Assess the total set of mechanical loads and mechanical properties of vessel wall and plaque constituents involved in plaque rupture

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The possibility to identify the risk of rupture of a carotid plaque will have tremendous impact in clinical decision making. Selection of candidates from surgery is based mainly on duplex ultrasonography, where now only the size of the stenosis is...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Observational invasive

Summary

ID

NL-OMON39249

Source
ToetsingOnline

Brief title
Assessment of mechanical properties of the carotid atherosclerotic plaque

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
atherosclerose, vessel occlusion

Research involving
Human

Sponsors and support

Primary sponsor: Technische Universiteit Eindhoven

Source(s) of monetary or material Support: CTMM;Fp7

Intervention

Keyword: atherosclerosis, carotid, mechanical properties, ultrasound

Outcome measures

Primary outcome

Investigation of the mechanical properties of the plaque and underlying vessel

wall ex vivo.

Determination of the plaque geometry.

Determination of the deformation of the plaque.

Secondary outcome

Correlation of 3D ultrasound in vivo with ex vivo ultrasound and histology.

Study description

Background summary

Cardiovascular disease (CVD) is the leading cause of death of the aging population worldwide. Annually 17,5 million people decease because of CVD. CVD is the term used for high blood pressure, coronary heart disease, heart failure, stroke and congenital heart diseases. CVD affects all socio-economic classes and both men and women. The number of deaths due to CVD is expected to rise in the coming years, notably as more and more children are threatened by the combined impacts of tobacco, alcohol, obesity and physical inactivity (World heart federation, 2007). In Europe CVD causes over 1 million deaths each year, which is nearly half of all deaths in Europe (48%).

Atherosclerosis is a vascular disease, where the arterial wall thickens as the result of a build up of fatty material, such as cholesterol. The fatty deposits are called plaques, and if they become too big, the flow of blood is restricted. A vulnerable plaque is considered to have a large necrotic core, a thin fibrous cap, the presence of inflammatory cells, intraplaque hemorrhage and/or neovascularisation (vaso vasorum). It is hypothesized that, when the stress in the fibrous cap exceeds the strength of the cap, rupture of the cap can occur (thus likely in vulnerable plaques). If rupture occurs a thrombus

will be formed which for example can travel to the brain and cause a stroke.

Study objective

The possibility to identify the risk of rupture of a carotid plaque will have tremendous impact in clinical decision making. Selection of candidates from surgery is based mainly on duplex ultrasonography, where now only the size of the stenosis is considered. Symptomatic patients with a 30-69% stenosis, are currently not operated upon according to the guidelines. Identification of the risk of plaque rupture could identify patients who have a high risk of recurrent stroke, and would therefore benefit of carotid intervention, such as endarterectomy or stent placement. This could potentially prevent a substantial number of strokes. Furthermore, in all symptomatic patients with a 70-99% stenosis carotid intervention should be considered, according to the guidelines. However, only one out of six patients with a 70-99% stenosis benefits from a carotid intervention . Summarizing, the size of stenosis alone is not a reliable predictor for plaque rupture. Plaque composition and activity are thought to be useful predictors of future thromboembolic events as well.

A vulnerable plaque is considered to have a large necrotic core, a thin fibrous cap, the presence of inflammatory cells, intraplaque hemorrhage and/or neovascularisation (vasa vasorum). The micro vascular networks are thought to play a central role in the early process of plaque progression and vulnerability. Another important hypothesis is that, when the stress in the fibrous cap exceeds the strength of the cap, rupture of the cap will occur. Therefore, identification of patients at high risk of stroke (i.e. with unstable/vulnerable plaques) in an early stage would permit timely intervention while substantially reducing unnecessary overtreatment of stable plaques.

Study design

In order to identify those patients, new methods for plaque rupture prediction are explored. These new methods use finite element analysis (FEA) of imaged intact plaques to calculate wall stresses and relate these results with prediction of rupture in patient-specific geometries. These models seem to better estimate the risk of rupture than stenosis size alone. Wall stress and strain calculations with FEA incorporate blood pressure data, stenosis geometry, wall and plaque composition and thickness.

In this study pre-operative 3D ultrasound will be performed to obtain patient-specific geometry and deformation. During endarterectomy the plaque will be dissected very carefully, to obtain an intact plaque (tube like structure) in order to apply sufficient loads in the ex-vivo experimental set up. By making use of ultrasound, a pressure radius relation can be obtained from this experiment, moreover the wall strains can be determined with dedicated software. After the loading experiment the plaque will be tested

locally by indentation experiments, to determine the material stiffness of the different plaque components. Finally histology will be performed to determine the exact components. Data from all these experiments will be used as input for the plaque rupture prediction model.

The main goal of this study is to assess the total set of mechanical loads and mechanical properties of the vessel wall and plaque constituents involved in plaque rupture.

Study burden and risks

nvt

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

age > 60, symptomatic and asymptomatic patient are both necessary for this research, Candidate for endarterectomy of carotid artery, > 70% stenosis

Exclusion criteria

Unable to give written informed consent
Obstructed carotid arteries
Assymetric EEG

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-06-2012
Enrollment:	104
Type:	Actual

Ethics review

Approved WMO

Date:	19-10-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	29-11-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	NL33040.060.10