THE PRICE OF DEFUSING MINES

RADIOLOGICAL IMAGING AFTER MICROSURGERY FOR INTRACRANIAL ANEURYSMS

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LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following publications, referred in the text by their Roman numerals:

I Kivisaari RP, Salonen O, Öhman J: Basal brain injury in aneurysm surgery. Neurosurgery 46:1070-1076, 2000.

II Kivisaari RP, Salonen O, Hernesniemi JA, Servo A, Autti T, Öhman J: Magnetic Resonance Imaging after Aneurysmal Subarachnoidal Hemorrhage and Surgery: A Long-term Follow-up Study. AJNR 22:1143-1148, 2001.

III Kivisaari RP, Porras M, Öhman J, Siironen J, Ishii K, Hernesniemi JA: Routine cerebral angiography after surgery for saccular aneurysms – is it worth it? Neurosurgery 55:1015-1024, 2004.

IV Kivisaari RP, Porras M, Öhman J, Piippo A, Karatas A, Hernesniemi JA: How to control results of microsurgical aneurysm clipping? Submitted manuscript.

ABBREVIATIONS

AComA	anterior communicating artery
CT	computed tomography
CTA	computed tomography angiography
DSA	digital subtraction angiography
GOS	Glasgow Outcome Scale
GR	good recovery
HH	Hunt and Hess classification
ICA	internal carotid artery
MCA	middle cerebral artery
MD	moderate disability
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
Peric	pericallosal artery
SAH	subarachnoid hemorrhage
SD	severe disability
VB	vertebral and basilar arteries
VS	vegetative state
VSP	cerebral arterial vasospasm
WFNS	World Federation of Neurosurgical Societies grading

INTRODUCTION

Even nowadays, aneurysmal subarachnoid hemorrhage (SAH) is a devastating disease with overall mortality rate of 50%.[46,75,90,132] It is estimated that 10 - 60% of the patients with SAH die before receiving medical attention[46,64,74,75,133,145,165,179,183] and only 60% of patients reaching medical attention recover to normal life.[170] The mortality rate of conservatively treated patients is high, only 35-40% of the nonsurgically treated patients survive more than three months.[145,149] Initial bleeding, rebleeding and delayed cerebral arterial vasospasm (VSP) are the major causes of mortality and morbidity.[12,64,86,101,141,142,181] VSP is seen in angiograms of up to 70-90% of the patients in the first two weeks following SAH.[75,99] Moreover, up to 50% of the patients with angiographic vasospasm develop ischaemic neurologic deficits.[117]

To prevent rebleeding of a ruptured aneurysm or the growth and subsequent rupture of an unruptured aneurysm, the complete closure of the aneurysm is essential.[2,30,46,64,92,94,95,141] This can be achieved by open surgery[29], since 1960's by microsurgery[213] and increasingly by endovascular coiling.[17,55,56,62,67] When an aneurysm is clipped, the neck of the aneurysm is closed and the walls are apposed for a continuous endothelial lining. If the clip is perfectly positioned, this occludes the aneurysm completely and leaves the parent vessels intact. The probability of rebleeding encourages most neurosurgeons to operate early; this also allows early and aggressive prevention and treatment of VSP with calcium antagonists and triple-H therapy.[65,102,141,142,170]

It is obvious that the angry red swollen brain tissue is more vulnerable during the acute operation.[141,142] The frequency of all surgical complications is reported to vary between 3% and 10%.[48,101-103,119,170,186] Although several authors have reported lesions possibly caused by retractor pressure to the basal areas of frontal and temporal lobes at early operation, the frequency of these lesions caused by surgery is not known.[81,150,157,158] Magnetic resonance imaging (MRI) is superior

to computed tomography (CT) in imaging hypodense areas consistent with infarctions, especially so in the basal regions of the brain where beam-hardening artifacts from bony structures of the skull base reduce the ability of CT to detect lesions.[11] Moreover, in MRI scans the aneurysm clip causes artifacts of only 20-30 mm in diameter [68,81,157] whereas in CT scans the basal region is often unreadable after clipping or coiling of an aneurysm.[126] Furthermore, MRI is superior to CT in detecting small lacunar lesions; particularly those located deep within the cerebral hemispheres and in the brain stem and cerebellum.[39,40,51,52] Modern aneurysm clips are MRI-compatible and there are several studies pointing out the safety of modern nonferromagnetic clips in the magnetic field.[37,81,96,157]

The difficulty in predicting the presence of residual or unclipped aneurysm suggests that all patients should undergo angiographic control.[25,122,187] Digital subtraction angiography (DSA) is safe and reliable method to evaluate the completeness of the closure of an aneurysm.[25,112,122,187,211]

In many neurosurgical units, computed tomographic angiography (CTA) has become the primary diagnostic method for detection of intracranial aneurysms among patients with subarachnoid hemorrhage. The quality and accuracy of CTA is almost that of catheter DSA, which is the golden standard study for patients with cerebral aneurysm.[6,7,66,97,210,212] The main advantage of CTA is its noninvasiveness meaning lower risk of complication as compared with DSA. CTA can also be performed by far much quicker, making it more suitable for critically ill or unstable patients. CTA is also less expensive than DSA.[97]

This study was carried to discover any permanent damages and the probable surgical damage of the brain tissue seen on a late MRI. We also wanted to evaluate the postoperative angiographic studies to examine the number of patients in risk for rebleeding or aneurysm regrowth after surgical repair and to assess whether the noninvasive CT angiography could replace DSA.

REVIEW OF THE LITERATURE

1.*Subarachnoid hemorrhage: Incidence and natural history of intracranial aneurysms*

Rupture of an intracerebral aneurysm leads to a catastrophic cascade of events known as subarachnoid hemorrhage. In 1875, Sir William Gowers presented the correlation of sudden death with the finding of blood over the surface of the brain and a ruptured aneurysm at autopsy.[53]

According to autopsy and MRA studies, the prevalence of intracranial aneurysms in general population varies from 0.2% to 9%, partly due to different study methods. The incidence rate of aneurysmal subarachnoid hemorrhage is 20-23 /100000 in Finland and Japan, and the worldwide mean incidence is 10.5 / 100 000.[116,162,195]

The incidence of familial aneurysms (at least two affected first-degree relatives in the same family) among SAH patients is 6% to 10% and 10% to 17% of asymptomatic relatives in affected families may have incidental aneurysms.[160-162,172,174,197] First-degree relatives of patients with SAH have a 3- to 7-fold increased risk of being struck by the same disease, but in second-degree relatives, the incidence of SAH is similar to that found in the general population.[21,172,197]

Women and cigarette smokers are at increased risk for intracranial aneurysm formation and growth.[88,116] Race, cigarette smoking, size of the unruptured intracranial aneurysm, alcohol consumption and age, inversely, are important risk factors for aneurysm rupture.[4,20,76,87,89,91,94,140,188] The use of oral contraceptives may increase the risk of SAH but the evidence is controversial.[83,188]

The incidence of SAH is also associated with specific heritable disorders of connective tissue, but these patients account for only a very small fraction of all patients with SAH. Autosomal dominant polycystic kidney disease is the most common heritable disorder associated with SAH, but it is

found in only 2% of all patients with SAH.[173] Weak association between SAH and Ehlers–Danlos disease IV and neurofibromatosis type 1 have also been reported.[28,171]

The peak incidence of rebleeding occurs in the first 24 hours after the initial hemorrhage, and the cumulative risk of rebleeding during the next two weeks is 20% which is also the time-period for the highest rates of morbidity and mortality following aneurysmal SAH.[46,64,79,86,101,102,145]

Besides initial bleeding and rebleeding, delayed cerebral arterial vasospasm is a major cause of mortality and morbidity.[64,101,141] It classically occurs during a time period ranging from 4 to 12 days after initial bleeding with a peak incidence on the seventh day.[99,149] Vasospasm is seen in angiograms up to 70-90% of the patients in the first two weeks following SAH.[73,99] Moreover, without treatment up to 50% of the patients with angiographic vasospasm develop ischaemic neurologic deficits or die.[117] The presence of cerebral vasospasm has been correlated with a 1.5- to 3-fold increase in mortality in the first 2 weeks after SAH. Vasospasm may last for days or weeks, in most cases vasospasm resolves after three weeks and is followed by a phase of vasodilatation.[109]

The risk factors associated with aneurysm rupture are better understood than the natural history of unruptured intracranial aneurysms.[5,78,87,91,124,156] The International Study of Unruptured Intracranial Aneurysms (ISUIA) stirred the consensus over the natural history of unruptured aneurysms. The study suggested markedly lower rupture rates of aneurysms less than 10mm in diameter (0.05%/a) than previously reported (1.5-2.4%/a).[59,61,76,79,93,94,154,206]

2. Surgical treatment of ruptured aneurysms

The introduction of cerebral angiography in 1927 by Moniz[135] allowed attempts at treating ruptured aneurysms and the first direct treatment of an intracranial aneurysm with success was by Dott in 1931.[32,33] In 1937 was the first time when a ruptured intracranial aneurysm was successfully clipped using a silver clip, this was done by Dandy.[29]

In the beginning of surgery for intracranial aneurysms, the results were far from optimal. McKissock et al. demonstrated that conservative therapy resulted in better outcome than direct surgery on anterior communicating aneurysms.[130] Because of the high morbidity in direct surgery and conservative treatment, indirect methods became more prevalent, mostly ligations of the parent arteries[120], or carotid arteries [191]. The ligation of the vertebral artery was also used at this time for treatment of vertebral and basilar aneurysms due to the very high mortality associated with direct surgery of posterior circulation aneurysms.

The beginning of microsurgery with the introduction of operating microscope in the 1960s brought new light to the results of aneurysm surgery.[213] Better understanding of the intracranial anatomy combined with delayed surgery, lead to acceptable low morbidity in good-grade patients.[48,100,192,200,213]

Advances in many aspects of management have contributed to better results, including the development of better microsurgical instruments and techniques. Also progress in neuroanaesthesic and intensive-care management, improved diagnostic facilities, and the development of vascular neurosurgery as a subspecialty all have reduced the risks of intracranial surgery.

Timing of surgery

Prior to operating microscope ruptured aneurysms were approached acutely with poor results. In their series of 100 patients with aneurysms of the anterior communicating artery operated within 21 days after ictus Norlen and Olivecrona published in 1953 an operative mortality rate of 3% which supported operating late.[137] Even though the large multi-institutional prospective, non-randomized, study of the timing of aneurysm surgery by Kassell et al in 1990 showed no significant difference in outcome between patients operated on early or late, most neurosurgeons began to operate early.[102,200] In 1989 Öhman and Heiskanen published the first randomized study where

early surgery combined with nimodipine treatment yielded in better results by preventing rebleeds and reducing the effects of vasospasm.[141]

Outcome

In 1968, Hunt and Hess published a grading system for the clinical condition of patients after SAH, in order to assess better the value of various methods of treatment. In a series of 64 patients operated on in the first four days after SAH, 87 % of Grade I and II patients and of Grade III patients had an excellent outcome, but only one of 13 grade IV-V patients had a good outcome.[72] In a series of 104 aneurysm patients operated on early published by Hunt and Miller in 1977 there was a 72 % overall survival rate.[71]

In a population based study Fogelholm et al comparing outcomes in the years 1976-1978 with the years 1980-1987 noted that active treatment policy including early surgery improved survival only marginally, but the quality of life of the survivors improved significantly.[46] Advances in treatment and prevention of complications have also occurred, but these have led to only modest improvement in overall outcome.[69,118,140,169]

In a population based study Johnston et al found a steady SAH mortality decrease and increase in the mean age of death – from 57 to 60 - between 1979 and 1994. The mortality has declined from a rate of 3.1 to 2.5 per 100,000 (19%). The decrease in mortality was most profound for black males, in whom rates declined by 35% over the time period, and least among black females, who showed no decline.[85] The median age of death from SAH was 59 years, more than 10 years younger than from intracerebral haematoma (median age, 73 years), and 20 years younger than from ischaemic stroke (median age 81 years).[85] This increase in age is also confined by others.[85,140]

In 1993 Hernesniemi et al published results of 1150 patients of which 1007 were operated (55% within 3 days).[64] Grade I and II patients recovered well with 88% and 80% of the patients

respectively reaching good recovery (GOS), mortality on grade IV and V patients was 44% and 59% respectively.

In a recent prospective study of 177 poor-grade (WFNS Grades IV and V) patients with aneurysmal subarachnoid hemorrhage with a management policy of aggressive ultraearly surgery (within 12hrs of SAH) outcome assessment at 3 months in the 132 surgical patients revealed that 40% were independent, 15% were dependent, and 45% had died.[110]

In a review of population-based studies from 1960 onward, the weighted average case fatality was 51%. Of those surviving the hemorrhage, one-third remain dependent.[69] Recovery to independence does not o guarantee good outcome, as the study of Hop et al on quality of life after SAH showed: more than 80% patients who were independent 4 months after the hemorrhage had significant reduction in quality of life.[70] At 18 months after ictus the outcome had improved considerably, but still almost 70% of the patients had reduction in the quality of life.[195] The improvement in the first year and a half shows that long-term follow-up is essential when evaluating the functional outcome after SAH.[195] When only 50% of the SAH patients ever reach hospital, and 50% of the hospitalized patients die leaving one third of the surviving patients dependent and two thirds independent, altogether approximately only 10% of all patients with SAH have truly good outcome.[127,128,164,195] The poor outcome combined with the young age of patients suffering SAH explain why the loss of years of potential life from SAH is tremendous and comparable to that of ischaemic stroke.

Radiological results of surgical treatment

Parenchymal lesions

The reported frequencies of all surgical complications vary from 3% to 10%.[8,60,101-103,111,119,148,170,182] In these studies a complication is defined either as death, a neurological deficit or pathological finding in CT scan. Among the surgical complications, several authors have

reported lesions caused by retractor pressure to the basal areas of frontal and temporal lobes at early operation.[8,36,81,150,158] However, the frequency of these lesions caused by surgery is not known. Moreover, it is not known whether the same factors that increase the risk of ischaemic lesions after SAH, i.e., amount of blood on the primary CT scan, vasospasm on postoperative angiogram and history of hypertension, would apply to this kind of lesion.[136,141] Hypodense areas consistent with infarctions seen on CT correlate well with cognitive deficits[208,209] – but also there have been reports of patients with severe cognitive deficits without CT findings.[207] In these cases MRI might be a useful diagnostic tool.

Angiographic results

Depending on definition the reported incidence of residual neck after surgical clipping of an aneurysm ranges between 3.8% and 18%.[30,34,36,44,107,114,122,178,199] The incidence of aneurysm neck remnant after surgery is relatively rare in the anterior circulation and in small aneurysms, and higher in the posterior circulation, midline aneurysms and in large or giant aneurysms.[34,36,178,199]

In a 25 year period (1979 – 2004), there are only seven series published in which routine postoperative angiography was performed after surgical clipping of intracranial aneurysms.[1,30,44,104,122,151,153] Feuerberg et al. reported in 1987 a 3.9% rate of residual aneurysms in 715 patients on follow-up angiography.[44] In 1997, Acevedo et al. reported a 6.3% rate of residual aneurysms in 217 patients on follow-up angiography.[1] Also in 1997, Proust et al. reported a 2.3% rate of residual aneurysms in 43 patients on postoperative angiography.[151] Rauzzino et al. published in 1998 a series of 227 patients with 312 aneurysms who underwent postoperative angiography, with residual filling found in 4.2% of the aneurysms.[153] In 1993, Macdonald et al. reported a series of 66 patients with 78 aneurysms of which 14% had residual filling on postoperative angiography.[122] David et al. reported in 1999, residual filling in 8.2% of 147 aneurysms. In their study the late (3 years after operation) angiographic follow-up demonstrated 2 (1.5%) recurrent

aneurysms of 135 aneurysms that initially were considered completely cured. Of eight "dog ear" residual necks, two grew, and of four broad-based residual necks, three grew. In addition, eight *de novo* aneurysms were found (risk, 1.8%/yr).[30]

Unexpected major vessel occlusions harbor a great risk for the patient – although many occur without any symptoms.[36,98,122] MacDonald et al. published in a thorough analysis a rate of 12% of unexpected major vessel occlusions.[122] Allcock and Drake found major vessel occlusions in 9% of 70 cases with unruptured aneurysms.[3] In a post-mortem study by Karhunen there were seven (11 %) major vessel occlusions in 28 patients among the 63 consecutive patients who died after aneurysm surgery.[98]

Recently the good results of intraoperative angiography in prevention of vessel occlusion and residual aneurysm necks have been well documented.[25,106,187] Two series using intraoperative angiography show that suboptimal clip placement and arterial occlusions are detected in about 9% of patients following aneurysm surgery.[13,125] Unexpected residual aneurysm neck remnants can be found in the normal postoperative DSA even if intraoperative angiography has been performed.[13]

If a vessel occlusion is diagnosed early, an immediate reoperation most likely prevents ischaemic damage to the brain. Small residual necks detected on a postoperative angiography may remain because of very difficult conditions at surgery (large and giant aneurysms), and reoperation would not give better result.

3. Endovascular treatment of ruptured and unruptured aneurysms

Serbinenko started endovascular treatment of aneurysms by the introduction of proximal artery occlusion with detachable balloon.[175] The first large series of endovascular occlusion of ruptured intracranial aneurysms with preservation of the parent vessel was by Romodanov and Shcheglov in 1979.[159] The introduction of electrolytically detachable coils by Guglielmi et al.[55,56] was the next step of endovascular occlusion of intracranial aneurysms. The first prospective study comparing

endovascular and surgical treatment by Koivisto and Vanninen demonstrated comparative results of the methods; endovascular treatment had more favorable angiographic results with posterior circulation aneurysms – whereas anterior circulation aneurysms were better occluded by surgery.[107,199] Also clinical and neuropsychological outcomes were similar, but endovascular occlusion was markedly less-often associated with MRI-detectable brain injury.[107,199]

Now endovascular aneurysmal occlusion has become a competitive alternative to microsurgical clipping for many aneurysms, particularly those with a relatively narrow neck and especially in circumstances where the patient is in poor medical or neurological condition. The long-term efficacy in preventing rebleeding still remains to be seen.[15,50,67,84,139,180,190,198,203]

In selected cases endovascular coiling of aneurysmal remnants after surgical treatment offers an alternative to reoperation. In reported small series endovascular treatment of remnants has proven safe.[14,47,57,189]

Recent prospective randomized international multicenter study comparing endovascular treatment with surgery (ISAT) was interrupted because of the better outcomes in the endovascular group. This study concluded that in patients with a ruptured intracranial aneurysm, for which endovascular coiling and neurosurgical clipping were equal treatment options, good outcome at 1 year is significantly more frequent with endovascular coiling. The data provided by the study also suggest that the long-term risks of further bleeding from the treated aneurysm are low with either method.[134] But in one year follow-up time there is a trend towards more rebleedings from the aneurysms treated endovascularly (3.2%) than from the aneurysms treated surgically (1.3%). In long term this may effect significantly the overall outcome.[138]

4.Imaging

Computed tomography

CT scanning is the standard investigation in search of SAH because of the ability of CT to detect fresh extravasated blood in the basal cisterns.[195] Also the maximum of the hemorrhage often suggests the location of the ruptured aneurysm.[196] The amount of hemorrhage on an admission CT scan is highly associated with VSP and thus the outcome of the patient.[45,49]

The sensitivity of CT scans for SAH decreases with time from the onset of symptoms and aneurysmal SAH cannot be excluded even if no blood is found.[177] If CT is performed within 12 hours after the hemorrhage studies are negative in ~2% of patients with SAH.[193] Lumbar puncture is more sensitive than CT for SAH and should be assessed in the setting of a negative CT scan. Unfortunately, sometimes traumatic lumbar puncture leads to false-positive diagnoses and subsequently to unnecessary angiographies.[168,204]

Intra-arterial digital subtraction angiography

Conventional DSA is the gold standard of pre- and post operative imaging of intracranial aneurysms. It is invasive and has morbidity, including locally at the puncture site, systemic complications and stroke. DSA is relatively safe in patients without atherosclerotic disease. The combined transient and reversible neurologic complication rate of cerebral angiography has been reported to be as low as 0.4% and as high as 12.2%. The reported permanent neurologic complication rate varies from 0% to 5.4%.[31,38,41,43,54,58,113,123,129,143,202,211] Pryor et al and Setton et al report in the 4 years (1992-1995) in 1802 angiograms complications occurred in four procedures, three with temporary neurological deficit (0.17%) and one with permanent neurological deficit (0.05%).[152,176] The Asymptomatic Carotid Atherosclerosis Study (ACAS) reports stroke rates from angiography of 1.2% and 1.6%.[185] The mean age of patients with subarachnoid hemorrhage is lower than patients suffering from ischaemic stroke, which results in lower neurologic complication rate in this patient group.[195,211] Ischaemic stroke has been reported to be a

risk factor in cerebral angiography and the neurologic complication rate to be lower in patients with subarachnoid hemorrhage, intracerebral aneurysm, or arteriovenous malformation.[26,38,41,43,58,113,129] Saitoh et al reported a 4.8% incidence of aneurysmal rebleeding during angiography within 6 hours after initial aneurysm rupture. Rerupture caused by angiography was estimated to occur in 1.4% (2/144) of cases.[166] Komiyama et al revealed a rebleeding rate of 3.3% during diagnostic angiography within 6 hours after SAH. In this study the mortality rate was 80%.[108] The outcome after a rebleed during angiography is worse than in cases when rebleeding has occurred in other circumstances.[214]

The non-invasive angiographies: computed tomography angiography and magnetic resonance angiography

The ideal investigation is non-invasive, has no morbidity, has a high sensitivity and specificity, and low cost together with wide availability.

The results of a meta-analysis of studies published between 1988 and 1998 show that CT angiography and MR angiography equally detect intracranial aneurysms, with an accuracy of approximately 90%.[205] Small size of aneurysm reduces sensitivity markedly, beneath 3 mm the sensitivity for aneurysm detection with CT angiography or MR angiography decreases, from 96% to 61% and from 94% to 38%, respectively.[205] A trend toward better results in the CT angiography studies published after 1995 compared with those published before. The future of such noninvasive methods that steadily keep on improving seems bright. During the same time period the results of MR angiography were not markedly improving.[205]

The quality of CTA is approaching that of DSA, the golden standard diagnostic study for patients with cerebral aneurysms.[7,16,24,80,97,147,194,210,212] The development of multislice-technique has improved the quality of CTA images markedly.[97] In a recent small (20 patients) series Otawara et al showed that multislice CTA can also detect angiographic vasospasm after SAH with accuracy equal

to that of DSA.[144] The advantages of CTA compared with DSA are: non-invasiveness, meaning lower risk of complication or morbidity, CTA can be performed much more quickly, it demands less resources, it is not painful to the patient, usually it does not require sedation, and it is suitable for critically ill and unstable patients.[66] So far, studies using CTA as a postoperative control in aneurysm surgery have not been published.

MRA is a particularly suitable method for screening studies as compared with DSA: imaging time is relatively short, the procedure is totally non-invasive, and it has no known risks for patient. However, compared with DSA, MRA has less specificity and sensitivity, with the best estimates suggesting sensitivity and specificity of 90 - 95%.[9,10,163,201] The disadvantages of CTA in comparison to MRA are the ionizing radiation of CTA and the use of contrast medium in the imaging. In contrast MRA has longer imaging time, making it often unsuitable for critically ill patient with SAH.[201]

Magnetic resonance imaging

MRI has well documented advantages over CT. Due to better resolution; MRI is more reliable in detecting ischaemic lesions in brain tissue.[11,39,51] This comes even more evident in the basal regions of the skull where CT is compromised with artifacts from bony structures, and especially after treatment for intracranial arterial aneurysms when the aneurysm clip or coils cause artifacts on a CT scan.[51,68,126] In MRI scans the diameter of aneurysm clip artifacts is only 20-30 mm.[22,51,52,68,81,157] Furthermore, MRI is superior to CT in detecting small lacunar lesions, particularly those located deep within the cerebral hemispheres and in the brain stem and cerebellum.[39,51]

AIMS OF THE STUDY

The purpose of the present study was:

I To evaluate the incidence of surgical damage to the brain tissue after surgery for ruptured intracranial aneurysms.

II To evaluate the permanent focal and degenerative changes of the brain tissue after subarachnoid hemorrhage and surgery for ruptured intracranial aneurysms.

III To evaluate the completeness of closure of ruptured and unruptured intracranial aneurysms after surgery with digital subtraction angiography.

IV To evaluate the completeness of closure of ruptured and unruptured intracranial aneurysms after surgery with computed tomography angiography.

PATIENTS AND METHODS

Patients

I-II *The incidence of surgical damage to the brain tissue and the permanent focal and degenerative alterations of the brain tissue after subarachnoid hemorrhage and surgery for ruptured intracranial aneurysms*

Helsinki is the only neurosurgical unit in Southern Finland serving a population of 2 million – there are no admission biases as all the patients – also those in poor condition or moribund are admitted. Out of a total of 433 patients with aneurysmal subarachnoid hemorrhage (SAH) - admitted to our hospital from April 1st 1992 to November 30th 1994 - a consecutive series of 147 (34%) patients with early surgery (both sexes; age 16-70 yr.), was scrutinized. The diagnosis of SAH had been made based on CT findings. If no blood was visible on the CT scans the patient was excluded from the study. The aneurysms were verified by DSA. Patients selected for the study were surgically treated within 72 hours after hemorrhage (=early surgery). Patients with rebleeding either before or after admission were excluded, as were patients with posterior circulation aneurysms, or late surgery. Other exclusion criteria were intraparenchymal hematomas in CT scans, pregnancy, severe complicating illness (hepatic or renal failure, recent myocardial infarction, terminal malignancy, AIDS), severe psychiatric illness and coagulation disorders or anticoagulant medication. Moreover, the presence of severe vasospasm (>50% narrowing of the vessel lumen) in angiograms obtained at admission indicating earlier SAH excluded patients from the study. Ten patients with multiple aneurysms were operated on for an unruptured aneurysm after a recovery period (1-5 months).

The patients were invited by telephone and letter for follow up MR brain studies of the brain from Oct 1st 1994 to June 30th 1998, which was 2-6 years (mean 3.3 years) postoperatively. A total of 14 patients died during the follow up period. Twenty-six patients did not reply to the invitation, one

patient was too heavy for our equipment, and the MR scanning had to be interrupted for two patients who suffered from claustrophobia. A total of 104 patients, aged 21 to 73 years (mean 48.8 years) went through the MRI studies (Table 1). Patients with pericallosal aneurysm were not included for the study of surgical lesions thus leaving 101 patients.

III *The completeness of closure of ruptured and unruptured intracranial aneurysms after surgery, studied with digital subtraction angiography*

Of 932 patients with SAH or an unruptured saccular intracranial aneurysm treated at our hospital between August 1, 1998, and December 31, 2001, a consecutive series of 622 patients (41% men, 59% women; age range, 23–81 yr.) was studied retrospectively. Excluded were 32 patients with fusiform aneurysm, 103 patients who had nonaneurysmal SAH, and 44 patients who underwent endovascular treatment or surgery other than clipping (e.g., trapping or bypass). In addition, 77 patients with no control digital subtraction angiogram were excluded. The reasons for not performing control DSA included: severe calcifications at the aortic arch and its branches, a complication in obtaining the diagnostic digital subtraction angiogram, or perfect visualization of the anatomy at operation. All patients with saccular aneurysm were treated, with the exception of 54 moribund or rapidly deteriorating or extremely old (>85 yr.) patients. Patients with large hematomas also were treated and included in the study. 12 surgeons operated on the aneurysms; the senior author (JH) performed most of the aneurysm operations (68%). The 622 patients presented with 955 aneurysms. Of these, 808 aneurysms were clipped, and the results were monitored postoperatively by angiography. A total of 121 patients (19%) had no history of SAH, i.e., they had incidental aneurysms. A total of 493 of the aneurysms (61%) were ruptured causing SAH; 315 (39%) of the 808 aneurysms were unruptured. (Table 2)

IV *The completeness of closure of intracranial aneurysms after surgery, studied with computed tomography angiography*

Of the 308 patients with SAH or unruptured saccular intracerebral aneurysm treated at our hospital between January 1st, 2003, and December 31st, 2003, a consecutive series of 160 patients (M 34%, F 66%; age 26-38 yr.), was retrospectively scrutinized. Excluded were, patients with fusiform aneurysm (12), patients who suffered non-aneurysmatic SAH (27), patients who had no control CTA after surgery (53) and patients with endovascular treatment or other surgery than clipping (trapping, bypass, etc.) (28). All patients with saccular aneurysm were treated, except 28 moribund or rapidly deteriorating or extremely old (>85 yr.) patients. Even patients with large hematomas were also included.

The 160 patients presented with a total of 327 aneurysms. Of these, 218 aneurysms were clipped and the result was postoperatively controlled with CTA. A total of 89 patients had no history of SAH i.e. they had incidental aneurysms. A total of 93 of the aneurysms were ruptured causing SAH; 125 out of the 218 aneurysms were unruptured. The demographic features of the patients are summarized in Table 3.

2.Computed tomography in I & II

A CT scan (Philips, Tomoscan) was performed 3 months after the SAH and surgery (127 patients) at the time of clinical follow up. An experienced neuroradiologist evaluated the CT scans with no knowledge of patient's clinical course or neurological status.

3.Magnetic resonance imaging in I & II

MRI study was performed on a total of 104 patients. A Magnetom- SP-42 scanner (1.0 T; (Siemens, Erlangen, Germany)) was used for 40 patients, and a Magnetom Vision (1.5T; Siemens) was used for 64 patients. Standard axial T1-weighted (TR, 570 – 600 ms; TE, 15 ms; Matrix, 256 x 256) and T2-weighted (TR, 2000 – 3500 ms; TE, 85 – 93 ms; Matrix, 190 x 256) sequences were obtained. Also coronal T2 weighted and gadolinium-DTPA (Magnevist®, Schering, Berlin./ Omniscan®, Nycomed, Oslo. 0,2 mmol / kg b.w.) enhanced axial T1 scans were obtained. Fluid attenuated inversion recovery sequence (FLAIR) (TR, 9999 ms; TE, 85 ms; Matrix, 154 x 256) was available and used in the 1.5 T Vision for 64 patients.

An experienced neuroradiologist who was not aware of patient's clinical course or neurological status or the previous CT findings analyzed the scans. Number of areas of high signal on T2 and FLAIR and low signal on T1 indicating infarction was counted and their size was measured, small high signal foci on T2 and proton density images were counted. Degree of leukoaraiosis was scored using a four-point scale: 0) normal, 1) mild, 2) moderate, 3) severe.[215]

Measurements of signal intensity were done for 18 patients with a ruptured aneurysm of the middle cerebral artery as their only presenting aneurysm and who were imaged at 1.0 T. The measured areas were: I) basal ganglia (thalamus, head of caudate nucleus and putamen), II) deep white matter on the levels of third ventricle and roof of lateral ventricles, III) centrum semiovale, IV) frontal cortex. Measurement was not included if a visible area of high signal intensity consistent with infarction was part of the region of interest. Two independent readers did the measurements.

4.Intra-arterial digital subtraction angiography in III

Preoperatively patients were examined by CTA or DSA where both carotid arteries and at least one vertebral artery were examined. Postoperative DSA (Integris V3000, Philips, The Netherlands. Matrix 1024x1024) was performed within 24 hours after the operation. At least 4 different projections per vessel were taken. All angiographic studies were analyzed by experienced

neuroradiologist who has assessed nearly 10 000 intracranial aneurysms. The analysis focused on 1) the completeness of the closure of the aneurysm and on 2) the occlusion of any major artery or branch or perforator. The closure of the aneurysm was considered incomplete even if a smallest neck remnant e.g.1mm or more, or fundus of the aneurysm was reliably visible. Incomplete closures were divided into two categories: 1) neck remnant only or 2) residual filling of fundus of the aneurysm. The size of the aneurysm was approximated in millimeters as compared with the intra-cavernotic part of internal carotid artery (5mm) and the middle part of the basilar artery (3mm).

5.Computed tomography angiography in III & IV

Patients were assessed preoperatively by CTA or catheter DSA where both carotid arteries and at least one vertebral artery were assessed. Postoperative CTA was performed within 24hrs after the operation. A multislice helical CT scanner with four detector rows (GE Lightspeed QX/i; GE Medical Systems, Milwaukee, WI) was used for CTA. An experienced neuroradiologist (MP) analyzed all CTA studies. The analysis focused on 1) the completeness of the closure of the aneurysm and on 2) the occlusion of any major artery or branch or perforator. The closure of the aneurysm was considered incomplete even if a small neck remnant e.g.1mm or more, or fundus of the aneurysm was reliably visible. Incomplete closures were divided into two categories: 1) neck remnant only or 2) residual filling of fundus of the aneurysm.

RESULTS

I *The incidence of surgical damage*

A total of 36 (16 males, 20 females) of the 101 patients presented with an area of high signal intensity on the T2- weighted images and low signal intensity on T1- weighted images in the basal temporal and basal frontal lobes. In every case this lesion appeared on the operated side. Of these

lesions two thirds (24 patients) were located in the basal temporal lobe, one third (10 patients) in the basal frontal lobe, and the remaining had lesions in the insular cortex.

A total of 25% (11/44) of the patients with ruptured aneurysm of the anterior communicating artery (AComA) presented the basal lesion (8 temporal, 3 frontal), whereas 41% (4 temporal, 3 frontal) and 45% (12 temporal, 4 frontal, 2 insular) of the patients with ruptured aneurysm of the ICA and MCA, presented with this lesion respectively. This difference, however, was not statistically significant.

Ten patients were operated for an unruptured aneurysm on the contralateral side after a recovery period from the operation of ruptured aneurysm (1-5 months). One patient had a bilateral lesion. Other nine patients had no signs of tissue damage in the basal frontotemporal region.

At the time of the MRI study 95 patients had good outcome, five patients were moderately and one patient was severely disabled. There was no significant difference between the groups with detectable lesions or no lesions when compared for the GOS at three months and at the time of the MRI.

None of the parameters analyzed for correlation to the lesion in the basal area showed any differences between the two groups; these parameters were: age of the patient, history of hypertension, pre- and postoperative angiographic vasospasm and circulation, pre- and postoperative Fisher grade and ventricular enlargement on the CT scans, the duration and depth of hypotension during the operation, duration of operation, premature rupture of the aneurysm at the operation, swelling or injury of the brain during the operation. The radiological findings are summarized in Table 4.

II *The frequency of the permanent focal and degenerative alterations of the brain*

Eighty-four of the 104 patients (81%) presented a total of 152 larger areas (>5mm) of increased signal intensity on T2 and FLAIR sequences and lowered signal intensity on T1 consistent with

infarction. Thirty-seven (24%) lesions were caused by surgery [105], 115 lesions were considered to be vascular in origin, 77 (51%) of which were caused by SAH and the rest 38 (25%) were not typically either surgical or SAH- related. (Tables 5 and 6)

Ninety-seven patients underwent imaging with both modalities (CT at 3 months and MRI). Of these 97 patients, 77 (79%) had infarction seen at MRI, whereas in the CT scan only 57 patients (59%) had hypodense areas in the brain ($p < 0.005$; chi-square). Sixteen patients presented with lesion in the frontal lobe in the CT scan. Out of the same 97 patients 47 patients presented a lesion in the frontal area when imaged with MRI. (16 vs. 48; $p < 0.001$; chi-square).

Signs of hemosiderin was present in 8 (7%) of the areas of increased signal intensity. Sixty-four patients (62%) presented small high signal foci (< 5mm) on the T2 weighted images. Eight patients (8%) had more than 50 of these lesions, 11 patients (11%) had 10-50 of these lesions and 45 patients (43%) had 1-9, forty patients (38%) did not have any small high signal foci on the T2-weighted images. The number of these foci increases with age. 50% of patients having more than 50 foci were 61 or older, no one under 41 years had more than 50 foci.

Leukoaraiosis (LA) was grading 0 in 71 (68%) of the patients, Grade I in 22 (21%) patients, Grade II in 9 (9%) patients and Grade III in two (2%) patients. The length and depth of hypotension, measured as the time period of systolic arterial pressure below 100 mm Hg and the lowest mean arterial pressure during operation, did not effect on presence or severity of LA.

In MRI all of the patients had an artifact from the clip; some of the patients had numerous clips. The average size of the artifact was 23 x 19-x 26 mm for one clip.

We measured the signal intensity of gray matter, deep white matter and the basal ganglia of 18 patients. We compared the absolute values between the two hemispheres, no significant differences were found between the sides with the initial bleeding and the contralateral side.

III *The completeness of closure of ruptured and unruptured intracranial aneurysms after microsurgery, studied with digital subtraction angiography.*

Complete closure of aneurysm was achieved in 711 (88%) of the total of 808 aneurysms (Table 7). Roughly two-thirds (59) of the 97 incomplete closures were unexpected and one third (38) of the incomplete closures were planned, to save a major vessel, because of calcifications or thick aneurysm wall. The frequency of the unexpected incomplete closure was extremely high at following locations; AComA (84% of all incomplete closures were unexpected), ICA (73% of all incomplete closures were unexpected) and pericallosal arteries (71% of all incomplete closures were unexpected) (Table 8). Of the 493 ruptured aneurysms 424 (86%) were completely occluded, 46 of the 69 incomplete closures were unexpected. Of the 94 unruptured aneurysms, which were operated at the same operation with a ruptured aneurysm, 83 (88%) were completely occluded, 6 of the 11 incomplete closures were unexpected. 221 unruptured aneurysms were operated without SAH or after a 2-3 months recovery period after SAH. Of the 221 aneurysms 204 (92%) were completely occluded. 7 of the 17 incomplete closures were unexpected. Altogether there were 315 unruptured aneurysms of which 287 (91%) were completely occluded. The difference in the number of completely closed aneurysms between ruptured and all unruptured aneurysms is significant (p = 0,003 Chi-squared) (Table 7).

The WFNS grade[27] on admission of the SAH patient or timing of surgery had no influence on the success rate of complete closure (Table 9).

The closure percentage (expected and unexpected) of the ruptured vertebro-basilar aneurysms (74%) was significantly lower than that of ruptured middle cerebral, internal carotid or anterior communicating artery aneurysms. Also, the closure percentage of the ruptured aneurysms of the middle cerebral artery (92%) was significantly higher than that of ruptured pericallosal or anterior communicating artery aneurysms, while other differences were not statistically significant. The

unruptured vertebro-basilar aneurysms were also significantly less often completely secured (77%) than the unruptured aneurysms of the carotid (97%) and middle cerebral arteries (92%) (Table 8).

The size of the aneurysm had a significant impact on closure rate (Table 8 and Table 10). Of the 20 large (15-24mm) ruptured aneurysms only 12 (60%) were completely occluded - whereas 92% and 84% of the small (2-7mm) and medium size (8-14mm) unruptured aneurysms, respectively, were completely occluded. Of the unruptured aneurysms 95% of small aneurysms were completely occluded whereas only 85% of medium, 50% of large and 57% of giant aneurysms were completely occluded.

24 of the total of 59 aneurysms (41%) with unexpected incomplete closure were reoperated, and 7 were treated with endovascular coiling (12%). After these treatments 4 aneurysms still had neck remnants.

There were 44 major vessel or branch of a major vessel occlusions, 32 were unexpected. Furthermore, the frequency of the unexpected major vessel occlusion was high at the locations of ICA (75% unexpected of all occlusions), MCA (79%) and pericallosal arteries (83%) (Table 11). Major vessel occlusion lead to reoperation in 14 patients. Two occlusions were treated with EC-IC bypass operation. In 12 occlusions a repositioning of the aneurysm clip was done with good angiographic result in 9 patients.

Altogether the control DSA led to reoperation or coiling in 45 patients.

Despite the by far greater number of large, giant and posterior circulation aneurysms, there were fewer fundus remnants in the aneurysms operated on by the senior author (with an experience of more than 2500 aneurysms treated) compared with other 11 surgeons together 2,4% vs. 6,1% (p=0.0192). The percentages of neck remnants were 10,1% vs. 11,7% (ns.) as giant and posterior circulation aneurysms were operated on by the senior author.

Outcome at three months of the patients is presented in table 12.

IV *The completeness of closure of intracranial aneurysms after microsurgery, studied with computed tomography angiography.*

Complete closure of aneurysm was achieved in 214 (98%) of the 218 aneurysms. All 4 incomplete closures were unexpected. Of the 93 ruptured aneurysms 89 (96%) were completely occluded, all of the 4 incomplete closures were unexpected. Of the 9 unruptured aneurysms, which were operated at the same operation with a ruptured aneurysm, all were completely occluded. 116 unruptured aneurysms were operated without SAH or after a 2-3 months recovery period after SAH. Of the 116 aneurysms all were completely occluded. Altogether there were 125 unruptured aneurysms. The difference in the number of completely closed aneurysms between ruptured and all unruptured aneurysms is significant (P = 0.019 Chi-squared) (Table 13).

Three of the incompletely ligated aneurysms were anterior communicating artery aneurysm, one was internal carotid artery aneurysm. Two of the incompletely ligated aneurysms were small - two were medium sized. (Table 14)

In 11 patients there were postoperatively both CTA and DSA. In one patient DSA showed slow circulation in the posterior temporal lobe which was not visible in the CTA. In one patient CTA showed a neck remnant that was not visualized in the DSA.

There were 3 major vessel or branch of a major vessel occlusions, all were unexpected. Major vessel occlusion lead to reoperation in 1 patient. Altogether the control CTA led to reoperation or coiling in 2 patients.

DISCUSSION

I *The incidence of surgical damage*

MRI is superior to CT in imaging the basal regions of the brain where the artifacts from the bone structures compromise the ability of CT to detect lesions.[68] Furthermore, after clipping or coiling of

an aneurysm the basal region is often unreadable in CT scan, whereas in MR image the diameter of an aneurysm clip artifact is only 20-30 mm.[22,81,157,158]

We found lesions at the operative site in 36 of 101 patients. These lesions were noted to be permanent in contrast to a previous report.[150] None of these lesions were seen on the pre- or postoperative CT-scans - nor were these lesions observed in any of the control CT scans obtained at 3 months. This finding emphasizes the superiority of the MRI in the basal regions of the skull, where the beam hardening effects from the bony structures and the aneurysm clip compromise the reliability of the CT.

The significance of this lesion in the basal frontotemporal area is not clear. In the present study, it seems that these lesions do not affect patient outcomes. There are more detailed and functional outcome scales (Karnofsky or Rankin scale) which could have revealed less obvious differences.

Jenkins et al. reported local edema or contusion at the operative site in all of the 10 patients who went through MRI right after operation for ruptured intracranial aneurysm.[81] Twelve of 20 (60%) patients had frontal or temporal tissue loss in the study of Romner et al[158], whereas Proust et al reported reversible hypodense areas in CT scans, which were associated with retractor-related surgical trauma for only 16 patients in a series of 200 patients.[150] In the present study lesions in the late MRI were seen in 36% of the patients, which is less than in either of the previous studies with MRI. This indicates that in the study of Jenkins et al. most of the areas of high intensity were edema related to the acute phase after the operation rather than permanent damage.[81] We did not record tissue loss but pathological signal of the brain tissue. Recording also tissue loss could have increased the number of these lesions. The fact that the MRI was performed a mean of 3.3 years after the operation, defines that these lesions are permanent rather than reversible as reported by Proust et al.[150]

No significant difference between patients with or without the basal lesion was found when compared for pre- or postoperative angiographic vasospasm. Neither was there difference in the

duration or depth hypotension during the operation between the two groups. These findings support the theory that this kind of lesion is mechanical of origin. Nor did the duration of the operation effect on occurrence the lesion.

Most of the lesions occurred in the temporal apex although routinely the retractor is also placed on the base of the frontal lobe. This could indicate that the temporal apex is more vulnerable than the basal frontal area. Damage to the bridging veins of the temporal apex causes disturbances in the blood flow and thus increases the risk of ischemic lesions to this region.

All of the lesions were at the same side as the surgical approach to the aneurysm. Ten patients were operated for an unruptured aneurysm on the contralateral side. One patient who underwent craniotomies on both sides for intracranial aneurysms presented with bilateral lesions.

The reason why patients with a ruptured aneurysm of the AComA have fewer of these lesions remains unclear. One would expect even more lesions for these patients due to the distance to the aneurysm from the dural opening and thus a greater demand for retraction. Significant differences were not detected.

Several authors have emphasized the importance of removing the sphenoid wing, to achieve a bony opening that is as flush with the floor of the middle fossa as possible. This provides the surgeon with more space and better visibility with less retraction, thus reducing the probability of damage to the brain tissue.[45,213] The swelling of the brain in the acute phase can be minimized with better neuroanesthesia and medical treatment thus allowing operation with less retraction. Monitoring of the retractor pressure during the operation, intermittent retraction[8] or developing operative technique without retractors could minimize the possibility of causing this damage.

II *The frequency of permanent focal and degenerative alterations of the brain*

Many lesions that were visible on the MRI at 2-6 years after surgical treatment of SAH are either undetected on the CT scan at 3 months postoperatively or did not exist at that time. On the CT scan

obtained at 3 months postoperatively no hypodense areas in the brain tissue of 41% of the 97 patients who underwent both imaging methods were shown. With MRI imaging the percentage of the same patients without tissue damage was as low as 21%. Especially remarkable is the increase of lesions detected in the frontal lobes - 16 versus 47, many of which might be related to surgery. This calls for further investigation for the significance of this finding. Some of the new lesions could be explained by the time interval between the CT and MRI scans (1.8 - 5.4, mean 3.1 years), but considering the age of the patients (mean 48.8.years) it is not likely.

Infarctions seen on CT correlate well with cognitive deficits.[208] However, there also have been reports of patients with severe cognitive deficits without CT findings.[207] In these cases MRI is evidently beneficial for establishing the diagnosis.

Small, high signal foci in the white matter are common incidental findings in T2 - weighted images, particularly in older patients. These asymptomatic lesions have no known clinical importance.[39,146] In this study the number of high signal foci was similar to the numbers in earlier reports and the number increases with age as the number did in earlier reports.[19,167]

Leukoaraiosis occurs more often in patients with history of stroke and in individuals with cognitive deterioration of presumed vascular origin.[11,23,77,121,184] The risk factors associated with leukoaraiosis are aging, arterial hypertension, diabetes mellitus, and cardiac diseases.[19,42,115,121,146] Moreover, a correlation of leukoaraiosis with hypotensive crises has been reported.[131] Patients with normal pressure hydrocephalus have a high prevalence of alterations in the white matter that are detectable by either CT or MRI.[18] In this study leukoaraiosis was present in 33 of 104 patients (32%). In 11 patients (11%) leukoaraiosis was considered moderate or severe. In our material the frequency of leukoaraiosis was greater among patients with history of hypertension (36% vs. 23%), the difference was not statistically significant ($p= 0.09$, chi-square).

Hemosiderin was visible in 8 (8%) patients images only, compared with 23 (22%) patients with intracerebral hematoma in the postoperative CT (104 patients).

Thus it appears that surgery for anterior circulation aneurysms or SAH itself does not increase the frequency or severity of degenerative brain alterations seen in MRI.

III *The completeness of aneurysm closure assessed with digital subtraction angiography*

An incompletely treated aneurysm may re-grow and lead to recurrent symptoms of hemorrhage or mass effect. The rebleeding rate of aneurysms with residual necks is between 3.5% and 28%.[34-36,44,64] In the long-term follow-up in extremely complex aneurysms as reported by Drake the rebleeding rate was 10%.[36] Aneurysm re-growth has been reported to occur in 3.5 to 15% of patients.[35,36,44] The high rebleeding rate over the long term (10-20 yr.) emphasizes the importance of perfect clipping. However, aneurysms treated with perfect clip placement also may rupture or regrow with mass effect[35] and this is also our long-term experience in Finland.[64,136]

Depending on definitions and the use of control angiograms, the reported incidence of residual neck after surgical clipping of an aneurysm ranges from 3.8 to 18%.[34,36,44,64,107,114,122,178,199,213] Despite our extensive experience, our overall results of 12% incomplete closures and 7.4% unexpected incomplete closures are within this wide range. This might be attributable to nonselection of patients for surgery but also to our strict criteria of the small neck remnants that might be considered successful surgical results in some other series. In our study, even the slightest “dog ear” was considered a neck remnant. Such neck remnants may not be recognized on routine control angiograms or considered as failures in other series. Furthermore, postoperative control angiography is not routinely performed in many institutions, and many surprises with partially ligated or filling aneurysms or occluded vessels remain hidden even in the most experienced neurosurgical hands. The few institutions that have presented excellent postoperative morphological results may not represent the average results achieved by surgery, or the criteria for aneurysm remnants are different. However, in the series by Drake et al. (Drake and Peerless have a total surgical experience of 5000 aneurysm operations) of 1767 vertebrobasilar aneurysms, total

obliteration was achieved in only 82.5% of aneurysms.[36] This result is biased by the extremely difficult aneurysms in relation to site and size that were treated. In addition, in our study, the frequency of unexpected incomplete closure was extremely high at the location of the anterior communicating artery (84% unexpected of all incomplete closures), internal carotid artery (73% unexpected of all incomplete closures), and pericallosal arteries (71% unexpected of all incomplete closures). Specifically, the high frequency of unexpected closure of the anterior communicating artery was surprising. This must depend on its complicated and difficult vascular anatomy. In clipping aneurysms at these locations, intraoperative angiography may be required in addition to careful handling.

In the study on timing of operation Kassell et al reported increased tightness of the brain at early surgery. It was surprising that this finding did not result in more difficult dissection of the aneurysm.[102] Accordingly, in our study, the timing of surgery did not affect the number of incomplete closures despite the tight conditions caused by the red and swollen brain tissue at early surgery. The most important thing in acute and early aneurysm surgery is to achieve a slack brain before beginning to clip the aneurysm(s). This can be achieved by anesthesiological means and especially by opening of the lamina terminals or frontal ventriculostomy. These maneuvers markedly reduce the need of retraction, which results in brain contusion and damage when use of brain spatulas is necessary.[105]

The difference of occlusion rate between unruptured and ruptured aneurysms is significant, and it might be explained by the bold dissection of unruptured aneurysms and smaller aneurysm size. In previous studies, the incidence of aneurysm neck remnants after surgery is relatively rare in the anterior circulation and in small aneurysms and much higher in the posterior circulation and midline, large, or giant aneurysms.[34,36,178] In our study, the incidence of aneurysm neck remnants in posterior circulation aneurysms hidden deep in small gaps was significantly higher than in middle cerebral artery aneurysms, which are the most common aneurysms in Finnish series.[145,155] Large

aneurysms were more often left with residual neck, often intentionally so as not to occlude any branches.

The reported high rates of unexpected major vessel occlusions, which also were observed in our series, harbor a great risk for the patient; many occur without symptoms, and they occur in the very best hands[36,64,98,122] Those who do not obtain control angiograms never see the unexpected findings. At surgery, it is often difficult to predict the presence of residual aneurysm or major vessel occlusion.[122] Use of mini-Doppler ultrasonography has improved the situation, but many vessels are too distal to be visualized. The good results of intraoperative angiography in prevention of vessel occlusions and residual aneurysms have been well documented in three recent studies.[25,106,187] Because vessel occlusion is diagnosed early, an immediate repositioning of the clip probably prevents ischaemic damage to the brain. All efforts should be made during surgery to save the vessels and replace the clip; this is the golden moment for the patient and the surgeon.

Small residual necks detected on a postoperative angiogram are left alone because of very difficult conditions at surgery (large and giant aneurysms), and reoperation probably would not achieve a better result. This leaves the responsibility to the experienced surgeon, who must make a judgment regarding each patient and aneurysm individually. In 7% of all patients, findings lead to reoperation or coiling. Considering the risk of both residual aneurysms and ischaemic deficits caused by major vessel occlusion, virtually all patients should undergo intraoperative angiography. We have tested the value of intraoperative angiography in complex (large, giant, fusiform, and vertebrobasilar artery) aneurysms. If a simpler method were made available, intraoperative angiography should be used even in patients with uncomplicated aneurysms. Control angiography and postoperative computed tomography are recommended even when surgeons are highly experienced, as surprising findings can be observed despite the good condition of the patient.

The prevalence of MCA aneurysms is typically high in the Finnish population. In addition, the female-to-male ratio usually has been 50:50. In this series, the most common ruptured aneurysm is

the anterior communicating artery aneurysm, and the number of female patients is somewhat higher than that of males. The reason for this is unknown. The study group has undergone 3 months of follow-up at our clinic. This is a short recovery period for aneurysmal SAH. For complete recovery, up to 2 years is needed, and a longer follow-up period probably would have demonstrated better results.

The conclusion to be drawn from Eastern Finland[107,199] and the ISAT study[134] is that only competent aneurysm surgeons should continue open aneurysm surgery. In the presence of inexperience, the aneurysms should be treated endovascularly, even if the expected results are inferior to those that might be achieved via surgical clipping.[63] Competent aneurysm and endovascular surgeons should form neurovascular teams to discuss and tailor an individual treatment plan for each patient and ensure satisfactory results.[139] Furthermore, today and in the future, a great amount of research effort should involve identification and treatment of aneurysms before their rupture, which will improve management results far more than any technical or medical advance.

IV *The completeness of aneurysm closure assessed with computed tomography angiography*

The overall rate of 2% of incomplete closures in this present series is remarkably low. This may due to selection bias – patients with difficult aneurysms may have been controlled with DSA and not with CTA. More likely reason is the artifacts around the clip area that make the evaluation of the aneurysm base very difficult. The low figures on for residual necks raises question on the reliability of the CTA in postoperative evaluation of operatively treated aneurysms.

The high frequency of unexpected closure of the anterior communicating artery aneurysms was expected and similar to our previous experience.[104] This is due to the complicated vascular anatomy of the communicans anterior region. The difference of occlusion rate between unruptured and

ruptured aneurysms is significant, and might be explained by the more bold dissection of unruptured aneurysms.

The question raises does CTA miss such small residuals which would be beyond resurgery or endovascular treatment. In present series 1% of all patients, findings lead to reoperation or coiling. In our previous study 7% of all patients, findings lead to reoperation or coiling.[104] We may assume that in the present series we missed close to 10 patients who would have had reclipping or coiling of the residual aneurysm if they had been examined with DSA. Simple intraoperative angiography will detect these patients, and lead to immediate reapplication of the aneurysm clip.

There are virtually no artifacts around titanium clips. But we have abandoned the use of titanium clips after trials due to weak closing force after reapplication. The development in the imaging technology has been very rapid. Maybe in the near future the CT technology overcomes the artifacts around the metal objects such as the aneurysm clip.

CONCLUSIONS

- Signs of tissue damage was identified in MR images in 36% of the 101 operated patients in the basal frontal and temporal areas. We suspect that they are retractor induced or due to disturbances in venous flow.
- Patients suffering from SAH because of a ruptured anterior circulation aneurysm harbor more lesions in the brain tissue at 2 to 6 years from ictus than might be suspected on the basis of early CT studies, especially in the frontal lobes.
- Complete aneurysm closure was achieved in 88% of aneurysms, a neck remnant was discovered in 9%, and a fundus remnant was revealed in 3%. Of 493 ruptured aneurysms, 86% were completely occluded. Of 315 unruptured aneurysms, 91% were completely occluded. The results for clipping of complex aneurysms, i.e., posterior circulation or large to giant aneurysms, were significantly inferior to those for small and anterior circulation aneurysms. In one-third of the large and giant aneurysms, a part of the base was left intentionally because of calcifications or strong wall or to prevent occlusion of any branches. In the series, a significant 5% complication rate of major vessel occlusion was detected.
- CT-angiography may serve as a reasonable compromise between invasive DSA with risk for complication, bigger costs and workload and no control at all. If in doubt, DSA should be done.

SUMMARY

It is estimated that 10 - 60% of the patients with SAH die before reaching medical attention and only 60% of patients reaching recover to normal life. Initial bleeding, rebleeding and delayed cerebral arterial vasospasm are the major causes of mortality and morbidity.To prevent the rebleeding of a ruptured aneurysm or the growth and rupture of an unruptured aneurysm, the complete closure of the aneurysm is essential. This can be achieved by microsurgery or endovascular coiling. The probability of rebleeding encourages most neurosurgeons to operate early; this also allows early and aggressive prevention and treatment of vasospasm with triple-H therapy and calcium antagonists. It is possible that the brain tissue is more vulnerable during the acute operation. Lesions possibly caused by retractor pressure to the basal areas of frontal and temporal lobes at early operation have been reported. However, the frequency of these lesions caused by surgery is not known. The difficulty in predicting the presence of residual or unclipped aneurysm suggests that all patients should undergo angiographic control. Digital subtraction angiography (DSA) is safe and reliable method to evaluate the completeness of the closure of an aneurysm. The quality and accuracy of computed tomographic angiography (CTA) is that of catheter DSA, which has been the golden standard study for patients with cerebral aneurysm. The advantage of CTA is its noninvasiveness meaning lower risk of complication as compared with DSA.

This study was carried to find out the permanent damages and the probable surgical damage of the brain tissue seen on a late MRI. We also wanted to evaluate the postoperative angiographic studies to find out the number of patients in risk for rebleeding or aneurysm regrowth after surgical repair and to find whether the noninvasive CT angiography could replace DSA.

104 patients operated early for a ruptured anterior circulation aneurysm were imaged with MRI 2 to 6 years (mean 3.3 years) postoperatively. To evaluate the number of patients in risk for rebleeding or aneurysm regrowth after surgical repair we analyzed retrospectively pre- and postoperative DS angiograms of 622 patients with 493 ruptured and 315 unruptured intracranial aneurysms. To find out whether the noninvasive CT angiography could replace DSA we retrospectively analyzed pre- and postoperative CT angiograms of 160 patients with 93 ruptured and 125 unruptured intracranial aneurysms.

MR images showed signs of surgical tissue damage in 36% of the patients. We suspect that they are retractor induced or due to disturbances in venous flow. DSA showed complete aneurysm closure in 88% of aneurysms. Of 493 ruptured aneurysms, 86% were completely occluded. Of 315 unruptured aneurysms, 91% were completely occluded. A significant 5% complication rate of major vessel occlusion was detected. CTA showed complete aneurysm closure in 98% of aneurysms. CT-angiography may serve as a reasonable compromise between invasive DSA with risk for complication, bigger costs and workload and no control at all.

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Table 1. Patients with aneurysmal SAH between April 1st , 1992, and November 30th , 1994; with late MRI control (I & II)

		No	*%*
Patients	TOTAL	104	
	Male	50	48
	Female	54	52
	Age (Mean at SAH)	45.5	
HH	1	21	20
	2	42	40
	3	31	30
	4	10	10
FISHER	0	0	0
	1	32	31
	2	53	51
	3	19	18
Aneurysm location	AComA	44	42
	MCA	40	38
	Peric	3	3
	ICA	17	16
GOS (at 3 months)	GR	79	76
	MD	15	14
	SD	10	10
	VS	0	0
	Dead	0	0
GOS (at MRI)	GR	98	94
	MD	5	5
	SD	1	1
	VS	0	0

HH, Hunt and Hess classification[72]; GOS, Glasgow Outcome Scale[82]; AcomA, anterior communicating artery; MCA, middle cerebral artery; ICA, internal carotid artery; Peric, pericallosal artery; GR, good recovery; MD, moderate disability; SD, severe disability; VS, vegetative state.

Table 2. Patients with postoperative DSA between August 1, 1998, and December 31, 2001. (III)

		Ruptured Aneurysm		*Unruptured Aneurysm*	
		No.	*%*	*No.*	*%*
Patients	TOTAL	493		222	
	Male	210	43	81	36
	Female	283	57	141	64
	Age (Mean)	53 (23-81)		52 (28-81)	
	Patients with multiple aneurysms	152	31	144	65
	Incidental unruptured aneurysms			121	
WFNS	1	207	42		
	2	89	18		
	3	27	5		
	4	84	17		
	5	85	17		
	NA	1	0		
	TOTAL	493	100		
Aneurysm location	ICA	98	20	64	20
	MCA	143	29	163	51
	AComA	174	35	44	14
	Peric	31	6	14	4
	VB	47	10	30	9
	TOTAL	493	100	315	
Aneurysm size	Small (< 7mm)	218	44	215	68
	Medium (7-14mm)	238	48	78	25
	Large (15-24mm)	20	4	8	3
	Giant (>24mm)	4	1	7	2
	NA	13	3	7	2
	TOTAL	493	100	315	100
Timing of surgery	< 24h	288	58		
	< 72h	400	81		
	3-10 days	63	13		
	> 10 days	30	6		
	TOTAL	493			
GOS (at 3 mo)	GR	227	46	98	81
	MD	99	20	13	11
	SD	94	19	7	6
	VS	20	4	1	1
	Dead	50	10	2	2
	NA	3	1		
	TOTAL	493		121	

WFNS, World Federation of Neurosurgical Societies grading [27]; GOS, Glasgow Outcome Scale[82]; AcomA, anterior communicating artery; MCA, middle cerebral artery; ICA, internal carotid artery; Peric, pericallosal artery; VB, vertebral and basilar arteries; GR, good recovery; MD, moderate disability; SD, severe disability; VS, vegetative state; NA, not available

Table 3. Patients with postoperative CTA between January 1st, 2003, and December 31, 2003 (IV)

		Ruptured Aneurysm No.	*%*	*Unruptured Aneurysm No.*	*%*
	Male	28	30	34	36
	Female	65	70	55	64
	TOTAL	93		89	
	Age (Mean)	55 (26-83)		54 (28-73)	
WFNS	1	13	14		
	2	47	51		
	3	3	3		
	4	18	19		
	5	10	11		
	NA	2	2		
	TOTAL	93	100		
Aneurysm location	ICA	19	20	29	23
	MCA	31	33	69	55
	AComA	34	37	9	7
	Peric	4	4	7	6
	VB	5	5	11	9
	TOTAL	93	100	125	100
Aneurysm size	Small (< 7mm)	51	55	86	69
	Medium (7-14mm)	38	41	26	21
	Large (15-24mm)	4	4	2	2
	Giant (>24mm)	0	0	2	2
	NA	0	0	9	7
	TOTAL	93	100	125	100
Timing of surgery	< 24h	42	45		
	< 72h	73	78		
	3-10 days	16	17		
	> 10 days	4	4		
	TOTAL	93	100		
GOS (at 3 mo)	GR	36	39	81	91
	MD	22	24	5	6
	SD	16	17	1	1
	VS	0	0	0	0
	Dead	17	18	1	1
	NA	2	2	1	1
	TOTAL	93		89	

WFNS, World Federation of Neurosurgical Societies grading [27]; GOS, Glasgow Outcome Scale[82]; AcomA, anterior communicating artery; MCA, middle cerebral artery; ICA, internal carotid artery; Peric, pericallosal artery; VB, vertebral and basilar arteries; GR, good recovery; MD, moderate disability; SD, severe disability; VS, vegetative state; NA, not available

Table 4. The baseline data correlated to basal injury and GOS at three months. (I)

		Basal lesion		*No basal lesion*	
		No.	*%*	*No.*	*%*
Fisher	1	0	0	0	0
	2	10	28	21	32
	3	20	56	32	49
	4	6	17	12	18
	TOTAL	36		65	
Aneurysm location	ICA	7	41	10	59
	MCA	18	45	22	55
	AComA	11	25	33	75
	TOTAL	36		65	
Vasospasm	None	5	14	20	31
	Mild	9	25	19	29
	Moderate	8	22	14	22
	Severe	14	39	12	18
	TOTAL	36	100	65	100
GOS (at 3 mo)	GR	34	94	61	94
	MD	2	6	3	5
	SD	0	0	1	2
	TOTAL	36	100	65	100

WFNS, World Federation of Neurosurgical Societies grading[27]; GOS, Glasgow Outcome Scale[82]; AcomA, anterior communicating artery; MCA, middle cerebral artery; ICA, internal carotid artery; Peric, pericallosal artery; VB, vertebral and basilar arteries; GR, good recovery; MD, moderate disability; SD, severe disability; VS, vegetative state

Table 5. The number and cause of infarctions correlated with the grade of the patient (HH). (II)

HH	*CAUSED BY SURGERY*	*%*	*CAUSED BY SAH*	*%*	*OTHER*	*%*	*Total No. of infarctions*
1	7	23	16	53	7	23	30
2	16	30	21	40	16	30	53
3	11	25	26	59	7	16	44
4	3	12	14	56	8	32	25
TOTAL	37	24	77	51	38	25	152

HH, Hunt and Hess classification[72]

Table 6. The number and cause of infarctions correlated with the Fisher grade.[45](II)

FISHER GRADE	*CAUSED BY SURGERY*	*%*	*CAUSED BY SAH*	*%*	*OTHER*	*%*	*Total No. of infarctions*
2	10	30	20	61	3	9	33
3	21	26	38	46	23	28	82
4	6	16	19	51	12	32	37
TOTAL	37	24	77	51	38	25	152

Table 7. The Results of Control Angiograms. (III)

	TOTAL CLOSURE	*%*	*NECK REMNANT*	*%*	*NECK AND FUNDUS REMNANT*	*%*	*MAJOR VESSEL OCCLUSION*	*%*	*Total*
RUPTURED	424	86	52	11	17	3	30	6	493
UNRUPTURED	287	91	17	5	11	3	14	4	315
TOTAL	711	88	69	9	28	3	44	5	808

Table 8. The expected and unexpected incomplete closures in control angiogram. (III)

		NO. OF EXPECTED INCOMPLETE CLOSURES	*%*	*NO. OF UNEXPECTED INCOMPLETE CLOSURES*	*%*
Aneurysm location	ICA	4	27	11	73
	MCA	14	58	10	42
	AcomA	5	16	26	84
	Peric	2	29	5	71
	VBA	13	65	7	35
	TOTAL	38	39	59	61
Size of aneurysm	Small (< 7mm)	6	21	22	79
	Medium (7-14mm)	18	36	32	64
	Large (15-24mm)	8	62	5	38
	Giant (>24mm)	4	100	0	0
	NA	2	100	0	0
	TOTAL	38	39	59	61

AcomA, anterior communicating artery; MCA, middle cerebral artery; ICA, internal carotid artery; Peric, pericallosal artery; VB, vertebral and basilar arteries; NA, not available

Table 9. The Complete Closures of aneurysms on Control Angiogram. (III)

		RUPTURED COMPLETE CLOSURE	*%*
WFNS	1	178	86
	2	82	92
	3	23	85
	4	68	81
	5	73	86
	Total No. of aneurysms	424	86
Timing of surgery	< 72h	347	87
	3-10days	54	86
	>10 days	23	77
	Total No. of aneurysms	424	86

WFNS, World Federation of Neurosurgical Societies grading[27].

Table 10. The Complete Closures on Control Angiogram. (III)

		COMPLETE CLOSURE	*%*
Aneurysm location	ICA	147	91
	MCA	282	92
	AComA	187	86
	Peric	38	84
	VB	57	74
	Total No. of aneurysms	711	88
Size of aneurysm	Small (< 7mm)	405	94
	Medium (7-14mm)	266	84
	Large (15-24mm)	15	54
	Giant (>24mm)	7	64
	NA	18	
	Total No. of aneurysms	711	88

AcomA, anterior communicating artery; MCA, middle cerebral artery; ICA, internal carotid artery; Peric, pericallosal artery; VB, vertebral and basilar arteries; NA, not available

Table 11. The unexpected major vessel occlusions in control angiogram. (III)

		NO. OF EXPECTED MAJOR VESSEL OCCLUSION	*%*	*NO. OF UNEXPECTED MAJOR VESSEL OCCLUSION*	*%*
Aneurysm location	ICA	3	25	9	75
	MCA	3	21	11	79
	AComA	2	40	3	60
	Peric	1	17	5	83
	VB	3	43	4	57
	TOTAL	12	27	32	73
Size of aneurysm	Small (< 7mm)	3	17	15	83
	Medium (7-14mm)	3	16	16	84
	Large (15-24mm)	2	67	1	33
	Giant (>24mm)	4	100	0	0
	TOTAL	12	27	32	73

AcomA, anterior communicating artery; MCA, middle cerebral artery; ICA, internal carotid artery; Peric, pericallosal artery; VB, vertebral and basilar arteries;

Table 12. The Outcome in various WFNS – grades at three months. (III)

GOS		*GR*	*%*	*MD*	*%*	*SD*	*%*	*VS*	*%*	*Dead*	*%*	*Total*	*%*
WFNS	1	154	73	36	17	12	6	2	1	4	2	208	42
	2	43	48	19	21	20	22	2	2	5	6	89	18
	3	7	26	7	26	8	30		0	5	19	27	5
	4	19	21	26	30	26	31	1	1	12	14	84	17
	5	6	7	12	14	28	33	15	18	24	28	85	17
TOTAL		229	46	100	20	94	19	20	4	50	10	493	100

WFNS, World Federation of Neurosurgical Societies grading [27]; GOS, Glasgow Outcome Scale[82];GR, good recovery; MD, moderate disability; SD, severe disability; VS, vegetative state

Table 13. The Results of Control CTA. (IV)

		COMPLETE CLOSURE	*%*
Aneurysm location	ICA	47	98
	MCA	100	100
	AComA	40	93
	Peric	11	100
	VB	16	100
	Total no of aneurysms	214	98
Size of aneurysm	Small (< 7mm)	135	99
	Medium (7-14mm)	62	97
	Large (15-24mm)	6	100
	Giant (>24mm)	2	100
	NA	9	
	Total No. of aneurysms	214	98

AcomA, anterior communicating artery; MCA, middle cerebral Artery, ICA, internal carotid artery; Peric, pericallosal artery; VB, vertebrobasilar arteries.

Table 14. Patients with incomplete closure on CTA (IV)

	WFNS GRADE	*FISHER*	*ANEURYSM*	*SIZE*	*REMNANT*
F 54	II	III	AComA	7mm	Neck
M 39	I	II	AComA	8mm	Neck
F 66	IV	IV	ICA	12mm	Fundus
F 45	IV	III	AComA	7mm	Neck

WFNS, World Federation of Neurosurgical Societies grading[27]; AcomA, anterior communicating artery; ICA, internal carotid artery.

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