

Study of the genetic causes of disorders of the aorta, arteries and cardiac valves

Published: 18-03-2014

Last updated: 23-04-2024

To gain a better insight into the genetic factors that play a role in the etiology of the thoracic aortic aneurysm with the following specific aims: 1. Study of specific genetic factors that play a role in the pathogenesis of both syndromic and non-...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac disorders, signs and symptoms NEC
Study type	Observational non invasive

Summary

ID

NL-OMON39758

Source

ToetsingOnline

Brief title

Aorta

Condition

- Cardiac disorders, signs and symptoms NEC
- Cardiac and vascular disorders congenital
- Aneurysms and artery dissections

Synonym

aortic dilatation, heart valve malformation

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud

Source(s) of monetary or material Support: ERC grant Bart Loeys

Intervention

Keyword: Aortic aneurysm, Bicuspid aortic valve, Genetics, Marfan syndrome

Outcome measures

Primary outcome

Identification of the genetic factors underlying thoracic aortic aneurysms or modify the phenotypic severity.

Secondary outcome

nvt

Study description

Background summary

Within the thoracic aortic aneurysms and dissection, two main groups can be distinguished: syndromic and non-syndromic forms. Within the syndromic group, such as Marfan syndrome, Ehlers-Danlos syndrome and Loeys-Dietz syndrome, very often other connective tissue symptoms and signs (affecting eyes, skin, joints, internal organs,*) are present. For this syndromic group, the genetic basis of most disorders is known but very little is known about the genetic factors that modify the phenotypical severity. Within the non-syndromic group about 20% of the patients have a positive family history indicating a strong genetic predisposition. Some of the genes underlying non-syndromic thoracic aortic aneurysm and dissection have been identified but for the majority the genetic cause is unknown. An important group within the non-syndromic forms, are the thoracic aneurysms associated with bicuspid aortic valve. Bicuspid aortic valves are the most common congenital heart defect in humans with a prevalence of 1-2% of the population. The genetic basis of bicuspid related thoracic aortic aneurysm is unknown.

Study objective

To gain a better insight into the genetic factors that play a role in the etiology of the thoracic aortic aneurysm with the following specific aims:

1. Study of specific genetic factors that play a role in the pathogenesis of both syndromic and non-syndromic aortic aneurysms.
2. Identify the role of modifiers of the phenotypical variation in genetic forms of aortic aneurysm, eg Marfan syndrome.

3. Unravel the genetic basis van bicuspid aortic valve related aneurysms.

Study design

Gathering and genetic analysis of DNA from blood sampling of patients with thoracic aortic aneurysm and/or valve defects. In rare case, investigations will also happen via skin biopsies (fibroblast culture) or via restmaterial obtained from cardiovascular surgery (heart valve, aortic wall)

Study burden and risks

Blood test: causes a short pain when the needle penetrates the skin. Prolonged bleeding can occur at the place of puncture. A blue discoloration of the skin can appear. This disappears within a fortnight. There is a limited risk of fainting or infection.

Skin biopsy: A biopsy of the skin of maximum 5mm is taken from a non-visible place (mostly at the inner upper arm). This is done under local anaesthesia. The skin defect will be stitched or sometimes closed with Steristrips. The injection of the local anaesthetic can briefly cause pain. There is a small risk of bleeding or infection afterwards. The wound normally heals within a fortnight. Occasionally, a small round scar remains visible.

Aortic/valve biopsy: For these procedures only material that normally would be destroyed will be used.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adolescents (12-15 years)

Adolescents (16-17 years)

Adults (18-64 years)

Children (2-11 years)

Elderly (65 years and older)

Inclusion criteria

Inclusion criteria

1. Patients and familymembers with thoracic aortic aneurysm and dissection
2. Patients and familymembers with Marfan syndrome and related conditions
3. Patients and familymembers with bicuspid aortic valve, specifically if associated with aortic aneurysm or history of sudden death or aortic dissection
4. Patients and family members with arterial aneurysms and/or valve abnormalities

No restriction for age or sex.

Exclusion criteria

None

Study design

Design

Study type:	Observational non 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): 01-06-2014
Enrollment: 500
Type: Actual

Ethics review

Approved WMO
Date: 18-03-2014
Application type: First submission
Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO
Date: 26-06-2014
Application type: Amendment
Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO
Date: 01-11-2016
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

CCMO

ID

NL42357.091.13