The GLOBAL Study (Genetic Loci and the Burden of Atherosclerotic Lesions) Protocol# CR0001

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

Summary

ID

NL-OMON38542

Source
ToetsingOnline

Brief title
The GLOBAL Study

Condition

- Coronary artery disorders

Synonym
coronary artery disease heart disease

Research involving
Human

Sponsors and support

Primary sponsor: Biotechnologische Industrie
Source(s) of monetary or material Support: industry

Intervention

Keyword: atherosclerotic, lesions

Outcome measures

Primary outcome

The primary objective of this study is to understand novel genomic associations of CAD by using advanced cardiovascular imaging for CAD phenotyping and next-generation whole genome genotyping and sequencing.

Secondary outcome

A secondary objective of this study is to understand novel gene expression, metabolomic, lipidomic and proteomic associations of CAD by using advanced cardiovascular imaging and state-of-the-art biomarker approaches.

Study description

Background summary

Atherosclerosis is responsible for coronary artery disease (CAD) and cerebrovascular disease, the first and third leading causes of morbidity and mortality in both the United States and worldwide, as well as for peripheral arterial disease, which is the leading medical cause of limb loss. Atherosclerosis, as any other disease, is the result of very complex interactions between genetic susceptibility and the environment. Genetic information is encoded in the deoxyribonucleic acid (DNA) is fully inherited and changes minimally during one*s lifetime. While over 99.9% of the genetic code (DNA) is identical in all human beings, differences in the remaining 0.1% are responsible for individual traits as well as for disease activities; 80% of such these differences are so-called *single nucleotide polymorphisms*, or *SNP*s*. To date, approximately 4 million SNP*s have been identified. These genetic susceptibilities interact with environmental factors and result in the expression of genes in the blood and tissues in the form of ribonucleic acid (RNA). Gene expression (RNA) manifests itself as actual traits, or *phenotypes* (intermediate phenotypes), such as lipid and lipoprotein levels, inflammatory milieu, blood pressure, glycemic environment, etc., and these traits act in concert in the development of diseases (ultimate phenotype), such

as atherosclerosis, culminating in sudden cardiac death, heart attack, stroke and critical limb disease.

Study objective

The purpose of the GLOBAL study is to perform whole-genome genotyping, next-generation deep resequencing, gene expression profiling, metabolomics, lipidomics and proteomics of atherosclerosis in patients phenotyped using advanced CT-based imaging modalities of atherosclerosis. If successful, results of this study may help in developing diagnostic tests that will assist physicians in identifying individuals at greatest risk for significant CAD.

Study design

The GLOBAL study is an international multi-center, prospective study designed to enroll up to 10,000 consecutive eligible subjects who are clinically referred for coronary CT angiography for assessment of suspected coronary artery disease (CAD). Subjects will be enrolled at up to 50 clinical institutions globally.

Study burden and risks

The risks associated with the Study (for the blood draw) are related to blood draw risks as follows: The safety of phlebotomy has been well established. When blood is drawn from a vein, there may be temporary discomfort and a minimal risk for local bruising, infection, or blockage of the vein. Fainting occurs rarely. All phlebotomy in this study will be performed in accordance with standard hospital policy and suitable precautions will be taken to minimize all risks. There is a rare risk that the contents of the PAXgene tube (RNA stabilizing agent) could reflux into the vein. The GLOBAL Study Laboratory Manual contains instructions regarding drawing the PAXgene tubes after blood flow has been established with the other blood tubes and maintaining the PAXgene tube below the stick level and at an appropriate angle, for minimizing these risks.

There are no anticipated benefits in immediate care to subjects participating in this Study and no clinical management decisions are being made with information from the study. If successful, results of this study may benefit future patients through development of diagnostic tests that will assist physicians in identifying individuals at greatest risk for significant CAD.

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

1. Ages 18-90
2. White and of Non-Hispanic or Non-Latino origin
3. Referral for coronary CT angiography to evaluate for presence of CAD
4. The patient has signed the appropriate Institutional Review Board approved Informed Consent
Form

Exclusion criteria

General Exclusion Criteria
1. Immunosuppressive or immunomodulatory therapy including any dose of systemic corticosteroids
in the preceding 30 days (except if steroids are administered as pre-medication prior to contrast
administration for CT scan within 24 hours)

2. Chemotherapy in the preceding year
3. Major surgery in the preceding 2 months
4. Blood or blood product transfusion in the preceding 2 months
5. Subjects for whom coronary CT angiography is contraindicated per institutional standard of care
6. Subjects with previous coronary arterial revascularization (PCI or CABG)
7. Subjects with atrial fibrillation/flutter or frequent irregular or rapid heart rhythms, which occurred
within the past 3 months
8. Subjects with a pacemaker or implantable cardioverter-defibrillator implant
9. Active congestive heart failure or the presence of known non-ischemic cardiomyopathy
10. Known genetic disorders of atherosclerosis, lipid or lipoprotein metabolism

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-10-2013
Enrollment:	600
Type:	Actual

Ethics review

Approved WMO Date:	17-09-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-12-2013

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-12-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
ClinicalTrials.gov	NCT01738828
CCMO	NL44384.091.13