Unruptured Cerebral Aneurysm: prediction of evolution: a prospective multi-centre study

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Our primary aim is to evaluate in clinical practice the predictive value of unruptured intracranial aneurysm wall enhancement for aneurysm growth. It will allow to set up a secure, efficient and personalized follow-up.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Aneurysms and artery dissections
Study type	Observational invasive

Summary

ID

NL-OMON50892

Source
ToetsingOnline

Brief title
UCAN

Condition

- Aneurysms and artery dissections

Synonym
Unruptured intracranial aneurysm - protuberance of a blood vessel in the brain

Research involving
Human

Sponsors and support

Primary sponsor: Nantes University Hospital
Source(s) of monetary or material Support: Hartstichting

Intervention

Keyword: Aneurysm growth, Follow-up imaging, Intracranial aneurysm, Unruptured

Outcome measures

Primary outcome

In order to evaluate the predictive value of arterial wall enhancement for unruptured intracranial aneurysm growth, we will consider as primary endpoint the growth of the unruptured intracranial aneurysm after the complete follow-up at 3 years.

This event could occur at any time during the follow-up if an unruptured intracranial aneurysm becomes symptomatic but will be systematically assessed at 1 year and 3 years by MRI.

UIA growth will be assessed independently by two expert neuroradiologists, routinely involved in UIA management and disagreement will be solved by consensus with involvement of a third expert.

UIA wall enhancement status will be defined independently by two different expert neuroradiologists, with > 5years experience in intracranial vessel wall imaging. Disagreement will be solved by consensus with involvement of a third expert.

Secondary outcome

Our secondary objectives are:

- Determination of clinical and anatomical factors related to the growth of UIA.

- Determination of clinical and anatomical factors related to rupture of UIA.

- Detection of other arterial wall enhancement variation patterns related to growth during the follow-up in order to improve the follow-up of UIA patients.

Our secondary endpoints are:

- Clinical and anatomical features recorded.

- Incidence of growth, stratified by clinical and anatomical features.

- Incidence of intracranial aneurysm rupture, stratified by clinical and anatomical features.

- Construction and evaluation of an automatized tool of AWE patterns, as compared to the visual analysis of experts, in the form of a decision-making tool.

Study description

Background summary

Unruptured intracranial aneurysms (UIAs) have a prevalence of 3.2% in the general population. UIAs usually remain asymptomatic, but if they subsequently rupture there are often severe clinical consequences. In selected groups, the risk of rupture may be <1% per year. Those risks associated with the natural history have to be balanced against the well-known treatment-related mortality and morbidity in seeking to secure a UIA, as the overall treatment-associated mortality and morbidity ranges from 0.5% to 0.7% and 3% to 17%, respectively. Past and current studies have suggested that UIAs may be classified as presenting a high or low rupture risk based on their location and size. However, the majority of UIAs is small. Additionally, the impact of any management strategy on health-related quality of life or cognition remains poorly investigated. Clinical decision making thus mainly relies on general risk factors organized in prognostic scores, such as the PHASES score. The balance between risk and benefit makes the identification of a specific, individual-based marker for higher risk of rupture a valuable addition to therapeutic decision-making processes.

There is strong evidence to suggest that growing aneurysms are at higher risk of rupture. A systematic review of the literature reveals an estimation of a yearly growth probability of 3.85% (95% CI 3.4% to 4.3%) with a total follow-up of 7799 patient-years and 300 growth events observed in 3079 patients and 3855 UIAs. Several studies having suggested that growing UIAs have an increased risk of rupture, hence follow-up imaging of untreated UIAs is recommended. However, guidelines from the American Heart Association and European Stroke Organization

lack recommendations on which patients should be considered for follow-up imaging and at what time interval it should be performed.

Preliminary studies have demonstrated that aneurysmal wall enhancement (AWE), using high-resolution vessel wall MRI, is linked to aneurysm instability (i.e., ruptured, symptomatic, or growing over time). Indeed, recent cross-sectional studies that included both ruptured intracranial aneurysms and UIAs suggested that, on 3.0-T vessel wall MRI, circumferential AWE more frequently manifests in unstable (i.e., ruptured, symptomatic, or having a morphologic structure that changes over time) rather than in stable (i.e., incidental or non-evolving) intracranial aneurysms. Although the prevalence of circumferential AWE was over 80% in unstable intracranial aneurysms, reflecting a high sensitivity to determine unstable status, 30% of stable UIAs also presented this pattern, reflecting the low specificity of this finding. Having an individually based imaging for UIA instability would allow physicians to characterize aneurysms as appropriate for conservative management or requiring invasive treatment to prevent rupture.

With the U-CAN project using a combination of innovative aspects in terms of approach, interdisciplinary collaboration and technologies, we aim to improve the prediction of aneurysm growth by identifying advanced but routinely accessible imaging parameters as well as clinical and anatomical risk factors for aneurysm growth. This project establishes new directions for optimal and personalized management of UIAs to decrease the impact of futile follow-up and the risk of unrecognized, evolving UIA. Overall, we could also expect to improve the impact of follow-up on the patient*s quality of life.

Study objective

Our primary aim is to evaluate in clinical practice the predictive value of unruptured intracranial aneurysm wall enhancement for aneurysm growth. It will allow to set up a secure, efficient and personalized follow-up.

Study design

A prospective observational international multicenter study

Study burden and risks

The proposed study adds administration of gadolinium to the MRA-protocol for additional aneurysm wall imaging. The use of gadolinium is safe and painless and is often used in clinical practice. In rare cases the use of gadolinium can cause an allergic reaction. In this case, the radiology staff will handle according to the protocol of allergic reactions. Furthermore, included patients have to complete a questionnaire about possible risk factors (ethnic origin, use of cigarettes/alcohol, medical history, medication use). The extent of

burden and risks for participants of this study are estimated to be negligible.

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

- Subject carrying unruptured and untreated typical intracranial aneurysm of bifurcation < 7mm.
- Ability to be followed-up 3 years,
- Age > 18 years old,
- Subject planned to have regular MRI scan in the context of the usual medical follow-up of UIA (MRI scan planned at least at inclusion, at year 1 and at year 3).

Exclusion criteria

- Mycotic, fusiform-shaped, or dissecting intracranial aneurysm, intracranial aneurysm in relation with arteriovenous malformation.
- Unruptured intracranial aneurysm scheduled for preventive occlusion within 3 years.
- Family history of polycystic kidney disease, Ehlers-Danlos syndromes, Marfan*s syndrome, or Moyamoya disease.
- Failure to obtain informed consent.
- MRI or constrast injection contraindication.
- Cavernous or partially thrombosed unruptured intracranial aneurysm.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-09-2021
Enrollment:	45
Type:	Actual

Ethics review

Approved WMO

Date:	12-08-2021
Application type:	First submission
Review commission:	METC NedMec

Approved WMO Date:	16-09-2021
Application type:	Amendment
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
ClinicalTrials.gov	NCT04578808
CCMO	NL75460.041.21