AtheroGenic LipoprothEinS in Ischemic Stroke: The AGELESS Study

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

Summary

ID

NL-OMON55996

Source
ToetsingOnline

Brief title
AGELESS

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
carotid narrowing, Carotid stenosis

Research involving
Human

Sponsors and support

Primary sponsor: Universitätsspital Basel
Source(s) of monetary or material Support: Funding: Schweizerischer Nationalfonds (32003B_200573 / 1)

Intervention

Keyword: Carotid, Intraplaque Hemorrhage, Lipoproteins, Stroke

Outcome measures

Primary outcome

For the first aim, the endpoint is presence of carotid IPH on MR-Plaque imaging at baseline. Baseline means either acquired during the hospitalization for the index stroke or during the enrolling visit at the outpatient consultation of the neurovascular clinic.

Secondary outcome

For the second aim, the endpoint is an ischemic, hemispheric, ipsilateral stroke, i.e. on the same side of the carotid stenosis, on baseline brain MR-DWI. For the third aim, the endpoint is a recurrent ischemic, hemispheric, ipsilateral stroke in the 3-month follow-up brain MR-DWI or at any time during the follow-up. The 3-month follow-up brain MR-DWI is conceived to detect covert strokes, i.e. clinically asymptomatic strokes, as recurrences tend to occur short after the first stroke.

Study description

Background summary

Atherogenic lipoproteins, also called ApoB lipoproteins, circulate in the blood and can be trapped into the arterial wall, where they initiate and drive atherosclerosis. All atherogenic lipoproteins are coated by apolipoprotein (apo) B. ApoB lipoproteins include: (1) the cholesterol-rich low-density lipoprotein (*bad cholesterol*), (2) lipoprotein(a) (Lp(a)) and (3) the triglyceride-rich very-low density lipoprotein.1 There are pharmacological treatments to lower ApoB blood levels. Statins lower apoB levels by lowering low-density lipoprotein cholesterol (LDL-C) and reduce the risk of ischemic

stroke caused by atherosclerosis.2 However, even among patients achieving very low LDL-C blood levels, there is a relevant residual risk of stroke. Factors who can contribute to the residual risk include: (1) atherogenic Lp(a) - whose blood levels are genetically determined and are increased by statins3 - and (2) a hemorrhage within the carotid atherosclerotic plaque - a marker of plaque vulnerability - as seen on Magnetic Resonance (MR) Plaque Imaging4. Recently, we completed a prospective cohort study with 1759 participants showing that increased Lp(a) levels were associated with an increased risk of ischemic stroke linked to carotid atherosclerosis independent of LDL-C (manuscript submitted). In a separate cohort study, carotid intraplaque hemorrhage was associated with an increased risk of ischemic stroke.4 However, so far, no study assessed - within the same cohort of patients - the link between apoB, Lp(a) and carotid intraplaque hemorrhage with ischemic stroke. Important questions remain yet unanswered, for instance - are patients suffering no ischemic stroke despite carotid intraplaque hemorrhage protected by low apoB and Lp(a) levels? Do patients who suffer ischemic stroke despite low apoB and Lp(a) levels have more frequently carotid intraplaque hemorrhage?

Study objective

AGELESS has 3 specific aims - they all refer to patients with carotid atherosclerosis:
1. To compare patients with and without carotid intraplaque hemorrhage, as assessed with MR-Plaque Imaging, in terms of apoB, Lp(a) levels and traditional cardiovascular risk factors.
2. To assess the risk of first-ever ischemic stroke in relation to apoB, Lp(a) levels, and presence of intraplaque hemorrhage, after adjusting for traditional cardiovascular factors.

3. To assess the risk of recurrent ischemic stroke in relation to apoB, Lp(a) levels, and presence of intraplaque hemorrhage, after adjusting for traditional cardiovascular factors.

Study design

A multicenter cohort study over four years - the AGELESS study.

Study burden and risks

The potential benefit of the enrolled patients is small except that these patients will be monitored more closely than usual by MRI scans that will be clinically evaluated for insidious pathology. Risks are smell since there are no known risks associated with MRI acquisition.

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 > 18 years
- Atherosclerotic carotid stenosis NASCET 30 - 99%
- Ability to undergo a neck MR for carotid plaque imaging
- Ability to undergo a follow-up of at least 1 year
- For the prospective, longitudinal part: hemispheric ischemic stroke or retinal ischemia ipsilateral to the carotid stenosis, with symptom onset within 24 hours.
- Written informed consent

Exclusion criteria

- Carotid stenosis due to causes other than atherosclerosis (e.g. carotid dissection)
- Contraindication to MRI
- Lack of informed consent by patient or legal representative

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-01-2024
Enrollment:	25
Type:	Actual

Ethics review

Approved WMO Date:	12-09-2023
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	14-09-2023
Application type:	First submission
Review commission:	METC NedMec

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	NL84508.041.23