Screening for Intracranial Aneurysms

Prof. Dr. Tommy Andersson, MD, PhD

Karolinska University Hospital and
Karolinska Institutet
Stockholm, Sweden🇸🇪

AZ Groeninge
Kortrijk, Belgium🇧🇪

Disclosures

<u>Consultant:</u>

- Ablynx
- Amnis Therapeutics
- Anaconda
- Cerenovus – Neuravi Ltd
- Medtronic - Covidien
- Rapid Medical

Purpose of screening

- Increase number of quality years
- Not to treat every single AA detected

Counselling before screening

- Risks of SAH
- Treatment risks
- All detected AA may not be treated
- Repeated entire life
- Not 100%
- Life insurance/flying/driving

Screening technique – reported by a specialist

- CTA
  - Sensitivity 93-100%, less with AA ≤3mm
  - Specificity 83-100%

- MRA
  - Sensitivity 87-100% for ≥3mm
  - Specificity 86-100% for ≥3mm
  - 3T – better spatial resolution

Reason for screening - 1

Familial aneurysms

Familial aneurysms

= ≥2 first degree relatives:

- Higher risk of rupture - SAH + Smaller AA rupture
  - Broderick et al 2009
    - Found AA in 21% of 548 screened individuals
    - Rupture rate of 1,2% per year
    - Ruptured AA were 3-4 mm

Original Contribution

Comparison of Rupture Risk of Intracranial Aneurysms Between Familial and Sporadic Patients

Liselore A. Mensing, MD; Jacoba P. Greving, PhD; Tessa A. Verhoeff, BSc;
Gabriel J.E. Rinkel, MD; Ynte M. Ruigrok, MD, PhD

Background and Purpose—A much higher rupture rate for patients with familial intracranial aneurysms (IA) compared with patients with sporadic IA has been reported in a study with highly selected familial aneurysms using sporadic patients from other populations a controls. We aimed to validate these findings in a large independent series of Dutch patients with familial and sporadic IA.

Methods—We conducted a secondary analysis of our institutional cohort of patients who were screened for IAs between 1994 and 2016. We assessed the incidence of aneurysmal subarachnoid hemorrhage between familial, defined as ≥2 affected first-degree relatives with aneurysmal subarachnoid hemorrhage and unruptured IA (UIA), and sporadic patients with UIA with Cox regression analysis.

Results—We identified 62 familial IA patients with 91 UIA and 412 sporadic IA patients with 542 UIA. Despite familial aneurysms being smaller and more often located at low risk sites than sporadic IA, 3 familial patients had aneurysmal subarachnoid hemorrhage (0.77 ruptures per 100 aneurysm-years [95% CI, 0.20–2.09]) compared with 7 sporadic patients (0.51 ruptures per 100 aneurysm-years [95% CI, 0.22–1.01]). As compared to sporadic UIA, familial UIA seems to have a 3-fold higher risk of rupture (hazard ratio, 2.9 [95% CI, 0.6–14]).

Conclusions—Our results suggest a slightly increased risk of aneurysm rupture for familial compared with sporadic IA, although we were not able to demonstrate this with statistical significance. However, the rupture risk seems less strongly increased than found in a previous study. Based on our results, we recommend to treat familial UIA more aggressively. (***Stroke*. 2019;50:00-00. DOI: 10.1161/STROKEAHA.118.023783.**)

Mensing et al - 1

- Incidence of SAH comparing familial and sporadic aneurysms
- Familial 3-fold higher risk of rupture
- But, 62 familial patients with 91 aneurysms – 3 ruptures – not significant
- *"…rupture risk less seems less strongly increased…recommend to treat familial UIA more aggressively"*

RESEARCH ARTICLE

Difference in Aneurysm Characteristics between Patients with Familial and Sporadic Aneurysmal Subarachnoid Haemorrhage

Liselore A. Mensing[1]*, Gabriel J. E. Rinkel[1], Monique H. M. Vlak[3], Irene C. van der Schaaf[2], Ynte M. Ruigrok[1]

1 Department of Neurology and Neurosurgery, Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht, the Netherlands, **2** Department of Radiology, University Medical Center Utrecht, Utrecht, the Netherlands, **3** Department of Neurology, Medical Center Haaglanden, The Hague, the Netherlands

* L.A.Mensing-3@umcutrecht.nl; liseloremensing@gmail.com

Abstract

Object

Patients with familial intracranial aneurysms (IA) have a higher risk of rupture than patients with sporadic IA. We compared geometric and morphological risk factors for aneurysmal rupture between patients with familial and sporadic aneurysmal subarachnoid hemorrhage (aSAH) to analyse if these risk factors contribute to the increased rupture rate of familial IA.

Methods

Geometric and morphological aneurysm characteristics were studied on CT-angiography in a prospectively collected series of patients with familial and sporadic aSAH, admitted between September 2006 and September 2009, and additional patients with familial aSAH retrieved from the prospectively collected database of familial IA patients of our center. Odds ratios (OR) with corresponding 95% confidence intervals (95% CI) were calculated to compare the aneurysm characteristics between patients with familial and sporadic aSAH.

Results

We studied 67 patients with familial and 184 with sporadic aSAH. OR's for familial compared with sporadic aSAH were for oval shape 1.16(95%CI:0.65–2.09), oblong shape 0.26 (95%CI:0.03–2.13), irregular shape 0.83(95%CI:0.47–1.49), aspect ratio $\geq$ 1.6 0.94(95% CI:0.54–1.66), contact with the perianeurysmal environment (PAE) 1.15(95%CI:0.56–2.40), deformation by the PAE 1.05(95%CI:0.47–2.35) and for dominance of the posterior communicating artery (PCoA) in case of PCoA aneurysms 1.97(95% CI:0.50–7.83).

Conclusions

The geometric and morphological risk factors for aneurysm rupture do not have a higher prevalence in familial than in sporadic aSAH and thus do not explain the increased risk of IA

Mensing et al - 2

- Compared geometrical and morphological factors
- E.g. irregular shape, aspect ratio, contact with environment
- *"…no higher prevalence…do not explain higher rupture risk…"*

Risk factors for aneurysm formation

- Smoking
- Excessive alcohol
- Uncontrolled hypertension
- Female gender
- ADPKD
- + family history

Risk factors for aneurysm rupture

- Smoking
- High shear stress
- Morphology: size, shape and location
- Presence of other, ruptured aneurysms
- + family history

Probable cause: genetics

- Genetic predisposition - not possible to find association to specific gene – formation/rupture

- Familial form with higher prevalence (10%)
- Screening: ≥ 2 first degree relatives with known aneurysms

- Still, modifiable risk factors play a greater role for *rupture*

Risk factors are *additive!*

Risk factor	Relative risk	Population risk %
Family history	6,6	11
ADPKD	4,4	0,3
Excessive alcohol	5,6	21
Hypertension	2,8	17
Smoking	1,9	20

Rinkel 2009

Reason for screening - 2

Autosomal Dominant Polycystic Kidney Disease

Autosomal Dominant Polycystic Kidney Disease

- 10% have IC AA
- 85% chromosome 16p (the rest mostly 4p)
- SAH at lower age
- Mostly MCA – larger size (25% ≥10mm)
- Less females – less related to hypertension

Reason for screening - 3

Coarctatio Aortae

Coarctatio Aortae

- Around 10% have AA
- 2/3 male – Md age 29 y
- Mean diameter 4 mm
- Often missed by cardiologists/cardiac radiologists
- Hypertension? Unknown inherited pathology?

ORIGINAL RESEARCH

S.L. Curtis
M. Bradley
P. Wilde
J. Aw
S. Chakrabarti
M. Hamilton
R. Martin
M. Turner
A.G. Stuart

Results of Screening for Intracranial Aneurysms in Patients with Coarctation of the Aorta

BACKGROUND AND PURPOSE: IAs are found in 2.3% of adults; the mean age at detection is 52 years. Prevalence is <0.5% in young adults. Early studies suggest that 10%–50% of patients with aortic coarctation have IAs. Screening recommendations are variable. We sought to examine the prevalence of IAs through screening with MRA.

MATERIALS AND METHODS: Consecutive patients older than 16 years of age with coarctation undergoing brain MRA between May 1999 and October 2007 were included. MRA was performed by using a 1.5T scanner with a 3D time-of-flight protocol; simultaneous MR imaging was performed of the heart and aorta. Cerebral MRAs were double-reported by a neuroradiologist. Statistics are described as mean ± SD and median ± range. Continuous variables were compared by using Student *t* tests and Mann-Whitney *U* tests (categoric variables, by using the Fisher exact test).

RESULTS: One hundred seventeen MRAs were double-reported. The median age was 29 ± 11 years (range, 16–59 years). IAs were found in 12 patients (10.3%). The mean diameter of IAs was 3.9 mm (range, 2.0–8.0 mm). Patients with aneurysms were older (median, 37 years; range, 16–50 years) than those without (median, 23 years; range, 16–59 years; $Z = -2.01$, $P = .04$). Hypertension was more common in those with IAs (IA 83% versus no IA 43%, $P = .01$). There was no association between ascending aortopathy, bicuspid aortic valves, and IAs.

CONCLUSIONS: Patients with coarctation have a higher prevalence of IAs, occurring at an earlier age than in population studies. Whether routine screening is appropriate for this group of patients is unclear. Hypertension is likely to be an important pathophysiologic factor.

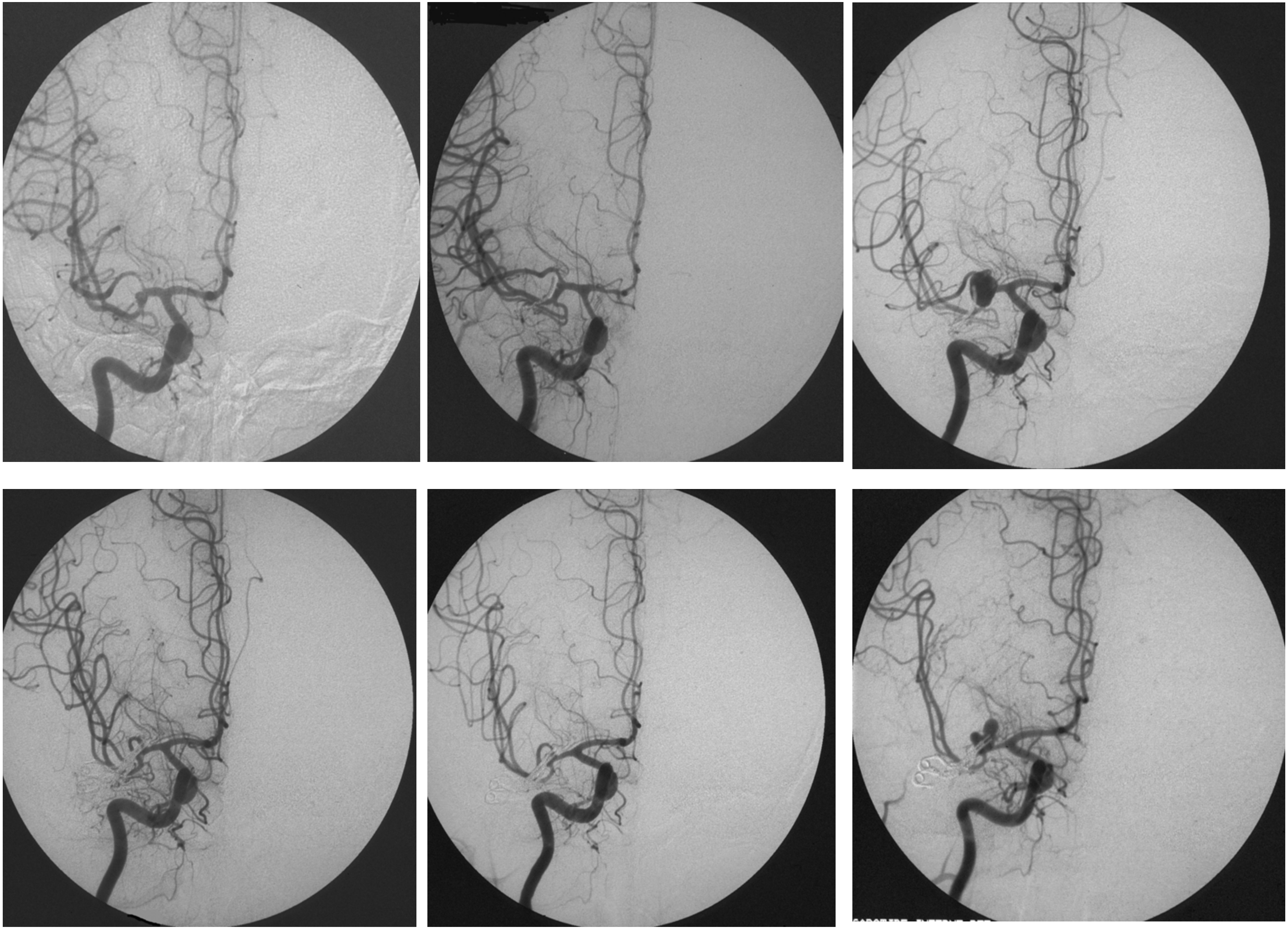
How often screening?

- Familial aneurysms, Bor et al 2010:
  - Every 2 years from 20 to 80 yo: largest health benefit but expensive and difficult for patients
  - Prevention of SAH depends on interval

- When QALY added: every 7 years from 20 to 80
  - Cost effective
  - Several assumptions

What about previous SAH?

- Recurrence?
- De novo formation?



Previous SAH

- Recurrence after clipping
  - 2% in 10 years / 9% in 20 years
  - 30-50x higher than general!

- Annual Incidence de novo AA: 0,3-1,8%

- So, *there is* a risk for recurrence and de novo, but:
  - Not all ruptures (risk in ISAT 0,04% each for de novo and additional AA) and not all detected are treated (20% in ASTRA)
  - Followed for life?

Effectiveness and costs of screening for aneurysms every 5 years after subarachnoid hemorrhage

Marieke J.H. Wermer, MD
Hendrik Koffijberg, MSc
Irene C. van der Schaaf, MD
For the ASTRA Study Group*

Address correspondence and reprint requests to Dr. M.J.H. Wermer, Department of Neurology: G03.228, University Medical Center Utrecht, Heidelberglaan 100, 3500 GA Utrecht, The Netherlands
m.wermer@umcutrecht.nl

ABSTRACT

Background: Patients who survive after subarachnoid hemorrhage (SAH) are at risk for a recurrence despite successful treatment of the ruptured aneurysm and may therefore benefit from screening for new aneurysms.

Methods: We screened 610 patients with SAH with CT angiography 2–18 years after clipping of the aneurysms. Results of screening were used as input for a Markov decision model. We compared the expected number of recurrent hemorrhages, life expectancy, quality-adjusted life-years (QALYs), and costs associated with the strategies "screening every 5 years" and "no screening."

Results: Screening individuals with previous SAH prevented almost half of the recurrences, slightly increased life expectancy (from 21.06 to 21.08 years), but reduced QALYs (from 12.18 to 12.04) and increased costs (from $2,750 to $4,165 per patient). Screening was cost-saving without increasing QALYs in patients with a more than twofold risk above baseline of both aneurysm formation and rupture and it was cost-saving while increasing QALYs if both risks were at least 4.5 times higher. In patients with reduced quality of life because of fear for a recurrence, screening increased QALYs at a maximum cost of $17,422 per QALY.

Conclusions: In general, screening patients with previous subarachnoid hemorrhage (SAH) cannot be recommended. Screening can save costs and increase quality-adjusted life-years (QALYs) in patients with a relatively high risk of both aneurysm formation and rupture, and increases QALYs at acceptable costs in patients with fear for a recurrence. More data are needed on risk factors for aneurysm formation and rupture in patients with previous SAH and on management of fear for a recurrence to identify patients who can benefit from screening. *Neurology*® 2008;70:2053–2062

Follow-up after coiling /clipping

Coiling

- 6 mo DSA (or MRA)
- 2 y MRA
- 5 y MRA
- 10 y MRA
- ?

Clipping

- 5-8 d DSA
- 6 mo DECT
- 2 y DECT
- 5 y DECT
- 10 y DECT
- ?

Summary - who?

1. 2 or more first degree relatives
   - Risk of having an AA: 8% (Rinkel 2005)
   - 10 years risk of SAH: 7%

2. Autosomal Dominant Polycystic Kidney Disease

3. Coarctatio Aortae

4. Identical twins

5. Consider following treated patients

Summary - how, when and why?

- MRA or CTA every 5 (2-3) years from 18 yo (or even younger) to 70-80 yo (?)

- Consider treatment for ≥ 3mm

- Familial AA rupture
  - Younger age
  - Smaller size - <6mm 17x increased risk compared to ISUIA

- Risk factors are additive
  - Hypertension
  - Smoking
  - Alcohol excess

Intracranial aneurysm screening: indications and advice for practice

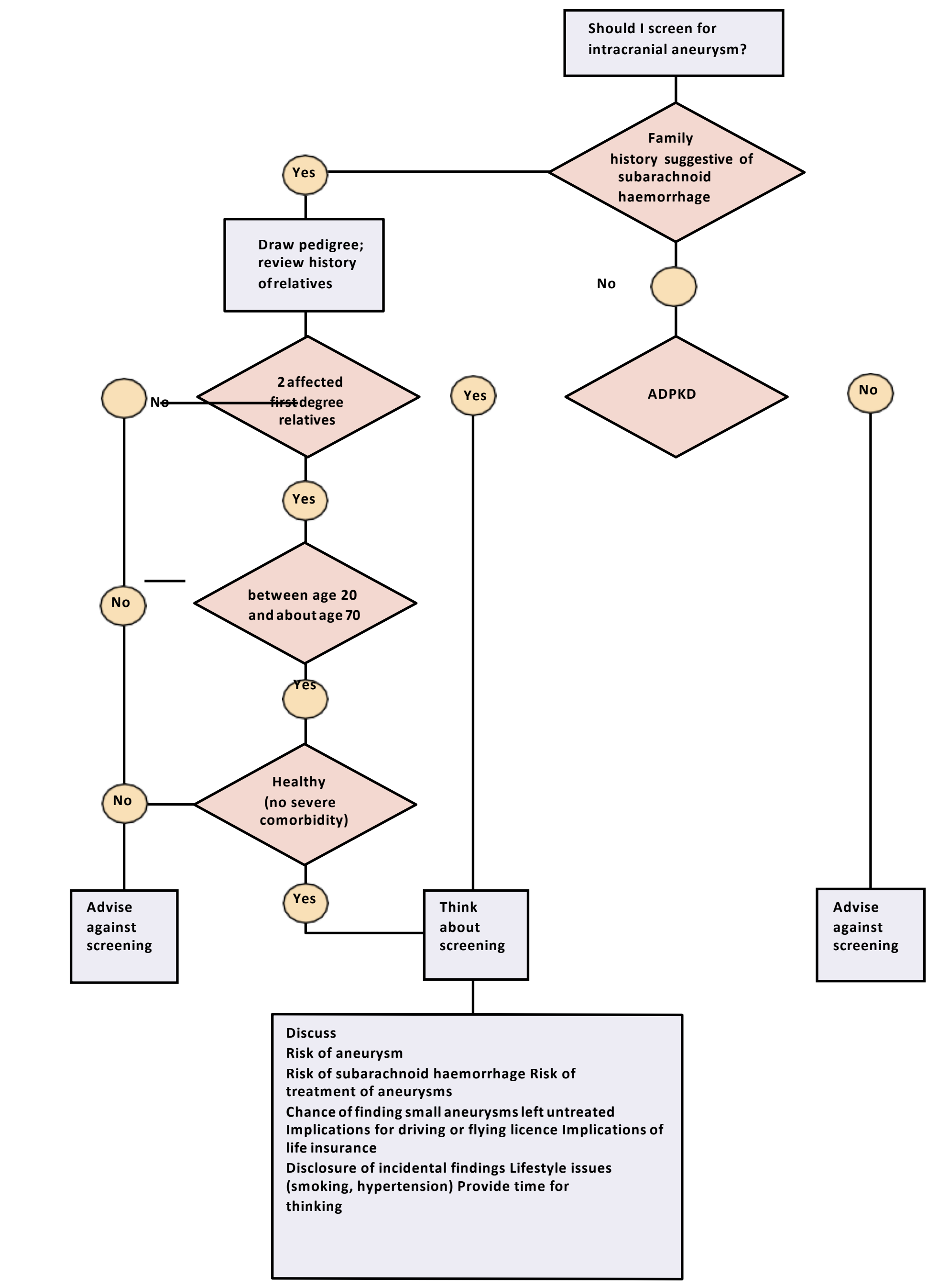
Lancet Neurol 2005; 4: 122–28

Gabriel JE Rinkel

Department of Neurology, University Medical Centre Utrecht, Netherlands (Prof GJE Rinkel MD)

Correspondence to: Prof Gabriel JE Rinkel, Department of Neurology, University Medical Centre Utrecht, PO box 85500, 3508 GA Utrecht, Netherlands g.j.e.rinkel@neuro.azu.nl

The advent of non-invasive methods of imaging intracranial blood vessels has facilitated screening for intracranial aneurysms in people who are at risk. A strong risk factor for intracranial aneurysm, which causes subarachnoid haemorrhage, is a positive family history, defined as two or more first-degree relatives with subarachnoid haemorrhages (relative risk [RR]=6·6). The greatest familial risk is associated with an affected sibling. Another strong risk factor is polycystic kidney disease (RR=4·4). People who have these risk factors are potential candidates for screening. Even if screening does not find abnormality, there is a high risk of new aneurysms 5 years later. Repeated screening might be done, although the optimum interval between screening assessments and the duration of repeated screening is unclear. Patients who have survived a subarachnoid haemorrhage are at increased risk of another from a newly developed aneurysm, but whether screening is beneficial in such patients is not clear. Most occurrences of subarachnoid haemorrhage in the general population are related to the more common risk factors of hypertension (RR=2·8) and smoking (RR=1·9). Therefore, screening of individuals who have a family history of subarachnoid haemorrhage or polycystic kidney disease will have little effect on the incidence of subarachnoid haemorrhage in the general population. When patients present for screening, the construction of a family tree and discussion of the history of relatives with stroke can be revealing. Before referring a patient for non-invasive imaging of the circle of Willis, the physician should discuss the risks and benefits of screening, the implications for holding a licence to drive or fly and for life insurance, and whether or not the patient wants to be informed about other incidental findings.



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Diploma Examination 2019

Monday Sept 2:

- 13-16 ECMINT Written Exam (arrival minimum 30 mins in advance)
- 13-19.30 EXMINT Oral Exam (you will have a time-slot of 45 mins, exact personal times will be announced later)

Tuesday Sept 3:

- 9-12 EXMINT Written Exam (arrival minimum 30 mins in advance)
- 9-16 ECMINT Oral Exam (you will have a time-slot of 45 mins, exact personal times will be announced later)

ECMINT
European Course of
Minimally Invasive Neurological Therapy

Dear ECMINT course member,

Our hearty congratulations on your great achievement fulfilling the criteria to be eligible to sit for the ESMINT Diploma! We look very much forward to welcoming you in Nice!

The ESMINT Diploma Examination 2018 will take place on ***Wednesday, 5 September at Hotel Le Méridien at 1 Promenade des Anglais in Nice***. The test will consist of three independent parts even though the two oral tests are done consecutively for each student. The three parts are:

- A written, computer-based test
- An oral exam with no cases
- A case presentation part

The written exam will start at 9 and finish at 12. ***You need to arrive no later than 8.30 so that we can start at 9 o'clock sharp.*** This theoretical part will contain 100 questions with 4-5 sub-questions in each, partially derived from the previous Oxford courses including anatomy, as well as some entirely new questions. As we have completed two full course cycles, the old questions will be identical or very similar between the two cycles and the new questions will mainly concern information that is of general interest or was given on both occasions. It should not matter in which cycle you participated. Please note, however, that some of the old questions may have been changed substantially, which means that if you think you recognize a certain question, you must consider that it may or may not have been altered. You consequently have to read every question carefully before answering, not just answer directly from memory. This theoretical part is completely computer based and similar to the final quizzes held at the courses. ***You have to bring your own laptop*** for this part and you will need 80% correct answers to pass. It is not allowed to view any other web-page during the test, anyone found doing that will be immediately disqualified.

After that we will have lunch and the oral exams start at 13.00. The examiners work in pairs, i.e. two examiners per student. Each participant will be given a time slot in the morning, which is chosen randomly: 13.00, 13.45, 14.30, 15.15 (15 min brake 16.00-16.15) 16.15, 17.00, 17.45, 18.30. The oral part is 45 minutes, 25 minutes for questions and 20 minutes for cases. Unfortunately, some of you will have to wait quite a long time for your slot but there will be a room prepared with drinks, sandwiches etc for this purpose. You may also leave the hotel but remember to return well in time for your oral exam.

ECMINT
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Dear ESMINT Diploma Examination participants,

Please find included the time-slots, the examination rooms and the examiners for the oral exams (question and cases) in the ESMINT Diploma Examination. A room (Espace Mougins) will be prepared for you with access to coffee, tea, soft drinks and snacks. The time-slots and the examiners have of course been randomly awarded.

We would also like to inform you that you will face three different kinds of questions in the written test:

1. Questions that are identical from the previous quizzes
2. Questions from the previous quizzes that have been changed
3. Completely new questions

This means that if you think you recognize a certain question, you have to please note that it may or may not have been altered. You consequently have to read every question carefully before answering, not just answer directly from memory.

Please remember, ***you have to bring your own laptop*** for this part. It is not allowed to view any other web-page during the test, anyone found doing that will be immediately disqualified.

We wish you the best of luck in the examination and are looking forward to meeting you in Nice!

Tommy Andersson
Shelley Renowden
James Byrne
Matthias Gawlitza

Schedule for the ESMINT Diploma Examinations at the Hotel Le Méridien:

Time		**Room**
08:30h	Arrival of all students	Biot
09:00h-12:00h	Theoretical Part	Biot
12:00h-13:00h	Lunch	Restaurant Le Colonial
13:00h-19:15h	Oral Part	Pls. see other document

Thank you!!!