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Vorstand: Univ.-Prof. Dr. med. J.-C. Tonn

Endovascular treatment of posterior circulation aneurysms

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Clemens Maria Schirmer
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Berichterstatter: Priv. Doz. Dr. med. R. Schmid-Elsaesser
Mitberichterstatter: Prof. Dr. U. Hoffmann
Prof. Dr. K.-J. Pfeifer
Dekan: Prof. Dr. med. Dr. h. c. K. Peter
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1 Introduction

1.1 Aneurysms of the posterior circulation

The definition of an aneurysm is a swelling along a blood vessel. The majority of aneurysms is saccular in shape and develops from a combination of factors including degeneration and weakening of the internal elastic lamina and collagen fibers of the arterial wall, as well as hemodynamic effects of fluid pulsations, which can be adversely increased by the presence anatomical variants. Very few of the aneurysms countered develop in utero or in childhood and it may be assumed that the majority of these lesions develop in adults. Aneurysms of the posterior intracranial circulation mainly consisting of the intracranial portion of the vertebral artery and the basilar artery and its branches tend to present with subarachnoidal hemorrhage in severe conditions that belies their incidence of about 10 -15% of all intracranial aneurysms. They most often pose challenge to a surgical approach with regards to their location and close relationship with eloquent perforating arteries (Peerless and Drake 1982; MacFarlane et al. 1983; Solomon and Stein 1988; Kassell et al. 1990; Kassell et al. 1990; Hillman et al. 1996).

Endovascular treatment of intracranial aneurysms by percutaneous endovascular coil embolization using Guglielmi electrolytically detachable coil (GDC) has been described as an alternative form of treatment with an increasing incidence in the literature (Guglielmi et al. 1992; Bavinzski et al. 1999; Byrne et al. 1999; Lempert et al. 2000).

Although the general usefulness of this method has been recognized and it is increasingly being considered an alternative to surgical clipping in selected patients (Pierot et al. 1996; Pierot et al. 1997; Eskridge and Song 1998; Kuether et al. 1998; Lempert et al. 2000)., the utility, efficacy, and safety in distinct patient populations are still in the process of being defined (Guglielmi et al. 1991; Guglielmi et al. 1992; Bavinzski et al. 1999; Brilstra et al. 1999; Byrne et al. 1999; Gruber et al. 1999; Lempert et al. 2000).

This work describes the safety and efficacy of GDC coil embolization in patients harboring aneurysms of the posterior circulation followed up over a period of up to 9 years.

1.2 Endovascular treatment

External placement of wires into intracranial aneurysms through a craniotomy was the original concept of a way of treating aneurysms through induction of thrombosis. Not entirely surprisingly this technique failed to gain widespread acceptance. Serbinenkow (Serbinenko 1974) and Shcheglov (Shcheglov and Romodanov 1982) in Russia developed a system of detachable latex balloons initially used for the treatment of carotid-cavernous sinus fistulas and the management of large and giant aneurysms of proximal location such as cavernous carotid aneurysms, which were treated by parent vessel occlusion. Later this technique was extended to intracranial aneurysms and Debrun introduced the technique in western Europe in the 1970s (Debrun et al. 1981).

Although encouraging results of this technique were obtained by Moret and Hieshima after refinement of the method, the principle of inflating a balloon inside of a previously ruptured aneurysm caused many to hesitate to adopt its use (Hieshima et al. 1981; Moret et al. 1991). These limitations prompted others to use the thrombogenic potential of fiber platinum coils originally developed for vessel occlusion, Hilal (Hilal et al. 1989) and Casasco (Casasco et al. 1993) reported first results that led to a fairly extensive use. This was superseded however by the development of the electrolytically detachable platinum coil device, developed in cooperation between G. Guglielmi at the UCLA Medical center and I. Sepetka, an engineer working for Target Therapeutics (Guglielmi et al. 1991; Guglielmi et al. 1991). Prominent feature of this device is the electrolytic detachment mechanism that allows for safe, reliable and atraumatic detachment of the coil after satisfactory placement has been obtained. Despite the original research objective that the application of the direct electrical current could produce an electrothrombotic effect, it turned out to be the obstruction of the blood flow into the aneurysm fundus that produced the thrombotic effect. After approval in European countries in 1992 and 1993 and from the United States FDA in 1995 it has been rapidly adopted and used in the management of selected patients with ruptured and unruptured aneurysms in

excess of 25000 patients worldwide by 1998. Early results that were obtained as part of the FDA approval process were reported by Vinuela (Vinuela et al. 1997).

The anatomical objective of endovascular treatment is complete obliteration of the aneurysm fundus in a stable configuration of the coil mass without compromising blood flow through the parent vessel. The relationship between anatomical degree of occlusion of an aneurysm and the risk of future hemorrhage is still uncertain and part of the questions asked in this thesis.

Criticism of endovascular therapy stems from the potential for rebleeding from partially occluded aneurysms. The need to demonstrate complete obliteration of the sac has been emphasized (Raymond and Roy 1997; Cognard et al. 1998), and the terms dog-ears, neck remnants, and residual aneurysm have been used in the literature to describe the angiographic appearance of partially occluded aneurysms. The long-term natural history of partially occluded aneurysms is not yet clear. As the pool of data for endovascular therapy increases, it is becoming clear that it is a viable alternative to surgical clipping in selected patients. Moreover, in certain situations, it might be regarded as the treatment of choice. A variety of mechanisms may lead to thromboembolic complications, including stasis of the distal flow in the parent vessel through occlusion and manipulation of the parent vessel. Distal embolization may then lead to neurological deficits. The same may occur when preexisting thrombus inside the aneurysm dome becomes dislodged during the coiling process. The coiling process might be incomplete, leaving either coil mass within the parent vessel lumen or a remnant, both can lead to formation of new thrombus. Qureshi et al. report a rate of 8.2% for thromboembolic complications in a comprehensive literature review (Qureshi et al. 2000).

Nowadays we still lack conclusive randomized controlled trials directly comparing surgery with endovascular therapy, but the criteria for the ideal "endovascular candidate" are beginning to emerge. The aim of this thesis is to discuss the current literature that is concerned with the comparison of surgical treatment and endovascular treatment exemplified by aneurysms of the posterior circulation, detailing population demographics; outcomes; and morbidity, mortality, rebleeding, and complication rates.

1.3 Posterior inferior cerebellar artery aneurysms

The posterior inferior cerebellar artery (PICA) commonly arises approximately 15mm proximal to the vertebrobasilar junction and supplies blood flow to the medulla, cerebellar tonsil, inferior vermis and the suboccipital aspect of the cerebellar hemisphere. The PICA is divided into five segments (I-V) (Lister et al. 1982; Hudgins et al. 1983): the anterior medullary segment (I) including its origin off of the vertebral artery where the artery is anterior to the medulla, the lateral medullary segment (II), the tonsillomedullary segment (III) traversing the fibers of cranial nerves IX, X, XI with its characteristic caudal loop, the rostral loop of the telovelotonsillar segment (IV) with the choroidal point at its apex leading to the final cortical segment (V). Aneurysms along the course of the PICA represent fewer than 0.5% to 1% of all intracranial aneurysms (Yamamoto et al. 1984), seem not to have a gender predominance and occur mostly proximal to the choroidal point (Beyerl and Heros 1986).

Usual presentations include sixth or lower cranial nerve symptoms, and in deficits arising from structural compression secondary to mass effect.. In patients presenting with a ruptured aneurysm the concomitant presence of acute subarachnoid hemorrhage with the associated cerebral edema and adhesion of aneurysm to the surrounding thrombus may increase the difficulty of safely accessing PICA aneurysms with open microsurgical technique, especially if located near deep brain stem structures with interposed cranial nerves and perforator arteries. Aneurysm of the distal PICA may also present with fourth-ventricular hemorrhage (Urbach et al. 1995), mass (Alexander et al. 1966; Yamaura et al. 1980), or intraparenchymal hematoma that may be mistaken for spontaneous cerebellar hemorrhage.

1.4 Superior cerebellar artery aneurysms

Aneurysms involving the superior cerebellar artery (SCA) without a mycotic origin are rare. Two large case series suggest a rate between 0.25% and 0.66% of all aneurysms of the posterior circulation (Locksley 1966; Yoshimoto et al. 1978). The SCA arises near the termination of the basilar artery, and passes lateralward, immediately below the oculomotor nerve, which separates it from the posterior cerebral artery. It then winds around the cerebral peduncle, close to the trochlear nerve, and, arriving at the upper surface of the cerebellum, divides into branches into

the pia mater and anastomoses with those of the inferior cerebellar arteries. It gives several branches to the pineal body, the anterior medullary velum, and the tela chorioidea of the third ventricle (Gray et al. 1995).

Infarction of the SCA, rarely encountered may lead to ipsilateral ataxia, ipsilateral intention tremor, ipsilateral Horner's syndrome, contralateral pain and temperature, and contrapulsion of saccades. Due to the supply pattern of the cerebellum between SCA, anterior inferior cerebellar artery (AICA), and posterior inferior cerebellar artery (PICA) an infarction of the SCA has a propensity to cause serious cerebellar swelling. Sequelae may also be vertigo secondary to ischemia of the fastigial nucleus or its outflow tracts in the superior cerebellar peduncle.

There have been occasional reports of cases where clipping of aneurysms with preservation of the parent vessel was successful (Papo et al. 1977; MacFarlane et al. 1983; Matricali and Seminara 1986; Collins et al. 1992), however especially for peripheral lesions the occlusion of the parent artery and/or trapping of the aneurysm with surgical clips has been the more common surgical approach (Mabuchi et al. 1992). This may itself lend to a prove of principle that a sufficient treatment of at least some SCA aneurysms is the occlusion of the parent artery, a goal that may also be achieved using endovascular coil embolization with Guglielmi electrolytically detachable coils. This may be a attractive alternative to surgical clipping, sparing the patient the longer and sometimes more hazardous time to full recovery after undergoing a craniotomy and surgical clipping. This work presents a series of 17 patients who underwent endovascular treatment of SCA aneurysms. This is the largest series of SCA aneurysms treated with this modality.

Presentation of SCA aneurysms varies, many suffer from the subarachnoidal hemorrhage (Locksley 1966) associated with rupture of the aneurysm, however there may be only subtle involvement of the adjacent cranial nerves (Papo et al. 1977; MacFarlane et al. 1983; Matricali and Seminara 1986).

1.5 Aneurysms of the vertebrobasilar junction

The aim of this study is to demonstrate the safety and efficacy of endovascular treatment of aneurysms of the vertebrobasilar junction. Morphology and geometry of

the vertebrobasilar junction was put in relationship to the location and morphology of the aneurysms.

The basilar artery is the only large artery in the human body that emerges from the junction of two arteries and contains the combined flow of these two.

Aneurysms of the vertebrobasilar junction are uncommon, comprising about 1-2% of all aneurysms of the posterior circulation. And in some patients they present in association with a fenestration of the basilar artery.

The anatomy in this area is usually complex, great variability of the anatomy of the larger vessels is contrasted by fairly constant anatomy of the perforators. Four zones have been identified, where small caliber perforators leave the arterial system near the vertebrobasilar junction and enter the brainstem (Grand et al. 1997). Additionally several cranial nerves in this area deny the surgeon easy access and clipping of the aneurysms, however the major obstacle seems to be the necessity to remove a portion of the petrous bone to gain direct view (Lawton et al. 1997; Aziz et al. 1999). A number of innovative skull base approaches have been developed that grant the surgeon the possibility of direct access to the aneurysm, however, they harbor non-trivial technical aspects (Solomon and Stein 1988; Lawton et al. 1997; Aziz et al. 1999).

1.6 Basilar apex aneurysms

Treatment of basilar tip aneurysms before the advent of endovascular therapy has been a surgical challenge. They are deeply located, with eloquent perforating arteries and cranial nerves in the immediate vicinity complicated by the small confines of the surgical exposure (MacFarlane et al. 1983; Solomon and Stein 1988; Batjer and Samson 1989; Kassell et al. 1990; Kassell et al. 1990; Hillman et al. 1996). Even after the development of innovative approaches to the skull base and technical improvements (Day et al. 1997; Lawton et al. 1997; Aziz et al. 1999) the morbidity and mortality rates associated with their exposure remain high (Drake 1979; Hernesniemi et al. 1992; Hillman et al. 1996).

Endovascular occlusion of intracranial aneurysms using Guglielmi electrolytically detachable coils (GDCs) has been accepted as a valuable therapeutic alternative to

surgical clipping of basilar tip aneurysms in patients who were not candidates for surgical intervention because of their presentation in poor condition, advanced age or the difficult nature of their lesion (Guglielmi et al. 1992; Peerless et al. 1994; Bavinzski et al. 1995; Nichols et al. 1997; Kuether et al. 1998; Bavinzski et al. 1999; Byrne et al. 1999). Basilar tip aneurysms in particular are well suited for endovascular approaches as for the distinct angiographic features of most of them. The efficacy and optimal risk stratification for endovascular treatment is currently in the process of being defined (Guglielmi et al. 1992; Bavinzski et al. 1995; McDougall et al. 1996; Nichols et al. 1997; Kuether et al. 1998; Bavinzski et al. 1999; Brilstra et al. 1999; Byrne et al. 1999; Steiger et al. 1999).

1.7 Objectives of this study

The aim of this study is to analyze the results and the outcome in patients with aneurysms of the posterior circulation which underwent endovascular treatment as the primary treatment option.

2 Patients and methods

From June 1991 to January 2000, a total number of 153 patients presented at the University of California San Francisco Medical Center, underwent diagnostic evaluation and endovascular treatment of the intracranial aneurysm with the use of Guglielmi detachable coils (GDC) (Target Therapeutics). The patients' hospital records, outpatient charts, operative reports, all angiographic, computed tomography, and magnetic resonance studies were subjected to careful retrospective analysis and review. Clinical examination and angiographic follow-up studies were also supplemented by telephone interviews. There was no prospective protocol for the follow-up, dates for follow-up examinations and angiographies were scheduled by the responsible surgeon based on the clinical course of the patient. Two serial angiographies over a time interval of more than 6 months warranted continuation of the follow-up on a clinical basis only.

Twenty-three patients had aneurysms of the posterior inferior cerebellar artery (PICA), and 17 patients were found to have aneurysms of the superior cerebellar artery (SCA). In 12 patients the aneurysms were situated at the vertebrobasilar junction (VBJ), and 101 patients harbored an aneurysm of the apex of the basilar artery (basilar-tip aneurysms, BTA).

Due to particularities of the admitting scheme at UCSF Medical Center at that time and constraints of the capacity of the cerebrovascular neurosurgeons all patients in this study represent a large and unbiased share of all patients admitted with intracranial aneurysms during that time. There was no triage process involved that tagged patients into a surgical and an endovascular category.

2.1 Angiographic Analysis

Quantitative measurement of aneurysm size was performed as previously described (Lempert et al. 2000) using digital subtraction angiographic projections obtained with externally placed 1-cm reference washers to correct for geometric magnification. Studies performed after 1996 employed an on-board angiographic digital computer (Toshiba Corporation, Tustin, CA) for measurement of aneurysm height, width, and neck size. The analysis included determination of aneurysm shape, degree of

aneurysm occlusion, and extent of aneurysm recanalization. The angiographic projections of the aneurysm used during initial treatment and subsequent follow-up studies were separately analyzed by two neurointerventional radiologists to determine the rate of occlusion of the aneurysm, which the proportion of the projected area of the aneurysm which was occluded by coil placement. A third independent Neuroradiologist was called upon for arbitration in cases of discrepancy. One hundred percent (100%) occlusion was assigned only to aneurysms with dense packing, and no contrast filling of the aneurysm fundus or neck. Aneurysm neck remnants were determined with respect to the total projected area of the aneurysm.

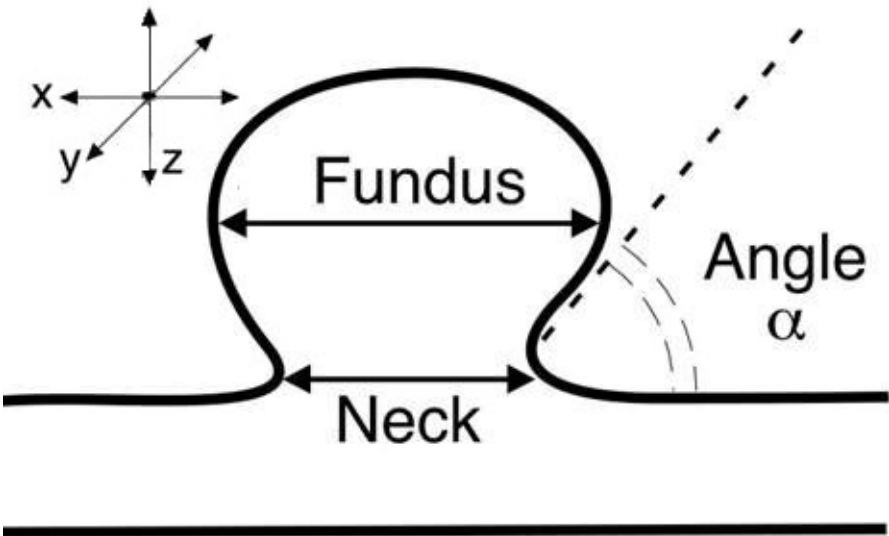


Figure 2-1 – Measurements taken from radiographic projections of the aneurysms after performing digital subtraction angiographies. Fundus and neck dimensions represent the maximal dimensions obtained from anterior-posterior and oblique views.

2.2 Clinical Outcome Measures

Clinical condition at the time of treatment was evaluated using the Hunt/Hess method (Hunt and Hess 1968). Clinical outcome was measured using the Modified Rankin scale (van Swieten et al. 1988), the Quality of Life Outcome Scale (QOL) (Stachniak et al. 1996) (in which QOL 1 corresponds to a patient with normal lifestyle, QOL 2 to a patient with minor neurological dysfunction but who is able to perform activities of daily living without help, QOL 3 to a patient needing assistance with daily activities, QOL 4 to one unable to perform activities of daily living and requiring full-time care, and QOL 5 to death), and the Glasgow Outcome Scale (GOS) (Jennett and Bond

1975) (where GOS 1 corresponds to good recovery and resumption of normal life despite minor deficits, GOS 2 to a moderately disabled but independent patient, GOS 3 to a severely disabled (but conscious) patient who is dependent on others for daily support, GOS 4 to a persistently vegetative state, and GOS 5 to death). Clinical data were obtained from neurological examinations by UCSF Cerebrovascular Neurologists during follow-up angiographic studies, examinations by patients' referring Neurosurgeons and Neurologists, and by telephone interviews with a Neurosciences Clinical Nurse Specialist.

2.3 Clinical Management and Technical Complications

Additional information included the interval between subarachnoid hemorrhage and treatment, dates of retreatment, medical history and complications, initial signs and symptoms and their progression or resolution, rebleeding, presence or absence of vasospasm, treatment of vasospasm, adverse events at diagnostic angiography, during GDC coil embolization, and delayed complications. Adverse events were categorized by type of adverse event, imaging characteristics, and adverse event outcome.

2.4 Statistical Analysis

Clinical information, procedural information, follow-up, and angiographic data of all endovascular aneurysm treatments performed at UCSF since 1991 were maintained in a database, and statistical analysis was performed with the SAS Institute software package (SAS Institute, Cary, NC). ANOVA was used to compare outcome scores versus presentation and treatment characteristics, and the Turkey-Kramer honestly significant difference correction was used for comparison as appropriate. Categorical values were compared with the Wilcoxon rank-sum test. Additionally, Pearson's χ^2 -test was used to determine marginal homogeneity among nominal variables. A p value of 0.05 or less was considered statistically significant. Regarding the relatively small n of this study a significant result may still be questionable concerning the appropriateness of Pearson's χ^2 -test in this case.

A categorical response model was used to show the dependency of categorical prognostic factor for an outcome parameter. The model compares subgroup

probabilities against overall probabilities in a constant response model. The negative log-likelihood test was used to assess significance.

2.5 Endovascular Embolization Method

2.5.1 Guglielmi Detachable Coils Embolization

2.5.1.1 Approach and anticoagulation

The method of aneurysm coil embolization used by our group has been previously described in detail (Lempert et al. 2000). A 6F or 7F vascular access sheath (Avanti, Cordis Endovascular) was inserted in the common femoral artery. Complete diagnostic high-resolution angiography was performed using digital subtraction angiography (DSA) to evaluate the presence and extent of vasospasm and other intracranial vascular anomalies prior to endovascular treatment. After determining the optimal orthogonal view for embolization, a baseline activated clotting time (ACT) was obtained and the patient was administered a weight-based bolus of intravenous heparin (70 units/kg of body weight) to achieve an ACT value between 250 and 300 seconds, and maintained by hourly boluses (35 units/kg of body weight). This is done because the risk of thromboembolism is regarded as dominant over the risk of hemorrhage even after recent subarachnoidal hemorrhage. In cases of ruptured aneurysms, the heparin was reversed with an appropriate dose of intravenous protamine sulfate at the end of the procedure, while in unruptured cases, the anticoagulation was allowed to decay or was maintained overnight in cases of partial branch compromise or thrombus around the coil mass.

2.5.1.2 Guide catheters

After confirming therapeutic anticoagulation, a 6 French (Envoy, Cordis) thin-walled straight guide catheter was carefully placed in the dominant vertebral artery, while avoiding flow occlusion. The hydrophilic coating of the catheter enables a very distal position to be obtained in the vertebral artery with minimal associated risk. It also offers a combination of a very soft flexible distal tip combined with a reasonably stiff shaft to provide a stable position in the parent artery during manipulation of the microcatheter.

2.5.1.3 Catheter selection and shaping

Using magnified real-time fluoroscopy and digital road-mapping techniques, a microcatheter (0.010-0.018 French) was placed coaxially through the guide catheter and directed into the aneurysm with the aid of a microguidewire (0.010-0.016 French). A stable position of the microcatheter within the aneurysm is most important for successful and reliable results. This may require steam shaping of the catheter tip to achieve an appropriate configuration according to the relation between parent vessel and aneurysm neck and dome.

2.5.1.4 Coil selection and placement

There is a larger range of GDC coils of different sizes and strengths available ranging from GDC 18 (20 mm) to GDC 10 soft coils with a 2 mm helix. The selection is operator-dependent and usually based on measurements made using the fluoroscopy equipment.

GDC coil embolization of aneurysms was performed using either GDC T10 or T18 (Target Therapeutics, Fremont, CA) electrolytically detachable coils, aiming to obliterate the aneurysm fundus without impinging on the parent vessel. Due to its preeminent importance the first coil should be accurately matched to the diameter of the aneurysm fundus to form a basket which provides a stable platform for subsequent dense packing. After successful placement and detachment of the first coil the sizing of the subsequent coils is normally progressively smaller by 1-2 mm helix size to achieve progressive central packing of the initial basket. After deployment of each coil it is essential to check both the anterior-posterior and lateral plane to avoid herniation of loops into the parent vessel or rupture of the aneurysm fundus. It will also allow the operator to judge the density of the packing based on the radiographic appearance.

Detachment is achieved by connecting a ground needle electrode to the groin of the patient and the positive electrode to the end of the coil wire. Direct current is applied from an isolated, battery driven system and in most situations detachment occurs after 1-3 minutes.

The availability of soft coils, in particular the GDC 10 soft coils fosters the packing of aneurysms due to the excellent deforming properties, allowing for denser packing and improved long term outcome.

In cases with saccular aneurysms that had a definable neck, coils were used to obliterate the aneurysm fundus without impinging on the parent vessel. In fusiform ruptured aneurysms, the coils were used to occlude the aneurysmal segment of the parent vessel. Following embolization, the patient was transferred to the Neurointensive Care Unit.

2.5.1.5 Coil removal

For wide-necked aneurysms with an adverse neck-to-dome ratio Moret et al. (Moret et al. 1997) described a remodeling technique, more results were later reported by Aletich et al. (Aletich et al. 2000) and Malek et al. (Malek et al. 2000). It involves placement of a separate balloon microcatheter over the neck of the aneurysm in the parent artery and inflating it during deployment of the coil within the aneurysm. This ensures that the coil mass is stably retained within the aneurysm dome and allows for tighter packing of the aneurysm neck.

2.5.2 Parent vessel occlusion

Some patients in this series were treated by complete occlusion of the parent vessel rather than selective embolization of the aneurysm. This was mostly caused by anatomical considerations and the individual aneurysm geometry, as e.g. present in fusiform aneurysms of the posterior inferior cerebellar artery. The course of the procedure in general is the same as described above; patients were monitored carefully after the procedure and managed perioperatively in a similar fashion.

3 Results

3.1 Posterior inferior cerebellar artery aneurysms

3.1.1 Patient Population and Presentation

The median age of the patients who were found to have an aneurysm of the posterior inferior cerebellar artery (PICA) was 59 years; age ranged from 1 to 87 years. There were 14 women (61%) and 9 men (39%). Of all patients in this series 13 patients (57%) presented with acute or subacute subarachnoidal hemorrhage (SAH) after rupture of the aneurysm. The median time to treatment after initial SAH was 2 days ranging from same day intervention to 75 days. The stratification of treated patients according to the Hunt-Hess grading system was as follows: grade I in 5 patients (5 of 13 patients, 38.5%), grade II in 3 patients (23.1%), grade III in 4 patients (30.8%), grade IV in 1 patient (8%), and grade V in 1 patient (8%). See also table 1 for a summary of the presentation.

3.1.2 Morphology and Location

Of all aneurysm in this series 17 were found to be in the proximal portion (74%), which included 10 that were located right at the origin of the PICA from the vertebral artery (43%), and 6 aneurysms, which came off segment 1 clearly distinct to the origin (26%). There were 4 aneurysms located in segment 2 (17%), 2 (9%) in segment 3, 1 in segment 4 (4%), while none occurred in segment 5. These were summarized to be in the distal portion (6 of 23 aneurysms, 26%), see also Figure 3-1.

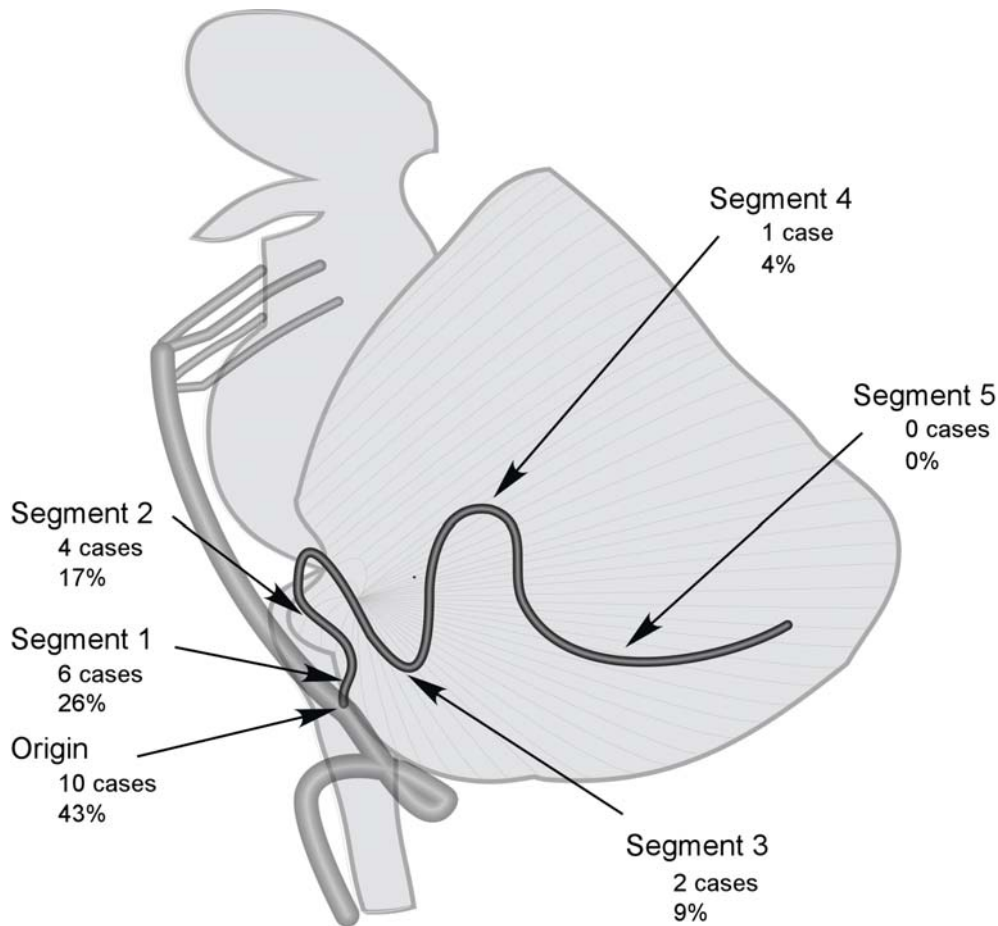


Figure 3-1 – Posterior inferior cerebellar artery and its relationship with important structures (simplified). Also depicted are the different segments of the PICA and the relative prevalence of aneurysms of this study in each segment. There were 10 aneurysms located at the origin of the PICA (43%), 6 aneurysms in the anterior medullary segment (segment 1) (26%), 4 aneurysms in the lateral medullary segment (segment 2) (17%), 2 aneurysms in the tonsillomedullary segment (segment 3) (9%), one aneurysm in the telovelotonsillar segment (segment 4) (4%). No aneurysm was found in the cortical segment (segment 5).

In 13 patients (13 of 23 patients, 57%) the neck diameter was less than 3 mm, in 2 cases between 3-5 mm, and in 2 cases between 5-7 mm (9%) each, and on patient had an aneurysm with greater than 10 mm neck diameter (4%). The fundus dimension was less than 4 mm in 1 patient (1 of 23 patients, 4%), between 4 and 7 mm for 11 patients (48%), between 7 and 10 mm for 7 patients (30%), and two patients each had a maximal fundus diameter between 10 and 13 mm (9%), and greater than 13 mm (2 of 23 patients, 9%). See Figure 3-2 for histograms of the neck and fundus dimension. The neck to dome ratio varied considerably between

individual aneurysms, however less than 25% of the aneurysms had unfavorable ratios of more than 0.51.

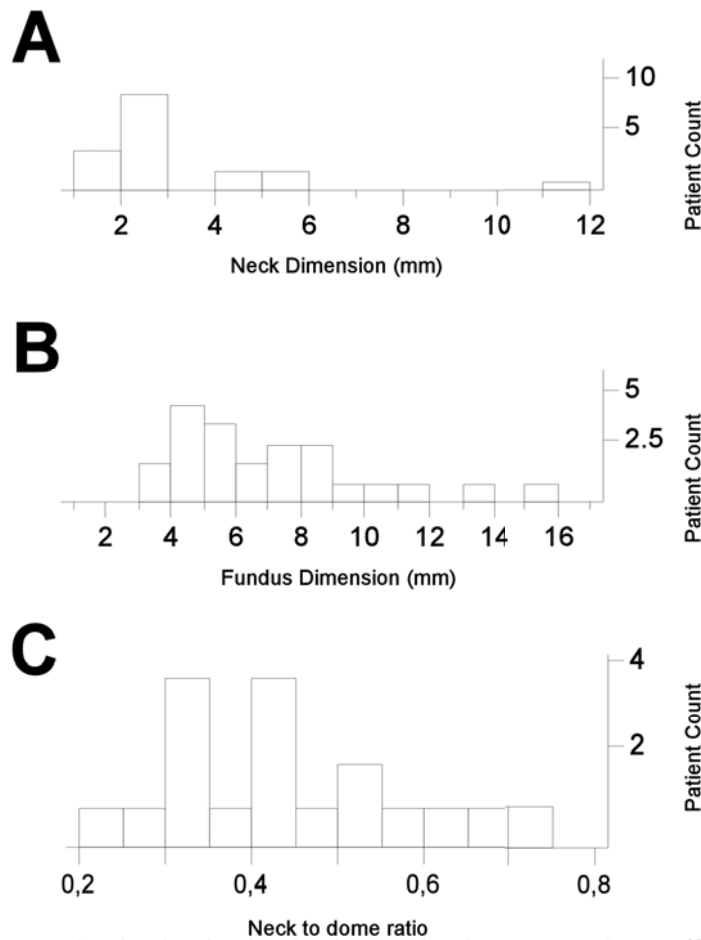


Figure 3-2 - Morphology and angiographic characteristics of PICA aneurysms. (A) Neck dimension distribution. (B) Distribution of the largest angiographic fundus diameter. (C) Diagram representation of the neck-to-dome ratios found in this subgroup of posterior circulation aneurysms.

Ten of the 23 aneurysms were located on the left side (43.5%), and 14 were located on the dominant side of the vertebral artery (60.9%). In five patients the parent vessel was co-dominant (21.8%) and in 2 patient non-dominant (8.9%) ($p < 0.0003$). Two were on the dominant side in association with an arteriovenous malformation (8.9%). Of note is that all of the left-sided aneurysms were in a dominant location (7 of 7 patients, 100%), whereas there were 2 non-dominant parent-vessels of aneurysms located on the right side (2 of 9 patients, 22%).

3.1.3 Technical Success and Angiographic Outcome

Endovascular treatment was successfully performed in 23 of 23 patients (100%), i.e. superselective catheterization of the aneurysm dome was reached and GDC coil deployment was performed, one patient (4%) needed to undergo retreatment due early recanalization of the aneurysm. Refer also to Table 1 for a summary of the technical success and angiographic outcome. In this case of a wide (>4mm) saccular aneurysm of the proximal PICA a loop of the used coil extended into the vertebral artery and the patient was treated with aspirin. Due to the fusiform shape and proximal location of 9 aneurysms (39%) an occlusion of the parent PICA was unavoidable.

Angiographic follow-up was obtained in 19 of 23 patients (83%), with a median angiographic follow-up duration of 7 ± 1.7 months, the extremes ranging from 0 to 32 months. See Figure 3-3 for a histogram presentation. The initial mean occlusion rate for all aneurysms (n=23) was 96.6% with a final occlusion rate of 96.9% with a SEM 1.2 and 1.2 respectively. The difference was non-significant. Of these 15 (66%) were embolized to 99% to 100%, 4 (17%) were occluded to 95% to 99%, 4 (17%) were incompletely occluded to <90%.

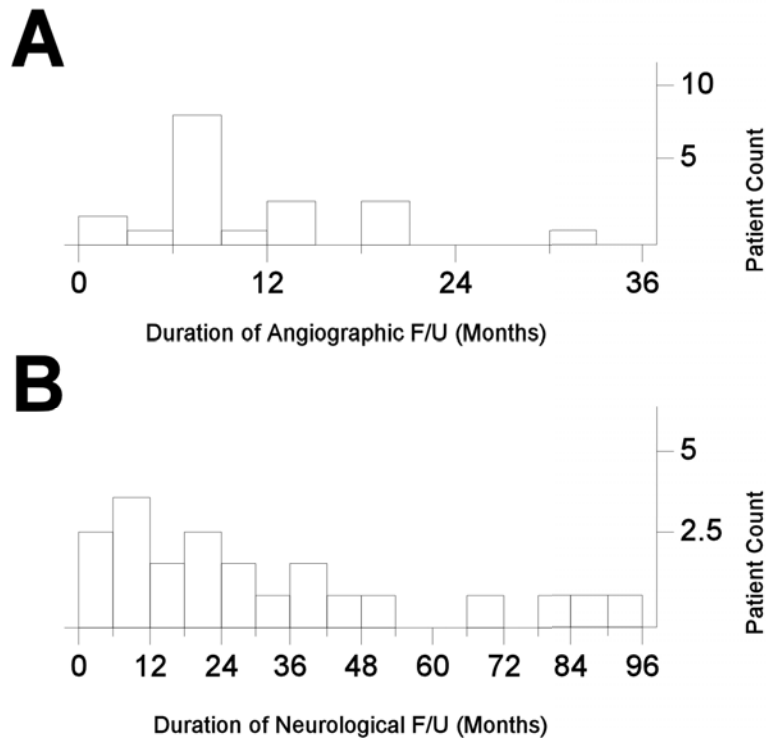


Figure 3-3 - Duration between embolization of PICA aneurysms and latest angiographic (A) and neurological (B) follow-up examination in 19 of 23 patients treated.

Parameters of aneurysm dimensions, i.e. neck and largest fundus diameter were found to be weakly correlated with a decreased percentage of final occlusion. In 2 of 23 patients evidence for partial recanalization of the aneurysm was found (8%) and these underwent a second successful treatment.

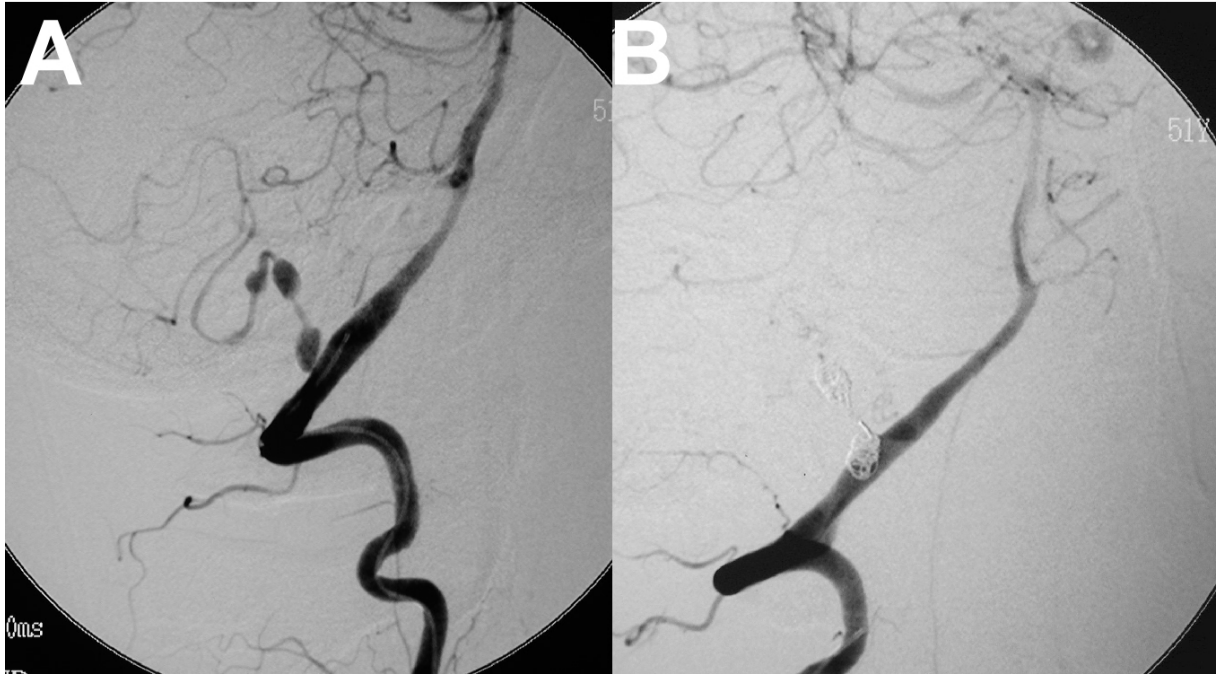


Figure 3-4 - Case #16 - 51 year-old male suffered from Hunt-Hess grade III SAH after rupture of a fusiform aneurysm involving segments II and III of the PICA. (A) Injection of the right dominant vertebral artery reveals the fusiform aneurysm with a probably dissecting origin in segment II of the PICA and three visible aneurysmal dilations. (B) The aneurysm was treated by parent vessel occlusion by deployment of multiple GDC coils, which lead to complete cessation of flow in the PICA and the aneurysm. The patient did not suffer from a neurological deficit and was discharged from the hospital in excellent condition. At follow-up he did not have any symptoms.

3.1.4 Clinical Follow-up and Outcome

Clinical follow-up was achieved in 22 of 23 treated patients (96%), the median duration of the follow-up was 23 ± 5.9 months, ranging from 3 to 92 months. At latest follow-up, 83% (19/23) of patients showed good recovery (GOS I), 9% (2/23) had moderate disability (GOS II), 4% (1/23) were severely disabled (GOS III), no patient was vegetative (GOS IV), and 4% (1/23) was dead (Figure 3-6). Overall, 91% (21/23) of patients had good recovery or moderate disability (GOS I and II) at the time of final follow-up. Notably enough patients with an adverse outcome (GOS III and IV) initially presented with a ruptured aneurysm. All patients (10/10 patients, 100%) with a non-ruptured aneurysm and eight patients (11/13 patients, 85%) with a ruptured aneurysm presenting with SAH had good recovery or moderate disability (GOS I and II) upon final assessment.

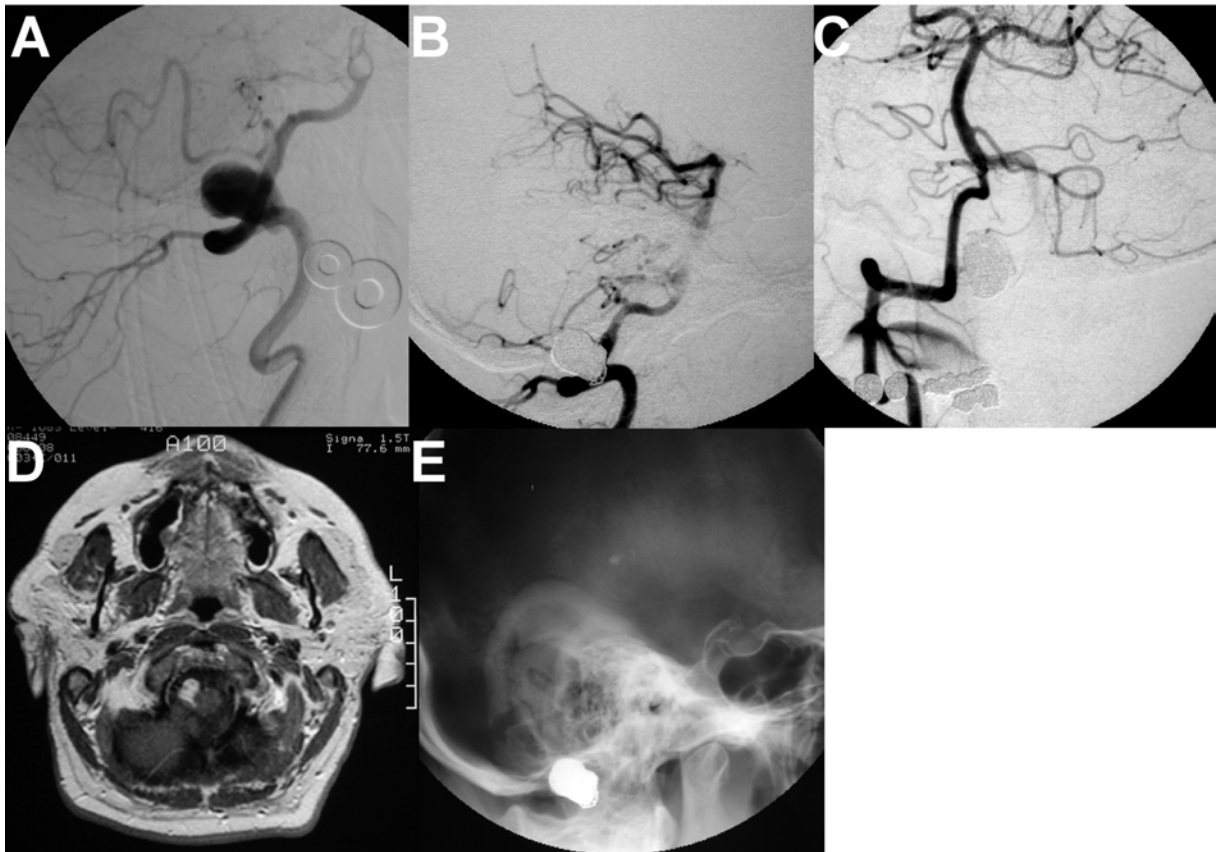


Figure 3-5 - Case No. 1: 43 year-old male with an unruptured right-sided large fusiform aneurysm of the lateral medullary (II) segment of the PICA. Injection of the right vertebral artery revealed a 15 mm fusiform aneurysm (A), which subsequently was successfully occluded with GDC coils (B). Follow-up angiography seven months later showed stable occlusion of the aneurysm and the distal PICA. (C) During his postoperative course the patient did not develop a neurological deficit. Of note is the rare extracranial location of the aneurysm, which is demonstrated on a plain skull film (E) and on axial MRI (D) (Chen and Chen 1997; Andoh et al. 2001).

There is a statistically significant correlation between Hunt-Hess grade at presentation and final GOS outcome score ($\chi^2 = 30.6$, $p < 0.01$) (Figure 3-7A). Of the 10 patients presenting with unruptured aneurysms 60% (6/10) had an initial GOS I which was unchanged upon final evaluation, 40% (4/10) had an initial GOS II, of which 3 patients (75%) improved to a final GOS score of I, and 25% (1 of 4 patients) remained unchanged GOS II. All 5 patients presenting in Hunt-Hess grade I had a final score of GOS I. Of the 3 patients presenting in Hunt-Hess grade II, 100% (3/3) improved to a final score of GOS I. Of the four patients presenting in Hunt-Hess grade III, 50% (2/4) improved to GOS I after presenting with an initial GOS III, 50% (1/2) deteriorated to GOS III after initially presenting with a GOS II, and one remained

stable grade II GOS. One patient presenting with Hunt-Hess grade IV markedly improved from GOS IV upon presentation to GOS I at the final assessment. The only patient presenting with Hunt-Hess grade V failed to improve and even deteriorated to GOS V from an initial GOS IV. Overall, of the 17 patients presenting in Hunt-Hess grades I to II or with unruptured aneurysms, 94% (16/17) achieved a GOS I outcome score on final follow-up, and 100% (17/17) had a GOS score of II or I upon final evaluation.

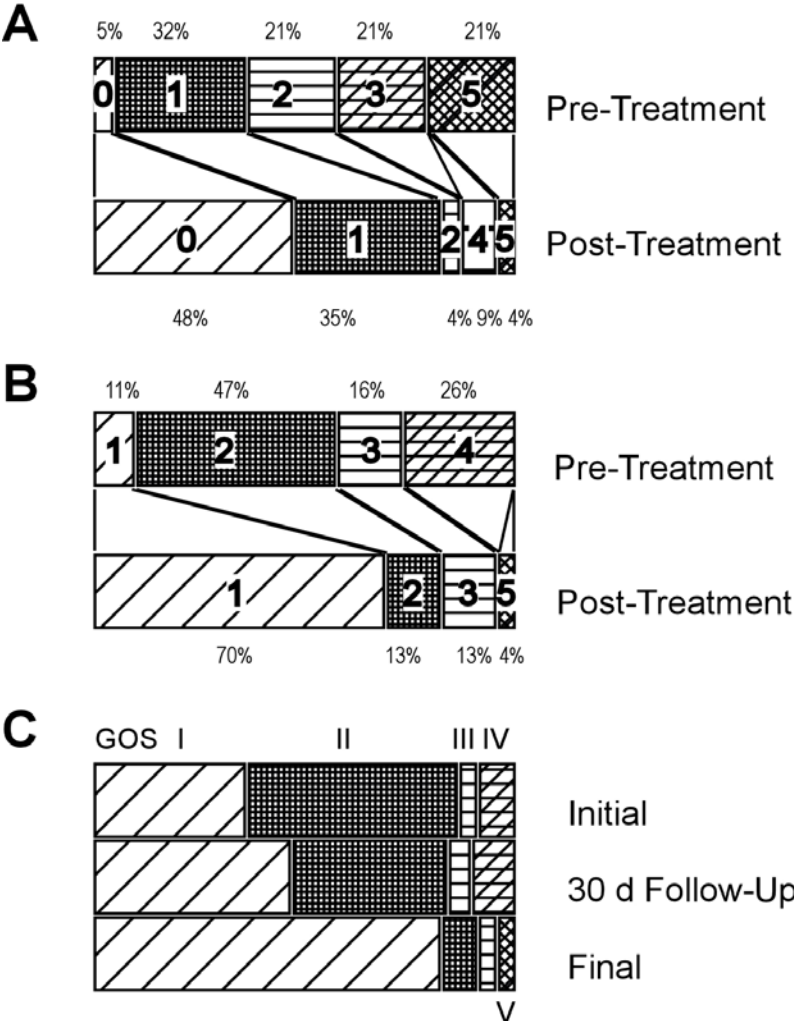


Figure 3-6 - Relative relationship between subgroups for the Modified Rankin Score (A) and the Quality of Life Scale (B) before and after treatment. (C) shows the development of the Glasgow Outcome Score.

The QOL scale was used to assess the status of treated patients at final follow-up. A statistically significant relationship between Hunt-Hess grade at presentation and final QOL score was demonstrated ($\chi^2 = 32.4, p < 0.006$) (see Figure 3-7B). A similar

analysis of the modified Rankin outcome at latest follow-up established a significant correlation with Hunt- Hess grade at time of presentation ($\chi^2 = 38.3$, $p < 0.009$) (see Figure 3-7C). The patient (1/23, 4%), who presented without any symptoms (modified Rankin scale 0) and five of the six (83%) patients presenting without significant disability despite symptoms (mRankin scale 1) harbored a non-ruptured aneurysm. Of these 6 had an excellent outcome (mRankin scale 0) (60%), 3 (30%) had remaining non-disabling symptoms (mRankin scale 1) and one (10%) patient deteriorated to mRankin scale 2. Of the 13 patients with a ruptured aneurysm, 5 (38%) had an excellent (mRankin scale 0), and 5 (38%) had a good outcome (mRankin scale 1), in contrast with moderate to severe disabilities (mRankin scale 4) in 2 patients (15%) and a severely disabled state in one (8%) patient (mRankin scale 5). Patient age, sex, the presence of recanalization, the need for subsequent retreatment, and the location of the aneurysm and the presence of vasospasm were not significantly correlated with patient clinical outcome.

		GOS at final F/U						
		I	II	III	IV	V		
A	Hunt-Hess Grade	0	8	1	0	0	0	9
	I	5	0	0	0	0	0	5
	II	3	0	0	0	0	0	3
	III	2	1	1	0	0	0	4
	IV	1	0	0	0	0	0	1
	V	0	0	0	0	0	1	1
		19	2	1	0	1		23

		Quality of Life Scale						
		1	2	3	4	5		
B	Hunt-Hess Grade	0	7	2	0	0	0	9
	I	4	1	0	0	0	0	5
	II	2	0	1	0	0	0	3
	III	2	0	2	0	0	0	4
	IV	1	0	0	0	0	0	1
	V	0	0	0	0	0	1	1
		16	3	3	0	1		23

		Modified Rankin Score								
		0	1	2	3	4	5	6		
C	Hunt-Hess Grade	0	5	3	1	0	0	0	0	9
	I	2	3	0	0	0	0	0	0	5
	II	1	2	0	0	0	0	0	0	3
	III	2	0	0	0	2	0	0	0	4
	IV	1	0	0	0	0	0	0	0	1
	V	0	0	0	0	0	1	0	0	1
		11	8	1	0	2	1	0		23

Figure 3-7 - (A) Final GOS score with respect to Hunt-Hess grade at presentation for patients with ruptured posterior circulation aneurysms shows a statistically significant correlation by Pearson's test ($\chi^2 = 30.6$, $p < 0.01$). (B) Quality of life index with respect to the Hunt-Hess Grade at presentation. Pearson's rank test demonstrates a significant relationship ($\chi^2 = 32.4$, $p < 0.006$). (C) Modified Rankin score index at latest follow-up with respect to Hunt-Hess grade at presentation ($\chi^2 = 38.6$, $p < 0.009$).

3.1.5 Complications

No patient from this series suffered from late rebleeding. Also there were no cases of procedure-related mortality in the series. Overall, there was one complication leading to permanent morbidity, for a rate of 4.4% (1/23 cases) (table 2). Two procedure-related complications were encountered that did not lead to a neurological deficit and were transient, for a rate of 8.7% (2/23 cases). These were 2 cases of herniation of a portion of a GDC into the parent vessel. Technical problems were encountered during coil removal in one of these two cases, where the coil broke upon attempted removal in such a fashion that one end of the coil extends into the basilar artery with the other end was stuck in the anterior inferior cerebellar artery (AICA), so a fragment of coil extends from the PICA to the AICA, across the basilar artery. The other case was successfully treated with aspirin.



Figure 3-8 - Case #8 - 72 year-old female presenting with an unruptured wide-neck saccular aneurysm located at the origin of the left PICA (A). Endovascular treatment with GDC coil embolization does not impede distal flow in the parent vessel. (B) Follow-up angiography 7 months later shows stable configuration of the coiled aneurysm (C).

There were two cases of a major neurological deficit, one case of major stroke on computer tomography in an area supplied by the posterior cerebral artery upon follow-up, and one case of infarction of the right cerebral peduncle. In the former case the parent artery remained patent after coiling, in the latter case the parent PICA was occluded. This case is the only one of 9 cases (11%) of occlusion of the parent vessel, where follow-up was close and imaging studies to reveal possible perfusion deficits even in the absence of clinically significant ischemic infarction were obtained in all patients, which resulted in a neurological deficit or abnormality of post-procedural imaging.

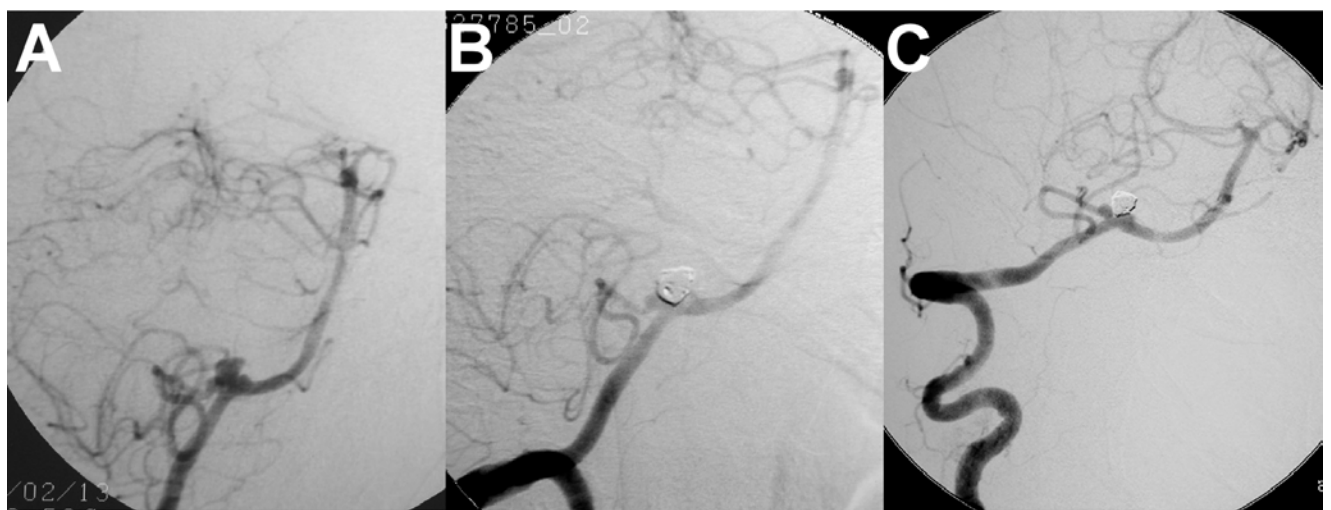


Figure 3-9 - Case #8 - 59 year-old female presenting with Hunt-Hess grade IV SAH and GOS score IV. Injection of the left vertebral artery showed a saccular aneurysm with a narrow neck located at the origin of the left PICA (A), which was treated successfully (B). Follow-up angiography at 18 months shows stable configuration with a small remnant (C). After demonstrating excellent recovery, she denied any symptoms upon final follow-up (modified Rankin scale 0).

None of the patients of this series died from either procedure related or unrelated reasons, however one patient (4.4%), who initially presented with SAH HH grade V died after successful treatment of the aneurysm of an unrelated medical problem.

3.1.6 Summary

The subgroup of 23 patients (14 Female; age 1-87) harboring PICA aneurysms (14 ruptured) was treated over a nine-year interval. In this series 16 aneurysms involved the proximal PICA (70%) and 7 aneurysms were located in the distal portion (30%). All 24 aneurysms in this subgroup of patients were successfully catheterized and treated with endovascular coil embolization either with preservation of the parent vessel in the case of saccular aneurysms (14/23, 61%) or with parent vessel occlusion in fusiform lesions (9/23, 39%). There was one periprocedural non-fatal major stroke (4.4%) and no procedure related deaths. During the follow-up period no re-hemorrhage occurred, and one patient died from an unrelated cause (4.4%). The mean final angiographic occlusion rate was 97%. At latest clinical follow-up the outcome on the modified Rankin scale was: grade 0 in 11 patients (48%), grade 1 in 8 patients (35%), grade 2 in 1 patient (4%), grade 4 in 2 patients (9%), and grade 5 in 1 patient (4%).

Table 1 – Demographics and presentation of the patients with PICA aneurysms in this series

Case No.	Age (yr) /Sex	Ruptured	Hunt-Hess grade	Location (Segment)	Side	Shape ^a	Size (mm)		Parent vessel occlusion	Re-Tx	Complications	Initial Occlusion (%)	Intermediate Occlusion (%)	Final follow-up			
							Fundus	Neck						Occlusion	Duration	GOS	mRankin
1	43/M	No	0	II	Right	Fusiform	15.	11.	Yes			95	95-99	100	18	I	0
2	72/M	No	0	Origin	Right	irregular narrow neck	9	4.5	No			99	95-99	99	.	I	0
3	59/M	No	0	Origin	Right	multilobed narrow neck	5.8	2.5	No			100	100	100	0	II	0
4	87/F	No	I	III - IV	Left	AVM, Fusiform, other ^b	4.5	2.5	No			100	100	100	.	I	0
5	51/F	No	0	I	Left	Giant? wide neck,	7.7	1.8	No			95	95-99	95	0,3	I	2
6	72/F	No	0	I	Left	Saccular wide neck	8	2.4	No			99	95-99	100	7	I	0
7	71/F	No	0	Origin	Left	Saccular wide neck	13.	5.8	No	X1	Coil extends into parent vessel	99	95-99	85	13	I	1
8	60/M	No	0	II	Right	Fusiform	10	.	Yes			100	100	100	18	I	0
9	1/M	No	0	II	Right	Saccular	8.3	2.5	No			80	<95	100	6	I	1
10	78/M	No	0	Origin	Right	pica-pica graft, enlarged	5.2	2.2	No			100	100	85	6	I	1
11	47/F	Yes	I	I	Right	Fusiform	4.5	2	Yes			100	100	100	7	I	1
12	70/F	Yes	III	I	Left	multilobed narrow neck	3.3	2	No			95	95-99	95	13	I	0
13	38/M	Yes	I	Origin	Left	Saccular narrow neck	6	2	No			100	100	100	6	I	1
14	79/F	Yes	V	Origin	Left	Fusiform	5.7	.	Yes			100	100	100	.	V	5
15	51/M	Yes	III	I - III	Right	Fusiform	4	.	Yes			100	100	100	10	I	0
16	69/F	Yes	II	Origin	Right	irregular wide neck	6.1	4	No			95	95-99	95	32	I	1
17	49/F	Yes	I	Origin	Right	AVM, Saccular wide	11	5	Yes		Coil extends into parent vessel	85	<95	95	7	I	1
18	41/M	Yes	I	I	Left	Fusiform	7.7	1.9	Yes			100	100	100	6	I	0
19	59/F	Yes	IV	Origin	Left	Saccular narrow neck	4.3	1.8	No			99	95-99	99	18	I	0
20	50/F	Yes	II	II - III	Right	Fusiform	7	.	Yes			100	100	100	.	I	0
21	73/F	Yes	III	I	Right	multilobed narrow neck	5.8	2	No		major stroke on CT	85	<95	85	7	II	4
22	42/F	Yes	III	Origin	Left	irregular	4.7	1.7	No			100	100	100	5	II	4
23	62/F	Yes	II	II	Right	Fusiform	8.2	.	Yes		Partial infarct of right cerebral	100	100	100	13	I	1

^a AVM associated designates cases where an AVM of the posterior fossa was at least partially supplied by the distal PICA, the more proximal aneurysm was the source of the SAH

^b another aneurysm of the anterior communicating artery gave rise to the SAH

Table 2 – Complications that occurred in the patients with PICA aneurysms

Pt. No.	Age/Sex	Aneurysm location and morphology	Ruptured/SAH HH Grade	Nature of complication	Treatment	Outcome	Comment	Final GOS
12	70/F	Distal PICA, multilobed narrow neck	Yes / III	Vasospasm bilobed aneurysm with small 0.8 mm diameter lobe opposite to the inflow region: impossible to embolize endovascularly.	HHH No Treatment	Improved Improved		II
17	49/F	Proximal PICA, saccular wide neck	Yes / I	Coil extends into parent vessel	Coil not removed - coil broke upon attempted	No change	"coil extends into BA. end was stuck in the AICA, so a fragment of coil extends from the PICA to the AICA, across the BA"	I
7	71/F	Proximal PICA, saccular wide neck	No	Coil extends into parent vessel	Aspirin	Improved		I
23	62/F	Proximal PICA, fusiform	Yes / II	Partial PICA infarction, cerebral peduncle infarction after PVO	N/A	Improved		I
21	73/F	Proximal PICA, multilobed narrow neck	Yes / III	Major stroke on Head CT F/U	N/A	No change		III

3.2 Superior cerebellar artery aneurysms

3.2.1 Patient Demographics and Clinical Presentation

The median age for the 17 patients harboring a superior cerebellar artery (SCA) aneurysm was 52 years, ranging from 16 to 77 years (mean 49 ± 5 years). Of the 10 female and 7 male patients a total number of 12 patients (71%) presented with acute or subacute subarachnoidal hemorrhage (SAH) after rupture of the aneurysm. The remaining aneurysms were incidental findings found on imaging studies of the head made for a variety of unrelated reasons. The severity of the SAH was graded using the Hunt-Hess grading system; there were three patients in each of the categories I to IV (25%), no patient presented with a grade V SAH. The median time between rupture and treatment was 4 days, ranging from 1 to 45 days (mean 9.3 days). Please see Table 3 for more details of the demographics and the presentation of the patients.

3.2.2 Aneurysm Characteristics and Morphology

All 17 patients included in this study had at least one aneurysm of the superior cerebellar artery. The average neck-to-dome ratio of the aneurysms was 0.403 ± 0.12 ; there were 7 aneurysms with a neck diameter of less than 3 mm (58%), 4 measured between 3 and 5 mm (31%), 2 aneurysm necks measured between 5 and 7 mm (17%), while non aneurysm in this series had a wider neck. The largest fundus dimension was used to characterize the morphology of the dome of the aneurysm. There were 2 aneurysms measuring less than 4 mm (12%), 3 between 4 and 7 mm (24%). The biggest group was measuring between 7 and 10 mm, 8 aneurysms in this range (47%), 2 were measuring between 10 and 13 mm (12%), and only one aneurysm had a dome larger than 13 mm (6%). Four of the 17 aneurysms (24%) were associated with arteriovenous malformations (AVMs), however, as in the group of patients with PICA aneurysms, these were not the cause of the SAH.

Table 3 – Characteristics of the patient population with SCA aneurysms in this series at the time of presentation.

Feature	n=17
Gender ratio (M/F)	0.7 (7/10)
Age (yr)	48.82±4.8
Ruptured (%)	12 (70.6%)
Time to treatment after rupture (d)	9.3 (1-45)
Hunt-Hess grade	
I	3 (17.6%)
II	3 (17.6%)
III	3 (17.6%)
IV	3 (17.6%)
V	0 (0.0%)
Initial Glasgow Outcome Score	
I	6 (35.3%)
II	4 (23.5%)
III	5 (29.4%)
IV	1 (5.9%)
V	0 (0.0%)
Aneurysm fundus size (mm)	n=17
0-4	2 (11.7%)
4-7	4 (23.5%)
7-10	8 (47.0%)
10-13	2 (11.7%)
>13	1 (5.8%)
Aneurysm neck size (mean /mm)	n=13
0-3	7 (58.3%)
3-5	4 (30.7%)
5-7	2 (16.7%)
>7	0 (0.0%)
Aneurysm neck-to-dome ratio	0.40±0.12

3.2.3 Angiographic and Neurological Follow-Up, Technical Success

Angiographic follow-up was obtained in 15 of the 17 patients (88%), the median follow-up time was 6 months, ranging from 0 to 18 months. Patients also underwent neurological follow-up examinations, 16 of 17 patients (94%) had clinical follow-up. The median neurological follow-up interval was 20 months, ranging from 2 to 84 months.

All aneurysms (17 of 17 patients, 100%) underwent successful endovascular treatment, i.e. the aneurysm was catheterized superselectively and GDC coils were deployed. One patient had to undergo repeat treatment due to 15% recanalization, when an acceptable angiographic outcome was reached.

3.2.4 Angiographic Outcome and Recanalization

After undergoing endovascular coil embolization of the SCA aneurysms, 15 of 17 patients (88%) underwent subsequent angiographic follow-up to assess the long-term degree of occlusion. In 5 of 17 patients the location and/or shape of the aneurysm made occlusion of the parent vessel unavoidable (29%). The mean initial rate of occlusion was $96.7 \pm 3.0\%$, the average rate of occlusion at final follow-up was $95.1 \pm 3.0\%$. See also Table 4 for more parameters of therapeutic success. Twelve of the 17 aneurysms were occluded to 99 - 100% (71%), 3 had a 95% rate of occlusion (18%), and one aneurysm was occluded to 50% and 85% respectively (6% each). One was an irregular shaped aneurysm where the neck was too small to reach an adequate packing density. The other patient harbored a multilobed aneurysm, where the smaller daughter lobe failed to lend itself to successful packing. The patient ultimately rebled from this uncoiled daughter aneurysm and died.

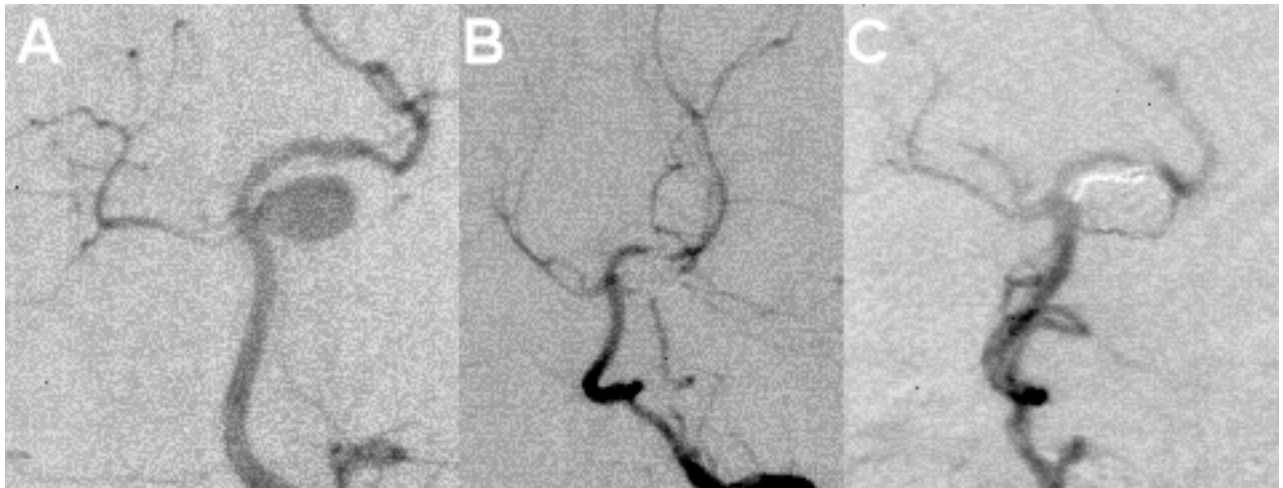


Figure 3-10 – Patient #6 - This 18-year-old male was transferred in a somnolent state from an outside Medical Center where he was diagnosed with a left superior cerebellar artery aneurysm after he suffered a subarachnoid hemorrhage. Angiography of the left vertebral artery demonstrates the aneurysm arising from the left superior cerebellar artery (A). The aneurysm projects directly laterally and has a 2 to 3 mm neck and is 7 mm in mediolateral extent and approximately 4 mm in craniocaudal extent. (B) Angiography performed after coil-placement shows complete obliteration of the aneurysm lumen, with no evidence of compromise of the basilar artery. (C) Follow-up angiography one year later demonstrates the coil mass in an unchanged and stable configuration.

Two patients demonstrated partial recanalization at angiographic follow-up. One case showed 15% recanalization after 100% initial rate of occlusion, and a final rate of 95%. The other case was initially 95% occluded, showed 5% recanalization with an unchanged final rate of occlusion of 95%. The neck-to-dome ratio of these aneurysms was high (0.63, and 0.5) compared to the average ratio of 0.40.

Table 4 – Characteristics of the patients with SCA aneurysms in this series after treatment and final outcomes.

Parameter	n=17
Modified Rankin Scale	
0 No symptoms at all	7 (41%)
1 No significant disability with	2 (12%)
2 Slight disability	2 (12%)
3 Moderate disability	1 (6%)
4 Moderately severe disability	2 (12%)
5 Severe disability; bedridden	0 (0%)
6 Death	3 (18%)
Glasgow Outcome Score	
I Good recovery	11 (65%)
II Moderate disability	3 (18%)
III Severe disability	0 (0%)
IV Persistent vegetative state	0 (0%)
V Death	3 (18%)
Rate of rebleeding	3 (18%)
Rate of recanalization	2 (13%)
Rate of maximal % recanalization	10
Rate of retreatment	0.058
Final occlusion (%)	95.1

3.2.5 Clinical Outcome

In 16 of 17 patients (94%) neurological follow-up examination was achieved, at latest follow-up after a median interval of 10 months, ranging from 2 to 84 months, 11 patients showed good recovery on the Glasgow outcome score (GOS I) (65%), 3 patients of 17 showed a moderate disability (GOS II) (18%), and 3 patients were dead (18%). All patients who lived at final clinical follow-up had good recovery or a moderate disability (GOS I and II) (82%).

The Quality of Life score was used to evaluate the status of treated patients at the final follow-up. Eight of the patients reported a normal lifestyle (QOL 1) (47%), 2 complained about minor neurological dysfunctions, however were able to perform activities of daily life without help (QOL 2) (12%), 3 patients needed help with some

activities of daily life (QOL 3) (18%). Only one patient (6%) was not able to perform activities of daily life without help (QOL 4), and the three patients were dead (18%).



Figure 3-11 – Patient #13 - This is a 67-year-old oriental female patient who suffered a subarachnoid hemorrhage. The patient was initially Hunt and Hess Grade 4 and subsequently improved to Grade 1 and was transferred definitive management of her aneurysm. Angiography of the left vertebral artery demonstrates the patient's aneurysm arising between the left superior cerebellar artery and the left posterior cerebral artery projecting posteriorly and slightly laterally. (A) The largest diameter of the aneurysm is approximately 3 mm and the aneurysm is slightly deeper than 3 mm. (B) Angiography performed after placement of 2 GDC electrolytically detachable coils shows significant stasis of flow in the lumen of the aneurysm. (C) Follow-up angiography demonstrates the coil mass in a stable configuration. The patient died during follow-up after 1 month from a repeat subarachnoidal hemorrhage.

The modified Rankin scale was used to evaluate the neurological outcome of the treated patients in a more strict fashion compared with the GOS. 41% (7 of 17 patients) denied any symptoms (modified Rankin 0), 12% (2 of 17 patients) had no significant disability despite having symptoms and were able to carry out previous activities (modified Rankin 1), and 12% (2 of 17 patients) had a slight disability and were not able to carry out previous activities (modified Rankin 2). One patient (6%) had a moderate disability, requiring some help but able to walk without assistance (modified Rankin 3), and two had a moderate to severe disability and was unable to walk without assistance (modified Rankin 4) (12%). Four patients (24%) were dead (modified Rankin 6), while no patients fell under modified Rankin category 5.

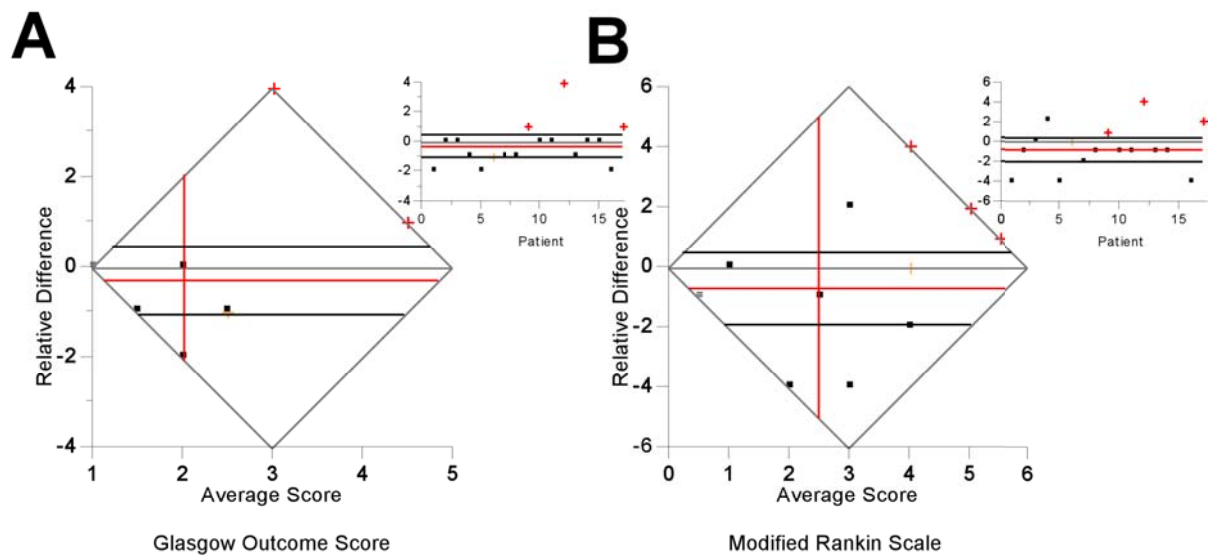


Figure 3-12 – Graphic display of the average grade of improvement drawn against the average score for a given patient, for (A) the GOS score, and (B) the modified Rankin scale. The inserts show the average difference for the patient population. Crosses mark patients with ultimately fatal outcome. Negative relative differences represent improvements of the outcome.

Except for three patients with an ultimately fatal outcome all 14 surviving patients improved both on the GOS score and the modified Rankin scale, see Figure 3-12 for a detailed graphical display. The mean improvement on the GOS score was 0.3grades, from an average grade 2.2 to grade 1.9. The difference is not significant ($p=0.2$). On the modified Rankin scale the mean difference was 0.7 from an average initial mRankin scale 2.9 to a final follow-up scale 2.2, however this difference is not significant either ($p=0.1$). By excluding the patients with fatal outcome from the analysis the GOS difference significantly changes to 0.8 from an average initial score 2 to 1.2 at final follow-up ($p<0.002$), and the mean difference on the modified Rankin scale also changes significantly to 1.4 from an average initial scale 2.7 to an average scale 1.3 at final follow-up ($p<0.008$).

3.2.6 Complications

Three patients of this series suffered from late rebleeding (18%), there was one case of major morbidity (5.8%), and three patients (18%) died after having suffered from rebleeding.

In one patient the possibility of clot formation, which was adherent to the coil mass was entertained toward the end of the procedure. As there were no definitive signs or symptoms arising from a non-occlusive embolus postoperatively, the need for a required follow-up angiography was stated. The patient was heparinized and underwent an unremarkable follow-up angiography.

One patient demonstrated one episode of dysmetria which was thought to be symptom of a transient ischemic episode (TIA) in the absence of vasospasm. Treatment with hypervolemia, hypertension and hemodilution was initiated and the condition improved and there was no neurological residual.

In a patient with a ruptured fusiform aneurysm, who presented with Hunt-Hess grade III, placement of an extraventricular drainage was necessary after the development of hydrocephalus. On follow-up the condition improved, there was no neurological residuum left at final follow-up.

One patient with a ruptured saccular wide-neck aneurysm, presenting with SAH Hunt-Hess grade III, suffered from a major stroke after inadvertent occlusion of the parent vessel and despite heparinization. With modified Rankin scale 2 as final outcome this case represents the only major morbidity in this series (1 of 17 patients, 5.8%).

While there were no cases of procedure related mortality, three patients (18%) died during follow-up. These three patients presented after rupture of the aneurysm with Hunt-Hess grade II or IV (2 cases). None of these cases developed vasospasm, and all three patients suffered from ultimately fatal rebleeding of the same or a daughter aneurysm, the morphology of which did not make endovascular treatment possible.

Of the 5 patients where occlusion of the parent vessel was unavoidable one developed a transient ischemic episode which resolved under hypertensive hemodilution therapy, one patient rebleed and demonstrated major hemorrhage on a follow-up computer tomography with an ultimately fatal outcome, and one patient developed a hydrocephalus requiring placement of a ventricular drain.

In summary the combined morbidity and mortality rate of this series is 4 of 17 patients (23%).

3.2.7 Summary

In the subgroup of patients with SCA aneurysms 12 of 17 patients (7 female, 10 male) presented with SAH after rupture of the aneurysm. All patients (17 of 17, 100%) underwent successful endovascular treatment. One patient had to undergo repeat treatment due to 15% recanalization, when an acceptable angiographic outcome was reached. The average rate of occlusion at final follow-up was $95.1 \pm 3.0\%$. In 16 of 17 patients (94%) neurological follow-up examination was achieved, 11 patients showed good recovery on the Glasgow outcome score (GOS I) (65%), 3 patients of 17 showed a moderate disability (GOS II) (18%), and 3 patients were dead (18%). All patients who lived at final clinical follow-up had good recovery or a moderate disability (GOS I and II) (82%).

Table 5 – Demographics and presentation characteristics of the seventeen patients with SCA aneurysms in this series.

Case No.	Age (yr) /Sex	Ruptured	Hunt-Hess grade	Location (Segment) ^a	Shape	Size (mm)		Parent vessel occlusion	Re-Tx	Complications	Initial Occlusion (%)	Intermediate Occlusion (%)	Final follow-up			
						Fundus	Neck						Occlusion	Duration	GOS	mRankin
1	16/F	No	N/A	SCA	Giant wide neck	9,5	3,6	Yes		TIA	100	100	100	7	I	1
2	77/F	No	N/A	SCA	Saccular wide neck	10	5	No			99	95-99	94	6	I	0
3	31/M	No	N/A	SCA, AVM	Saccular narrow neck	6,4	1,9	No			100	100	100	8	I	2
4	57/F	No	N/A	SCA	Fusiform	5,3	1,5	No			100	100	100	18	I	0
5	74/F	No	N/A	SCA	Saccular wide	9,3	4	No			99	95-99	99	0,06	I	0
6	18/M	Yes	III	SCA	Saccular narrow neck	7,1	2,5	No			100	100	100	7	I	1
7	47/F	Yes	I	SCA	Saccular	3	1,5	No		Clot adherent to	100	100	100	7	I	0
8	48/M	Yes	II	SCA, AVM	Fusiform	9	.	No			96	95-99	95	1	I	4
9	50/F	Yes	III	SCA	Fusiform	9	.	Yes			100	100	100	7	I	0
10	31/M	Yes	II	SCA	Fusiform	17	.	Yes			100	100	100	.	II	4
11	53/F	Yes	IV	SCA	Irregular	12,	5,5	No			50	<95	50	0,1	II	3
12	66/M	Yes	I	BTA/SCA	Saccular wide neck	6,4	4	No	1		99	95-99	95	14	I	0
13	67/F	Yes	IV	SCA	Saccular narrow neck	3,3	1,7	No		Rebleed	99	95-99	99	0,3	V	6
14	52/F	Yes	III	SCA	Saccular wide neck	9	2,5	No			99	95-99	99	0,3	II	2
15	18/F	Yes	II	SCA, AVM	Fusiform	8	2	Yes		Rebleed	100	100	100	0	V	6
16	54/M	Yes	I	SCA, AVM	Fusiform	7,3	.	Yes			100	100	100	.	I	0
17	71/M	Yes	IV	SCA	Saccular	6	4,3	No		Rebleed	85	85	85	0,2	V	6

3.3 Aneurysms of the vertebrobasilar junction

3.3.1 Demographical features and presentation of the patients

The 3 male and 9 female (75%) patients had a median age of 42.5 ± 4.2 years, ranging from 18 to 64. 10 of the twelve aneurysms were ruptured at the time of presentation (83%), the severity of the acute or subacute subarachnoidal hemorrhage was graded using the Hunt-Hess grading system. One patient presented with HH grade I (8%), two with grade II (17%), three each with grade III or IV (25% each), and one with grade V (8%). The median time between rupture and treatment was 5 ± 3.8 days. See Table 6 for details on the patient demographics and presentation

3.3.2 Morphological characteristics

Of the twelve VBJ aneurysms, refer to Figure 3-13, four also had a concomitant fenestration of proximal portion of the basilar artery. There were 8 aneurysm with a distinguishable neck diameter, of these 3 measured between 0 and 3 mm (3 of 8 aneurysms, 38%), 2 were between 3 and 5 mm in size (25%), and 3 were larger than 7 mm (37%). The average neck dimension was 5.1 ± 1.3 mm. The largest fundus dimension was distributed in a similar fashion, of the 12 aneurysms, 1 was less than 4 mm in largest diameter (8%), 4 measured between 4 and 7 mm (33%), 2 each between 10 to 13 mm, and 13 to 16 mm (17% each), and three were measuring more than 16 mm (25%). Ranging from 2.8 to 50 mm, the average maximal fundus dimension was 14.2 ± 4.0 mm.

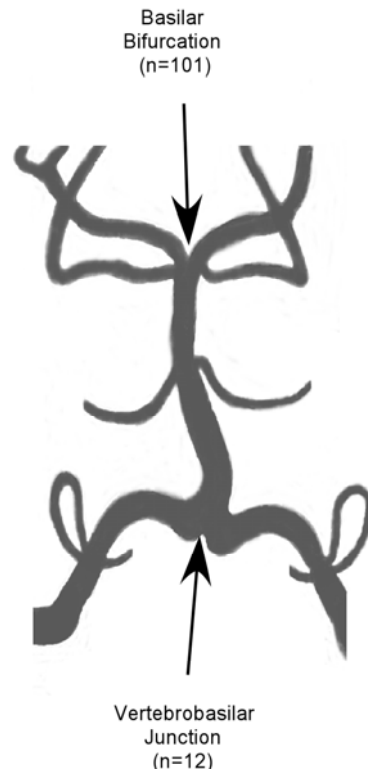


Figure 3-13 – Graphical depiction of the anatomical location of vertebrobasilar junction aneurysms treated.

Of the other 4 aneurysms 2 were fusiform, one was a giant fusiform, and one aneurysm had an irregular shape. Seven of the 12 aneurysms (58%) pointed towards the right side, 2 of these were directed anterior and caudal (2 of 7 aneurysms, 29%), 5 of these were directed towards posterior and cranial (5 of 7 aneurysms, 71%). The other five were pointing towards the left side (42%), 2 of these were pointing anterior and cranial (40%), and one aneurysm each towards the other three possible directions (anterior-caudal, posterior-cranial, and –caudal). Of the 4 cases harboring a fenestration of the basilar artery, two had the aneurysm on the left and two on the right side, three had aneurysms pointing posterior-cranial, and one anterior-cranial. Six of the 12 aneurysms were pointing away from the dominant vertebral artery (50%), the remaining 6 aneurysms were associated with a dominant vertebral artery on the same side (5 of 12 aneurysms, 42%), or a bilaterally non-dominant VA (1 case, 8%).

3.3.3 Angiographical outcome

Angiographic follow-up was obtained in 11 of the 12 patients (92%) with a median follow-up duration of 12 months, ranging from 3 days to 88 months (mean 23.9 ± 9.5 months).

Immediate post-operative and follow-up angiographies of 11 of the 12 patients were used to assess the degree of obliteration of the aneurysm. The average rate of occlusion immediately after the embolization was $88 \pm 5.8\%$, in 4 patients complete (100%) occlusion was demonstrated. In 2 patients nearly complete (95%) occlusion was reached, in three patients only partial occlusion was reached (50 - 85%). At final follow-up the mean rate of occlusion was $92 \pm 3.8\%$, in 5 of 11 patients 100% occlusion was shown (45%), in 3 patients 95% occlusion was demonstrated (27%), 2 patients had between 80% and 90% occlusion (18%), one patients showed partial 60% occlusion (9%). Both patients with an unruptured aneurysm had complete occlusion at follow-up.

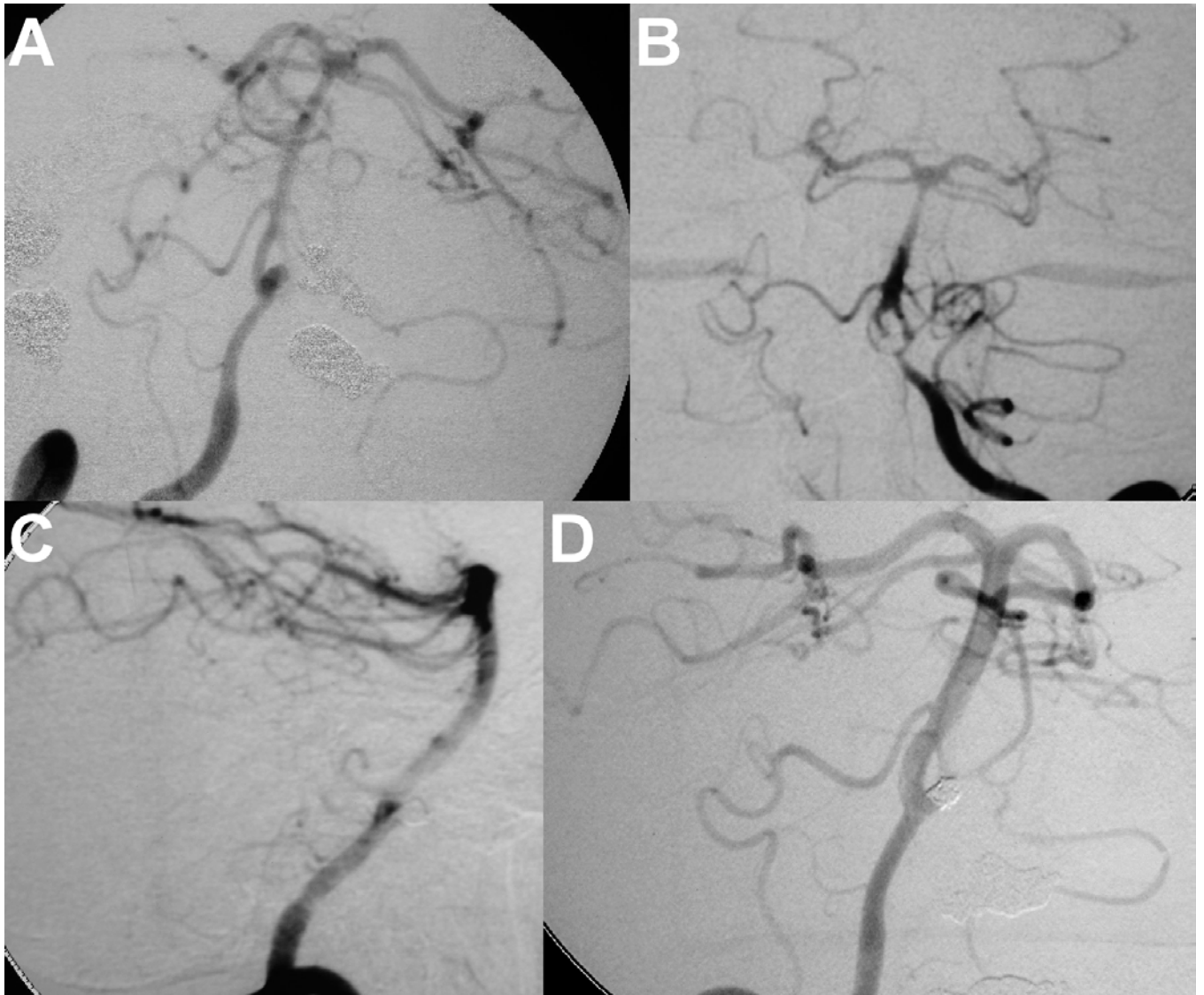


Figure 3-14 – Patient #4 - A 40 year-old female presented with subarachnoidal hemorrhage Hunt-Hess grade V. Injection of the right vertebral artery revealed a saccular aneurysm at the vertebrobasilar junction (A). Successful obliteration of the aneurysm fundus was reached using GDC coils (B, C) At follow-up angiography 7 months later stable coil configuration was demonstrated.

There was one case, where regrowth and a 50% recanalization of a neck remnant of the aneurysm occurred (8%), and a repeat treatment was necessary. In two more cases multiple procedures were necessary to achieve an acceptable result: one case required two, and one case required three courses of treatment (3 of 12 patients, 25%). No re-hemorrhage occurred in this series (0%).

In two cases vasospasm developed (17%), both patients underwent successful percutaneous angioplasty; one of the patients was treated with papaverine in addition to the utilization of hypervolemia, hypertension and hemodilution.

One patient underwent endovascular intervention, at this point encroachment of the parent vessel was noted, which necessitated occlusion of the parent artery, which was tolerated without neurological sequelae.

3.3.4 Neurological outcome

Neurological follow-up evaluations were performed in 11 of the 12 patients (92%), the longest follow-up interval ranging from 1 to 91 months, with a median of 24 months (mean 26.7 ± 10.3 months).

At clinical follow-up examination 24 months later in average, there were 10 patients with an excellent follow-up on the GOS score (GOS I) (83%). These were all ruptured aneurysms but one, and the initial GOS was I in 3 patients, II in 2 patients, and III in 5 patients. They also recovered well on the QOL scale, 9 claimed a normal lifestyle (QOL 1) at final follow-up (9 of 12 patients, 75%), 1 patient claimed minor neurological dysfunction, but was able to perform activities of daily life without help (QOL 2) (8%). The preoperative modified Rankin scale of these patients was distributed: 3 had no significant disability despite symptoms and were able to carry out normal activities (mRankin 1), 1 patient each had a moderate disability, still able to walk without help (mRankin 3), or a moderate to severe disability and requiring assistance to walk (mRankin 4), and 4 patients were bedridden with a severe disability (mRankin 5). At final follow-up, 7 patients had no symptoms at all (mRankin 0) (7 of 12 patients, 58%), two patients fell into the mRankin 1 category, and one patient was mRankin 2. They also had score between 90 and 100 on the Barthel scale. One patient with a ruptured aneurysm had a final GOS score of III, along with an inability to perform activities of daily life (QOL 4) and was not able to walk without assistance (mRankin 4). A score of 25 was reached on the Barthel scale. In a patient with an unruptured aneurysm an ultimately fatal outcome occurred.

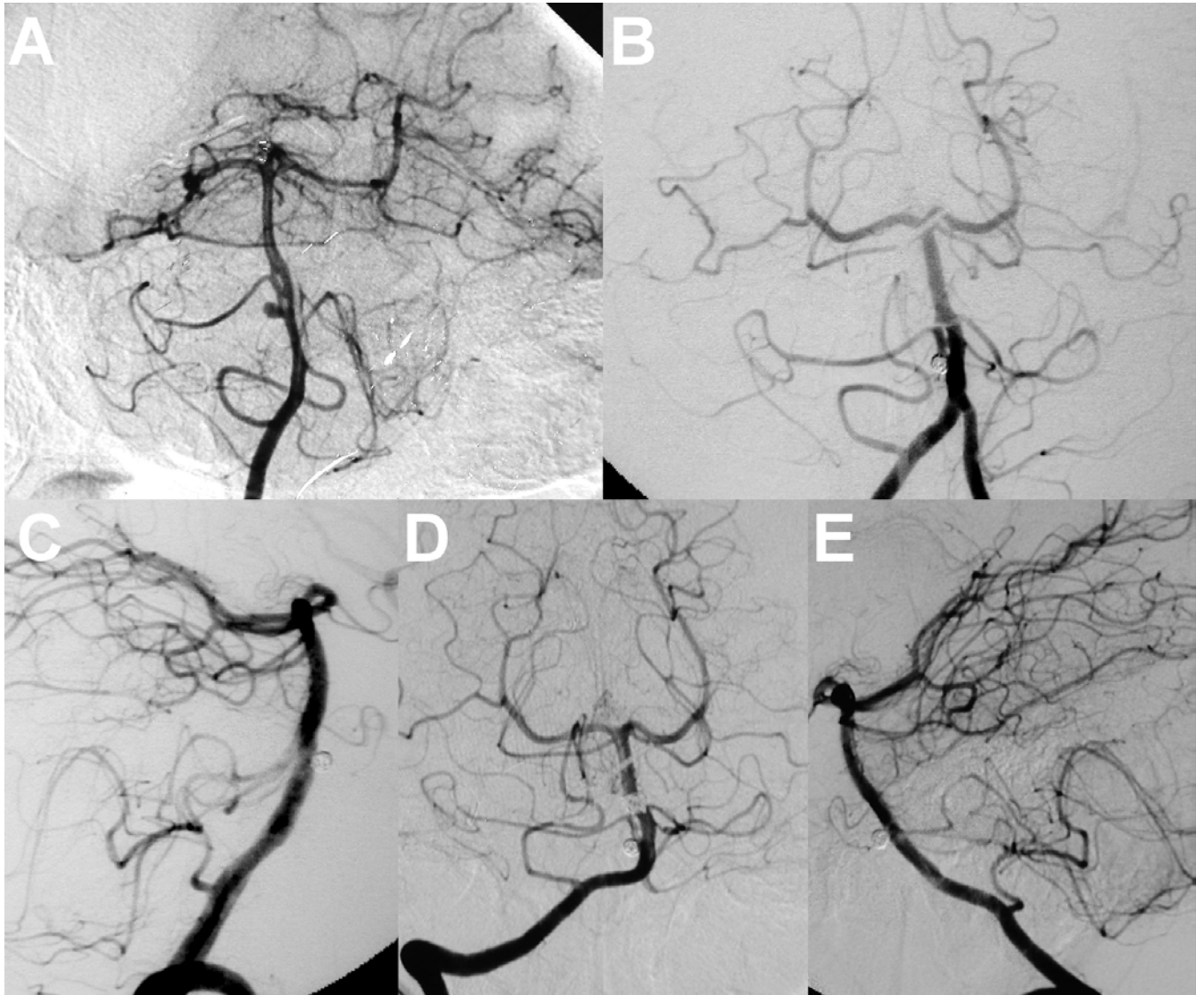


Figure 3-15 – Patient #2 - This 38 year-old female has been diagnosed with an aneurysm at the vertebrobasilar junction by angiographic means (A). The patient also harbored an aneurysm of the internal carotid artery and an anterior communicating artery aneurysm which was surgically clipped after presentation with a subarachnoid hemorrhage. GDC coil embolization was successfully performed (B, C), and follow-up angiography after 12 months demonstrated a stable configuration of the coil mass (D, E).

This patient had a dolichoectatic aneurysm and died of causes related to also having undergone surgery. In this case bilateral occlusion of the vertebral arteries using GDC embolization and balloon occlusion was necessary; the patient also underwent surgery to construct a bypass between the external carotid artery and the superior cerebellar artery. From there he rebled with an ultimately fatal outcome (8%). There was no procedure-related mortality (0%). There was no case of major or permanent neurological morbidity.

3.3.5 Summary

There were 12 patients (9 female and 3 male) with aneurysms of the vertebrobasilar junction, including 4 patients with a concomitant fenestration of the basilar artery underwent endovascular coil embolization. Ten patients (83%) presented with SAH. There was one case of aneurysm recanalization and regrowth (8%), requiring repeat treatment. At final neurological follow-up 7 patients had a modified Rankin scale grade 0 (58%), 2 had grade 1 (17%), 1 grade 2 (8%), 1 grade 4 (8%), 1 grade 6 (8%). Overall mortality in this series is 8%, there was no procedure related morbidity.

Table 6 – Demographics, presentation and outcome of the 12 patients with VBJ aneurysms in this series.

Case No.	Age (yr) /Sex	Ruptured	Hunt-Hess grade	Side	Fenestration	Shape ^a	Size (mm)		Parent vessel occlusion	Re-Tx	Complications	Initial Occlusion (%)	Intermediate Occlusion (%)	Final follow-up			
							Fundus	Neck						Occlusion	Duration	GOS	mRankin
1	60/F	No	-	Left		Giant fusiform	50	n/a								V	6
2	38/F	No	-	Right	Yes	Saccular narrow neck	4.5	2	No		100	100	100	12	I	1	
3	45/M	Yes	IV	Left		irregular wide neck	15	9.2	No	3	80	<95	85	85	I	0	
4	40/F	Yes	V	Left	Yes	Saccular narrow neck	5	3	No		95	95-99	95	7	I	1	
5	62/F	Yes	III	Right		Saccular narrow neck	11.	6.9	No		95	98	95	0,08	I	0	
6	39/F	Yes	II	Right		Saccular narrow neck	13.	5	No	1	70		80	88	I	0	
7	39/F	Yes	III	Right		Saccular wide neck	16.	4	No		100	100	100	24	I	0	
8	55/M	Yes	IV	Right	Yes	Fusiform	10	n/a	No	2	50	<95	60	5	I	2	
9	18/F	Yes	II	Left		Fusiform	32	n/a	Yes		100	100	100	12	I	0	
10	28/F	Yes	I	Right		Saccular narrow neck	4	1.5	No		100	100	100	17	I	0	
11	64/M	Yes	III	Right		Saccular narrow neck	2.8	2			.	100	100	7	I	0	
12	58/F	Yes	IV	Left	Yes	Saccular narrow neck	5	n/a			.	95	95	6	III	4	

3.4 Basilar apex aneurysms

3.4.1 Patient demographics and clinical presentation

101 patients underwent endovascular treatment of 101 aneurysms of the tip of the basilar artery complex utilizing the Guglielmi electrolytically detachable coil (GDC) system. See Figure 3-16 for the location of the aneurysms. The study population, consisting of 78 female (77%) and 23 male (23%) patients, had a median age of 53 years, ranging from 32 to 86 years. Of the total number of 101 aneurysms treated, 28 (28%) were unruptured, and 72% (73 of 101 patients) presented after rupture. All patients in this series were classified according to Hunt-Hess (Hunt and Hess 1968) (HH), using grade 0 for unruptured aneurysms. The median time between presentation with acute or subacute subarachnoidal hemorrhage (SAH) and treatment was 6 days with a range from 0 to 540 days (mean 22 ± 9 days). The stratification for the aneurysms treated was as follows: 28 were unruptured and classified as grade 0 (28%), grade I in 18 cases (18%), grade II in 17 cases (17%), grade III in 14 cases (14%), grade IV in 20 cases (20%), and 4 cases presented with grade V (4%). 40 patients (40%) had multiple aneurysms: one additional aneurysm was found in 25 patients, two were discovered in 10 patients, and three or more were found in 5 patients. See table 5 for details of the presentation.

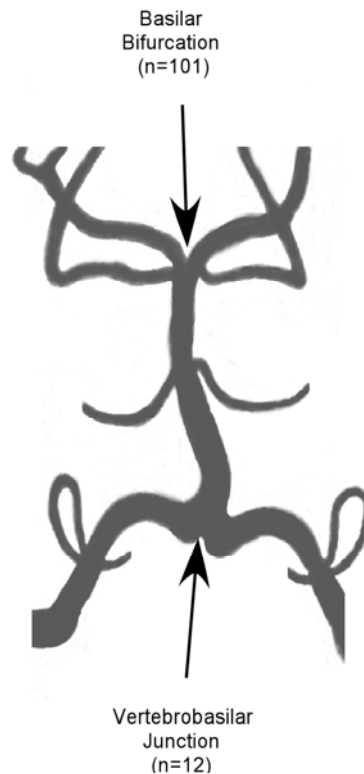


Figure 3-16 – Graphical depiction and histogram of the anatomical location of basilar artery aneurysms treated using GDC coil embolization.

3.4.2 Aneurysm characteristics and morphology

Of the treated aneurysms 26 (30%) were saccular in shape and had a narrow neck (< 4mm), 17 (19%) were saccular shaped with a wide (> 4mm) neck, 10 were fusiform (11%) including one giant fusiform aneurysm, 11 were of irregular shape (7 harboring a wide neck and 4 a narrow neck), 9 were multilobed (6 with a wide neck), 11 were giant aneurysms with wide necks (12%), and two did not fall into one of the categories above (2%). Twenty three of the 101 aneurysms had a neck diameter less than 3 mm (23%), 48 aneurysm necks measured between 3 and 5 mm (48%), and 16 between 5 and 7 mm (16%), and 10 neck diameters greater than 7 mm (11%). Figure 3-17 shows histograms of the distributions of the neck diameter (A) and the largest fundus dimension (B). For 6 aneurysms the largest fundus diameter was less than 4 mm (6%), there 35 aneurysms measuring between 4 and 7 mm (35%), 24 (24%) had a largest diameter between 7 and 10 mm, and for 19 (19%) between 10 and 13 mm. 17 aneurysms were larger than 13 mm in the largest fundus dimension (17%). The median neck-to-dome ratio was 0.44 ± 0.02 , with a mean ratio of 0.49.

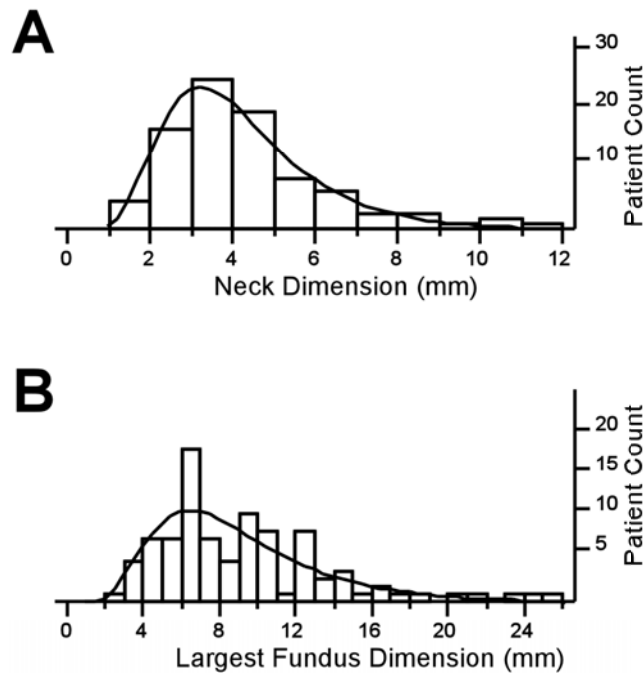


Figure 3-17 - Morphology and angiographic characteristics of basilar tip aneurysms. (A) Histogram illustrating the distribution of aneurysm neck dimensions. (B) Histogram of the largest angiographic aneurysm fundus dimension.

3.4.3 Angiographic and neurological follow-up

Angiographic follow-up was obtained in 79 of 101 patients (78%) treated, with a median angiographic follow-up of 10 ± 2.4 months (mean 18.2 months, range, 0 to 90 months). Clinical follow-up was achieved in 96 of 101 treated patients with a median duration of 25 ± 2.5 months (95%; mean duration, 31.3 months ranging between 1 to 91 months). See Figure 3-18 for histograms showing the duration of the follow-up in both modalities over time.

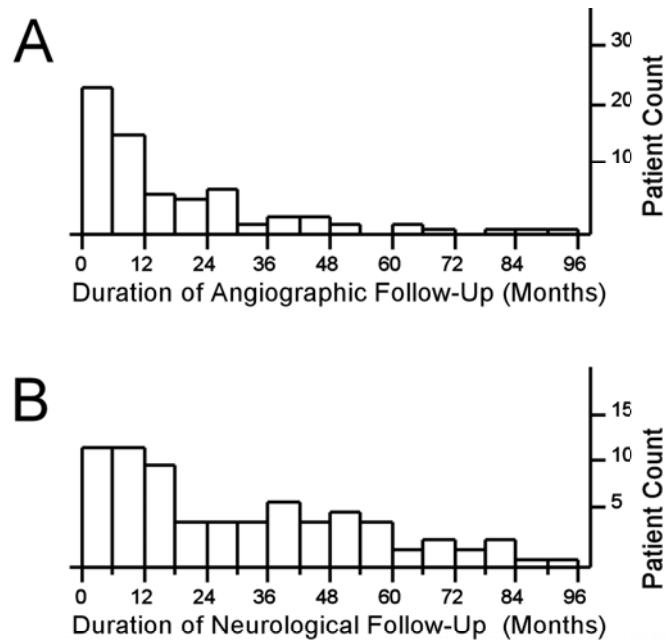


Figure 3-18 - Histogram of the duration between initial embolization and latest angiographic follow-up in 99 out of the 123 aneurysms not treated by parent vessel occlusion (A). Histogram of the duration between aneurysm embolization and latest neurological follow-up in 107 out of 123 treated patients (B).

3.4.4 Technical Success

Endovascular treatment was successfully performed in 97 of 101 cases (96%), in 3 cases (3%) a wide neck prevented successful embolization while risking inadvertent dislocation of the coil mass in to the parent vessel. In one case (1%) the morphology of tandem fusiform basilar tip aneurysms with a daughter on the anterior aneurysm prevented complete occlusion of the aneurysm without occluding basilar artery. An attempt to place a stent across base of daughter aneurysm failed.

3.4.5 Angiographic Outcome

In the presented series 101 patients underwent endovascular treatment of 101 aneurysms of the vertebrobasilar complex with preservation of the parent vessel. The initial mean occlusion rate for the 97 treated aneurysms was $95.6 \pm 0.8\%$ with a final occlusion rate of $93.7 \pm 1.0\%$. The difference is not significant. Of these 46 (47%) were embolized to 99% to 100%, 20 (21%) were incompletely occluded to 95% to

99%, 14 (14%) were incompletely occluded to 90% to 94%, 13 (14%) were incompletely occluded to 75% to 90%, and 4 (4%) were partially occluded to <75%. Only 4 of 101 patients suffered from re-hemorrhage (4%), these patients had an initial occlusion rate of 80%-90%.

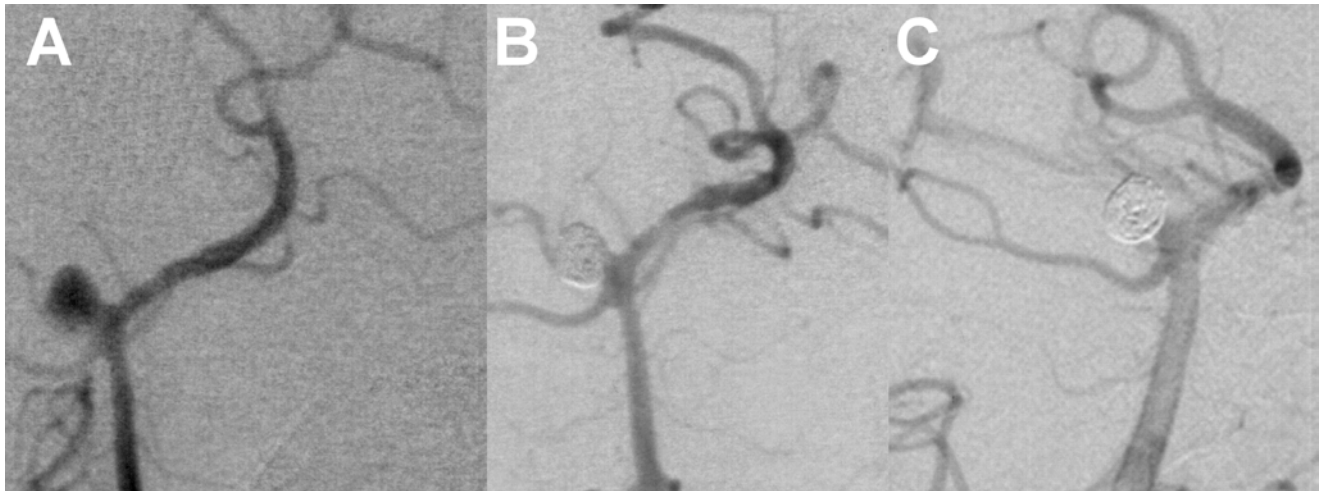


Figure 3-19 – 41 year-old male patient presented with a Hunt-Hess grade I subarachnoidal hemorrhage. Cerebral angiography revealed a narrow-neck basilar tip aneurysm (neck to dome ratio 0.4) (A). After successful endovascular treatment the aneurysm dome is completely occluded with electrolytically detached coils. At this point a neck remnant is visible. (B) Follow-up angiography after 15 months demonstrates a stable coil mass, a stable neck remnant and good flow in the parent vessels.

Parameters of aneurysm dimensions, i.e. neck and largest fundus diameter are correlated with a decreased percentage of final occlusion (R^2 is 0.145 for the neck diameter, $p < 0.0002$, R^2 is 0.079 for the largest fundus diameter, $p < 0.007$). The neck diameter correlated with the largest dimension, and the neck-to-dome ratio is not a good predictor for final occlusion, as shown in Figure 3-20.

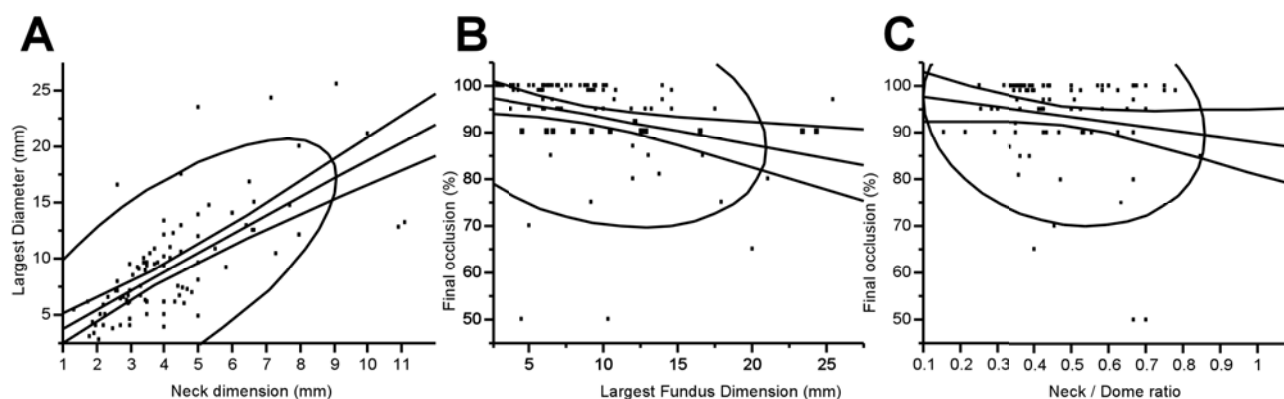


Figure 3-20 – Neck dimension correlates well with the largest dimension(A), and largest angiographic fundus dimension (B) correlate with a decreasing rate of angiographic occlusion of the aneurysm upon final follow-up. The neck-to-dome ratio is not a good predictor of the final occlusion (C).

3.4.6 Recanalization after Treatment

Of the 79 aneurysms with angiographic follow-up, 65% (59 of 79 cases) showed no evidence for recanalization, while 35% (28 of 99 patients) did. The mean rate of recanalization was 8.7%. Analysis of this subgroup of aneurysms revealed that there is a significant relationship between parameters of aneurysm location and morphology and the probability of recanalization on angiographic follow-up studies. In a logistic regression model the probability of recanalization can be fitted as a function of the neck dimension ($R^2 = 0.067$, $\chi^2 = 13.4$, $p < 0.001$) and with less certainty as a function of the largest fundus dimension ($R^2 = 0.049$, $\chi^2 = 10.2$, $p < 0.007$). Three patients with 100% initial occlusion showed evidence of recanalization on follow-up angiography. No evidence was found to support those other parameters of aneurysm morphology e.g. the neck/largest fundus diameter ratio were significantly correlated with the risk of recanalization.

3.4.7 Clinical Outcome

Clinical follow-up for >1 month was achieved in 91% (91 of 101 patients). At latest follow-up, 70% (70/101) of patients showed excellent recovery (GOS I), 9% (9/101)

had moderate disability (GOS II), 6% (6/101) were severely disabled (GOS III), no patient was vegetative (GOS IV), and 11% (11/101) were dead (see Figure 3-21). Overall, 79% (79/101) of patients had good recovery or moderate disability (GOS I and II) at the time of final follow-up. Notably enough 88% (15/17) of the patients with an adverse outcome (GOS III through V) initially presented with a ruptured aneurysm. Almost all patients (23/25) patients, 92%) with a non-ruptured aneurysm and 79% of the patients with a ruptured aneurysm presenting with SAH (56 of 71 patients) had good recovery or moderate disability (GOS I and II) upon final assessment.

There is statistically significant correlation between Hunt-Hess grade at presentation and final GOS outcome score ($\chi^2 = 43.6, p < 0.0001$) (see Figure 3-22A for details).

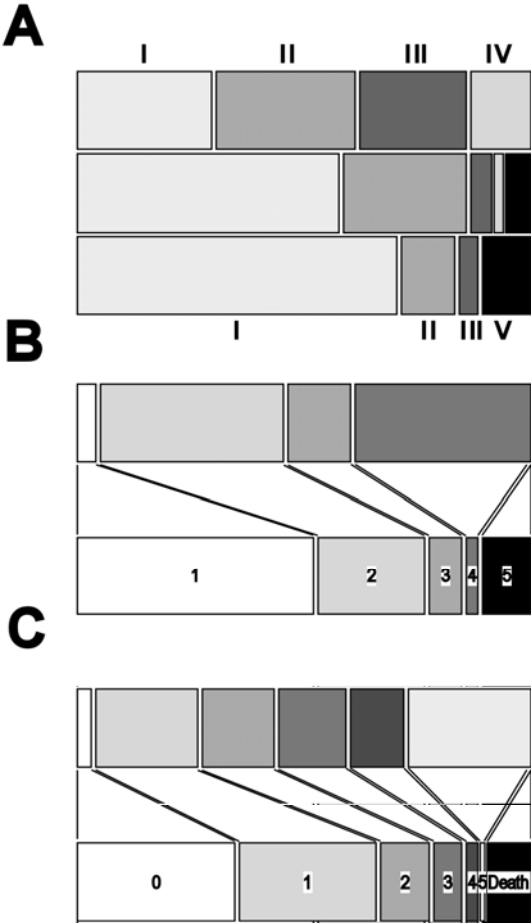


Figure 3-21 – (A) Change in distribution of GOS scores from the initial assessment (top row), over the 30 day follow-up evaluation (middle row) to the final follow-up GOS score (bottom row). (B) Proportional change of the quality of life score between initial and final evaluation (top and bottom row respectively). (C) Change of the proportions of the modified Rankin score from the initial assessment (top row) to the final assessment (bottom row).

The QOL was used to assess the ability of treated patients to deal with daily activities at the time of final follow-up. A statistically significant relationship between Hunt-Hess grade at presentation and final QOL score was demonstrated ($\chi^2 = 43.8$, $p \leq 0.002$) (Figure 3-22B). A similar analysis of the modified Rankin outcome at latest follow-up established a significant correlation with Hunt-Hess grade at time of presentation ($\chi^2 = 61.125$, $p \leq 0.001$) after the treatment (Figure 3-22C). There were 43 patients (44%) without symptoms upon final follow-up (modified Rankin score 0), 16 had some symptoms without disability (16%) (modified Rankin score 1), 7 (7%) had a slight disability (modified Rankin score 2), 5 (5%) a moderate disability (modified Rankin score 3), 2 (2%) a moderately severe disability (modified Rankin score 4), 1 suffered from a severe disability (1%) (modified Rankin score 5), and 23 (24%) were dead (modified Rankin score 6).

Repeat evaluation at the time of latest neurological follow-up showed a still significant, yet less strong correlation ($\chi^2 = 44.6$, $p \leq 0.04$) between the modified Rankin score at that time and the initial presenting Hunt-Hess score. Stratification of the data for presentation after rupture of the aneurysm using the Cochran Mantel-Haenszel test yields a higher level of significance: a low HH grade at presentation is associated with a low final GOS in both patients who present with a ruptured aneurysms and in unruptured aneurysms ($p < 0.01$). A similar result reveals the stratification of the QOL outcomes ($p < 0.01$) and the modified Rankin scale outcomes ($p < 0.003$).

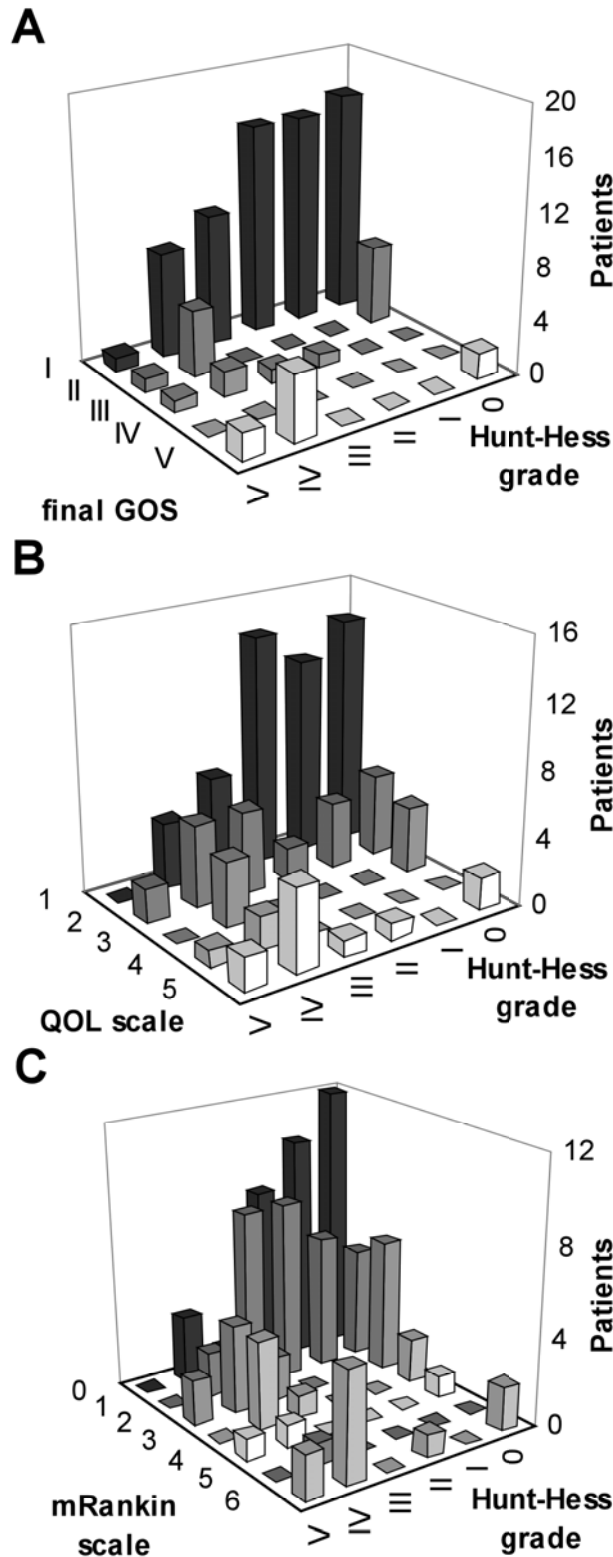


Figure 3-22 – (A) Representation of the final Glasgow Outcome Score with respect to Hunt Hess grade at presentation for patients with ruptured posterior circulation aneurysms shows a statistically significant correlation by Pearson’s test ($\chi^2 = 41.4, p < 0.0005$). (B) Representation of Quality of Life (QOL) index with respect to Hunt-Hess grade at treatment indicates a statistically significant correlation ($\chi^2 = 54.6, p < 0.00001$). (C) Representation of patient’s modified Rankin score index at latest follow-up with respect to Hunt-Hess grade at presentation ($\chi^2 = 71.1, p < 0.00001$).

3.4.8 Complications

3.4.8.1 Aneurysm rerupture after unsuccessful coiling

Four patients suffered late rebleeding (4/101 patients, 3%). One was a patient with a giant basilar tip aneurysm (largest fundus dimension 18 mm) who initially presented with Hunt-Hess grade III, GDC placement yielded 95% occlusion, subsequently developed post-procedural vasospasm, suffered from recurrent hemorrhage, and ultimately died from related complications. The second patient suffered from rupture of tandem fusiform basilar tip aneurysms with 8.9 mm largest fundus diameter, which were found unsuitable for endovascular therapy. The patient underwent craniotomy and die one week after pontine hemorrhage. The third patient had a giant wide neck basilar tip aneurysm, unruptured upon presentation with a largest fundus dimension of 21 mm and a 10 mm neck, who suffered from a fatal recurrent subarachnoidal hemorrhage. The fourth patient died 11 days after unsuccessfully attempted coiling of a too wide necked (4.3 mm, largest fundus dimension 6 mm) basilar tip aneurysm from complications related to massive subarachnoidal hemorrhage after presenting with a ruptured aneurysm.

3.4.8.2 Procedure-Related Mortality and Morbidity

There were no cases of procedure-related mortality in the series. Overall, there were 2 complications leading to permanent morbidity, a rate of 2% (2/101 cases) (refer to table 6 for a detailed listing of complication). Three procedure-related complications with non-permanent neurological sequelae were encountered, for a rate of 3% (3/101 cases). These include a case of parent artery encroachment, a coil extending into the parent basilar artery and a case of asymptomatic aneurysmal rupture.

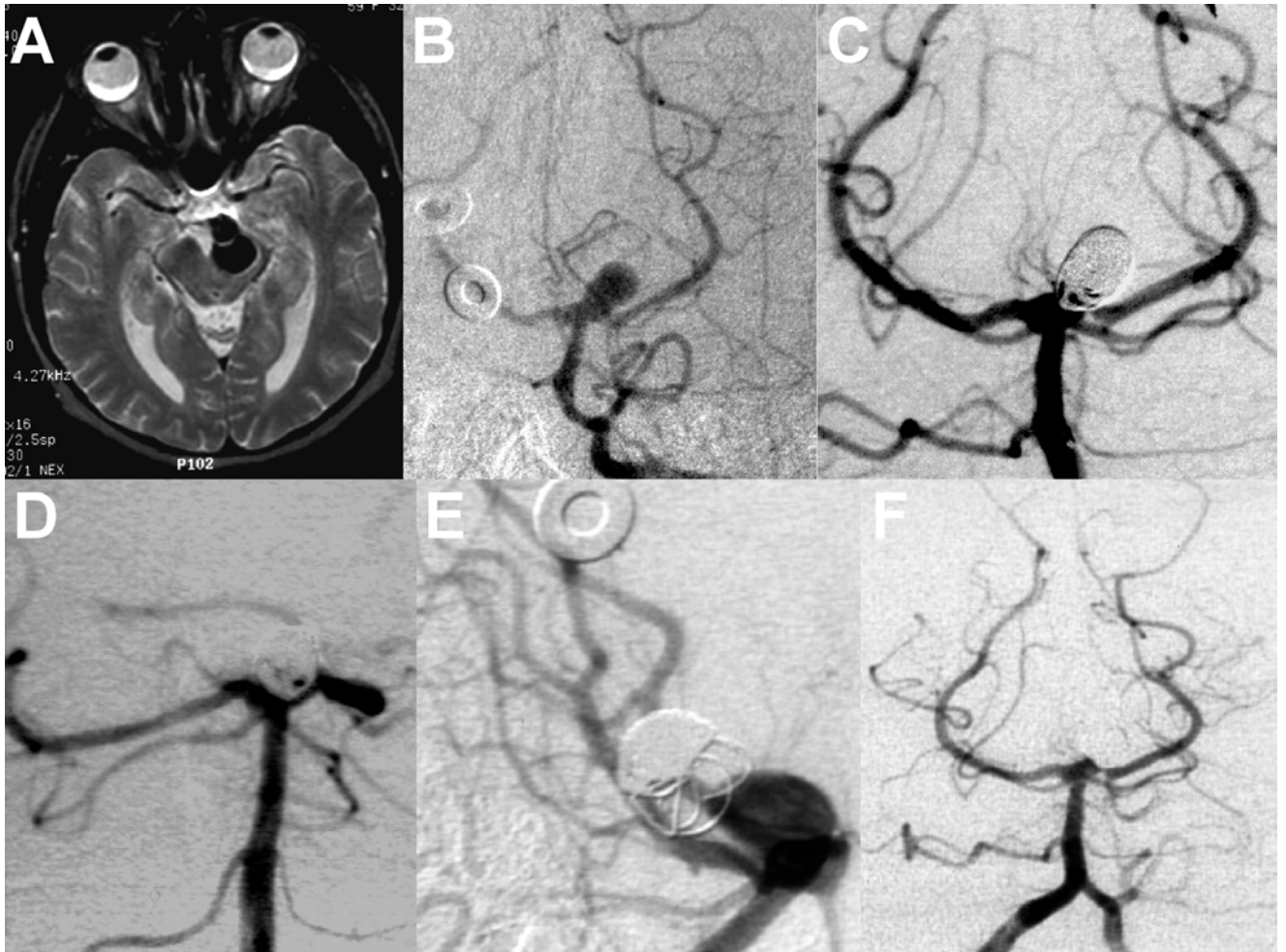


Figure 3-23 – A 59 year-old female patient presented with an incidental unruptured basilar tip aneurysm revealed by MRI imaging (A), and cerebral angiography (B). After successful coil embolization (C) a six-month follow-up angiography was unremarkable (D). On the 15 month follow-up regrowth of the aneurysm was demonstrated (E), which lead to repeat treatment with near-complete occlusion of the aneurysm at final follow-up (F).

3.4.8.3 Medical Complications

Eight patients in this cohort suffered concurrent medical complications, some of which were related to SAH, for a rate of 8% (8 of 101 patients).

Table 7 – Overview of complications that lead to permanent morbidity or mortality in the group of patient with basilar apex aneurysms.

Age/S	Aneurysm Location	SAH HH Grade	Nature of complication	Symptoms	Treatment	Outcome
49/M	Basilar tip – giant	II	Recanalization	Mass effect	Surgery	Death
66/M	Basilar tip –	IV	Severe vasospasm		HHH	Death
41/F	Basilar tip –	II	Minor perforation and rebleed	hydrocephalus	EVD	Improved
49/F	Basilar tip	IV	Bilateral MCA stroke		N/A	Death
44/M	Basilar tip –	III	Minor perforation and rebleed		Self sealed	Improved
64/F	Basilar tip –	IV	Nonocclusive embolus		N/A	Death
86/F	Basilar tip – fusiform	IV	Not coilable, major stroke		N/A	Death
67/F	Basilar tip – giant	III	Parent artery encroachment, regrowth,	Vasospasm	N/A	Improved
45/F	Basilar tip –	0	Coil extend into parent basilar artery,		Urokinase	Major
44/F	Basilar tip -fusiform	V	Complications of SAH		N/A	Death
47/F	Basilar tip – giant	0	Rerupture	Major stroke	N/A	Death
54/M	Basilar tip –	IV	Failed to recover from SAH		N/A	Death
64/F	Basilar tip –	IV	Failed to recover from SAH		N/A	Death
59/M	Basilar tip –	V	Vasospasm		HHH	Death
51/M	Basilar tip –	IV	Vasospasm		PTA,	Improved
42/F	Basilar tip –	IV	Vasospasm, Branch occlusion, coil #1 could		HHH	Improved
52/M	Basilar tip –	IV	Vasospasm, Hydrocephalus	Minor stroke	HHH, EVD	Major
71/M	Basilar tip – wide	IV	Not coilable, rebleed		N/A	Death

3.4.8.4 Mortality

Twenty three patients of this series died (23/101 patients, 23%) during the course of follow-up, overall 8 patients from causes related to complications of subarachnoidal hemorrhage or rebleed (12 of 23 patients, 52%; 12 of 101 patients, 12%), two patients without having received treatment due to the untreatable morphology of one fusiform giant and one wide neck basilar tip aneurysm. 12 of the 23 patients presented initially with a SAH HH grade IV or V (52%). This subset of patients demonstrated poor initial neurological condition, often refractory vasospasm with subsequent infarction, and co-morbid medical conditions (pneumonia, sepsis, congestive heart failure, and pulmonary edema). None of these patients improved neurologically or with regards to the outcome scores after endovascular treatment and before death. Two patients presented with HH grade II and III after rupture of a giant wide neck basilar tip aneurysm. In one case recanalization lead to a fatal outcome, the other case exhibited Regrowth and fatal re-rupture of the aneurysm. In one case a giant wide neck basilar tip aneurysm bled after successful treatment and benign initial presentation. Three patients died from complications of surgery performed after unsuccessful endovascular treatment or as therapeutic modality (13%). Nine patients died of other medical reasons after discharge from the hospital (39%).

In summary a total number of 9 complications occurred (9%), five of which were procedure related (55%) with permanent morbidity in two cases (22%), four patients suffered from recurrent hemorrhage after incomplete embolization of the aneurysm (3%), in one patients recurrence of hemorrhage occurred after recanalization of the aneurysm. Of the total number of 28 patients with either recurrent hemorrhage or recanalization or both (28%) 12 required further treatment (42%).

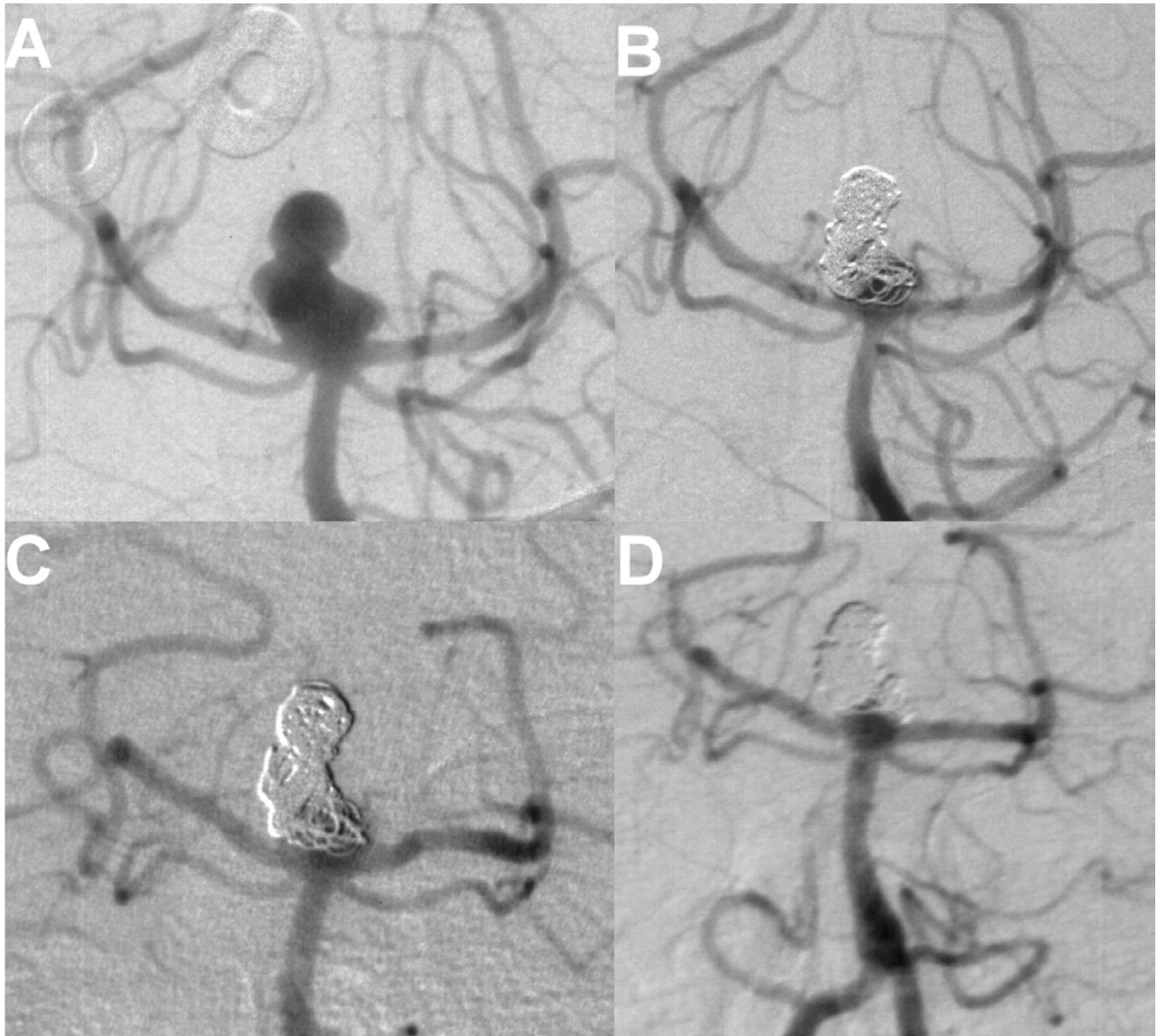


Figure 3-24 – After rupture this 46 year-old male patient presented with Hunt-Hess grade I subarachnoidal bleed to the team. Angiography of the cerebral vasculature revealed a multilobed, wide necked (neck to dome ratio 0.5) basilar tip aneurysm (A), which was nearly completely occluded by deployment of electrolytically detachable coils (B). Follow-up angiography after 14 months revealed a stable coil mass without signs for recanalization or regrowth.

3.4.9 Outcome of a Subgroup with Small Aneurysms

A subgroup of 65 patients (65 of 101 patients, 64%) with small fundus aneurysms using an arbitrary 10 mm cutoff for the largest fundus dimension was identified. There were slightly different admission characteristics of the subgroup compared with the

subgroup of aneurysms with greater than 10 mm largest fundus diameter (36 patients,36%). While the mean age was not significantly different, as was the rate of rupture, and the distribution of Hunt-Hess grade upon presentation, more, but non significantly so, women were found in the subgroup with the largest fundus dimension <10 mm.

Table 8 - Characteristics of the patients with basilar apex aneurysms in the series compared with the two subgroups of patients with fundus dimensions less and larger than 10 mm at hospital admission.

	Subgroup with largest fundus diameter <10 mm (n= 65)	Subgroup ≥10 mm (n=36)	p	Whole series (n=101)
Gender ratio (M/F)	0.275 (14/51)	0.33 (9/27)	ns	0.295 (23/78)
Median age (yr)	52±11.2	53±11.2	ns	53±12.2
Ruptured	49 (75.4%)	24 (66.7%)	ns	73 (72%)
Hunt-Hess Grade				
I (%)	12 (18%)	6 (17%)	ns	18 (18%)
II (%)	9 (14%)	8 (22%)	ns	17 (17%)
III (%)	11 (17%)	3 (8%)	ns	14 (14%)
IV (%)	14 (22%)	6 (17%)	ns	20 (20%)
V (%)	3 (5%)	1 (3%)	ns	4 (4%)
Fundus size (mean /mm)	6.49±1.90	14.24±4.13		
0-4 mm	6 (9%)	N/A		6 (6%)
4-7 mm	35 (54%)	N/A		35 (35%)
7-10 mm	24 (37%)	N/A		24 (24%)
>10 mm	N/A	36 (100%)		36 (36%)
Neck size (mean /mm)	3.28±0.95	5.98±2.14	<0.0001	
0-3 mm	22 (34%)	1 (3%)		23 (23%)
3-5 mm	36 (55%)	12 (33%)		48 (48%)
5-7 mm	4 (6%)	12 (33%)		16 (16%)
>7 mm	0	11 (31%)		10 (10%)
Aneurysm neck-to-dome ratio	0.532	0.438	<0.001	0.502
Rupture – Treatment Interval (days)	4 ; 29.2±13.5	2 ; 7.29±4.1	ns	6

For more detail on the distribution of the parameters of aneurysm size, see table 5. The neck-to-dome ratio in the subgroup was significantly higher (0.532) than in the larger size aneurysm subgroup (0.438, $p<0.001$).

Comparing these two subgroups (see table 6 for details) shows that the angiographic outcome differs considerably between the two subgroups. The rate of rebleeding is non-significantly different, each subgroup hosts 2 of the total of 4 cases, that suffered from rebleeding (3% and 6% in the small aneurysm subgroup and the large aneurysm subgroup, respectively). Large aneurysms recanalized more readily (17 cases, 47%) compared with small aneurysms (11 cases, 17%, $p<0.0001$), the maximal angiographic rate (in %) of recanalization exhibits a similar significant difference (5.5% for small aneurysms compared with 14.0% for large aneurysms, $p<0.0001$). Patients with small aneurysms subsequently underwent retreatment less frequently, with a rate of 0.06 per patient, compared with 0.25 in the large aneurysm group ($p<0.0007$). In the large aneurysm group multiple re-treatments were necessary, whereas the 4 patients with small aneurysms needed to undergo repeat treatment only once. The rate of occlusion at final angiographic follow-up is 96.0% in the group of small aneurysms compared to 89.6% in the group of large aneurysms ($p<0.0001$).

The clinical outcome differed only non-significantly, however there were 48 patients in the group of small aneurysms with a good recovery at final follow-up (77%), whereas only 22 patients (65%) in the group with large aneurysms had such an outcome. Five (8%) and 4 patients (12%), respectively, had a moderate disability at final follow-up. See table 6 for more details. A similar picture shows the modified Rankin scale outcome after treatment: 32 patients (52%) with small aneurysms had no remaining symptoms, compared to only 11 patients (31%) of the large aneurysm group. Grade I on the modified Rankin scale was reached by 10 patients (16%) with small aneurysms, and by 6 patients (17%) with large aneurysms. These differences in outcome are not significant. See table 6 for more details. The death rate did not differ significantly.

Table 9 - Characteristics of the patients in the series compared with the two subgroups of patients with fundus dimensions less and larger than 10 mm at hospital discharge.

	Subgroup with largest fundus diameter <10 mm (n= 65)	Subgroup ≥10 mm (n=36)	p	Whole series (n=101)
Modified Rankin Scale			ns	
0 No symptoms at all	32 (52%)	11 (31%)		43 (44%)
1 No significant disability with symptoms	10 (16%)	6 (17%)		16 (16%)
2 Slight disability	5 (8%)	2 (6%)		7 (7%)
3 Moderate disability	3 (5%)	2 (6%)		5 (5%)
4 Moderately severe disability	1 (2%)	1 (3%)		2 (2%)
5 Severe disability; bedridden	0 (0%)	1 (3%)		1 (1%)
6 Death	11 (18%)	12 (34%)		23 (24%)
Glasgow Outcome Score			ns	
I Good recovery	48 (77%)	22 (65%)		70 (73%)
II Moderate disability	5 (8%)	4 (12%)		9 (9%)
III Severe disability	3 (5%)	3 (9%)		6 (6%)
IV Persistent vegetative state	0 (0%)	0 (0%)		0 (0%)
V Death	6 (10%)	5 (15%)		11 (11%)
Rate of rebleeding	2 (2.7%)	2 (3.8%)		4 (3.2%)
Rate of recanalization	11 (17%)	17 (47%)	<0.0001	28 (35%)
Rate of maximal % recanalization	5.5	14.0	<0.0001	8.7
Rate of retreatment	0.06	0.25	<0.0007	0.14
Final occlusion (%)	96.0	89.6	<0.0001	95.6

3.4.10 Prognostic Factors

The clinical outcome was measured using the Modified Rankin scale (van Swieten et al. 1988), the QOL scale (Stachniak et al. 1996) and the Glasgow Outcome Scale (GOS) (Jennett and Bond 1975). The angiographic outcome has been qualitatively and quantitatively described by the rate of occlusion, Regrowth, and recanalization.

Several parameters were evaluated for a possible role for a reliable prediction of the outcome.

3.4.10.1 Age and Gender

Univariate logistic regression analysis failed to reveal a significant correlation between age and the clinical outcomes on the GOS scale (basilar tip $\chi^2 = 7.08$, $p=0.07$). A different picture gives the correlation between age and the QOL outcome with a significant result for basilar tip aneurysms ($\chi^2 = 5.2$, $p<0.04$). A similar picture results from correlation of the age with the modified Rankin scale, the regression analysis shows a non-significant result for basilar tip aneurysms ($\chi^2 = 13.0$, $p<0.05$). Sex was not found to be a significant factor.

There was no correlation between age and the degree of initial occlusion (t ratio - 1.15, $p= 0.26$), as was sex ($\chi^2 =0.1$, $p= 0.76$), however the rate of occlusion at final follow-up was not significantly correlated with age (t ratio -0.23, $p = 0.81$) or sex ($\chi^2 =0.15$, $p = 0.67$). The rate of recanalization and re-growth of the aneurysms was not significantly related to age ($\chi^2 = 4.57$, $p=0.1$, and $\chi^2 = 5.54$, $p=0.051$, respectively) or to sex ($\chi^2 = 0.56$, $p=0.76$, and $\chi^2 = 0.63$, $p=0.73$, respectively).

3.4.10.2 Aneurysm size and location

The clinical outcome in this series tended to be stable against variation of parameters of aneurysm location. In an univariate logistic regression analysis the neck dimension of the aneurysms was not significantly correlated with the clinical outcome (GOS: $\chi^2 = 2.51$, $p=0.47$, QOL scale $\chi^2 = 3.8$ $p=0.054$, modified Rankin scale $\chi^2 = 8.8$, $p=0.18$), as was not the largest fundus dimension (GOS: $\chi^2 = 4.1$, $p=0.26$, QOL scale $\chi^2 = 2.16$, $p<0.04$, modified Rankin scale $\chi^2 = 10.3$, $p=0.11$).

The morphologic parameters of aneurysm dimensions were significantly correlated with a decreased rate of initial occlusion (for the neck diameter: t ratio = -3.24, $p<0.002$, for the largest fundus diameter: t ratio = -2.71, $p<0.009$), as was the final occlusion (neck diameter: t ratio = -4.28, $p<0.0001$, largest fundus diameter: t ratio = -2.81, $p<0.006$). Of note is the higher rate of recanalization in relation to an increasing neck diameter in a univariate negative logarithmic likelihood regression analysis ($\chi^2 = 9.21$, $p< 0.01$). A similar relationship can be shown for the largest

fundus diameter ($\chi^2 = 10.19, p < 0.007$). The rate of regrowth was not correlated with the neck and fundus dimension ($\chi^2 = 3.06, p = 0.22$ and $\chi^2 = 1.55, p = 0.46$, respectively). However it was correlated to the calculated neck-to-dome ratio ($\chi^2 = 7.85, p < 0.02$).

3.4.10.3 Time interval between SAH and Treatment

The time interval between the event of subarachnoidal hemorrhage and endovascular treatment was not significantly correlated with the clinical outcome measures (GOS: $\chi^2 = 4.12, p = 0.25$, QOL scale $\chi^2 = 3.12, p = 0.25$, modified Rankin scale $\chi^2 = 6.84, p = 0.34$).

Final angiographic outcome was not significantly related to the number of days between the rupture and the treatment of the aneurysms (t ratio = 0.11, $p = 0.91$). The rate of recanalization and regrowth were not significantly related ($\chi^2 = 1.21, p = 0.55$ and $\chi^2 = 3.4, p = 0.18$ respectively).

3.4.10.4 Vasospasm

In this series the occurrence of vasospasm did not show correlation with the modified Rankin scale ($\chi^2 = 7.91, p = 0.24$), nor with the GOS score ($\chi^2 = 2.91, p = 0.41$), or the QOL score ($\chi^2 = 3.46, p = 0.06$).

In the presence or late development of vasospasm goes along with an initial rate of occlusion of 97.24 ± 5.22 %, while the rate is 94.85 ± 7.44 % in the absence of vasospasm, the difference is non-significant ($p = 0.28$). A slightly different, yet non-significant result yield the comparison upon final follow-up: 94.4 ± 7.36 % without vasospasm against 92.13 ± 13.52 % in patients that had vasospasm ($p = 0.81$). The occurrence of late recanalization and regrowth was not significantly related to vasospasm ($\chi^2 = 1.41, p = 0.56$ and $\chi^2 = 1.49, p = 0.49$ respectively).

3.4.11 Prognostic Models

Prognostic factors for univariate regression were identified in the previous paragraph. The prognostic value of combinations of these can be tested using logistic regression models.

Table 10 – Modelling the risk of recanalization as an outcome parameter using a negative log-likelihood model. In this model morphological parameters of aneurysm size and derivations were combined to predict the chance of recanalization. All included parameter contributed significantly to the angiographic outcome parameter recanalization except for the neck-to-dome ratio.

Factor	L-R χ^2	Probability > χ^2
log Neck diameter/Area	8.21	<0.02
Neck diameter/Area	6.08	<0.05
Largest fundus dimension	11.00	<0.005
Neck/Dome ratio	4.23	0.1206

The final rate of angiographic occlusion was significantly related to the largest fundus dimension, and the logarithmic neck/dome ratio ($p < 0.001$ and $p < 0.007$, respectively), see Table 11 for details. The rate of recanalization significantly related to the logarithmic neck to area ratio, area being fundus height multiplied by fundus width ($p < 0.02$), see Table 10 for details. It was also related to the neck-to-area ratio and the largest fundus dimension ($p < 0.05$ and $p < 0.005$ respectively).

Table 11 – Final angiographic occlusion rate predicted by a model incorporating parameters of aneurysm size. Only the largest fundus diameter and logarithmic neck diameter to area ratio contributed significantly.

Factor	Sum of Squares	F Ratio	Probability > F
Log Neck diameter/Area	342,41201	7,8870	<0.007
Neck diameter/Area	92,17282	2,1231	0,1506
Largest Dimension	929,77561	21,4161	<0.0001
Neck/Dome ratio	157,63243	3,6308	0,0618
Number of coils used	1,13625	0,0262	0,8721

A nominal logistic fit was used to elicit a relationship between the QOL score post-treatment and age, the initial presenting GOS score, the Hunt-Hess grade, the interval between a rupture and the treatment if applicable, and the presence of vasospasm during or after treatment. In this model only the age is a significant predictor for the QOL outcome ($p < 0.004$), all other parameters contributed non-significantly. When the QOL score elicited upon final follow-up was used, the same model failed to predict the outcome ($p = 0.1$). The prediction remained valid ($p < 0.02$) in a reduced model incorporating only age, Hunt-Hess grade and initial GOS score. In contrast the GOS score outcome after treatment was significantly related to the presence of vasospasm ($p < 0.007$), and age ($p < 0.05$), the remaining parameters only contributing non-significantly. When the final GOS outcome was used, the same factors contributed significantly (age: $p < 0.02$, presence of vasospasm $p < 0.05$).

Table 12 – Post treatment modified Rankin scale predicted by a model including age, Hunt-Hess grade upon presentation if applicable, initial GOS score, number of days between rupture and treatment if applicable, and the presence of vasospasm. Only age, the presence of vasospasm, and the interval between rupture and treatment seemed to be a significant contributors to the final modified Rankin scale outcome.

Factor	L-R χ^2	Probability $> \chi^2$
Age	17,0080445	<0.001
Hunt-Hess grade at treatment	23,2275698	0.5064
Initial GOS score	24,874442	0.1284
Days post SAH	16,4134968	<0.02
Vasospasm	18,8285381	<0.005

In a reduced model, incorporating only age, Hunt-Hess grade, and initial GOS score all were significant factors (age: $p < 0.04$, Hunt-Hess grade $p < 0.05$, initial GOS score $p < 0.03$). The post-treatment modified Rankin scale correlated only with the initial GOS score in a model fitting age, Hunt-Hess grade and initial GOS score ($p < 0.007$). For the modified Rankin score at final follow-up age became a significant factor ($p < 0.02$) (initial GOS: $p < 0.02$, Hunt-Hess grade $p = 0.065$). In an extended model with

additional parameters (interval between rupture and treatment if applicable, and presence of vasospasm) age became a significant factor ($p<0.01$), as were the interval between rupture and treatment ($p<0.02$), and the presence of vasospasm ($p<0.005$) in predicting the final modified Rankin-scale (see Table 12 for details).

3.4.12 Summary

There was a subgroup of 101 aneurysms of the basilar apex in 101 patients (78 female and 23 male) that underwent endovascular therapy. In 28 patients (28%) the aneurysm was unruptured. The procedure resulted in successful coil delivery and embolization in 97/101 of cases (96%) in this subgroup of patients with basilar apex aneurysms. The mean angiographic occlusion rate, or projected area of the aneurysm occluded by the coils, for all 97 successfully treated aneurysms was 94%. At latest clinical follow-up, 43/97 patients (44%) denied any symptoms (modified Rankin 0), 16/97 (16%) had remaining symptoms without accompanying disability (mRankin 1), and 15 (15%) had various degrees of impairment (mRankin 2-5), and 23 (24%) were dead. Of the subset of 49 patients with Hunt-Hess grades I-III, 46 (94%) achieved a good clinical outcome (GOS I). A statistically significant correlation was demonstrated between Hunt-Hess grade at presentation and final modified Rankin outcome score ($\chi^2 = 44.6$, $p<0.04$). Procedure-related permanent morbidity was 2.8% (3/109 patients). Repeat hemorrhage was observed in 4 patients (4%). Eight (8%) patients died from SAH related causes.

4 Discussion

4.1 Posterior inferior cerebellar artery aneurysms

The aim of endovascular treatment of PICA aneurysms is the prevention of initial or repeated hemorrhage and its devastating consequences (Schievink et al. 1995). Rarely the relief of focal symptoms is the primary goal. The clinical experience from a series of ruptured aneurysms treated conservatively has demonstrated a 37% risk of rebleeding at 4 weeks and an overall mortality rate from repeated hemorrhage and its sequelae of 34% to 42% (Nishioka et al. 1984; Nishioka et al. 1984). In the context of this poor natural history, the results presented here for ruptured intracranial posterior circulation aneurysms indicate that GDC embolization confers a protective effect. There was no recurrent SAH in the acute phase after endovascular embolization encountered. Furthermore, no aneurysm of this series, all of which were occluded to greater than 85% by angiographic criteria rebled during the follow-up period.

With regard to the small total number of patients in this study (n=23) the absence of recurrent rate (0%) of SAH and rebleeding due to repeat rupture after primary treatment could be accounted for by sampling bias. Nevertheless this may very well be comparable to those reported in other endovascular series, which range from 0%/y to 3%/y (Kuether et al (Kuether et al. 1998), 1.4%; Eskridge et al (Eskridge and Song 1998), 3%; Pierot et al (Pierot et al. 1997), 0%). Tsutsumi et al (Tsutsumi et al. 1998) calculated the rate of recurrent SAH between 1.4% and 1.8% in a group of 220 patients treated with surgical clipping during a follow-up period ranging from 3 to 21 years. The cumulative risk for recurrent SAH was estimated to be 0.5%, 2.2%, and 5.5% at 5, 10, and 15 years postoperatively, respectively (Tsutsumi et al. 1998).

4.1.1 Angiographic Outcome

Small aneurysms with narrow necks and saccular shape demonstrated excellent initial and final occlusion rates. Overall, 83% (19/23) of the treated non-parent vessel occlusion aneurysms were occluded in the 90% to 100% range. A multicenter study of 150 basilar apex aneurysms (Eskridge and Song 1998) noted 75% of aneurysms at 90% to 100% occlusion after GDC embolization. Other series of posterior circulation aneurysms, mainly of the basilar artery treated with GDC embolization

report complete and near-complete (90% to 100%) angiographic occlusion in a mean of 59,8% of patients (range, 42% to 75%), compared with 83% in this series (Bavinzski et al. 1995; Pierot et al. 1996; Raymond et al. 1997; Eskridge and Song 1998; Gruber et al. 1999). Of note however is that distal PICA aneurysms may be technically more challenging to embolize and easier to clip, which is not reflected in pure numbers. In surgical series, Heros et al. (Heros 1995) reported an 88% rate of an uneventful postoperative course after complete clipping, with one reversible serious complication (lateral medullary infarction) and on death after a large hemorrhage. Very good results on the Botterell scale in 59 of a series of 69 patients (85%) with PICA aneurysms presenting with HH grade I or II were reported by Peerless and Drake (Peerless and Drake 1982) with 2 deaths. Lee et al. (Lee et al. 1989) describe a series of 14 patients with 11 excellent outcomes postoperatively (79%) and 2 deaths. Others describe similarly good results (Yamaura et al. 1981; Salcman et al. 1990). In a review of the literature on peripheral PICA aneurysms a 83% rate of good or excellent outcome was found with a mortality of about 1% (Beyerl and Heros 1986). Peerless et al. (Peerless et al. 1994) reported an 87.4% rate of total occlusion after clipping, with a neck remnant seen in 5.8% and residual aneurysm body or fundus in 6.8%. Less than complete occlusion was in almost all cases due to complex aneurysm geometry. In the present series, 22% of treated aneurysms harbored a wide neck (≥ 4 mm), and 17% measured ≥ 10 mm in largest diameter. The difficulty in attaining complete obliteration of these complex aneurysms is shared with surgical series, which have similarly reported greater difficulty in complete occlusion by clipping in this group (Peerless et al. 1994; Samson et al. 1999). Incomplete aneurysm occlusion by endovascular coil placement may still offer a measure of protection from re-hemorrhage, as shown by the absence of repeated rupture rate in this and other series, although the necessary degree of occlusion needed to result in such protection needs further elucidation.

4.1.2 Clinical Outcome

The initial clinical grade of the patient at presentation was a strong predictor of the patient outcome. In this series, 94% of good-grade patients (Hunt-Hess 0, I or II) had good recovery leading to a GOS I outcome at final follow-up, with 100% in the GOS I or II group. The 4 intermediate-grade patients (Hunt-Hess III) reached GOS I (2/4

patients, 50%), GOS II (1/4 patients, 25%), and GOS III (1/4 patients, 25%) outcome. Taking the small number of patients (n=4) of this subgroup into account, this finding is consistent with other series that have reported lower percentages of good outcome for grade III patients: 55%, (Cognard et al. 1998), 57%, (Malisch et al. 1997), and 100% (Kuether et al. 1998). Of the two poor-grade patients (Hunt- Hess IV and V), only one recovered to a good final outcome (GOS I). All measured indices, including GOS, modified Rankin, and QOL, showed improved outcomes after GDC embolization when adjusted for the initial neurological condition. Late deterioration resulted from vasospasm (4.2%, 1/24), and delayed complications (4.2%, 1/24). The overall final excellent/ good clinical outcome in this series (GOS I/II) of 91% (21/23) is comparable to the 69% to 91% (average of 78%) GOS I/II outcomes seen in other series (Bavinzski et al. 1995; Pierot et al. 1996; Raymond and Roy 1997; Eskridge and Song 1998; Gruber et al. 1999; Lempert et al. 2000).

4.1.3 Complications

There were no cases of procedure-related mortality in this series (0%), compared with rates ranging from 0% to 3% in other endovascular series (Bavinzski et al. 1995; Pierot et al. 1996; Raymond et al. 1997; Eskridge and Song 1998; Gruber et al. 1999). The permanent morbidity rate of 4.4% (1/23 patients) is comparable with other endovascular series having reported combined morbidity and mortality rates between 5% and 16.9% (Bavinzski et al. 1995; Pierot et al. 1996; Raymond and Roy 1997; Eskridge and Song 1998; Gruber et al. 1999; Lempert et al. 2000). A recent meta-analysis (Brilstra et al. 1999) of 48 eligible endovascular studies totaling 1383 patients reported permanent complications in 46 of 1256 patients (3.7%; 95% CI, 2.7% to 4.9%). Even when taking the small size of the patient population into account endovascular coiling of PICA aneurysms does not seem to impose increased risks compared with other locations. Important to note is that the rather drastic measure of total occlusion of the parent vessel – most often in cases with a fusiform aneurysm – seems to be well tolerated in this series since used in conjunction with aggressive fluid management and optimization of the hydration status and blood pressure. Used in 9 of 23 patients (39%), only in one case (1/9, 11%) a noticeable neurological deficit (infarction of the cerebral peduncle on the affected side) of change on imaging studies was demonstrated. The clinical symptoms are known to correlate well with

the imaging studies (Cormier et al. 1992). Although perforating branches of the PICA are considered predominant in supplying the medulla (Lister et al. 1982; Amarenco and Hauw 1989; Amarenco et al. 1989; Grand et al. 1997), perforating branches of the vertebral artery are more recently considered as important. The definitive terminal distribution of the vessels perforating the brainstem has been recently challenged (Lister et al. 1982; Yamaura 1988; Amarenco and Hauw 1989; Amarenco et al. 1989; Grand et al. 1997), a more plexiform network of small vessels equally arising from the PICA, vertebral artery, basilar artery, anterior inferior cerebellar artery, especially between the two former ones (Lister et al. 1982; Akar et al. 1994). This may explain the demonstrated low rate of ischemic complications from occlusion of the PICA after treatment of fusiform aneurysms.

Despite the limitations in comparing surgical and endovascular studies, the retrospective nature of this study, and potential selection and referral bias, and the small size of the patient population, results of 0% direct mortality, 4.4% overall mortality, and 91% overall excellent/good outcome (GOS I and II) compare favorably with published surgical results of series that include both ruptured and unruptured posterior inferior cerebellar artery aneurysms (Lee et al. 1989; Yamaura et al. 1991; Zingale et al. 1994; Bertalanffy et al. 1998; Ogilvy and Quinones-Hinojosa 1998; Kaptain et al. 1999; Dinichert et al. 2000). The findings confirm that GDC embolization is effective in preventing recurrent hemorrhage of PICA aneurysms over a follow-up period, which is longer than in other series of endovascularly treated aneurysms.

4.2 Superior cerebellar artery aneurysms

Patients with aneurysms of the superior cerebellar artery represent only a small subset of the patients harboring intracranial aneurysms. They represent about 0.25% to 0.66% of all aneurysms of the posterior circulation. (McDonald and Korb 1939; Locksley 1966) They, with a higher than usual rate, seem to be associated with arteriovenous malformations, as it was the case in this series, where 24% of the aneurysms were part of AVM feeding vessels.

The majority of SCA aneurysms presents after rupture with acute or subacute subarachnoidal hemorrhage. Nevertheless more subtle presentations involving only

the cranial nerves that are adjacent to the SCA are possible, Collins et al. reported a case where palsy of the trochlear nerve was the only symptom of a SCA aneurysm (Collins et al. 1992). In this series 71% of the patients presented with ruptured aneurysms. Of these, only two patients had an aneurysm with the largest fundus dimension being less than 5 mm, which contrasts with other published reports. However this fits to the conclusion drawn from other larger series not concentrating on SCA aneurysms, that 5mm may be a cutoff size to determine the risk of rupture and hemorrhage (Matricali and Seminara 1986). It has arguably been considered the minimum size at which intracranial aneurysms are statistically likely to bleed (Crompton 1966). Gacs et al (Gacs et al. 1983) theorized that these peripheral aneurysms tended to rupture at a smaller size because of a thinner aneurysm wall. The subset of un-ruptured aneurysms in this series (5 patients) did not differ significantly from the subset with a ruptured aneurysm regarding largest fundus and neck dimension.

Symptomatic aneurysms arising from the peripheral segments of both supratentorial and infratentorial cerebral arteries are rare and have frequently been noted to stem from either traumatic or mycotic origins (Ferry and Kempe 1972; Cockrill et al. 1977; Jellinger 1977; Quattrocchi et al. 1990). Peripheral aneurysms involving the superior cerebellar artery are particularly uncommon; findings in two large case series suggest a rate of occurrence of 0.25% to 0.66% of all aneurysms of the posterior circulation (McDonald and Korb 1939; Locksley 1966). Furthermore, peripheral aneurysms involving the cerebellar arteries are associated more frequently than expected with cerebral arteriovenous malformations (Gacs et al. 1983)

Occlusion of the parent SCA is often required by open surgical treatment (McDonald and Korb 1939; Ferry and Kempe 1972; Cockrill et al. 1977; Mabuchi et al. 1992; McDermott and Sellar 1994), yet it seems to be well-tolerated (Ferry and Kempe 1972; Gacs et al. 1983; Mabuchi et al. 1992). A number of factors seem to contribute to this intrinsic stability against ischemic damage after occlusion of the SCA. In general there is a very well established network of collateral circulation between the superior cerebellar artery and both the anterior inferior cerebellar artery and the posterior inferior cerebellar artery through the vermian arcade (Lasjaunias et al. 2001). After proximal occlusion of the superior cerebellar artery, retrograde flow with reconstitution of the distal branches may be established through this network as has

been described above in 4.1.3. Also the ventral brainstem, which is partially supplied by proximal perforators from the superior cerebellar artery, possesses good collateral flow from basilar artery perforators, thus diminishing the likelihood of ischemic damage to these areas. This may explain a paucity of perforators arising from the anterior pontine and lateromesencephalic portions of the SCA. The area suffering most from an ischemic insult following occlusion of the superior cerebellar artery seems to be the cerebellar cortex, yielding less of a definitive neurological deficit than other insults in the posterior fossa. Critical swelling of the brain following an insult or subarachnoidal hemorrhage after rupture may result in a fatal outcome (Chaloupka et al. 1996).

Considering the relatively high mortality rate of 23% in the series of patients with SCA presented above, which fails to compare favorably with surgical series recommendations can be made only in a very cautious manner. Endovascular therapy is a safe and efficacious method when technical success is reached, however the conjunction of the opposite may not be valid. Given the small number of cases of SCA aneurysms in the presented series the results found here may not be definitive.

4.3 Aneurysms of the vertebrobasilar junction

Aneurysms located at the vertebrobasilar junction are associated with complex geometry of the large vessels, multiple adjacent perforating arteries to the brain stem, proximity of the roots and fibers of the lower cranial nerves, and possible additional fenestration of the basilar artery. The seemingly non-trivial task of obtaining adequate surgical exposure of these aneurysms makes surgical clipping difficult (Drake 1968; Matricali and van Dulken 1981; Nakasu et al. 1982; Hernesniemi et al. 1992). Endovascular treatment of these aneurysms using GDC coil embolization provides an alternative treatment (Graves et al. 1996).

In large autopsy series the incidence of basilar fenestrations was between 1.3% and 6% (Wollschlaeger et al. 1967; Hoffman and Wilson 1979), a discrepancy to the rate of 0.02% to 0.6% in angiographic series (Takahashi et al. 1973; Teal et al. 1973; Sanders et al. 1993). Very thin and angiographically occult dividers, and often a view obscured by the aneurysm, may explain the difference between autopsy and angiographical series.

When a fenestration is noted in a patient, the incidence of an associated aneurysm present is reported to be 7% (Sanders et al. 1993), whereas in the presence of a vertebrobasilar junction aneurysm the incidence of a concomitant fenestration was reported to be 35.5% (Campos et al. 1987). In this series there were 4 fenestrations for a rate of 33%.

Failure of the paired fetal neural arteries to fuse along the whole length of the basilar artery leads to fenestration, commonly during the fifth week of fetal development between 29 and 32 days of development (embryo length 4-6mm). This failure may occur at any given point of the basilar artery, however the more prevalent location is the proximal portion (Padget 1948), where the vertebral arteries form only at 32 to 35 days (embryo length 7 to 12mm).

The lateral walls of a fenestrated artery show a normal intrinsic histology, whereas the medial walls function as a septation, which divides the artery into two distinct vascular canals. Focal defects are located at both end of the medial septation, with local absence of the media and discontinuous elastin. Proximally thin subendothelium thickens towards the distal end. All these changes are comparable to those seen in bifurcations of cerebral arteries (Finlay and Canham 1994).

Complex hemodynamics are a function of the special geometry of the vertebrobasilar junction, especially in the presence of a concomitant basilar fenestration.

Ravensbergen et al. describe a model of the vertebrobasilar junction and demonstrate that the angle of confluence and a sharp versus a blunted geometry of the junction are two major factors that govern the wall shear stress of the vessels. The angle of confluence influences both the velocity of flow near and far distal of the junction (Ravensbergen et al. 1997). With increasing angles in junctions with a sharp geometry a region of low flow velocities increases in size, and recirculation occurs resulting in a low shear stress region, whereas the same phenomenon occurs for blunt-angle junctions with decreasing confluence angles.

Although the theoretical hemodynamic changes from a laminar flow pattern at the vertebrobasilar junction are consistent with the theory of development of intracranial berry aneurysms, as proposed by Stehbens (Stehbens 1989), and the presence of aneurysms may be partially accounted for by these, no prediction of the direction or

the side to which a particular aneurysm points could be made. There is no model that in any way accounts for the brainstem and other adjacent structures near the aneurysm, and may give more valid predictions.

Direct surgical access to aneurysms at the vertebrobasilar junction is blocked by the petrous bone (Lawton et al. 1997; Aziz et al. 1999), however a number of innovative skull base approaches have been developed to deal with this problem. A dramatic reduction in morbidity and mortality rates associated with surgery could be reached through reduced need of retraction of neural structures. These approaches include the transpetrosal approach, the retrolabyrinthine transigmoidal approach, and the combined supratentorial and infratentorial approach (Solomon and Stein 1988). Utilization of accessory instruments such as intraoperative temporary balloon occlusion of the vertebral artery and hypothermia with circulatory arrest have been described to facilitate successful clipping of large or giant aneurysms of the vertebrobasilar junction or the basilar trunk (Spetzler et al. 1988; Lawton et al. 1997).

Embolization of intracranial aneurysms using GDC coils was introduced into clinical practice in 1991. The presence of two distinct arterial approaches to the vertebrobasilar junction or the basilar artery via the vertebral arteries provides the means for safe and simple catheterization and endovascular navigation.

Small perforators seem to almost never arise from the dome of an aneurysms, the endovascular approach thereby decreases the chance of compromising blood supply to the brainstem through one of these arteries. Inadvertent migration of the coil mass or the resultant thrombus into the neck of the aneurysm or the parent artery however may lead to accidental occlusion of perforating arteries.

Although the vertebral artery provides a most direct access to vertebrobasilar junction aneurysms, it may also be the limiting factor in treating these lesions. A tortuous course and small diameter may increase the risk of dissection of the artery.

As vertebrobasilar junction aneurysms receive blood flow from both vertebral arteries, which leads to an increased risk of recanalization and requirement for permanent occlusion of one or both vertebral arteries. Uda et. al. report that 60% of the vertebrobasilar junction aneurysm required this additional measure, and that two

thirds of all ischemic complications in their series occurred in patients with vertebrobasilar junction aneurysms (Uda et al. 2001).

Compared with aneurysms of the anterior circulation, aneurysms of the posterior circulation in general have a worse prognosis in association with higher morbidity and mortality rates. The international cooperative study describes a 31% mortality for 266 aneurysms of the vertebrobasilar system (Kassell et al. 1990).

The outcome of the subgroup of patients in this series with VBJ aneurysms compares favorably with other series (Uda et al. 2001), that used endovascular intervention, or surgical series (Kassell et al. 1990) showing that endovascular therapy for VBJ aneurysms using GDC coils is a valuable treatment option in selected cases.

4.4 Basilar apex aneurysms

Since the introduction of GDCs into clinical practice in 1991 basilar tip aneurysms were in the early phases of the experience with this technique the most common type of aneurysms treated. These and other types of aneurysms of the basilar artery pose challenge to a surgical approach with regards to their location and close relationship with eloquent perforating arteries (Peerless and Drake 1982; MacFarlane et al. 1983; Solomon and Stein 1988; Kassell et al. 1990; Kassell et al. 1990; Hillman et al. 1996). Instead of their location, embolization of aneurysms is rather dependent on their anatomic configuration (Fernandez Zubillaga et al. 1994). The straight course of the intracranial portion of the vertebral artery and basilar artery and the anatomic disposition of many basilar artery aneurysms are favorable for endovascular navigation and aneurysm catheterization (Fernandez Zubillaga et al. 1994).

This technique by no means solves general problems associated with these aneurysms that tend to be most difficult to treat surgically. A wide neck and large fundus imposes a great risk of sub optimal outcome both with surgical clipping and endovascular treatment. Optimal angiographic imaging of the neck of the aneurysm is required for treatment of the most difficult neck-portion of the aneurysm and the whole aneurysm without encroachment on the parent vessel or risking thromboembolism. Previous studies related the degree of initial or short-term occlusion with the size of the aneurysm neck and reported a 85% to 100% occlusion

rate for small-necked aneurysms, but only around 15% for wide-necked aneurysms (Guglielmi et al. 1992; Fernandez Zubillaga et al. 1994).

Although there still is not much long-term follow-up data available for patients who underwent endovascular treatment for basilar artery aneurysms in the literature this work reports about angiographic follow-up as long as 90 months (with a mean angiographic follow-up of 17.9 ± 2.2 months), and similarly clinical follow-up as long as 91 months (mean duration 31.3 ± 2.5 months) in the majority of the patient population. The mean follow-up time is longer than in other series, especially in patients with sub-optimal occlusion upon initial treatment or follow-up who underwent repeat follow-up. Uda et al. obtained follow-up angiograms in 29 patients with 31 aneurysms with a mean follow-up period of 17 months. No recanalization was observed in the eight completely occluded aneurysms. In 19 lesions with small neck remnants, seven (36.8%) had further thrombosis, three (15.8%) remained anatomically unchanged, and nine (47.3%) had recanalization caused by coil compaction. In one patient (2.6%) the aneurysm rebled 8 years after the initial embolization (Uda et al. 2001). Tateshima et al. performed a follow-up angiography after 6 months for all patients and unspecified additional follow-up angiographies based on risk assessment (Tateshima et al. 2000). In respect to the question how long these patients would have to be followed (McDougall et al. 1996), the conclusion is that there is still a lack of sufficient data to support any limitation in follow-up.

Not contrary to expectation this series demonstrates that partial occlusion is partially protective at best concerning the risk of future hemorrhage. The 4 patients that rebled during the duration of the follow-up all had initial rates of occlusion between 80% and 90%, hence a lower rate of initial occlusion failed to be a predictor of re-hemorrhage. This is no surprise regarding current knowledge about incompletely clipped aneurysms (Drake and Vanderlinden 1967; Feuerberg et al. 1987; Lin et al. 1989). The data presented here suggest that the reduction of risk of hemorrhage, initial or repeat, outweighs the risk of the endovascular procedure.

Many of these patients would not be considered surgical candidates; hence comparison with surgical series of clipped aneurysms is not entirely valid and only warranted by the lack of conclusive endovascular data. The results in this series

compare favorable with the natural history of ruptured aneurysms (Jane et al. 1985), the feasibility of this comparison remains to be determined.

To further the assessment of pre- and intra-operative risk this work seeks to identify prognostic factors that were associated with the angiographic and clinical outcome parameters of this series. No attempt was undertaken to revise an existing grading system or even propose a new one. In reference to the previous chapter several prognostic factors contributing to outcome using both univariate and multivariate regression analysis were identified.

Age and gender overall had a very variable role in contributing to both clinical and angiographic outcome. Overall both QOL score and modified Rankin scale were influenced by age, showing a decreasing percentage of patients with good and excellent outcomes in the older age groups. The results of several series of patients with ruptured and unruptured intracranial aneurysms, where patient age has been identified in as an independent predictor of long-term clinical outcome were similar (Kassell et al. 1990; Kassell et al. 1990; Hernesniemi et al. 1993; Deruty et al. 1995; Yoshimoto and Kwak 1995; Khanna et al. 1996). Gender did not contribute significantly, which is also in agreement with previously published data.

The clinical outcome seems not to be associated with aneurysm size and location, as has been previously noted (Ogilvy and Carter 1998), in contrast to significant associations between aneurysm size and angiographic outcome (Guglielmi et al. 1992; Fernandez Zubillaga et al. 1994). In the multivariate model described above this association only held for the largest fundus dimension and a derived neck-to-fundus ratio, which compares well with previously known results (Guglielmi et al. 1992; Fernandez Zubillaga et al. 1994). This can be deduced from both the comparison of the subgroups with a largest fundus diameter of less or more than 10 mm and the uni- and multivariate models. Especially the final rate of occlusion and the rate of retreatment and recanalization differ significantly and impressively between the two subgroups. Although the clinical outcome measured by GOS, QOL and modified Rankin scale appears to be different by numbers it cannot be ruled out that these differences are attributable to chance. Still the results highlight the efficacy and safety of endovascular treatment especially for small aneurysms with a largest diameter less than 10 mm. In contrast to the literature (Fernandez Zubillaga et al.

1994) the neck-to-dome ratio was not found to be a predictor of favorable outcome, but it was still significantly different between the subgroups with small and large aneurysms.

Vasospasm has been known as one strong predictor of clinical outcome (Brouwers et al. 1993; Gerber et al. 1993; Rabb et al. 1994), yet in this series using univariate analysis only the modified Rankin scale relates to the presence of vasospasm, in contrast to the GOS, and QOL score, and angiographic outcomes. Utilizing the multivariate models, vasospasm becomes also a predictor of the final GOS.

Angiographic and clinical outcomes in 101 consecutive patients with basilar artery aneurysms treated with the GDC technique were analyzed retrospectively. The immediate angiographic outcomes confirm that this technology achieves good results in basilar artery aneurysms with favorable neck-to-dome ratio. However, the angiographic outcomes are less than satisfactory in small aneurysms with wide necks, as well as in large and giant aneurysms. Results from subgroup analysis and modeling analysis suggest that the largest fundus dimension is a stronger predictor of at least angiographic success than the neck-to-dome ratio.

Despite the significant proportion of difficult aneurysms and poor Hunt and Hess grades in this study population, the overall morbidity and mortality rates in this series compare favorably with those of most published neurosurgical series.

4.5 Endovascular versus surgical treatment

A common endpoint in discussions about the superiority of either treatment modality was the reference that there were no randomized controlled trials that addressed the question. The international subarachnoid aneurysm trial was designed to alleviate this lack of evidence (Molyneux et al. 2002). After screening about ten-thousand patients suffering from a subarachnoid hemorrhage from an intracranial aneurysm patients, where both a neurosurgeon and an interventional neuroradiologist agreed that both could treat the aneurysm, were enrolled into the trial. They were then randomized to one of the two treatment modalities. The interim outcome analysis after one year showed that there was both a 22.6% reduction of the relative risk of an unfavorable outcome (modified Rankin scale 3-6) or death and a 6.9% reduction of the absolute risk, respectively for patients that underwent the endovascular path.

Although tempting, this does certainly not warrant apodictic statements which have been given by prominent interventional neuroradiologists (Molyneux 2002). Other authors caution that the main question will not be addressed by the comparison of outcome after one year and point out that the majority of aneurysms initially screened in the trial failed to meet inclusion criteria (Nichols et al. 2002). Economic considerations gain increasing importance in today's medicine and hence it may turn out that one of the factors decisive for one or the other treatment modality will be cost of the treatment itself and related costs such as length of hospital stay and follow-up costs. There is increasing evidence that endovascular treatment is economically more effective (Jordan et al. 1996; Johnston et al. 2000), and a subset analysis of the ISAT trial addressing this issue will be revealing, since there was specific consideration towards the collection of economic data in the protocol (Molyneux 2002; Molyneux et al. 2002).

At this point there is unequivocal agreement that endovascular treatment of intracranial aneurysms is a feasible treatment modality for selected patients and aneurysm types. Dispute starts with the question what could be criteria to select these patients in a prospective fashion in clinical practice, and it ends with the problem of grading evidence in a rapidly evolving field of medicine.

Endovascular therapy provides the means to access the aneurysm in a minimally invasive fashion. This is a clear advantage in aneurysms in a difficult location, where an adequate exposure may be difficult to obtain by open surgery. In an acute stage after rupture of the aneurysm brain swelling may provide an additional incentive to avoid a craniotomy. The clear disadvantage of this technique is the still limited experience with treatment and follow-up. Although the data presented above may provide supporting evidence it still has to be shown that endovascular therapy reaches adequate occlusion rates with acceptable rates of regrowth and recanalization in comparison with surgical series.

5 References

- Akar, Z. C., M. Dujovny, et al. (1994). "Microsurgical anatomy of the intracranial part of the vertebral artery." *Neurol Res* **16**(3): 171-80.
- Aletich, V. A., G. M. Debrun, et al. (2000). "The remodeling technique of balloon-assisted Guglielmi detachable coil placement in wide-necked aneurysms: experience at the University of Illinois at Chicago." *J Neurosurg* **93**(3): 388-96.
- Alexander, E., Jr., C. H. Davis, Jr., et al. (1966). "Aneurysm of the posterior inferior cerebellar artery filling the fourth ventricle. Case report." *J Neurosurg* **24**(1): 99-101.
- Amarenco, P. and J. J. Hauw (1989). "[Anatomy of the cerebellar arteries]." *Rev Neurol (Paris)* **145**(4): 267-76.
- Amarenco, P., J. J. Hauw, et al. (1989). "[Cerebellar infarction in the area of the posterior cerebellar artery. Clinicopathology of 28 cases]." *Rev Neurol (Paris)* **145**(4): 277-86.
- Andoh, K., K. Tanohata, et al. (2001). "The posterior inferior cerebellar artery arising from the extracranial segment of the internal carotid artery via the hypoglossal canal without an interposed segment of the basilar artery: a persistent primitive hypoglossal artery variant." *Clin Imaging* **25**(2): 86-9.
- Aziz, K. M., H. R. van Loveren, et al. (1999). "The Kawase approach to retrosellar and upper clival basilar aneurysms." *Neurosurgery* **44**(6): 1225-34; discussion 1234-6.
- Batjer, H. H. and D. S. Samson (1989). "Causes of morbidity and mortality from surgery of aneurysms of the distal basilar artery." *Neurosurgery* **25**(6): 904-15; discussion 915-6.
- Bavinzski, G., M. Killer, et al. (1999). "Treatment of basilar artery bifurcation aneurysms by using Guglielmi detachable coils: a 6-year experience." *J Neurosurg* **90**(5): 843-52.
- Bavinzski, G., B. Richling, et al. (1995). "Endosaccular occlusion of basilar artery bifurcation aneurysms using electrically detachable coils." *Acta Neurochir (Wien)* **134**(3-4): 184-9.
- Bertalanffy, H., U. Sure, et al. (1998). "Management of aneurysms of the vertebral artery-posterior inferior cerebellar artery complex." *Neurol Med Chir (Tokyo)* **38 Suppl**: 93-103.
- Beyerl, B. D. and R. C. Heros (1986). "Multiple peripheral aneurysms of the posterior inferior cerebellar artery." *Neurosurgery* **19**(2): 285-9.
- Brilstra, E. H., G. J. Rinkel, et al. (1999). "Treatment of intracranial aneurysms by embolization with coils: a systematic review." *Stroke* **30**(2): 470-6.
- Brouwers, P. J., D. W. Dippel, et al. (1993). "Amount of blood on computed tomography as an independent predictor after aneurysm rupture." *Stroke* **24**(6): 809-14.
- Byrne, J. V., M. J. Sohn, et al. (1999). "Five-year experience in using coil embolization for ruptured intracranial aneurysms: outcomes and incidence of late rebleeding." *J Neurosurg* **90**(4): 656-63.

- Campos, J., A. J. Fox, et al. (1987). "Saccular aneurysms in basilar artery fenestration." *AJNR Am J Neuroradiol* **8**(2): 233-6.
- Casasco, A. E., A. Aymard, et al. (1993). "Selective endovascular treatment of 71 intracranial aneurysms with platinum coils." *J Neurosurg* **79**(1): 3-10.
- Chaloupka, J. C., C. M. Putman, et al. (1996). "Endovascular therapeutic approach to peripheral aneurysms of the superior cerebellar artery." *AJNR Am J Neuroradiol* **17**(7): 1338-42.
- Chen, C. J. and S. T. Chen (1997). "Extracranial distal aneurysm of posterior inferior cerebellar artery." *Neuroradiology* **39**(5): 344-7.
- Cockrill, H. H., Jr., J. P. Jimenez, et al. (1977). "Traumatic false aneurysm of the superior cerebellar artery simulating posterior fossa tumor." *J Neurosurg* **46**(3): 377-80.
- Cognard, C., A. Weill, et al. (1998). "Intracranial berry aneurysms: angiographic and clinical results after endovascular treatment." *Radiology* **206**(2): 499-510.
- Collins, T. E., T. F. Mehalic, et al. (1992). "Trochlear nerve palsy as the sole initial sign of an aneurysm of the superior cerebellar artery." *Neurosurgery* **30**(2): 258-61.
- Cormier, P. J., E. R. Long, et al. (1992). "MR imaging of posterior fossa infarctions: vascular territories and clinical correlates." *Radiographics* **12**(6): 1079-96.
- Crompton, M. R. (1966). "Mechanism of growth and rupture in cerebral berry aneurysms." *Br Med J* **5496**: 1138-42.
- Day, J. D., T. Fukushima, et al. (1997). "Cranial base approaches to posterior circulation aneurysms." *J Neurosurg* **87**(4): 544-54.
- Debrun, G., A. Fox, et al. (1981). "Giant unclippable aneurysms: treatment with detachable balloons." *AJNR Am J Neuroradiol* **2**(2): 167-73.
- Deruty, R., I. Pelissou-Guyotat, et al. (1995). "Level of consciousness and age as prognostic factors in aneurysmal SAH." *Acta Neurochir (Wien)* **132**(1-3): 1-8.
- Dinichert, A., D. A. Rufenacht, et al. (2000). "Dissecting aneurysms of the posterior inferior cerebellar artery: report of four cases and review of the literature." *J Clin Neurosci* **7**(6): 515-20.
- Drake, C. G. (1968). "The surgical treatment of aneurysms of the basilar artery." *J Neurosurg* **29**(4): 436-46.
- Drake, C. G. (1979). "The treatment of aneurysms of the posterior circulation." *Clin Neurosurg* **26**: 96-144.
- Drake, C. G. and R. G. Vanderlinden (1967). "The late consequences of incomplete surgical treatment of cerebral aneurysms." *J Neurosurg* **27**(3): 226-38.
- Eskridge, J. M. and J. K. Song (1998). "Endovascular embolization of 150 basilar tip aneurysms with Guglielmi detachable coils: results of the Food and Drug Administration multicenter clinical trial." *J Neurosurg* **89**(1): 81-6.

- Fernandez Zubillaga, A., G. Guglielmi, et al. (1994). "Endovascular occlusion of intracranial aneurysms with electrically detachable coils: correlation of aneurysm neck size and treatment results." *AJNR Am J Neuroradiol* **15**(5): 815-20.
- Ferry, D. J., Jr. and L. G. Kempe (1972). "False aneurysm secondary to penetration of the brain through orbitofacial wounds. Report of two cases." *J Neurosurg* **36**(4): 503-6.
- Feuerberg, I., C. Lindquist, et al. (1987). "Natural history of postoperative aneurysm rests." *J Neurosurg* **66**(1): 30-4.
- Finlay, H. M. and P. B. Canham (1994). "The layered fabric of cerebral artery fenestrations." *Stroke* **25**(9): 1799-806.
- Gacs, G., F. Vinuela, et al. (1983). "Peripheral aneurysms of the cerebellar arteries. Review of 16 cases." *J Neurosurg* **58**(1): 63-8.
- Gerber, C. J., D. A. Lang, et al. (1993). "A simple scoring system for accurate prediction of outcome within four days of a subarachnoid haemorrhage." *Acta Neurochir (Wien)* **122**(1-2): 11-22.
- Grand, W., J. L. Budny, et al. (1997). "Microvascular surgical anatomy of the vertebrobasilar junction." *Neurosurgery* **40**(6): 1219-23; discussion 1223-5.
- Graves, V. B., C. M. Strother, et al. (1996). "Vertebrobasilar junction aneurysms associated with fenestration: treatment with Guglielmi detachable coils." *AJNR Am J Neuroradiol* **17**(1): 35-40.
- Gray, H., P. L. Williams, et al. (1995). *Gray's anatomy : the anatomical basis of medicine and surgery*. New York, Churchill Livingstone.
- Gruber, A., M. Killer, et al. (1999). "Clinical and angiographic results of endosaccular coiling treatment of giant and very large intracranial aneurysms: a 7-year, single-center experience." *Neurosurgery* **45**(4): 793-803; discussion 803-4.
- Gruber, D. P., G. A. Zimmerman, et al. (1999). "A comparison between endovascular and surgical management of basilar artery apex aneurysms." *J Neurosurg* **90**(5): 868-74.
- Guglielmi, G., F. Vinuela, et al. (1991). "Electrothrombosis of saccular aneurysms via endovascular approach. Part 2: Preliminary clinical experience." *J Neurosurg* **75**(1): 8-14.
- Guglielmi, G., F. Vinuela, et al. (1992). "Endovascular treatment of posterior circulation aneurysms by electrothrombosis using electrically detachable coils." *J Neurosurg* **77**(4): 515-24.
- Guglielmi, G., F. Vinuela, et al. (1991). "Electrothrombosis of saccular aneurysms via endovascular approach. Part 1: Electrochemical basis, technique, and experimental results." *J Neurosurg* **75**(1): 1-7.
- Hernesniemi, J., M. Vapalahti, et al. (1992). "Management outcome for vertebrobasilar artery aneurysms by early surgery." *Neurosurgery* **31**(5): 857-61; discussion 861-2.
- Hernesniemi, J., M. Vapalahti, et al. (1993). "One-year outcome in early aneurysm surgery: a 14 years experience." *Acta Neurochir (Wien)* **122**(1-2): 1-10.

- Heros, R. C. (1995). Aneurysms of the vertebral artery and its branches. *Surgical management of neurovascular disease*. R. G. Ojemann. Baltimore, Williams & Wilkins: 291-304.
- Hieshima, G. B., V. S. Grinnell, et al. (1981). "A detachable balloon for therapeutic transcatheter occlusions." *Radiology* **138**(1): 227-8.
- Hilal, S., A. Khandji, et al. (1989). "Obliteration of intracranial aneurysms with preshaped highly thrombogenic coils." *Radiology* **173**: 250-7.
- Hillman, J., H. Saveland, et al. (1996). "Overall management outcome of ruptured posterior fossa aneurysms." *J Neurosurg* **85**(1): 33-8.
- Hoffman, W. F. and C. B. Wilson (1979). "Fenestrated basilar artery with an associated saccular aneurysm. Case report." *J Neurosurg* **50**(2): 262-4.
- Hudgins, R. J., A. L. Day, et al. (1983). "Aneurysms of the posterior inferior cerebellar artery. A clinical and anatomical analysis." *J Neurosurg* **58**(3): 381-7.
- Hunt, W. E. and R. M. Hess (1968). "Surgical risk as related to time of intervention in the repair of intracranial aneurysms." *J Neurosurg* **28**(1): 14-20.
- Jane, J. A., N. F. Kassell, et al. (1985). "The natural history of aneurysms and arteriovenous malformations." *J Neurosurg* **62**(3): 321-3.
- Jellinger, K. (1977). "Pathology of intracerebral hemorrhage." *Zentralbl Neurochir* **38**(1): 29-42.
- Jennett, B. and M. Bond (1975). "Assessment of outcome after severe brain damage." *Lancet* **1**(7905): 480-4.
- Johnston, S. C., C. B. Wilson, et al. (2000). "Endovascular and surgical treatment of unruptured cerebral aneurysms: comparison of risks." *Ann Neurol* **48**(1): 11-9.
- Jordan, J. E., M. P. Marks, et al. (1996). "Cost-effectiveness of endovascular therapy in the surgical management of cerebral arteriovenous malformations." *AJNR Am J Neuroradiol* **17**(2): 247-54.
- Kaptain, G. J., G. Lanzino, et al. (1999). "Posterior inferior cerebellar artery aneurysms associated with posterior fossa arteriovenous malformation: report of five cases and literature review." *Surg Neurol* **51**(2): 146-52.
- Kassell, N. F., J. C. Torner, et al. (1990). "The International Cooperative Study on the Timing of Aneurysm Surgery. Part 1: Overall management results." *J Neurosurg* **73**(1): 18-36.
- Kassell, N. F., J. C. Torner, et al. (1990). "The International Cooperative Study on the Timing of Aneurysm Surgery. Part 2: Surgical results." *J Neurosurg* **73**(1): 37-47.
- Khanna, R. K., G. M. Malik, et al. (1996). "Predicting outcome following surgical treatment of unruptured intracranial aneurysms: a proposed grading system." *J Neurosurg* **84**(1): 49-54.
- Kuether, T. A., G. M. Nesbit, et al. (1998). "Clinical and angiographic outcomes, with treatment data, for patients with cerebral aneurysms treated with Guglielmi detachable coils: a single-center experience." *Neurosurgery* **43**(5): 1016-25.

- Lasjaunias, P., A. Berenstein, et al. (2001). The anterosuperior cerebellar artery. *Clinical vascular anatomy and variations*. P. Lasjaunias, A. Berenstein and K. G. t. Brugge. Berlin, Springer-Verlag. **Vol. I:** 538-540.
- Lawton, M. T., C. P. Daspit, et al. (1997). "Technical aspects and recent trends in the management of large and giant midbasilar artery aneurysms." *Neurosurgery* **41**(3): 513-20; discussion 520-1.
- Lee, K. S., D. J. Gower, et al. (1989). "Surgical repair of aneurysms of the posterior inferior cerebellar artery--a clinical series." *Surg Neurol* **31**(2): 85-91.
- Lempert, T. E., A. M. Malek, et al. (2000). "Endovascular treatment of ruptured posterior circulation cerebral aneurysms. Clinical and angiographic outcomes." *Stroke* **31**(1): 100-10.
- Lin, T., A. J. Fox, et al. (1989). "Regrowth of aneurysm sacs from residual neck following aneurysm clipping." *J Neurosurg* **70**(4): 556-60.
- Lister, J. R., A. L. Rhoton, Jr., et al. (1982). "Microsurgical anatomy of the posterior inferior cerebellar artery." *Neurosurgery* **10**(2): 170-99.
- Locksley, H. B. (1966). "Natural history of subarachnoid hemorrhage, intracranial aneurysms and arteriovenous malformations. Based on 6368 cases in the cooperative study." *J Neurosurg* **25**(2): 219-39.
- Mabuchi, S., H. Kamiyama, et al. (1992). "Distal aneurysms of the superior cerebellar artery and posterior inferior cerebellar artery feeding an associated arteriovenous malformation: case report." *Neurosurgery* **30**(2): 284-7.
- MacFarlane, M. R., V. L. McAllister, et al. (1983). "Posterior circulation aneurysms. Results of direct operations." *Surg Neurol* **20**(5): 399-413.
- Malek, A. M., V. V. Halbach, et al. (2000). "Balloon-assist technique for endovascular coil embolization of geometrically difficult intracranial aneurysms." *Neurosurgery* **46**(6): 1397-406; discussion 1406-7.
- Malisch, T. W., G. Guglielmi, et al. (1997). "Intracranial aneurysms treated with the Guglielmi detachable coil: midterm clinical results in a consecutive series of 100 patients." *J Neurosurg* **87**(2): 176-83.
- Matricali, B. and P. Seminara (1986). "Aneurysm arising from the medial branch of the superior cerebellar artery." *Neurosurgery* **18**(3): 350-2.
- Matricali, B. and H. van Dulken (1981). "Aneurysm of fenestrated basilar artery." *Surg Neurol* **15**(3): 189-91.
- McDermott, V. G. and R. J. Sellar (1994). "Superior cerebellar artery aneurysms associated with infratentorial arteriovenous malformations." *Clin Imaging* **18**(3): 209-12.
- McDonald, C. and M. Korb (1939). "Intracranial aneurysms." *Arch Neurol Psychiatry* **42**: 298-328.
- McDonald, C. A. and M. Korb (1939). "Intracranial aneurysms." *Arch Neurol Psychiatry* **42**: 298-328.

- McDougall, C. G., V. V. Halbach, et al. (1996). "Endovascular treatment of basilar tip aneurysms using electrolytically detachable coils." *J Neurosurg* **84**(3): 393-9.
- Molyneux, A. (2002). Comments on the ISAT trial. C. M. Schirmer. Ludwigshafen, Germany.
- Molyneux, A., R. Kerr, et al. (2002). "International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial." *Lancet* **360**(9342): 1267-74.
- Moret, J., A. Boulin, et al. (1991). "Endovascular treatment of berry aneurysms by endosaccular balloon occlusion." *Neuroradiology* **33**(Suppl): 135-6.
- Moret, J., C. Cognard, et al. (1997). "[Reconstruction technic in the treatment of wide-neck intracranial aneurysms. Long-term angiographic and clinical results. Apropos of 56 cases]." *J Neuroradiol* **24**(1): 30-44.
- Nakasu, Y., S. Nakasu, et al. (1982). "Aneurysm at the fenestration of basilar artery--case report." *Nippon Geka Hokan* **51**(2): 344-8.
- Nichols, D. A., R. D. Brown, Jr., et al. (2002). "Coils or clips in subarachnoid haemorrhage?" *Lancet* **360**(9342): 1262-3.
- Nichols, D. A., R. D. Brown, Jr., et al. (1997). "Endovascular treatment of ruptured posterior circulation aneurysms using electrolytically detachable coils." *J Neurosurg* **87**(3): 374-80.
- Nishioka, H., J. C. Torner, et al. (1984). "Cooperative study of intracranial aneurysms and subarachnoid hemorrhage: a long-term prognostic study. II. Ruptured intracranial aneurysms managed conservatively." *Arch Neurol* **41**(11): 1142-6.
- Nishioka, H., J. C. Torner, et al. (1984). "Cooperative study of intracranial aneurysms and subarachnoid hemorrhage: a long-term prognostic study. III. Subarachnoid hemorrhage of undetermined etiology." *Arch Neurol* **41**(11): 1147-51.
- Ogilvy, C. S. and B. S. Carter (1998). "A proposed comprehensive grading system to predict outcome for surgical management of intracranial aneurysms." *Neurosurgery* **42**(5): 959-68; discussion 968-70.
- Ogilvy, C. S. and A. Quinones-Hinojosa (1998). "Surgical treatment of vertebral and posterior inferior cerebellar artery aneurysms." *Neurosurg Clin N Am* **9**(4): 851-60.
- Padget, D. H. (1948). "The development of the cranial arteries in the human embryo." *Contrib Embryol* **32**: 205-261.
- Papo, I., G. Caruselli, et al. (1977). "Aneurysm of the superior cerebellar artery." *Surg Neurol* **7**(1): 15-7.
- Peerless, S. J. and C. G. Drake (1982). Management of aneurysms of posterior circulation. *Neurological surgery : a comprehensive reference guide to the diagnosis and management of neurosurgical problems*. J. R. Youmans. Philadelphia, Saunders: 1715-1763.
- Peerless, S. J., J. A. Hernesniemi, et al. (1994). "Early surgery for ruptured vertebrobasilar aneurysms." *J Neurosurg* **80**(4): 643-9.

- Pierot, L., A. Boulin, et al. (1996). "Selective occlusion of basilar artery aneurysms using controlled detachable coils: report of 35 cases." *Neurosurgery* **38**(5): 948-53; discussion 953-4.
- Pierot, L., A. Boulin, et al. (1997). "The endovascular approach in the management of patients with multiple intracranial aneurysms." *Neuroradiology* **39**(5): 361-6.
- Quattrocchi, K. B., S. L. Nielsen, et al. (1990). "Traumatic aneurysm of the superior cerebellar artery: case report and review of the literature." *Neurosurgery* **27**(3): 476-9.
- Qureshi, A. I., A. R. Luft, et al. (2000). "Prevention and treatment of thromboembolic and ischemic complications associated with endovascular procedures: Part II--Clinical aspects and recommendations." *Neurosurgery* **46**(6): 1360-75; discussion 1375-6.
- Rabb, C. H., G. Tang, et al. (1994). "A statistical analysis of factors related to symptomatic cerebral vasospasm." *Acta Neurochir (Wien)* **127**(1-2): 27-31.
- Ravensbergen, J., J. K. Krijger, et al. (1997). "The influence of the blunting of the apex on the flow in a vertebro-basilar junction model." *J Biomech Eng* **119**(2): 195-205.
- Raymond, J. and D. Roy (1997). "Safety and efficacy of endovascular treatment of acutely ruptured aneurysms." *Neurosurgery* **41**(6): 1235-45; discussion 1245-6.
- Raymond, J., D. Roy, et al. (1997). "Endovascular treatment of acutely ruptured and unruptured aneurysms of the basilar bifurcation." *J Neurosurg* **86**(2): 211-9.
- Salcman, M., D. Rigamonti, et al. (1990). "Aneurysms of the posterior inferior cerebellar artery-vertebral artery complex: variations on a theme." *Neurosurgery* **27**(1): 12-20; discussion 20-1.
- Samson, D., H. H. Batjer, et al. (1999). "Current results of the surgical management of aneurysms of the basilar apex." *Neurosurgery* **44**(4): 697-702; discussion 702-4.
- Sanders, W. P., P. A. Sorek, et al. (1993). "Fenestration of intracranial arteries with special attention to associated aneurysms and other anomalies." *AJNR Am J Neuroradiol* **14**(3): 675-80.
- Schievink, W. I., E. F. Wijdicks, et al. (1995). "The poor prognosis of ruptured intracranial aneurysms of the posterior circulation." *J Neurosurg* **82**(5): 791-5.
- Serbinenko, F. A. (1974). "Balloon catheterization and occlusion of major cerebral vessels." *J Neurosurg* **41**(2): 125-45.
- Shcheglov, V. and A. Romodanov (1982). Intravascular occlusion of saccular aneurysms of the cerebral arteries by means of a detachable balloon catheter. *Advances and technical standards in neurosurgery*. H. Krayenbuhl. Zurich, Springer. **9**: 25-48.
- Solomon, R. A. and B. M. Stein (1988). "Surgical approaches to aneurysms of the vertebral and basilar arteries." *Neurosurgery* **23**(2): 203-8.
- Spetzler, R. F., M. N. Hadley, et al. (1988). "Aneurysms of the basilar artery treated with circulatory arrest, hypothermia, and barbiturate cerebral protection." *J Neurosurg* **68**(6): 868-79.

- Stachniak, J. B., A. J. Layon, et al. (1996). "Craniotomy for intracranial aneurysm and subarachnoid hemorrhage. Is course, cost, or outcome affected by age?" *Stroke* **27**(2): 276-81.
- Stehbens, W. E. (1989). "Etiology of intracranial berry aneurysms." *J Neurosurg* **70**(6): 823-31.
- Steiger, H. J., R. Medele, et al. (1999). "Interdisciplinary management results in 100 patients with ruptured and unruptured posterior circulation aneurysms." *Acta Neurochir (Wien)* **141**(4): 359-66; discussion 366-7.
- Takahashi, M., Y. Tamakawa, et al. (1973). "Fenestration of the basilar artery. Report of three cases and review of the literature." *Radiology* **109**(1): 79-82.
- Tateshima, S., Y. Murayama, et al. (2000). "Endovascular treatment of basilar tip aneurysms using Guglielmi detachable coils: anatomic and clinical outcomes in 73 patients from a single institution." *Neurosurgery* **47**(6): 1332-9; discussion 1339-42.
- Teal, J. S., C. L. Rumbaugh, et al. (1973). "Angiographic demonstration of fenestrations of the intradural intracranial arteries." *Radiology* **106**(1): 123-6.
- Tsutsumi, K., K. Ueki, et al. (1998). "Risk of recurrent subarachnoid hemorrhage after complete obliteration of cerebral aneurysms." *Stroke* **29**(12): 2511-3.
- Uda, K., Y. Murayama, et al. (2001). "Endovascular treatment of basilar artery trunk aneurysms with Guglielmi detachable coils: clinical experience with 41 aneurysms in 39 patients." *J Neurosurg* **95**(4): 624-32.
- Urbach, H., B. Meyer, et al. (1995). "Posterior inferior cerebellar artery aneurysm in the fourth ventricle." *Neuroradiology* **37**(4): 267-9.
- van Swieten, J. C., P. J. Koudstaal, et al. (1988). "Interobserver agreement for the assessment of handicap in stroke patients." *Stroke* **19**(5): 604-7.
- Vinuela, F., G. Duckwiler, et al. (1997). "Guglielmi detachable coil embolization of acute intracranial aneurysm: perioperative anatomical and clinical outcome in 403 patients." *J Neurosurg* **86**(3): 475-82.
- Wollschlaeger, G., P. B. Wollschlaeger, et al. (1967). "Experience and result with postmortem cerebral angiography performed as routine procedure of the autopsy." *Am J Roentgenol Radium Ther Nucl Med* **101**(1): 68-87.
- Yamamoto, I., R. Tsugane, et al. (1984). "Peripheral aneurysms of the posterior inferior cerebellar artery." *Neurosurgery* **15**(6): 839-45.
- Yamaura, A. (1988). "Diagnosis and treatment of vertebral aneurysms." *J Neurosurg* **69**(3): 345-9.
- Yamaura, A., H. Ise, et al. (1981). "Radiometric study on posterior inferior cerebellar aneurysms with special reference to accessibility by the lateral suboccipital approach." *Neurol Med Chir (Tokyo)* **21**(7): 721-33.
- Yamaura, A., K. Isobe, et al. (1991). "Dissecting aneurysms of the posterior inferior cerebellar artery." *Neurosurgery* **28**(6): 894-8.

Yamaura, A., K. Isobe, et al. (1980). "Posterior inferior cerebellar aneurysm in the fourth ventricle." *Surg Neurol* **13**(4): 297-9.

Yoshimoto, T., T. Kayama, et al. (1978). "Distribution of intracranial aneurysm." *Tohoku J Exp Med* **126**(2): 125-32.

Yoshimoto, Y. and S. Kwak (1995). "Age-related multifactorial causes of neurological deterioration after early surgery for aneurysmal subarachnoid hemorrhage." *J Neurosurg* **83**(6): 984-8.

Zingale, A., I. Chiaramonte, et al. (1994). "Distal posterior inferior cerebellar artery saccular and giant aneurysms: report of two new cases and a comprehensive review of the surgically-treated cases." *J Neurosurg Sci* **38**(2): 93-104.

6 Summary

Aneurysms of the posterior circulation including posterior inferior cerebellar artery (PICA), superior cerebellar artery (SCA), vertebrobasilar junction (VBJ) and basilar tip (BTA) presently are often very difficult to access and often require complex skull base approaches with consequent retraction of brainstem structures. These features make these aneurysms well suited for endovascular therapy.

From June 1991 to January 2000, a total number of 153 patients presented at the University of California San Francisco Medical Center, underwent diagnostic evaluation and endovascular treatment of the intracranial aneurysm with the use of Guglielmi detachable coils (GDC) (Target Therapeutics). The patients' hospital records, outpatient charts, operative reports, all angiographic, computed tomography, and magnetic resonance studies were subjected to careful retrospective analysis and review. Clinical examination and angiographic follow-up studies were also supplemented by telephone interviews.

Twenty-three patients had aneurysms of the posterior inferior cerebellar artery (PICA), and 17 patients were found to have aneurysms of the superior cerebellar artery (SCA). In 12 patients the aneurysms were situated at the vertebrobasilar junction (VBJ), and 101 patients harbored an aneurysm of the apex of the basilar artery (basilar-tip aneurysms, BTA).

The subgroup of 23 patients (14 Female; age 1-87) harboring PICA aneurysms (14 ruptured) was treated over a nine-year interval. In this series 16 aneurysms involved the proximal PICA (70%) and 7 aneurysms were located in the distal portion (30%). All 24 aneurysms in this subgroup of patients were successfully catheterized and treated with endovascular coil embolization either with preservation of the parent vessel in the case of saccular aneurysms (14/23, 61%) or with parent vessel occlusion in fusiform lesions (9/23, 39%). There was one periprocedural non-fatal major stroke (4.4%) and no procedure related deaths. During the follow-up period no re-hemorrhage occurred, and one patient died from an unrelated cause (4.4%). The mean final angiographic occlusion rate was 97%. At latest clinical follow-up the outcome on the modified Rankin scale was: grade 0 in 11 patients (48%), grade 1 in

8 patients (35%), grade 2 in 1 patient (4%), grade 4 in 2 patients (9%), and grade 5 in 1 patient (4%).

In the subgroup of patients with SCA aneurysms 12 of 17 patients (7 female, 10 male) presented with SAH after rupture of the aneurysm. All patients (17 of 17, 100%) underwent successful endovascular treatment. One patient had to undergo repeat treatment due to 15% recanalization, when an acceptable angiographic outcome was reached. The average rate of occlusion at final follow-up was $95.1 \pm 3.0\%$. In 16 of 17 patients (94%) neurological follow-up examination was achieved, 11 patients showed good recovery on the Glasgow outcome score (GOS I) (65%), 3 patients of 17 showed a moderate disability (GOS II) (18%), and 3 patients were dead (18%). All patients who lived at final clinical follow-up had good recovery or a moderate disability (GOS I and II) (82%).

There were 12 patients (9 female and 3 male) with aneurysms of the vertebrobasilar junction, including 4 patients with a concomitant fenestration of the basilar artery underwent endovascular coil embolization. Ten patients (83%) presented with SAH. There was one case of aneurysm recanalization and regrowth (8%), requiring repeat treatment. At final neurological follow-up 7 patients had a modified Rankin scale grade 0 (58%), 2 had grade 1 (17%), 1 grade 2 (8%), 1 grade 4 (8%), 1 grade 6 (8%). Overall mortality in this series is 8%, there was no procedure related morbidity.

There was a subgroup of 101 aneurysms of the basilar apex in 101 patients (78 female and 23 male) that underwent endovascular therapy. In 28 patients (28%) the aneurysm was unruptured. The procedure resulted in successful coil delivery and embolization in 97/101 of cases (96%) in this subgroup of patients with basilar apex aneurysms. The mean angiographic occlusion rate, or projected area of the aneurysm occluded by the coils, for all 97 successfully treated aneurysms was 94%. At latest clinical follow-up, 43/97 patients (44%) denied any symptoms (modified Rankin 0), 16/97 (16%) had remaining symptoms without accompanying disability (mRankin 1), and 15 (15%) had various degrees of impairment (mRankin 2-5), and 23 (24%) were dead. Of the subset of 49 patients with Hunt-Hess grades I-III, 46 (94%) achieved a good clinical outcome (GOS I). A statistically significant correlation was demonstrated between Hunt-Hess grade at presentation and final modified Rankin outcome score ($\chi^2 = 44.6, p < 0.04$). Procedure-related permanent morbidity

was 2.8% (3/109 patients). Repeat hemorrhage was observed in 4 patients (4%). Eight (8%) patients died from SAH related causes.

GDC coil embolization provides an effective therapy for prevention of recurrent hemorrhage in the treatment of both saccular and fusiform PICA and SCA aneurysms. The angiographic and clinical outcomes compare favorably with open surgical treatment. It is a safe and efficacious method of treatment for aneurysms of the vertebrobasilar junction and the basilar tip, requiring a technically less complex procedure compared to surgical clipping in this group of high-risk patients.

7 Zusammenfassung

In der hinteren Zirkulation einschließlich A. cerebelli posterior inferior (PICA), A. cerebelli superior (SCA), vertebrobasilären Verzweigung (VBJ) und der Spitze der A. basilaris (BTA) gelegene Aneurysmen sind chirurgisch teilweise nur schwer zugänglich und erfordern häufig komplexe Schädelbasischirurgie und Retraktion der umgebenden Hirnstrukturen oder des Hirnstammes. Diese Charakteristika machen diese Aneurysmen zu aussichtsreichen Kandidaten für endovaskuläre Therapie.

Zwischen Juni 1991 und Januar 2000 unterzog sich eine Gesamtanzahl von 153 Patienten am UC San Francisco Medical Center nach der Diagnose einer anschließender endovaskulären Behandlung eines intrakraniellen Aneurysma unter Gebrauch von elektrolytisch ablösbaren Platinspiralen nach Guglielmi (GDC) (Target Therapeutics). Die Krankenakten der Patienten, Operationsberichte, alle Angiographien, Computertomographien sowie Magnetresonanztomographien wurden einer genauen retrospektiven Analyse unterzogen. Klinische Untersuchungen und angiographische Folgeuntersuchungen wurden durch Telefoninterviews ergänzt.

Dreiundzwanzig Patienten hatten Aneurysmen der A. cerebelli posterior inferior (PICA), und bei 17 Patienten wurden Aneurysmen der A. cerebelli superior (SCA) gefunden. Bei 12 Patienten wurden Aneurysmen an der vertebrobasilären Verzweigung (VBJ) festgestellt, und 101 Patienten hatten ein Basilarispitzenaneurysma (BTA).

Die Untergruppe von 23 Patienten (14 weiblich; Alter 1-87) mit PICA Aneurysmen (14 rupturiert) wurde über einen Zeitraum von 9 Jahren behandelt. In dieser Serie waren 16 Aneurysmen im proximalen Anteil der PICA (70%) gelegen und 7 Aneurysmen im distalen Teil (30%). Alle 24 Aneurysmen dieser Untergruppe von Patienten wurden erfolgreich katheterisiert und endovaskulär mit Platinspulen embolisiert, entweder unter Schonung des Muttergefäßes bei sakkulären Aneurysmen (14/23, 61%) oder bei fusiformen Läsionen durch Verschluss der Muttergefäßes (9/23, 39%) behandelt. Periprozedural kam es zu einem nichttödlichen Schlaganfall (4.4%), es traten keine mit der Therapie ursächlich in Verbindung stehenden Todesfälle auf. Während der Nachsorge trat keine Reruptur auf, ein Patient starb an einer anderen internistischen Erkrankung (4.4%). Die abschließende angiographische Verschlussrate war 97%.

Zum Zeitpunkt der letzten Nachsorgeuntersuchung wurde auf der modifizierten Skala nach Rankin den Wert 0 bei 11 Patienten (48%), 1 bei 8 Patienten (35%), 2 bei 1 Patienten (4%), 4 bei 2 Patienten (9%), und 5 bei 1 Patienten (4%) erreicht.

In der Untergruppe der Patienten mit SCA Aneurysmen wurden 12 von 17 Patienten (7 weiblich) mit SAB nach Ruptur des Aneurysma vorgestellt. Alle Patienten wurden erfolgreich endovaskulär behandelt. Ein Patient musste sich aufgrund einer 15% Rekanalisierung einer Zweitbehandlung unterziehen, nach deren Abschluss ein gutes angiographisches Resultat erzielt wurde. Die durchschnittliche Verschlussrate war 95.1 ± 3.0 %. Bei 16 von 17 Patienten (94%) wurde neurologische Folgeuntersuchungen durchgeführt, sie zeigten bei 11 Patienten gute Erholung auf der Glasgow Outcome Skala (GOS I) (65%), 3 Patienten von 17 zeigten mäßig schwere Folgeerscheinungen (GOS II) (18%) und 3 Patienten waren verstorben (18%). Alle Patienten, die bei der letzten Folgeuntersuchung am Leben waren, hatten sich gut erholt oder litten nur unter mäßig schweren Folgen (GOS I und II) (82%).

Es gab 12 Patienten (9 davon weiblich) mit Aneurysmen an der vertebrobasilar Verzweigung, einschließlich 4 Patienten mit einer begleitenden Fensterung der A. basilaris. 10 Patienten (83%) stellten sich mit einer subarachnoidalen Blutung vor. In einem Fall erforderten Rekanalisierung und nachträgliches Wachstum (8%) des Aneurysmas eine Zweitbehandlung. Bei der abschließenden neurologischen Folgeuntersuchung erreichten 7 Patienten Grad 0 auf der modifizierten Skala nach Rankin (58%), 2 Grad 1 (17%), 1 Patient Grad 2 (8%), 1 Grad 4 (8%), und 1 Patient Grad 6 (8%). Die Gesamtsterblichkeit in der Gruppe war 8%, es gab keine mit der eigentlichen Intervention zusammenhängende Morbidität.

Es gibt eine Untergruppe von 101 Basilariskopfaneurysmen (101 Patienten, 78 weiblich). Bei 28 Patienten (28%) war das Aneurysma nicht rupturiert, bei 97/101 Fällen (96%) in dieser Untergruppe konnte eine erfolgreiche Embolisation durchgeführt werden. Die mittlere angiographische Verschlussrate der erfolgreich behandelten Aneurysmen war 94%. Bei der letzten klinischen Anschlussuntersuchung verneinten 43/97 Patienten (44%) jegliche Symptome (mRankin 0), 16/97 (16%) hatten Folgesymptome, die keine Beeinträchtigung nach sich zogen (mRankin 1), 15 (15%) hatten verschiedene Beeinträchtigungen (mRankin 2-5), und 23 (24%) waren verstorben. In der Untergruppe von 49 Patienten mit Hunt-Hess Grad I-III war

bei 46 (94%) ein gutes klinisches Resultat (GOS I) erzielt worden. Eine statistisch signifikante Korrelation wurde zwischen Hunt-Hess Grad zum Aufnahmezeitpunkt und dem endgültigen Ergebnis auf der modifizierten Rankinskala gefunden ($\chi^2 = 44.6$, $p < 0.04$). Die prozedural bedingte permanente Morbidität war 2.8% (3/109 patients). Erneute Blutung wurde bei 4 Patienten (4%) gesehen, 8 (8%) Patienten verstarben an Blutungsbedingten Folgeerscheinungen.

Die Embolisierung von intrakraniellen Aneurysmen mit elektrolytisch ablösbaren Platinspulen nach Guglielmi (GDC) stellt eine wirkungsvolle Therapie für Verhinderung der erneuten Blutung bei der Behandlung von sakkulären und fusiformen PICA und SCA Aneurysmen dar. Die angiographischen und klinischen Resultate sind im Vergleich mit der offenen chirurgischen Behandlung mindestens gut. Auch ist es eine sichere und wirkungsvolle Behandlungsmethode für Aneurysmen an der vertebrobasilären Verzweigung und am Basilariskopf. Für diese Gruppe von Hochrisikopatienten ist somit, verglichen mit der chirurgischen Behandlung mittels Clips, ein technisch weniger komplexes Verfahren verfügbar.

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9 Curriculum vitae

Name Clemens Maria Schirmer

Geburtstag 4. Mai 1976

Geburtsort München

Schulbildung:

1986- 95 Wittelsbacher Gymnasium München

1994 Summer School University of California Berkeley, CA, USA (Political science, Quantum physics) (3 Monate)

Studium:

1995 - 2002 Studium der Medizin an der Ludwig-Maximilians Universität München

1997 - 2002 (Doppel)Studium der Physik an der Ludwig-Maximilians Universität München

1998 - 2001 Studentischer Mitarbeiter, Physiologisches Institut, LMU München

9/1998 Interdisziplinäre Sommer Akademie der Deutschen Studienstiftung in Olang, Italien (Plant-Pathogen Interaction)

4/1999 Clerkship in Ophthalmology am Wilmer Eye Institute, Johns Hopkins University, School of Medicine, Baltimore, MD, USA

8/1999 Interdisziplinäre Sommer Akademie der Deutschen Studienstiftung und der Université La Rochelle, La Rochelle, Frankreich ("Intelligent Materials")

10/1999 Elective in pediatric surgery am Children's Hospital, Harvard Medical School, Boston, MA, USA

4/2000 Elective in Neurosurgery am Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Praktisches Jahr:

3/2001-4/2002 Praktisches Jahr/ Final year an der Harvard Medical School und LMU München

1. Terial: *Innere Medizin:* core clerkship, Beth Israel Deaconess Hospital und subinternship in internal medicine, Mt. Auburn Hospital, Harvard Medical School, Boston, MA, USA

2. Terial: *Chirurgie:* subinternship in cardiac surgery und in surgery (thoracic surgery), Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Neurochirurgie: Klinik und Poliklinik für Neurochirurgie, Klinikum Großhadern, LMU

3. Terial: *Neurologie:* subinternships in neurology am Beth Israel Deaconess Hospital, Harvard Medical School, Boston

Prüfungen:

4/98, 3/99, 3/01 Physikum, 1., 2. und 3. Staatsexamen Medizin, LMU München

7/99, 9/01, 6/02 United States Medical Licensing Examination (USMLE) Step 1 und Step 2, Clinical Skill Assessment Examination (CSA)

11/00, 11/01, 6/02 Vordiplom in Physik und Diplom in Physik (Teil I und II), LMU München

Wehrdienst:

1996- 97 Wehrdienst, Sanitätsakademie der Bundeswehr, Neuherberg, München

Forschung:

- 1998-2001 Arbeitsgruppe Entwicklungsneurobiologie, Physiologikum der LMU, Prof. Dr. B. Sutor
2002-2003 Dissertation zum Dr. med. über endovaskuläre Therapie von intrakraniellen Aneurysmen bei PD. Dr. Schmid-Elsaesser

Veröffentlichungen - Abstracts:

CM Schirmer, VV Halbach, CF Dowd, RT Higashida, AM Malek: Endovascular Treatment of Basilar Apex Aneurysms: Clinical and Angiographic Outcomes, New England Neurosurgical Society, 2002

CM Schirmer, VV Halbach, CF Dowd, RT Higashida, AM Malek: Treatment of Posterior Inferior Cerebellar Artery Aneurysms Using Endovascular Coil Embolization, New England Neurosurgical Society, 2002

- Publikationen:

B Sutor, C Schmolke, B Teubner, C Schirmer, W Willecke: Myelination defects and neuronal hyperexcitability in the neocortex of connexin 32-deficient mice. *Cereb Cortex*. 2000 Jul;10(7):684-697.

- Andere Veröffentlichungen:

Schirmer CM, Tutorialfall für den NERV-Kurs 2002, Blind oder nicht blind - ..., Medizinische Fakultät LMU München, 2002

Preis und Stipendien:

- 1998- Vollstipendium der Studienstiftung des deutschen Volkes
2000- e-fellows.net Online Stipendium, gesponsert von McKinsey & Company, Georg von Holtzbrinck Group, Deutsche Telekom AG, SAP and Compaq
2000 1. Preis Benjamin Franklin Wettbewerb, Freie Universität Berlin, Berlin
2001 Harvard Munich Alliance for Medical Education – Stipendium für das final year -program an der Harvard Medical School (6 Monate klinischer Rotationen in innerer Medizin und Chirurgie)
2001 Stipendium für das Academic Year Program des Biomedical Sciences Exchange Program between North America and Europe (BMEP) in Kooperation mit dem Deutschen akademischen Austauschdienst (DAAD) und der Carl-Duisberg-Stiftung an der Harvard Medical School (4 Monate klinischer Rotationen in Chirurgie und Neurologie, 4 Monate Forschung)