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Investigating the contents of atherosclerotic plaques using novel imaging techniques including PET/MRI

Submission date	Recruitment status	[_] Prospectively registered
04/01/2021	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
05/01/2021	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
11/08/2021	Circulatory System	

Plain English summary of protocol

Background and study aims
Atherosclerosis is the deadliest disease worldwide. It is caused by the buildup of fats, cholesterol and other substances in and on the artery walls (plaque), which can restrict blood flow. Most deaths are caused by the rupture (bursting) of plaques, leading to arterial thrombosis (blood clot) and occlusion (blockage), resulting in a heart attack or stroke. Early detection of rupture-prone plaques would provide opportunities for treatment before fatal or disabling cardiovascular events. Previous research has shown that factors strongly associated with plaque rupture are inflammation and elevated contents of fat (the lipid core) and blood (hemorrhage within the plaque). Therefore, these plaque characteristics are associated with a high risk of cardiovascular events.
Researchers have developed a new and validated MRI technique for measuring fat and blood within plaques. In this study, for the first time, the aim is to measure not only fat and blood, but also plaque inflammation. The study of correlations between these high-risk plaque features will provide new information on atherosclerotic plaque biology, and will hopefully lead to new methods to identify high-risk individuals.

Who can participate?
Patients aged 80 or under with high-grade carotid stenosis (narrowing of the carotid arteries)

What does the study involve?
All patients undergo one MRI scan and one whole-body PET/MRI scan in order to create images of the carotid arteries.

What are the possible benefits and risks of participating?
The PET scan involves a low dose of radiation, 5 mS. However, the risk to the patients of developing any side effects related to this is considered very low, as their mean age is over 70. The benefit is the possibility that the study contributes to the development of better tests for plaque risk assessment in the future.

Where is the study run from?
Linköping University and Uppsala University (Sweden)

When is the study starting and how long is it expected to run for?
June 2017 to October 2018

Who is funding the study?
1. Henry och Ella Margareta Ståhls Stiftelse (Henry and Ella Margareta Ståhl's Foundation) (Sweden)
2. Swedish Heart-Lung Foundation (Sweden)

Who is the main contact?
Dr Elin Good
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Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 1

Study information

Scientific Title
The DTP FDG-PET-MRI study for assessment of inflammation, lipid-rich necrotic core and intraplaque hemorrhage in the atherosclerotic plaque

Acronym
CARMA-PET

Study objectives
The degree of inflammation in the atherosclerotic plaque is correlated to the quantity of fat (lipid-rich necrotic core) and the quantity of blood (intraplaque haemorrhage), as all these three are associated with plaque rupture.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/01/2018, Swedish Ethical Review Authority (Swedish Ethical Review Authority, Box 2110, 750 02 Uppsala; +46 (0)10 475 08 00; registrator@etikprovning.se), ref: 2017/545-31

Study design
Multicenter observational prospective trial

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Atherosclerotic plaque composition in patients with high-grade carotid stenosis

Interventions

In patients with high-grade carotid stenosis the extent of lipid-rich necrotic core and intraplaque hemorrhage is quantified from fat and R2* maps acquired with a previously validated four-point Dixon MRI sequence in a stand-alone MRI. PET/MRI is used to measure 18F-FDG uptake.

Intervention Type
Device

Phase
Not Applicable

Primary outcome(s)
1. Lipid-rich necrotic cores (fat) and intraplaque hemorrhage (blood) in atherosclerotic plaques are measured using a novel and thoroughly validated quantitative MRI (qMRI) technique at study baseline
2. Inflammation measured using 18F-fluoro-deoxyglucose (18F- FDG) uptake quantified in the same plaques on images acquired using a simultaneous whole-body PET/MRI scanner at study baseline, as close in time to the qMRI assessment as possible

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
26/10/2018

Eligibility

Key inclusion criteria
≥50% carotid stenosis (corresponds to a Doppler flow velocity ≥1.3 m/sec at a Doppler angle of 50-60°)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
12

Key exclusion criteria
1. Previous carotid endarterectomy
2. Carotid occlusion
3. Diabetes mellitus

4. Renal failure (GFR <45 ml/min/1.73m²)
5. Inflammatory diseases including malignancies, immunologic disorders
6. Treatment with immunosuppressive/anti-inflammatory agents

Date of first enrolment
01/04/2018

Date of final enrolment
01/10/2018

Locations

Countries of recruitment
Sweden

Study participating centre
Linköping University
Department of Health, Medicine and Caring Sciences
Linköping University Hospital
Linköping
Sweden
58183

Study participating centre
Uppsala University
Department of Surgical Sciences
Section of Radiology & Molecular Imaging
Uppsala University Hospital
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Sponsor information

Organisation
Henry och Ella Margareta Ståhls Stiftelse (Henry and Ella Margareta Ståhl's Foundation)

Funder(s)

Funder type
Charity

Funder Name
Henry och Ella Margareta Ståhls Stiftelse (Henry and Ella Margareta Ståhl's Foundation)

Funder Name
Hjärt-Lungfonden

Alternative Name(s)
Swedish Heart-Lung Foundation

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Sweden

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Elin Good (elin.good@liu.se). Individual participant data that underlie the results reported in published manuscripts will be available immediately following publication, after deidentification (text, tables, figures, and appendices). This information may be shared with investigators whose proposed use of the data has been approved by an independent review committee identified for this purpose. The information may be used to achieve aims in the approved proposal. Proposals may be submitted up to 36 months following article publication. After 36 months the data will be available in the University's data warehouse but without investigator support other than deposited metadata. Written informed consent from all participants was obtained. All data is anonymized.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	09/07/2021	11/08/2021	Yes	No
Participant information sheet			04/02/2021	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes