Microvascular Function in Non-ST-segment Elevation Acute Coronary Syndrome

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Observational invasive

Summary

ID

NL-OMON42844

Source
ToetsingOnline

Brief title
DEFINE NSTEMI

Condition

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

Synonym
microvascular dysfunction, NSTEMI

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Doppler coronary flow, Microvascular function, NSTEMI, Thermodilution coronary flow

Outcome measures

Primary outcome

To document the magnitude of microvascular resistance in patients with NSTE-ACS versus patients with stable coronary artery disease, as obtained from Doppler flow velocity-derived and thermodilution mean transit time-derived surrogates of coronary flow.

Secondary outcome

To document the relative magnitude of absolute coronary flow and coronary flow reserve in patients with NSTE-ACS versus patients with stable coronary artery disease, as obtained from Doppler flow velocity-derived and thermodilution mean transit time-derived surrogates of coronary flow.

To determine the relationship between Doppler flow velocity-derived and thermodilution-derived mean transit time-derived surrogates of coronary flow, coronary flow reserve, and the derived indices of microvascular resistance.

To determine the effect of intravenous versus intracoronary administration of adenosine on maximal coronary flow and coronary flow reserve.

To determine the relevance of correction of coronary flow and coronary flow reserve for the loss of perfusion pressure after intravenous administration of

adenosine.

To determine the potential of advanced analysis of the coronary angiogram for the assessment of coronary flow and resistance parameters through fluid dynamic modelling.

Study description

Background summary

Although the use of coronary physiology techniques in contemporary clinical practice is dominated by the use of coronary pressure to guide epicardial revascularization, a comprehensive assessment of coronary physiology only can be achieved by measuring both coronary pressure and flow simultaneously. The resistance of a vascular compartment is defined as the ratio of the pressure drop over it to the flow through it, the measurement of both coronary pressure and flow simultaneously during cardiac catheterization allows the selective interrogation of the resistance to coronary flow induced by the epicardial and microvascular compartments of the interrogated coronary vascular bed. Evidence is accumulating that the resistance induced by the coronary microcirculation is an important contributor to the occurrence of myocardial ischemia, importantly influences the diagnosis of the functional severity of epicardial coronary stenoses by coronary pressure measurements, and even poses an independent risk factor for adverse clinical outcome when it is abnormal, both in stable coronary artery disease and ST-segment elevation myocardial infarction patients (STEMI).
These findings indicate an important role of coronary microvascular function in the spectrum of coronary artery disease. Although the spectrum of acute coronary syndromes is considered a sliding scale in terms of ischemic burden to the myocardium, increasing in severity from unstable angina pectoris to STEMI, the clinical outcome of NSTE-ACS is counter intuitively equivalent to that of STEMI. Considering the well-documented influence of microvascular function on clinical outcome, both in stable coronary artery disease and STEMI-populations, it may be considered that the functional consequences of the ischemic event in the setting of NSTE-ACS may precipitate adverse outcome in a similar manner as in STEMI. Unfortunately, clinical coronary physiology data in the setting of NSTE-ACS is minimal. Moreover, the available data has been obtained with different equipment and methodology than that used in the pivotal stable coronary artery disease and STEMI studies.

Study objective

The purpose of this study is to advance our understanding of the behaviour of the coronary microcirculation in the setting of NSTE-ACS, to provide insights into the relationship between Doppler flow velocity and thermodilution-derived coronary physiological parameters and their use in advanced physiological indices of coronary resistance, and to identify the effect of systemic versus local administration of vasodilators on coronary flow and flow reserve and potential for its correction. Hence, this study aims to document 1) the magnitude of microvascular resistance, maximal coronary flow and coronary flow reserve in the setting of NSTE-ACS relative to a stable coronary artery disease population 2) the relationship between Doppler flow velocity-derived and thermodilution mean transit time-derived coronary flow, and the derived indices of stenosis and microvascular resistance, and 3) the effect of intravenous versus intracoronary administration of adenosine on maximal coronary flow and coronary flow reserve, and the pertinence of correction for loss of perfusion pressure.

Study design

This study is designed as a single-center, cross-sectional randomized studie with invasive measurements.

Study burden and risks

The use of sensor-tipped guide wires in diseased coronary arteries is considered safe. The appearance of damaging of the vessel wall occurs in approximately 1 of 1000 procedures. The appearance of vessel wall damaging in healthy vessels is even considered lower. The measurements will be conducted according study protocol and are not standard cardiac care. However, since the measurements are considered safe with a risk of vessel wall damaging of less then 1 in a 1000, the extra risks coherent to the study protocol are negligible. Therewithall, the measurements offer additional information regarding the spectrum of coronary artery disease which are of therapeutical and prognostic value. It has already been proven that microvascular dysfunction can be considered as an important contributor to adverse clinical outcome in patients with stable coronary artery disease or in the setting of STEMI. The additional intracoronary measurements allow an early diagnostics of a compromised microcirculation on which the treating doctor can anticipate in an early setting. The advantages of the additional measurements outweight the limited risk profile of intracoronary measurements.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Stable angina (CCS class I to III, or Braunwald class I) or NSTE-ACS (Chest pain within the preceding 5 days and an index event >24 hours from time of angiography but within the previous 7 days).;2. Scheduled for percutaneous coronary intervention or intracoronary evaluation of functional stenosis severity (diagnostic catheterization).;3. The presence of at least one normal or minimally diseased reference coronary artery (<30% diameter stenosis on visual assessment) with a vessel diameter of more than 2.5 mm.

Exclusion criteria

1. Younger than 19 or older than 80 years of age.;2. Recent ST-segment elevation myocardial infarction (<6 weeks prior to enrollment).;3. Inability to receive intravenous adenosine (for

example, severe reactive airway disease, marked hypotension, or high-grade AV block without pacemaker).;4. Known renal insufficiency (eGRF according to MDRD <30 mL/min/m2).;5. Known severe valvular abnormalities.;6. Known severe left ventricular dysfunction (LV ejection fraction <30%) or known myocardial hypertrophy (septal wall thickness at echocardiography of >13 mm).;7. Extremely tortuous or calcified coronary arteries precluding intracoronary physiologic measurements.;8. Women of child bearing age not on active birth control;9. 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.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-02-2017
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	10-11-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL58034.018.16