Durability of endovascular treatment for intracranial aneurysms
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Citation for published version (APA):
1 Introduction and outline of the thesis
INTRODUCTION

Intracranial aneurysms

Intracranial aneurysms are intimal outpouchings due to focal weakness of the medial layer of the vessel wall of cerebral arteries, and are present in 0.4 to 6% of the general population. In a small number of patients, intracranial aneurysms rupture, causing a bleeding in the brain (subarachnoid hemorrhage or SAH) with high morbidity and mortality rates. Annual incidence of SAH from an intracranial aneurysm is estimated to be 0.04-1.2%, leading to approximately 1200 hospital admissions due to SAH per year in the Netherlands (source: Netherlands Heart Foundation 2004). Early securing of the aneurysm is vital to prevent a frequently fatal early recurrent hemorrhage.

Diagnosis and treatment

Intracranial aneurysms are mostly discovered during imaging work-up in the acute situation of a SAH by Computed Tomography Angiography (CTA), Magnetic Resonance Angiography (MRA) or Digital Subtraction Angiography (DSA). Unruptured aneurysms may be found as additional aneurysms in patients with another ruptured aneurysm, in patients presenting with neurologic symptoms due to mass effect, or be found incidentally.

For long, the standard treatment for intracranial aneurysms was to place a micro-neurosurgical clip over the aneurysm neck, excluding the aneurysm from the circulation with the goal to prevent a (recurrent) hemorrhage. In the early '90s, an endovascular approach has been developed. The introduction of micro catheters and a detachable coil system allowed the operator to selectively catheterize the aneurysm and fill the aneurysm lumen with platinum coils to prevent recurrent hemorrhage. Aneurysm coiling has gradually replaced surgery as the first line treatment of choice, since, in 2002, a large multicenter randomized controlled trial showed that patients had better short-term outcome after coiling compared to clipping.

Although coiling has become the preferred treatment for both ruptured and unruptured intracranial aneurysms, and clipping has become only indicated for aneurysms not suitable for coiling, it has several shortcomings. First, not all aneurysms can be completely occluded at first treatment, leaving the patient at risk for early recurrent hemorrhage. Second, a substantial part of coiled aneurysms shows instability with time. Aneurysms may reopen due to coil compaction, growth of the aneurysm, coil migration into intraluminal thrombus, or dissolving of intraluminal thrombus.
**Imaging follow-up**

To assess aneurysm occlusion and discover possible reopening, it is important to perform imaging follow-up in patients with coiled intracranial aneurysms. Aneurysm occlusion is commonly described in a 3-point scale (complete, near-complete with a remaining small neck remnant and incomplete) or in a 2-point scale (adequate and incomplete occlusion), where no distinction is made between complete and near-complete occlusion. Incomplete aneurysm occlusion leaves the patient at risk for a SAH, and retreatment is often advocated.

Possible determinants for initial incomplete aneurysm occlusion are unfavorable aneurysm anatomy and vessel geometry and types of coils that are used. Possible risk factors for reopening of a coiled aneurysm over time are large aneurysm size, presence of intraluminal thrombus, low packing density, initial incomplete occlusion, duration of follow-up, ruptured aneurysms, location in the posterior circulation, and a large neck–dome ratio. The magnitude of separate contributions of these risk factors to aneurysm reopening are not clear, since studies differ in design, selection of aneurysms and method of follow-up.

Longer time after treatment as a risk factor for aneurysm reopening is under debate. Some studies reported more first-time aneurysm reopenings with longer follow-up and prolonged imaging follow-up has been recommended. However, interpretation of these studies is impeded by a wide variety in time intervals of first follow-up angiography. Reopenings that were detected on first follow up angiography some years after coiling, may have had developed much earlier. Recently, studies have found that almost all aneurysm reopenings may occur in the first 6 months after coiling, and that late reopening (>6 months after coiling) is rare. If indeed, late aneurysm reopening is rare, and almost all reopened aneurysms can be detected at first imaging follow-up after 6 months, long-term follow-up may not be necessary for a large subgroup of patients.

Another important reason for imaging follow-up of patients with coiled intracranial aneurysms is the detection of newly developed aneurysms or growth of small untreated additional aneurysms. Patients with a treated intracranial aneurysm frequently have additional aneurysms. Incidence of growth of additional aneurysms varies in different studies, with annual risks ranging from 1.51% to 22.7%. The annual risk of developing a de novo aneurysm is lower, 0.3-1.8%. The concern of newly developing aneurysms and growth of untreated aneurysms is the increased risk of rupture, because size is an important determinant of the risk of rupture and possibly also because enlarging
Aneurysms are unstable.\textsuperscript{24} Overall, the annual rupture rate of unruptured intracranial aneurysms is low, 0.04-1.2% per year.\textsuperscript{25,26}

**AIMS AND OUTLINE OF THIS THESIS**

This thesis is focused on the long-term clinical and angiographic outcome of patients with coiled intracranial aneurysms.

The main objectives of this thesis are:

- To evaluate the yield and psychological effect of MRA screening long term after coiling in patients with adequate aneurysm occlusion at first angiographic follow-up after 6 months
- To systematically review the literature on angiographic outcome and retreatments after coiling of intracranial aneurysms
- To assess long-term clinical and angiographic outcome in patients with incomplete aneurysm occlusion at first angiographic follow-up 6 months after coiling
- To assess long-term clinical and angiographic outcome after endovascular treatment of patients with partially thrombosed intracranial aneurysms

The results of a systematic review and meta-analysis of 42 studies with imaging follow-up of patients with coiled intracranial aneurysms are presented in CHAPTER 2. We evaluated reopening and retreatment rates and risk factors for aneurysm reopening and retreatment.

We performed a multicenter imaging follow-up study with MRA at 3 Tesla >4.5 years after coiling, in 400 patients with 440 adequately occluded aneurysms at first (6-months) angiographic follow-up. In CHAPTER 3 we describe the yield of long-term follow-up screening with MRA in these patients in terms of detection of late (>6 months after coiling) aneurysm reopening and indication for retreatment. Additional aneurysms detected 5 years ± 0.5 years after coiling on the long-term follow-up MRA of 276 patients were compared with previous imaging to assess formation of de novo aneurysms and growth of small untreated additional aneurysms. Five-year incidence of de novo aneurysm formation and growth of untreated aneurysms is described in CHAPTER 4. Patients who participated in the LOTUS study (screening with MRA long-term after coiling of an intracranial aneurysm) may experience feelings of anxiety. On the other hand, findings of persistent occlusion of the aneurysm may reassure the
patient, and thus reduce feelings of anxiety with time. In CHAPTER 5 we studied the effect of screening with MRA on mood and anxiety in 120 participants in the long-term follow-up study after coiling of intracranial aneurysms.

Although the majority of coiled aneurysms is adequately occluded at first angiographic follow-up, a significant part is incompletely occluded. Patients with previously ruptured incompletely occluded aneurysms are at risk of a recurrent SAH. Often, retreatment is performed and imaging follow-up intensified in these patients, exposing them to the risk of procedural complications. In CHAPTER 6 we describe all aneurysm related late adverse events in 124 patients with incompletely occluded aneurysms at first angiographic follow-up 6 months after coiling.

The most consistent risk factor for aneurysm reopening is the presence of intraluminal thrombus in aneurysms. Partially thrombosed intracranial aneurysms are rare and form a high-risk subgroup of intracranial aneurysms. In CHAPTER 7 we assessed long-term clinical and angiographic outcome of 56 patients with endovascular treatment of partially thrombosed aneurysms. Outcomes of two different treatment modalities were investigated; parent vessel occlusion (PVO) and coiling.
REFERENCES

15. Sluzewski M, Menovsky T, van Rooij WJ, Wijnalda D. Coiling of very large or giant cerebral