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Follow-up screening after subarachnoid haemorrhage: frequency and determinants of new aneurysms and enlargement of existing aneurysms

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Intracranial aneurysms have long been considered a once in a lifetime event. Nevertheless, patients who survive after subarachnoid haemorrhage (SAH) may be at risk for new aneurysms. In a cohort of patients with clipped aneurysms, we studied the yield of screening in the years after the SAH and we tried to identify risk factors for formation of new aneurysms as well as for enlargement of aneurysms that were already present at the time of the SAH. We screened 610 patients who had been admitted between 1985 and 2001 for SAH by means of CT-angiography. Risk factors were evaluated by Cox regression analyses. With screening we detected 129 aneurysms in 96 (16%) patients, after a mean interval of 8.9 years. Of these, 24 (19%) were located at the site of the previously ruptured and clipped aneurysm and 105 (81%) at a site remote from the clip site. Of the aneurysms at a remote site 59 could be compared with the initial (CT)-angiogram. Of these, 19 were truly *de novo* (32%) and 40 (68%) were already visible in retrospect. Of the 53 aneurysms that were followed over time 13 (25%) had enlarged. Risk factors for aneurysm formation and growth were presence of multiple aneurysms at time of SAH (HR 3.2, 95% CI 1.2–8.6), current smoking (HR 3.8, 95% CI 1.5–9.4) and hypertension (HR 2.3, 95% CI 1.1–4.9). These results suggest that intracranial aneurysms should not be considered as a single event in a lifetime but rather as a continuous process. Patients with a previous SAH have a substantial risk for new aneurysm formation and enlargement of untreated aneurysms. Screening these patients might be beneficial, especially in patients with multiple aneurysms, hypertension and a history of smoking. The risks and benefits of screening, however, should be carefully weighed, for example, in a decision model.

Keywords: aneurysm; epidemiology; screening; subarachnoid haemorrhage

Abbreviations: CTA = CT-angiography; HR = hazards ratio; IA-A = intra-arterial angiography; MCA = medial cerebral artery; ROC = receiver–operator characteristic; SAH = subarachnoid haemorrhage

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Introduction

Subarachnoid haemorrhage (SAH) from a ruptured aneurysm is often considered a once in a lifetime event. However, the rarity of intracranial aneurysms under the age of 20 and the presence of multiple aneurysms in up to 30% of patients with SAH suggest that there is an ongoing development of aneurysms during life (Rinkel *et al.*, 1998). Patients with a history of SAH may, therefore, be at risk for new aneurysms despite successful treatment of the ruptured aneurysm at time of the SAH.

New aneurysms can develop at a new site (*de novo*) or adjacent to the clip or coil from the previous treatment (regrowth). Data on the incidence of *de novo* or regrowth aneurysms after treatment of ruptured aneurysms are sparse. Also the risk factors for formation of new aneurysms or the

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enlargement of additional (unruptured) aneurysms in patients with a history of SAH are not well known. In previous studies the incidence of *de novo* aneurysms has been reported as between 0.8 and 2.2% per year and the incidence of regrowth aneurysms after clipping ~0.5% per year (Juvela *et al.*, 1993; David *et al.*, 1999; Tsutsumi *et al.*, 2001). However, these series were small and often inhomogeneous.

Nowadays screening can be performed relatively easily with screening techniques that are not or only minimally invasive, such as CT-angiography (CTA) and MR-angiography (MRA). We assessed the number of aneurysms detected with screening by means of CTA in a cohort of patients who had been admitted with SAH between 1985 and 2001 and studied risk factors for new aneurysm formation and enlargement of already existing aneurysms.

Methods

Patients

After approval from the hospital ethics committees we selected from our databases of patients admitted with SAH, all patients who met the following inclusion criteria: (i) admission between 1985 and 2001 to the University Medical Centre Utrecht or admission between 1987 and 1998 to the Academic Medical Centre Amsterdam, (ii) confirmation of the SAH by CT and an aneurysm proven by CTA or conventional intra-arterial angiography (IA-A), (iii) treatment of the ruptured aneurysm by clipping, (iv) recovery to an at least partly independent state after treatment (defined as a score of $\leq$3 on the modified Rankin scale) (Bamford *et al.*, 1989) and (v) age between 18 and 70 years at the time of screening. Excluded were patients (i) who were not able to communicate well enough to give informed consent, (ii) those with severe co-morbidity or reduced life expectancy or (iii) patients in whom one or more aneurysms had been treated by coiling.

For all patients meeting the inclusion criteria we contacted the general practitioner to see if the patient was still alive and had not moved to a nursing home. Subsequently, we invited all patients to visit our outpatient clinic for more detailed information about the study. At the outpatient clinic we recorded the medical history, actual blood pressure, family history of intracranial aneurysms and possible other risk factors for aneurysm formation.

CTA and conventional intra-arterial angiography

CTA of the brain was performed by means of a multislice (MS)-CTA. One hospital used a 16-detector MS-CT (UMC), the other hospital used a 4-detector MS-CT (AMC). In patients with an allergy to iodinated contrast agents a 1.5 T MRA was performed. Two neuroradiologists in each hospital independently evaluated all CTAs. In case of disagreement the neuroradiologists tried to reach consensus in a common reading. If there was still disagreement after the consensus reading a third neuroradiologist was asked to provide a final decision. In all patients in whom, on CTA, an aneurysm was suspected at the clip site, IA-A was performed for confirmation. In patients with an aneurysm at a site remote from the clip site, IA-A was subsequently performed if the estimated size of the aneurysm was $\geq$3 mm. Patients with an aneurysm <3 mm were offered a control CTA after 1 year. IA-A was not performed in patients with a normal CTA.

Classification of aneurysms

If an aneurysm had already been described in the patient discharge letter or in the report of the angiogram at the time of the SAH, but was left untreated, we classified it as already known. If an aneurysm was detected that had not been described before, first, the neuroradiologists were asked to classify it either as an aneurysm at a location remote from the originally clipped aneurysm or as an aneurysm located at the clip site from the previous operation. Secondly, for all detected aneurysms the neuroradiologists had a second look at the angiograms that had been performed at time of the SAH, if still available. The hard copies of the angiogram or the digital datasets of the CTA at time of the SAH were available only in patients who had been admitted after 1992. The aneurysms at sites remote from the clip were subdivided into (i) *de novo* aneurysm (not visible on the initial CTA/IA-A), (ii) additional aneurysm (visible only in retrospect but not identified on the CTA/IA-A at the time of the SAH), (iii) probable *de novo* aneurysm (CTA or four-vessel IA-A performed at time of SAH, no aneurysm reported but CTA or angiogram no longer available for review) or (iv) unknown (unknown if a complete four-vessel IA-A was performed or if an incomplete IA-A was performed at time of SAH). The aneurysms located at the site of the clip were classified as (i) regrowth aneurysm (post-operative angiogram showed complete clipping of the aneurysm); (ii) remnant (post-operative angiogram showed incomplete clipping of the aneurysm); or (iii) unknown if post-operative angiography had not been performed or was not available for review.

Thirdly, the observers measured the size of all newly detected aneurysms. On the CTA the size of the aneurysm was measured directly. On IA-A the size of the aneurysm was related to the size of the carotid artery. If an aneurysm had already been present at time of the original SAH (additional or already known aneurysms), the neuroradiologists measured if the aneurysm had increased in size in the intervening years.

Data analysis

We recorded the overall number and proportion of aneurysms detected at screening and the number and proportion of different subgroups of aneurysms (*de novo*, regrowth, additional) with corresponding 95% CIs. We also calculated the number of aneurysms in the different subgroups per patient-year of screening. In addition we assessed the location and the size of the detected aneurysms and the frequency and rate of enlargement of aneurysms in patients with an additional or already known aneurysms.

We used Cox regression to calculate hazard ratios (HR) and corresponding 95% CIs of factors associated with aneurysm formation and enlargement. For the Cox regression analyses and the calculations of the number or aneurysms per patient-year of screening we assumed that the new aneurysms had developed at halfway between the SAH and the screening. Risk factors for aneurysm formation were analysed by comparing the characteristics of patients with a definite *de novo* or a regrowth aneurysm with those of patients with a negative screening. Similarly, risk factors for aneurysm enlargement were analysed by comparing the characteristics of patients who had an additional or already known aneurysm that had grown in the time after the SAH with those of patients who had an additional or already known aneurysm that had not enlarged in size. In a second analysis we included both the patients with a newly developed aneurysm (definite *de novo* or regrowth) and the patients with an aneurysm

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Table 1 Characteristics of all patients and different subgroups of patients

Characteristic	All (*N* = 610)	No aneurysm (*N* = 498)	*De novo* (*N* = 14)	Regrowth (*N* = 3)	Enlargement (*N* = 13)
Age at time of screen (mean years)	53	53	50	55	55
Age at SAH (years)					
<40	196 (32%)	162 (32%)	8 (57%)	1 (33%)	3 (23%)
40–60	384 (63%)	313 (63%)	6 (43%)	2 (66%)	8 (62%)
>60	30 (5%)	23 (5%)	0 (0%)	0 (0%)	2 (15%)
Women	391 (64%)	315 (63%)	12 (85%)	2 (66%)	9 (69%)
Current smoker	312 (51%)	246 (49%)	11 (79%)	2 (66%)	9 (69%)
Former smoker	190 (31%)	153 (31%)	3 (21%)	1 (33%)	2 (15%)
Never smoker	108 (18%)	99 (20%)	0 (0%)	0 (0%)	1 (8%)
Alcohol use >5 drinks a day	27 (4%)	22 (4%)	1 (7%)	0 (0%)	1 (8%)
Former use >5 drinks a day	22 (4%)	20 (4%)	0 (0%)	0 (0%)	0 (0%)
Alcohol use <5 drinks a day	396 (65%)	323 (65%)	7 (50%)	3 (100%)	7 (54%)
Never	165 (27%)	133 (27%)	6 (43%)	0 (0%)	5 (38%)
Family history of IA	96 (16%)	83 (17%)	9 (64%)	1 (33%)	2 (15%)
History of hypertension	264 (43%)	208 (42%)	7 (50%)	2 (66%)	9 (69%)
Number aneurysms at SAH*					
1	481 (79%)	432 (87%)	9 (64%)	2 (66%)	0 (0%)
2	89 (15%)	46 (9%)	3 (21%)	1 (33%)	9 (69%)
3	32 (5%)	17 (3%)	2 (14%)	0 (0%)	3 (23%)
4	8 (1%)	3 (1%)	0 (0%)	0 (0%)	1 (8%)
Location of aneurysm at SAH†					
ACA	261 (43%)	230 (46%)	7 (50%)	1 (33%)	4 (31%)
ICA	168 (27%)	133 (27%)	2 (14%)	1 (33%)	5 (38%)
MCA	137 (23%)	102 (20%)	3 (21%)	1 (33%)	4 (31%)
Vertebrobasilar	44 (7%)	33 (7%)	2 (14%)	0 (0%)	0 (0%)

*Number of aneurysms at SAH = number of aneurysms at time of SAH including the aneurysms that were not described at time of SAH but could be identified in retrospect. †ACA, anterior communicating artery; ICA, internal communicating artery; MCA, medial cerebral artery.

that had enlarged and compared the risk factors in these two groups together with those in patients with a negative screening.

The following characteristics were included in the analyses: age at time of SAH (continuous), sex, smoking (dichotomous: current versus former plus never smokers and categories), alcohol use (categories: never drink, <5 drinks a day, former use of >5 drinks a day and current use of >5 drinks a day), history of hypertension, blood pressure values at time of screening [categories: normal (systolic blood pressure (SBP) <140 mmHg and/or diastolic blood pressure (DBP) <90 mmHg), borderline (SBP 140–160 mmHg and/or DBP 90–95 mmHg) or hypertension (SBP >160 mmHg and/or DBP >95 mmHg)], family history of intracranial aneurysms (defined as ≥1 first-degree relative(s) with a verified aneurysm or a history very suggestive of SAH, such as relatives who died after sudden very severe headache), location of the ruptured aneurysm at the time of SAH [categories: internal carotid artery, anterior cerebral artery, medial cerebral artery (MCA), vertebrobasilar and dichotomous: MCA versus other locations] and the number of aneurysms at the time of SAH (dichotomous: one versus multiple). We performed univariate Cox regression analysis for all risk factors and multivariate Cox regression analysis with forward selection of variables with probability values <0.20 in the univariate analysis. We tried to find a combination of variables that most accurately predicted the occurrence of new aneurysm development or enlargement. We used receiver–operator characteristic (ROC) curves to evaluate the information content of the predictive model. The higher an ROC curve is located in the upper left corner of the graph, the more is the area under the curve and the higher are both sensitivity and specificity for the prediction of new formation of enlargement of an aneurysm.

Results

Frequency of detected aneurysms

In the period 1985–2001 (UMC, Utrecht) and the period 1987–1998 (AMC, Amsterdam) a total of 1455 patients were discharged after treatment of the ruptured and all additional aneurysms. From these 1455 patients 396 were excluded because they were too young or too old, 125 because they had died after discharge, 87 because they stayed in a nursing home or had severe co-morbidity, 59 because they were coiled and 13 for other reasons like language problems. In 10 of the 125 patients who died after discharge the cause of death was a recurrent SAH, and in 2 of the 87 patients who stayed in a nursing home the cause of admission was disability from a recurrent SAH. In total, 775 patients met the inclusion criteria. Of these patients, 99 declined screening, 21 had moved abroad, 14 were lost to follow-up and 31 were not approached (because the study had already ended). We screened a total of 610 patients. Their mean age was 53.5 years (range: 24–70); 391 (64%) were women (Table 1). The age and sex distribution of the non-participants was comparable with the distribution of the screened patients. The mean interval after the SAH was 8.9 years (range: 2.3–18.8). We found 129 new aneurysms in 96 of the 610 patients (16%; 95% CI 13–19%), i.e. aneurysms not identified at the time of the presenting SAH. In addition, 22 aneurysms in 17 patients were already known to be present. In total, we found

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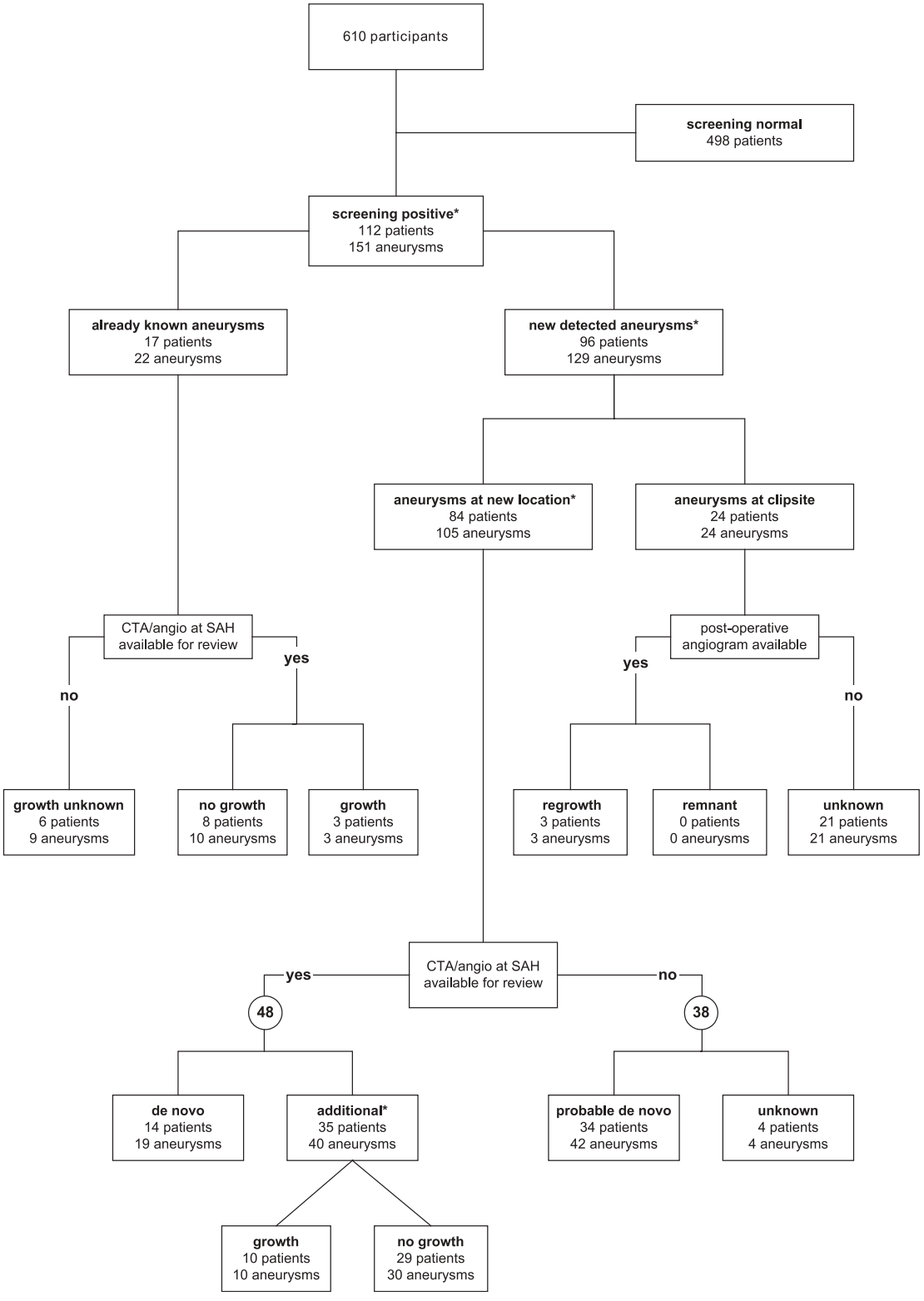

Fig. 1 Different subgroups of aneurysms detected at screening. *The number of patients in the subcategories does not always add up to the number of patients in the main categories because patients are sometimes classified in more than one subcategory.

151 aneurysms in 112 (18%; 95% CI 15–22%) of the 610 patients (Fig. 1).

Of the 129 aneurysms that were not described at the time of the SAH, 24 (19%) were located at the site of the clip placed at the previous operation and 105 (81%) were located at a site remote from the clip site. For 59 of the 105 aneurysms that were detected at a remote site the CTA/IA-A at the time of the SAH was available for review. Of these 59 aneurysms 19 (32%)

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were classified as definitely being *de novo* and 40 (68%) were classified as additional. In 3 of the 24 patients with an aneurysm at the clip site a post-operative angiogram was available for review, which showed no aneurysm; these 3 aneurysms were therefore classified as regrowth. The size and location of the different aneurysms are shown in Fig. 2 and an example of a regrowth and a *de novo* aneurysm is shown in Fig. 3.

Out of 112 patients with aneurysms, 84 (75%) had a single aneurysm at screening, 18 (16%) had two aneurysms, 9 (8%) had three aneurysms and 1 (1%) patient had four aneurysms.

New aneurysm formation

In the first 5 years after SAH a *de novo* aneurysm was found in 1 of 120 patients (0.8%; 95% CI 0–5.2%) and in 8 of 365 patients (2.2%; 95% CI 1.0–4.4%) in the first 10 years after SAH and overall in 14 of 610 patients (2.3%; 95% CI 1.3–3.9%). In the total number of 5078 years of follow-up we found 19 definite *de novo* aneurysms (in 14 patients) and 42 probable *de novo* aneurysms (in 34 patients), which corresponds with an annual incidence of *de novo* aneurysms between 0.37 (95% CI 0.23–0.60%) and 1.20% (95% CI 0.93–1.55%). The mean interval for the detection of the 19 definite *de novo* aneurysms was 9.1 years after SAH (range: 4.4–13.7).

An aneurysm at the clip site occurred in the first 5 years after SAH in 2 of 120 patients (1.7%; 95% CI 0.3–6.5%), in the first 10 years after SAH in 10 of 365 patients (2.7%; 95% CI 1.4–5.1%) and overall in 24 of the 610 (3.9%; 95% CI 2.6–5.9%) patients. The total of 24 aneurysms at the clip site in 24 patients (including three definite regrowths) in 5078 years of follow-up corresponds to an annual incidence between 0.06% (95% CI 0.02–0.19%) and 0.47% (95% CI 0.31–0.71%). The mean interval after which we detected an aneurysm at the clip site was 10.6 years after SAH (range: 4.3–15.5). The three certain regrowth aneurysms were detected 13, 14 and 15 years after treatment.

Enlargement of already present aneurysms

For 53 of the 62 aneurysms that were already present at the time of the SAH (40 additional and 13 already known) the initial CTA/IA-A was available for assessment of enlargement. In the first 5 years after SAH 4 of 18 aneurysms enlarged (22.2%; 95% CI 7.4–48.1%), in the first 10 years after SAH 9 of 45 aneurysms had enlarged (20.0%; 95% CI 10.1–35.1%) and overall 13 of 53 aneurysms enlarged (24.5%; 95% CI 14.2–38.6%) between the SAH and the screening. Four patients had one additional aneurysm that had enlarged and another additional aneurysm that had remained stable. Eleven aneurysms enlarged 1–3 mm, one enlarged 3–5 mm and one aneurysm enlarged >5 mm. The mean enlargement rate per aneurysm varied between 0.12 and 1.3 mm per year.

Risk factors for aneurysm formation and enlargement

In the univariate Cox regression analysis current smoking (HR 3.2, 95% CI 1.0–9.7), a positive family history of intracranial aneurysms (HR 2.7, 95% CI 1.0–7.4), and the presence of multiple aneurysms at time of the SAH (HR 3.3, 95% CI 1.2–8.9) were significantly related with the formation of a *de novo* or regrowth aneurysm. Sex was not statistically significant in the univariate analyses but had a *P*-value of <0.2 (HR for men 0.4, 95% CI 0.1–1.3) and was therefore included in the multivariate analyses. In the multivariate forward Cox regression analyses current smoking (HR 3.1, 95% CI 1.0–9.4) and multiple aneurysms (HR 3.2, 95% CI 1.2–8.6) were both statistically significant risk factors. The predictive model with these two characteristics had an ROC area under the curve of 0.68.

In the univariate Cox regression analysis for enlargement only current smoking had a *P*-value < 0.20 (HR 4.5, HR 0.99–20.1), hence we performed no multivariate analyses for risk factors for enlargement.

In the univariate Cox regression analysis for the formation of new aneurysms and the enlargement together, current smoking (HR 3.5, 95% CI 1.4–8.7), sex (HR 0.5 for men, 95% CI 0.2–1.2) and history of hypertension (HR 1.9, 95% CI 0.9–4.4) were related to formation or enlargement of aneurysms and included in the multivariate analysis. In the multivariate analysis, current smoking (HR 3.8, 95% CI 1.5–9.4) and a history of hypertension (HR 2.3, 95% CI 1.1–4.9) remained statistically significant. The predictive model with these two characteristics had an ROC area under the curve of 0.69.

Discussion

We found that screening in patients with a history of SAH has a high yield; in one-sixth of the patients an aneurysm was detected that had not been described before. In half of the patients in whom the CTA/IA-A at the time of the SAH was available for review, the detected aneurysm was *de novo* or had increased in size. This high risk of recurrent aneurysms indicates that development of intracranial aneurysms should not be considered as a once in a lifetime event but rather as a continuous process. Also, small aneurysms cannot always be considered stable lesions.

Important risk factors for aneurysm development and enlargement of the already existing aneurysms were multiple aneurysms, a history of hypertension and current smoking. Other risk factors in the univariate analysis were a positive family history and female sex. These risk factors, except of course the presence of multiple aneurysms, are similar to those for intracranial aneurysms and SAH in general. Smoking and female sex have been identified before as an important risk factor for new aneurysm formation and enlargement of already present aneurysms in patients with a history of intracranial aneurysms or SAH (Juvela *et al.*, 2001). Our predictive model for aneurysm formation and enlargement may help to identify the patients at the highest risk for recurrent aneurysms and SAH. However, before it can be used in clinical practice it should be validated in a new group of patients. Nevertheless, the present data indicate that

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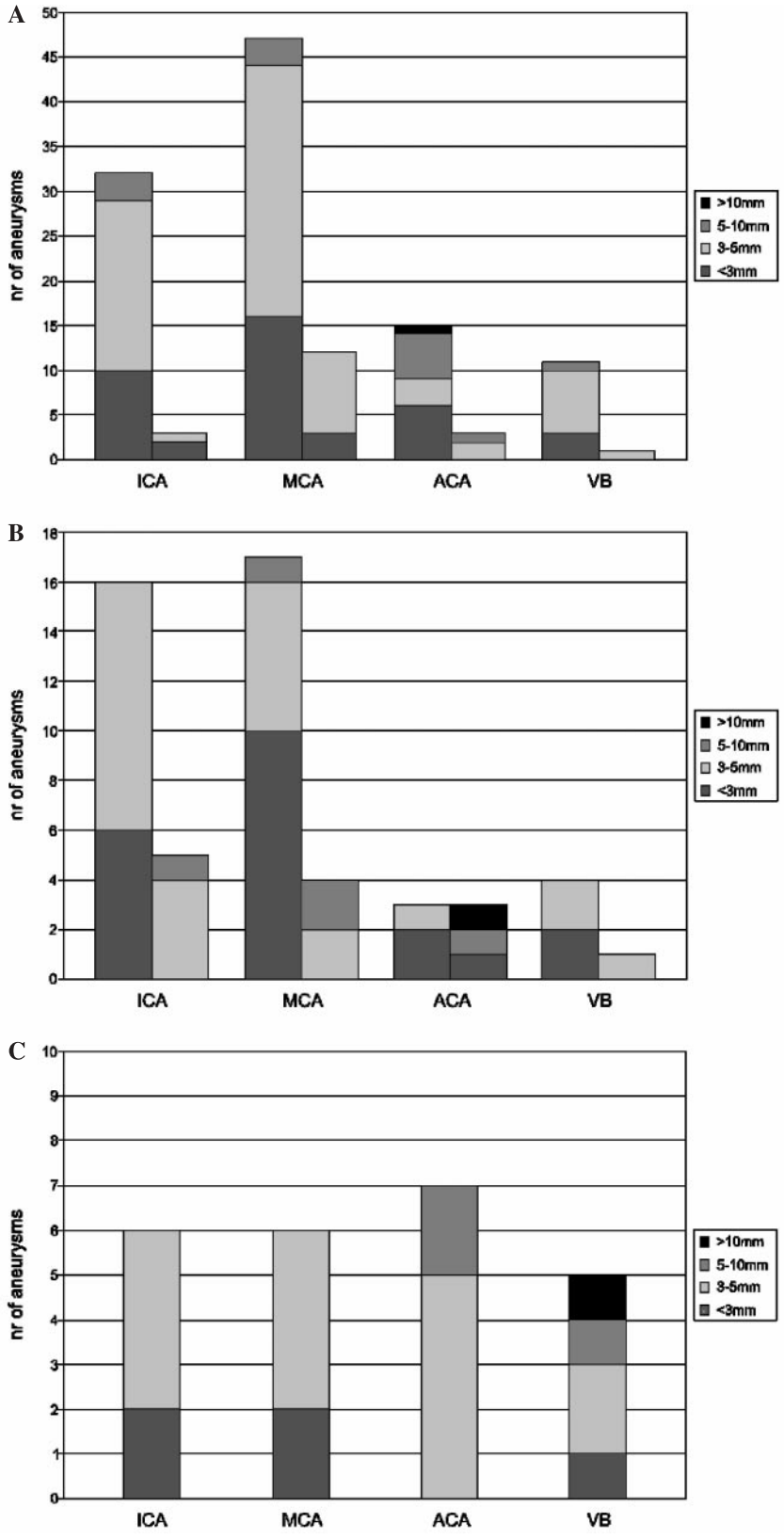

Fig. 2 Size and location of different subgroups of aneurysms: *x*-axis, location; *y*-axis, number of aneurysms. (**A**) All new aneurysms detected at another location than the clip site and all definite *de novo* aneurysms. The left bars represent all aneurysms detected at a location remote from the clip site ($n = 105$). The right bar presents the subgroup of the *de novo* aneurysms ($n = 19$). (**B**) Aneurysms already present at time of SAH (already known or additional). The left bars represent all aneurysms that remained stable in size ($n = 40$). The right bars represent all aneurysms that enlarged over time ($n = 13$). (**C**) All aneurysms detected at the clip site ($n = 24$).

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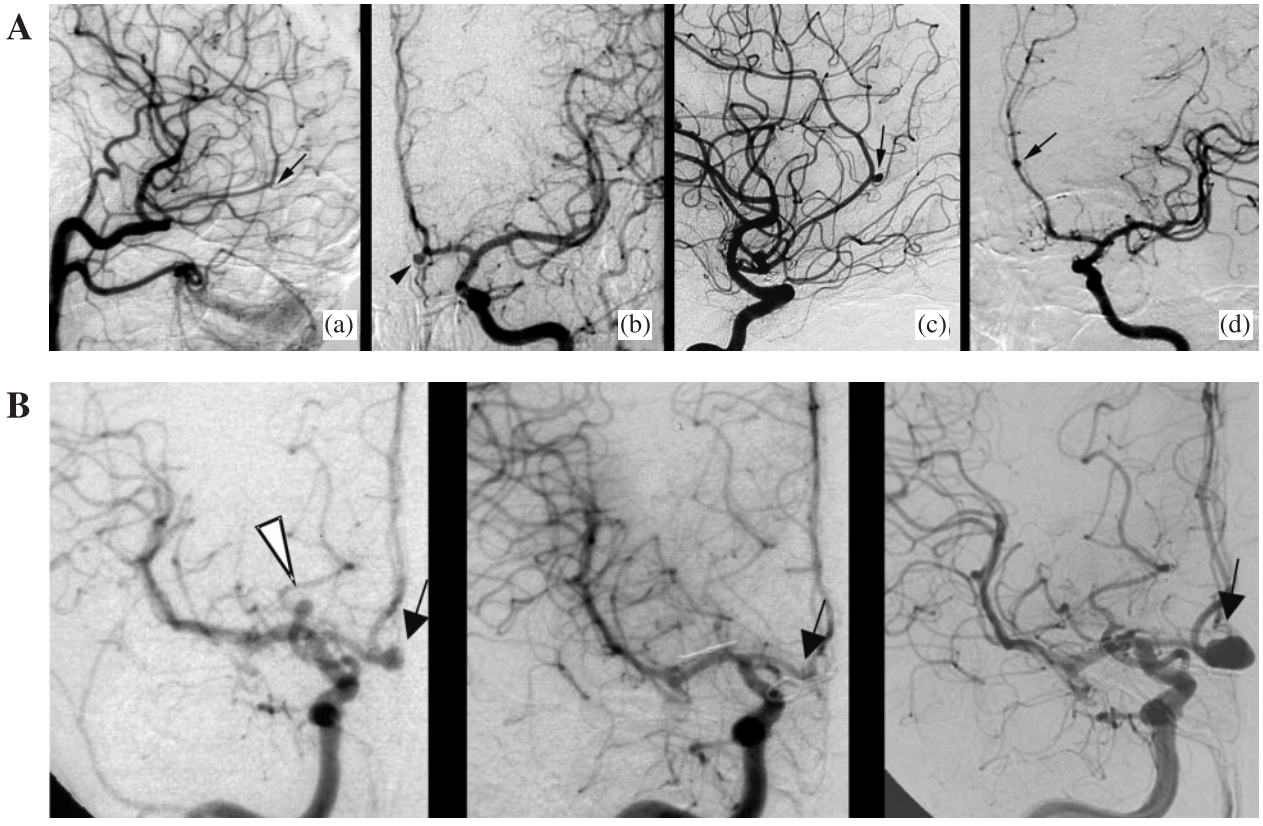

Fig. 3 An example of a *de novo* and a regrowth aneurysm. (**A**) IA-A of 1993 (a and b). Left common carotid artery injection with lateral view (a) and anteroposterior view (b) of the internal carotid artery showing an anterior communicating artery aneurysm (arrowhead) and no aneurysm on the pericallosal artery (arrow) IA-A of 2003 (c and d) 10 years after clipping of the anterior communicating artery aneurysm. Lateral (c) and anteroposterior view (d) after selective left internal carotid artery injection demonstrating an anterior communicating artery aneurysm adjacent to the clip site (arrowhead) and a *de novo* pericallosal aneurysm (arrow). (**B**) IA-A (anteroposterior view) of 1992 (left and middle) and 2003 (right). Left: IA-A at time of SAH with an aneurysm on the anterior communicating artery (Acom) (arrow) and the right middle cerebral artery (MCA) (arrowhead). Middle: post-operative IA-A with completely clipped aneurysms of the Acom and right MCA. Right: follow-up IA-A shows a regrowth Acom aneurysm at the clip site (arrow).

hypertension should be closely monitored and treated, and that patients should strongly be discouraged from starting or continuing smoking.

To assess risk factors for formation of new aneurysms and enlargement of existing aneurysms we first analysed these events separately and subsequently together. The mechanisms of formation and enlargement may be rather similar, since for formation of an aneurysm enlargement from very small irregularities can be assumed. Moreover at surgery often weak spots in vessels are observed that possibly develop into an aneurysm.

For the Cox regression analyses and the calculations of the number of new aneurysms per patient-year screening we assumed that the new aneurysms had developed halfway between the SAH and the date of screening. It is, however, unknown at what time the aneurysms we detected truly developed. In additional analyses we assumed that the new aneurysms had occurred at the date of screening. In this analysis the HR and the incidences of new aneurysm formation changed no more than 5% compared with the original analyses. We feel, therefore, confident that our assumption regarding the timing of aneurysm formation hardly affects the results of our study.

MS-CTA is a technique that is suitable for screening since it is minimally invasive and has no vascular complications as in IA-A. The diagnostic properties of MS-CTA in detecting aneurysms in clipped patients are comparable with IA-A for aneurysms at new locations (Wintermark *et al.*, 2003). However, for aneurysms adjacent to the clip site the test characteristics are less favourable because of clip artefacts (Teksam *et al.*, 2004). We, therefore, have probably underestimated the number of aneurysms that developed at the clip site. In all three patients in whom a post-operative angiogram was available for review, the IA-A demonstrated complete clipping of the ruptured aneurysm. This shows that, as in coiling, the long-term durability of clipping is not perfect.

Because of the age criteria for our study the population examined was somewhat younger than expected in an unselected population 9 years after SAH. We did not include patients in our study who were older than 70 years at the time of the screening since the risk of complications of

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treatment of aneurysms in this patient group is high and the life expectancy is relatively short. Therefore, if an aneurysm is detected at screening in most of these cases treatment will not be recommended. Our results, therefore, only apply for patients younger than 70 years at the time of screening.

In the study hospitals aneurysms <3 mm are not treated but followed over time. Since IA-A is not without risks, patients with a small aneurysm on CTA did not undergo IA-A for confirmation. We therefore cannot exclude the possibility that in some of these patients the finding classified as aneurysm will be an infundibulum or a venous overprojection.

From the 125 patients who had died and the 87 patients who stayed in a nursing home after discharge, the cause of death or disability was a recurrent SAH in 12. By not including these patients in our calculations on the risk of *de novo* and regrowth aneurysms we have underestimated this risk. Conversely, had these 12 patients been included in the analysis of the study we would have overestimated the incidence of *de novo* and regrowth aneurysms by confounding by indication. The reason for this confounding is that many patients died and others became disabled after recovery from the SAH from other causes than from recurrent SAH. For proper analysis, the follow-up years of these patients and the presence or absence of new aneurysms at the time of death or disability from other causes should have been included. Obviously, no screening in these patients was performed and therefore, some of them might also have had *de novo* or regrowth aneurysms. Including these patients as having no aneurysm would cause dilution of the true incidence of *de novo* and regrowth aneurysms. We, therefore, decided not to include these 12 patients in our calculations. The incidence of recurrent aneurysms in our study is, therefore, the risk found in a population that is alive and clinically suitable for screening. Our present study was not designed to assess the prevalence of recurrent SAH in patients with a history of SAH.

The CTA/IA-A at the time of SAH was available only for patients admitted for SAH after 1992. In these patients where the screening CTA could be compared with the initial CTA/IA-A the proportion of definite *de novo* aneurysms was one-third. The remaining aneurysms detected at screening were, in retrospect, already present at time of the SAH. If the same proportion of *de novo* aneurysms is assumed in the patients for whom the initial CTA/IA-A was no longer available for comparison, the average risk of a *de novo* aneurysm was 0.65% per person year, with a relatively low risk in the first years after SAH and a relatively high risk thereafter. This risk is slightly lower than in previously published estimates of *de novo* aneurysms, but in those studies it is unclear if all angiograms at time of the SAH were available for review and therefore, additional aneurysms might have been classified as *de novo* aneurysms (Juvela *et al.*, 1993; David *et al.*, 1999; Tsutsumi *et al.*, 2001). In our study we included only patients with aneurysms treated by neurosurgical clipping. It is likely that the number of *de novo* aneurysms in coiled patients will be comparable with the number of *de novo* aneurysms we found for the clipped patients. The numbers of regrowths or remnants caused by impaction of coils, however, might differ from those after clipping.

A quarter of the aneurysms that were already present at the time of the SAH subsequently enlarged. Enlarging aneurysms have a relatively high risk of rupture, because size is an important determinant of the risk of rupture and perhaps also because enlarging aneurysms are unstable (Juvela *et al.*, 2001; Wiebers *et al.*, 2003). Small additional aneurysms that cannot be treated by coiling and that cannot be occluded at the same time as the ruptured aneurysm may need regular monitoring by CTA or angiography, but the yield and frequency of such monitoring requires a separate study.

We showed that screening in patients with a history of SAH reveals many previously undetected aneurysms. The outcome of a recurrent SAH is as poor as that from a first episode of SAH (Wermer *et al.*, 2005). Routine follow-up screening might, therefore, be efficient after SAH, especially in patients with additional risk factors. Screening, however, also has disadvantages. Although with the advent of coiling the majority of aneurysms can be treated with relatively low risk of complications, preventive treatment can lead to disability and even death. Furthermore, small aneurysms will often not be treated. The knowledge of having an untreated aneurysm can lead to a decrease in quality of life (van der Schaaf *et al.*, 2002). Before screening after SAH is implemented in clinical practice, the risk and benefits of screening should, therefore, be carefully weighed, for example, in a decision model.

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