# Prevalence of vulnerable plaque in type 2 Diabetes Mellitus and its predictive value for future ischemic strokes

Published: 25-11-2015
Last updated: 13-04-2024

Primary:2. To investigate the prevalence of vulnerable plaques, i.e. plaques with intraplaque hemorrhage on MRI, in individuals with type 2 diabetes, impaired and normal glucose tolerance and a minimal plaque thickness of 2mm on ultrasonography. To...

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Will not start |
| **Health condition type** | Cardiac disorders, signs and symptoms NEC |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON41735

**Source**
ToetsingOnline

**Brief title**
Type 2 Diabetes Mellitus Plaque Study

### Condition

- Cardiac disorders, signs and symptoms NEC
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

**Synonym**
atherosclerosis, diabetes

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** Europees Fonds voor Regionale

Ontwikkeling;Stichting de Weijerhorst;CARIM;NUTRIM;Stichting Annadal

## Intervention

**Keyword:** Atherosclerosis, Carotid artery, Diabetes Mellitus Type 2, MR imaging

## Outcome measures

### Primary outcome

Presence of a vulnerable carotid plaque with intraplaque haemorrhage on MRI (on the left and/or right-hand side) in asymptomatic individuals with type 2 diabetes, impaired and normal glucose tolerance and a 2 mm plaque as identified by an ultrasound examination.

Number of new ischemic stroke events after 10 years of follow-up.

### Secondary outcome

Presence of brain infarct(s) on brain MRI.

Number of cardiovascular events after 10 years of follow-up

Subject characteristics (age, gender, cardiovascular risk factors, previous cardiovascular symptoms)

Glucose tolerance tests

# Study description

### Background summary

More than 240 000 people have suffered from a stroke in the Netherlands. One third of the strokes causes sudden death and another third of the patients remains permanently disabled. A stroke frequently occurs unannounced, e.g. without any previous neurological symptoms. The presence of a carotid plaque accounts for 15-20% of ischemic strokes. A large multi-centre randomised surgery trial has shown that asymptomatic individuals younger than 75 years of age with 60-90% carotid stenosis benefit from carotid endarterectomy, although the benefit of surgery is only marginal. Therefore, in the Netherlands, these

individuals are generally not operated on. However, still 13.4% of these individualswill suffer from a stroke within 10 years. Therefore, it would be highly beneficial if there would be better measures to identify indviduals with increased stroke risk, beyond the degree of stenosis. It is well known that rupture of a vulnerable plaque is an important underlying cause of stroke. Recently, it was demonstrated in several studies that MRI is able to identify carotid plaque vulnerability, and that intraplaque haemorrhage as detected with MRI can predict a stroke. In parallel, it is also well known that type 2 Diabetes Mellitus is a strong risk factor for stroke. However, little is known about the prevalence of vulnerable plaques in individuals with type 2 Diabetes Mellitus, impaired glucose or normal glucose tolerance, its relation with (silent) brain infarcts, and its associated risk for future stroke.

## Study objective

Primary:
2. To investigate the prevalence of vulnerable plaques, i.e. plaques with intraplaque hemorrhage on MRI, in individuals with type 2 diabetes, impaired and normal glucose tolerance and a minimal plaque thickness of 2mm on ultrasonography. To determine the predictive value of intraplaque hemorrhage for future ischemic stroke in individuals with and without type 2 diabetes mellitus.
Secondary:
2e. To determine the predictive value of plaque features, i.e. intraplaque hemorrhage, plaque volume, normalized wall index and volume of calcifications as identified with carotid MRI for future cardiovascular disease.
2f. To relate the presence of intraplaque hemorrhage and other plaque features, i.e. plaque volume, normalized wall index and volume of calcifications with the presence of (silent) brain infarcts on brain MRI in type 2 diabetes, impaired and normal glucose tolerance.
2g. To compare plaque features of plaques, i.e. intraplaque hemorrhage, plaque volume, normalized wall index and volume of calcificationsfrom asymptomatic individuals with plaques from symptomatic patients (on the symptomatic and asymptomatic side). Note that symptomatic patients are currently being enrolled in another ongoing study within the azM (the PARISk study; METC 09-2-082 14).
2h. To study the inter-scanner reproducibility of the 3.0 Tesla MRI protocol in a small subgroup.

## Study design

The present study is a prospective cohort MRI study on 1680 individuals with type 2 diabetes, impaired glucose tolerance or normal glucose tolerance. Participants will be recruited from DMS and followed for an average duration of 10 years, to determine the predictive value of carotid plaque features for ischemic stroke and cardiovascular disease (objective 1 and 2a). Ischemic strokes due to carotid stenosis is defined as an ischemic stroke and a

significant (>50%) stenosis or occlusion at the carotid territory and no cardiac source of emboli. Cardiovascular disease is defined as the total of coronary heart disease, heart failure and stroke.
Recruitment
Subjects will be approached by an investigator after the carotid ultrasound scan as assessed by DMS. The plaque in the carotid artery should have a wall thickness of at least 2 mm determined from the ultrasound scan performed by DMS. The minimal wall thickness of 2 mm was chosen based on the following considerations:
* it is expected that the majority (95%) of individuals that will experience an ischemic stroke, due to carotid stenosis, during ten years of follow-up, have a wall thickness of >2mm at baseline
* a carotid wall of 2 mm is of sufficient thickness taking into account the resolution of the MRI scans, and
* as atherosclerosis is a progressive disease it is expected that the carotid plaque is at least of similar size (* 2mm) than during the ultrasound scan by DMS.

MRI protocol
All subjects will undergo the MR imaging on a 3.0 Tesla unit. First, the carotid bifurcation will be identified by means of MR angiography without contrast material enhancement. Subsequently, transverse images will be obtained from about 7 mm caudal to 2 cm cranial of the carotid bifurcation, so that the complete plaque will be imaged for all individuals. Multisequence MR imaging will be performed to assess carotid plaque features, including intraplaque hemorrhage, plaque volume, normalized wall index and volume of calcifications, no contrast agent will be injected. Total scan duration is approximately 40 minutes.

Future ischemic stroke and cardiovascular disease
DMS*s annual follow-up comprises of an annual follow-up questionnaire, linking of participant data to hospital and pharmacy records and collection of mortality data through existing up-to-date databases from Statistics Netherlands (CBS). With the participant*s written permission (according to DMS informed consent), we will use these data to classify the outcome measure: ischemic stroke (objective 1) and cardiovascular disease (objective 2a).

Secondary Objectives
A cross-sectional approach will be used for objectives 2b and 2c.
On a subset of the participants, brain MRIs are performed by DMS. The brain MRIs will be used to identify participants with (silent) brain infarct (objective 2b).
For objective 2c, asymptomatic participants of the Type 2 Diabetes Mellitus Plaque Study will be compared with symptomatic patients that are currently being enrolled in an ongoing study within the azM (the PARISk study; METC 09-2-082 14).
Participants of the Type 2 Diabetes Mellitus Plaque Study are scanned on the

Siemens 3T MRI system, while in the ongoing PARISk study the scans are performed on the Philips 3T MRI system. To analyze differences in characteristics of asymptomatic and symptomatic plaques, it is important to know the inter-scanner reproducibility (objective 2d). Therefore, twenty participants will be selected for an additional scan on the Philips MRI system within 7 days before or after the Siemens MRI scan. The scan time for the second scan will be approximately 40min.

**Study burden and risks**

not applicable

## Contacts

**Public**
Academisch Medisch Centrum

P. Debyelaan 25
Maastricht 6229 HX
NL
**Scientific**
Academisch Medisch Centrum

P. Debyelaan 25
Maastricht 6229 HX
NL

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

### Inclusion criteria

* Subjects enrolled in "de maastricht studie"
* Subjects who have atherosclerotic plaques * 2mm, demonstrated in the carotid artery during vascular ultrasound in "de maastricht studie".

### Exclusion criteria

* Pregnancy.
* Standard contra-indications for MRI (ferromagnetic implants like pacemakers or other electronic implants, metallic eye fragments, vascular clips, claustrophobia, etc).

## Study design

### Design

**Study type:** Observational invasive

| | |
|---|---|
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Basic science |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Will not start |
| Enrollment: | 1680 |
| Type: | Anticipated |

## Ethics review

Approved WMO

| | |
|---|---|
| Date: | 25-11-2015 |
| Application type: | First submission |
| 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 | NL51869.068.15 |