Noninvasive Imaging of Vulnerable Inflammatory Coronary Plaque using Cardiac PET/CT in Humans: a feasibility study

Published: 08-09-2013
Last updated: 22-04-2024

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

Summary

ID

NL-OMON44976

Source
ToetsingOnline

Brief title
Imaging of coronary vulnerable inflammatory plaques

Condition

- Coronary artery disorders

Synonym
Coronary artery disease, unstable angina

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: Reserve budget van de afdeling cardiologie VUmc.

Intervention

Keyword: CCTA, PET, Vulnerable Inflammatory Plaque

Outcome measures

Primary outcome

This feasibility study will test different tracers for their feasibility to

detect culprit lesions of patients with an ACS. Endpoints will be sufficient

target to background uptake of tracer beyond 1.2 that coincides with the

culprit lesion identified with general clinical information / CAG / OCT

characteristics.

Secondary outcome

Kinetics of the three different PET tracers (11C-PK11195, 18F-AS101, or

18F-Galacto-RGD)

Study description

Background summary

Coronary artery disease (CAD) is the leading cause of death in the western world. Traditional strategies for the detection and treatment of CAD are aimed at detecting flow limiting coronary atherosclerotic lesions and subsequently restoring coronary flow either by percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) for symptom relief. Although this strategy is suitable for patients with stable CAD, it does not identify patients at risk to develop an acute coronary syndrome (ACS). The latter syndrome is caused by coronary plaque rupture provoking thrombosis leading to unheralded events such as unstable angina and myocardial infarction.(Naghavi et al. Circulation 2003, Finn et al. ATVB 2010) These plaque ruptures often occur in non-obstructive lesions, which generally outnumber symptomatic stenotic plaques.(Libby et al. Circulation 1995) Consequently, an ACS with potential devastating effects is frequently the initial presentation of CAD in previously

asymptomatic patients. Next to obstructive severity, therefore, plaque morphology assessment could play a pivotal role in the evaluation of CAD to predict plaque stability.
Imaging of plaque biology and constitution is therefore of interest to potentially identify those lesions that are prone to rupture. Positron emission tomography (PET), in conjunction with a positron emitting labeled compound of interest, allows to track biochemical pathways in vivo noninvasively. Studies using PET have documented that the positron-labeled glucose analogue 18F-fluorodeoxyglucose (18F-FDG) is actively taken up in atheromata of the carotid arteries and aorta.(Rudd et al. Circulation 2002, Rudd et al. J Nucl Med 2008) Thus, increased uptake of 18F-FDG may provide a marker for metabolically active inflammatory cells in plaque. Unfortunately, attempts to use 18F-FDG PET for detection of inflammatory coronary plaques have been disappointing.Therefore novel probes are required to specifically visualize the biological characteristics of the coronary vulnerable plaque that are not metabolized by the myocardium itself and yield a sufficient target-to-background ratio. In recent years, several tracers have been developed for this purpose. Among these are tracers that bind to macrophages (11C-PK11195), matrix-metalloptroteinase (18F-AS101), or integrins (18F-galacto-RDG).(Lamare et al. J Nucl Med 2010, Quillard et al. ATVB 2011, Laitinen et al. Circulation Cardiovasc Imaging 2009) Each of these probes has demonstrated their ability to detect inflammatory atheromata in animal experiments. In addition, human studies have showed that 11C-PK11195 can also be detected with PET in inflamed carotid artery plaques.(Gaemperli et al. Eur Heart J 2012) Studies to evaluate the feasibility to image coronary vulnerable plaques are, however, lacking.

Study objective

The objective is to study the feasibility of different PET tracers to detect vulnerable plaques in patients with a recent acute coronary syndrome and co-localize these inflammatory lesions with anatomical plaque features obtained with CT based coronary angiography (CCTA).

Study design

Twenty-four patients (35-75 years) admitted to the coronary care unit with an ACS and no prior history of percutaneous coronary intervention, coronary artery bypass surgery, or myocardial infarction will be included. Prior to ESC guidelines indicated ICA all patients will undergo a PET/CT-scan. The scanning sequence will consist of a CCTA, which will be fused with PET images using an investigational tracer to potentially identify the vulnerable plaque. In a serial manner, each tracer will be tested for feasibility purposes in eight patients per tracer (either 11C-PK11195, 18F-AS101, or 18F-Galacto-RGD). Tracer kinetics will be quantified and co-registered with the coronary tree as obtained with CCTA. After PET/CT, ICA will be performed in combination with

optical coherence tomography (OCT) to identify vulnerable plaque invasively. PCI will subsequently be performed according to the current ESC guidelines on myocardial revascularization.

Intervention

PET-tracer (11C-PK11195, 18F-AS101, or 18F-Galacto-RGD)

Study burden and risks

Patients will receive contrast during CCTA with risk of allergic reactions or renal failure. Renal function will be tested during regular care and will be available for considering participation. All patients with estimated glomerular filtration rate < 45 ml/min will be excluded to avoid any risk of renal failure. During CCTA one of the investigator will be present to monitor any allergic effects to the contrast agent. Appropriate measures will be executed when necessary. Patients will receive 6 * 8 mSv during PET/CT protocol. There will be no direct benefit to participate in this study for patients individually. Improvement of clinical healthcare is the main purpose of this study and is considered beneficial by the investigators.

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

* Patients with an acute coronary syndrome and accompanying ECG abnormalities (unstable angina / non-ST-elevation myocardial infarction.
* Clinical indication for invasive coronary angiography within 72 hours upon admission based on ESC guidelines pertaining treatment of patients with unstable angina or non-ST segment elevation myocardial infarction.
* Age 35-75 years

Exclusion criteria

* Prior percutaneous coronary intervention, coronary artery bypass surgery, or myocardial infarction
* History of systemic inflammatory disease
* Current cardiac arrhythmia
* Renal failure with estimated glomerular filtration rate < 45 ml/min
* Refusal or inability to give informed consent

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	29-07-2016
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nvt
Generic name:	[11C]PK11195
Product type:	Medicine
Brand name:	nvt
Generic name:	18F-AS101
Product type:	Medicine
Brand name:	nvt
Generic name:	18F-Galacto-RGD

Ethics review

Approved WMO Date:	08-09-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-09-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-04-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-04-2017
Application type:	Amendment
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
EudraCT	EUCTR2013-002670-40-NL
CCMO	NL44913.029.13