The assessment of the Plaque At RISK by non-invasive (molecular) imaging and modelling (ParisK): Prospective clinical study for diagnosis efficacy for high risk plaque and stroke.

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The main objective is to show whether imaging characteristics assessed at baseline can predict clinical events in patients with a 30-69 % symptomatic carotid stenosis.

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

Summary

ID

NL-OMON43700

Source
ToetsingOnline

Brief title
ParisK

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
atherosclerotische plaques, hardening of the arteries

Research involving
Human

Sponsors and support

Primary sponsor: Radiologie
Source(s) of monetary or material Support: CTMM (Center for Translational Molecular Medicine),Esaote Europe,Philips,Pie Medical Imaging,VisualSonics BV

Intervention

Keyword: atherosclerosis, imaging, plaque, stroke

Outcome measures

Primary outcome

The primary study endpoint is recurrent ischemic stroke, or TIA and/or new ipsilateral brain lesions on follow-up brain MRI. For the primary analysis we will assess the following parameters: 1) presence of IPH as assessed on ipsilateral MRI of carotid plaque, 2) ipsilateral carotid plaque ulceration as assessed on MDCTA, 3) ipsilateral carotid plaque volume as assessed on MRI, and 4) the proportion of calcifications with respect to the ipsilateral carotid plaque volume as assessed with MDCT.

Secondary outcome

Secundary endpoints:

- Plaque progression or regression assessed by repeated imaging.
- Detection of (new) subclinical vascular brain damage by MRI
- Emboli detection assessed by TCD.
- In case patients with recurrent events will undergo carotid intervention before the two year follow-up, repeat imaging using MRI, MDCT, US and TCD will be done in those patients before carotid endarterectomy.

Study description

Background summary

The possibility of the identification of the risk of rupture of a carotid plaque will have tremendous impact in clinical decision making. Firstly, in symptomatic patients with a 30-69% stenosis, who are currently not operated upon according to the current guidelines, identification of the risk of rupture plaque 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. Secondly, 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. Identification of patients with a high risk of a recurrent stroke would reduce the number of unnecessary interventions substantially (Rothwell et al. 1999). Hence, a diagnostic imaging test with high accuracy for recurrent stroke prediction has tremendous clinical impact in patients with carotid artery disease.
Previous studies have evaluated the use of imaging to assess carotid plaque vulnerability, mostly showing a good correlation between imaging and histology and/or clinical characteristics. Plaque vulnerability is defined by a large necrotic core, a thin fibrous cap, the presence of inflammatory cells, intraplaque hemorrhage and/or neovascularisation (vasa vasorum). However, previous studies have focused on single modalities (magnetic resonance imaging [MRI], multidetector-row computed tomography [MDCT], ultrasonography [US], or transcranial Doppler [TCD]), and have used relatively small cohorts (Altaf et al. 2008, Takaya et al. 2006, Wintermark et al. 2008, Li et al. 2008, Underhill et al. 2008, Cappendijk et al. 2005, Fayad et al. 2004, Yuan et al. 2002, Henneman et al. 2008, Markus et al. 2005), This could be the reason why carotid artery imaging studies so far have not changed the therapeutic guidelines. In addition, the imaging modalities so far may not have delivered the necessary sensitivity to achieve the goal of changing the guidelines. Therefore, a clinical trial will be performed in symptomatic patients with a 30-69% stenosis (n=244) who are not scheduled for carotid intervention. Participating patients will undergo baseline imaging, which includes 3T MRI of the carotid atherosclerotic plaque and brain, MDCT and US of the plaque, and TCD registration for emboli detection in the middle cerebral artery (which is a measure of plaque thrombogenicity). At baseline, a blood sample will also be taken to assess the presence of certain biomarkers, which may provide additional information on plaque vulnerability (Lobbes et al. 2006). Patients will be followed-up yearly until the end of the study. After two years all imaging modalities will be repeated for the first 150 patients. For the remaining patients, brain MRI will be repeated.

Study objective

The main objective is to show whether imaging characteristics assessed at baseline can predict clinical events in patients with a 30-69 % symptomatic carotid stenosis.

Study design

Prospective study.

Study burden and risks

Participating patients will undergo an MRI, MDCT, US and TCD examination. In addition, a blood sample will be taken for detection of biomarkers.

Burden:
-During the MRI examination, one is laying in the supine position for approximately 10 minutes and subsequently for another 45 minutes. This does not have to be a problem, but it can be difficult for patients with back problems. The MRI scanner produces a lot of noise during the examination, which can be unpleasant for the patient. Therefore, participating patients will use a protecting head set or ear plugs. During the MRI examination, a contrast agent will be intravenously administered. During injection, patients may experience a cold feeling in their arm. The MRI scanner is a kind of tube, with openings in the front and back. Still, some patients may feel uncomfortable when laying in the tube.
-During the CT examination, one is laying in the supine position for approximately 10 minutes. This does not have to be a problem, but it can be difficult for patients with back problems. During the CT examination, a contrast agent will be intravenously administered, and patients can experience a warm feeling. The CT scanner is a kind of tube, with openings in the front and back. Still, some patients may feel uncomfortable when laying in the tube.
-During the US examination, one is laying in the supine position on a bed for approximately 10 minutes. Most patients experience the US examination as comfortable. The TCD examination will take four hours. The TCD examination is harmless. However, the mobile TCD device may cause some discomfort after a while.
-For biomarker detection, a blood sample (30 ml) will be taken from a vein in the arm.

Risks:
-MRI does not using ionizing radiation. However, patients with pacemakers, metal implants, vessel clips, or metal splinters in the eye will be excluded from this study. The side effects of the MRI contrast agent (Gadobutrol) are rare and are amongst others nausea (0.25%), vomiting (0.05%), urticaria (0.04%), feeling of warmth, tachycardia, wheals (for each 0.03%), dizziness,

itching, vasodilatation, itchy throat (for each 0.02%) and cough, dyspnoea, flushing, hives, generalized itching, oral dryness, facial redness, sensation of heat, skin disorder and aggravated nausea (for each, (0.01%). In severe cases, an allergic reaction and shock could occur. In most cases side effects occur immediately after contrast injection, and therefore patients will remain in the hospital for 30 minutes after injection. The administration of the contrast agent is relatively safe and side effects are rare. At the place of injection of the contrast agent, (temporary) bruising or swelling may occur, and the place may be sensitive. In rare cases, an infection could occur at this place.
-An MDCT examination is not harmful for one*s health. However, MDCT uses ionizing radiation: The radiation dose of an MDCT examination is approximately 2.2 mSv. The radiation dose for the perfusion CT is approximately 7.2 mSv. The CT contrast agents (iodixanol and iopromide) are associated with a low rate of side effects. The most reported side effects are feeling of warmth (1.3 %) and nausea (0.3%). In severe cases, contrast-induced nefropathy could occur. However, the use of the CT contrast agents are relatively safe and adverse effects rarely occur. At the place of injection of the contrast agent, (temporary) bruising or swelling may occur, and the place may be sensitive. In rare cases, an infection could occur at this place.
-The US and TCD examinations are harmless (no associated health risks).
-Blood sampling is not dangerous and will be performed by an experienced nurse or medical doctor. At the place of blood sampling, (temporary) bruising or swelling may occur, and the place may be sensitive.

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

-Patients with neurological symptoms due to ischemia in the carotid artery territory and with a carotid stenosis between 30% and 69% according to ECST criteria will be included (n<=244).
-Asymptomatic patients with a carotid stenosis between 30 and 69% according to ECST criteria will be included in the MUMC (n<=20) to study reproducibility 3T MRI.
-Healthy volunteers recruited in the MUMC (n<=15) to optimalize the 3T MRI protocol.

Exclusion criteria

- Patients with a probable cardiac source of embolism (rhythm disorders, mitral valve stenosis, prolapse or calcification, mechanical cardiac valves, recent myocardial infarction, left ventricular thrombus, atrial myxoma, endocarditis, dilated cardiomyopathy, patent foramen ovale) or a clotting disorder.
- Patients with evident other cause of neurological symptoms than carotid stenosis due to atherosclerotic disease (like demyelinating diseases, epilepsy, congenital brain disorders, aneurysms, fibromuscular dysplasia, etc.).
- Patients already scheduled for carotid endarterectomy or stenting
- Severe co-morbidity, dementia, or pregnancy.
- Standard contra-indications for MRI (ferromagnetic implants like pacemakers or other electronic implants, metallic eye fragments, vascular clips, claustrophobia etc).
- Patients who have a documented allergy to contrast media are not eligible to undergo contrast-enhanced MRI or contrast-enhanced CT.
- Patients with a renal clearance <30 ml/minute are not eligible to undergo contrast-enhanced MRI. Patients with a renal clearance of <60 ml/minute are not eligible to undergo contrast-enhanced CT.
- Patients who had a TIA or minor stroke more than 3 months before inclusion

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):	20-05-2010
Enrollment:	244
Type:	Actual

Ethics review

Approved WMO Date:	07-12-2009
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-03-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	07-05-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	02-07-2010
Application type:	Amendment

Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	19-08-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	07-02-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	19-12-2011
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	20-12-2011
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	25-07-2013
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	19-05-2014
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	03-02-2015
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC 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	NL29116.068.09