Genetics and genomics of hypertension associated with microinflammation, oxidative stress, chronic renal disease and heart failure.

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To investigate the genetic, genomic and proteomic basis of hypertension and susceptibility to hypertension-related target-organ damage (renal insufficiency and heart failure).

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Observational invasive

Summary

ID

NL-OMON33614

Source
ToetsingOnline

Brief title
InGenious HyperCare

Condition

- Heart failures
- Nephropathies
- Vascular hypertensive disorders

Synonym
essential hypertension, high blood pressure

Research involving
Human

Sponsors and support

Primary sponsor: Interne Geneeskunde
Source(s) of monetary or material Support: zesde kaderproject van de Europese Unie

Intervention

Keyword: Genetics, Hypertension, Proteomics, Target Organ Damage

Outcome measures

Primary outcome

To analyse genetic and genomic factors involved in the pathogenesis of hypertension.

To analyse genetic, genomic and proteomic factors involved in changes in microalbuminuria.

To analyse genetic, genomic and proteomic factors involved in changes in cardiac and large artery structure and function.

Secondary outcome

To analyse the proteomic factors involves in the pathogenesis of hypertension.

To explore the role of oxidative stress and microinflammation in the pathogenesis of hypertension.

To analyse genetic, genomic and proteomic factors associated with renal phenotypes in hypertensive subjects: elevated urinary albumin excretion (microalbuminuria, proteinuria) salt-sensitivity, reduced GFR, and end-stage renal disease.

To analyse genetic, genomic and proteomic factors associated with presence or development of heart dysfunction and failure in hypertensive patients.

Study description

Background summary

Hypertension and its cardiovascular consequences are a major cause of mortality and morbidity. The knowledge and experience in the mechanisms of blood pressure control, the development of hypertension and hypertension related organ damage is still very fragmented. The InGenious HyperCare network aims to integrate this knowledge and to build up comprehensive databases of common phenotypes, genotypes and proteomic data from hypertensive subjects. The current Joint Research Project (JRP A2-B2-B3) focuses on the so-called *mechanomics* of hypertension: genetic, genomic and proteomic markers of disturbances in the major mechanisms (inflammation and oxidative stress) involved in the development of hypertension and hypertension related organ damage (renal insufficiency and heart failure). Hypertension-related organ disease results from arterial and arteriolar damage. Important mediators of this damage are activation of the renin-angiotensin system, fibrosis, hypertrophy and inflammation. Inflammation is thought to be an important link between hypertension, endothelial dysfunction, oxidative stress and ultimately organ damage. Both hypertension and oxidative stress are known to cause endothelial dysfunction and an inflammatory cascade involving expression of endothelial adhesion molecules. These molecules facilitate leukocyte infiltration of the extracellular matrix, leading to altered cell-signalling, production of growth factors, production of matrix proteins and proliferation of vascular smooth muscle cells, all contributing to vascular damage. Genetic factors seem to play a prominent role in these mechanisms. This is supported by the fact that both hypertension in itself and hypertension related renal disease have a strong familial occurrence. Nevertheless, studies investigating the link between genetics and different cardiovascular phenotypes have not given univocal results. Therefore, the present study aims to investigate genetic, genomic and proteomic factors involved in inflammation and oxidative stress in hypertension and its related organ damage.

Study objective

To investigate the genetic, genomic and proteomic basis of hypertension and susceptibility to hypertension-related target-organ damage (renal insufficiency and heart failure).

Study design

The present study is a large, multicenter, observational family-study with follow-up moments after 2 and 4 years. Subjects and family-members will undergo extensive cardiovascular phenotyping involving a complete medical history, physical examination, measurement of the carotid Intima Media Thickness (cIMT),

Pulse-wave velocity, ECG, cardiac ultrasonography, ambulatory blood-pressure measurement (ABPM) and laboratory tests of blood and urine. Data is collected from over 30 research-centres in Europe and is integrated in a large central database.

Study burden and risks

Subjects will visit the research-laboratory for two hours on two consecutive days. During these visits the medical history, physical examination and the other investigations will be performed. Blood samples will be obtained by venipuncture. There is a risk of hematoma-development after venipuncture. In addition are subjects required to collect a morning-sample of urine on two days. The investigations will be repeated after two and four years.

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

- Men or women between 18 and 60 years of age at time of enrolment
- Essential hypertension diagnosed before the age of 50 years.
- At least 3 first-degree relatives of whom at least 1 should have hypertension and at least one from a different generation, willing to participate in the study.
- Written informed consent

Exclusion criteria

- Any known form of secondary hypertension,
- Any known previous clinical complications of hypertension (angina, myocardial infarction, stroke, TIA, peripheral artery disease) at any time
- known renal disease, including GFR < 60 mL/min/1.73 m2 as estimated by the abbreviated MDRD formula, or kidney stones
- Kidney or other organ transplantation
- Type 1 diabetes mellitus
- Heart failure stage D (AHA/ACC criteria)
- Any malignant concomitant diseases or history of malignant diseases within the last five years, with exception of treated squamous skin cancer or basalioma
- Clinical or laboratory signs of acute infection.
- Systemic inflammatory diseases,
- Steroids or any other immunosuppressive drug
- Severe known liver disease (ALT or gamma-GT above three-fold of upper normal limit)
- Current alcohol consume of more than 21 drinks/week or drug abuse
- Pregnancy

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-09-2009
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO Date:	20-02-2009
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-10-2009
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL26082.068.08