronary function testing regardless of whether formal criteria for abnormal vasoconstriction or abnormal vasodilatation are met.

5. Health status EQ5D[13]

Assess the participants' general health status and self-reported quality of life using the EQ5D questionnaire.

6. Cost effectiveness analysis

Costs related to coronary function test guided versus angiography guided treatment, including cost utility analysis from a societal perspective with the costs per prevented cardiac event and the costs per QALY as the respective primary health economic outcomes (using a quality-of-life questionnaire and a health care resource use questionnaire).

7. Wireless diagnosis in ANOCA

Agreement of angiography-based assessment of stenosis severity

(angiography-derived FFR), and angiography-derived coronary flow reserve and

microvascular resistance for the correct diagnosis of abnormal vasodilatation.

Study description

Background summary

Historically, the diagnosis of angina pectoris focuses on detecting obstructive epicardial coronary artery disease (CAD). The identification of coronary artery obstruction may subsequently lead to evidence-based treatment including guideline-directed medical therapy and coronary revascularization[1]. However, among almost 400,000 patients undergoing coronary angiography for chest pain syndromes in the United States between 2004 and 2008, 39.2% had no evidence of epicardial CAD[2]. Such patients are usually reassured that no coronary stenosis is present, and their symptoms remain unaddressed[3]. It has been shown that patients with undiagnosed chest pain (including those who have undergone cardiac investigations) are at increased risk of cardiovascular events in the longer term and have high medical expenses due to ongoing symptoms, re-catherization and hospital admissions, highlighting the importance of reaching a diagnosis of the respective vasomotor abnormalities.[4], [5] Although the reasons for a *negative* coronary angiogram are multifactorial, many of these patients have a disorder of coronary artery function accounting for myocardial ischemia of non-obstructive origin [6]. Such disorders can relate to the occurrence of abnormal vasoconstriction in the epicardial coronary artery or the microvasculature, or to the occurrence of abnormal vasodilatation upon an increase in myocardial demand due to structural or functional alterations in the microvasculature[7][8]. Naturally, pharmacological treatment for each of these endotypes of vascular dysfunction should be substantially different. Therefore, early recognition of these specific disorders is of great importance[9]. However, since routine coronary angiography does not inform about the presence of disorders in coronary artery function[10][11], prescription of effective treatments (i.e. those addressing the causes of myocardial ischemia and/or anginal pain) requires additional tests providing key information on the underlying pathophysiology. The *CorMicA*-randomized, sham-controlled, blinded, clinical trial first reported on the efficacy of routine coronary function test-guided treatment in patients with angina and non-obstructive coronary artery disease (ANOCA) in two hospitals in Scotland[12]. Significant improvements in angina and quality of life at 6 months were sustained during longer term follow-up, suggesting an

important benefit of routine ICFT-guided treatment of ANOCA in clinical practice[13].

ILIAS ANOCA is a multi-centre, prospective, double-blind, randomized clinical trial comparing a coronary function test-guided treatment approach with standard clinical care for patients with stable angina pectoris without obstructive coronary disease on invasive coronary angiography. The coronary function test guided approach involves a standardized coronary function testing protocol, structured interpretation of the results, and subsequent stratified guidance on medical therapy.

Study objective

6.2.1 Primary objective
The primary objective is to assess the effectiveness of a stepwise medical therapy approach guided by coronary function testing in reducing angina burden of patients with angina pectoris and no obstructive epicardial coronary artery disease, compared with the control of angina provided by standard clinical care not guided by coronary function testing.

6.2.2 Secondary objectives
1. To identify the relevance of endothelial dysfunction in the spectrum of ANOCA endotypes

2. To evaluate the appropriateness of current criteria for abnormal vasoconstriction and abnormal vasodilatation to sensitively rule-out significant abnormalities in coronary function.

3. To compare angiography-derived coronary flow reserve and microvascular resistance versus invasive coronary flow reserve and microvascular resistance measurements.

4. To assess the cost-effectiveness of a stepwise medical therapy approach guided by coronary function testing compared with standard clinical care not guided by coronary function testing.

5. To assess the prognostic value of biomarkers (hs-troponin, NT-proBNP, CRP) at baseline across the ANOCA-endotypes.

6. To assess sex-differences across the various ANOCA-endotypes and the impact of sex-differences on diagnosis, treatment and health status.

Study design

Multi-center, prospective, double-blind, randomized, sham-controlled clinical

trial

Intervention

The intervention consists of disclosure of intracoronary function-testing and contemporary therapeutic advice.

Study burden and risks

Compared to local practice standards that recommend physiological-guided revascularization, no additional risks are related to the present study. It is in general considered that the use of sensor-equipped guide wires is safe. The appearance of vessel wall damaging occurs in approximately 1 of 1000 procedures, hence the adoption of sensor-equipped guide wires is considered as local standard care.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Inclusion criteria

• Age >=*18 years.
• Patient referred for elective coronary angiography for suspected angina (and/or angina-like) symptoms as defined by current clinical practice guidelines[1].
• Absence of obstructive coronary artery disease evident in a main coronary artery (diameter stenosis<50%, iFR>0.89, or FFR >0.80).

Exclusion criteria

• A noncoronary indication for invasive angiography, e.g., valve disease, hypertrophic obstructive cardiomyopathy
• Coronary angiography performed in the evaluation of elevated cardiac troponin (myocardial infarction with no obstructed coronary arteries).
• A life expectancy of less than 2 years.
• Inability to sign an informed consent, due to any mental condition that renders the subject unable to understand the nature, scope, and possible consequences of the trial or due to mental retardation or language barrier.
• Potential for non-compliance towards the requirements for follow-up visits.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-09-2021

Enrollment:	120
Type:	Actual

Ethics review

Approved WMO Date:	04-05-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-03-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-06-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-01-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

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	NL76384.018.21