Transcriptome analysis of circulating monocytes from patients with stable plaques and patients with unstable plaques.

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

Summary

ID

NL-OMON29831

Source
ToetsingOnline

Brief title
Transcriptome analysis of circulating monocytes.

Condition

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

Synonym
Cardiovascular disease, Hardening or furring of the arteries

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Acute coronary syndrome, Atherosclerosis, Biological risk markers, Genomics

Outcome measures

Primary outcome

Relative gene expression levels in monocytes from different inflammatory

disease patient groups.

Secondary outcome

A questionaire concerning the habits and the disease progression of the

patients will be conducted. This will be used in later correlation studies. A

folow-up questionaire will be taken after 12 months

Study description

Background summary

Multiple lines of evidence indicate an intense interaction between circulating monocytes and atherosclerotic plaques. The role of monocyte infiltration in the arterial wall and the differentiation into lipid-laden macrophage foam cells, is well recognized in the pathogenesis of atherosclerosis. Macrophage foam cells play a key role in disease progression, both as scavengers of lipid and as inflammatory mediators. Moreover, recent literature indicates that a substantial population of macrophage foam cells emigrates from atherosclerotic plaques, which permits their re-entry into the blood and genes were identified that are differentially expressed between the circulating monocytes of patients undergoing carotid endarterectomy and normal subjects.
Studies of the mononuclear-phagocyte system using monoclonal antibodies for cell-surface antigens (e.g. L-selectin, chemokine receptors), have shown heterogeneity in the phenotype of monocytes and macrophages in atherosclerotic plaques. In line with phenotypic heterogeneity, our lab has recently identified differences between the gene expression profiles of macrophages from

atherosclerotic plaques and non-atherosclerotic macrophages isolated from spleen, liver and lungs, demonstrating that heterogeneity is also present on transcriptome level. Likewise, we hypothesize that an increased inflammatory status, such as reported for vulnerable plaques, will go together with changes in the transcriptome of blood monocytes.
Overlap between the expression profiles of the identified set of genes on the pathway level, might give insights in the molecular mechanism of atherosclerosis.

Study objective

The primary objective is identification of a set of genes as candidate monocyte markers for acute coronary complications and subsequent identification of a prognosis classifier to discriminate vulnerable, stable, and control subjects, based on the expression of the identified set of genes.

Study design

This study is an observational cross sectional study to study the differences in the transcriptome of monocytes from stable and unstable patients using rheumatoid arthritis patients as a control group. Unstable patients are identified in the emergency room as highly suspected for the presence of ruptured coronary plaques, because of a recent history of unstable angina (i.e. with ECG abnormalities indicating subendocardial ischemia or postischemic conditions, but without elevated levels of troponin-T), i.e. unstable angina IIA, IIIA, IIB and IIIB-Tneg. Patients shown to have atherosclerotic lesions in the past during coronary catheterization, treated for more than 3 months for stable angina pectoris in the Hart-en Vaatcentrum Maastricht, but without any history of previous AMI or cerebro-vascular event, are considered as stable patients. As a control group for other inflammatory genes age- and gender matched patients suffering from rheumatoide arthritis, without clinical evidence of cardiovascular disease will be included in close cooperation with Prof Dr P. Geussens, Internal Medicine, azM.
Monocytes will be isolated from blood that will be drawn from the patients by venapunction. At first, of all groups at least 20 patients will be included for transcriptome analysis on genome-wide micro-arrays. Secondly, the gene expression results will be utilized in the design of a custom array containing approximately 500 genes mostly related to the disease state. Then the transcriptome of 250 patients of both the stable and unstable patient groups is analysed. Subsequently a prognosis classifier gene-set will be designed based on the gene-expression levels in 70% of the subjects. Finally the prognosis classifier gene-set will be evaluated on the remaining 30% of the gene-expression data.

Study burden and risks

The risk to and burden for the individual subjects is very low because a venapunction is a standard procedure with negligible risks and low burden.

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

Unstable angina (IIA, IIIA, IIB, IIIB-Tneg): Clinical symptoms secondary to recent coronary plaque rupture, history of recent unstable angina, ECG repolarization abnormalities, statin treatment (> 2 months).
Stable angina patients: Stable atherosclerotic lesion(s) identified during coronary angiography, treated for more than 2 months for angina pectoris,
statin treatment (> 2 months).
Rheumatoid arthritis patients: Diagnosed as having Rheumatoid Arthritis for longer than 12 months, statin treatment (> 2 months).

Exclusion criteria

Unstable angina (IIA, IIIA, IIB, IIIB-Tneg): Recent history of acute myocardial infarction (in the past year), elevated troponin-T levels, diabetic, smoker, under 18 yrs of age, clinical manifestation of extracardiac atherosclerotic disease.
Stable angina patients: Recent history of unstable angina or Acute Myocardial Infarction, diabetic, smoker, under 18 yrs of age, clinical manifestation of extracardiac atherosclerotic disease.
Rheumatoid arthritis: Clinical symptoms of atherslerotic disease, diabetic, smoker, under 18 yrs of age.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-01-2007
Enrollment:	779
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	15-11-2006
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit

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	NL13305.068.06