Genetic polymorphisms and immunologic profiles in arteriogenesis

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Determining the role and influence of genetics, their polymorphisms and immunologic phenotype in arteriogenesis in patients with obstructive coronary artery disease (CAD).

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

Summary

ID

NL-OMON44569

Source
ToetsingOnline

Brief title
GLACIER study

Condition

- Coronary artery disorders

Synonym
Obstructive coronary artery disease and collateral artery growth

Research involving
Human

Sponsors and support

Primary sponsor: VU University Medical Center
Source(s) of monetary or material Support: NIRM

Intervention

Keyword: Arteriogenesis, CTO, Genetics, Immunology

Outcome measures

Primary outcome

Main study endpoints: the main study endpoints are collateral flow, as

determined by CFI, arteriogenic polymorphism, determined by DNA-profile and

immunologic phenotype.

Secondary outcome

Heart function

Study description

Background summary

Obstructive coronary artery disease brings along morbidity and mortality in millions of patients worldwide. Despite the success of techniques like retrograde revascularization by coronary artery bypass grafting (CABG) and antegrade revascularization by percutaneous coronary intervention (PCI), these forms of treatment are not suited for all patients due to complexity of the lesions or co-morbidity and high surgical risks. Therefore new alternative treatment options are warranted to alleviate symptoms and improve survival and quality of life in these estimated 20% of patients without revascularization options. One of the body*s physiologic mechanisms to maintain tissue perfusion is the growth of collateral vessels. Due to an increasing gradient in the presence of a arterial stenosis, the caliber of pre-existing collateral vessel is increased, This process is known as arteriogenesis and is in concept the prototype of retrograde vascularization using natural bypasses already present in myocardial tissue. This potent process is capable to largely compensate for perfusion deficits in coronary artery disease (CAD) and its mechanisms have been under extensive research in the past decades. Coronary collaterals are already prevalent in some extent in every person, but there are great differences in the arteriogenic response between individuals. These differences have been attributed to both genetic variation (i.e. polymorphism) and immunologic phenotype. Interestingly, only about one third of the patients with obstructive coronary artery disease develops a fully functional collateral circulation. Especially in patients with a chronic total occlusion (CTO), where one of the coronary arteries is fully occluded for >=3 months and downstream vital myocardium is fully dependent on collateral perfusion. This collateral perfusion can be determined by the collateral flow index (CFI). By measuring the pressure gradient between the aortic pressure and the post CTO coronary

wedge pressure, CFI can be calculated. In this way CFI is directly correlated with the amount of collateral perfusion and thereby arteriogenesis. Analyzing the correlations between CFI with both genetic an immunologic profile helps us further unravel the mechanisms of arteriogenesis, thereby opening the way for possible future clinical applications.

Study objective

Determining the role and influence of genetics, their polymorphisms and immunologic phenotype in arteriogenesis in patients with obstructive coronary artery disease (CAD).

Study design

This study is designed as a single center prospective cohort study.

Study burden and risks

The burden of the research is small. Patients included in the study will undergo a single additional invasive measurement following the PCI. Furthermore, 120ml blood will be taken for lab investigation, and patients will undergo MRI and PET scans. The risks are minimal. The intracoronoary pressure-flow measurement is a single invasive procedure like many which are done in every standard PCI procedure, the risk of which are <1%.

Contacts

Public
VU University Medical Center

De Boelelaan 1117
Amsterdam 1081HV
NL
Scientific
VU University Medical Center

De Boelelaan 1117
Amsterdam 1081HV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

>18 years old
present chronic total occlusion of one of the coronaries
Patients who undergo succesfull PCI

Exclusion criteria

-refusal or inabilty to give informed consent
-Age >80
-Immunologic disorder of disease, recent use of immunosuppressive drugs.
-haemodynamic unstablility

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	12-06-2015
Enrollment:	50

Type:	Actual

Ethics review

Approved WMO Date:	09-06-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-11-2016
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
CCMO	NL47521.029.14