Investigating retinal vascular atrophy as an indicator of brain degeneration in glaucoma

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Ethical review	Approved WMO
Status	Pending
Health condition type	Glaucoma and ocular hypertension
Study type	Observational non invasive

Summary

ID

NL-OMON57362

Source
ToetsingOnline

Brief title
Vascular atrophy as indicator of brain degeneration in glaucoma

Condition

- Glaucoma and ocular hypertension
- Structural brain disorders

Synonym
Glaucoma; POAG

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,Europese Unie:

Horizon Europe - Marie Sk□odowska-Curie Actions (MSCA)

Intervention

Keyword: Angiography, Glaucoma, Neurodegeneration, Neuroimaging

Outcome measures

Primary outcome

The primary outcomes are:

• Retinal nerve fiber layer thickness, as assessed using OCT

• Perifoveal vessel density, as assessed using OCTA

• Optic disc flow index, as assessed using OCTA

• Fixel based metrics in the visual system, as derived from DWI

• fiber density

• fiber cross section

• Integrated measures

Secondary outcome

The secondary outcomes are:

• Course of white matter tracts, as derived from DWI

• Averaged retinal nerve fiber layer thickness, as derived from OCT

• Retinal nerve fiber layer distribution, as derived from OCT

• Visual field mean deviation, as derived from HFA

• Degeneration of the retinal nerve fiber layer, as derived from OCT

• Degeneration of pfVD and odFI, as derived from OCTA

• Cerebral blood perfusion, as assessed using ASL (MRI)

Study description

Background summary

Glaucoma is one of the leading causes of irreversible blindness worldwide. The traditional view of glaucoma is that of an eye disease in which an elevation of intraocular pressure (IOP) causes the death of retinal ganglion cells (RGCs) through mechanical stress, leading to peripheral visual field (VF) defects and eventually blindness.

Earlier studies suggest that glaucoma is a neurodegenerative brain disease, in which glaucomatous changes in the retina give rise to degeneration of white and grey matter in the brain. Numerous MRI studies investigating structural changes in the brain have shown that neurodegeneration takes place in the entire visual system in people with glaucoma. One of the objectives of glaucoma research is to relate this neurodegeneration of the brain to structural and functional damage at the retinal level. This will give us a more complete overview of the consequences of glaucoma and potentially may allow us to better predict progression, and, in the future, even recovery.

Structural damage in the retina is commonly measured using the retinal nerve fiber layer (RNFL) thickness, which is obtained using an Optical Coherence Tomography (OCT) scan. An OCT scan is part of standard clinical practice. This RNFL thickness is reduced in people with glaucoma due to the RGC degeneration.

However, RNFL thickness as a measure of progression of glaucoma stops to be useful at a certain level due to a floor effect. In advanced glaucoma cases, the RNFL thickness becomes so thin that further thinning cannot be observed. Vascular atrophy has been described in several studies as a better indicator of glaucoma progression than RNFL thickness as it does not show this floor effect. Based on recent literature, the following metrics for describing structural damage via vascular atrophy are proposed: perifoveal vessel density (pfVD) and optic disk flow index (odFI). These changes can be observed using Optical Coherence Tomography Angiography (OCTA).

In this study, an investigation of vascular atrophy as an indicator of structural damage to the white matter of people with glaucoma will be performed. Structural properties of the white matter can be assessed using diffusion magnetic resonance imaging (dMRI). Fixel-based analysis provides the most clinically relevant metrics since these directly relate to the structure of white matter. By comparing the metrics of participants with glaucoma to those of controls, we can assess white matter changes. We expect that the changes in people with glaucoma will be reflected by a) structural changes in the visual system (lower fiber density and fiber cross-section in white matter), b) lower vessel density, c) lower blood perfusion, d) a correlation between the structural changes in the brain and vascular atrophy. We expect

this correlation to be higher than between the structural changes in the brain and the RNFL thickness.

Study objective

The primary objective of this study is to be able to better assess progression of visual pathway damage in advanced glaucoma cases in particular. For this, we will use a unique combination of OCTA and dMRI techniques. In particular, we aim to relate the retina's vascular information, derived from OCTA, to changes in the structural properties of the visual white matter in the brain, as assessed with dMRI. The main question we would like to answer in this study is *Is there a positive linear relationship between vascular measures in the eye and structural measures of white matter metrics in the primary visual pathway of the brain (optic nerve, optic chiasm, optic tract, optic radiation) in people with primary open angle glaucoma?* Such finding would be clinically relevant as OCTA is commonly used in clinical practice and is a cheaper and quicker alternative to MRI to assess structural changes to the visual pathway in the brain.

Study design

The study will be an observational, cross-sectional study with an emphasis on late disease stage and its association with relevant variables (fixel based metrics (FD, FC, FDC) and metrics of vasculature (pfVD, odFI, cortical blood flow). Sex and age will be taken into account in the analysis as potential confounders. The study will consist of two parts: ophthalmologic examinations (including an OCTA scan), and a (d)MRI experiment.

Study burden and risks

There are no direct risks associated with the proposed study. The planned ophthalmological examination is akin to the standard examination one receives on a visit to an ophthalmologist, which involves no risks. The MRI scanner that will be used has a magnetic field strength of 3 Tesla, which is a very common field strength used extensively in both clinical practice and research. No side effects have been reported so far from the use of such scanners.

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
Able to understand and actively participate in experiments
Signed written consent form
Able to walk independently or by using a rollator
Diagnosed with primary open angle glaucoma in at least one eye

Exclusion criteria

Other ophthalmic disorders, currently and/or in the past
MR contraindications (e.g., having a pacemaker or being claustrophobic)
Gross abnormalities/lesions in MRI scans

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2024
Enrollment:	34
Type:	Anticipated

Ethics review

Approved WMO

Date:	11-03-2025
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL85990.042.24