



# Additional Relevant Intracranial Findings in Persons Screened with MR for Intracranial Aneurysms

Philippine B. van Wijngaarden<sup>a,\*</sup>, Gabriel J.E. Rinkel<sup>a</sup>, Irene C. van der Schaaf<sup>b</sup>, Liselore A. Mensing<sup>a</sup>, Ynte M. Ruigrok<sup>a</sup>, Mervyn D.I. Vergouwen<sup>a</sup>

<sup>a</sup> Department of Neurology and Neurosurgery, UMC Utrecht Brain Centre, University Medical Centre Utrecht, Utrecht University, Utrecht, the Netherlands

<sup>b</sup> Department of Radiology, University Medical Centre Utrecht, Utrecht University, Utrecht, the Netherlands

## ARTICLE INFO

### Keywords:

Unruptured intracranial aneurysm  
Subarachnoid haemorrhage  
MRA  
Incidental findings  
Additional relevant findings

## ABSTRACT

**Background:** Radiological screening for intracranial aneurysms (IAs) may identify other relevant intracranial findings. We investigated their prevalence on MR in persons screened for IAs.

**Methods:** We included all persons who were screened for the presence of IAs with brain MRI/MRA between 1996 and 2022 because of a family history of aneurysmal subarachnoid haemorrhage (aSAH) or autosomal dominant polycystic kidney disease (ADPKD). We reviewed radiology reports of initial and repeated brain MR to identify additional intracranial findings that needed follow-up or treatment, or carried a risk of becoming symptomatic.

**Results:** We included 766 persons (positive family history of aSAH:  $n = 681$ ; ADPKD:  $n = 85$ ) who had 1446 MRI/MRAs. At initial screening, 49 additional relevant intracranial findings were reported in 47 persons (6.1%, 95% CI 4.7–8.1%). Of all included persons, 338 (44%) underwent one ( $n = 154$ ) or more ( $n = 184$ ) follow-up screenings (total MRI/MRAs at follow-up:  $n = 680$ ). In 15/338 persons (4.4%, 95% CI 2.7–7.2%), 16 new additional relevant findings were reported at a median follow-up duration of 10 years (IQR 5–12).

**Conclusions:** Persons who are counselled for screening for IAs should be informed that there is a six percent chance of identifying an additional finding that requires follow-up or treatment, or may become symptomatic. Additionally, after 10-year follow-up screening there is a four percent chance of identifying a new additional relevant finding. The impact of such findings on quality of life needs further study.

## 1. Introduction

Persons with a positive family history of aneurysmal subarachnoid haemorrhage (aSAH) and patients with autosomal dominant polycystic kidney disease (ADPKD) have an increased lifetime risk of aSAH [1–3]. Several studies showed that screening for IAs with Magnetic Resonance Angiography (MRA) and preventive treatment of detected aneurysms is cost-effective in these persons [4–7]. However, such screening may also show additional relevant intracranial findings [8]. It remains unclear how often such findings are reported during screening for IAs. These data are important when counselling persons at high risk of aSAH who are considering screening for IAs. Therefore, we aimed to assess the prevalence of additional relevant intracranial findings on brain MRI/MRA in persons screened for IAs.

## 2. Methods

### 2.1. Study population

The Institutional Review Board of the University Medical Centre (UMC) Utrecht waived individual patient consent and formal ethics approval for this study since data available from routine care were used. We included persons who underwent screening for IAs with brain MRI/MRA because of a positive family history of aSAH or a patient history of ADPKD between May 1996 and August 2022. These persons were identified through an automatic search of patient files for persons screened with MRA for IAs in the UMC Utrecht, which is a tertiary referral centre for unruptured IAs (UIAs) and aSAH in the Netherlands. For this study, a positive family history of aSAH was defined as at least one first-degree relative (parent, sibling, or child) with aSAH, or at least one first-degree relative with a UIA who had a first-degree relative with

\* Corresponding author at: Department of Neurology and Neurosurgery, UMC Utrecht Brain Centre, University Medical Centre Utrecht, Utrecht University, Heidelberglaan 100, 3584 CX Utrecht, the Netherlands.

E-mail address: [p.b.vanwijngaarden-5@umcutrecht.nl](mailto:p.b.vanwijngaarden-5@umcutrecht.nl) (P.B. van Wijngaarden).

<https://doi.org/10.1016/j.jns.2024.123160>

Received 27 March 2024; Received in revised form 9 July 2024; Accepted 28 July 2024

Available online 30 July 2024

0022-510X/© 2024 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

aSAH. We excluded persons who had a previous medical history of aSAH or UIA. If a patient underwent screening and a UIA was identified on MRA, we excluded the subsequent scans since these were made for radiological monitoring of the detected UIA and no longer for screening.

## 2.2. Data collection

We collected the following patient characteristics: age at time of first screening, sex, history of hypertension, hypercholesterolemia, diabetes mellitus, smoking status, alcohol abuse, use of recreational drugs, neurological history, family history of aSAH, and ADPKD. Hypertension was defined as a systolic blood pressure of >140 mmHg or a diastolic blood pressure of >90 mmHg, or a history of hypertension, or the use of antihypertensive drugs. Hypercholesterolemia was defined as a history of hypercholesterolemia or the use of lipid lowering drugs. Diabetes mellitus was defined as a history of diabetes mellitus or the use of antidiabetic medication. Smoking status was categorized into never, former, and current. Alcohol abuse was defined as more than 2 glasses per day or 14 glasses per week.

## 2.3. Imaging

In our hospital, we usually screen around the ages of 40 and 55 in case of one affected first-degree family member, and every 5 years until the age of 75 in case of two or more affected first-degree family members or in case of ADPKD. Some persons only had the initial screening for one or more of the following reasons: 1) because we included patients until August 2022 (and therefore not enough time passed by to have the follow-up MRI/MRA); 2) because screening showed an intracranial aneurysm resulting in exclusion from our analyses for the follow-up screening; 3) because the patient reached the upper age limit for screening; or 4) because the patient developed severe comorbidities which did not justify further IA screening. The imaging protocol of a person who was screened for the presence of an IA included the following sequences at initial screening: MRA 3D TOF, T1 SE (sag), T2

TSE (tra), T2 FLAIR (tra) and SWI (tra). The imaging protocol for follow-up screening included less sequences: MRA 3D TOF and T2 FLAIR (tra).

## 2.4. Radiology reports

We reviewed the radiology reports of the included persons for additional relevant intracranial findings. These findings were defined as previously undetected intracranial abnormalities that required follow-up or treatment, or carried a risk of becoming symptomatic. Normal variations such as ventricular asymmetry, enlarged cisterns, cavum septum pellucidum, enlarged Virchow–Robin spaces, and anatomical variations in the Circle of Willis, were not considered as relevant findings. Since vascular and non-specific white matter lesions are extremely common (in 95% of persons aged 45–59 years, with an even higher prevalence in older persons) [8], we did not consider these lesions as relevant findings either. If a patient had previous brain imaging and a known additional relevant finding, it was not considered an additional finding in our study. But if an additional relevant finding was in retrospect already present at previous brain imaging but not previously reported, we did consider this an additional finding. In case an additional finding was reported for which further diagnostic tests were performed to assess a final diagnosis we used the final diagnosis to describe the additional finding.

## 2.5. Data analysis

We determined the proportions of IAs found upon screening and the proportion of additional relevant findings for the total cohort and for persons with a positive family history of aSAH and patients with ADPKD separately. The prevalence of additional relevant findings was reported separately for the first screening and all follow-up screenings combined. Confidence intervals were calculated using the Wilson score interval.

**Table 1**

Person characteristics at time of first screening.

Number of persons screened	Total N = 766	Positive family history of aSAH N = 681	ADPKD N = 85
Median age, years (IQR)	41 (29–52)	41 (29–51)	45 (30–54)
Female sex, (%)	424 (55)	381 (56)	43 (51)
Hypertension (%)	181 (24)	133 (20)	48 (56)
Hypercholesterolemia (%)	50 (7)	38 (6)	12 (14)
Diabetes mellitus (%)	10 (1)	8 (1)	2 (2)
Smoking (%)			
Current smoker	121 (16)	115 (17)	6 (7)
Former smoker	144 (19)	126 (19)	18 (21)
Never	235 (31)	204 (30)	31 (36)
Unknown	268 (35)	236 (35)	31 (36)
Alcohol abuse (%) <sup>a</sup>	27 (4)	24 (4)	3 (4)
Recreational drugs (%)			
Current drug use	12 (2)	11 (2)	1 (1)
History of drug use	19 (3)	19 (3)	–
Relevant neurological history(%) <sup>b</sup>			
Migraine	33 (4)	28 (4)	5 (6)
Epilepsy	7 (1)	5 (1)	2 (2)
Transient ischemic attack	5 (1)	5 (1)	–
Cavernous malformation	1 (0)	1 (0)	–
Hydrocephalus	1 (0)	1 (0)	–
Haemorrhagic stroke	1 (0)	–	1 (1)
Ischemic stroke	1 (0)	1 (0)	–
Meningioma	1 (0)	1 (0)	–
Meningitis	1 (0)	–	1 (1)
Multiple sclerosis	1 (0)	–	1 (1)
Prolactinoma	1 (0)	1 (0)	–
Schwannoma	1 (0)	–	1 (1)

ADPKD: autosomal dominant polycystic kidney disease; aSAH: aneurysmal subarachnoid haemorrhage.

<sup>a</sup> (>2 glasses/day or > 14 glasses/week).

<sup>b</sup> Known imaging abnormalities from previous medical history were not considered incidental intracranial findings.

**Table 2**

Number of reported unruptured intracranial aneurysms and number of additional relevant intracranial findings on first screening MRI/MRA.

Number of persons screened	Total N = 766 (n, %)	Positive family history of aSAH N = 681 (n, %)	ADPKD N = 85 (n, %)
Unruptured intracranial aneurysms	54 (7)	46 (7)	8 (9)
<i>Additional relevant intracranial findings</i>			
Arachnoid cyst	14 (2)	8 (1)	6 (7)
Cerebral infarction	13 (2)	11 (2)	2 (2)
Pineal gland cyst	5 (1)	5 (1)	–
Developmental venous anomaly	3 (0)	3 (0)	–
Megadolichobasilar artery	3 (0)	2 (0)	1 (1)
Cavernous malformation	2 (0)	1 (0)	1 (1)
Low-grade glioma	2 (0)	1 (0)	1 (1)
Arteriovenous malformation	1 (0)	1 (0)	–
Brain capillary telangiectasias	1 (0)	1 (0)	–
Colloid cyst	1 (0)	1 (0)	–
Meningioma	1 (0)	1 (0)	–
Multinodular and vacuolating neuronal tumour	1 (0)	1 (0)	–
Neuroglial cyst	1 (0)	1 (0)	–
Subependymoma	1 (0)	1 (0)	–

ADPKD: autosomal dominant polycystic kidney disease; aSAH: aneurysmal subarachnoid haemorrhage.

### 3. Results

We included 766 persons with a total number of 1446 MRI/MRAs. Patient characteristics at baseline are shown in Table 1. Of these 766 persons, 681 (89%) had a positive family history of aSAH, and 85 (11%) ADPKD (Table 1). The median age at time of first screening was 41 years (IQR 29–52), and 424 of the screened persons (55%) were female.

#### 3.1. Results of first screening

In the total cohort, during the first screening, 54 IAs were identified in 47 persons (6.1%, 95% CI 4.7–8.1%), and 49 additional relevant intracranial findings in 47 persons (6.1%, 95% CI 4.7–8.1%) (Table 2). The most frequently reported additional findings were arachnoid cysts (1.8%, 95% CI 1.1–3.0%). Of the persons screened at initial screening with an additional relevant intracranial finding, four persons (8.5%, 95% CI 3.4–19.9%) needed follow-up imaging for their additional findings (colloid cyst, low-grade glioma, multinodular and vacuolating neuronal tumour, and subependymoma), two persons (4.3%, 95% CI 1.2–14.3%) were surgically treated (arteriovenous malformation, low-grade glioma), and one person (2.1%, 95% CI 0.4–11.1%) needed further diagnostic assessment with imaging for the brain capillary telangiectasias but declined this.

#### 3.2. Results of subsequent screenings

A total of 338 persons (44%, family history of aSAH:  $n = 307$ ; ADPKD:  $n = 31$ ) underwent one ( $n = 154$ ) or more ( $n = 184$ ) follow-up screenings (total:  $n = 680$  scans) with a median of 2 scans per person (IQR 1–2) during a median follow-up between the first and last scan of 9 years (IQR 5–13). The median age at the time of follow-up screening was 45 years (IQR 34–55). During follow-up screening, at a median duration

of follow-up of 5 years (IQR 5–10), 26 new IAs were identified in 23 persons (6.8%, 95% CI 4.6–10.0%). Of these 26 newly found IAs, seven were retrospectively already present during the prior screening. At a median duration of follow-up of 10 years (IQR 5–12), 16 new additional relevant intracranial findings were reported in 15 persons (4.4%, 95% CI 2.7–7.2%) (Table 3). The most frequently reported new additional findings were cerebral infarctions (1.8%, 95% CI 0.8–3.8%). Of the persons with an additional relevant intracranial finding at follow-up screening, one person (6.7%, 95% CI 1.2–29.8%) needed surgical treatment for the newly found additional relevant finding (schwannoma).

#### 3.3. Subgroup analyses

In 681 persons with a family history of aSAH, the first screening identified 46 IAs in 41 persons (6.0%, 95% CI 4.5–8.1%), and 38 additional relevant intracranial findings in 38 persons (5.6%, 95% CI 4.1–7.6%) (Table 2). Follow-up screening was done in 307 persons with a family history of aSAH. During follow-up screening, at a median duration of follow-up of 5 years (IQR 5–10), 23 new IAs were identified in 20 persons (6.5%, 95% CI 4.3–9.9%). At a median duration of follow-up of 7 years (IQR 5–11), 14 new additional relevant intracranial findings were identified in 13 persons (4.2%, 95% CI 2.5–7.1%) (Table 3).

In 85 patients with ADPKD, the first screening identified 8 IAs in 6 persons (7.1%, 95% CI 3.3–14.6%), and 11 additional relevant intracranial findings in 9 persons (10.6%, 95% CI 5.7–18.9%) (Table 2). Follow-up screening was done in 31 patients with ADPKD. During follow-up screening, at a median duration of follow-up of 9 years (range 4–16), 3 new IAs were identified in 3 persons (9.7%, 95% CI 3.4–24.9%). At a median duration of follow-up of 16.5 years (range 16–17), 2 new additional relevant intracranial findings were reported in 2 persons (6.5%, 95% CI 1.8–20.7%) (Table 3).

**Table 3**

Number of newly reported unruptured intracranial aneurysms and number of additional relevant intracranial findings on follow-up MRI/MRA.

Number of persons screened	Total N = 338 (n, %)	Positive family history of aSAH N = 307 (n, %)	ADPKD N = 31 (n, %)
Unruptured intracranial aneurysms	26 (8)	23 (7)	3 (10)
<i>Additional relevant intracranial findings</i>			
Cerebral infarction	6 (2)	5 (2)	1 (3)
Arachnoid cyst	3 (1)	3 (1)	–
Cavernous malformation	2 (1)	2 (1)	–
Developmental venous anomaly	1 (0)	1 (0)	–
Heterotopia	1 (0)	1 (0)	–
Major artery stenosis*	1 (0)	1 (0)	–
Meningioma	1 (0)	–	1 (3)
Schwannoma	1 (0)	1 (0)	–

ADPKD: autosomal dominant polycystic kidney disease; aSAH: aneurysmal subarachnoid haemorrhage. \* &gt;50% intracranial carotid artery stenosis

### 3.4. Additional diagnostic without additional relevant findings

At initial screening, four persons (0.5%, 95% CI 0.2–1.3%) had additional diagnostic imaging because of a potential additional relevant finding. In all four persons, additional diagnostic imaging consisted of an MRI with gadolinium. Three out of four persons had an additional intracranial finding that did not need follow-up or treatment, nor carried a risk of becoming symptomatic (i.e., no additional relevant intracranial finding). The other person did not have any additional finding at the diagnostic follow-up imaging.

## 4. Discussion

In persons screened for IAs because of a family history of aSAH or ADPKD, additional intracranial findings that require follow-up or treatment, or carry a risk of becoming symptomatic are reported in approximately six percent of the persons at first screening. At serial screening, new additional relevant intracranial findings are reported in approximately four percent of the persons after a median follow-up duration of 10 years.

The prevalence of additional relevant intracranial findings in our study is lower than reported in a study on incidental findings in the general population (13.6%) [8]. The following explanations may contribute to this lower prevalence. First, the mean age in the population-based study was higher than in our study, leading to a higher prevalence of asymptomatic infarctions and meningiomas in the population-based study [8–11]. Second, we, on purpose, excluded IAs as additional findings, because the indication for the MR was screening for IAs. In the population-based study, IAs were included as incidental findings. Third, the definition of additional findings differed between the two studies, with, for example, also inclusion of Type I Chiari malformations as incidental findings in the population-based study.

Our study has several strengths. First, we studied a large cohort of persons undergoing screening for IAs. This enabled us to perform subgroup analyses for the two groups that most commonly undergo IA screening, namely persons with a positive family history of aSAH and patients with ADPKD. Second, the long follow-up duration allowed for investigating the chance of identifying new additional relevant intracranial findings at follow-up screening. Both strengths increase the internal validity and generalizability of our findings to persons screened for IAs because of a family history of aSAH or patient history of ADPKD. We also need to address some limitations. First, the additional findings in our study were retrospectively analysed using radiology reports. The scans were reported by several neuroradiologists who may vary in their accuracy to report additional findings. Because the actual scans were not reviewed for the presence of additional relevant intracranial findings, our method may have resulted in an underestimation of the overall prevalence of these findings. However, since we only included additional intracranial findings that needed follow-up or treatment, or carried a risk of becoming symptomatic, we assume that the degree of underreporting was small. Moreover, by not reviewing the scans for research purposes but using the original report as data source, we ensured that our study remained as close as possible to clinical reality. Second, the follow-up scans consisted of less sequences, which may have resulted in a lower sensitivity to detect additional relevant findings compared to the first screening. Finally, we included scans from 1996 onward. Over time, the scan-quality and hereby the sensitivity for detecting additional findings has increased [11].

The clinical implication of our study is that persons who are counselled for IA screening should be informed, prior to performing imaging, about the six percent chance of finding an additional relevant intracranial finding at initial screening and the four percent chance at 10-year follow-up screening for a newly found additional relevant intracranial finding. Future studies are needed to investigate the impact of additional intracranial findings on quality-of-life.

## Funding

Dr. Vergouwen was supported by a Clinical Established Investigator grant by the Dutch Heart Foundation (2018T076). This study was funded by a grant from the Dutch Heart Foundation, CVON2015-08 ERASE (optimal Early Recognition of persons at high risk of Aneurysmal Subarachnoid hemorrhage).

## Informed consent

The Institutional Review Board of the University Medical Centre (UMC) Utrecht waived individual patient consent for this study since data available from routine care were used.

## Ethical approval

Formal ethical approval for this study was waived by The Institutional Review Board of the UMC Utrecht since data available from routine care were used. This study was completed in accordance with the Helsinki Declaration as Revised in 2023.

## CRediT authorship contribution statement

**Philippine B. van Wijngaarden:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Gabriel J.E. Rinkel:** Writing – review & editing, Writing – original draft, Supervision, Resources, Methodology, Conceptualization. **Irene C. van der Schaaf:** Writing – review & editing, Writing – original draft, Supervision, Methodology. **Liselore A. Mensing:** Writing – review & editing, Writing – original draft, Methodology. **Ynte M. Ruigrok:** Writing – review & editing, Writing – original draft, Supervision, Methodology. **Mervyn D.I. Vergouwen:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Conceptualization.

## Declaration of competing interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Acknowledgements

None.

## References

- [1] A.S. Bor, G.J. Rinkel, J. van Norden, M.J. Wermer, Long-term, serial screening for intracranial aneurysms in individuals with a family history of aneurysmal subarachnoid haemorrhage: a cohort study, *Lancet Neurol.* 13 (385–392) (2014) 20140305, [https://doi.org/10.1016/s1474-4422\(14\)70021-3](https://doi.org/10.1016/s1474-4422(14)70021-3).
- [2] I. Rasing, Y.M. Ruigrok, P. Greebe, et al., Long-term risk of aneurysmal subarachnoid hemorrhage after a negative aneurysm screen, *Neurology* 84 (912–917) (2015) 20150130, <https://doi.org/10.1212/wnl.0000000000001310>.
- [3] E.M. Hopmans, Y.M. Ruigrok, A.S. Bor, et al., A cost-effectiveness analysis of screening for intracranial aneurysms in persons with one first-degree relative with subarachnoid haemorrhage, *Eur. Stroke J.* 1 (320–329) (2016) 20161019, <https://doi.org/10.1177/2396987316674862>.
- [4] G.J. Rinkel, Y.M. Ruigrok, Preventive screening for intracranial aneurysms, *Int. J. Stroke* 17 (30–36) (2022) 20210617, <https://doi.org/10.1177/17474930211024584>.
- [5] Z. Zhou, Y. Xu, C. Delcourt, et al., Is regular screening for intracranial aneurysm necessary in patients with autosomal dominant polycystic kidney disease? A systematic review and Meta-analysis, *Cerebrovasc. Dis.* 44 (75–82) (2017) 20170513, <https://doi.org/10.1159/000476073>.
- [6] A. Flahault, D. Trystram, F. Nataf, et al., Screening for intracranial aneurysms in autosomal dominant polycystic kidney disease is cost-effective, *Kidney Int.* 93 (716–726) (2018) 20171020, <https://doi.org/10.1016/j.kint.2017.08.016>.
- [7] A. Malhotra, X. Wu, C.C. Matouk, et al., MR angiography screening and surveillance for intracranial aneurysms in autosomal dominant polycystic kidney disease: a cost-effectiveness analysis, *Radiology* 291 (400–408) (2019) 20190219, <https://doi.org/10.1148/radiol.2019181399>.

- [8] M.W. Vernooij, M.A. Ikram, H.L. Tanghe, et al., Incidental findings on brain MRI in the general population, *N. Engl. J. Med.* 357 (2007) 1821–1828, <https://doi.org/10.1056/NEJMoa070972>.
- [9] D.E. Sunny, M. Amoo, M. Al Breiki, et al., Prevalence of incidental intracranial findings on magnetic resonance imaging: a systematic review and meta-analysis, *Acta Neurochir.* 164 (2751–2765) (2022) 20220508, <https://doi.org/10.1007/s00701-022-05225-7>.
- [10] S.E. Vermeer, P.J. Koudstaal, M. Oudkerk, et al., Prevalence and risk factors of silent brain infarcts in the population-based Rotterdam scan study, *Stroke* 33 (2002) 21–25, <https://doi.org/10.1161/hs0102.101629>.
- [11] Z. Morris, W.N. Whiteley, W.T. Longstreth Jr., et al., Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis, *Bmj* 339 (b3016) (2009) 20090817, <https://doi.org/10.1136/bmj.b3016>.