The assessment of the Plaque at RISK by non-invasive (molecular) imaging and modelling (ParisK): Validation of imaging techniques with histology

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Primary- MRI: correlation between neovascularisation in carotid atherosclerotic plaque characteristics assessed by dynamic 3.0 Tesla MRI and carotid atherosclerotic plaque at histology. - CT: correlation between size of lipid-rich-necrotic-core in…

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

Summary

ID

NL-OMON39382

Source
ToetsingOnline

Brief title
ParisK

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
atherosclerotic plaque, hardening of the arteries

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht

Source(s) of monetary or material Support: CTMM,Esaote Europe,Philips,Pie Medical Imaging,VisualSonics BV

Intervention

Keyword: atherosclerosis, imaging, plaque

Outcome measures

Primary outcome

- MRI: correlation between neovascularisation in carotid atherosclerotic plaque characteristics assessed by dynamic 3.0 Tesla MRI and carotid atherosclerotic plaque at histology.

- CT: correlation between size of lipid-rich-necrotic-core in dual-energy CT and histology.

Secondary outcome

- MRI: correlation between volume of LRNC, fibrous cap status, and volume of calcifications in carotid atherosclerotic plaques visualised by MRI and carotid atherosclerotic plaques at histology.

- Ultrasound: correlation between deformation pattern and plaque composition and volume of LRNC at histology.

- TCD: relation between number of recorded MES and fibrous cap status.

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. Hence, a diagnostic imaging test with high accuracy for recurrent stroke prediction has tremendous clinical impact in patients with carotid artery disease.
A vulnerable plaque is considered to have a large necrotic core, a thin fibrous cap, the presence of inflammatory cells, intraplaque haemorrhage and/or neovascularisation (vasa vasorum).
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. However, they have focused on single modalities (magnetic resonance imaging [MRI], mutidetector-row computed tomography [MDCT], ultrasonography [US] or transcranial Doppler [TCD]), and have used relatively small cohorts. So far, only 2 studies investigated the validation of 3.0 Tesla MRI in detection of the characteristics of the vulnerable plaque. One of these studies is a clinical case report with one single patient. The other study compared 1.5 Tesla MRI with 3.0 Tesla MRI but didn*t compare the results with histology.
Regarding, transcranial Doppler, several studies have been performed using microembolic signals (MES) as a marker of embolic activity and the relation with different clinical endpoints (stroke, TIA, functioning after surgery). Mackinnon investigated the relevance of prolonged measurements in symptomatic and asymptomatic patients. He showed that is worth detecting embolies during more than one hour.
Given the studies mentioned above, we will perform a validation study in symptomatic patients with carotidstenosis (n=50), who are scheduled for carotid endarterectomy (CEA). Participating patients will undergo a 3.0 Tesla MRI of the carotid atherosclerotic plaque, dual energy CT, ultrasound and TCD registration for emboli detection in the middle cerebral artery during 4 hours at least one day prior to the surgery. During surgery, the carotid endarterectomy specimen will be collected and supervised by members of the pathology research laboratory. The data obtained from the imaging will be compared with the histological findings; especially focussing on the characteristics of the vulnerable plaque.

Study objective

Primary
- MRI: correlation between neovascularisation in carotid atherosclerotic plaque characteristics assessed by dynamic 3.0 Tesla MRI and carotid atherosclerotic plaque at histology.
- CT: correlation between size of lipid-rich-necrotic-core in dual-energy CT and histology and between neovascularisation in carotid atherosclerotic plaque

characteristics assessed by perfusion CT and carotid atherosclerotic plaque at histology.
Secondary
- MRI: correlation between volume of LRNC, fibrous cap status, and volume of calcifications in carotid atherosclerotic plaques visualised by MRI and carotid atherosclerotic plaques at histology.
- Ultrasound: correlation between deformation pattern and plaque composition and volume of LRNC at histology.
- TCD: relation between number of recorded MES and fibrous cap status.

Study design

Validation study

Study burden and risks

The side effects of the MRI contrast agent (Gadovist) are rare amongst others nauseau (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%). Out of 14 299 patients, two serious ADRs occurred (0.01%), which were considered by the treating physician to be probable associated with the administration of Gadovist; one patient had a severe anaphylactoid reaction and the other presented with itching and swelling in the throat. 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 agents is relatively safe and side effects are rare. To minimize the risk of contrast-induced nefropathy, patients with a renal clearance of less than 30 mL/min/1.73 m2 will not receive the MR contrast agent.
The radiation dose of an MDCT examination is approximately 9.4 mSv. The CT contrast agent (Ultravist 300) is associated with a low rate of side effects. The most reported side effects are heat sensation (1.14%) and nausea (0.52%). To minimize the risk of contrast-induced nefropathy, patients with a renal clearance of less than 60 mL/min/1.73 m2 will not undergo the MDCT scan.

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 a carotid artery stenosis, who are scheduled for carotid endarterectomy
- age 18 years or older (no maximum age)
- informed consent by signing informed consent form regarding this study
- inclusion criteria carotid endarterectomy:
* symptomatic carotid artery stenosis 70-99% within 3 months of neurologic symptoms
* symptomatic carotid artery stenosis 50-99% in man within 2 weeks of neurologic symptoms
* asymptomatic carotid artery stenosis 70-99% with contralateral occlusion

Exclusion criteria

* 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 MRI or CT contrast media
* Patients with a renal clearance <30 ml/min are not eligible to undergo contrast-enhanced MRI
* Patients with a renal clearance <60 ml/min are not eligible to undergo dual-energy CT

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):	23-08-2011
Enrollment:	71
Type:	Actual

Ethics review

Approved WMO Date:	06-12-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-08-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	07-10-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-10-2013
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	NL32741.068.10