Long term follow-up of patients with coiled intracranial aneurysms
Sprengers, M.E.S.

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Chapter 6

MR angiography follow-up 5 years after coiling: frequency of new aneurysms and enlargement of untreated aneurysms

Marieke E.S. Sprengers
Willem Jan van Rooij
Menno Sluzewski
Gabriël J.E. Rinkel
Birgitta K. Velthuis
Gerard A.P. de Kort
Charles B.L.M. Majoie

ABSTRACT

**Background and purpose:** Patients with intracranial aneurysms are at risk for future development of new aneurysms and growth of additional untreated aneurysms. Since in previous long-term follow-up studies duration of follow up varied widely, the time interval after which screening could be effective remains largely unknown. The purpose of this study was to assess incidence of de novo aneurysm formation and growth of additional untreated aneurysms in patients with coiled aneurysms followed with MRA after a fixed period of 5 years.

**Materials and Methods:** In 65 patients with a coiled intracranial aneurysm, high resolution 3.0T MRA was performed 5.1 ± 0.2 years after coiling. MRA follow up imaging was compared with angiography or CTA at the time of coiling. Additional aneurysms detected at MRA follow up were classified as unchanged, grown, de novo or incomparable with previous imaging.

**Results:** In 13 of 65 patients (20%), 24 additional aneurysms were found. Four aneurysms were incomparable with previous imaging and 2 of these were clipped. Of the remaining 20 additional aneurysms one was de novo, one had slightly grown and 18 were unchanged. Incidence of de novo aneurysm formation after 5 years was 1.54% (95%CI 0.01-9.0%). For additional aneurysms known at the time of initial coiling and for the one de novo aneurysm, no treatment was judged indicated.

**Conclusion:** MRA screening five years after coiling for detection of de novo aneurysms and for growth of additional untreated aneurysms has a low yield in terms of finding aneurysms that need to be treated.
INTRODUCTION

In a substantial proportion of patients presenting with an intracranial aneurysm, small additional aneurysms are found. Some of these additional aneurysms may be surgically or endovascular treated in the same or a repeat procedure, but many will be left untreated because of small size, unfavorable aneurysm geometry or location remote from the target aneurysm. Apart from this, patients with treated intracranial aneurysms are at risk for developing new aneurysms with time. Little is known about the frequency of de novo aneurysm formation and pace of growth of small additional aneurysms that were left untreated. In particular, the time period after which screening for these events could be effective, is unknown. In a recent study of 610 patients with ruptured aneurysms that were clipped, after 2-18 years of follow-up de novo aneurysms had developed in 3% of patients and 25% of additional aneurysms had enlarged. Since follow up intervals varied widely, the time of first development or growth remained obscure. The purpose of the current study was to assess incidence of de novo aneurysm formation and determine natural history of additional untreated aneurysms in 65 patients with coiled intracranial aneurysms after a fixed follow up period of 5 years.

PATIENTS AND METHODS

Patients

This study was approved by the Institutional Review Board of the three participating hospitals in The Netherlands (St. Elisabeth Ziekenhuis Tilburg, Academisch Medisch Centrum Amsterdam and Universitair Medisch Centrum Utrecht) and written informed patient consent was obtained. From the databases of the three centers we selected all patients with a ruptured or unruptured aneurysm coiled in the period January 1, 1995 – December 31, 2002, and with adequate aneurysm occlusion (complete occlusion or small neck remnant) at 6 months angiographic follow-up. Further inclusion criteria were current age between 18-70 years, independent functional state, and no contra-indication for 3.0T-MRI. All aneurysms were treated with Guglielmi Detachable Coils (Boston Scientific, Fremont, CA).

We contacted the general practitioner of all eligible patients to find out if the patient was still alive. If patients had died we asked for the date and the cause of death. If a patient had died in a hospital or other facility, we reviewed the medical records. The patients who were still alive received a letter with background information and an invitation to participate in this MR follow-up study. Patients who consented were invited for MR imaging. A written report of the MR findings was sent to the general practitioner and patients were informed about results by telephone or at the outpatient clinic. The long-term follow-up MR data were analyzed for assessment of long term stability of coiled intracranial aneurysms with adequate occlusion at 6 months. For the purpose of this study, we selected those patients with MRA follow-up of 5 years.

MRI and MRA follow-up protocol

MR examinations were performed on a 3.0-T system (Philips Intera R10, Philips Medical Systems, Best, The Netherlands) using the sensitivity encoding (SENSE) phased array head coil (MRI Devices, Gainesville, FL). MR imaging protocol included axial T2-weighted fast spin echo and multiple overlapping thin slab acquisition 3-dimensional time of flight (MOTSA 3D-TOF) MRA sequences. Imaging parameters for the T2-weighted fast-spin echo sequence were 3394/80
(TR/TE), 400x400 matrix (reconstructed to 512x512), 230-mm field of view, 5 mm thick sections with a 0.5 mm gap. The volume of the MOTSA 3D-TOF MRA was localized on a sagittal 2D phase-contrast scout image. A presaturation band was applied above the imaging volume to saturate incoming venous blood. For the MOTSA 3D-TOF MR sequence the parameters were: 3D fast field echo T1-weighted sequence, 21/4 (TR/TE), flip angle 20º, 512x512 matrix (reconstructed to 1024x1024), 200 mm field of view, 85% rectangular field of view, 1.0 mm thick sections, interpolated to 0.5 mm, 160 slices acquired in 8 chunks. The measured voxel size of the MOTSA 3D-TOF MR sequence was 0.39x0.61x1 mm and the reconstructed voxel size was 0.2x0.2x0.5 mm. Acquisition time of the high-resolution MOTSA 3D TOF sequence was reduced by SENSE parallel imaging. Total MR examination time was 20 minutes. Usefulness of this 3.0T-MRA protocol in follow-up of coiled intracranial aneurysms was validated in a previous study. 3

MRI and MRA evaluation

MRI and MRA imaging (axial source images, maximum intensity projections and volume rendered images) was evaluated and compared with previous imaging studies in 2 institutions by 2 experienced neuroradiologists (M.S. and C.M. or B.V. and G.K) independently. Discrepancies were resolved in consensus.

Location and size of additional aneurysms were recorded and compared with angiography or CTA at the time of coiling. Subsequently, these aneurysms were classified as unchanged, grown, de novo or incomparable with previous imaging.

Clinical implication in terms of treatment advice and change of follow up imaging policy of these 5-year-follow-up findings was assessed.

RESULTS

Between January 1, 1995, and December 31, 2002, 666 aneurysms in 612 patients were coiled in the 3 participating centers (Tilburg, 483 [76%]; Utrecht, 105 [16%]; and Amsterdam, 24 [8%]). Of 612 patients, 457 with 497 aneurysms had 6-month follow-up angiography, and 316 aneurysms in 297 patients were adequately occluded at this first angiographic follow-up (Fig 1). Of 297 eligible patients with 316 aneurysms, 84 were excluded for the following reasons: dependent functional state in 5, age older than 70 years in 39, 3T MR imaging contraindication in 27 (clipped additional aneurysms in 18, claustrophobia in 4, and a pacemaker in 5), unrelated death in 13 (cancer in 6, cardiovascular disease in 3, old age in 1, and unknown but unlikely subarachnoid hemorrhage in 3). Seventy-three patients could not be traced, but many of these patients had previous clinical or angiographic follow-up beyond the 6-month interval. The remaining 140 patients were invited to participate in the study, of which 36 declined. Thus, 104 patients (Tilburg, 74 [71%]; Utrecht, 25 [24%]; and Amsterdam, 5 [5%]) with 111 aneurysms were followed up with MRA.

Of the total 104 patients 39 patients with 46 aneurysms had a follow-up interval of more than 5 years. Sixty-five patients with 65 coiled aneurysms had a consistent MRA follow-up of 5.1 ± 0.2 years after coiling. These patients are the subject of this study. There were 46 women and 19 men with a mean age of 54 years (39-70 years). Of 65 coiled aneurysms, 54 were ruptured and 11 unruptured.

In 13 of 65 patients (20.0%), 24 additional aneurysms were found. Patient and aneurysm characteristics of patients with additional aneurysms on 5 year MRA follow-up are displayed in the Table. Eight patients had 1 additional aneurysm, 2 patients had 2 and 3 patients had 3 or more
additional aneurysms. In 3 of 24 additional aneurysms, no previous imaging was available and these aneurysms were classified as incomparable. In another 1 mm choroidal artery aneurysm, the projections of the initial carotid artery angiogram did not allow verification of its presence or absence and this aneurysm was also classified as incomparable. The remaining 20 additional aneurysms could be compared to previous imaging: 18 of 20 were classified as unchanged, 1 as grown and 1 as de novo.

The 18 unchanged additional aneurysms were present in 11 patients. Sizes ranged from 1-6 mm, an example is provided in figure 2. The only additional aneurysm that had grown was a pericallosal artery aneurysm in a patient with 5 additional aneurysms that increased in size from 1.5 mm to 2.5 mm in 5 years (fig. 3). The only definite de novo aneurysm was a 3 mm middle cerebral artery aneurysm (fig 4).

The 4 additional aneurysms that could not be compared with previous imaging were present in 2 patients. One patient had the 1 mm choroidal artery aneurysm that could not be verified on the available projections of the carotid angiogram. The other patient had four additional aneurysms, 3 of which were not imaged before. Location and size of these 3 aneurysms was one on the superior cerebellar artery (3 mm) and 2 on the left middle cerebral artery (3 and 6 mm) (fig. 5).

Incidence of de novo aneurysms
Five years after coiling a de novo aneurysm was found in 1 of 65 patients (1.54%; 95% CI 0.01-9.0%)

Clinical implications of 5 year follow-up
Of 24 additional aneurysms, 2 left middle cerebral aneurysms in 1 patient classified as incomparable with previous imaging were clipped without complications. For the remaining 22 additional aneurysms, treatment was considered not indicated and no specific follow-up policy was advised. Thus, for additional aneurysms that were known at the time of initial coiling and for the one de novo aneurysm, no treatment was considered needed.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Characteristics of 13 patients with 24 additional aneurysms detected on 5 years MRA follow up.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>12 (92%)</td>
</tr>
<tr>
<td>Age</td>
<td>mean 52; range 40-70 years</td>
</tr>
<tr>
<td>Ruptured aneurysms</td>
<td>11 (85%)</td>
</tr>
<tr>
<td>aneurysm size</td>
<td>mean 3.1; range 1-6 mm</td>
</tr>
<tr>
<td>&gt;1 additional aneurysm</td>
<td>5 (38%)</td>
</tr>
<tr>
<td>anterior cerebral artery</td>
<td>4</td>
</tr>
<tr>
<td>middle cerebral artery</td>
<td>10</td>
</tr>
<tr>
<td>posterior circulation</td>
<td>3</td>
</tr>
<tr>
<td>internal carotid artery</td>
<td>7</td>
</tr>
<tr>
<td>de novo aneurysms</td>
<td>1</td>
</tr>
<tr>
<td>Unchanged</td>
<td>18</td>
</tr>
<tr>
<td>Grown</td>
<td>1</td>
</tr>
<tr>
<td>Incomparable</td>
<td>4</td>
</tr>
</tbody>
</table>
Figure 1
Flowchart of the total cohort and included patients.
Figure 2
54-year-old woman with 3 untreated additional aneurysms unchanged after 5 years.
A and B: right internal carotid angiogram (A) and vertebral angiogram (B) show additional aneurysms on the carotid cavernous sinus, middle cerebral artery and superior cerebellar artery (arrows).
C: MRA after 5 years demonstrates unchanged size of all three aneurysms (arrows).

Figure 3
25-year-old woman with multiple additional untreated aneurysms
A. Initial lateral view of internal carotid angiogram shows 1.5 mm pericallosal artery aneurysm.
B. Five year follow up MRA reveals growth to 2.5 mm.
C. Angiogram confirms MRA findings.
Figure 4
56-year-old woman with a de novo 3 mm middle cerebral artery aneurysm.
A. Initial angiogram of the middle cerebral artery
B. MRA after 5 years shows 3 mm de novo aneurysm (arrow)

Figure 5
5 year MRA follow up in a 42-year-old woman with a coiled right middle cerebral artery aneurysm demonstrates 2 left middle cerebral artery aneurysms and a superior cerebellar artery aneurysm (arrows) without available previous imaging. The 2 middle cerebral artery aneurysms were clipped.
DISCUSSION

MRA 5 years after coiling of an intracranial aneurysm to detect de novo aneurysms and growth of additional untreated aneurysms has a low yield: in 65 patients only one small de novo aneurysm was detected and one of 20 untreated additional aneurysms showed slight enlargement. For none of these aneurysms treatment was considered indicated and no specific follow-up policy was advised.

In some patients, both angiography at the time of coiling and short-term follow up angiography was incomplete. As a consequence, on follow-up MRA 4 additional aneurysms (in 2 patients) were detected without previous angiograms. Two of these aneurysms in one patient were clipped. This event emphasis the importance of complete imaging of cerebral vessels when angiography is used as the only diagnostic tool.

Although our study is retrospective with a limited number of patients, it is the first follow-up study with a fixed interval of 5 years. Our 3.0T MRA technique without intravenous contrast enhancement provides high resolution images of the intracranial vessels without artefacts of inserted coils. Therefore, it is unlikely that aneurysms were missed.

The incidence of de novo aneurysm formation after 5 years in this study was 1.5%. This figure is in concordance with a previous CTA follow up study on 610 clipped patients with a variable follow up of 2-18 years: in the first 5 years after SAH a de novo aneurysm developed in 1 of 120 patients (0.8%). Further, in our study one of 20 additional aneurysms (5%) had enlarged 1 mm after 5 years. In the cited CTA follow-up study, in the first 5 years after SAH 4 of 18 aneurysms (22%) had enlarged with a rate of 0.12-1.3 mm per year.

It must be kept in mind that these figures are only valid for patients that survived at least 5 years after treatment of an aneurysm without recurrent SAH. The risk of recurrent SAH after treatment was assessed in a follow-up study after clipping of ruptured aneurysms. In this study the incidence rate of recurrent SAH in the first 10 years after clipping was 286 per 100.000 while in the general population this figure is 9-10 per 100.000. However, during the first 33 months, no recurrent SAH was observed from de novo or regrowth aneurysms. In another study, short-term (1-2 years) CTA follow up of small aneurysms detected at screening in patients with a history of SAH or with familiar aneurysms, did not eliminate the risk of recurrent SAH: 2 of 93 patients had a recurrent SAH, one from the clipped aneurysm and one from a new dissecting aneurysm. In that study, 3 of 93 patients, the small aneurysm detected at screening had enlarged slightly.

Combining these data suggests that the risk of de novo aneurysm formation and significant enlargement of additional untreated aneurysms is low with subsequently an extremely low risk of SAH from these aneurysms. This low risk seems particularly true for the first 5 years and probably also for the first 10 years. Therefore, screening all patients within the first 5 years after aneurysm treatment seems not beneficial, both in terms of preventing SAH and for detection of aneurysms that need treatment. From the patients’ perspective, follow up screening may work two-sided: in patients with fear for a recurrence it may increase quality of life when no such recurrence is found but screening may have a negative impact when aneurysms are detected that remain untreated.

A limitation of our study is the small sample size of 65 patients. However, the consistent MRA follow-up period of 5 years makes this group rather unique for comparison of angiographic data. Another limitation of our study is that we did not search for risk factors. In view of the low event rate, large patients groups are needed to identify risk factors. Such studies have been performed and showed that risk factors for aneurysm development and enlargement of existing aneurysms are: presence of multiple aneurysms, a history of hypertension and current smoking. Other risk factors
are a positive family history and female gender. These risk factors, except of course the presence of multiple aneurysms, are similar to those for intracranial aneurysms and SAH in general. Although current available data suggest a low yield of MRA screening at 5 years for patients with treated aneurysms in general, this may be different for subgroups of patients with increased risk such as young patients with multiple aneurysms, patients with a positive family history or patients with proved growth of additional aneurysms. Until now, not enough data are available and larger follow-up studies, preferably with fixed follow-up intervals, are needed to identify subgroups that might benefit from screening at 5 years.

Conclusion

MRA screening five years after coiling for detection of de novo aneurysms and for growth of additional untreated aneurysms has a low yield in terms of finding aneurysms that need to be treated: After 5 year follow-up MRA in this group of 65 patients with coiled intracranial aneurysms we found one small de-novo aneurysm and one small additional aneurysm showed a minimal growth. Treatment for these aneurysms was judged not indicated.

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REFERENCES