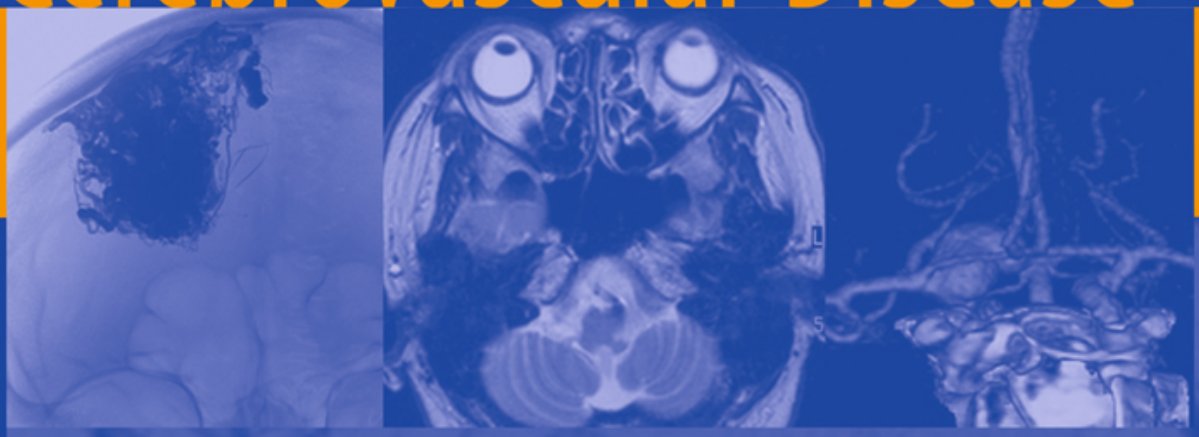
A. Laakso · J. Hernesniemi
Y. Yonekawa · T. Tsukahara
Editors

Surgical Management of Cerebrovascular Disease



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Edited by
Aki Laakso, Juha Hernesniemi, Yasuhiro Yonekawa, Tetsuya Tsukahara

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Preface

In July 2008, European and Japanese specialists in neurosurgery, neurology, interventional neuroradiology, and neurointensive care joined together to discuss the latest developments in the management of cerebrovascular disorders for the fourth time. The 4th European Japanese Joint Conference on Stroke Surgery (formerly Swiss Japanese Joint Conference on Cerebral Stroke Surgery) was held on July 4th–6th, this time in Helsinki, Finland. The meeting was chaired by Prof. Juha Hernesniemi from Helsinki and Prof. Tetsuya Tsukahara from Kyoto, and Prof. Yasuhiro Yonekawa from Zurich was the Honorary Guest of the meeting.

During those 3 days of Arctic Finnish Summer at its peak, the participants presented papers on aneurysm surgery and management of subarachnoid hemorrhage and stroke, arterial dissection, intracranial arteriovenous malformations and fistulas, and microneurosurgical bypass and revascularization techniques, among other topics. Many of these contributions have now been collected to form this book, which will be published along the tradition of the meeting. We hope the professionals involved in the management of cerebrovascular disease will find this compilation helpful and interesting for their daily work. The organizers of the meeting wish to express their gratitude to the Japanese Ministry of Health, Labour, and Welfare (Research Grant for Cardiovascular Disease (18C-5)), the Finnish Neurosurgical Society, and all the participants for making the meeting, and eventually this volume, possible once again.

A. Laakso, J. Hernesnieni,
Y. Yonekawa, T. Tsukahara

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Part I
Intracranial Aneurysms and Subarachnoid Hemorrhage

Chapter 1
Microsurgical Principles for Anterior Circulation Aneurysms

Rossana Romani, Aki Laakso, Mika Niemelä, Martin Lehecka, Reza Dashti, Puchong Isarakul, Özgür Celik, Ondrej Navratil, Hanna Lehto, Riku Kivisaari, and Juha Hernesniemi

Abstract Microneurosurgical techniques introduced by Prof. Yaşargil have been modified by the senior author (JH) when treating more than 4,000 patients with aneurysms at two of the Departments of Neurosurgery in Finland, Kuopio and Helsinki, with a total catchment area of close to three million people. This experience is reviewed, and the treatment of anterior circulation aneurysms by simple, fast, normal anatomy preserving strategy is presented.

Most of the aneurysms of the anterior circulation are treated by using the lateral supraorbital approach, a less invasive, more frontally located modification of the pterional approach. To avoid extensive skull base surgery, a slack brain is needed and achieved by experienced neuroanesthesia and by surgical tricks for removal of CSF.

Diagnosis of cerebral aneurysm before rupture improves treatment results more than any technical advances. Until this is realized, we continue to treat cerebral aneurysms by simple, fast, preserving normal anatomy-strategy, which has served our patients well.

Patients with cerebral aneurysms should be treated at specialized neurovascular centers.

Keywords Lateral supraorbital approach · Microsurgical technique · Cerebral aneurysm · Anterior circulation · Skull base surgery

Introduction

Since the introduction of endovascular surgery by the Russian school, and its further improvement by the French and Italian schools, many alternative methods have been developed to manage cerebral aneurysms [1–5]. With a growing number of aneurysms treated by the endovascular route, microsurgical experience is becoming less frequent.

Microneurosurgical techniques as introduced by Yaşargil [6–8] have been modified by the senior author (JH) while treating more than 4,000 patients with aneurysms at two institutes in Finland, Kuopio and Helsinki [9, 10]. We operate on most of the aneurysms of the anterior circulation by using the lateral supraorbital approach (LSO), a less invasive, and by far faster, more frontally located modification of the pterional approach [11]. To avoid extensive skull base surgery and to minimize the surgical approach, a slack brain is needed which is achieved by experienced neuroanesthesia and by surgical tricks for the removal of CSF [12].

Diagnosis of cerebral aneurysm before rupture improves treatment results more than any technical advances. Until this is realized, we continue to treat anterior circulation aneurysms by simple, fast, preserving normal anatomy-strategy, which has served our patients well [9, 10, 13–15]. Open surgery should be less invasive, fast, and with minimal retraction and manipulation of the brain, similar to the approach of endovascular surgeons [14]. In this paper we present highlights of our experience in the treatment of anterior circulation aneurysms.

Materials and Methods

This review is based on the experience of two Finnish neurosurgical centers, Kuopio and Helsinki, in the treatment of more than 11,000 unselected aneurysm patients. These two centers have a catchment area close to three million people. Sites of aneurysms in the Finnish population are shown in Table 1.

Most (4/5) of the patients with ruptured aneurysms undergo operation during the first 24 h after bleeding. Aneurysms are diagnosed in all patients with 3D computed

R. Romani, A. Laakso, M. Niemelä, M. Lehecka, R. Dashti, P. Isarakul, Ö. Celik, O. Navratil, H. Lehto, R. Kivisaari, and J. Hernesniemi (✉)
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Table 1 Frequency of aneurysm sites in the Finnish population, Helsinki, and Kuopio

Location of aneurysms	%
Middle cerebral artery	38
Anterior communicating artery	26
Internal carotid artery	23
Pericallosal artery	6
Vertebrobasilar arteries	7

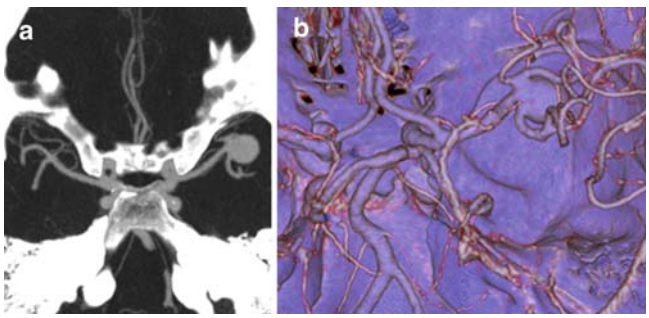

Fig. 1 2D (**a**) and 3D (**b**) computed tomography angiography (CTA) showing the relationship between a right medium sized middle cerebral artery bifurcation aneurysm with the greater sphenoid wing

tomography angiography (CTA) which is fast, non-invasive and gives information about bony landmarks and the surgical view with 3D recontructions (Fig. 1).

Surgical approach

Nearly all aneurysms of the anterior circulation except those of the pericallosal artery have been treated via the LSO approach. This approach has been used by the senior author (JH) for more than 20 years both in the management of vascular [14–19] and neoplastic lesions of the anterior cranial fossa [11]. This approach is a less-invasive modification of the pterional approach located more frontally with the bone flap about 3–4 cm in diameter. It has been described previously in detail [11], and demonstrated on video in our article on M1 aneurysms (M1As) of the middle cerebral artery (MCA) in our aneurysm series published in *Surgical Neurology* [14, 17–19].

Briefly, the head is fixed to the Sugita frame and is 1) elevated clearly above the cardiac level; 2) rotated 15–30° toward the opposite side; 3) tilted slightly downward to have a good exposition of the deeper part of the anterior circulation (Fig. 2a). It is our practice to adjust the position of the fixed head and body during the operation as needed [11, 15]. After minimal shaving and injection of a vasoconstrictor agent, skin incision (7–9 cm) is performed behind the hairline (Fig. 2b). One-layer skin–muscle flap is retracted frontally with spring hooks, and the superior orbital rim and the anterior zygomatic arch are exposed. The upper and more anterior part of the temporal muscle is split and retracted towards the zygomatic arch (Fig. 2c). The extent of the craniotomy depends on the surgeon's experience and preferences. It may be tailored according to the location and size of the aneurysm. Usually, a small LSO craniotomy is all that is necessary. A single burr hole is placed just under the temporal line in the bone, i.e. the superior insertion of the temporal muscle (Fig. 2d). A bone flap of 3×4 cm is detached mostly by side-cutting drill, and the basal part can be drilled before lifting (Fig. 2d, e). Dura is incised curvilinearly with the base sphenoidally. Dural edges are elevated by multiple stitches, extended over craniotomy dressings (Fig. 2f). From this point on, all surgery is performed under the operating microscope, including skin closure. A special set of instruments for aneurysm surgery is depicted in Fig. 3. Our general policy is to use as few instruments as possible [9].

In order to avoid extensive skull base approaches and brain retraction, in unruptured and in ruptured aneurysms, it is mandatory to have a slack brain [14]. An extensive review of our neuroanesthesia technique during aneurysm surgery has previously been published [12]. However, the surgical tricks to drain CSF by opening the lamina terminalis and/or basal cisterns, especially the Liliequist membrane, or through puncturing lateral ventricles or less invasively lumbar CSF space are equally important [9, 10, 13–19].

Complex intracranial aneurysms

Some anterior circulation aneurysms may be considered "complex" due to their size, morphology, location, or specific wall properties (intramural thrombus, atherosclerosis, calcification, dissection). Treatment of complex aneurysms needs special microneurosurgical skills such as aneurysmectomy with reconstruction of the vessel wall or revascularization followed by trapping of the parent artery. Both low and high flow bypass techniques are used for revascularization. The high flow ELANA technique developed by Prof. Tulleken has made fast progress recently and has been used in our institution for the last six years.

With the increasing use of endovascular surgery the number of those complex aneurysms that need further surgical treatment is growing. Coils make the aneurysm rigid, obscure the surgical field and reduce the space for applying the clip, thus increasing the intraoperative rupture of aneurysms. Sometimes it is necessary to remove the coils to gain space and free the base of the aneurysm, and this can be dangerous because part of the coils can penetrate or are attached to the wall of the aneurysm and/or the parent artery.

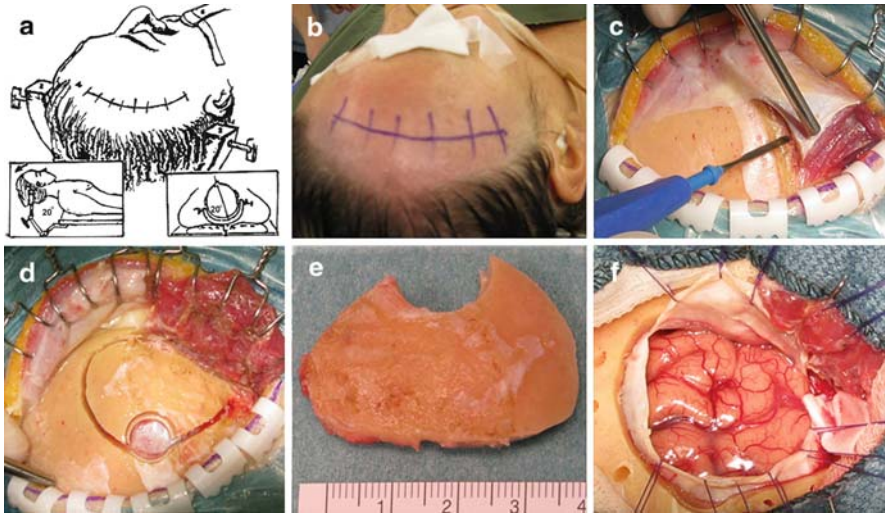

Fig. 2 Surgical steps to perform the lateral supraorbital (LSO) approach (**a**) Position of the head. (**b**) Skin incision, 7–9 cm are enough. (**c**) The antero-superior part of the temporal muscle is splitted to expose the superior orbital rim and the anterior zygomatic arch. (**d**) Location of the burr hole and craniotomy. (**e**) Craniotomy size (3×4 cm). (**f**) Dural edges are elevated by multiple stitches

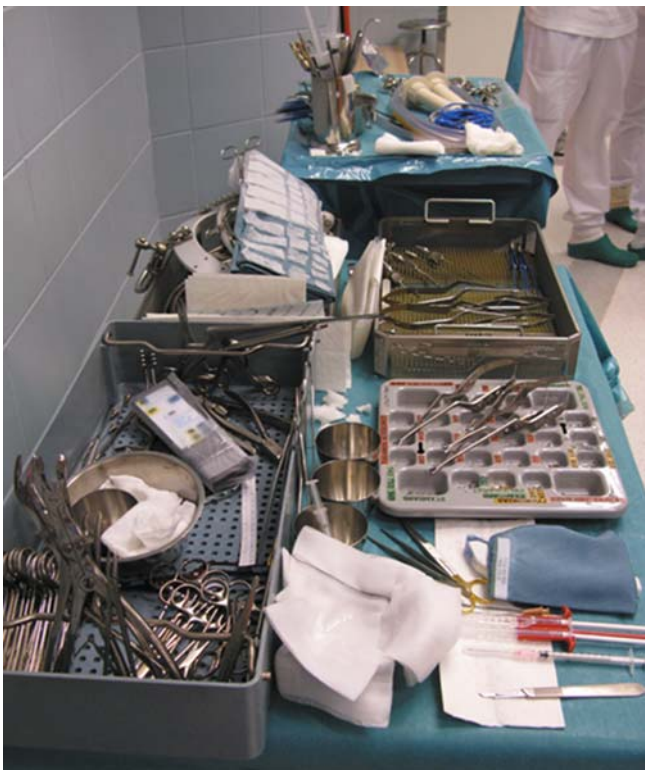

Fig. 3 Regular set of surgical instruments used in aneurysm surgery

Discussion

During accumulation of the extensive personal experience of the senior author (JH) in the microneurosurgical management of intracranial aneurysms, it became apparent that extension of the pterional approach to include the middle fossa is not necessary, and over the years the so-called "lateral supraorbital" approach (LSO) was developed [11]. In most anterior circulation aneurysms, LSO approach has served our patients well. During the treatment of most anterior circulation aneurysms, including complex MCA aneurysms (the most common aneurysm in the Finnish population) (Table 1), optimal exposure can be obtained by the LSO approach. We do not recommend fronto-orbito-zygomatic craniotomy as swelling of the orbital contents can obscure most of the extra space achieved. Distal anterior cerebral artery aneurysms (6% of our patients) naturally require a different approach, and this is a small frontal paramedian, nearly always right sided, craniotomy [20–24].

In selected cases such as proximal internal carotid artery aneurysms the anterior clinoid process can be removed simply by means of an ultrasonic aspirator (Sonopet Omni, Model UST-2001 Ultrasonic surgical system, Synergetics, Inc., Miwatec CO., LTD, Kawasaki, Japan). The space achieved by removing the anterior clinoid process provides optimal proximal control or access to the base of the aneurysm [14].

In 2009 we are in the era of minimally invasive techniques, but the future will belong to the era of biologic solutions identifying aneurysms before their rupture. We are studying how to identify the gene defect carriers, and thereafter follow those patients who can develop these often deadly sacks. We also need to identify aneurysms prone to rupture with molecular imaging. This goal can be achieved by understanding the pathobiology of the aneurysm wall itself, e.g. the role of inflammation in the growth and rupture, to be able to image molecular changes [14]. Research on the aneurysm wall has just begun, and will eventually render

both the microsurgical and endovascular approach completely obsolete. In fact, we believe that in a few decades many, if not most, aneurysms will be treated by local delivery of some agents to strengthen the aneurysm wall, and eventually by pharmaceutical therapy [25–32].

At present, with the growing number of aneurysms treated by the endovascular route omitting microsurgical possibilities, microsurgical experience is becoming less frequent. Consequently, in order to minimize complications, cerebrovascular patients should be referred to few specialized centres. This is especially true for patients with large or giant aneurysms, possibly needing a bypass for their treatment, or for posterior circulation aneurysm surgery.

Conclusion

In the coming years we will have to develop very simple low or high flow bypasses for a combined treatment of many complex aneurysms. At the same time we will give up some of the most extensive skull base approaches in favor of minimally invasive approaches. "Simple, fast, preserving normal anatomy" is the goal [33]. There is already some weak progress regarding the best timing of aneurysm surgery: operation, either exo- or endovascular, before aneurysm rupture. This will improve the management more than any technical innovation or improvements in personal skills [14].

Conflicts of interest statement We declare that we have no conflict of interest.

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Chapter 2
Treatment of Ruptured Cerebral Aneurysms – Clip and Coil, Not Clip Versus Coil

Yasuhiko Kaku, Kentarou Yamashita, Jouji Kokuzawa, Naoki Hatsuda, and Takashi Andoh

Abstract *Background and aims*: Recent advances in neurosurgery and interventional neuroradiology have brought us a new aspect in the treatment of cerebral aneurysms. The present single-surgeon series provides a balanced overview of the treatment of ruptured aneurysms in surgical clipping and coil embolization.

Clinical materials and methods: One hundred consecutive patients with ruptured cerebral aneurysms underwent surgical clipping or endovascular coil embolization between January 2005 and December 2007. All patients underwent clipping or coil embolization of at least one ruptured cerebral aneurysm by a single neurosurgeon (YK) who performed both the surgical clipping and endovascular coiling.

Results: Of the 48 surgically treated patients, 37 (77.1%) achieved a favorable outcome. Of the 52 patients who underwent endovascular embolization, 37 (71.2%) achieved a favorable outcome. No significant difference was observed regarding the proportion of favorable outcomes between the two treatment modalities. Five patients (9.6%) who underwent endovascular embolization needed re-treatments, while no re-treatment was necessary in the surgically treated patients. The rates of symptomatic vasospasm and shunt dependent hydrocephalus were 18.8% and 14.6%, respectively, in the clipped patients, and 19.2% and 21.2%, respectively, in the coiled patients. Endovascular coiling of ruptured aneurysms has a tendency towards a higher risk of developing shunt dependent hydrocephalus.

Conclusion: A combined microsurgical-endovascular approach can achieve the best outcomes for patients with ruptured cerebral aneurysms. Our findings support the policy of "Clip and Coil, not Clip versus Coil."

Keywords Cerebral aneurysm · Subarachnoid hemorrhage · Microsurgery · Coil embolization

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Introduction

Recent advancements in neurosurgery and interventional neuroradiology have led us to develop new strategies in the treatment of cerebral aneurysms. There is now a choice of several therapeutic alternatives for the management of cerebral aneurysms. The present series provides a balanced overview of the treatment of aneurysms in surgical clipping and coil embolization. Our findings thus support the policy of "Clip and Coil, not Clip versus Coil."

Clinical Material and Methods

A total of 100 consecutive patients with ruptured cerebral aneurysms underwent endovascular embolization and/or surgical clipping at Murakami Memorial Hospital, Asahi University, over the period of January 2005 to December 2007. All patients suffered aneurysmal subarachnoid hemorrhage (SAH) and were admitted within 48 h after onset of SAH, 30 patients were male, and 70 were females ranging in age from 23 to 93 years (63.4 $\pm$ 9.3 years (mean$\pm$SD)).

Decisions on how to treat an aneurysm were made on a case-by-case basis, depending on the 3D CT angiography findings (aneurysm location, size, shape, dome–neck ratio, incorporation of normal branches, and tortuosity of the proximal vessels) and the clinical data (patient age, baseline neurological condition, and systemic comorbidities). Endovascular treatment was chosen as the first-line treatment for patients with aneurysms that had the following characteristics; a dome–neck ratio $>$1.25, neck $<$5 mm and no incorporation of normal branches. Patients over 80 years of age or with poor medical condition and poor grade patients (WFNS grade 4) were also candidates for endovascular treatment as first choice treatment. Surgical clipping was applied to other patients and it was also performed in the instance of either failed or attempted endovascular treatment.

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All endovascular and surgical procedures were performed by the first author. All endovascular procedures were performed under local anesthesia with/without intravenous infusion of Propofol. A bolus of 3,000 units of heparin was administered after the first coil delivery and full heparinization was maintained thereafter. The trans-brachial approach was performed in most of the cases. GDC coils (Boston Scientific, Fremont, CA) were used for dome embolization. No balloon assisted remodeling technique or stent assisted technique was applied in this series.

All surgical procedures were performed within 48 h of aneurysmal rupture. A simple and less invasive pterional approach or supraorbital approach with a small craniotomy was applied in most cases to avoid any unnecessary insult to the brain parenchyma and vascular structures. Only related cisterns were opened to gain access to the aneurysm, and a minimal amount of the subarachnoid clot was removed around the aneurysm. Titanium clips were routinely used. No drainage catheter was inserted into the CSF pathway, unless hydrocephalus was confirmed.

Postoperatively, all patients were monitored in the stroke care unit until day 14 post SAH. A regimen of normovolemia and normotension was administered for each patient. The daily use of 80 mg of Ozagrel sodium and 90 mg of Fasudil hydrochloride was routinely continued for the prophylaxis of vasospasm. Induced hypertension was started immediately in cases of neurological deterioration attributed to vasospasm. Balloon angioplasty and/or superselective infusion of papaverine hydrochloride was applied for medically intractable symptomatic vasospasm. Either MR angiography for cases that underwent coil embolization or 3D CT angiography for cases that underwent surgical clipping was performed on day 7 post-SAH. Follow-up angiography was performed 6 months following the endovascular procedures, unless a plain craniogram demonstrated coil deformity.

All surviving patients were evaluated on an outpatient basis following hospital discharge. On follow-up, the patients were evaluated to measure their functional ability based on the Glasgow Outcome Scale at 6 months, 1 year and then annually after treatment.

Results

The patients' clinical conditions at the time of admission and the treatment modalities used are shown in Table 1, while the locations of the aneurysms and the treatment modalities used are shown in Table 2. Almost half of the patients underwent surgical clipping or coil embolization, and four cases underwent coil embolization followed by surgical clipping. The proportion of poor grade patients was higher in the coil embolization group than in the clipping group.

Table 1 Summary of clinical conditions at the time of admission and the treatment modalities in 100 patients with aneurysmal SAH

Grade	Clipping	Embolization	Coil→Clip	Total
1	21	19	1	41
2	10	7	1	18
3	5	4	0	9
4	12	18	2	32
Total	48	48	4	100

Table 2 Treatment modality in 100 cerebral aneurysms according to lesion location

Location	Clipping	Embolization	Coil→Clip	Total
ICA	15	13	1	29
MCA	20	5	1	26
ACA	9	23	2	34
BA	1	5	0	6
VA	2	1	0	3
PCA	1	1	0	2
Total	48	48	4	119

Of the 29 internal carotid artery (ICA) aneurysms, 15 (51.7%) were treated using surgical clipping, while 13 (44.8%) underwent endovascular embolization, and one patient underwent coil embolization followed by surgical neck clipping. Of the 26 middle cerebral artery (MCA) aneurysms, 20 (76.9%) were treated using surgical clipping, 5 (19.2%) underwent endovascular embolization, and one patient with a ruptured right MCA aneurysm with an ill-defined neck and mild vasospasm adjacent to the aneurysm underwent tentative coil embolization followed by definitive neck clipping in the chronic stage. Of the 34 anterior cerebral artery (ACA) aneurysms, 9 (26.5%) were treated using surgical clipping, 23 (67.6%) underwent endovascular embolization, and two cases underwent coil embolization followed by surgical neck clipping. Of the 11 posterior circulation aneurysms, four (36.4%) were treated using surgical clipping, including one patient with a posterior inferior cerebellar artery dissecting aneurysm treated by occipital artery to PICA anastomosis and surgical trapping, and seven (63.6%) underwent endovascular embolization.

In the follow-up of the 48 surgically treated patients, 37 (77.1%) achieved a favorable outcome (good recovery: GR and moderately disabled: MD). Of the 52 patients that underwent endovascular embolization, 37 (71.2%) achieved a favorable outcome. No significant difference was observed regarding the proportion of favorable outcome between the two treatment modalities. The outcome of the surgically treated group and the group of patients that underwent endovascular embolization, according to the admission WFNS grade, are summarized in Tables 3 and 4, respectively. The rates of symptomatic vasospasm and shunt dependent hydrocephalus were 18.8% and 14.6%, respectively, in the clipped patients, and 19.2% and 21.2%, respectively, in the coiled

Table 3 Outcome of the surgically treated group according to the admission WFNS grade

Grade	GR	MD	SD	V	D	Total
1	20	1	0	0	0	21
2	8	0	1	0	1	10
3	5	0	0	0	0	5
4	0	3	3	1	5	12
Total	33	4	4	1	3	48

Table 4 Outcome of the group of patients who underwent endovascular embolization according to the admission WFNS grade

Grade	GR	MD	SD	V	D	Total
1	19	0	0	0	1	20
2	7	0	1	0	0	8
3	1	2	1	0	0	4
4	6	2	4	4	4	20
Total	33	4	6	4	5	52

Table 5 Rates of symptomatic vasospasm and shunt-dependent hydrocephalus

	Clipping	Coil mobolization
Symptomatic vasospasm	9/48 (18.8%)	10/52 (19.2%)
Permanent shunt	7/48 (14.6%)	11/52 (21.2%)

Table 6 Causes of unfavorable outcome and death according to the treatment modality in 100 patients with aneurysmal SAH

Cause of unfavorable outcome	Clipping	Embolization
Effect of primary bleed	5	8
Complication of treatment	1	2
Rebleeding	0	1
Vasospasm	4	3
Systemic complication	1	1
Total	11	15

patients (Table 5). Endovascular coiling of ruptured aneurysms has a tendency towards a higher risk for developing shunt dependent hydrocephalus. There was, however, still no significant difference. The causes of unfavorable outcome (severely disabled: SD, Vegetative survival: V and Dead: D) of the surgically treated group and the group of patients that underwent endovascular embolization are listed in Table 6. One patient with a basilar apex aneurysm underwent endovascular embolization, had a rebleeding of the aneurysm 16 days after the initial endovascular treatment and died; another patient with an IC-P-com aneurysm had a minor rebleeding 22 months after the initial endovascular coiling, while no rebleeding was observed in the surgically treated patients. Five out of 52 patients (9.6%) who underwent endovascular embolization needed re-treatment following the initial endovascular treatment, while no re-treatment was necessary in the surgically treated patients.

Figures 1 and 2 demonstrate a typical case treated with efficient collaboration between two treatment modalities.

Discussion

Recent advances in neurosurgery and interventional neuroradiology have led us to develop new strategies in the treatment of cerebral aneurysms. The published reports of early clinical and angiographical results of endovascular treatment have been promising [1]. The International Subarachnoid Aneurysm Trial (ISAT) is a well-designed and well-executed, randomized, controlled trial on a large number of patients. These data provide the highest level of evidence supporting the use of detachable coils for patients with ruptured cerebral aneurysms suitable for endovascular therapy [2, 3]. The study data allow us to conclude that patients with subarachnoid hemorrhage and aneurysm indicating a high likelihood of success with endovascular therapy should be offered that option. The publication of the results of this trial has sparked heated debate regarding the best current treatment for ruptured intracranial aneurysms [4–6]. In Europe, particularly in the United Kingdom, the study has had a profound effect on the management of ruptured intracranial aneurysms. On the other hand, the ISAT has not had such a significant impact on the neurosurgical vascular practices in Japan and the US. A major criticism of the ISAT is that only a minority of the patients evaluated at the participating centers were indeed enrolled in the trial. For inclusion in the study, the patient in question had to have an aneurysm judged by both a neurosurgeon and a neurointerventionalist to be equally amenable to surgery or endovascular embolization. As a result, only 2,143 of the 9,559 patients screened at the participating centers were actually enrolled in the trial, 78% were excluded. Nine percent of the exclusions were for refusal to participate, while the remaining 69% were excluded from the study because the aneurysm could not be treated by either procedure. A large proportion of these aneurysms were excluded because they probably had a configuration that was not suitable or ideal for coiling. The results of this study therefore do not necessarily justify embracing endovascular embolization as the therapy of choice for the entire population of patients with ruptured intracranial aneurysms. Furthermore, the endpoint in ISAT was assessed at 1 year. The longer-term durability of endovascular therapy, however, remains to be determined. It is possible that an early gain in the lowered rate of periprocedural morbidity and mortality from endovascular therapy, such as that found in this study, could be offset to some degree by a later increase in morbidity and mortality from later aneurysm rebleeding related to aneurysm remnants or recurrences [7–11]. In fact, in the ISAT, the rate of post-procedural hemorrhage up to 1 year in the endovascularly treated patients was 2.6 times that in the surgically treated ones. The long-term follow-up data from the ISAT and other studies should therefore help provide an answer to these questions.

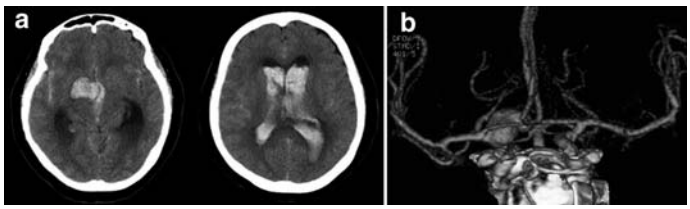

Fig. 1 A 64 year-old woman had a grade 4 subarachnoid hemorrhage due to rupture of a right IC large aneurysm. (**a**) CT demonstrating a small intracerebral hematoma and massive intraventricular hemorrhage. (**b**) 3D CT angiography demonstrating a ruptured right IC large aneurysm with a large bleb considered as a rupture point

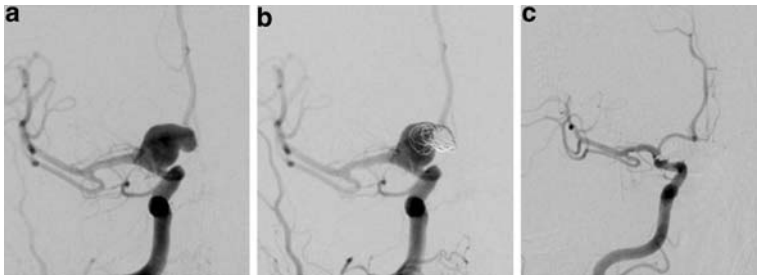

Fig. 2 The treatment strategy for this poor grade patient was as follows: at first tentative coiling for obliteration of the rupture point to prevent acute subsequent bleeding, whereas the configuration of the aneurysm was not suitable for coil embolization. Ventricular drainage was then set with intraventricular UK fibrinolysis. The definitive clipping was, finally, completed at the chronic stage following the recovery of neurological status. (**a**) Right carotid angiogram demonstrating a right IC large aneurysm with ill-defined neck. (**b**) Following the tentative coil embolization, angiogram demonstrating obliteration of the large bleb of the aneurysm. (**c**) Right carotid angiogram following the definitive surgical clipping, demonstrating complete obliteration of the aneurysm. The patient recovered well and achieved favorable outcome

When making case-by-case evaluation by a combined team of microsurgical and endovascular therapists based on the individual characteristics of each aneurysm, it is likely that a combined microsurgical-endovascular team approach will provide the means to achieve the best outcomes for the entire population of patients with ruptured intracranial aneurysms [12–15]. In treating an individual patient with a ruptured aneurysm, multiple factors must be considered when choosing the optimal course of treatment. Such factors include the aneurysm location, size, shape, and orientation; the tortuosity of the proximal vessels and the parent artery; the presence of calcifications at the aneurysm neck; neck–dome ratio; and patient's chronological and biological age, systemic comorbidities, life expectancy, and neurological condition. For example, it might be more appropriate for an elderly patient or a poor-grade patient with a limited life expectancy to receive no specific treatment or a treatment that is safer than one that provides decades of cure. Similarly, a young patient might forego a safer treatment for one that is more permanent. Excellent results can be obtained with complementary surgical clipping and coil embolization. The two treatment options can be successfully used interchangeably and at times in a complementary fashion to protect the patient from an aneurysm rupture while trying to minimize the complications related to treatment. To minimize complications, it is very important to assess the risk–benefit ratio constantly even in the advanced phases of surgical or endovascular procedures. If risks greater than those originally estimated or if unexpected findings are encountered while performing either surgery or endovascular embolization, the procedure can be halted and then the patient should be treated with an alternative method.

Conclusion

The selection of interventional neuroradiological techniques requires the careful consideration of the various available neurosurgical techniques, just as the selection of neurosurgical treatment requires an analysis of the endovascular alternatives. The method of treatment for each individual patient should be based on an objective selection of the safest and the most effective treatment, rather than the physician's preference for any specific treatment modality. It is likely that a combined microsurgical-endovascular team approach will provide the best means to achieve favorable outcomes for the entire population of patients with intracranial aneurysms.

Conflict of Interest Statement We declare that we have no conflict of interest

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Chapter 3
Distal Anterior Cerebral Artery Aneurysms

Martin Lehecka, Reza Dashti, Hanna Lehto, Riku Kivisaari, Mika Niemelä, and Juha Hernesniemi

Abstract *Background*: Distal anterior cerebral artery (DACA) aneurysms, also known as pericallosal artery aneurysms, represent about 6% of all intracranial aneurysms. They are located on the A2–A5 segments of the anterior cerebral artery and on its distal branches.

Methods: This paper summarizes present knowledge on radiological features, treatment options, treatment results, and long-term follow-up of DACA aneurysms.

Findings: Typical features of DACA aneurysms are small size, broad base, and branches originating from the base. When ruptured, they cause intracerebral hematoma in nearly half of the cases. DACA aneurysms are nowadays more often treated with microsurgical clipping than endovascular coiling due to their distal location and morphologic features. With clipping the results are same or slightly better than for aneurysms at other locations, coiling is often associated with more complications than in other aneurysms.

Conclusion: Clipping is a long-lasting treatment with very small recurrence rate, there is no long-term data available on efficacy of coiling yet. For ruptured DACA aneurysms the most important factors affecting outcome is the severity of initial bleeding and patient's age.

Keywords Aneurysm · Azygos · Clipping · Coiling · Distal anterior cerebral artery · Outcome · Pericallosal artery · Subarachnoid hemorrhage · Traumatic · Treatment

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Incidence and Location of DACA Aneurysms

Distal anterior cerebral artery (DACA) aneurysms, also referred to as pericallosal artery aneurysms, are located distally to the anterior communicating artery (ACoA) on the A2–A5 segments of the anterior cerebral artery (ACA) and its branches (Fig. 1) [1]. They are relatively rare, comprising about 6% (range 2–9%) of all IAs [2–16]. DACA aneurysms are further divided into subgroups based on their exact locations with respect to the segments of the ACA and the corpus callosum (Fig. 1).

Aneurysms of the ACA

Aneurysms of the ACA can be classified into five different groups: aneurysms of the A1 segment or proximal anterior cerebral artery aneurysms (A1As); anterior communicating artery aneurysms (ACoAAs); aneurysms of the A2 segment and its frontobasal branches or proximal pericallosal aneurysms (A2As); aneurysms of the A3 segment or classical pericallosal aneurysms (A3As); and aneurysms of the A4 and A5 segments and distal cortical branches or distal pericallosal aneurysms (AdistAs) [8, 17]. The last three groups represent the DACA aneurysms.

A2As (Proximal Pericallosal Aneurysms)

A2As are located either directly on the pericallosal artery, between the ACoA and the genu of the corpus callosum (A2 segment), or on one of its frontobasal branches (Fig. 1). Proximal pericallosal artery aneurysms (A2As) are rare. The reported incidence of A2As has been 0.2–1% of all IAs or about 5–22% of all DACA aneurysms [2–5, 7–10, 12–16, 18]. They are frequently involved with perforating

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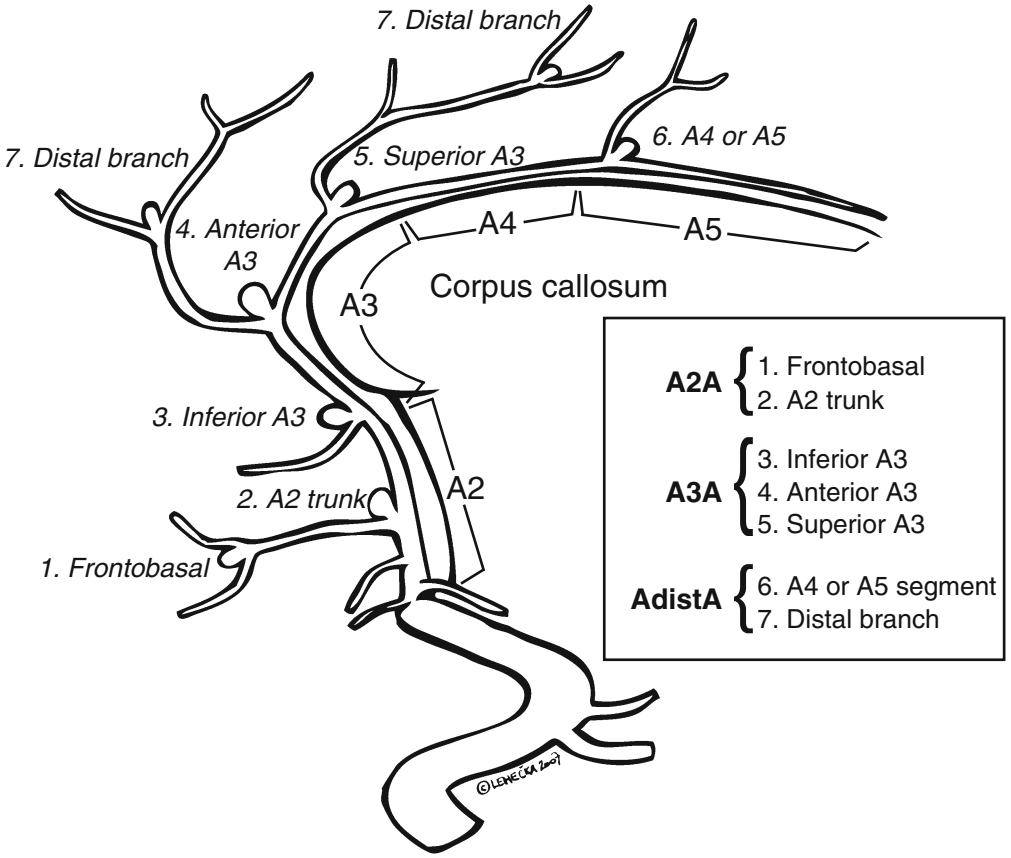

Fig. 1 A2 to A5 segments of the anterior cerebral artery (ACA) and their relation with the different groups of the DACA aneurysms

arteries arising from both the ACoA and the A2 segment, as well as arterial anomalies of this region [19–21].

A3As (Classical Pericallosal Aneurysms)

A3As are located at the A3 segment of the ACA at the genu of corpus callosum (GCC), often at the origin of the callosomarginal artery (CMA) (Fig. 1). They have also been called pericallosal artery–CMA junction aneurysms or "loco classico" pericallosal artery aneurysms. A3As are the most common of the DACA aneurysms. Their incidence is 2–7% of all IAs or 69–82% of all DACA aneurysms [2–5, 7–10, 12–16, 18].

AdistAs (Distal Pericallosal Aneurysms)

AdistAs are located at the A4 and the A5 segments of the ACA, distal to the GCC, or on the cortical branches that originate from the A3–A5 segments, e.g., the CMA (Fig. 1). AdistAs are the least frequent of all DACA aneurysms with an incidence of only 0.3–0.6% of all IAs or 5–20% of all DACA aneurysms [2, 3, 7, 8, 12, 13, 16, 18].

Clinical Symptoms

When DACA aneurysms rupture, they usually present with the same symptoms as seen in other ruptured aneurysms, i.e. headache, nausea, and loss of consciousness depending on the amount of bleeding [13]. Still, there are some unique neurological deficits which are more often seen in this aneurysm group, including akinetic mutism, bilateral leg weakness, behavioral changes and cognitive deficits [22–26]. These findings are thought to be related to bilateral damage to the vascular territory supplied by the distal ACA, especially the bilateral cingulate gyri and other limbic structures, and the supplementary motor area (SMA), caused either by mass effect after ICH, or infarction [22, 27].

Anatomic Features

Size

DACA aneurysms are small; even when ruptured their mean size varies from 5 to 8 mm [2, 3, 10, 12, 13, 28–30], with over 50% of the ruptured ones smaller than 7 mm [7, 8]. In addition, DACA aneurysms have often a broad base with possible neck calcifications and originating branches nearby [2, 3, 5, 9–14, 16, 31]. The broad base with base-to-dome ratio 1:2 or more has been seen in 81% of DACA aneurysms, and 94% of the DACA aneurysms had a branch originating at the base [8].

Multiple Aneurysms

DACA aneurysms are often associated with other aneurysms [2, 3, 7, 8, 10, 11, 16, 31]. Associated aneurysms have been reported in 25–55% of patients with DACA aneurysms [2–4, 7, 8, 10–14, 31, 32], which is higher than the usual 28–35% reported for other aneurysm locations [33–38].

ICH and IVH

DACA aneurysms tend to bleed into the adjacent brain tissue causing ICH in 17−73% of the patients [3, 7, 11–13, 32, 39, 40]. The highest density of blood in the subarachnoid space is in the distal interhemispheric fissure, pericallosal cistern, and lamina terminalis cistern [41]. The ICH is usually located in the frontal lobe, corpus callosum or cingulate gyrus (Fig. 2) [42]. The high incidence of ICHs, higher than for aneurysms elsewhere, is obviously related to the narrow pericallosal cistern and the dense attachments to the adjacent brain surface [11, 17]. IVH is seen in 25−30% of the patients, more frequently related to ruptured A2As and A3As than AdistAs [43–45]. Frontal ICHs are likely to cause late cognitive deficits [26].

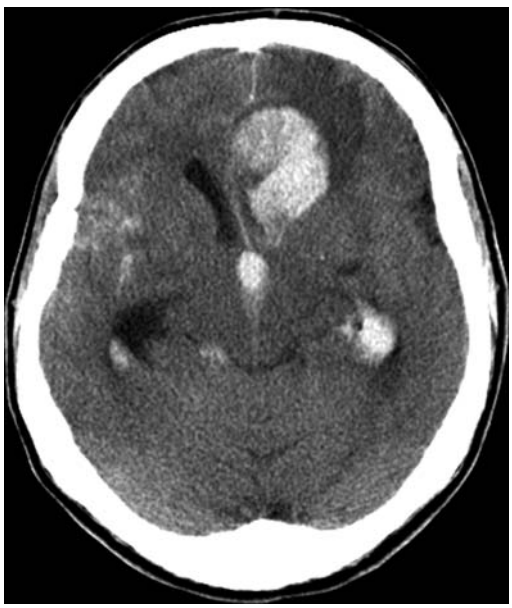

Fig. 2 Intracerebral hematoma caused by ruptured DACA aneurysm

Association with ACA Anomalies

DACA aneurysms are often associated with various anomalies of the ACA [3, 8, 13, 14], which are thought to cause greater blood flow and shear stress on the vessel wall, and thus increase the susceptibility to aneurysm formation at the bi-, tri-, and quadrifurcations of these arteries [46, 47]. Huber et al. reported an association between anomalies of the ACA and DACA aneurysms in an angiographic series [48]. In anatomic autopsy studies of patients without aneurysms, the azygos ACA was seen in 0.2–4%, the bihemispheric ACA in 0.2–12% and the triplication of ACA in 3–13% of patients [19, 20, 49–55]. However, in clinical series, different anomalies of the ACA have been observed in 7–35% of patients with DACA aneurysms, an incidence generally higher than in the autopsy studies [4, 5, 13, 28, 31]. Azygos ACA with only one ACA trunk has been seen in 4%, bihemispheric ACA with two ACA trunks – one of which rudimentary and one dominant – in 15%, and triplication of ACA with three similar size trunks in 4% of patients with DACA aneurysms [8].

Association with AVMs

In addition to ACA anomalies, DACA aneurysms are thought to be associated with cerebral arteriovenous malformations (AVMs) [3, 13, 14]. AVMs have been reported in 0−15% of DACA aneurysm patients [2, 5, 7, 8, 13, 14]. The variation is high among different series, and the incidence seems to be higher in certain metropolitan centers to which many difficult vascular cases are referred compared to centers functioning more on population basis.

Special Subgroups of DACA Aneurysms

Giant DACA Aneurysms

Giant DACA aneurysms (diameter ≥25 mm) are extremely rare. So far, there have been only little over 30 cases reported in the literature (Table 1). Only few of them were reported as

Table 1 Published cases of giant (≥25 mm) DACA aneurysms

Authors	Year	No. of giant DACA aneurysms
Snyckers and Drake [32]	1973	1
O'Neill et al. [67]	1979	1
Pia and Zierski [69]	1979	1
Pozzati et al. [70]	1982	1
Smith and Parent [73]	1982	1
Hayashi et al. [60]	1985	2
Yamagami et al. [76]	1986	1
Nitta et al. [66]	1987	1
Maiuri et al. [64]	1990	1
Mishima et al. [65]	1990	1
Hashizume et al. [59]	1992	1
Hernesniemi et al. [3]	1992	1
Preul et al. [71]	1992	1
Shiokawa et al. [72]	1993	2
Farias et al. [58]	1997	1
deSousa et al. [2]	1999	2
Kanemoto et al. [61]	2000	1
Koyama et al. [62]	2000	1
Miyazawa et al. [9]	2000	1
Türe et al. [75]	2001	1
Topsakal et al. [74]	2003	1
Biondi, et al. [57]	2006	2
Dinc et al. [56]	2006	1
Lawton et al. [63]	2006	1
Steven et al. [13]	2007	2
Lehecka et al. [7]	2008	(1+1)[a]
Park et al. [68]	2008	1
Total		32

[a]One of the two cases was previously reported in Hernesniemi et al. 1992 series

part of a larger series on DACA aneurysms [2, 3, 7, 9, 13, 32, 56], most as case reports [57–76]. Since giant DACA aneurysms may mimic the symptoms of frontal tumors, MRI and Digital subtraction angiography (DSA) are essential for reaching a correct diagnosis. CT and CTA are helpful in identifying calcifications at the aneurysm base.

Aneurysms Associated with Azygos ACA

As mentioned earlier (see Section "Multiple Aneurysms") DACA aneurysms are frequently associated with anomalies of the ACA. Of such anomalies, the azygos ACA has received the most attention. In larger series on DACA aneurysms, an azygos ACA has been observed in 3−22% of patients [2, 4–6, 8–10, 13, 28, 30, 32, 77–82]. In addition, there exists a large number of case reports on the subject [46–48, 59–61, 65, 72, 74, 76, 83–110]. It seems that the incidence of azygos ACAs compared to bihemispheric ACAs in connection with DACA aneurysms has been overestimated. It is actually very difficult to distinguish between these two anomalies in the normal DSA, even with compression of the contralateral carotid artery [19, 99]. CTA or rotational DSA give more accurate information for making the distinction between the two anomalies.

Traumatic DACA Aneurysms

Aneurysms of traumatic origin represent less than 1% of all IAs aneurysms [39, 111, 112] and traumatic DACA aneurysms are even more rare [4]. Traumatic DACA aneurysms have been described in only some case reports [7, 13, 111–140]. They are typically found in young patients or children [125, 126, 134, 140]. The pericallosal artery is thought to be prone for formation of traumatic aneurysms after a head trauma, since the lower margin of the falx may directly damage the arterial wall of the pericallosal artery [140]. Traumatic DACA aneurysms are usually fusiform, with thin walls and poorly defined necks [118], which makes their treatment very challenging. Wrapping, proximal occlusion, excision, trapping, parent artery occlusion with preoperative bypass, and reconstruction can be considered for these aneurysms [141–144]. Sometimes even a preoperative bypass, side-to-side A3–A3 bypass [145] or arterial translation (e.g., STA-ACA) is needed [146–149].

Imaging of DACA Aneurysms

DSA is still the valid gold standard in many centers [150]. Recently, multislice helical CT-angiography (CTA) has begun to replace DSA as a noninvasive, safe, and quick imaging method with sensitivity and specificity comparable to DSA in aneurysms larger than 2 mm [151–159]. In addition, it allows disclosure of calcifications in the arterial walls and quick reconstruction of 3D images (Fig. 3) [160]. In giant or partially thrombosed DACA aneurysms, MRI is valuable for evaluating the presence and extension of intraluminal thrombus. Nowadays, 3T magnetic resonance angiography (MRA) shows good potential in identifying small details of the vasculature without the side effects of radiation [161, 162].

Treatment of DACA Aneurysms

The first surgery on DACA aneurysm was reported by Sugar and Tinsley in 1948, in a 19-year old girl in whom proximal pericallosal artery was ligated [163]. The first aneurysm

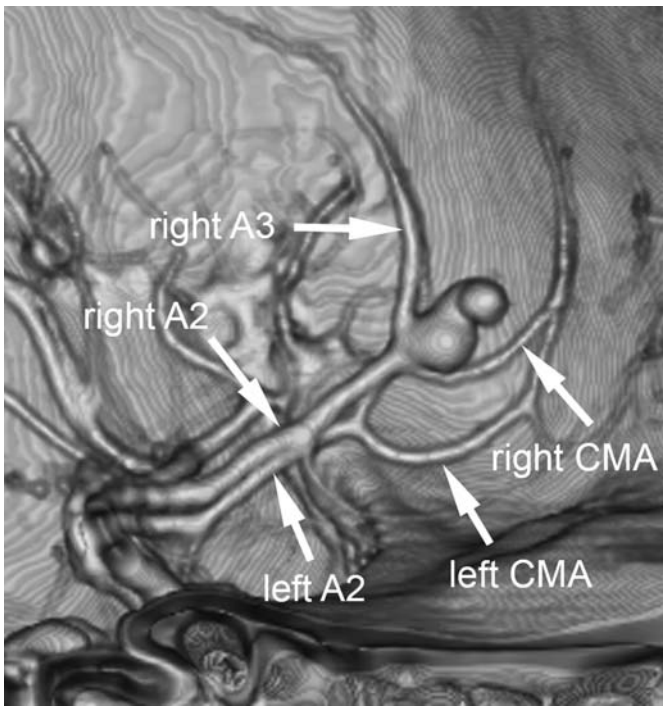

Fig. 3 3D reconstruction of DACA aneurysm

series dedicated to DACA aneurysms came from Laitinen and Snellman in Finland in 1960, who reported 14 patients, 10 of whom where treated surgically [5]. Conservative treatment for ruptured DACA aneurysms was abandoned after the Cooperative Study of Intracranial Aneurysms in 1966, which reported mortality rate as high as 75% at 1 year follow-up [164]. Since then clipping has become the primary treatment for DACA aneurysms, first without magnification and later with microsurgical techniques.

Microsurgical Clipping

The first report on microneurosurgical management of DACA aneurysms came from Yaşargil and Carter in 1974 describing 13 consecutive patients operated on by Yaşargil under operating microscope since 1967 [15]. The general microneurosurgical technique for treatment of DACA aneurysms described in this paper is very similar to the one still in use. The major advances over time are related to better preoperative imaging, refined instruments, and certain microneurosurgical technical nuances developed over the years by different authors [2, 3, 10, 31, 43–45]. After Yaşargil's first paper, a number of reports were published on microneurosurgical management of DACA aneurysms (Table 2). The fact that most of these series were small, with less than 30 patients [4, 12, 14, 28, 30, 31, 40, 56, 78, 80, 82, 165–167], shows how infrequent DACA aneurysms are and how difficult it is to obtain experience in their treatment even at one institution (Table 2). Most DACA aneurysms are operated via the anterior interhemispheric route [2, 3, 10, 31, 43–45]. Partial resection of the genu of corpus callosum is not advisable as it may lead to neuropsychological problems [168].

The largest series on DACA aneurysm by far, with 258 ruptured and 104 unruptured DACA aneurysms treated with microsurgical clipping, was published by Lehecka et al. in 2008 [7]. They reported 91% total occlusion of the DACA aneurysms with clipping. Intraoperative rupture was seen in 22% of the ruptured and 7% of the unruptured cases. Morbidity related to treatment was 15% and 12% for the ruptured and unruptured DACA aneurysms respectively. Surgery related mortality was only 0.4% for the ruptured and 1% for the unruptured aneurysms. Favorable outcome, as Glasgow Outcome Score 4 or 5, at 1 year was 75% for the ruptured and 94% for the unruptured DACA aneurysms. These results were similar to what other authors have reported earlier with much smaller series [2, 3, 9–11, 13].

Microneurosurgical clipping of DACA aneurysms presents certain specific difficulties when compared with other aneurysm locations [31]. These difficulties are related to the approach deep inside the narrow interhemispheric space, lack of anatomic landmarks, dense attachments and embedding of the aneurysm dome in surrounding brain tissue, and morphological features of the DACA aneurysms such as

Table 2 Series on treatment of DACA aneurysms published before 2009

Author(s)	Year	No. cases	Clipped	Coiled	Indirect surgery	Conservative
Before microneurosurgery						
McKissock and Walsh [175]	1956	7	4	0	1	2
Hamilton et al. [176]	1959	6	3	0	3	0
Laitinen and Snellman [5]	1960	14	9	0	1	4
Pool and Potts [177]	1965	3	2		1	0
Wilson et al. [178]	1965	4	4	0	0	0
Fisher and Ciminello [179]	1966	4	3	0	0	1
Skultety and Nishioka [180]	1966	65	27	0	12	26
Dechaume et al. [181]	1973	12	6	0	0	6
Snyckers and Drake [32]	1973	24	15	0	0	9
Kinoshita and Matsukado [79]	1975	10	8	0	0	2
Nukui and Aiba [81]	1978	26	22	0	0	4
Becker and Newton [77]	1979	12	9	0	0	3
Yoshimoto et al. [16]	1979	34	34	0	0	0
Microneurosurgery						
Yasargil and Carter [15]	1974	13	13	0	0	0
Kuwabara et al. [80]	1984	18	17	0	0	1
Mann et al. [40]	1984	11	11	0	0	0
Yasargil [31]	1984	23	23	0	0	0
Ogasawara et al. [82]	1987	18	12	0	0	6
Wisoff and Flamm [14]	1987	20	20	0	0	0
Kawamura et al. [78]	1988	29	20	0	0	9
Sindou et al. [12]	1988	19	16	0	0	3
Ohno et al. [10]	1990	42	34	0	0	8
Fukushima et al. [165]	1991	26	26	0	0	0
Hernesniemi et al. [3]	1992	84	67	0	0	17
Martines et al. [166]	1996	11	11	0	0	0
Proust et al. [11]	1997	43	43	0	0	0
Inci, et al. [4]	1998	14	14	0	0	0
Ng et al. [30]	1998	30	25	0	0	5
deSousa, et al. [2]	1999	72	72	0	0	0
Miyazawa et al. [9]	2000	54	54	0	0	0
Chhabra et al. [28]	2005	28	28	0	0	0
Dinc et al. [56]	2006	26	24	1	0	1
Oshiro et al. [167]	2007	20	20	0	0	0
Kim et al. [182]	2007	12	12	0	0	0
Steven et al. [13]	2007	59	58	1	0	0
Lehecka et al. [7]	2008	501	405	17	8	71
Lee et al. [6]	2008	126	117	9	0	0
Endovascular						
Pierot et al. [170]	1996	8	0	8	0	0
Menovsky et al. [29]	2002	12	0	12	0	0
Keston et al. [171]	2004	18	0	17	0	1
Nguyen, et al. [172]	2007	26	0	25	0	1
Pandey et al. [173]	2007	41	13	28	0	0
Waldenberger et al. [174]	2008	45	12	29	0	4
Vora et al. [183]	2008	28	0	28	0	0

small size and broad base with branching arteries close to the base. Despite these challenging features, microsurgical clipping still offers good treatment results, high initial occlusion rate, and only 0.4% rebleeding rate in 10-year median follow-up [169].

Coiling

Since the first report on endovascular treatment of DACA aneurysm by Pierot et al. in 1996 [170], the number of coiled DACA aneurysms has been increasing, although, not to an

extent comparable to other aneurysm locations (Table 2). Coiling is considered to be more demanding for DACA aneurysms than for most other aneurysms, and thereby also the complication rate has been higher with 7–18% being reported [170–174]. Reruptures during coiling were seen in 3–18% [171, 172, 174], aneurysm recurrence/recanalization rate was also relatively high occurring in 18–53% [172–174], and the initial total occlusion has been achieved in only 25–90% [170–174]. On the other hand, in all of these series, patients with SAH due to ruptured DACA aneurysm had a similar outcome as in most surgical series [170–174].

It seems that, using the present technology, endovascular occlusion of DACA aneurysms is demanding because of their small size, relatively wide neck, branches originating close to the base, small caliber of the parent artery, and distal location of the aneurysm [170–174]. DACA aneurysms are difficult to reach via small diameter parent arteries and there is often a lack of stability and support for optimal coil deployment. Suboptimal initial coiling results easily in aneurysm recurrence [172]. Only a long-term follow-up will indicate what is the durability of coiling in DACA aneurysms.

Outcome for Ruptured DACA Aneurysms

Short-Term Outcome

Microsurgical series of patients with ruptured DACA aneurysms have reported favorable outcomes in 58−83% and management mortality in 7−21%, respectively [2, 3, 10–14, 30, 40]. The results vary depending on how selected the patient material is, what is the timing of the surgery, and whether the short-term outcome is evaluated at discharge or later e.g. at 1 year. Mortality at 1 year due to ruptured DACA aneurysm has been shown to be lower than for other aneurysm locations (13% vs. 24%), but the overall favorable outcome (Glasgow Outcome Score $\geq$ 4) was similar (74% vs. 69%) [7]. This means that DACA aneurysms cause less frequently fatal ruptures, but cognitive problems due to frontal lobe injury are more often encountered [3, 26].

The known independent predicting factors for unfavorable outcome in patients with ruptured DACA aneurysms are: age; Hunt and Hess grade; rebleeding before treatment; ICH; IVH; and severe preoperative hydrocephalus [7, 9, 13, 173].

Long-Term Outcome

The only study on long-term follow-up of patients with ruptured DACA aneurysms showed that re-bleeding from a previously treated DACA aneurysm is exceptional, with only one such case observed during 10 year median follow-up of 280 patients [169]. During the first 3 years after the initial SAH most patients (72%) died directly from the SAH or its sequelae. Later, after 10 or more years the most common causes of death were cardiovascular disease and cancer like in general population [169]. Excess mortality was seen in patients with ruptured DACA aneurysms only during the first 3 years, after that their life expectancy was the same as for matched general population [169].

Unruptured DACA Aneurysms

DACA aneurysms are usually small, over 50% have been less than <7 mm in diameter when ruptured [7, 8]. This means that it is probably beneficial to treat even small unruptured DACA aneurysms [7]. Clipping has been shown to be a long-lasting method in the treatment of these aneurysms. There was only one recurrent SAH in 262 clipped DACA aneurysms during 10 year median follow-up [169]. There is no such long-term data available on the effects of coiling. Clipping of unruptured DACA aneurysms was related with 12% morbidity and 94% favorable outcome at 1 year [7]. The most important factor determining the outcome in these patients is the presence or absence of acute SAH caused by other aneurysm. Clearly, patients in whom the unruptured DACA aneurysm was treated during the acute SAH phase did worse than those treated later on after recovery; the latter group had the same excellent results as patients with no history of SAH [7]. In patients with acute SAH, associated unruptured DACA aneurysm(s) should be treated only when they can be reached easily via the same microsurgical approach, i.e. only if the SAH is caused by another DACA aneurysm [2, 7]. In all other cases one should wait for the patient to recover from the SAH and its primary treatment and then treat the unruptured DACA aneurysm in a separate session together with other possible associated aneurysms.

Conclusions

Even when ruptured, DACA aneurysms are usually small with wide neck and branches originating from their base. Most of them are found on the A3 segments of the anterior cerebral artery, anterior to the genu of corpus callosum. Anatomic anomalies of the ACA are frequently associated with these aneurysms. Microsurgical clipping provides high initial occlusion rate of the aneurysm, has very small re-bleeding rate in the long-term follow-up and the treatment

related complication rate is similar to other aneurysm locations. Coiling of DACA aneurysms is often associated with more complications than coiling of more proximal aneurysms and the initial occlusion rate is often relatively low. The long-term follow-up data on coiled DACA aneurysms is lacking. With active treatment, three out of four patients with ruptured DACA aneurysm achieve favorable outcome at 1 year, the prognosis is slightly better than for aneurysms at other locations. Severity of the initial SAH is the most important prognostic factor for outcome.

Conflicts of interest statement We declare that we have no conflict of interest.

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Chapter 4
Treatment of Complex Intracranial Aneurysms of Anterior Circulation Using Multiple Clips

Hirotoshi Sano

Abstract *Objective*: To evaluate the efficacy of multiple clip application for the occlusion of complex intracranial aneurysms, analyzing the technique and outcome of big and giant cerebral aneurysms clipped in our institution.

Method: A total of 259 giant and large intracranial aneurysms (65 ruptured and 193 unruptured) were treated at Fujita Health University Hospital by clipping from January 1975 till December 2008. All patients were treated by multiple clipping according to our multiple clipping technique with reconstruction of the parent vessel. All patients underwent preoperative 3D computed tomography and some patients in addition received digital subtraction angiography. We examined the patients' clinical records and pre- and postoperative case notes, diagnostic and intraoperative images. There were 97 (giant 43, big 54) ICA aneurysms, 105 (giant 45, big 60) MC aneurysms and 32 (giant 7, big 25) AC aneurysms, 25 (giant 14, big 11) VB aneurysms. All patients underwent thorough pre-surgical planning of approach and clipping technique.

Surgical technique involved the use of multiple clips with the initial clip securing the deepest neck part and the others successively occluding the rest by remnant clips, occluding along the best plane of neck obliteration.

Results: Out of 193 cases, 165 cases were without any complications. Temporary complications were seen in 18 cases and permanent in 10. In our 65 ruptured aneurysms operated on, outcome was in line with standard outcome according to the SAH grade on admission (H&H, WFNS grade). In total, 183 cases had good results (94.8%).

Conclusions: The "multi" clip method for the treatment of complex intracranial aneurysms can be a safe and effective method where a single clip cannot obtain complete neck closure. Proper preoperative understanding of the three-dimensional anatomy of the aneurysm and appropriate preoperative planning and selection of suitable clipping method, using an appropriate combination of clips, definitely can reduce the morbidity and mortality in these patients.

Keywords Complex intracranial aneurysm · Multiclip method · Intraoperative doppler · Intraoperative neuroendoscopy

Introduction

In spite of the advances in microsurgical and endovascular techniques, complex intracranial aneurysms remain a difficult neurosurgical problem [1]. If a single clip is used for obliteration of these aneurysms, they have probably a higher incidence of re-growth because parts of the aneurysmal wall remain exposed to hemodynamic factors. Many of these aneurysms have a large calcified neck, may directly involve parent and/or branching arteries, may be partly thrombosed, may have sac projections inconvenient for clipping, and usually have complex anatomical relations to the adjacent neural and vascular structures [2]. To overcome these challenges successfully with minimal morbidity and mortality, we have resorted to the use of the "multi clip" method. Aneurysm clips of different shape, size, fenestrated or not can be applied on the neck of these aneurysms for reconstruction of the artery and at the same time to avoid any perforator being clipped. We recommend application of an appropriate first clip to the deepest part of the neck in the operative field followed by successive, more superficial clip placements, using different types of blade shapes. By properly adjusting different clips to the aneurysmal neck, both inner walls of the neck can be approximated, achieving contact between the normal intimae all around the neck orifice. The use of a single clip may not achieve such precise clipping, and one may end up with residual aneurysm or a high incidence of postoperative complications.

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Patients and Methods

Between January 1975 and December 2008, 258 patients with complex intracranial aneurysms (65 ruptured and 193 unruptured), of which 97 were ICA aneurysms (giant 43, big 54), 105 MC aneurysms (giant 45, big 60), 32 AC aneurysms (giant 7, big 25), and 25 VB (giant 14, big 11), were treated at the Department of Neurosurgery, Fujita Health University Hospital, Japan. We defined three types of "multiclipping" technique: (1) precision clipping type, (2) perforator preservation type, and (3) reconstruction type.

Preoperative imaging studies, including three-dimensional computed tomography and, in some patients, digital subtraction angiography, were very important for the preoperative understanding and planning of the appropriate method and selection of clip type.

Intraoperative doppler ultrasound, ICG and neuroendoscopy were used in all patients to ensure proper clipping and to avoid complications. All patients underwent standard pterional craniotomy and splitting of the sylvian fissure. All patients had irregular neck shape on preoperative imaging, and intraoperatively it was impossible to clip them with a single clip as this could have caused narrowing or kinking of the parent vessel or sacrifice of a perforator or branch vessel(s). We clipped the distal or deep part of the aneurysm sac at the beginning using a standard clip, and then successively occluded the dome by placing multiple clips called the "remnant" clips. This was the most appropriate method to achieve exact and complete clipping and to avoid postoperative morbidity and mortality in these patients with complex aneurysms.

Results

Surgery for patients in chronic stage post-SAH or unruptured aneurysms was performed in 193 cases. All aneurysms in this series could be clipped precisely and were completely excluded from the circulation. At follow-up 165 cases were without any complications, temporary complications were seen in 18 cases and permanent ones in 10 cases (Table 1). We also treated 65 ruptured aneurysms and outcome was related to the grading score on admission (Table 2).

Table 1 Operative results in chronic operation of incidental cases (193 cases)

EX		165	183 (94.8%)
Comp	Temporary	18	
	Permanent	10	

EX – Excellent Recovery, Comp – Complications

Table 2 Operative results in early operation. Total 65 cases

GR	32 (I/II:13, III:12, IV:5, V:2)
MD	9 (III:5, IV:4)
SD	7 (III:2, IV:3, V:2)
V	3 (IV:2, V:1)
D	14 (IV:4, V:10)

(GR – 49.2%, MD – 13.9%, SD – 10.8%, V – 4.6%, D – 21.5%). GR – Good Recovery, MD – Moderately Disabled, SD – Severely disabled, V – Vegetative, D-Dead

Illustrative Cases

The first case (Fig. 1) shows our method of treating complex anterior communicating (Acom) artery aneurysm. The sylvian fissure was dissected widely and a very small part of the gyrus rectus on the left side was excised. The aneurysm and the anterior cerebral arteries (bilateral A1 and A2 arteries) were exposed all around the aneurysm. Initially, the standard clip was applied to the neck as shown in Fig. 1b. This initial partial occlusion reduced the flow in the aneurysm and thus also its size and allowed better visualization of the residual parts and adjacent normal anatomy. Once the first standard clip was secured, the superficial part of the aneurysm was obliterated using fenestrated clips and appropriate mini clips in succession or tandem manner for total exclusion. Complete exclusion and preservation of blood flow in normal vessels was confirmed intraoperatively by indocyanine-green study and intraoperative doppler ultrasound followed by intraoperative endoscopy. Good postoperative clinical results also proved the safety and efficacy of this multiclip method.

Another illustrative case (Fig. 2) is a ruptured complex giant intracranial aneurysm with schematic representation of the multiclip method. After standard pterional craniotomy and adequate dissection of the left sylvian fissure, the anterior communicating artery complex was exposed. The right anterior cerebral artery (A1) was hypoplastic and the aneurysm was filling from the left. The left gyrus rectus was excised partially to completely expose the aneurysm anatomy. Intraoperative endoscopy was performed to visualize the anatomy in a better way and to understand the three-dimensional orientation of this complex aneurysm. The first standard clip was applied to the deepest part of the neck to obliterate partially the neck, preventing stenosis or kinking of the normal adjacent arteries and perforators. Then fenestrated and mini clips were applied sequentially to obliterate the aneurysm completely. Intraoperative ICG Doppler ultrasound and endoscopy were performed to confirm proper positioning of the clips, exclusion of the aneurysm from circulation, and preservation of the normal blood flow. The patient recovered well postoperatively and had no additional neurological deficit.

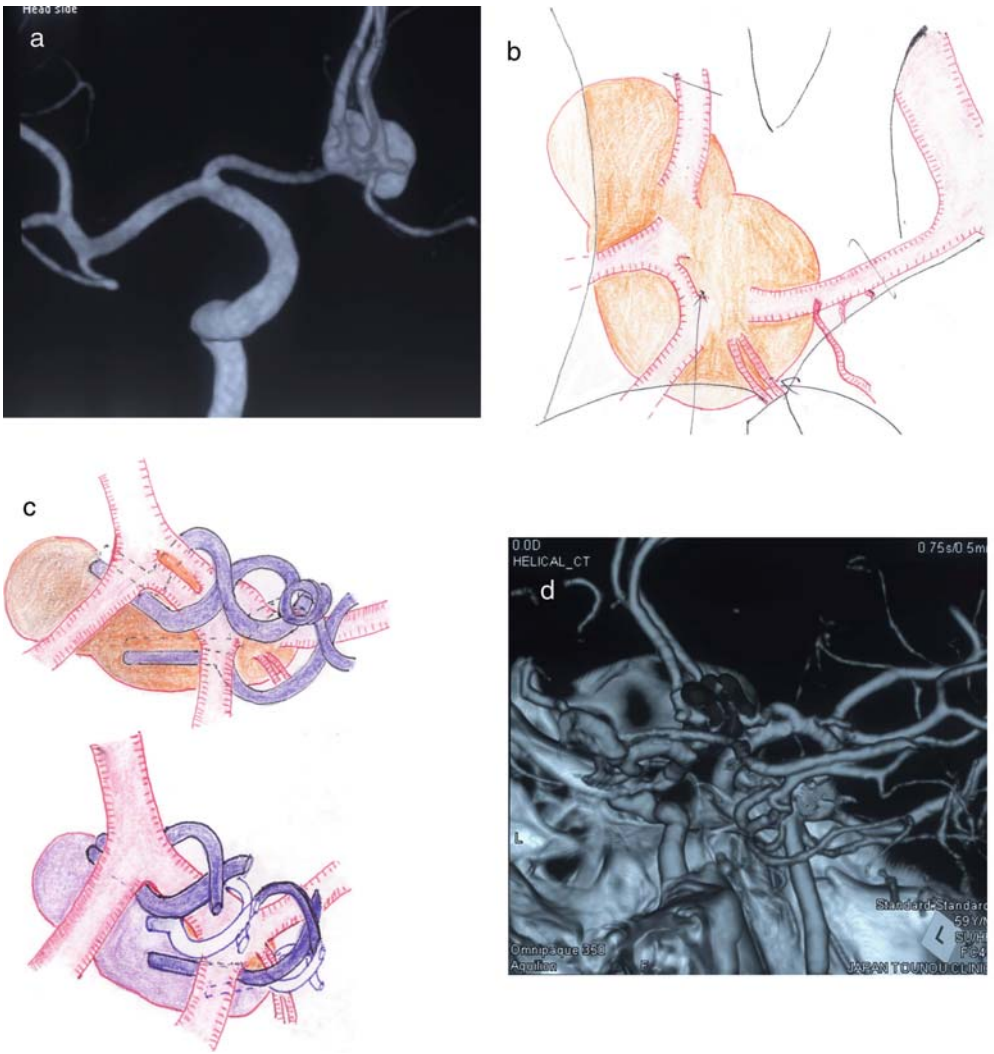

Fig. 1 (**a**) CT Angiography showing a Complex ACom Artery Aneurysm (**b**) Complex Acom artery Aneurysm (**c**) Precise clipping using appropriate multiple clips with preservation of perforators (**d**) Post operative CT Angiography showing the Complex ACom Artery Aneurysm to be excluded from the circulation with perforators preserved

The third case shows the clipping technique of a complex wide neck giant middle cerebral artery aneurysm. After standard right pterional craniotomy and dissection of the sylvian fissure the aneurysm, proximal and distal vessels were exposed adequately and the aneurysm was trapped for a short period of time to prevent rupture from the evident bleb. Then initial partial occlusion of the aneurysm neck was performed, followed by successive reconstruction of the middle cerebral artery using fenestrated and mini clips (Fig. 3b). Thereafter, intraoperative Doppler ultrasound and ICG was applied to confirm the reconstruction and preservation of normal blood flow in the middle cerebral artery.

The following case shows the clipping of a large complex aneurysm on internal carotid-posterior communicating (PCOM) artery. After the standard operative exposure of the aneurysm and intraoperative endoscopy, clipping was initiated by using first a standard fenestrated clip as shown in Fig. 4b. This was followed by successive application of fenestrated and mini clips, completely occluding the aneurysm, reconstructing the internal carotid and PCOM arteries with preservation of normal flow in the perforators. This was again confirmed by ICG, intraoperative doppler ultrasound and endoscopy. The patient was neurologically intact after surgery.

Discussion

Complex intracranial aneurysms represent one of the challenging neurosurgical problems. Their shape, size, location, relation to parent arteries and perforators, calcifications at

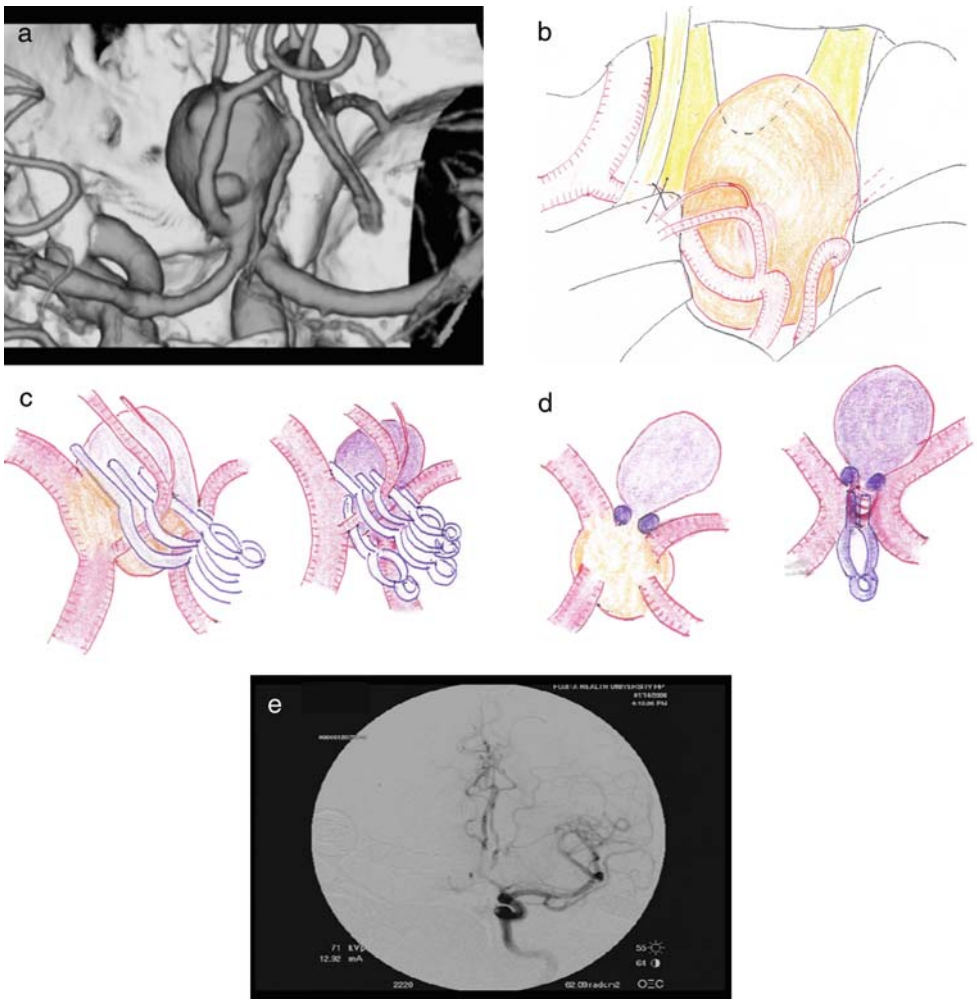

Fig. 2 (**a**) CT Angiography showing a Complex giant ACom Artery Aneurysm with hypoplastic right anterior cerebral artery (**b**) Ruptured complex giant Acom artery aneurysm with right anterior cerebral artery hypoplasia (**c**) Temporary clip on left anterior cerebral artery with initial permanent clip on the deeper part at the neck and followed by successive application of fenestrated clip toward surface or dome side with perforator preservation. (**d**) Reconstruction of the neck and complete occlusion of the aneurysm. (**e**) Post operative DSA Angiography showing a Complex giant ACom Artery Aneurysm now excluded from the circulation

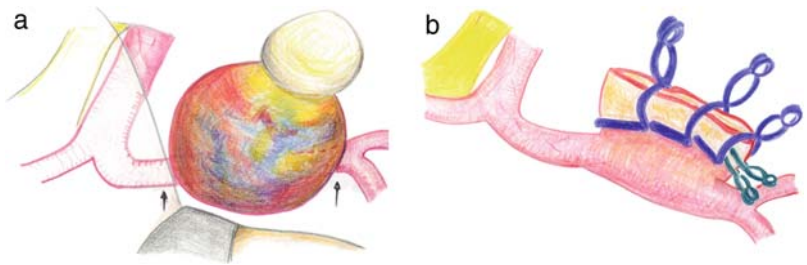

Fig. 3 (**a**) Giant wide neck middle cerebral artery aneurysm with bleb, (**b**) Trapping using temporary clips and reconstruction of parent vessel using multiclip method

the neck, thrombosis and direct involvement of the parent arteries show wide variations and complexities. All these cases require difficult decisions either because of the neck or complex aneurysm relation to the normal vessels [3]. The precise application of the clip to exclude the aneurysm completely is always the goal, but not an easy task to achieve [3]. Thorough preoperative planning is required to understand the complex anatomy and orientation of the three-dimensional configuration, often done by drawing schematic pictures. With the extreme variability of these aneurysms, a preoperatively chosen ideal single clip may eventually not be the ideal and practical solution, and the multiclipping method described by the senior author offers the most versatile solution. The preservation of normal flow with complete exclusion of the aneurysm from circulation also prevents re-growth. An important point is the application of a standard clip first to reduce the neck size and simultaneously the size of the whole aneurysm, so that the rest of the aneurysm can be visualized. This permits proper planning and appropriate application of suitable clips in succession. The perforators

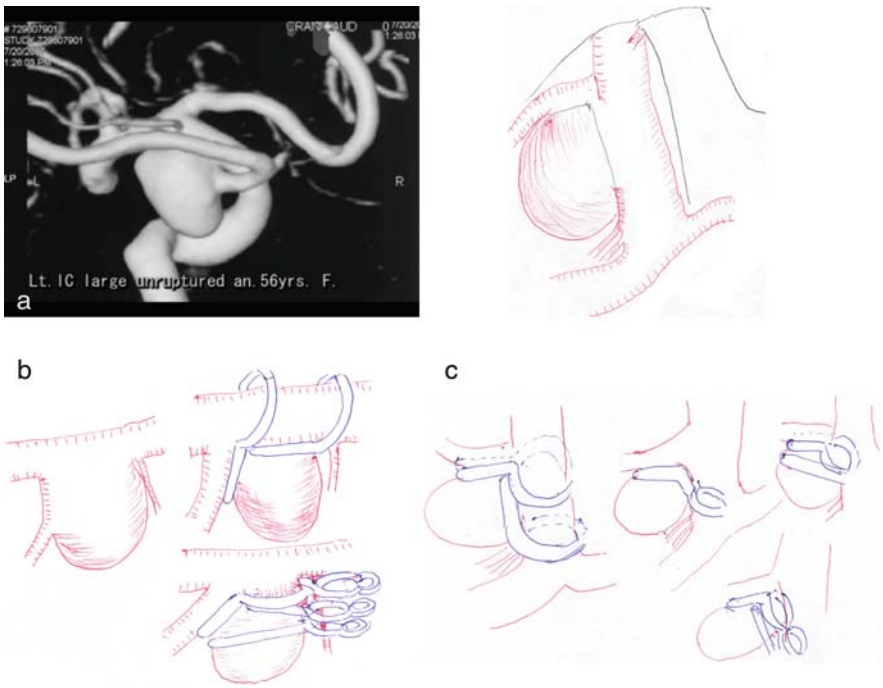

Fig. 4 (**a**) Another complex posterior communicating artery aneurysm, (**b**) Application of initial deep fenestrated clips to obliterate the neck followed by successive dome occlusion by means of various types of multiple clips, (**c**) Another view showing preservation of the perforators using the multiclipping method

arising from the parent artery near the aneurysmal neck are always a challenge to preserve. Using suitable multiple clips can definitely preserve the perforators and improve the outcome of aneurysm surgery. Complex aneurysms have thick walls that prevent approximation of the clip tips and complete closing of the aneurysm [4]. In such aneurysms, the "multiclip" method helps to achieve complete and accurate clipping. Although our short-term follow-up of these complex aneurysms has shown excellent results, the method may have some limitations because the space around the clipped aneurysm is reduced for introduction of the neuroendoscope or to apply tandem clips in succession.

Conclusions

Complex intracranial aneurysms are a challenging neurosurgical problem, and by using the multiclip method as demonstrated complete clipping can be accomplished with reduced complication rates, when compared to the use of a single clip. Hence the multiclip method is very useful and safe for the successful and precise clipping of complex cases. It should find broader application in contemporary open aneurysm surgery.

Conflicts of interest statement We declare that we have no conflict of interest.

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Part II
Cerebral Arterial Dissection

Chapter 5
Overview of Spontaneous Cervicocephalic Arterial Dissection in Japan

Tetsuya Tsukahara and Kazuo Minematsu

Abstract Spontaneous cervicocephalic arterial dissection (SCAD) has been recognized as an uncommon cause of cerebral stroke. Although it has been viewed as an important cause of stroke, especially in juvenile cases, its natural course and pathophysiology have yet to be fully clarified, and no treatment criteria have been established. Recent studies have suggested that clinical features of SCAD in Japan are different from those in European countries. Herein, we reviewed the current status of the management of SCAD in Japan, and clarified its clinical characteristics to establish an appropriate treatment.

Keywords Arterial dissection · Stroke · Carotid artery · Vertebral artery

Introduction and Background

In arterial dissection, since blood penetrates through an intimal tear of the arterial wall, splits the medial layer, and extends along the artery, a false lumen is created, resulting in stenosis or occlusion of the artery, or pseudaneurysm, which may induce bleeding extending through the outer layer. Spontaneous cervicocephalic arterial dissection (SCAD) has been recognized as an important cause of cerebral stroke, especially in juveniles. The recent development of diagnostic methods such as MRI and MRA has revealed that SCAD more frequently occurs and plays a more important role in cases of stroke than previously thought [1–6].

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The natural course and pathophysiology of SCAD are rather complicated and have yet to be fully clarified, since it can cause both ischemic and hemorrhagic stroke, and the healing mechanism or remodeling of the lesion may sometimes modify the pathophysiology. As for treatment, antithrombotic therapy has been performed for ischemic stroke, and surgical intervention has also been carried out to prevent the bleeding of the dissected lesion. Although the recent development of endovascular treatment has introduced alternative vascular reconstruction methods using stenting or coil embolization, the indication of treatment has yet to be established based on a prospective study with a high evidence level or a randomized clinical trial.

Recent clinical studies reported that the nature of SCAD in Japan may be very different from that of Europe and North America since a much higher incidence of SCAD of the intracranial vertebro-basilar artery and bleeding cases have been reported in Japanese patients. In order to clarify the pathophysiology of cerebral arterial dissection and to establish appropriate treatment in Japan, a study group has been organized supported by the Japanese Ministry of Health, Labour and Welfare research grant 18C-5; Spontaneous Cervicocephalic Arterial Dissections Study (SCADS). Herein, we reviewed the current status of SCAD management in Japan and clarified its clinical characteristics to establish appropriate treatment.

SCADS

SCADS is a multicenter registration study conducted by the SCAD Study Group supported by the Research Grant for Cardiovascular Diseases (18C-5) from the Ministry of Health, Labour and Welfare, Japan. Chair: K. Minematsu, National Cardiovascular Center and Vice Chair: T. Tsukahara, Kyoto Medical Center. The members of the Surgical Treatment working group of SCADS are: T. Tsukahara, National Hospital Organization (N.H.O.), Kyoto Medical Center

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Table 1 Site of SCADs registered in SCAD-1

Anterior Circulation	Right	Left	Bilateral	Total
ICA extracranial	5	6	0	11 (2%)
ICA intracranial	10	8	0	18 (4%)
MCA	7	9	0	16 (4%)
ACA	19	15	1	35 (8%)
Posterior Circulation	Right	Left	Bilateral	Total
VA extracranial	11	13	0	24 (5%)
VA intracranial	139	130	19	288 (63%)
BA	–	–	–	22 (5%)
PICA	8	18	0	26 (6%)
SCA	1	0	0	1 (0.2%)
PCA	3	3	1	7 (2%)
Multiple	–	–	–	6 (1%)

(M.C.), M. Yonekura, N.H.O., Nagasaki M.C., T. Inoue, N.H.O., Kyusyu M.C., K. Iihara, National Cardiovascular Center, A. Nishino, N.H.O., Sendai M.C., T. Takahashi, N.H.O., Nagoya M.C., S. Nakajima, N.H.O., Osaka M.C, H. Manabe, N.H.O., Hakodate M.C. A. Sato, Saitama Medical University, K. Hongo, Sinsyuu University.

SCADS is composed of two studies: SCADS-I is a retrospective multicenter registration study, and SCADS-II is a prospective multicenter registration study. In SCADS-I, 456 patients (men: 70%, median age of 54 years) were registered from 82 collaborating stroke and cardiovascular centers throughout Japan. A total of 288 patients (63%) had dissections of the intracranial vertebral arteries, and only 11 patients (2.4%) showed dissections of the extracranial carotid arteries. In this study, SCAD was diagnosed after ischemic stroke in 234 patients and after hemorrhagic stroke in 126 patients. Sixty-five patients were surgically treated (Table 1).

Etiology

SCADs are classified into those of the anterior circulation (carotid artery (ICDA)), and of the posterior circulation (vertebrobasilar artery (VADA)). The first clearly reported case of SCAD was a 41-year-old man with dissection of the left carotid artery described by Anderson and Schechter in 1959, followed by more detailed reports by Yamada et al. and Fisher et al [2, 8]. Since then, many European and North American reports have described dissection of the internal carotid artery (ICDA) [9–11]. Bogousslavsky et al. [12] analyzed 1,200 patients presenting with stroke, which was due to ICDA in 30 patients (2.5%). The outcome was poorer in these ICDA-related patients, with only 40% showing a favorable recovery.

On the other hand, the annual incidence of vertebral artery (VA) dissection is less frequent, being about 1/100,000 and 1.5/100,000 in the USA and Europe, respectively [6, 13–16]. The age at onset is slightly higher than in cases of carotid dissection.

VA dissection (VADA) can be classified into intra- and extracranial, with the latter being more frequent. The most commonly involved segments are V1 and V3 as they are highly mobile, while V2 is fixed within the transverse foramen. Dissecting aneurysm of the vertebral artery (DAVA) represents around 28% of the posterior circulation aneurysms and 3.3% of all intracranial aneurysms [17–20]. Subarachnoid hemorrhage (SAH) caused by DAVA may comprise less than 10% of all causes of non-traumatic SAH [14, 21], with a reported mortality ranging from 19 to 83% [22]. Intracranial dissection more generally causes SAH, while extracranial dissection leads to ischemia [11, 23–26]. In the series of Santos–Franco et al. [27], 73% of DAVA represented SAH, while 27% caused bulbar or cerebellar ischemic stroke.

In Japan, Yamaura et al. [28] performed a retrospective nationwide surveillance study in 1995, in which 357 non-traumatic intracranial arterial dissections were registered. According to this study, a markedly high incidence of SAH caused by VADA was noted as a Japanese characteristic of SCAD. SCAD-1 also showed that SCADs of Japanese occurred mainly in intracranial arteries, with the majority at the VA, followed by the anterior cerebral arteries (Table 1).

Symptoms

Symptoms of SCAD are divided into asymptomatic, ischemic, SAH, combined symptoms, and others. Over 75% of cases are accompanied by pain. Although most cases were formerly diagnosed after ischemic syndrome or SAH, the recent development of MR on CT scan has revealed many cases of asymptomatic SCAD or SCAD without neurological deficits other than headache. A characteristic clinical feature of ICDA is the sudden onset of pain of the unilateral head, neck, or face. ICDA in typical cases causes prominent neck and facial pain, headache, ipsilateral Horner's syndrome, episodes of ipsilateral cerebral ischemia, and retinal ischemia [1–4, 29]. Morki [3] reviewed 70 patients with ICDA, and reported that the most common symptom was headache (84%), followed by ischemic symptoms (TIA or stroke) in 61% and oculosympathetic paresis in 53%.

DAVA frequently causes SAH after rupture, as the wall of these aneurysms is sometimes extremely thin and friable [6, 14, 18, 21, 30–33]. The rebleeding rate is rather high, between 30% and 40%, most frequently within 24 h after the initial bleeding [3, 21, 33, 34]. Angiographic and autopsy-based studies reported that the healing process mediated by intimal hyperplasia begins 1 week after bleeding.

According to a Japanese study by Yamaura et al. [28], Japanese patients are more frequently accompanied by SAH or Wallenberg syndrome caused by VADA, since SCAD of intracranial arteries is more commonly accompanied by hemorrhagic symptoms.

Although in SCADS-1, more patients were registered by neurological clinics than in the previous study by Yamaura [28], in which more patients were registered by neurosurgical clinics, SAH comprised 28%, ischemic syndrome 52%, and others 14%. This shows that the characteristics of SCAD in Japanese are different from those in European patients.

Diagnostic Features of SCAD

The standard in diagnostic imaging is still represented by digital subtraction angiography (DSA). The diagnostic standard of SCAD shows arterial dilatation with stenosis or occlusion by angiography, such as double lumen or pearl and string signs. However, the recent development of MRI and MRA has facilitated the identification of lacerations of the arterial wall or thrombus adhesion. Hosoya et al. reported that a parallel MR view along the vertebrobasilar artery B-pasis useful for the diagnosis of VA dissection [35]. CTA or duplex ultrasonography can also show the double lumen (or intimal flap) of the dissected artery.

Treatment of SCAD

1. Medical treatment

Medical treatment using heparin or anti-platelet drugs has been recommended for ischemic symptoms caused by SCAD. The Japanese guideline for stroke treatment recommended preventive treatment by anti-platelet therapy as grade C1. In many ischemic cases of extracranial SCAD, cerebral infarction was frequently found in the distal arterial area including the cerebral cortex, which may be caused by artery-to-artery micro emboli from the dissected lesion. In such cases, anti-platelet therapy can prevent the enlargement of cerebral infarction. Indeed, it has been generally applied especially for SCAD of extracranial arteries. However, it may induce the enlargement of intramural hematoma in the dissected area. In cases of intracranial SCAD, as hematoma extension may induce fatal SAH, we have to select appropriate cases in which to apply anti-platelet therapy.

2. Surgical treatment

The indication for surgical intervention has not been fully established for ischemic cases, although vascular reconstructive surgeries have been performed and endovascular treatments using stents have been reported recently. For bleeding cases, there is mainly SAH surgical treatment, such as clipping for aneurysmal dilatation or the rupture site, trapping, or proximal ligation. However, a general consensus regarding the indication of this treatment has not been established.

1) Surgical treatment of SCAD of anterior circulation

For the prevention of ischemic symptoms caused by SCAD of extracranial carotid lesions, endarterectomy (CEA) or carotid stenting (CAS) may be considered as surgical intervention. However, the number of SCAD patients who have received these treatments is not large in Japan, because this is not a common lesion of SCAD among Japanese.

IC dorsal (anterior wall) aneurysm: ICDA arises from the anterior wall of the C1 or C2 portion of the internal carotid artery. Some of these aneurysms are recognized as dissecting aneurysms based on the intraoperative findings or postmortem pathology. Surgical treatment of ICDA is still a challenge because it may cause catastrophic bleeding during the operation.

A national surveillance study on ICDA in Japan was performed by Satoh et al. in 1996 [36]. In this study, a total of 365 cases of ICDA and 222 of SAH cases were registered. Twenty-three percent of the 222 SAH cases were diagnosed with dissecting aneurysms. According to the results of this study, the prognosis following surgical treatment for ICDA in the SAH acute phase was poor, but, on the other hand, the rebleeding rate was high with a delay in surgery. The establishment of a proper treatment guideline is necessary.

2) Surgical treatment of SCAD of posterior circulation

The management of DAVA is a technical challenge due to the histopathological features and localization [10, 37]. The proximal ligation of VA and trapping of VADA have been performed as surgical treatments for VADA. Although the proximal ligation of VA is not a technically complicated method, retrograde blood flow into the aneurysm sometimes causes enlargement of the AN and consequently rebleeding.

Although the trapping of VADA has also been performed with or without PICA reconstruction, the non-perfusion of small perforating arteries sometimes causes ischemia of the brain stem [13, 21, 23, 32, 35, 38, 39]. It is sometimes difficult to select patients who need reconstruction of PICA after trapping of VADA because the flow and the perfusion area of PICA are different in each case and intraparenchymal vascular anastomosis of the posterior circulation show a large variation. Surgical treatment working group of SCADS is now examining the necessity of PICA reconstruction after trapping of VADA.

3. Endovascular treatment of DAVA

1) Embolization of DAVA

Recent advances in endovascular treatment have facilitated the embolization of DAVA and proximal VA using a GDC coil. The balloon occlusion test (BOT) may be necessary when the occlusion area involves the origin of the PICA or the anterior spinal artery.

This technique is rather widely used and fairly satisfactory long-term results have been reported. However, severe and frequent complications have also been reported, such as ischemia of the brain stem or recanalization of the aneurysm [5, 31, 40–43].

Case 1:

Forty-six-year-old female

Present illness:

She was admitted to our hospital after the sudden onset of a severe headache. Although brain CT scan showed no intracranial bleeding, MRA and DSA angiography revealed a left VA aneurysm (Fig. 1a). Since the size of the aneurysm enlarged during the observation period, coil embolization was performed (Fig. 1b, c).

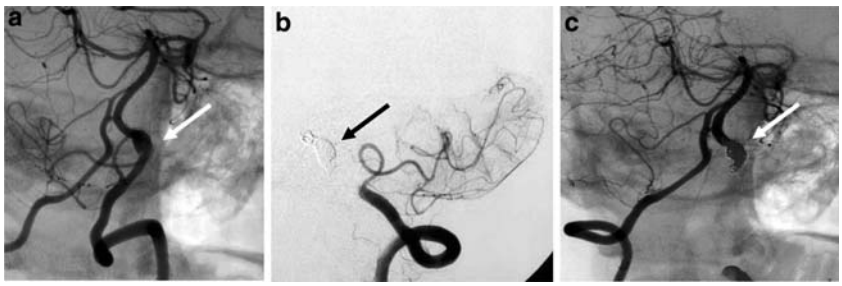

Fig. 1 (**a**) DSA angiography of the vertebrobasilar artery. A-P view showed a left vertebral artery aneurysm probably of a dissecting nature (*arrow*). (**b**) DSA angiography of the left vertebral artery after coil embolization. Lateral view showed complete embolization of the aneurysm (*arrow*) and the left vertebral artery with PICA preservation. (**c**) DSA angiography of the right vertebral artery after coil embolization. A-P view showed that the left vertebral artery aneurysm was embolized (*arrow*) and the basilar artery was well perfused from the right vertebral artery

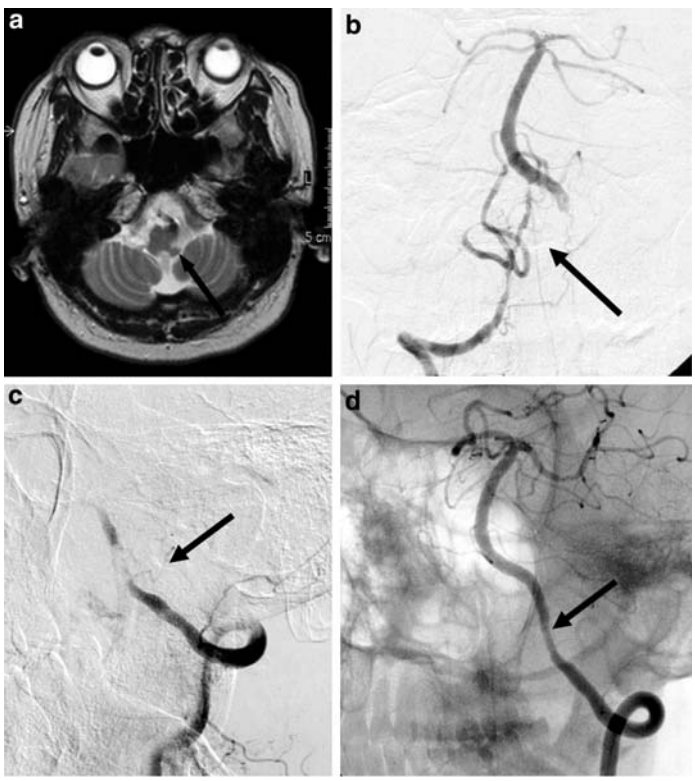

Fig. 2 (**a**) MRI T2WI on admission revealed infarction of the left lateral medulla (*arrow*). (**b**) and (**c**) DSA showed diffuse stenosis of the right vertebral artery (**b**; *arrow*) and severe tapered stenosis of the left vertebral artery (**c**; *arrow*). (**d**) left vertebral DSA showed that the stenotic lesion was well dilated after stent placement (**d**; *arrow*)

As the flow of the right VA was confirmed and the lesion was located in the distal PICA, coil embolization including the VA and aneurysm was performed without neurological complications.

1) Reconstructive procedure for DAVA

A reconstructive procedure has recently been developed. Endovascular stent placement can be performed for string-like stenosis or tapered occlusion of the VA when the ischemic symptom is progressive.

Larger, prospective series may be necessary to establish accurate criteria for the selection of appropriate cases for surgical management (clipping or trapping of the aneurysm) or endovascular treatment (coiling, stent-assisted coiling, or sole stenting)

Case 2:

Fifty-one-year-old female

She was admitted to the hospital after the sudden onset of ataxia and dysarthria. Brain MRI showed infarction of the left lateral medulla (Fig. 2a). Although medical treatment was performed using anti-platelet drugs, her ischemic symptom was progressive. DSA angiography showed diffuse stenosis of the right VA and severe left VA stenosis probably of a dissecting nature (Fig. 2b, c).

Endovascular VA reconstructive treatment was performed using a stent for the left VA stenosis (Fig. 2d). She was discharged from our hospital with mild dysarthria. Follow-up angiography 8 months after the treatment showed no restenosis of the left VA.

4. Hemorrhagic VA dissection

As for dissections of the vertebral arteries (VADA), which are most frequently reported in Japan, especially for bleeding cases, endovascular treatment is widely applied, particularly in Japan. At the time of selecting treatment, we have to consider the VA size of the contralateral side and PICA location. If the basilar artery is perfused by contralateral VA, the complication rate is lower after the trapping or coil embolization of AD, although an occlusion test may be necessary before surgery if the basilar artery is not perfused by contralateral VA or the contralateral VA is hyperplasic. In such a case, the reconstruction of PICA by OA–PICA anastomosis is necessary to prevent ischemic complications.

Surgical treatment – SCADS-1 in Japan

Sixty-five patients registered in SCADS-1 received surgery. As summarized in Table 2, eight different surgical procedures were performed for the affected arteries and seven other surgeries were performed. Statistical analysis may be not suitable since the number of surgeries was too small and the pathophysiology of each case was so varied, and so further analysis is necessary to investigate the surgical results regarding SCAD. However, the prognosis was not better in the surgically treated group overall when compared with the modified Rankin scale (mRS) of the endovascular treatment group 3 months after treatment (Table 3).

Table 2 Surgical treatment in SCAD-1

	Number of cases	Mean prognosis (mRS)
Clipping	7	3.86
Coating	1	6.00
Wrapping	2	0.50
Proximal ligation without bypass	4	1.25
Proximal ligation with bypass	7	2.71
Trapping without bypass	22	2.36
Trapping with bypass	10	1.60
Bypass	5	1.00
Others	7	4.43

Table 3 Prognosis following surgical treatment and endovascular treatment in SCAD-1

	mRS		0	1	2	3	4	5	6	Mean
SAH	Total	140	46	22	12	10	12	14	24	2.41
	Surgical	38	11	2	4	3	6	9	3	2.78
	Endovascular	73	26	13	7	6	7	6	8	2.07
CI		215	73	67	30	21	13	9	2	1.39
	Surgical	6	2	1	1	0	0	2	0	2.17
	Endovascular	13	2	4	4	2	0	0	1	1.85

The prognosis was not better in the surgically treated group overall
Further analysis of the surgical results regarding SCAD is necessary

In conclusion, SCAD-1 showed that SCADs of Japanese occurred mainly in intracranial arteries, with the majority at the VA, followed by the ACA and that ischemic stroke with SCADs was more common and associated with a better outcome compared to hemorrhagic cases. Further study is necessary to investigate the surgical results of SCADs.

Conflicts of interest statement We declare that we have no conflict of interest.

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Chapter 6
Incidence of Intracranial Arterial Dissection in Non-emergency Outpatients Complaining of Headache: Preliminary Investigation with MRI/MRA Examinations

Hiroshi Manabe, Kazuya Yonezawa, Takaaki Kato, Kentaro Toyama, Koichi Haraguchi, and Takeo Ito

Abstract *Purpose*: Headache is recognized as one of the specific signs of intracranial arterial dissection (ICrAD). We clarified the incidence of ICrAD in non-emergency outpatients complaining of headache and the nature of headache observed in case of ICrAD.

Patient population and methods: Consecutive non-emergency outpatients coming to the neurological and neurosurgical departments and who underwent MRI and MRA examinations were included in this study. The diagnosis of ICrAD was made when patients met the following two conditions: (1) pearl-and-string sign, pearl sign, or string sign on MRA, and (2) high arterial wall signal on T1 images or intimal flap on T2 images. If possible, cerebral angiography and/or black blood MRI and/or surface-image MRI was also performed in cases meeting these criteria.

Results: (1) Headache group (172 patients): severe headache was seen in five patients and headache of sudden onset in three. Arterial dissection was diagnosed in eight patients (4.7%, including seven cases of asymptomatic vertebral dissection and one of basilar dissection). The headache noted in most cases of ICrAD was similar to that experienced in daily life. (2) Non-headache group (201 patients): complaints included vertigo/dizziness in 52 patients, gait disturbance in 28, weakness of the arm or leg in 20, and limb numbness in 18, syncope attack in 14, and others in 69. Arterial dissection was diagnosed in six patients (3.0%, including one case of asymptomatic basilar and two of vertebral artery dissection, symptomatic two vertebral and one basilar dissection).

Conclusion: We obtained no evidence of significant difference in the incidence of ICrAD in non-emergency outpatients with (4.7%) and without headache (3.0%). The nature of the headache in the cases of ICrAD was similar to that experienced in daily life. ICrAD with nonspecific headache is more common than previously thought.

Keywords Intracranial arterial dissection · Headache · Incidence

Introduction

Headache is well known as a common symptom of cervical spontaneous arterial dissection, and is reported in 60~75% of cases of cervical internal carotid dissection (CIAD) and in about 70% of cases of cervical vertebral dissection (CVAD) [1]. The headache is the initial sign in about half of the cases of CIAD and in one-third of the case of CVAD, and typically occurs on the same side of the dissection, followed by neurological symptoms with a delay of several hours to several days, with about 20% of cases having a history of migraine [1].

Intracranial arterial dissection (ICrAD) mainly occurs in the vertebrobasilar artery and may cause both cerebral ischemia and intracranial hemorrhage [2–4]. Several reports have suggested that headache is also one of the symptoms of ICrAD, and that it is occasionally the initial sign of dissection followed by major stroke [2, 4, 5], as associated with cervical arterial dissection. According to one report, headache was the only symptom of dissection [6]. Hosoya et al. [2], in an examination of 31 cases of intracranial vertebrobasilar dissection, reported that severe headache without subarachnoid hemorrhage was seen in eight cases, while in 14 cases no headache was noted. This suggested that the nature of headache associated with ICrAD may vary.

Considering the variety of types of headache reported in cases of ICrAD, we hypothesized that patients complaining of mild headache similar to that experienced in daily life may have ICrAD. In this study, we performed Magnetic Resonance Imaging (MRI) and Magnetic Resonance Angiography (MRA) examinations to detect ICrAD in

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consecutive non-emergency outpatients, and clarified the incidence of ICrAD and the nature of headache in cases of ICrAD.

Clinical Materials and Methods

From June 2006 to June 2008, consecutive non-emergency outpatients were prospectively examined to detect ICrAD with 1.0, 1.5, or 3.0 Tesla MRI/MRA. Both of two criteria for the diagnosis of ICrAD had to be met: (1) Pearl-and-string sign, pearl sign, or string sign on MRA, and (2) high intensity arterial wall signal on T1 images or intimal flap on T2 images. Following the acquisition of informed consent from patients, angiography and/or surface-image MRI (3D Fast image employ steady state acquisition: 3D FIESTA, or Basiparallel anatomic scanning MR Imaging: BPAS) and/or black blood MRI was also performed to confirm arterial dissection. All patients were checked to determine whether they had headache, and the incidence of ICrAD was compared between patients with and without headache.

Results

Three hundred seventy-three patients were included in this study. Patient age ranged from 8~88 (mean 61.2) years, and there were 159 males and 214 females. Of them 172 patients complained of headache (headache group) while 201 patients complained of symptoms other than headache (non-headache group). ICrAD was detected in 14 cases (3.7%). In the 14 cases of ICrAD, no fresh infarction or bleeding related to ICrAD was detected on MRI.

Headache group (Table 1, Fig. 1). One hundred seventy-two patients were included. Patient age ranged from 8~84 (mean 57.2) years, and there were 67 males and 105 females. The headache was located mainly in the occipital region in 54 patients, temporal region in 12, frontal region in 11, periorbital region in 3, hemi-cranial region in 6, and was non-localized in 86. The headache was severe in 5 patients and mild in 167. The headache appeared suddenly in 3 patients and not suddenly in 169 patients.

In this group, eight patients with ICrAD were detected, so that the incidence of ICrAD in the headache group was 4.7%. Age ranged from 56 to 84 (mean 66.5) years. Four patients were male. ICrAD was on the vertebral artery in seven patients and on the basilar artery in one. In none of the eight patients we detected any findings of stroke related to the dissection on MRA. The pain was mild in all eight patients, and appeared suddenly in one of them. Headache was mainly in the occipital region in six patients and in the temporal region in one. In the other one patient, headache was not localized.

Table 1 Patient profile in headache group (172 patients)

Age	8~84 (mean, 52.7) years
Gender	Male/female: 67/105
Headache location:	
Nonlocalized	86
Hemi-cranial	6
Occipital	54
Temporal	12
Periorbital	3
Frontal	11
Nature	Severe/mild: 5/167
	Sudden/not sudden in appearance: 3/169
Dissection	8 (4.7%)
Age	56~84 (mean, 66.5) years
Gender	Male/female: 4/4
Location	Vertebral 7, basilar 1
Headache	
Location	Not localized 1, temporal 1, occipital 6
Nature	Severe/mild: 0/8
	Sudden/not sudden appearance: 1/7
Stroke	No 8, Yes 0

Non-headache group (Table 2, Fig. 2). Two hundred and one patients were included. Age ranged from 17 to 88 (mean 64.6) years. Ninety-one patients were male. The chief complaint was vertigo or dizziness in 52 patients, gait disturbance in 28, limb weakness in 20, limb numbness in 18, speech disturbance in 4, syncope in 14, tinnitus in 2, and others including head discomfort in 63.

In this group, six patients with ICrAD were detected, so that the incidence of ICrAD in the non-headache group was 3.0%. Of them, two presented with TIA, while the others were asymptomatic. Age ranged from 49 to 80 (mean 65.3) years. Four patients were male. ICrAD was on the vertebral artery in four patients and on the basilar artery in two. The chief complaint of patients with ICrAD in this group was vertigo in two patients, floating sensation in one, involuntary movement of a lower limb in one, limb weakness in one, and syncope in one.

Difference in the incidence of ICrAD between the groups. Incidence of ICrAD did not differ significantly between the headache and non-headache groups ($p=0.4$, $\chi 2$ test).

Discussion

Several reports have suggested that severe headache is the initial or only specific sign of ICrAD [2, 4]. As ICrAD occurs commonly on the vertrebrobasilar artery, the headache related to ICrAD has been believed to be severe occipital

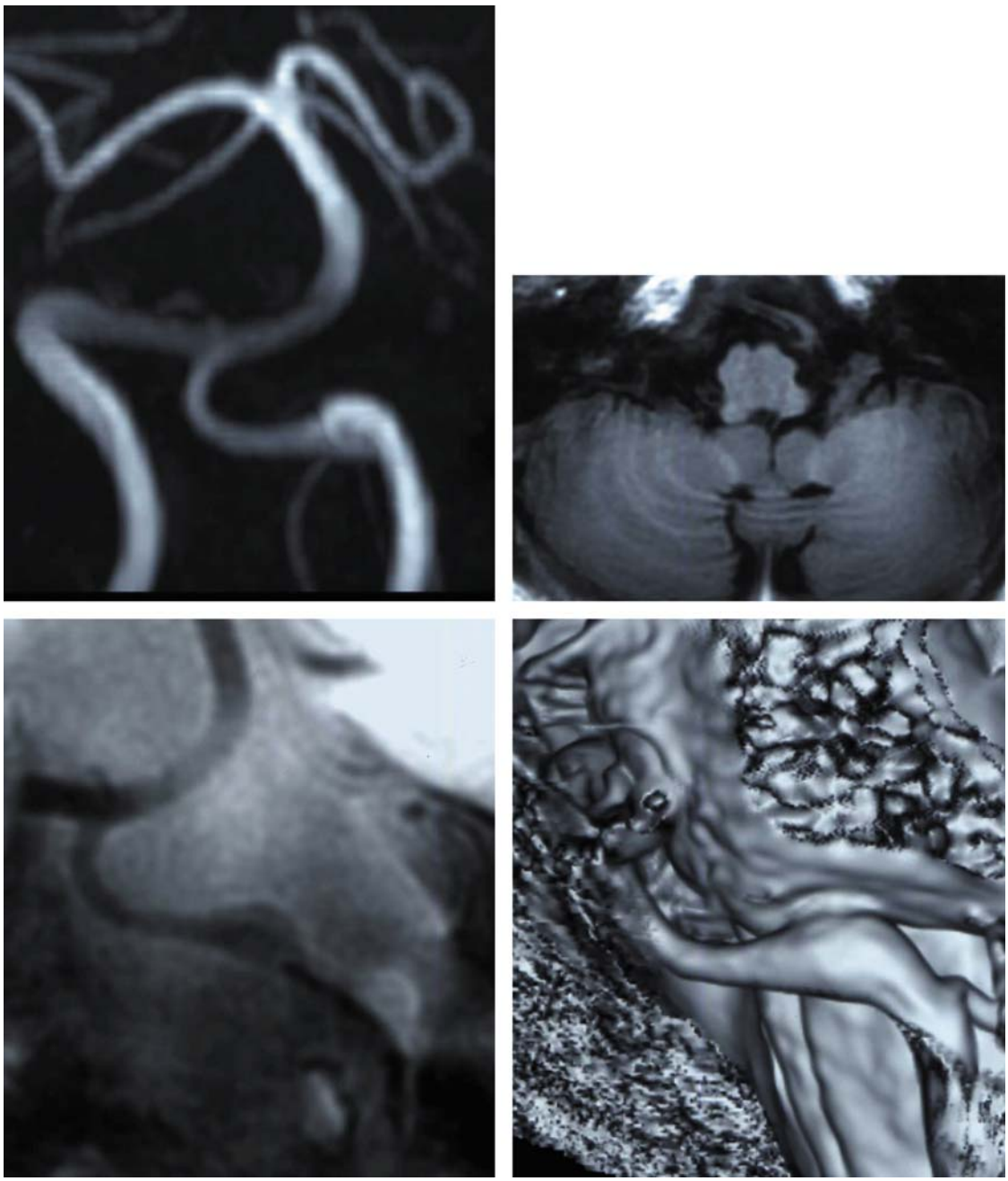

Fig. 1 Sixty-year-old man complaining of chronic mild occipital pain. He had no history of stroke. MRA showed fusiform dilatation of the left vertebral artery (*upper left*). A high-intensity area was seen in the left vertebral wall on T1 image (*upper right*). Black blood MRI revealed a slightly high intensity area in the dilated portion of the left vertebral artery (*lower left*). 3D FIESTA MRI revealed that the surface of the left vertebral artery exhibited a sausage-like dilatation (*lower right*)

pain. But this widely accepted recognition was based on limited data collected from cases suffering from SAH or major ischemic symptoms. Hosoya et al. [2] reported clinical features and neuroradiological findings of vertebrobasilar dissection among 31 patients, of which three were incidentally detected. In the report headache was noted in 17 cases (55%) including three cases of subarachnoid hemorrhage, and headache was not severe in six cases. This suggested that a severe headache may not always occur in case of ICrAD.

In this study, no difference was found in the incidence of ICrAD between the headache and non-headache groups, and that headache seen in all eight patients with ICrAC was not severe, but was similar to that experienced in daily life. This

Table 2 Patient profile in non-headache group (201 patients)

Age	17~88 (mean 64.6) years
Gender	Male/female: 91/110
Complaint	
Vertigo/dizziness	52
Gait disturbance	28
Limb weakness	20
Limb numbness/dysesthesia	18
Speech disturbance	4
Syncope	14
Tinnitus	2
Others	63 (discomfort of the head and others)
Dissection	6 (3.0%)
Gender	Male/female: 4/2
Age	49~80 (mean, 65.3) years
Complaint	
Vertigo/dizziness	2
Gait disturbance	1
Involuntary movement of lower limb	1
Transient limb weakness	1
Syncope	1
Location	Vertebral 4, basilar 2
Stroke	Yes 2 (TIA), No 4

suggests that ICrAD with nonspecific headache may be more common.

In this study, the incidence of ICrAD was 3.7%. All the ICrAD were in the vertrobasilar system. The incidence of ICrAD is still unclear. Postmortem pathologic investigation of the vertebral arteries of 94 patients who died suddenly of causes other than subarachnoid hemorrhage and aortic dissection in the Tokyo area, reported by Saito et al. at the Annual Meeting of the Japanese Neuropathological Society in 2003 in Nagoya, revealed that a gap of internal elastic lamina with organization, which was considered an initial pathological finding of arterial dissection, was observed in ten cases (10.9%). These findings suggest that asymptomatic vertebral dissection is not rare. We believe that asymptomatic IcrAD, especially in the vertebrobasilar system, may be more common than previously believed.

Conclusion

We found no evidence of significant difference in the incidence of ICrAD in non-emergency outpatients with (4.7%) and without headache (3.0%). The headache seen in many cases of ICrAD may be non-specific, similar to that experienced in daily life. Moreover, asymptomatic ICrAD may be more common than previously thought.

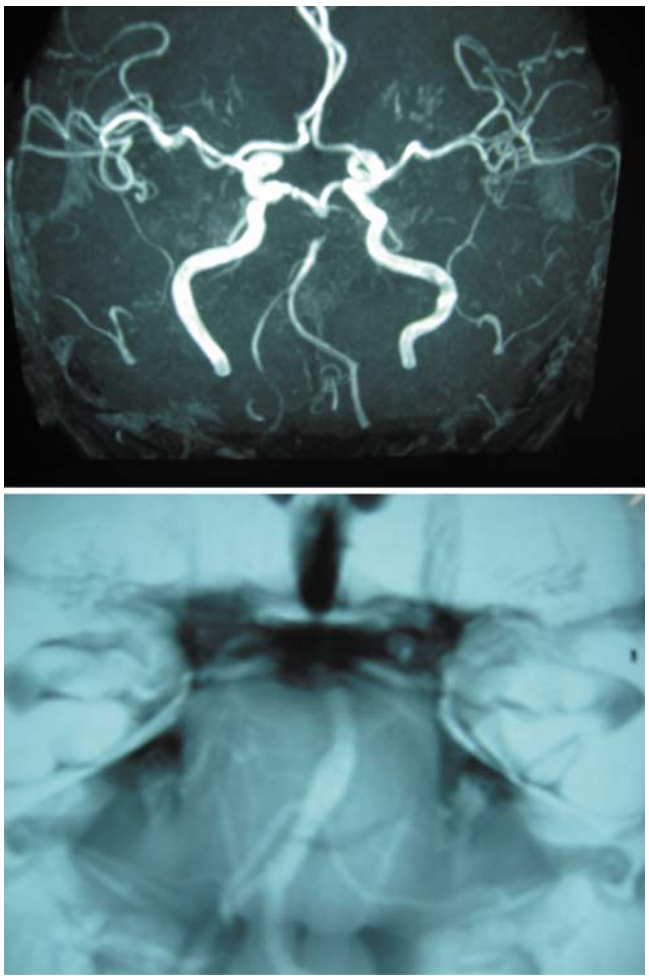

Fig. 2 Forty-nine-year-old female with transient right hemiparesis. She had had no headache. A high-intensity area was noted in the basilar artery on T1 image (*upper left*). MRA revealed occlusion of the upper basilar artery (*upper right*). Angiography revealed pearl-and-string sign on the basilar artery (*lower left*), the outer appearance of which was a sausage-like swelling on BPAS-MR imaging (*lower right*)

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Chapter 7
A Study of Vertebrobasilar Artery Dissection with Subarachnoid Hemorrhage

S. Nakajima, T. Tsukahara, and K. Minematsu

Abstract We retrospectively studied clinical characteristics of 368 patients with cerebral artery dissections who were diagnosed in 172 Japanese hospitals. Of these patients, 130 (35%) presented with subarachnoid hemorrhage, 217 (59%) with cerebral infarctions, and 21 (6%) with transient ischemic attacks. We analyzed 109 (84%) subarachnoid hemorrhage cases caused by vertebrobasilar artery dissection to evaluate conservative and surgical treatment from the viewpoint of postoperative rerupture and infarction.

Subsequent ruptures were observed in 14% of the 21 cases with nonsurgical treatment. For the preventive purpose of rerupture, 88 patients received surgical interventions: 68 trappings, 13 proximal occlusions, 6 aneurysmal sac occlusions and 1 stenting. Rerupture was experienced in 33% of the aneurysmal sac occlusion patients while not occurring in the other three surgical interventions. In the group without vascular anastomosis, postoperative cerebral infarction was observed in 25% of the trapping, none of the proximal occlusion and 33% of the aneurysmal sac occlusion cases.

In this study, aneurysmal sac occlusion treatments were more frequently complicated by rerupture or cerebral infarction postoperatively than the other treatment methods. It was difficult to determine which surgical treatment can achieve better surgical outcome among the proximal occlusion and trapping with or without vascular anastomosis.

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Keywords Vertebrobasilar artery dissection · Subarachnoid hemorrhage

Introduction

In the western countries, most of the cerebral artery dissections have been observed in carotid artery resulting in cerebral infarction [1, 2]. For this reason, the main purpose of the treatment is to prevent cerebral infarction using medication. However, the majority of cerebral artery dissection in Japanese people occurs in the vertebrobasilar artery area [3]. It can cause either cerebral infarction or subarachnoid hemorrhage so that the treatment strategy tends to become more complex [3]. Therefore, we conducted a retrospective observation study, Spontaneous Cervicocephalic Arterial Dissections Study Japan (SCADS-Japan) to determine which surgical treatment is more effective for vertebrobasilar artery dissection resulting in subarachnoid hemorrhage.

Materials and Methods

We studied 368 cervicocephalic dissection patients with either subarachnoid hemorrhage, cerebral infarction or transient ischemic attack from 172 hospitals registered for SCADS-Japan. Cerebral artery dissection was diagnosed by cerebral angiography, MR angiography or three-dimensional CT angiography between April 2003 and March 2006. There were 260 (71%) male patients with an average age of 53 (range 13–88). Of these patients, 130 (35%) presented with subarachnoid hemorrhage, 217 (59%) with cerebral infarctions, and 21 (6%) with transient ischemic attacks. In the 130 subarachnoid hemorrhage cases, 109 patients were caused by vertebrobasilar artery dissection. We analysed the results of these 109 patients to examine postoperative complications such as rerupture and infarction.

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Results

Outcome in Conservative Treatment

In the 109 cases with vertebrobasilar artery dissection resulting in subarachnoid hemorrhage, conservative treatment was selected in 21 patients and rerupture was experienced in 8 patients among them. The cumulative rerupture rate was 6.9% on the onset day, 11.1% on the following 2 days, and 14% thereafter.

Outcome in Surgical Treatment

Characteristics of four types of surgical treatment utilized in this study were shown in Fig. 1. Trapping, performed in craniotomy and endovascular surgery, is supposed to exclude blood flow from the dissecting region, having risks of subsequent cerebral infarction. Proximal occlusion is to reduce the blood flow of the region, inheres the risk of rerupture or infarction. Aneurysmal sac occlusion can keep the normal blood flow of the vessel but still has a risk of surgical complications. Stenting is a relatively new treatment to vertebrobasilar dissection in Japan.

Surgical treatment was performed in 88 patients (Fig. 2). The trapping was given to 68 patients (12 craniotomies and 56 endovascular) but 17 of them had postoperative infarction. The proximal occlusion was performed in 13 patients (five craniotomy and eight endovascular) with no complications. The aneurysmal sac occlusion was conducted for six patients (two craniotomy and four endovascular). Rerupture was experienced in two cases and postoperative infarctions in other two patients. There was the only one stenting treatment without postoperative events.

In the trapping surgery, to avoid postoperative infarction, bypass surgery between extracranial and intracranial arteries, for example, occipital artery (OA) and posterior inferior cerebellar artery (PICA) has been performed. Among 66 trapping cases with a single lesion of vertebrobasilar artery dissection, six cases had bypass surgeries but not the remaining cases. The percentages of postoperative infarction in the two groups with and without anastomosis were not statistically different.

Figure 3 shows the further breakdown by the locations of dissection. There are three types of dissecting locations such as distal to PICA, involvement of PICA and proximal to PICA. Superficial temporal artery–superior cerebellar artery anastomosis was performed in the bypass surgery for the region of distal to PICA. In any of three types of dissecting locations, there were no significant differences in the occurrence of postoperative infarction between the groups with bypass surgery and without.

Discussion

Epidemiology

We retrospectively investigated cervicocephalic artery dissections. Approximately 30% (109 cases) of the 368 cases presented subarachnoid hemorrhages due to vertebrobasilar dissections. The previous nationwide study of non-traumatic intracranial arterial dissection in Japan between 1995 and 1996 showed that subarachnoid hemorrhage was observed in 58% of the 357 cases and vertebrobasilar dissection was detected in 88% of the 322 cases with a single lesion [3]. In the western countries, on the contrary, dissection was experienced more extracranially than intracranially [4, 5], occurred more in carotid artery than vertebrobasilar artery, and resulted in more cerebral infarctions than subarachnoid hemorrhage [1, 2, 6].

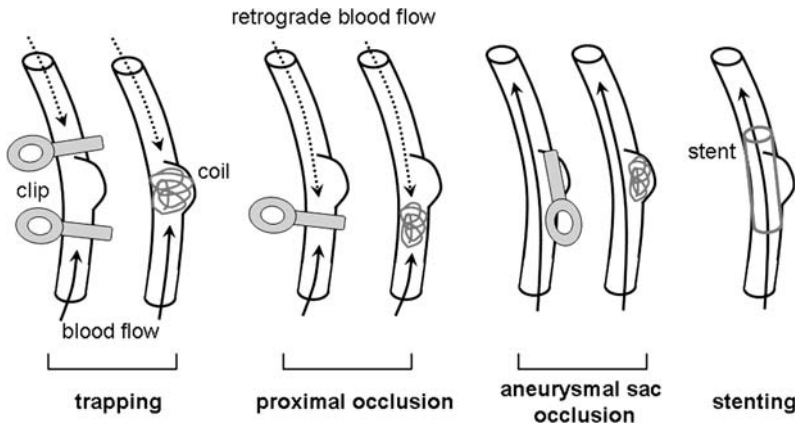

Fig. 1 Four types of surgical treatments: trapping, proximal occlusion, aneurysmal sac occlusion and stenting. The former three treatments can be performed by either craniotomy or endovascular surgery. Only in the proximal occlusion cases among four procedures, retrograde blood flow to the dissecting part still remains

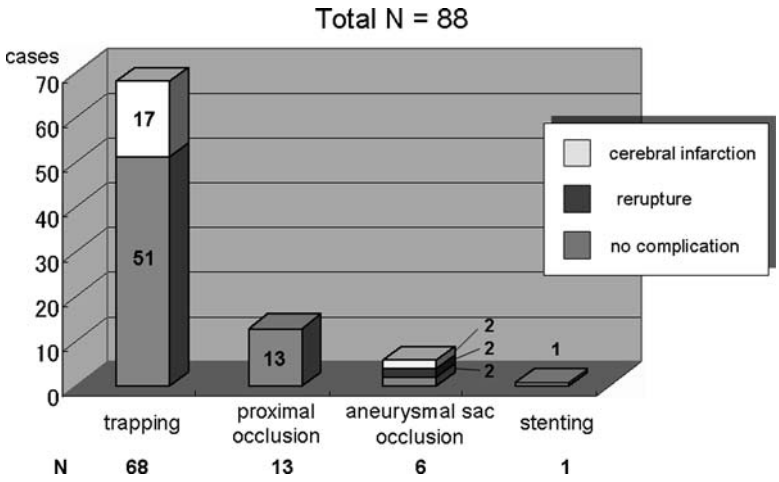

Fig. 2 Outcome of four types of surgical treatments. N: number of cases

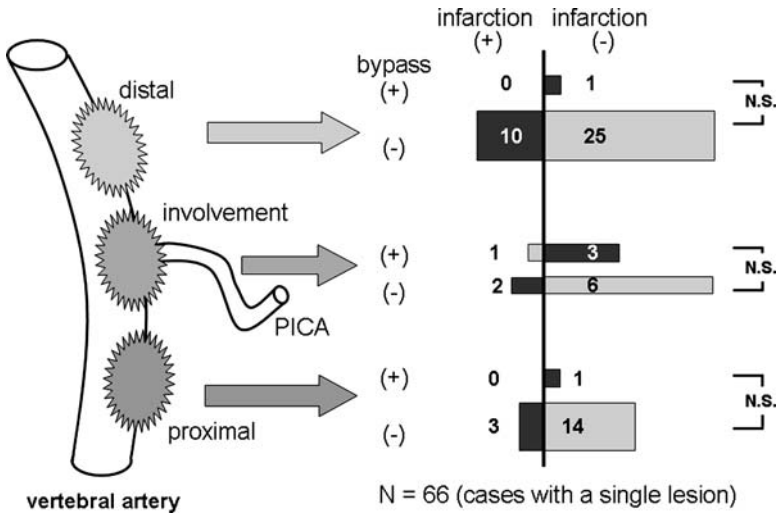

Fig. 3 Breakdown by locations of dissections. Dissecting locations were classified as three types: distal to PICA (posterior inferior cerebellar artery), involving PICA and proximal to PICA. There were no statistical differences in the occurrence of postoperative infarction between the groups with and without bypass surgery. N: number of cases. N.S.: not significant

Surgical Strategy

Some vertebrobasilar dissections with subarachnoid hemorrhage healed naturally [7–11], but many of the cases experienced rerupture in the acute phase and become critical in that situation [9, 11–13]. In our study, cumulative rerupture rate in the conservative treatment group was 14% after 3 days from the onset and thereafter. Thus, the main purpose of the treatment in the acute phase is to prevent rerupture [9, 12, 13].

Four major types of surgical treatments for vertebrobasilar dissection with subarachnoid hemorrhage such as trapping, proximal occlusion, aneurysmal sac occlusion and stenting have been utilized, combined with various vascular anastomosis when necessary [14]. Trapping, proximal occlusion and aneurysmal sac occlusion can be conducted in either craniotomy or intravascular therapy, while stenting is solely performed intravascularly [15]. In our study, there were 12 craniotomies and 56 endovascular surgeries for trapping, 5 craniotomies and 8 endovascular surgeries for proximal occlusion, and 2 craniotomies and 4 endovascular surgeries for aneurysmal sac occlusion.

Trapping

Trapping is performed in either craniotomy or intravascular surgery to prevent rerupture [8, 10, 14–19]. Postoperative infarction after trapping can occur due to hemodynamic changes or perforator injuries [20]. When a dissecting region is proximal to or including PICA, it could be effective to prevent postoperative infarction in the PICA region by bypass surgery, such as OA–PICA anastomosis [9, 19, 21]. There has been no study about whether there is a significant difference in the occurrence of postoperative infarction between trapping surgery with the OA–PICA bypass and without. In our study,

there was no significant difference between the bypass and no-bypass groups (% of infarction: 16% vs. 25%).

Proximal Occlusion

Proximal occlusion in craniotomy and intravascular surgery is known as another effective method for preventing rerupture of the dissections and postoperative cerebral infarction [7, 9–11, 14, 15, 17, 19, 20, 22, 23]. In our study there was no postoperative rerupture or no infarction in proximal occlusion cases, although we have to recognize that rerupture after proximal occlusion and postoperative infarction have been reported in several cases [7, 9, 11, 15, 16, 20, 23, 24].

Aneurysmal Sac Occlusion

Aneurysmal sac occlusion surgery can be another effective method [17, 23]. In our six experiences of aneurysmal sac occlusion surgery, reruptures were experienced in two cases as reported in previous studies [9]. We also had postoperative infarction in another two cases, although aneurysmal sac occlusion was expected to keep the original blood flow away from the region. The differences in surgical outcomes in various studies can be confounded by the limited number of cases, and variations of aneurysmal sac occlusion surgery [25, 26], complexity of anatomy [17], and surgeons' skills in each individual case.

Stenting

Stenting, as a reconstructive surgery, keeps the original blood flow while repairing the dissection. In Japan, there aren't sufficient data to evaluate the effectiveness of stenting for cervicocephalic artery dissection because it is not covered by Japanese universal health insurance. Stenting will become an effective therapeutic option for cervicocephalic artery dissection, considering that many clinical experiences with the use of stenting in other countries have shown better outcomes than conventional surgeries [27–31].

Conclusions

We studied 109 subarachnoid hemorrhage cases caused by vertebrobasilar artery dissection in Japan. The surgical outcome was evaluated by prevention of both postoperative rerupture and infarction. The trapping and proximal occlusion seemed to have the better outcome than aneurysmal sac occlusion. It was difficult to determine the better surgical method and the necessity of bypass surgery to achieve the therapeutic goal among the four types of interventions performed. Our result might be influenced by the limited number of cases as well as confounded by anatomical complexity, surgical skills and other factors in each individual case. Further study needs to be conducted.

Conflicts of interest statement We declare that we have no conflict of interest.

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Chapter 8
Surgical Treatment of Intracranial VA Dissecting Aneurysm

Koichiro Takemoto, Hiroshi Abe, Ken Uda, and Tooru Inoue

Abstract *Object*: Intracranial VA dissections are reported to cause headache, brain stem infarction, and SAH with an associated high morbidity and mortality. We aimed to clarify both the clinical characteristics and effectual treatment of intracranial VA dissections, and to present a retrospective analysis of our experience in the treatment.

Material and method: Between 1995 and 2007 we experienced 62 VA dissections in our institution. Fourteen of 62 (23%) cases of VA dissections were associated with aneurysm, and received surgical treatment. Five of fourteen cases presented with SAH, 8/14 cases with ischemia, 1/14 cases with headache.

Results: In the hemorrhagic group, internal trapping of aneurysm (ITA) was successfully performed in four cases. In one case, bypass surgery was followed by ITA, while one case with treatment-related complication was observed. But Glasgow Outcome Scale (GOS) of almost all cases was severe; 2/5 cases showed good recovery (GR), and 3/5 cases had severe disability. In the non-hemorrhagic group, proximal clipping or trapping was performed in 4/9 cases. Bypass surgery followed by proximal clipping or trapping was performed in 2/9 cases, and ITA in 1/9 case. One case showed treatment-related complication. GOS was GR in all cases.

Conclusion: Outcome in the hemorrhagic group was more severe as compared to the non-hemorrhagic group. The surgical strategy should be planned according to the location of the aneurysm and the origin of PICA.

Keywords Vertebral artery · Dissecting aneurysm · Direct surgery · Endovascular therapy

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Introduction

VA dissection has recently gained attention as a relatively common cause of stroke since the introduction of MRI as a diagnostic technique. This entity is mainly divided into two types: a hemorrhagic type, which presents with SAH, and a non-hemorrhagic type which presents with an ischemic symptom and/or a headache. Previous studies have shown that patients of the hemorrhagic type have a higher incidence of rebleeding (24–30%), and a high mortality rate at the time of recurrent bleeding. Therefore it has been proposed that these cases should undergo early repair of aneurysm by direct surgery or endovascular procedure. On the other hand, according to few large series that have been reported, the non-hemorrhagic type usually is of a benign nature. But an optimal management has not been established yet. We aimed to clarify the clinical characteristics and effectual treatment of intracranial VA dissections, and to present a retrospective analysis of our experience in the treatment of these dissections.

Materials and Methods

Between 1995 and 2007, we experienced 62 VA dissections at the National hospital organization Kyushu Medical Center. During this period, 14 cases comprising approximately 23% of the total number of VA dissections were associated with aneurysm and also received surgical treatment. In the hemorrhagic group, endovascular methods (internal trapping of the aneurysm or proximal occlusion of the parent artery) were performed as first line therapy. In the non-hemorrhagic group, direct surgery (trapping of the aneurysm or proximal clipping of the parent artery with or without bypass surgery) was performed as first line therapy. The diagnosis was made based on characteristic features demonstrated on both conventional angiography and MRI (pearl and string sign, string sign, tapered occlusion, intimal flap and intramural

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hematoma on T1 weighted image). The location of each aneurysm was classified into one of three groups: proximal to the PICA, involving the PICA, distal to the PICA. We reviewed the clinical treatment and examined the safety and management outcomes of our strategy retrospectively.

Results

Patient Population

Mean age of the 14 patients (12 men and 2 women) was 51.2 years (range 38–62 years). Five patients presented with SAH, eight with ischemic symptoms, and one with headache.

Hemorrhagic Group

Among the five patients presenting with SAH (four men and one woman) (Table 1), the aneurysms were located distal to the PICA in four patients, no aneurysms were located proximal to the PICA or involved the PICA. One aneurysm was located at the fenestrated VA, and the PICA originated from a different lumen. At admission, clinical grading based on H&K was assessed: grade III: two patients, grade IV: two patients, grade V: one patient. The representative case is described.

Case1: 54-year-old woman presented with H&K grade III SAH. The initial CT scan revealed diffuse SAH. Angiography revealed a dissecting aneurysm at the fenestrated right VA, and the PICA originated from another lumen of it. Contralateral VA was hypoplasia distal to the PICA. One month later, she underwent a balloon test occlusion (BTO) when a silicone balloon was placed within the right VA and was expanded for 15 min. The BTO was not tolerated, and so we performed the STA–SCA anastomosis in advance. Following the successful bypass surgery, the aneurysm was occluded with a pack of GDCs, preserving the lumen of the fenestrated VA that originated from the PICA. Follow-up angiography revealed complete obliteration of the aneurysm. There was no evidence of an ischemic lesion on diffusion-weighted MR images (Fig. 1).

Management Outcomes in the Hemorrhagic group

Complete obliteration of the aneurysm was obtained in all cases. ITA was performed without any treatment related

Table 1 Summary of patients with VA dissecting aneurysms with SAH

Case No.	age sex	H&K grade	aneurysm location	treatment		treatment-related morbidity	GOS	mRS
				procedure	Day post SAH			
1	54F	III	R. fenestration	STA-SCA/ITA	46/53	none	GR	0
2	62M	V	L. distal	ITA	59	none	SD	4
3	58M	IV	R. distal	ITA	1	none	GR	0
4	58M	IV	R. distal	ITA	1	none	SD	4
5	52M	III	L. distal	ITA	1	B.I.	SD	4

H&K grade: Hunt & Kosnik grade, GOS: Glasgow outcome scale, mRS: modified Rankin scale, M: male, F: female, ITA: Internal trapping of aneurysm, STA-SCA: STA-SCA bypass, GR: good recovery, SD: severe disability B.I.: Brain infarction.

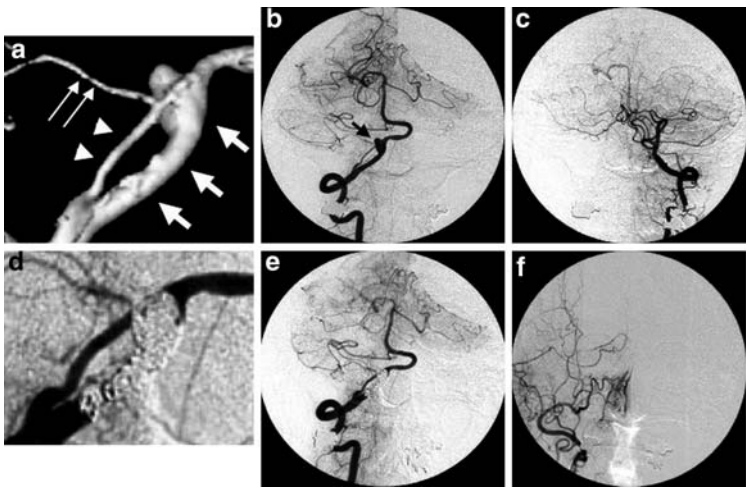

Fig. 1 *Case 1*. A 54-year-old woman presented with a H&K grade 3 SAH. (**a**, **b**) Angiography revealed a dissecting aneurysm at the fenestrated right VA (*large arrows*), and the PICA (*small arrows*) originated with another lumen of it (*arrow heads*). (**c**) Contralateral VA was hypoplasia distal to the PICA. (**d**, **e**) The aneurysm was occluded with a pack of GDCs, preserving the lumen of the fenestrated VA that originated with the PICA. (**f**) Right ECAG after STA–SCA anastomosis

complication in four patients. Only one patient in whom the aneurysm was located distal to the PICA experienced brainstem infarction after ITA. Treatment-related morbidity rate was 20%. Among the five patients who presented with SAH, the final outcomes were good recovery in two patients, severe disability in three patients (Table 1).

Non-Hemorrhagic Group

We experienced 57 non-hemorrhagic VA dissections. Of the 57 patients, 49 patients (86%) presented with ischemic symptoms, eight patients (14%) had headache as the initial symptom. Fifteen patients (26%) harbored aneurysmal dilatation. Indication for treatment was limited to cases with large aneurysm, progressive enlargement of an aneurysmal dilatation, and recurrent ischemic symptoms. Among the non-hemorrhagic group, the aneurysms were located at the PICA in two patients, involving the PICA in three patients, distal to the PICA in two patients, aplasia of the PICA in one patient, and the PICA origin in one patient. Management strategy was according to the location of the aneurysms: in cases involving the PICA and the PICA origin, OA–PICA anastomosis is necessary to preserve PICA. In cases proximal and distal to the PICA, trapping is not always necessary, as opposed to the hemorrhagic group. Finally eight patients were treated with direct surgery and one patient was treated with endovascular procedure. The aneurysms were located distal to the PICA in two patients, involving the PICA in three patients, proximal to the PICA in two patients, pure PICA in one patient (Table 2). The representative cases are described.

Case 5: This 38-year-old man presented with dysarthria and swallowing disturbance caused by brainstem infarction. The aneurysmal dissection was located distal to the PICA. Follow-up angiography 12 days after the initial angiography revealed enlargement of the aneurysmal dilatation. So the affected VA was on the dominant side, BTO was performed. After the patient tolerated a 15-min occlusion, surgical proximal clipping was performed. Two weeks after the initial procedure, he presented with a right Wallenberg syndrome. Angiography revealed a pearl and string sign on the right VA. This contralateral VA dissection was treated conservatively with antithrombotic agent. Follow-up angiography was performed after 9 days, 3 months, and 5 months, demonstrating improvement of the pearl and string sign (Fig. 2).

Case 9: This 52-year-old man presented with left Wallenberg syndrome caused by brainstem infarction at the lateral part of the medulla oblongata. Angiography revealed a left VA dissecting aneurysm involving the origin of the PICA. He was treated conservatively. Follow-up angiography performed 25 days later revealed an occlusive change of aneurysmal dilatation, but follow-up angiography performed 53 days later revealed a recanalization of the occlusive VA. To determine the feasibility of internal trapping of a dissected segment involving the origin of the PICA, BTO was performed. The patient passed the BTO following the OA–PICA anastomosis and surgical trapping of the aneurysm was performed. Follow-up angiography revealed complete obliteration of the aneurysm. The PICA territory was filled from the bypass and there was no evidence of a new ischemic lesion on diffusion-weighted MR images (Fig. 3).

Management Outcomes in the Non-Hemorrhagic Group

Complete obliteration of the aneurysm was obtained in all cases. Treatment-related complication was observed in only one patient that presented with diplopia. Treatment-related morbidity rate was 11%. The final outcomes were good

Table 2 Summary of patients with VA dissecting aneurysms with non-SAH symptoms

Case No.	age sex	presentation	aneurysm location	treatment		treatment-related morbidity	GOS	mRS	Indication
				procedure	timing after symptom onset				
1	61M	headache	R. proximal	ITA	1month	none	GR	1	large
2	47M	ischemia	R. noPICA	trapping	12month	none	GR	0	large
3	41M	ischemia	R. involved	proximal clipping OA-PICA	1month	none	GR	1	enlarged
4	42M	ischemia	R. distal	proximal clipping	2month	none	GR	1	large
5	38M	ischemia	L. distal	proximal clipping	0.5month	none (bil. dissection)	GR	1	enlarged
6	46M	ischemia	R. involved	trapping OA-PICA	7month	none	GR	1	enlarged
7	53M	ischemia	L. proximal	trapping	22month	none	GR	1	large
8	53F	ischemia	R. involved	trapping OA-PICA	1month	diplopia	GR	1	enlarged
9	52M	ischemia	L. PICA	trapping OA-PICA	2month	none	GR	0	change

GOS: Glasgow outcome scale, mRS: modified Rankin scale, M: male, F: female, ITA: Internal trapping of aneurysm trapping: surgical trapping, OA-PICA: OA-PICA bypass, GR: good recovery

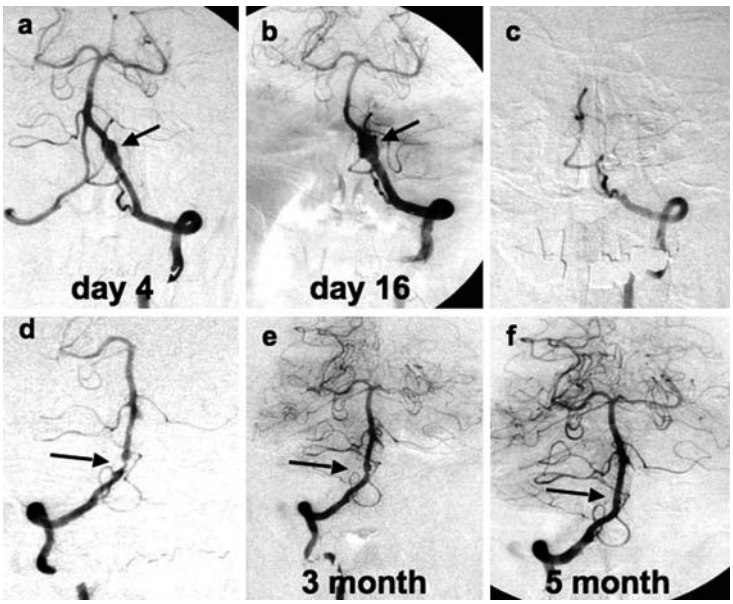

Fig. 2 *Case 5*. (**a**) Angiograms obtained in a patient with a left VA dissecting aneurysm distal to the PICA who presented with a brainstem infarction. (**b**) Follow-up angiography 12 days after the initial angiography revealed enlargement of the aneurysmal dilatation. (**c**) Surgical proximal clipping was performed. (**d**) Two weeks after the initial procedure, angiography revealed a pearl and string sign on right VA. (**e**, **f**) Follow-up angiography was performed at 3 months, and 5 months later, demonstrating improvement of the pearl and string sign

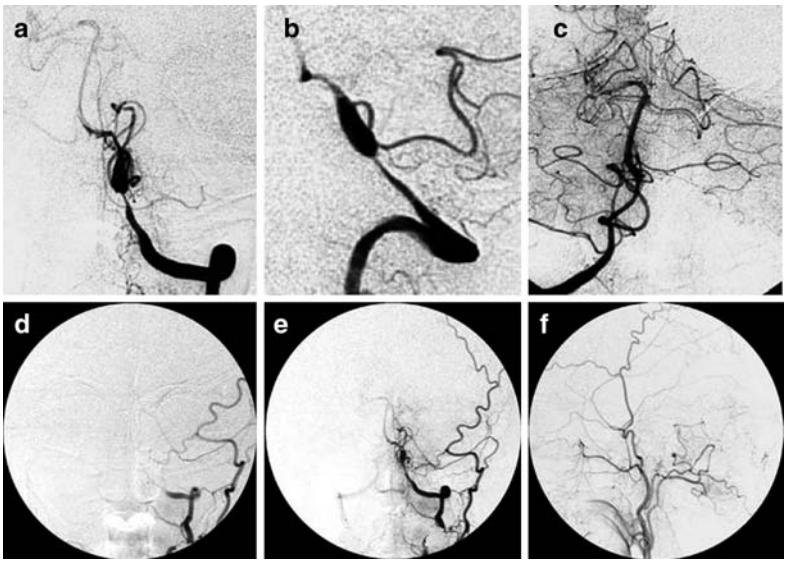

Fig. 3 *Case 9*. This 52-year-old man presented with left Wallenberg syndrome caused by brainstem infarction at the lateral part of the medulla oblongata. (**a**, **b**) Angiography revealed a left VA dissecting aneurysm involving the origin of the PICA. (**c**) Right vertebral angiography. He was treated conservatively. (**d**) Follow-up angiography performed 25 days later revealed an occlusive change of aneurysmal dilatation. (**e**) Follow-up angiography performed 53 days later revealed a recanalization of the occlusive VA. (**f**) Following OA–PICA anastomosis, surgical trapping of the aneurysm was performed

recovery in all patients. No recurrent ischemic symptoms or conversions to hemorrhage were seen following treatment.

Discussion

VA dissection has recently gained attention as a relatively common cause of stroke since the introduction of MRI as a diagnostic technique. It has been possible to identify 28% of all VA aneurysms and 3.2% of all intracranial aneurysms [1].

Surgical Indication and Optical Timing of the Treatment

It is known that VA dissecting aneurysms presenting with SAH are associated with a high risk of rebleeding, especially within the first 24 h after initial bleeding, and within the 1st week if left untreated [2]. Rebleeding rates were estimated at 71% of cases by Mizutani et al. with subsequent re-rupture of the aneurysms in 57%. A high mortality was associated with aneurysm re-rupture (46.7%), compared to 8% without re-rupture [3]. Therefore, we consider early treatment to be

essential to improve prognosis in these patients. On the other hand, the therapeutic indications for VA dissecting aneurysms with ischemic symptom, headache, and incidental findings remain an open question. Conservative treatment has been recommended for the non-hemorrhagic group because a relatively benign clinical course and outcome were shown in the majority of previous reports [4–6]. However, Nakagawa et al. reported serial angiographic changes in 88.2% of VA dissections, including subsequent enlargement [7]. Another recent report has shown that three patients of 21 VA dissecting aneurysms (14.3%) without SAH experienced subsequent SAH in conservative treatment [8]. Therefore we consider that a follow-up angiography must be performed during the early stage (within 3 weeks after onset of symptoms) to confirm formation or enlargement of the aneurysm. Treatment should be considered in cases of relatively large aneurysm, enlargement of aneurysm, and recurrence of ischemic symptoms.

Management Strategy of the Hemorrhagic VA Dissecting Aneurysm

Endovascular procedure is now deemed to be the best treatment of VA dissecting aneurysms following SAH, especially during the acute phase. This technique allows obliteration of the entire segment of the dissected site with coils more easily in a tight posterior fossa. However, such a radical treatment cannot be achieved in every patient during the acute phase. Originally, proximal occlusion or trapping was advocated as the treatment of choice for VA dissecting aneurysms if the contralateral VA was equal or greater in caliber. Such treatment should be avoided in cases where contralateral VA is hypo- or aplasia. When this case is encountered, preceding bypass surgery to preserve the perfusion of the affected VA will be needed before proceeding with trapping. Although it is possible to perform bypass surgery and trapping of the aneurysm during a single operation, this is technically much more demanding during the acute stage post SAH. Other options of treatment such as stent-supported coil embolization are also reported [9, 10].

Also problematic in the treatment of VA dissecting aneurysm are cases involving the PICA. The therapeutic goal for a VA dissecting aneurysm is complete exclusion of the lesion from the circulation. So revascularization of the PICA (OA–PICA or PICA–PICA anastomosis) and trapping of the aneurysm is the most ideal treatment. Another option is proximal VA occlusion. But in this treatment, the patient remains at risk of hemorrhage even if the slightest filling is present. In previous series, the overall morbidity rate in the management of PICA-involved VA dissecting aneurysms was as high as 40% [11]. The morbidity rate was much higher in the subgroup treated by trapping (60%) than in the subgroup that underwent proximal occlusion of VA (20%) [12].

Management Strategy of the Non-Hemorrhagic VA Dissecting Aneurysm

Surgical management of VA dissecting aneurysm without SAH is still controversial. In the hemorrhagic group, there are unfavorable conditions for direct surgery such as tight

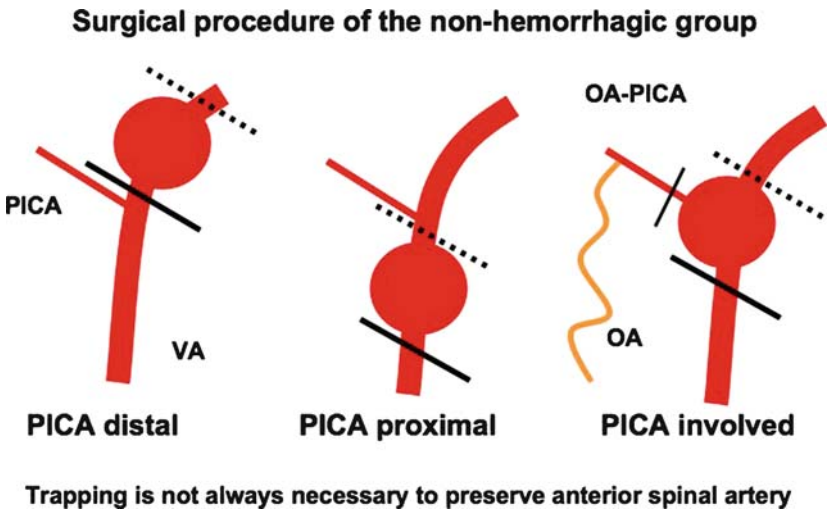

Fig. 4 The management strategy according to the location of the aneurysm: In case of the involving the PICA and the PICA origin, OA-PICA anastomosis is necessary to preserve PICA. In case of proximal and distal to the PICA, Trapping is not always necessary different from the hemorrhagic group

posterior fossa, and bloody CSF. On the other hand, in the non-hemorrhagic group, there is no limitation by these factors. During direct surgery, large perforating arteries often arise from dissecting aneurysms. Unruptured VA dissecting aneurysms with subsequent SAH usually rupture within 1 month in most cases [13]. Therefore, we believe that trapping is not always necessary as in the hemorrhagic group in chronic stage (Fig. 4). In our series, all cases of unruptured VA dissecting aneurysm except one case were treated with direct surgery (trapping or proximal clipping of the aneurysm). There is no case which presented with SAH during the follow-up.

Conclusion

Management strategy in the hemorrhagic group comprised endovascular methods as first line therapy. In the non-hemorrhagic group, direct surgery was performed as treatment of choice. This provided us with acceptable rates of procedural morbidity and prevention of rebleeding and ischemic event. But outcome of the hemorrhagic group was more severe as compared to the non-hemorrhagic group. This severe outcome of the hemorrhagic patients depended greatly on the patient's condition (Hunt & Kosnik grade) before treatment.

Conflicts of interest statement We declare that we have no conflict of interest.

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Chapter 9
Management of Spontaneous Dissection of the Cervical Carotid Artery

Ralf W. Baumgartner

Abstract This manuscript reviews the management of patients with spontaneous dissection of the cervical internal carotid artery (sICAD). Recommendations are not based on controlled-randomized trials, but on case-control and observational, hospital-based studies, and case reports. Vascular risk factors seem to be as prevalent in patients with sICAD as in age-matched, healthy volunteers. Stroke prevention includes the treatment of vascular risk factors and the administration of oral aspirin, which may be as effective as anticoagulation. The few available data indicate that most patients with sICAD causing severe stenosis or occlusion, or an aneurysm can be treated conservatively. Patients with sICAD were not excluded in the intravenous controlled-randomized thrombolysis trials with tissue plasminogen activator, but were excluded in the intraarterial controlled-randomized thrombolysis trials. Taking the few published case series and reports on thrombolysis in patients with sICAD into consideration, intravenous thrombolysis may be beneficial, whereas it remains unclear whether intraarterial thrombolysis is useful.

Keywords Aneurysm · Antithrombotic treatment · Carotid stenosis · Carotid occlusion · Dissection · Internal carotid artery · Stroke prevention · Thrombolysis · Vascular risk factors

Introduction

This manuscript reviews the management of patients with spontaneous dissection of the cervical internal carotid artery (sICAD). The first part will deal with stroke prevention, in particular the vascular risk factors, antithrombotic therapy, and the treatment of severe stenosis or occlusion, and dissecting aneurysm. The second part will discuss thrombolytic treatment of acute ischemic stroke due to sICAD.

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Stroke Prevention

Vascular Risk Factors

Arterial hypertension is the main independent risk factor for aortic dissection, and sudden, brief blood pressure changes are steeper in hypertensive compared to normotensive subjects [1]. It is thus fair to assume that it may also be involved in the pathogenesis of sICAD [2]. Two case-control studies in patients with spontaneous cervical artery dissection (sCAD) found no correlation between hypertension and sCAD [3, 4]. In a French case-control study, major vascular risk factors, body weight, body height and body mass index (BMI) of 239 patients obtained from a prospective hospital-based sCAD registry were compared with 516 age- and sex-matched healthy controls [3]. The overall frequency of hypertension did not differ between sCAD patients and controls [3]. An Italian case-control study compared the prevalence of hypertension in 153 consecutive patients with sCAD and 153 controls [4]. Again, the frequency of hypertension did not differ between the two groups. Both case-control studies showed a similar frequency of hypertension for men and women [3, 4]. In contrast, men had more often a history of hypertension than women (31% vs. 15%; $p < 0.0001$) in an observation study examining gender differences in 696 Swiss and French patients with sCAD [5].

In the Italian case-control study mentioned above hypertension was associated with brain infarction caused by sCAD (odds ratio (OR), 1.94; 95% confidence interval (CI), 1.01–3.70; $p = 0.045$), particularly when the ischemic lesion resulted from spontaneous vertebral artery dissection (OR 2.69; 95% CI 1.20–6.04; $p = 0.017$) [4].

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Diabetes mellitus, current and former smoking. The overall frequency of diabetes (patients: 1% of 236 cases; controls: 1% of 508 cases), current smoking (patients: 27% of 238 cases; controls: 31% of 516 cases), and past smoking (patients: 17% of 238 cases; controls: 19% of 516 cases) did not differ between sCAD patients and controls in the aforementioned French case-control study, and gender-specific subgroup analyses showed similar results for both sexes [3].

Hypercholesterolemia. In the French case-control study mentioned above, the frequency of hypercholesterolemia (patients: 68% of 178 cases; controls: 64% of 515 cases) and mean total plasma cholesterol level (patients and controls: 5.5 ± 1.1 mmol/L) did not differ between the two groups [3]. The frequency of hypercholesterolemia was lower in Swiss and French sCAD patients and normal subjects: it was 53% in 301 patients with sCAD [5], and about 60% in the Swiss MONICA center Vaud/Fribourg [6], Swiss military personnel [7] and 61,108 French subjects over 15 years of age who volunteered for a systematic medical check-up [8]. These data suggest that the frequency of hypercholesterolemia might be similar in sCAD patients and control subjects.

An observational study found that hypercholesterolemia occurred more often in sICAD that caused ischemic events compared to those sICAD that caused just local symptoms and signs on the side of dissection (head- and neck pain, pulsatile tinnitus, Horner syndrome or cranial nerve palsy) or remained clinically asymptomatic [9].

Homocysteine. Case-control and observational studies suggest that patients with sCAD have a mild elevation of total homocysteine (tHcy) levels, an increased prevalence of hyperhomocysteinemia, or both [10–13]. The tHcy levels in patients with sCAD (±ischemic stroke) are lower compared to those in patients with ischemic stroke not due to sCAD [10, 13–15]. Hyperhomocysteinemia damages the endothelium according to in vitro and animal studies [16–18], impairs endothelial-dependent and flow mediated vasodilation in humans [19], and is associated with premature peripheral and cerebrovascular disease and atherosclerosis in case-control studies [20, 21]. Gallai et al. [11] have suggested that tHcy levels slightly above normal predispose to the development of an intimal tear and sCAD without the occurrence of atherosclerosis, although the underlying mechanism remains elusive. Several arguments suggest that the small difference in tHcy levels between normals and patients with sCAD might be an artifact [10]: (1) tHcy levels are not assessed before, but after the onset of stroke. Even though the tHcy samples are collected soon after the ischemic event, there is still time for them to be affected by the stroke. (2) Homocysteine is assumed to be an acute-phase reactant [24, 25]. Therefore, elevated tHcy could be the consequence of cerebral ischemia or also an infection which has been shown to be associated with sCAD [26, 27] rather than a cause of the disease. Also, food deprivation increases the tHcy levels [28, 29]. In acute stroke, patients are kept fasting, and tHcy may therefore increase independently of the ischemic process [10].

In conclusion, hypertension might be a risk factor for sCAD causing ischemic brain infarction and sCAD in men. Mild hyperhomocysteinemia was found to be more prevalent in sCAD patients, although it is not clear whether this slight increase of the tHcy level is a risk factor for dissection or an artifact. The other vascular risk factors such as cigarette smoking, diabetes mellitus and hypercholesterolemia seem to be similarly frequent in patients with sCAD and healthy volunteers. These findings suggest that the vascular risk factors should also be assessed in patients with sCAD.

Body Height, Body Weight, and Body Mass Index

A French case-control study reported that (1) mean body height was higher in sCAD patients than in controls (171.3 ± 8.6 cm vs. 167.7 ± 8.9 cm, $p < 0.0001$), (2) sCAD patients had a lower mean body weight than controls (67.5 ± 12.2 kg vs. 69.3 ± 14.6) kg; $p < 0.001$), and (3) sCAD patients had a lower mean body mass index (22.9 ± 3.3 kg/m vs. 24.5 ± 4.2 kg/m; $p < 0.0001$) than controls [5]. This association was observed in both genders. Compared to healthy controls, the taller patients with sCAD might have a greater radius from the axis of neck rotation, the cervical spinal column, to the point of application of the force causing the intimal tear in the carotid artery. Consequently, the lever arm and the ensuing torque affecting the cervical ICA during neck movements might be greater in sCAD patients compared to normals. However, there are no data to prove this hypothesis, because the corresponding anatomical data were not measured. Genetic factors such as the increased frequency of connective tissue abnormalities in taller subjects might be another explanation. For example, patients with Marfan's syndrome are known to be taller than the normal population [30]. However, just two of 696 sCAD patients reported in the largest yet published series [5] suffered from this connective tissue disorder.

Antithrombotic Treatment

Brain imaging studies performed in patients with sICAD suggest that the essential mechanism of stroke is cerebral embolism [31]. These findings are underscored by transcranial Doppler sonography investigations, which reported

microembolic signals in middle cerebral arteries that were irrigated by dissected carotids [32]. These findings suggest that antithrombotic treatment for preventing embolic stroke is the key issue in patients with sICAD.

No controlled randomized or non-controlled study has compared the safety and efficacy of an antithrombotic treatment with placebo or different antithrombotic treatments (e.g. aspirin with anticoagulation) in patients with sICAD [33]. A systematic meta-analysis investigated in patients with sICAD, whether the outcomes “death from all causes” and “dead or disabled” differs after treatment with antiplatelet agents or anticoagulation [33]. There was no difference for the outcome "death from all causes" as 2% of 109 patients treated with antiplatelets and 2% of 218 patients treated with anticoagulation died. The endpoint "dead or disabled" did not differ between both groups (antiplatelet treatment: 24% of 59 patients; anticoagulation: 14% of 119 patients; Peto OR, 1.94; 95%-CI, 0.76–4.91).

In a recent study, prospectively collected data from 298 consecutive patients with sICAD treated with anticoagulants alone ($n = 202$) or aspirin alone ($n = 96$) was retrospectively analyzed [34]. Admission diagnosis was ischemic stroke in 165, transient ischemic attack (TIA) in 37, retinal ischemia in 8 and local symptoms and signs in 80 patients, while 8 patients were asymptomatic. Clinical follow-up was obtained after 3 months by neurological examination (97% of patients) or structured telephone interview. Outcome measures were (1) new cerebral ischemic events, defined as ischemic stroke, TIA or retinal ischemia, (2) symptomatic intracranial hemorrhage and (3) major extracranial bleeding. During follow-up, ischemic events were rare (ischemic stroke, 0.3%; TIA, 3.4%; retinal ischemia 1%); their frequency did not significantly differ between patients treated with anticoagulants (5.9%) and those treated with aspirin (2.1%). The same was true for hemorrhagic adverse events (anticoagulants, 2%; aspirin, 1%). These data suggest that (1) the frequency of new cerebral and retinal ischemic events in patients with sICAD is low and probably independent of the type of antithrombotic treatment (aspirin or anticoagulants), and (2) a randomized controlled trial comparing aspirin with anticoagulation is needed.

Complete recanalisation of a narrowed or occluded sICAD has been recently shown to occur mainly in the first 6 months after the onset of symptoms [35]. These findings indicate that antithrombotic treatment is mandatory during this 6-month period.

The long-term stroke risk of sCAD patients is low and ranges between 0.3% and 1.4% per year in French and Swiss series observing 92–459 patients during a mean follow-up of 2.6–6.7 years [36–38]. There is no study which analyzed whether specific subgroups have a higher long-term stroke risk and might benefit from long-term antithrombotic treatment. It is thus unclear whether patients with sCAD should undergo chronic antiplatelet treatment. Patients with persistent aneurysms after sCAD are usually treated with aspirin to prevent the development of thrombo-embolism, although no study has evaluated whether this treatment is beneficial.

Treatment of sICAD Causing Severe Stenosis or Occlusion

The rate of ischemic events and intracranial hemorrhage was investigated in patients with persistent ($n = 46$) and transient ($n = 46$) severe stenosis or occlusion of the ICA due to unilateral sICAD in a noncontrolled, long-term observational study [36]. Patients with transient carotid obstruction had a similar length of follow-up (7.2 ± 4.3 years) compared to patients with permanent carotid obstruction (6.2 ± 3.4 years). Antithrombotic treatment was similar in both groups, though it was administered at the discretion of the treating physician. Patients with permanent carotid obstruction showed annual rates of 0.7% for ipsilateral carotid territory stroke and of 1.4% for any stroke, whereas patients with transient carotid obstruction showed annual rates of 0.3% for ipsilateral carotid territory stroke and of 0.6% for any stroke. These results indicate that sICAD has a benign long-term prognosis with low rates of ipsilateral carotid territory and any stroke, and that the stroke rate in sICAD is not related to the persistence of severe carotid stenosis or occlusion. Accordingly, conservative treatment with antithrombotic agents is sufficient in most patients with sICAD causing severe stenosis or occlusion.

Treatment of Dissecting Aneurysm

Three monocenter, non-randomized observational studies evaluated the clinical and radiological course of cervical aneurysms caused by sICAD during mean follow-up periods ranging from 3 to 6.5 years [39–41]. The studies included 82 patients with 91 aneurysms of the cervical ICA. Antithrombotic treatment included mainly aspirin, a few patients were anticoagulated or had no antithrombotic therapy. During follow-up, aneurysms persisted in 64–100% with a decreasing size in 15–30%, whereas the remaining aneurysms resolved completely [39–41]. Long-term outcome of cervical aneurysm due to sICAD – regardless of location, size, and morphology – seems to be benign under conservative treatment including mainly aspirin, as no aneurysm ruptured or caused ischemia or new local symptoms or signs [39–41]. These findings suggest that conservative management is the treatment of choice in most patients with cervical aneurysms caused by sICAD [39–41].

Treatment of Acute Ischemic Stroke

No controlled randomized trial has investigated the safety and efficacy of intravenous (IVT), intraarterial (IAT) or mechanical (MT) thrombolysis in acute ischemic stroke caused by sICAD [42]. Therefore, all currently available data on this issue are derived from observational studies or case reports.

Intravenous Thrombolysis

Patients with ischemic stroke caused by sICAD were not excluded in any controlled, randomized IVT trial, which evaluated the effect of tissue plasminogen activator [23, 43–45]. SICAD is characterized by a false lumen containing the intramural hematoma and an intraluminal thrombus. An extension of the mural hematoma may cause local signs on the side of dissection or progression of luminal narrowing. Other potential complications include the development of an aneurysm, carotid rupture causing cervical or subarachnoid hemorrhage (SAH), and arterio-arterial embolism. Georgiadis et al. [42] summarized four studies reporting on 50 patients with sICAD causing ischemic stroke treated with IVT [46–48]. No new or worsened local signs, rupture of the dissected artery or SAH were observed [46–48]. One patient deteriorated during IVT, possibly due to recurrent thromboembolism [47]. Mortality was 8%, and a good outcome defined by a modified Rankin scale score of 0–2 points occurred in 40% of patients. These data reveal that IVT in ischemic stroke due to sICAD is probably safe.

Intraarterial and Mechanical Thrombolysis

Arterial dissection was an exclusion criterion in all controlled, randomized trials, which evaluated the effect of IAT in acute ischemic stroke [49–51]. In contrast, patients with sICAD were not excluded from the mechanical embolus removal in cerebral ischemia (MERCI) trial [52].

The potential adverse effects of IAT and MT include in addition to those mentioned for IVT the risk of catheter angiography including iatrogenic thrombo-embolism and catheterization of the false lumen with rupture of the dissected artery. In six patients with sICAD who underwent IAT, no rupture of the dissected vessel, cervical, subarachnoid or intracranial hemorrhage, or peri-interventional [50] arterial embolism was described [22, 53–55]. Nedeltchev et al. [56] reported a patient with sICAD causing symptomatic occlusion of the middle cerebral artery who underwent MT without adverse events. These limited data indicate that IAT and MT can be performed safely and successfully in selected patients with ischemic stroke due to sICAD.

Conflicts of interest statement We declare that we have no conflict of interest.

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Part III
Arteriovenous Malformations and Fistulas

Chapter 10
Natural History of Arteriovenous Malformations: Presentation, Risk of Hemorrhage and Mortality

Aki Laakso, Reza Dashti, Seppo Juvela, Mika Niemelä, and Juha Hernesniemi

Abstract Brain arteriovenous malformations (AVMs) are highly complex vascular lesions, which may become symptomatic by causing hemorrhagic stroke, epilepsy, chronic headache and/or focal neurological deficits. An increasing number of AVMs are also found incidentally in MRI and CT scans performed for other reasons. It is mandatory to understand the natural history and prognosis of these malformations when evaluating the risks that may be associated with the treatment. In this review, we discuss the symptomatology, hemorrhage risk and mortality associated with their natural course.

Keywords Arteriovenous malformation · Cerebrovascular · Intracerebral hemorrhage · Mortality · Stroke · Subarachnoid hemorrhage · Survival

Introduction

Brain arteriovenous malformations (AVMs) are vascular lesions of the brain in which arterial blood flows directly into draining veins without normal intervening capillary bed [1, 2]. Resulting high flow and direct transmission of arterial pressure to venous structures lead to pathological dilatation and growth of vessels, as well as disturbance of intracranial hemodynamics. AVMs are probably congenital, but not hereditary lesions, and their etiology remains unknown. The most serious complication of an AVM is its rupture, leading to hemorrhagic stroke. In addition to causing intracranial bleeding, AVMs may become symptomatic because of mass effect, irritation of surrounding cortex, or pathological changes in hemodynamics.

The large majority of AVMs are nowadays amenable to treatment by experienced neuromicrosurgical and endovascular teams. However, treatment of these highly complex lesions is one of the most formidable tasks encountered by the practicing neurovascular surgeon and is associated with a significant complication rate even using today's technology. It is mandatory that the treatment will not impose a greater risk upon the patient than the lesion being treated. In order to evaluate this, it is important to understand the natural prognosis of the disease.

Form of Presentation and Associated Symptoms

AVMs are rather rare lesions, with the estimated incidence of newly diagnosed AVMs being currently approximately 1 per 100,000 persons per year [1, 2]. The most common age of diagnosis is the third or fourth decade. They cause only 2% of all strokes, but their significance is amplified by the fact that they are the most common etiology of non-traumatic intracranial hemorrhage (ICH) in children and young adults. The pattern of symptoms by which AVMs are diagnosed is changing, however. With the rapidly increasing availability of noninvasive imaging methods, more and more incidental AVMs are found. Only few decades ago, over 70% of AVMs were diagnosed because of ICH [3, 4], whereas contemporary patient series report hemorrhagic presentation rates of less than 50% [5, 6]. Despite this, it still remains the most common type of presentation, since 45–72% (median 52%) of patients presented with ICH in ten large AVM series [3–12]. Anatomical and demographic factors associated with hemorrhagic presentation are shown in Table 1. However, it is very important to understand that risk factors associated with hemorrhagic presentation are not

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Table 1 Factors associated with hemorrhagic presentation of AVM, according to studies that have utilized univariate and/or multivariate statistical analyses (listed according to the sample size)

Authors	Cohort nationality	N	Risk factors for hemorrhagic presentation according to univariate analysis	Independent risk factors for hemorrhagic presentation according to multivariate analysis
Laakso et al. [25]	Finnish	623	Young age, small size, deep venous drainage	N/A
Stapf et al. [6]	U.S.	622	Old age, infratentorial location, deep location, deep venous drainage, associated aneurysms, small size, non-borderzone location	Deep location, deep venous drainage, associated aneurysms, small size, non-borderzone location
Kader et al. [10]	U.S.	449	Small size, infratentorial location, deep location, deep venous drainage	Small size, deep venous drainage
Yamada et al. [12]	Japanese	305	Small size, deep location, deep venous drainage	N/A
Langer et al. [5]	U.S.	100	N/A	Hypertension, small size, deep venous drainage
Spetzler et al. [26]	U.S.	92	Small size	N/A

necessarily the same as those which are risk factors for AVM rupture. For example, small AVM size is found consistently as a risk factor for hemorrhagic presentation, whereas large size seems to increase the risk for hemorrhage during the follow-up after the initial diagnosis (see below). This is most likely due to the fact that small AVMs are not easily diagnosed unless they bleed, whereas large AVMs may cause a variety of symptoms leading to diagnosis before they rupture.

It is commonly accepted that hemorrhage from AVM is, on average, less hazardous than the rupture of an intracranial aneurysm, but the actual short-term case fatality rate is not very well studied. However, it is probably less than 10% per bleeding (as compared to 50% in aneurysmal subarachnoid hemorrhage) [1, 2]. Nevertheless, as AVM rupture usually leads to intraparenchymatous hemorrhage, it may result in significant neurological disability, the type of which depends on the location of the lesion.

The second most common form of presentation is symptomatic epilepsy, with 18–35% (median 26%) of patients diagnosed because of seizures. Less common symptoms leading to diagnosis are chronic headache (unrelated to bleeding) in 6–14% of patients, and focal neurological deficit (temporary, fixed or progressive) due to mass effect or hemodynamic changes in 3–10%. The proportion of patients with incidentally found AVMs have increased from less than 2% in early studies to 10% in contemporary series.

Risk of Hemorrhage After Diagnosis

Several carefully done follow-up studies on the risk factors and hemorrhage rates in untreated AVM patients have been published. One of the most cited is a report by Ondra and coworkers [4], who had a follow-up study in 160 patients with a mean period of almost 24 years per patient, and suggested the annual bleeding rate of 4.0% in both previously ruptured and unruptured AVMs. Unfortunately, despite its laudable effort in gathering massively extensive follow-up, the report lacks sophisticated statistical analyses, which nowadays are more or less routinely used. In Table 2, we show long-term follow-up studies that have utilized Kaplan – Meier life-table analyses and univariate or multivariate models to identify various risk factors for AVM rupture. Based on these, the average annual AVM rupture rate in untreated patients is approximately 2–4%, and varies highly depending on various risk factors.

The figure used to describe the extent of a follow-up study is the length of the follow-up period in person-years (the sum of follow-up periods of all subjects). However, it may not be the same whether the person-years are accumulated by collecting a large patient population with short follow-up, or by collecting a smaller population with a long follow-up. First, the bleeding frequency in untreated AVMs may not remain constant over the years or decades. Many studies suggest a change in the bleeding rate over time; the bleeding rate being higher during the first years after the diagnosis [7, 9, 12, 13]. Second, many AVMs are not stable lesions, but can either grow, diminish (even disappear), or remain unchanged over time, even in the absence of any treatment attempts [14–16].

Among reported factors associated with the increased risk for AVM rupture during follow-up, previous rupture is probably the most consistent one [3, 6, 8, 11–13, 17], although even this is not a universal finding [18–20]. In our own series, hemorrhagic presentation almost tripled the risk of hemorrhage during the first 5 years after the diagnosis as compared with AVMs which had not bled [13].

Deep and infratentorial AVM locations, sometimes together with deep venous drainage pattern, are also consistently found to be associated with subsequent hemorrhage [6, 7, 12, 13, 20]. One might presume that this is because these lesions

Table 2 Long-term follow-up studies in untreated AVM patients, which have utilized univariate and/or multivariate statistical models to define risk factors for subsequent rupture after diagnosis (listed according to the length of follow-up)

Authors	Cohort nationality	N	Follow-up (person-years)	Follow-up (mean, years)	Average annual rupture rate	Risk factors from univariate analyses	Independent risk factors from multivariate models
Hernesniemi et al. [13]	Finnish	238	3,222	13.5	2.4%	-Young age -Previous rupture -Deep location -Infratentorial location -Deep venous drainage	-Previous rupture -Deep location -Infratentorial location -Large size (>5 cm)
Halim et al. [8]	US	790	3,156	4.0	2.1%	-Previous rupture	-Previous rupture
Crawford et al. [3]	UK	217	2,257	10.4	2%	-Previous rupture -Old age	N/A
da Costa et al. [27]	Canadian	678	1,932	2.8	4.6%	-Previous rupture -Deep venous drainage -Associated aneurysms	-Previous rupture
Stapf et al. [6]	US	622	1,412	2.3	2.8%	-Old age -Previous rupture -Deep location -Deep venous drainage	-Old age -Previous rupture -Deep location -Deep venous drainage
Stefani et al. [20]	Canadian	390	1,205	3.1	3.2%	-Deep location -Large size (> 3 cm) -Deep venous drainage -Deep feeders -Associated aneurysms -Single draining vein	-Deep location -Large size (> 3 cm)
Yamada et al. [12]	Japanese	305	892	2.9	4.7%	-Previous rupture Only in previously ruptured: -Young age -Female sex -Deep location	Only in previously ruptured: -Young age -Female sex -Deep location
Mine et al. [19]	Japanese	55	578	10.5	2.3%	-Large size -Deep or infratentorial location	N/A
Mast et al. [11]	US	281	239	0.9	8.8%	-Previous rupture	-Previous rupture -Male sex -Deep venous drainage

only lead to diagnosis if they bleed (and therefore they are more likely to bleed again during follow-up), but these locations have been found to be independent risk factors in multivariate models as well [6, 13, 20]. A more controversial risk factor is AVM size. As mentioned above, small AVM size is consistently associated with hemorrhagic presentation, but this does not automatically imply that it has to be a risk factor for future hemorrhage as well. In fact, small AVM size has not been a risk factor for hemorrhage in any study using multivariate models. On the contrary, four groups have found large AVM size to be a risk factor for subsequent rupture [13, 19–21], and many groups have not found AVM size to have any effect [3, 6, 8, 11, 12, 22]. Age and sex have been reported to influence the rupture frequency very inconsistently [6, 9, 12, 13], and no definite conclusions about their role can be drawn at present.

Mortality in Untreated AVM Patients

How AVM affects patient survival is not well studied. Simple annual mortality rate calculations suggest 0.7–2.9% overall annual mortality in AVM patients [3, 4, 9, 17, 19,

23, 24]. However, the only study with statistical comparison with general population was recently published by our group [25]. Our study with 623 AVM patients also included a subset of 155 untreated patients. As this was a retrospective analysis, this subgroup is obviously subject to some selection bias. However, these patients were admitted mostly in 1940s to 1970s, when the treatment policy was much more conservative than nowadays. In these patients, the overall annual mortality rate was 3.4% during a median follow-up period of 18.9 years. AVM-related (due to either acute case fatality or chronic sequelae of AVM-related morbidity) annual mortality rate in the same group was 1.6%. Comparison to the general population was done using relative survival ratio (RSR) as a measure; i.e. the survival of the patient population was compared to the survival of the whole population of Finland, matched for age, sex and historical era. Cumulative RSR in untreated AVM patients 30 years after diagnosis was 0.49 (i.e., over 50% excess in mortality compared with general population). For comparison, AVM patients in whom the AVM was completely obliterated, had cumulative RSR of 0.87 by 30 years. In other words, untreated AVM patients seem to have quite poor prognosis.

Conclusions

The most common form of presentation of an AVM is still intracranial hemorrhage, followed by epileptic seizures, headache and focal neurological deficits, although the number of incidentally found AVMs is rapidly increasing. The average annual risk of rupture of an untreated AVM is between 2 and 4%, although the risk may be significantly higher or lower, depending on individual characteristics of the lesion. Factors associated with increased rupture risk are previous rupture, deep and infratentorial location, and possibly large size. Untreated AVMs are associated with increased long-term mortality.

Conflicts of interest statement We declare that we have no conflict of interest.

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Chapter 11
Present State of Microneurosurgery of Cerebral Arteriovenous Malformations

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Abstract Microneurosurgical excision is known to be the definitive treatment for brain arteriovenous malformation (AVMs). The most important factors governing the operability of an AVM are location, size, age of the patient, and the neurosurgeon's and team's experience. We present in this review the surgical experience of the senior author (JH) in microneurosurgical treatment of brain AVMs. This consists of the following steps: (1) accurate preoperative embolization; (2) optimal selection of the surgical approach; (3) accurate definition and preservation of the normal arterial vessels of passage; (4) temporary clipping of the feeding arteries; (5) a special method of coagulation called "dirty coagulation" of the deep small difficult vessels inside apparently normal brain around the AVM; (6) removal of all AVM; (7) meticulous hemostasis; (8) intra- and postoperative digital subtraction angiography (DSA); (9) clinical and radiological follow-up. These steps are not possible in AVMs lying entirely within central eloquent areas. Nine out of ten small- and medium-sized arteriovenous malformations (AVMs) are suitable for direct surgery, but surgical complications increase drastically with the size of the AVM. Nevertheless, the actual results of combined treatment with preoperative Onyx embolization followed by microsurgery have decreased these risks.

Keywords Arteriovenous malformations · Microsurgical techniques · Multimodality treatment · Preoperative embolization · Onyx

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Introduction

The most challenging aspects of caring for a patient harboring an AVM is to decide rationally upon a management strategy. This is particularly true if the individual is young, and therefore has a high number of years at risk. A rough algorithm for the patient and relatives is that the risk to die in rebleeding from an untreated AVM during the remaining lifetime is (90-age)%, the percentage being higher for the probability of neurological disability. The new long-term results of the Helsinki AVM database allow the patient and the referring physician to grasp the risks of living with an AVM for a year or a decade rather accurately, and also demonstrates the high variability in the bleeding frequency of AVMs with different characteristics [1]. One should also have available – and experience with – the whole range of treatment options for AVMs; some are easily and safely treated by one method and are quite unsuitable for others [2–9]. Finally, the surgeon's own record of success or failure with these treatment modalities needs to be factored into the decision tree.

The best and definitive treatment of cerebral AVMs still remains complete microsurgical removal in experienced hands [1, 5, 10–13]. However, the microsurgical technique of complicated AVMs remains one of the most difficult tasks of microsurgery: unlike in tumor surgery incomplete removal is likely to lead to death or disability. The present state of our microsurgical techniques is described in the following, consisting of (1) accurate preoperative embolization; (2) optimal selection of the surgical approach; (3) definition and preservation of the normal arterial vessels of passage; (4) temporary clipping of feeding arteries; (5) a special method of coagulation called "dirty coagulation" of the deep small difficult vessels inside the apparently normal brain around the AVM; (6) removal of all AVM; (7) meticulous hemostasis; (8) intra- and postoperative digital subtraction angiography (DSA); (9) clinical and radiological follow-up. We explain all steps in this report.

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Patients and Diagnosis

Size and location of 623 arteriovenous malformations in the Helsinki AVM database are described elsewhere [14]. The experience of the senior author differs from this as one-third of the senior author's patients were operated on in Kuopio UH (1980–1997). For diagnosis we use computed tomography (CT) with angiography (CTA), followed by DSA. This is considered the gold standard and can provide dynamic data on the angio-architecture, real size, and location of AVM. CTA alone is used in our department only in small AVMs with large hematomas treated as emergencies. Magnetic resonance imaging (MRI) is done routinely, to better understand the AVM site and anatomy. Functional MRI and tractography are used in AVMs located in eloquent areas.

Surgical Indications

The senior author (J.H.) has treated the main part of patients with ruptured AVMs surgically since 1980, except for some elderly and/or moribund patients and few occasional cases refusing operation. AVMs diagnosed during the evaluation of epilepsy have usually been operated on, especially those causing intractable epilepsy. An increasing number of incidental AVMs have also been treated by microsurgery in patients of reasonable age.

Microsurgical Treatment

Preoperative Embolization

Large AVMs can often be reduced in size with preoperative embolization. The interventional neuroradiologic techniques occlude inflowing feeders and reduce the nidus of the shunt with particulate material, mainly by rapidly, or recently by slowly (Onyx) setting glue [6]. It has been rare that an AVM can be completely obliterated by regular embolization alone (10%), but with slowly setting glue (Onyx) even up to 50% of the selected cases can be totally occluded. In the remaining cases, partial occlusion is very valuable, making the final microsurgical total occlusion safer and straightforward. Preoperative Onyx embolization has revolutionized the treatment of large AVMs, as many of these can, after extensive filling with Onyx, be occluded and/or resected without difficulties [8, 15, 16].

Embolization is also very useful in obliterating deep feeding vessels difficult to reach microsurgically, making surgical obliteration technically more feasible [9]. Unfortunately, the deep small difficult vessels can seldom be embolized. Partial embolization alone is, according to our follow up, increasing the risk of rebleeding, and should be used only when followed by radio- or microsurgery (manuscript in preparation).

Positioning of the Patient and Approach

Operations are performed under moderate hypotension. The head is significantly elevated above the heart level for a semi-sitting position or nearly so, but a true sitting position is seldom used. Exceptions are the nowadays rarely microsurgically treated vein of Galen malformations and some of the midline posterior fossa AVMs [17, 18]. Lateral posterior fossa AVMs are operated upon in a park bench position, as are many of the more posterior temporally, parietally and occipitally located AVMs. The very mobile balanced model of the operating microscope and some microsurgical instruments are of special importance, and routine during the excision of cerebral AVMs. In fact, no AVM should be operated upon without a microscope or micro-instruments [19]. In microsurgery, our trend has been toward the use of rather small bone flaps (diameter of less than 2 inches) [10–13]. In AVM surgery, however, we have used larger openings to obtain better orientation of the AVM and its surroundings. Nevertheless, for deeply sited AVMs the keyhole principle is often applicable [1, 5, 14].

Dural Opening and Initial Dissection

After opening the skull, the dura mater is carefully inspected and opened under the operating microscope because many draining veins, and also the AVM itself, can be firmly adherent to the dura mater. Adherence is common in redo cases and after severe or several bleedings and/or several embolizations. Depending on the location and size of the AVM, we first attempt to locate the feeding arteries. These can be more easily visualized in superficial AVMs by using intraoperative ICG videoangiography. Draining veins are also identified and preserved until the last steps of the excision. Those AVMs having only one draining vein are more difficult to treat than those with multiple ones. In one parietal AVM the single huge draining vein was partially running inside the bone, and was torn during raising the flap. A catastrophic bleeding was treated by compressing a cotton patty on the bleeding site, and by suturing it circumferentially to the dura to seal the bleeding until the final stage of large AVM removal. In another posterior fossa redo surgery the huge single draining vein was injured when dissecting inside the scar, resulting in rapid swelling of the large AVM. Fast four-handed removal of the AVM by two experienced neurosurgeons saved the patient.

In a few cases of small AVMs, the draining vein was cut initially and used as a handle to help the dissection. In many cases, as larger feeders were severed, we placed a vascular clip into the distal part of the arterial feeder at the side of the AVM. This clip helped with orientation during the operation and could be used as a handle. The same maneuver was often used with the draining veins. In many cases, a silk ligature was connected to the clip and permitted a very careful application of some tension during excision of the AVM.

Further Dissection and Use of Temporary Clips

The borderline between the AVM and the surrounding brain is generally grayish and has some glial scarring, especially after hemorrhages. After embolization, small infarctions often surround the AVM, and this soft macerated tissue can easily be suctioned away. Many times the hematoma has dissected the brain so that the AVM is easier to find and remove. Signs of past bleeding were found in the absence of any previous clinical evidence of rupture in some AVMs; in these cases the bleeding may have been misdiagnosed as an epileptic seizure.

Identification of the cleavage plane between the AVM and the brain is extremely helpful when excising these formidable lesions. In the beginning of the operation a lot of time should be spent on careful dissection with a sharp needle, jewelers' forceps and sharp microscissors as well as water injections. This time pays back, as with a clear anatomical understanding the removal of even difficult looking AVMs is facilitated.

Feeding arteries are identified, after which we usually place a temporary clip on them until at a later stage they are coagulated and then cut. The duration of temporary clipping is monitored and recorded. Considering the often prolonged times (up to hours) the temporary clips are in place, surprisingly little or no adverse effect are seen. This is probably due to long-term adaptation of the circulation to "the vascular steal" caused by the fistulous nature of the AVM. Usually no permanent clips are used to seal small or large arteries (or veins); instead, after dividing, vessel ends are sealed with bipolar coagulation for the second time. It is our long-time experience that the placed clips may cause problems when accidentally touched.

Coagulation and Dissection of Small Feeders: "Dirty coagulation"

Endovascular treatment has helped in many ways in open microsurgery in the total removal of cerebral AVMs, but unfortunately the tiny vessels cannot be occluded by endovascular means. Hemostasis of small and thin-walled fragile feeders, most cumbersome in the close proximity of the ventricle, remains the most difficult part of the surgical procedure. Bleeding is difficult to control as these vessels have too little tissue for coagulation to be effective. They often burst and retract into the white matter, at which point bipolar coagulation is again continued until the bleeding stops. There is no possibility to tamponade these bleedings as they are profuse, and if multiple, the bleeding sites are difficult to find, and should be managed under very high magnification.

Earlier, as the last resort, we clipped these vessels with special microclips, and, indeed, in some cases, up to ten microclips were used. The accumulation of microclips in the operative area often complicated microsurgery, as they were later touched and new bleedings were produced. Instead of using the microclips by Sundt and Sugita to control bleeding from troublesome vessels, a small amount of brain substance is taken between the tips of a rather blunt bipolar coagulation forceps, and the small vessel is coagulated together with the brain substance. This is the process of dirty coagulation, called like that because the forceps used are blunt and large in relation to the vessels. Blunt, clean, and cold forceps prevent scarring and sticking. One of the miseries in the treatment of these small vessels is sticking of the forceps, producing a new bleeding and needing further patience and careful coagulation. Malis settings 20–25 are used, depending on the tip of the forceps. Dirty coagulation has produced frightening postoperative hematomas from these profusely bleeding small arteries, occurring as late as 1 week after the operation, an extreme rarity.

Final Stage of the AVM Removal

In large AVMs, the final stages of excision prove to be the most difficult. It is the senior author's (J.H.) experience that at the beginning of the operation of a large AVM, the feeling of being one of the world's best neurosurgeons in action may be present, just to change to being the worst one when the ultra-small feeders situated at the deepest part of the AVM bleed! In prolonged operations psychomotor weakness occurs easily, and small errors may be made, resulting in bleeding. If this happens, the team is alarmed by closing the radio, but usually the situation is recognized already at the screens of the OR. The blood pressure is lowered (systolic pressure even lower than 100 mmHg), suction may be changed to a bigger level, bleeding sites are sought and tamponaded with patties, followed by dirty coagulation. Seldom is the site packed with hemostatics and a new working area is sought, returning later to the bleeding site. When several bleeding sites occur, the AVM is excised as quickly

as possible. As the excision of complex AVMs involves many operative steps, we prefer to operate at a brisk pace (before fatigue sets in), except for the initial careful and time consuming study of the anatomy. Some large malformations with myriads of feeders and less experience required long operating times of up to 8 h; however, ordinary AVMs are excised within 2–4 h.

Glue Covering of the Surgical Bed and Final Hemostasis

All kinds of hemostatics: small muscle pieces, tissue glues, Oxycel (Becton Dickinson, Sandy, UT), Spongostan (Ferrosan, Denmark), or Avitene (Alcon, Puerto Rico) have been used to stop the bleeding. After resection of the AVM, our present and long-time policy is to touch the surface of the resection cavity gently with the tips of the bipolar forceps and cotton patties. If bleeding occurs, a small remnant of the AVM can usually be found, and this is controlled by bipolar coagulation. Finally, the resection cavity surface is covered with glue and Oxycel, which is pressed on the fresh glue all around the cavity.

Postoperative DSA and Care

We always perform intraoperative DSA after the removal of complex AVM and before closing. We use the regular Sugita head frame in intraoperative DSA; one or two good projections can be tailored with a C arm. After obtaining a perfect hemostasis, the patient is transferred to the intensive care unit. After closing the wound the DSA is repeated, usually in the OR. Patients with complex AVMs, especially those with myriads of nasty small vessels requiring heavy use of dirty coagulation, are usually maintained for several days in controlled moderate arterial hypotension (systolic pressure 100–120 mmHg); in some complex cases in deep hypotension for several days. Patients with small and straightforward medium-sized AVMs are wakened up immediately, and are usually discharged from the ICU to the ordinary inpatient ward the next day. Anticonvulsants are used routinely, and hypotensive drugs frequently.

Staged Operation

Earlier in the 1980s, some large AVMs were operated by first ligating the largest feeding vessels and later excising the whole AVM. In a few cases, an intraoperative embolization with Spongostan particles or tissue glue was done. This procedure has naturally been replaced by preoperative embolization. In the past 20 years, no two-step operations or intraoperative embolizations were used. Patients with large intracerebral hematomas were operated on as emergencies, usually removing the AVM in the same session.

Results

Due to our special admission policy, all patients are clinically evaluated several times postoperatively. Ninety percent of the patients with small and medium sized AVMs operated on are independent, with a Glasgow outcome score (GOS) of 4 or 5 [20].

Discussion

The decision to treat or not and how to treat a cerebral AVM is still debated. The following factors must be taken into consideration: (1) the presentation and natural history of the lesion; (2) the knowledge of (own) results of the available therapeutic choices; (3) patient's age and general medical condition; (4) presenting neurological status (level of consciousness, motor or sensitive deficits, epilepsy, headache, or asymptomatic); (5) the AVM-related factors including: location, size, number and flow pattern of the feeding vessels, location of the venous drainage; (6) the presence of a recent or remote hematoma. Each of these factors might be the most important one when making decisions for the individual patient.

The primary goal of AVM surgery is to prevent hemorrage and consequently seizures, neurological deficits, or death. This can be achieved only by total occlusion, in our case with microsurgical excision of the AVM [1, 5]. Incompletely treated AVMs may rebleed as the fistulous connection between arteries and veins in the nidus of the lesion will recruit surrounding vessels and rapidly make them as prominent as those that have been occluded. A prolonged follow-up of surgically treated patients is necessary in order to confirm permanent cure [14]. Patients with partial occlusion of their AVMs should have additional radiosurgical treatment, redo surgery, or additional embolization.

Surgical Treatment

The advent of microsurgical techniques has changed the operative treatment of AVMs. In the Helsinki historical series (1947–1973) [21], only 40% of the patients with

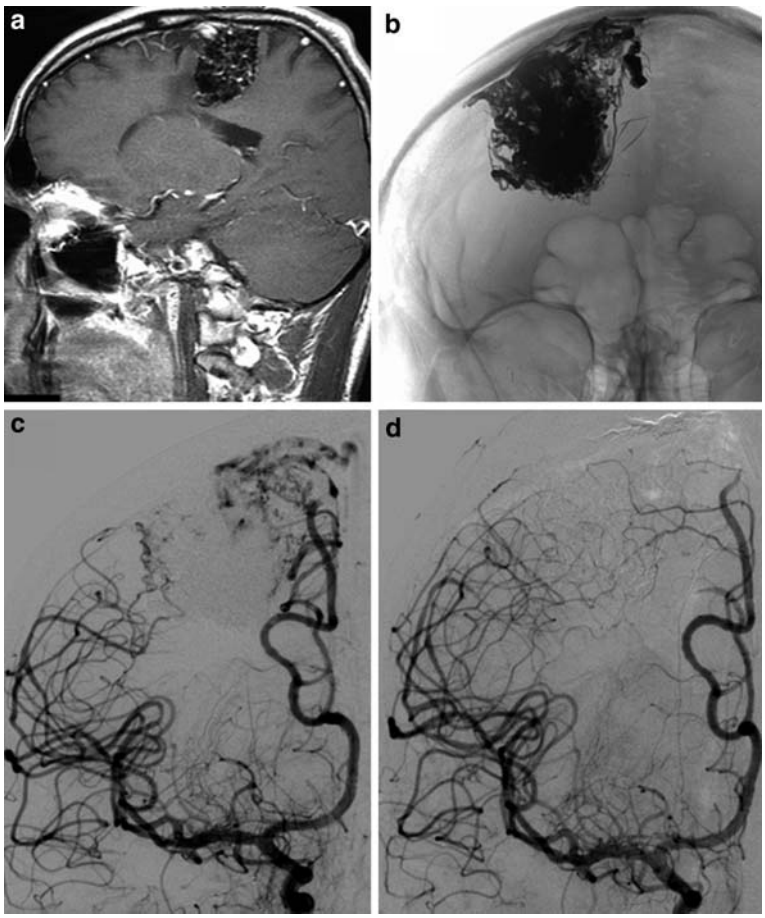

Fig. 1 Sagittal MRI (**a**) showing a parietal AVM preoperatively embolized with Onyx by Dr. Moret in Paris. Antero-posterior X-ray (**b**) and DSA (**c**) showing the Onyx and the parietal AVM. Post-operative DSA showing the removal of the parietal AVM (**d**). The patient, a male 25 years old, recovered from a slight left postoperative hemiparesis 1 month after the operation

AVMs were operated upon. In the present study, the large majority (90%) of patients were surgically treated [1, 5, 14]. With the present operative methods central, deep thalamic, and mesencephalic AVMs are inoperable, and should be treated by endovascular and/or radiosurgery [15]. Our experience is in line with the large series of Yasargil and many others [3, 4, 19, 22–25]. A large AVM located in the frontal pole is surgically removed without deficits for the patient, but a small, even tiny, malformation within the spinal cord, brain stem or thalamus may remain surgically inaccessible. Usually surgical complications increase drastically with the size of the AVM. However, the actual results of combined treatment with preoperative Onyx embolization followed by microsurgery have decreased those risks. After an earlier, more conservative approach to large parietal AVMs, with Onyx embolization we are very much encouraged to treat also these lesions with good results (Fig. 1a–d). These AVMs, previously inoperable in the hands of most skilled neurosurgeons, have become treatable ("practical" as Drake called those cases amenable to treatment) [3, 26]. Even now, and thus it will remain, no therapeutic interventions are possible in moribund patients where most severe bleeding may destroy in seconds the brain without any chances for recovery. Only diagnosis and treatment prior to such catastrophic bleedings might save these patients. However, our patients with large intraparenchymal hematomas operated on emergently would have died without acute surgery. Real general screening for cerebral AVMs is unlikely to happen in the near future, as their occurrence is not familiar.

Conclusions

The most important factors governing the operability of AVMs are their location and site, the age of the patient, and the experience of the neurosurgeon and the team. According to our experience, small- and medium-sized AVMs can be excised with good results in most cases, even in eloquent regions of the brain. A center(s) specializing in the surgery of arteriovenous malformations and aneurysms should be available in every country.

Conflicts of interest statement We declare that we have no conflict of interest.

Acknowledgment Authors guarantee that their paper has not been published in another journal nor will be submitted for publication in another journal.

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Chapter 12
Management of Dural Arteriovenous Fistulas – Helsinki and Kuopio Experience

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Abstract Dural arteriovenous fistulas (DAVFs) are complex disorders, some of them with aggressive clinical behaviour. During past decades their treatment strategy has changed due to increased knowledge of their pathophysiology and natural history, and advances in treatment modalities. In asymptomatic cases or cases with mild symptoms in the absence of cortical venous drainage (CVD) no treatment is necessarily required, whereas aggressive DAVFs should be treated promptly by endovascular or microsurgical means.

In our series of 323 patients with 333 fistulas, treated in two neurosurgical units in Finland since 1944, there were 265 true DAVFs and 68 Barrow type A caroticocavernous fistulas. Among the DAVFs there was a slight female predominance, 140 women (55%) and 115 men (45%), and the majority of the cases were located in the area of transverse and sigmoid sinuses. Mode of treatment in the early series was proximal ligation of feeding artery, and later craniotomy, endovascular treatment and radiosurgery, or combination of these treatments, with total occlusion rate being 53%.

Keywords Dural arteriovenous fistula · Intracranial hemorrhage · Microneurosurgery · Cerebrovascular · Endovascular · Embolization · Radiosurgery

Introduction

Intracranial dural arteriovenous fistulas (DAVFs) are abnormal fistulous connections between arterial feeder(s) and a dural venous sinus or leptomeningeal vein within dural leaflets. They comprise about 10–15% of all intracranial, 6% of supratentorial, 35% of infratentorial vascular malformations [1–3]. Recent advances in neuroradiology (particularly DSA) led to better understanding of the unique pathophysiology definition, natural history and symptoms properties of these lesions. Since DAVFs are rather complex disorders with heterogeneous behavior depending on location and angiographic aspects, especially pattern of venous drainage, and both surgical and endovascular treatment have a rather high risk of morbidity and mortality; their treatment must be carefully and individually tailored and done by only experienced microneurosurgeons and neuroradiologists.

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Rationale

Pathogenesis of DAVFs

The etiopathogenesis of DAVFs is not yet well understood, but is accepted to be acquired rather than congenital. The association of DAVFs with sinus thrombosis has been noted by many authors [4–7]. However, many DAVFs are not associated with any evidence of present or previous venous thrombosis [8]. In our series, any underlying cause of DAVF was not found in the majority of patients.

Sinus thrombosis causes venous hypertension when outflow is significantly compromised and collateral venous drainage is inadequate [9] resulting in passive congestion and decreased cerebral perfusion [6–8, 10, 11] and thereby hypoxia. To reverse hypoxia, expression of angiogenic stimulators and angiogenic activity is induced [9, 12–14] and new vascular connections are formed. In immunohistochemical studies of DAVFs expression of growth factors has been shown [8, 15, 16]. After initial shunting turbulent arterial blood flow probably directly and indirectly (intimal injury, luminal thrombosis, restriction of venous flow) exacerbates

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the intrasinusal pressure causing a vicious circle [9, 17, 18]. Disorders associated with sinus thrombosis such as tumor invasion of major sinuses, trauma, infections, dehydration, hormonal disorders and coagulopathies predispose to formation of DAVF by representing an environment that may be conducive to the development of a DAVF depending on individual host response [19].

Classification of DAVFs

DAVFs can be classified according to anatomical location, rate of shunting (high flow or low flow) or pattern of venous drainage [6, 20, 21]. As their clinical behavior depends on the pattern of venous drainage [20–24] the most commonly used classifications of DAVFs were done according to venous drainage pattern. Djiandjian first described a classification of DAVFs according to angioarchitectural aspects in 1978 [5]. Cognard and Borden proposed their classifications in 1995 [20, 21].

Caroticocavernous fistulas (CCF) are a special group of fistulas that can be classified according to many properties such as velocity and blood flow (high or low flow), etiology (spontaneous or traumatic) or pattern of shunting (direct or indirect). The classification described by Barrow et al. is the most commonly used in daily clinical practice [25]. According to that classification type B, C and D lesions are true dural arteriovenous fistulas while type A fistulas are direct high flow shunts between ICA and cavernous sinus through a defect on the cavernous part of the carotid wall.

Decision-Making

Symptoms

In Lasjaunias et al.'s review about previously reported cases of DAVFs with special attention to the mechanisms of manifestations, the symptoms are divided into artery, nidus and vein related [7]. Central nervous system symptoms dominantly seem to be related to venous hypertension and congestion whereas the peripheral cranial nerve symptoms are most likely due to arterial steal.

Most of the DAVFs are considered to be benign lesions. Their reported annual risk of hemorrhage is 1.8% [26]. However, DAVFs with cortical venous drainage (CVD) are known to behave more aggressively, causing intracranial hemorrhage (ICH) and subarachnoid hemorrhage (SAH). The Toronto Brain Vascular Malformation Group reported DAVFs with CVD to have an annual mortality rate of 10.4% and an annual hemorrhage and non-hemorrhagic neurological deficit (NHND) rate of 15% [24].

Radiological Findings

Computerized tomography (CT scan) is usually the initial radiological examination for patients who apply with acute symptoms and it can demonstrate acute intracerebral hemorrhage successfully. Patients who present with chronic symptoms frequently have magnetic resonance imaging (MRI) with cerebral artery MRA as initial radiological examination. Both modalities can demonstrate engorged cortical veins as well as evidence of venous congestion [19, 24]. However, they are insufficient to demonstrate the underlying pathology properly and can be used for primary diagnostics only. Digital subtraction angiography (DSA) is required for reliable diagnosis, and for treatment planning DSA is necessary to accurately image the feeding arteries, small draining veins and the exact location of DAVF.

Indications

As noted previously, the pattern of venous drainage determines the natural history of DAVF. Therefore, indications and strategy of treatment depend on the pattern of venous drainage. Borden type I lesions are called benign fistulas. Considering their benign course, asymptomatic cases or cases with tolerable limited symptoms do not need treatment. These benign fistulas, however, carry a 2% risk of changing into an aggressive type, and therefore they should be monitored both clinically and radiologically [27]. Patients who have intolerable symptoms, particularly caroticocavernous fistulas with progressive visual impairment, should be treated. Borden type II or III fistulas having leptomeningeal venous drainage are considered aggressive fistulas, and they require treatment to prevent intracerebral hemorrhage and neurological deficits. Therapeutic options include endovascular treatment, microneurosurgery and radiosurgery.

Treatment Strategy

Since the majority of these lesions can at least partially be treated by endovascular techniques, they should first be explored endovascularly with the intent of embolization to obtain a cure. Surgery is indicated when the fistula cannot be treated by endovascular means, or endovascular treatment

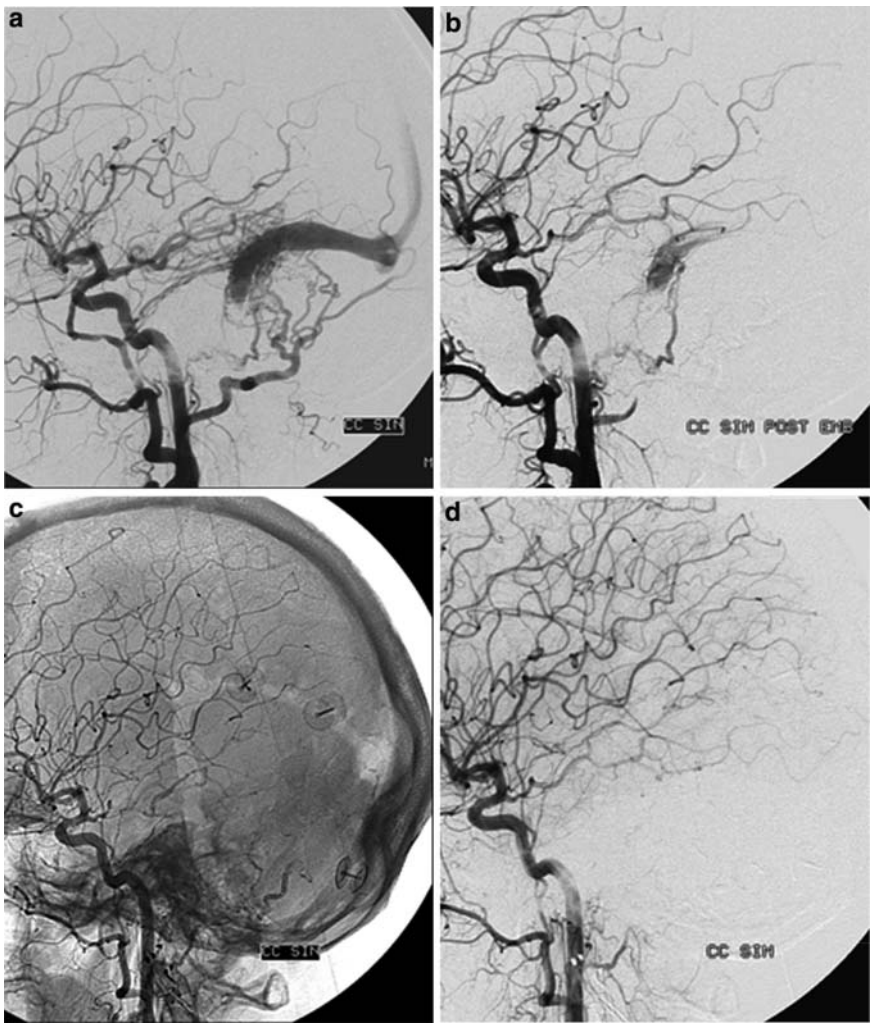

Fig. 1 (**a**) A left transverse-sigmoid sinus dural arteriovenous fistula (DAVF) with cortical venous drainage (CVD) in a 54-year-old female. (**b**) After embolization of feeders from the middle meningeal artery and occipital artery, craniotomy (**c**) via lateral suboccipital craniotomy and resection of left transverse-sigmoid sinus was made (**d**) resulting in the total occlusion of the DAVF

fails to obtain complete occlusion (Figure 1) and cure is needed, as in the case of aggressive fistulas or patients with severe symptoms. Endovascular treatment can be used as a complementary treatment if there is residual filling of fistula after surgery. Radiosurgery is also an effective treatment for DAVFs. However, obliteration of the shunt after this treatment requires time and not all fistulas respond to the treatment. Therefore, radiosurgery is not a recommended treatment for high risk DAVFs as a first step of treatment. It is indicated for patients who have benign fistula with moderate symptoms that can only be tolerated for some time and high risk fistulas refractory to endovascular treatment and microneurosurgery.

Patients and Methods

Since 1944 altogether 323 patients with 333 DAVFs and caroticocavernous fistulas have been treated in Helsinki and Kuopio Neurosurgical units. Sixty-eight of these fistulas are Barrow type A caroticocavernous shunts and 265 true DAVFs in 255 patients. Eight patients had multiple fistulas [2, 22, 25]. Among DAVF patients there was a slight female predominance, 140 women (55%) and 115 men (45%). Caroticocavernous shunts were equally distributed between sexes. Most of the DAVFs were located in the area of transverse and sigmoid sinuses, and the second common location was cavernous sinus (Table 1). The most common symptom in these patients was bruit (Table 2). At the time of diagnosis, 13% of the patients had hemorrhage. Until the early 1980s, the majority of cases were treated by proximal ligation of feeding artery or conservatively. Later, the main part of patients underwent preoperative embolization and

Table 1 Location of 265 dural arteriovenous fistulas (DAVFs) treated in Helsinki and Kuopio Neurosurgical units between 1944 and 2006

Transverse and sigmoid sinus	185
Cavernous sinus	26
Superior sagittal sinus	6
Frontobasal	5
Other	43

Table 2 Symptoms in patients with DAVF

Bruit	166
Headache	81
Chemosis	21
Seizure	16
Hemiparesis	15
Mental deterioration	7
Cardiac symptoms	3

Table 3 Mode of treatment in DAVFs

Embolization	79
Surgery	53
Ligation of proximal efferent vessel	16
Craniotomy	37
Embolization followed by surgery	68
Radiosurgery	4
Embolization followed by radiosurgery	11
Combined embolization, surgery, and radiosurgery	2
No treatment	48

Table 4 Mode of treatment in caroticocavernous fistulas (Barrow type A)

Embolization	23
Ligation of proximal efferent vessel	22
Embolization followed by surgery	3
No treatment	20

Table 5 Total occlusion rate

Location	No. of totally occluded (%)
Transverse and sigmoid sinus	110 (60%)
Cavernous sinus DAVFs	19 (73%)
Barrow type A fistulas	18 (26%)
Superior sagittal sinus	3 (50%)
Frontobasal	3 (60%)
Other	22 (51%)
Total	175 (53%)

subsequently craniotomy, and since the 21st century radiosurgery has increasingly been used in the treatment of DAVFs. The mode of treatment and results can be seen in Tables 3, 4 and 5.

Surgical Technique

Transverse and Sigmoid Sinus DAVFs

We prefer to operate these lesions via lateral suboccipital craniotomy as described by Hugosson and Sundt [28–30]. The patient is positioned in the park bench position. A lumbar drainage is used to gain extra space for exposing both sides and ligating the sinus. A question mark or slightly curved incision can be used. Enlarged occipital and posterior auricular arteries are cut and coagulated with heavy bipolar coagulation to prevent excessive bleeding. Bleeding from bone can be treated by monopolar coagulator or bone wax. A lateral suboccipital bone flap with three or four burr holes is elevated. Burr holes are heavily waxed if bleeding occurs. Craniotomy should be done fast to elevate the bone flap, especially if there is excessive bleeding from bone margins. Hot drilling with a large diamond drill is very effective to stop this kind of bleeding. All bleeders from dura should be coagulated by heavy bipolar coagulation. Dural tacking sutures are also helpful to prevent oozing from highly vascularized dura. If there is bleeding from the sinus, we prefer to use Oxycel, fibrin glue, and muscle to stop bleeding. At this point the surgical strategy is determined according to the angioarchitecture of the lesion. If the sinus is functional and provides the major route of venous drainage, skeletonization should be preferred. If the sinus is nonfunctional, thrombosed or there is retrograde flow to cortical veins, we prefer to remove the sinus. In that case, first the medial and subsequently the lateral part of sinus is ligated. After ligation, the sinus is resected. The vein of Labbé is the most vulnerable point in the surgical strategy. Partial resection of the transverse sinus should be done in the presence of a prominent vein of Labbé to preserve the flow.

Caroticocavernous Fistula

We prefer to operate these lesions via supraorbital lateral approach from the side the lesion is lateralized. After induction of anesthesia, the patient is positioned supine, and the head is elevated above the cardiac level. The head is fixed with three or four pin headrest with 45° rotation to the contralateral side and tilted slightly. After minimal shaving, a 7–9 cm frontotemporal incision which does not even extend in front of the ear is made just behind the hair line. Splitting of the temporal muscle is limited to the superior and anterior part to prevent late atrophy, and the musculocutaneous flap is elevated anteriorly until the margin of the orbital rim and anterior zygomatic arch are exposed. After placing a burr hole on the superior temporal line, the dura can be detached from the bone via this burr hole. A 3 × 4-sized free craniotomy flap is elevated with a high speed drill. The surgical microscope is brought to the surgical field. The dura along the sphenoid ridge and anterior clinoid process is separated from the bone. The lateral part of the sphenoid ridge is drilled by high speed drill with a diamond tip. The medial part of the sphenoid ridge, the roof of the optic canal and the anterior clinoid process are removed by ultrasonic surgical aspirator. After completion of the bone work, the dura propria over the temporal lobe is separated from the outer cavernous membrane. After exposing the wall

of the cavernous sinus, a very small incision is made to open it. We prefer to inject glue with a blunt applier and pack Oxycel from this opening. This procedure is repeated from different points of the cavernous sinus wall until it is ascertained that the fistula is completely occluded. During this, extreme attention should be paid to preserve the carotid artery and the flow in the carotid artery. We recommend using intraoperative DSA and Doppler USG to check the patency. If intraoperative DSA cannot be performed early, postoperative DSA is indicated.

Other Locations

The majority of ethmoidal DAVFs have feeders arising usually from the anterior or posterior ethmoidal arteries originating from the ophthalmic artery. Therefore, embolization of these feeders is usually impossible without the risk of visual system complications. We prefer to operate these lesions via the lateral supraorbital approach (LSO) as described previously from the side where the fistula is located. After craniotomy, drilling of the lateral sphenoid ridge and flattening of the superior wall of orbit is performed applying the hot drilling technique to prevent bleeding. The most important step is occlusion of the vascular connections between the dura of the cribriform plate area and the pial vessels [31]. If there is bilateral venous drainage, the falx can be split to reach contralateral draining veins to coagulate. Removal of frontobasal dura is not required but removal of the anterior aspect of falx is recommended if it is involved by the lesion [31].

Surgical approach of the superior sagittal sinus (SSS) and convexity DAVFs varies according to the angioarchitecture and location of the fistula. If there is a single fistulous point, a paramedian linear incision above the fistula point is sufficient to reach a single fistula, but in case of multiple fistulas with bilateral arterial supply, a linear midline incision above the sick part of SSS is used. Bilateral exploration along SSS is done to expose, identify, and coagulate the feeding arteries and the retrograde draining veins. To identify and preserve the normal bridging veins is the most important point. İntraoperative DSA might be helpful to confirm total occlusion of all fistulous structures.

How to Avoid Complications

The treatment of intracranial DAVFs has a high rate of complication and mortality. In our series the rate of treatment morbidity was 15% and mortality 4%. The reasons that led to morbidity and mortality were postoperative epidural hematoma, pulmonary embolism, sinus thrombosis, large brain infarction and severe brain swelling. Severe brain swelling and hemorrhagic infarction are the most dangerous of these complications. Gaining a good knowledge of DAVF anatomy by carefully reviewing the angiograms preoperatively is the best way to avoid venous ischemia. In case of transverse and sigmoid sinus DAVFs, location of the vein of Labbé should be studied. Preserving normal functional vasculature, especially venous structures, and identifying pathologic structures represents the main surgical strategy.

As noted previously, we have been using fibrin glue injection technique to cavernous sinus from a very small hole on the cavernous sinus wall. During this procedure there might occur heavy arterial bleeding preventing proper visibility. At that point, there is a high risk of carotid puncture and injection of fibrin glue into the carotid artery. Therefore we always use a blunt needle during fibrin glue injection.

DAVFs are highly vascularized lesions, thus having a high tendency for intraoperative bleeding during almost every step of surgery and risk of postoperative hematoma. We have been using Raney clips and strong spring hooks to prevent bleeding from skin incision, bone wax and hot drilling technique to prevent bleeding from bone margins, and dural tacking sutures, bipolar coagulation and fibrin glue to prevent epidural bleeding. Use of the operative microscope from an early stage of surgery is one of the most important strategies to visualize and control bleeding. After wound closure we recommend slight hypotension to prevent postoperative hematoma. A postoperative CT scan is performed a couple of hours after the procedure to reveal possible complications.

Tight closure of dura is nearly impossible in most of the cases especially in the area of transverse and sigmoid sinuses due to bristle tacking sutures and resection of the sinus. We recommend to use artificial dura and fibrin glue to prevent CSF leak. If mastoid air cells are opened during craniotomy we have used bone wax, muscle and fibrin glue to prevent rhinorrhea. Fascia latae patch has been used for reconstruction of the skull base in case part of it has been removed by hot drilling (for example anterior fossa skull base).

Conflicts of interest statement We declare that we have no conflict of interest.

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Chapter 13
The Rationale Behind "A Randomized Trial of Unruptured Brain AVMs" (ARUBA)

Christian Stapf

Abstract A Randomized Trial of Unruptured Brain AVMs is a multidisciplinary international randomized controlled clinical trial including 800 adult patients with the diagnosis of an unruptured brain AVM. Patients willing to participate are randomly assigned to either best possible invasive therapy (endovascular, neurosurgical, and/or radiation therapy) or medical management without intervention. The study protocol does not modify any routine treatment strategies in either arm. Patients will be followed for a minimum of 5 years and a maximum of 10 years from randomization.

The primary outcome measure is the composite endpoint of death from any cause or stroke (clinically symptomatic hemorrhage or infarction confirmed by imaging). The secondary outcome measure is long-term clinical status by Rankin Scale, NIHSS, SF-36, and EuroQol.

Patient enrollment was successfully started in 2007. Participating sites currently include multidisciplinary treatment centers in North and South America, Australasia, and Europe (including Australia, Austria, Brazil, Canada, Finland, France, Germany, Italy, Netherlands, Spain, South Korea, Switzerland, UK, and the USA).

The trial is sponsored and monitored by the US NIH/NINDS (NCT00389181).

Keywords Cerebral arteriovenous malformations · Clinical trial · Epidemiology · Stroke · Intracerebral hemorrhage · Subarachnoid hemorrhage

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Introduction

Current invasive treatment for brain arteriovenous malformations (AVMs) is highly specialized and includes neurosurgical removal, endovascular embolization, and stereotactic radiotherapy, either alone or in any combination. Carefully planned intervention generally leads to successful AVM eradication with relatively low treatment-related morbidity and mortality: a systematic meta-analysis of 2,425 from 25 single institutions suggests surgical mortality was 3.3% with a permanent postoperative morbidity of 8.6% for complete AVM eradication [1]. The 2005 overview on endovascular AVM therapy by the World Federation of Interventional and Therapeutic Neuroradiology showed frequencies of embolization-related complications in well-established international centers ranging between 9.1% and 11.9% [2]. A large prospective series of 308 patients receiving radiosurgery showed 10% radiation induced deficits and 9% unprevented new intracranial hemorrhages with an overall cure rate of 78% [3]. Another multi-centre analysis of 1,255 patients undergoing stereotactic radiotherapy showed that 8% developed a neurological deficit after radiation [4].

The growing availability of MR imaging has lead to a substantial increase in the detection of unruptured malformations ranging between 54% and 62% of all diagnosed AVM patients in modern population-based datasets [5–7]. Similar to intracranial aneurysms, the natural history of unruptured AVMs seems more favorable with an average bleeding risk of approximately 1% per year, as compared to more than 5% for those discovered after initial hemorrhage [8, 9]. The bleeding risk seems to be particularly low (0.9% per year) in the most frequent subgroup of patients harboring unruptured lobar AVMs with superficial venous drainage [10].

Recent data from the literature have raised the possibility that elective invasive treatment for unruptured AVMs may yield worse outcomes than managing patients with symptomatic therapy alone [11], while other series suggest that

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long-term outcome may be more favorable after intervention [10]. In the light of these figures, neurosurgical teams face the clinical dilemma of how to balance the inherent risk of intervention against the potentially low haemorrhage rates in patients harbouring an unruptured brain AVM. Unfortunately, no controlled clinical trials have yet been undertaken of the management of unruptured AVMs to address this growing clinical dilemma [12–14].

Methods

Patients and Interventions

A Randomized Trial of Unruptured Brain AVMs (ARUBA) has been designed as a randomized controlled trial in order to compare the long-term outcomes of patients who receive medical management for neurological symptoms (if any - e.g., headache, seizures, etc.) associated with an unruptured AVM to those who receive medical management and invasive therapy to eradicate brain AVM. The study design is a prospective, multi-center trial where the best possible invasive treatment strategy (free choice depending on the patient's individual profile and anatomic AVM characteristics) will be randomized against non-invasive management. The invasive therapy arm of the trial involves best possible standard interventions with a plan for AVM eradication (by means of neurosurgical eradication, endovascular embolization, and/or stereotactic radiotherapy).

The primary outcome measure is the composite endpoint of death from any cause or symptomatic stroke, i.e., a clinically symptomatic hemorrhage or infarction confirmed by imaging. The secondary outcome measure is long-term clinical status by Rankin Scale, NIHSS, SF-36, and EuroQal. Should patients in the medical management arm develop a symptomatic stroke related to their AVM, they would then be candidates for any single or combination of invasive therapy.

Statistics

From a statistical standpoint, invasive AVM treatment is considered the current standard of care, while the non-interventional group constitutes the "experimental" arm as justified by the expected low spontaneous morbidity in unruptured malformations [8, 9].

The trial will require 800 patients to detect the hypothesized 36.5% relative risk reduction in the event rate with 80% power in an intention-to-treat analysis. Practically speaking, the trial has been designed to test whether invasive therapy or non-invasive management ("deferred treatment") will reduce the risk of death or symptomatic stroke by an absolute magnitude of about 7.5% over 5 years.

Results

In its rigorous review process, the NIH/NINDS study section found scientific and ethical equipoise justifying randomization, and approved ARUBA for international funding. The 5-year follow-up is the expected minimum longitudinal study period based on NIH funding cycles and application policies. The overall length of the study will easily double, given alone the time needed to recruit 800 patients worldwide. Moreover, the independent Data and Safety Monitoring Board has already recommended a longer funding period to ensure a valid interpretation of the trial results and long-term projections based on a 10-year longitudinal observation.

Participating sites include neurovascular teams in North and South America (Brazil, Canada, USA), Australasia, and nine European countries including Austria, Finland, France, Germany, Italy, Netherlands, Spain, Switzerland, and the UK (a regularly updated list of sites open to enrollment is available at http://clinicaltrials.gov/ct2/show/NCT00389181). Eligibility criteria for study enrolment are summarized in Table 1.

Discussion

ARUBA offers the unique opportunity to address these uncertainties in an investigator initiated, multidisciplinary international study. An international consortium of vascular neurosurgeons, interventional neuroradiologists, and vascular neurologists helped designing the trial protocol and is overlooking the conduct and the progress of the trial. There is overall consensus that ARUBA will soon be able to provide reliable data on the natural history in unselected patients with unruptured brain AVMs. Major advantages of this collaborative international study design include a sound and statistically robust trial structure based on ethical equipoise. The inclusion criteria are sufficiently large to prevent systematic non-inclusion of eligible patients. The primary endpoint (i.e., symptomatic stroke and death) constitutes an objective, unbiased criterion highly relevant to clinical practice. The power calculations are based on a two-sided model considering invasive AVM treatment as standard of care. Also, the study protocol will not impose any predefined treatment plan, but will be able to document "real life"

Table 1 Predefined inclusion and exclusion criteria for patient enrollment in "A Randomized Multicenter Clinical Trial of Unruptured Brain AVMs" (ARUBA)

Inclusion criteria
1. Patient must have unruptured brain AVM diagnosed by MRI/MRA, CTA and/or angiogram
2. Patient must be 18 years of age or older
3. Patient must have signed informed consent
Exclusion criteria
1. Patient has a brain AVM presenting with evidence of recent or prior hemorrhage
2. Patient has received prior AVM therapy (endovascular, surgical, radiotherapy)
3. Patient has a brain AVM deemed untreatable by local team, or has concomitant vascular or brain disease that interferes with/or contraindicates any interventional therapy type (stenosis/occlusion of neck artery, prior brain surgery/radiation for other reasons)
4. Patient has a baseline Rankin scale score of 2 or more
5. Patient has concomitant disease reducing life expectancy to less than 10 years
6. Patient has thrombocytopenia ($<$100,000/μL)
7. Patient has uncorrectable coagulopathy (INR $>$1.5)
8. Patient is pregnant or lactating
9. Patient has multiple brain AVMs or harbours another intracranial vascular malformation (cerebral cavernous malformation, dural fistula, familial hemorrhagic telangiectasia, etc.)[a]

[a]Exclusion criteria truncated to most relevant items

therapy according to each site's longstanding experience and expertise of participating neurosurgical and neurovascular teams. Academic treatment centers providing multidisciplinary AVM therapy and treating ten or more AVM patients per year are welcome to join this clinically important international project. More detailed information and contact addresses are available at www.arubastudy.org.

Conflicts of interest statement There are no conflicts of interest.

Acknowledgments A randomized trial of Unruptured Brain AVMs (ARUBA) is funded by NIH/NINDS grants U01 NS051483 (PI: J.P. Mohr) and U01 NS051566 (PI: A.J. Moskowitz). The study is internationally registered as NCT00389181 and ISRCTN44013133. CERVCO (French Reference Center of Rare Vascular Diseases of the Brain and Eye, www.cervco.fr) is supported by public funds by the French Ministry of Health.

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Part IV
Cerebral Revascularization and Bypass Surgery

Chapter 14
Posterior Circulation EC–IC Bypass via Supracerebellar Transtentorial SCTT Approach Applied in a Young Patient with Congenital Multiple Occlusive Cerebrovascular Anomalies – Case Report and Technical Note

Yasuhiro Yonekawa

Abstract A case of remarkable vertebrobasilar insufficiency due to congenital multiple occlusive cerebro-vascular anomalies is presented. Anomalies are of the anterior and posterior circulation, presumably induced by "segmental vulnerability" and modified by infection of recurrent tonsillitis. Symptoms of repeated faintness and black-out attacks and deterioration of cognitive function compromised the quality of life considerably. Successful treatment was achieved by combination of a new type of posterior circulation revascularization procedure, namely occipital artery – superior cerebellar artery bypass via the supracerebellar transtentorial SCTT approach in the sitting position in combination with a standard superficial temporal artery STA–MCA bypass.

Keywords Vertebrobasilar insufficiency · Cerebrovascular occlusive disease · Segmental vulnerability · Posterior circulation revascularization · Transtentorial supracerebellar approach.

Introduction

Microsurgical EC–IC bypass in form of superficial temporal artery to middle cerebral artery (STA–MCA) anastomosis for the anterior circulation pioneered by Donaghy and Yasargil in 1967 [1] has developed into bypasses also for the posterior circulation; superficial temporal artery – superior cerebrellar artery STA–SCA bypass by Ausman (1978) [2], occipital artery–posterior inferior cerebellar artery OA–PICA bypass by Khodadad (1976) [3] and venous interposition graft from the STA to the posterior cerebral artery by Sundt (1982) [4]. Another type of posterior circulation EC–IC bypass via SCTT approach using the OA as donor and the SCA or PCA as recipient in the sitting position was reported by us in 2001 [5]. In this paper a case of peculiar congenital multiple cerebrovascular occlusive lesions is presented in which this type of posterior circulation revascularization procedure in combination with standard STA–MCA bypass was successfully applied as treatment. Technical details of this posterior circulation bypass are also described.

Case Report

The 21-year-old female had been suffering from exertion headache associated with nausea, swaying vertigo and black-out over a period of several months. Sometimes they were accompanied by faintness spells. Lately such episodes occurred almost every day. As soon as she lied down, the above mentioned symptomatology subsided. Furthermore, gradually and insidiously increasing problems of memory disturbance and speech disturbance were pointed out. Except for recurrent tonsillitis, her personal anamnesis was unobtrusive. Hence the patient underwent primarily thorough examination at an ORL clinic for the recurrent tonsillitis. In light of the multiple vascular anomalies seen on MRA and in the presence of a normal MRI, the patient was admitted to the department of neurosurgery University Hospital Zuerich in May 2007.

There were no abnormal neurological findings on admission which corresponded with the MRI findings of no abnormality. The only noticeable laboratory finding of blood chemistry at the time of admission was increased CRP (45 mg/L normally under 5 mg/L) associated with slight leucocytosis (12.14($\times 10^3$/μL) normally 3.0–9.6).

Digital subtraction cerebral angiography (DSA) (Fig. 1) disclosed hypoplasia of the left internal carotid artery (ICA) with its distal ICA of dysplastic configuration partly

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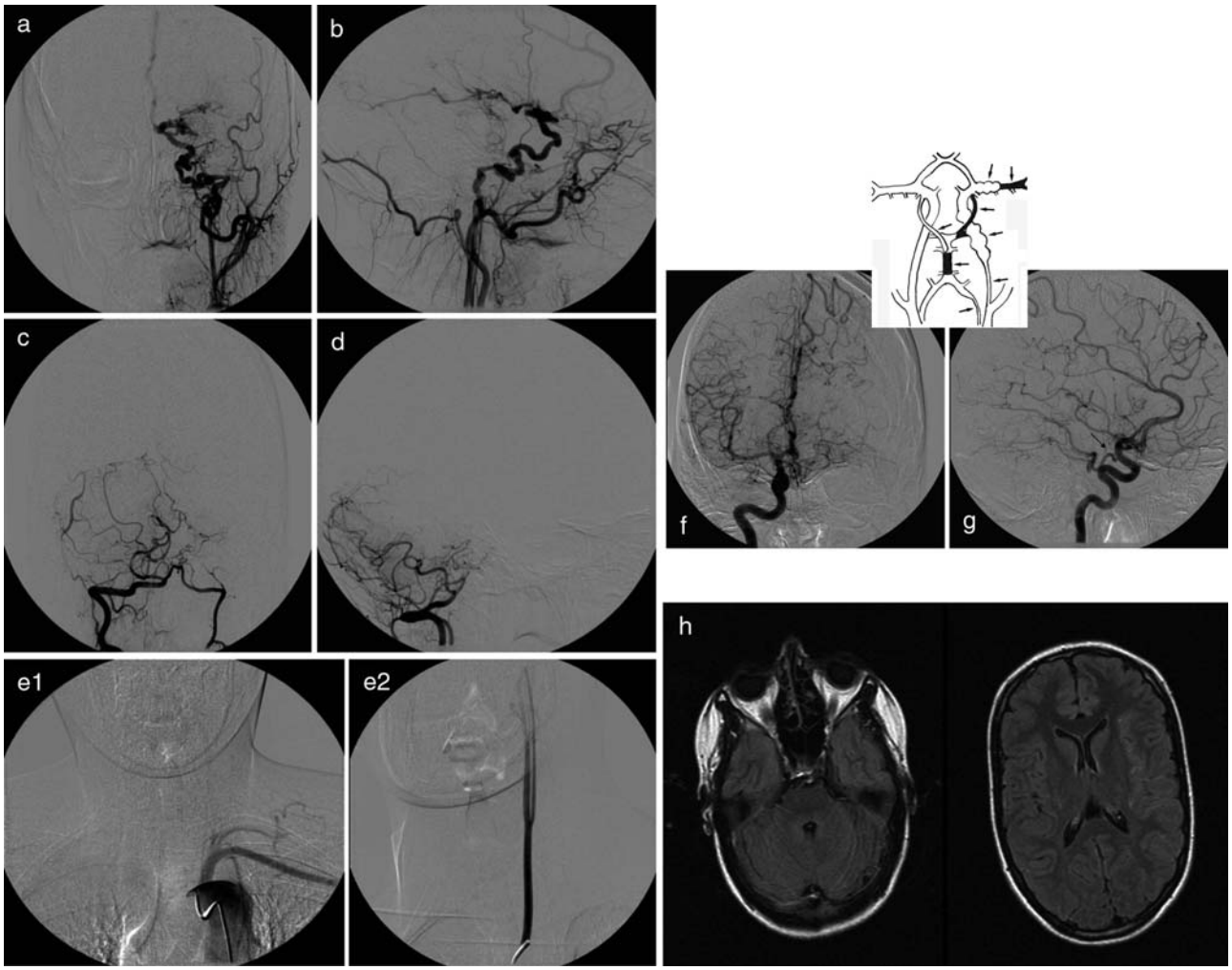

Fig. 1 Preoperative neuroradiology: DSA indicates multiple vascular anomalies including occlusion (**a**–**g**) along with normal MRI (H) (Courtesy of A. Valavanis Neuroradiology USZ): (**a**, **b**) left ICAGs show dysplastic segment partly simulating "string of beads" at C4 and C5. Similar dysplastic segment can be seen at M1 segment prior to complete occlusion. (**c**, **d**) right VAGs show retrograde filling of the right VA and complete occlusion of the BA distal to the VA union. The right PICA supplies partly the SCA and AICA territory. **e**1, **e**2 Hypoplasia of the left VA and the left ICA, respectively. (**f**, **g**) the carotid basilar anastomosis via the right dolicho-posterior communicating artery (*arrow*) where schematic representation of multiple pathologic anomalies is attached

simulating "string of beads" at the C4–C5 segment plus MCA occlusion after a similar dysplastic segment at its M1 portion. The right PCA, SCA and upper basilar artery BA trunk were filling via the right dolicho-posterior communicating artery PcomA, while the filling of the left PcomA–PCA could not be seen. The left VA was hypoplastic from its origin at the subclavian artery. Filling of the right VA was followed up to the VA–BA junction including retrograde filling of the left distal VA, giving the right PICA supplying the territory of the anterior inferior cerebellar artery AICA and the SCA. The BA trunk at its proximal segment was demonstrated neither from the ICA circulation nor from the VA circulation, hence without filling of the anterior inferior cerebellar artery AICA on both sides.

Positron emission CT PET using $H_2{}^{15}O$ with Diamox® loading (Fig. 2) showed low perfusion in the left temporo-parieto-occipital and left cerebellar regions, in which no practical increase on Diamox loading was seen, indicating compromised hemodynamic reserve identified as cerbrovascular reactivity CVR.

In order to augment cerebral blood flow CBF, an STA–MCA bypass was constructed on the left side and 3 days later an occipital artery – superior cerebellar artery (OA–SCA) bypass was performed on the left side as described below. The postoperative course was uneventful and the patient could be discharged on the 8th postoperative day after the second surgery.

The patient did well thereafter without any attacks of black-out and fainting spells. Cognitive dysfunction had

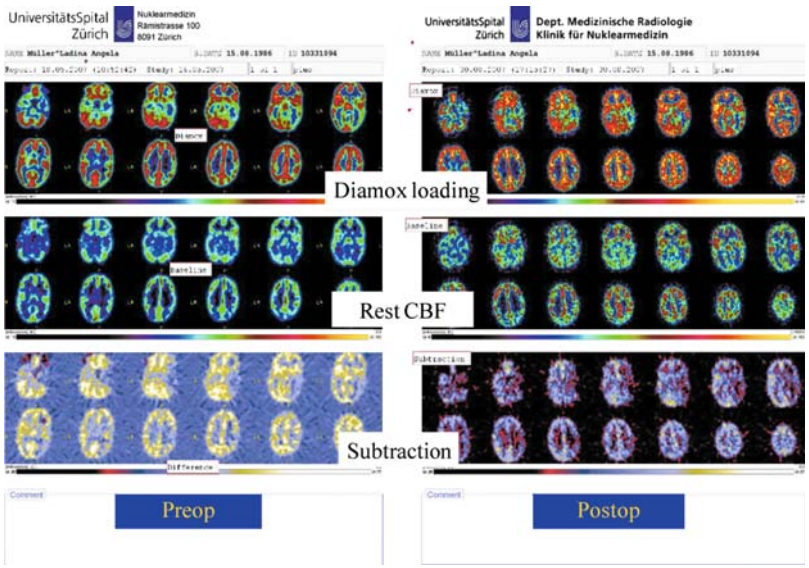

Fig. 2 Preoperative and postoperative $H_2{}^{15}O$-PET (Courtesy of A. Buck Nuclear medicine USZ) Comparison between preoperative and postoperative scans indicates improved CBF and hemodynamic reserve CVR although not complete. This improvement was sufficient to stop faintness and black-out attacks and to recover cognitive dysfunction

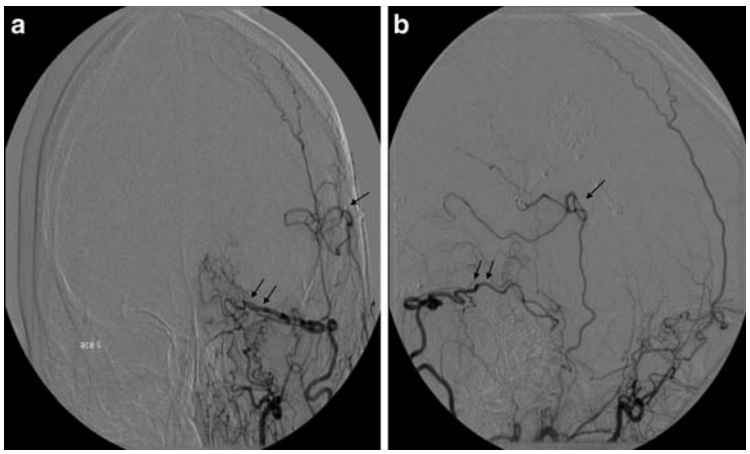

Fig. 3 Follow-up of selective ECAG indicates patent STA–MCA bypass (*arrow*) and OA–SCA bypass (*double arrows*)

also improved. The patient could return to her former job. The follow-up angiography and water-PET were performed after 3 months as inpatient in August 2007, which displayed functioning bypasses. Some cortical branches of the MCA were opacified by the STA and those of the SCA by the OA on selective external carotid angiography on the left side (Fig. 3). The PET scan showed increase of the CBF and of the hemodynamic reserve at the region where these had been impaired preoperatively (Fig. 2).

Surgery of OA–SCA Bypass

In the sitting position, the head is fixed with Mayfield's three point pin apparatus rotating about 30°, turned to the operating side and flexed about 20°. Technical details of the procedure were partly presented elsewhere (Fig. 4) [5]. After having checked the running course of the OA with Doppler sonography percutaneously, a linear skin incision is made over the OA followed by its dissection about 15 cm down to the medial corner of the processus mastoideus. The squama occipitalis is exposed by splitting and spreading the occpitito-nuchal muscles. After a paramedian occipito-sub-occipital craniotomy of 4–5 cm in diameter reaching down to the foramen magnum, the space between the tentorium and the cranial surface of the cerebellum is obtained by sacrificing one or two bridging veins between them. The arachnoid of the cisterna magna is opened at its lateral corner for the purpose of CSF drainage beforehand, so that the mentioned surgical space becomes more spacious. The tentorium is incised from midway towards the tentorial notch. The SCA marginal branch of 1 mm in diameter can be found together with the trochlear nerve at the cranio-anterior margin

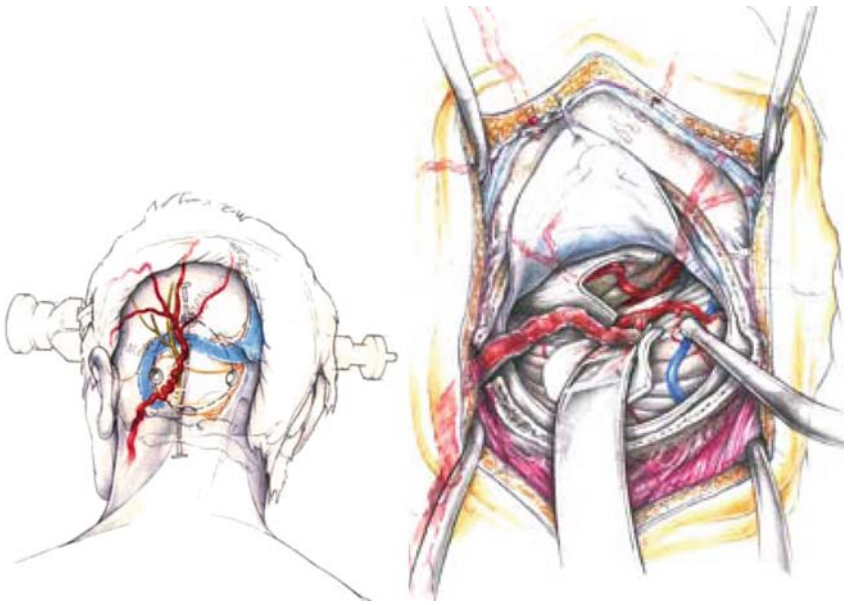

Fig. 4 Artist's drawing of the OA–SCA bypass via SCTT approach

of the lobulus quadrangularis. After dissection of the SCA branch, over a length of 1 cm, where sacrificing of tiny branches is hardly necessary, end-to-side microvascular anastomosis is performed using the dissected end of the OA of 1 mm in diameter in a similar fashion as standard STA–MCA bypass as described elsewhere with long micro-instruments [1, 6–8]. Dural closure, bone replacement and serial closure of muscles, fascia and skin in layers is achieved avoiding strangulation of the OA. There is no need for any drainage.

Discussion

The discussion section consists of two parts: etiology and pathophysiology of the vascular steno-occclusion of the patient and posterior circulation revascularization.

Anomaly and steno-occlusive lesion of this 21-year-old female consisted of at least eight sites, as was mentioned above and is shown in Fig. 1. By the way, the carotid basilar anastomosis was not via the primitive trigeminal artery as described in the standard textbook of neuroradiology [9], which is one of the peculiar points of the vascular anomalies of this patient.

What could have been the etiology of these multiple vascular anomalous occlusive pathologies of this young female patient? Moyamoya disease or moyamoya angiopathy MMA can be ruled out: no bilaterality, no pathology at the terminal portion of the ICA, no abnormal moyamoya-like vasculature at the base of the brain, and the age of this patient just between the predilection age of MMA lower than 10 years old and around 35 years old [10, 11]. Typical cervico-cephalic fibromuscular dysplasia FMD can also be ruled out: dyplastic "string of beads" is not bilateral and not at the level of C2 vertebral body and the patient is only 21 years old, while predilection age of FMD is around 50-year-old females [12].

It might be presumed that the congenital vascular anomaly during the stages of cranial artery development in embryology (vasculogenesis, angiogenesis and remodelling) has taken place being subject to "segmental identity hence vulnerability" after Lasjaunias [13]: occlusion, hypoplasia, dysplasia, elongation (dolicho) and carotid basilar anastomosis in various segments. This probably was the base of vascular insufficiency, which was accentuated by recurrent infections of tonsillitis indicated by a remarkable increase of CRP at the time of admission and which was the reason for the patient's first visit to the ORL clinic. By the way, recurrent infection was considered to be part of the etiology of MMA at the early stage of research [11]. Congenital vascular anomaly was also presumed as etiology of MMA at the very beginning of its research [11] and has gained a new insight under the concept of segmental vulnerability at the time of embryonal vascular development by Lasjaunias [13], later followed by Komiyama [14].

Concerning the OA–SCA and OA–PCA bypass by supracerebellar transtentorial SCTT in the sitting position, this was reported by us in 2001 [5]. The tentorial incision is made at the time of the OA–SCA bypass as this procedure allows a more spacious operative field and better illumination of it, although the procedure of the SCA dissection and anastomosis itself might be performed without doing this. Its incision enables dissection of the posterior temporal artery in case of

OA–PCA bypass. The type of bypass to the PCA does not need the use of PCA trunk itself as in the STA–PCA interposition graft bypass [4], so that the possible complication of hemianopsia or hemiparesis and considerable retraction of the temporal lobe can be avoided.

Advantages and disadvantages of this procedure in the sitting position have been discussed elsewhere [5, 15]. Advantages are: clean operative field as cerebrospinal fluid CSF and blood do not accumulate in the operative field, no need for a considerable temporal lobe retraction, which is usually necessary at the time of STA–SCA bypass and bypass surgery to the PCA, hence no possibility of compromise of the vein of Labbé. Possible disadvantages of the sitting position when performing posterior circulation revascularization have been pointed out by Khodadad [3]. Disadvantages of the sitting position i.e. mainly air embolism and circulatory instability can be managed and overcome by an experienced anesthesiology and operating team, especially by abundant watering of the operating field and by the use of tissue adhesives to seal the air entering points or bleeding points confirmed by jugular compression. Another remarkable disadvantage of the sitting position might be transient deterioration of neurological findings in cases of disturbed CSF absorption, namely in cases of hydrocephalus malresorptivus [15]. The air substituted CBF at the time of surgery remains longer than in cases without this problem representing nearly as "tension pneumocephalus," so that one has to know about this especially in aged patients with CBF disturbances. This young patient did not show such problem.

Conclusion

A case presenting with remarkable vertebrobasilar vascular insufficiency due to congenital multiple cerebro-vascular anomalies probably due to segmental vulnerability and presumably modified by infection has been presented. Symptomatology represented by repeated fainting spells and black-out attacks as well as cognitive function deterioration compromising the quality of life could be successfully treated by a new type of posterior circulation revascularization OA–SCA bypass via SCTT approach in the sitting position combined with a standard STA–MCA bypass.

Conflicts of interest statement We declare that we have no conflict of interest.

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Chapter 15
Superficial Temporal Artery-To-Middle Cerebral Artery Anastomosis with Encephalo-Duro-Myo-Synangiosis as a Modified Operative Procedure for Moyamoya Disease

Keisuke Ishii, Masaki Morishige, Mitsuhiro Anan, Kenji Sugita, Eiji Abe, Takeshi Kubo, Minoru Fujiki, and Hidenori Kobayashi

Abstract *Background*: Various types of revascularization surgery have been performed for moyamoya disease. Although the efficacies of these operations are well recognized, the optimal operative procedure remains undecided. In this report, we describe our modified surgical revascularization procedure for moyamoya disease and retrospectively analyze the results of such surgeries on six sides in six adult patients.

Methods: Our operative procedure, combining direct and indirect bypasses, is a superficial temporal artery to middle cerebral artery anastomosis with encephalo-duro-myo-synangiosis. The encephalo-duro-myo-synangiosis is an indirect bypass combining the encephalo-duro- and encephalo-myo-synangioses. This operative procedure has been used routinely in adult patients since 2002.

Results: Perioperative complications were noted in one of the six operations. This complication was transient and no attributive lesions were detected on CT or MRI. Revascularization was seen in cerebral blood flow studies in all patients, and the clinical outcomes were excellent or good. Effective neovascularization through the grafts was observed in all patients in follow-up angiographies.

Conclusions: This operative procedure provides needed revascularization and prevents ischemic deficits. This modified procedure is useful for responding to subsequent additional ischemia in the area of the anterior cerebral artery and should be considered one of the optimal procedures for treating moyamoya disease.

Keywords Moyamoya disease · Cerebrovascular disease · Stroke · Ischemia · Revascularization · Operative procedure · EC–IC bypass · Encephalo-duro-myo-synangiosis · Surgery

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Introduction

Moyamoya disease is a progressive occlusive cerebrovascular disease characterized by bilateral stenosis of the internal carotid arteries and the development of compensatory collateral vessels (moyamoya vessels) [1–3]. Various operative procedures to initiate revascularization have been reported to prevent the resulting ischemic deficits, including both direct and indirect bypass procedures. One such direct bypass procedure is the superficial temporal artery to middle cerebral artery (STA–MCA) anastomosis [4, 5], and the indirect bypass procedures include encephalo-duro-arterio-synangiosis (EDAS) [6], encephalo-myo-synangiosis (EMS) [7], encephalo-duro-arterio-myo-synangiosis (EDAMS) [8], encephalo-galeo-synangiosis (EGS) [9], omental transplantation onto the cortical surface [10], and the use of multiple burr holes [11, 12]. The procedures have been applied independently or in combinations of direct and indirect bypasses [7, 8, 13–15]. The operative procedure should be selected depending on age, clinical symptoms, general condition, ischemic lesion, cerebral blood flow (CBF) reserve, and individual surgeon preference. In this report, we describe the technique of STA–MCA anastomosis with encephalo-duro-myo-synangiosis (EDMS), modified to combine direct and indirect anastomoses, in six adult patients.

Methods

Patients

We performed STA–MCA anastomosis with EDMS in six consecutive adult patients (three males, three females) with moyamoya disease between 2002 and 2007. The ages of the patients at the time of operation ranged from 22 to 48 years (mean 30 years). Onset symptoms were transient ischemic

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Table 1 Characteristics of moyamoya disease patients who underwent STA-MCA–EDMS surgery

Case No	Age (year) / sex	Type of onset (side)	Presenting symptoms on admission	CT/MRI findings on admission	Angiographical stage (preoperative)	Operative side	Perioperative complications (side)	Follow-up period	Clinical outcome
1	28/F	TIA (R)	Dysarthria	Normal	R: 3, L: 2	R	None	6 years	Excellent
2	48/M	Infarction(R)	Dysarthria	Infarction (R frontal)	R: 4, L: 3	R	None	4 years	Excellent
3	22/F	TIA (R)	Involuntary arm movement(L)	Normal	R: 4, L: 1	R	None	2 years	Excellent
4	27/F	Hemorrhage	Consciousness disturbance	Intraventricular hemorrhage,	R: 1, L: 3	L	None	2 years	Good
		Infarction (L)	Total aphasia, Hemiparesis (R)	Infarction (L fronto-parietal)					
5	34/M	Infarction (L)	Motor aphasia	Infarction (L frontal)	R: 3, L: 4	L	None	1 year	Excellent
6	23/M	TIA (L)	None	Normal	R: 1, L: 4	L	TIA (L)	1 year	Excellent

TIA transient ischemic attack, *R* right, *L* left

attack (TIA) (three patients), infarction (three patients), and hemorrhage (one patient). The angiographic stages, according to Suzuki and Takaku [2], ranged from stage 1 to stage 4. Detailed characteristics of the six patients are summarized in Table 1.

Surgical Technique, STA–MCA Anastomosis with EDMS

A schematic diagram of the surgical procedure is shown in Fig. 1. A skin incision was made along the parietal branch of the STA and extended upward approximately 6 cm toward the frontal, taking caution not to cut the frontal branch of the STA. The parietal branch of the STA was dissected as a donor vessel for direct anastomosis. The small branches of the parietal branch of the STA were coagulated and cut. The temporal muscle was cut as wide as possible along the skin incision and the *linea temporalis*, and a fronto-temporal craniotomy (7–8 cm wide and 9–10 cm long in the frontal-temporal direction) was performed. We usually make two burr holes. The *dura mater* was cut without severing the main branch of the middle meningeal artery, and was turned over and attached to the brain surface. The STA–MCA anastomosis was then performed using 10-0 nylon suture thread. The parietal branch of the STA was anastomosed to the proper recipient of the frontal branch of the MCA. A dissected piece of temporal muscle, used as a graft, was attached to the surface of the cortex and sutured to the *dura mater*. The dural opening was covered with this temporal muscle. The free bone flap was moderately raised from its original position and fixed to avoid compression of the cortex by the temporal muscle. Subcutaneous and cutaneous layers were then closed separately.

Results

Perioperative complications were noted during one of the six operations. In this patient, the ischemic attack was transient and no attributive lesion was detected on either CT or MRI. To date, all patients have been followed up by neurological and radiological examinations, including angiography and CBF measured by single photon emission CT using ^{123}I-iodoamphetamine and ^{99m}Tc-d,l-hexamethyl-propyleneamine oxime. At follow-up, one of the patients (Case 4) exhibited slight right hemiparesis, but this neurological deficit was also present before the operation, and this patient continues to do well in daily life. The other five patients showed no neurological deficits.

CT/MRI scans, CBF studies, and angiographic studies were carried out both preoperatively and postoperatively for all patients. Cerebral infarction (Cases 2 and 5) and intraventricular hemorrhage (Case 4) were observed on CT or MRI images at admission. However, there were no new abnormal lesions reported after discharge. There were no remarkable abnormal findings on CT or MRI in the other three patients. CBF studies were conducted in all patients from 3 days to 36 months postoperatively. Blood flow reserve in the frontal and parietal lobes of the operative side were improved (excluding the infarction area) in all patients postoperatively. The interval from operation to the follow-up angiographic studies ranged from 9 days to 36 months; collateral circulation was supplied mainly through the direct bypass procedure. The deep temporal artery and

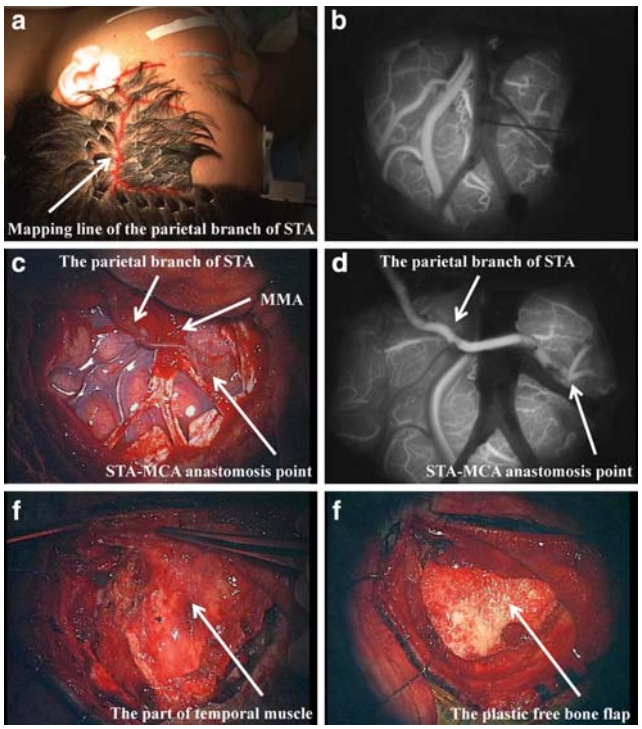

Fig. 1 Perioperative photographs illustrating the surgical procedure of superior temporal artery (STA) to middle cerebral artery (MCA) anastomosis with encephalo-duro-myo-synangiosis (EDMS). (**a**) A skin incision is made along the parietal branch of the STA and extended approximately 6 cm upward toward the anterior, using caution to not cut the frontal branch of the STA. (**b**) Indocyanine green videoangiography showing the middle meningeal artery (MMA). (**c**) The parietal branch of the STA is then dissected as a donor for the direct bypass. The temporal muscle is cut as wide as possible along the skin incision and the *linea temporalis* and a fronto-temporal craniotomy (7–8 cm wide and 9–10 cm long in the fronto-temporal direction) is performed. The *dura mater* is cut, without severing the main branch of the MMA. (**d**) Indocyanine green videoangiography showing the parietal branch of the STA and the point of anastomosis. (**e**) Following the STA–MCA bypass, a dissected part of the temporal muscle, used as a graft, is attached to the surface of the cortex and sutured to the *dura mater*. (**f**) The free bone flap is removed at the point of entrance of the temporal muscle graft, moderately raised from its original position, and fixed to avoid compression of the cortex by the temporal muscle

middle meningeal artery were the usual donors for neovascularization of the grafted tissue. Figures 2 and 3 show an illustrative case (Case 1).

Discussion

We have previously reported on the initiation of moyamoya disease [16] and on the long-term efficacy of revascularization surgery in most patients with moyamoya disease [17, 18]. We have also described our operative procedure and its effect of preventing ischemic insults, and discussed the surgical management of moyamoya disease [19]. In this report, we focus on the combined STA–MCA anastomosis with EDMS operative technique and discuss the possibility of it being one of the optimal procedures for treating moyamoya disease.

Various types of revascularization surgery have been used to treat patients with moyamoya disease [4–15, 19]. However, there is some controversy about the most optimal operative procedures. Both direct and indirect anastomoses have advantages and disadvantages. Previous studies reported that indirect bypass surgery might be more advantageous due to its simple and less-invasive nature [6, 8, 20]. However, in adult patients, the efficacy of indirect anastomosis remains controversial compared to that of direct anastomosis, and organic revascularization was not expected in indirect anastomoses [5, 21–23]. We have performed both direct and indirect anastomoses in adult patients, and consider direct anastomosis to be indispensable. The procedures of choice have been the STA–MCA for the direct anastomosis, and until 2002, EMS for the indirect anastomosis. After 2002, we changed the procedure of indirect anastomosis from EMS to EDMS. The EDMS is a modified procedure combining the EDS and EMS. We have greater expectations of widespread neovascularization due to the additional graft of *dura mater* along with the temporal muscle as shown in Fig. 2. The EDMS is technically not difficult and the time required is comparable to that of the EMS. The EDMS is different from the EDAMS, in that in the EDAMS, the STA

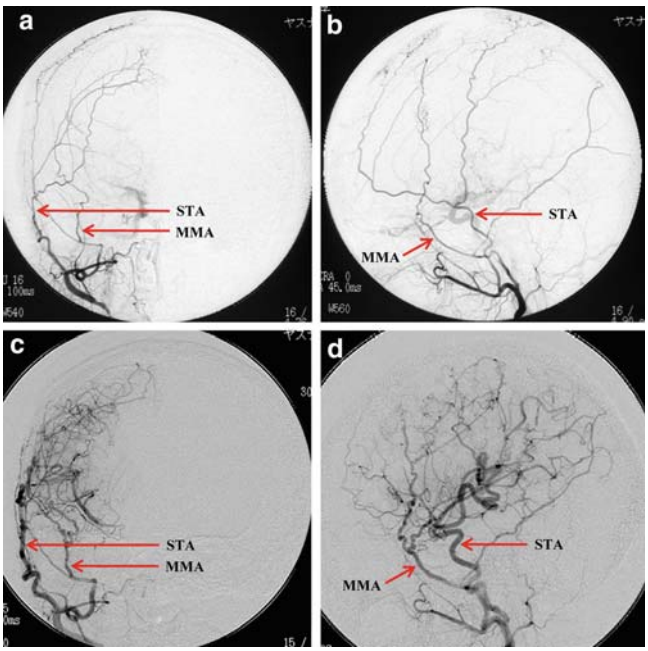

Fig. 2 Preoperative selective right external carotid angiography (Patient No. 1) seen from the anterior–posterior (**a**) and lateral (**b**) views. Postoperative (36 months) selective right external carotid angiography seen from the anterior–posterior (**c**) and lateral (**d**) views. Satisfactory collateral circulation can be observed resulting from the STA–MCA anastomosis and the EDMS. The donor arteries used for revascularization are dilated

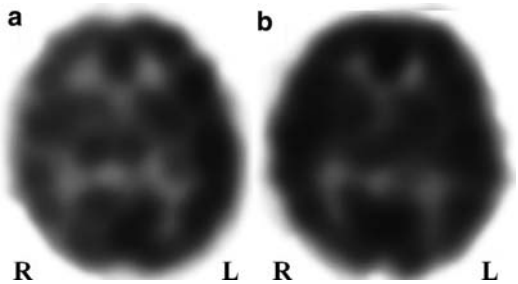

Fig. 3 (**a**) Preoperative and (**b**) postoperative (3 months) SPECT. Preoperatively, the CBF is decreased in the right (R) hemisphere and the postoperative image shows marked improvement

donor is usually the frontal branch, and the parietal branch is not cut. Instead, the parietal branch of the STA is secured for usage as a graft and is attached to the surface of the cortex, while in the EDMS that we use, the parietal branch of the STA is usually dissected as a donor vessel for direct anastomosis and the frontal branch is not harmed. An advantage of the EDMS is that, if additional revascularization in the area of the anterior cerebral artery (ACA) or the frontal lobe is needed, the frontal branch of the STA must be used as an additional option of a direct anastomosis to the ACA territory or as a main donor artery of an EGS to the frontal lobe. The EDMS has also the advantage of being less time-consuming than the EDAMS. One of the disadvantages not only of EDMS, but also EDS, EDAS, EMS, and EDAMS is their restriction to only the area of the MCA.

In the patients undergoing this combined surgery, there were no major complications due to the operative procedure, and postoperative clinical and radiographical outcomes have been good. Despite the limited number of cases examined and the short follow-up time, we believe that the STA–MCA anastomosis with EDMS could be a candidate for one of the optimal revascularization procedures for moyamoya disease, especially in adult patients.

Conflicts of interest statement We declare that we have no conflict of interest.

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Chapter 16
Long-Term Results of Carotid Endarterectomy and Carotid Stenting

Hideki Ogata, Tetsuya Tsukahara, Taketo Hatano, Takuya Nakakuki, Mamoru Murakami, Takako Aoyama, and Akinori Miyakoshi

Abstract *Introduction*: We report the long-term results of surgery for carotid stenosis in our institute, and suggest a better treatment strategy for high-risk patients.

Materials and methods: Our series of 352 carotid surgeries conducted between April 1998 and May 2007 were investigated. CEA comprised 134 (38%), whereas CAS comprised 218 (62%). In August 2007, we sent questionnaires to all patients, and analyzed responses up to May 2008. For patients undergoing regular follow-up, the data were gathered from the medical records. The questions were: (1) mRS at that time, (2) the cause of death if the patient was deceased, (3) newly diagnosed stroke, and (4) newly diagnosed coronary heart disease.

Results: The response rate was 68.8%. The average follow-up period was 31.2 months. The average differences in mRS pre- and postoperation were −0.33 and −0.48 in CEA and CAS, respectively. The mortality rate at >30days was 8.2% in CEA, and 5.0% in CAS. The leading cause of death was heart disease (31.8%).

Conclusion: Our report suggests that CAS is not inferior to CEA, and both procedures can be managed safely if all characteristics of the carotid lesions are considered.

Keywords Carotid endarterectomy · Carotid artery stenting

Introduction

The efficacy of carotid endarterectomy (CEA) for carotid stenosis is well documented, and has been generally accepted as a treatment for severe carotid stenosis [7]. In recent years carotid arterial stenting (CAS) has developed as an alternative treatment for carotid disease. However, the superiority of this endovascular procedure, in terms of safety, efficacy, and durability, has not been confirmed by randomized clinical trials (RCT) [2–5]. Some studies have suggested that CAS is more beneficial than CEA for high-risk patients [1, 5]. However, several points remain to be clarified. For example, is there a good indication for CAS other than the high risk of CEA? Are the long-term surgical results of CAS better than those of CEA?

Few studies have reported the long-term results of surgical treatment for carotid stenosis, especially for CAS. In this study, we retrospectively evaluated the long-term results of CAS and CEA in our hospital, and suggest an appropriate treatment strategy for high-risk patients.

Materials and Methods

Patient Population

Between April 1998 and May 2007, we surgically treated 352 patients with carotid stenosis. One hundred thirty-four lesions were treated by CEA and 218 by CAS (Table 1). Surgical indications (CEA or CAS) were: (1) angiographically severe stenosis (60–99% stenosis), (2) sonographically severe stenosis (75–99% stenosis), and (3) symptomatic stenosis with intra-luminal ulceration. Although CEA was considered the first choice for severe stenosis, CAS was selected when CEA was considered to be risky for patients with: (1) a contra-lateral ICA lesion, (2) distal ICA lesion, (3) higher level lesion (higher than the C2 vertebral level), and (4) medical risk factors such as coronary heart disease. The patient population undergoing CEA or CAS is shown in Table 1.

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Table 1 Patient population

	Cases (%)	Age (mean (range))	S:A (%)	Preoperative stenotic rate
CEA	134 (38)	69.2 (42–82)	68:32	83%
CAS	218 (62)	71.4 (54–94)	62:38	65%

S symptomatic lesions, *A* asymptomatic lesions

Surgical Procedure

CEA was performed under general anesthesia with intra-operative monitors such as INVOS (SaO2), EEG, and SEP. Intra-operative carotid arterial shunt was used for limited cases in which cross-clamping was considered too risky [6]. CAS was performed under local anesthesia. We performed pre-dilatation after the protection device (ParcSurge®) was positioned in the distal part of the lesion. Self-expanding stents (Smart®, Wallstent ®, and Precise®) were used. After dilatation, the embolus was removed by the aspiration catheter.

Data Analysis

In August 2007, questionnaires were sent to the patients who underwent CEA or CAS in our center. The questions covered the following: (1) the condition at that time (mRS 0–6), (2) cause of death if the patient was deceased, (3) newly diagnosed stroke after the operation, and (4) newly diagnosed coronary heart disease after the operation. A total of 165 (46.8%) responses were received up to May 2008. Regarding patients we followed up regularly, the data were gathered from the medical records. We took 77 patient data sets from the medical records (21.8%). Therefore, a total of 242 (68.8%) data sets were available.

Results

Perioperative Results

Revascularization was successful in all cases. The mortality rate for CEA was 0.75% (1/134), and that for CAS was 0.46% (1/218) at 30 days. At 30 days, minor and major stroke cases numbered 3 (2.24%) and 0, and 1 (0.46%) and 3 (1.38%) in CEA and CAS groups, respectively.

Long-Term Results

The pre- and postoperative modified Rankin scales at more than 30 days are shown in Figs. 1 and 2. Both in the pre- and postoperative conditions, average mRS values of CEA patients (1.47 and 1.86, respectively) were a little higher than those of CAS patients (1.18 and 1.64, respectively), although these differences were not significant ($P < 0.05$). The average differences between the pre- and postoperative mRS values were −0.33 in the CEA group and −0.48 in the

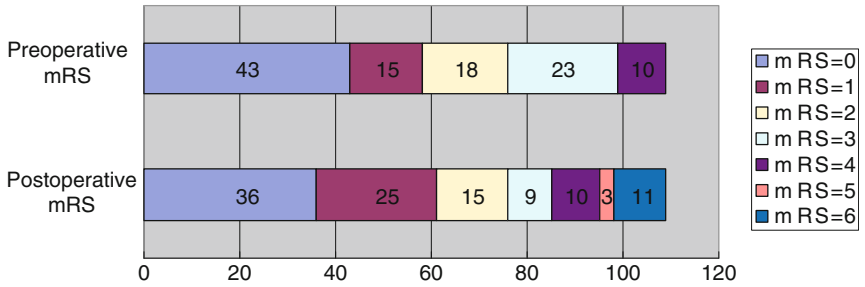

Fig. 1 Perioperative mRS in CEA

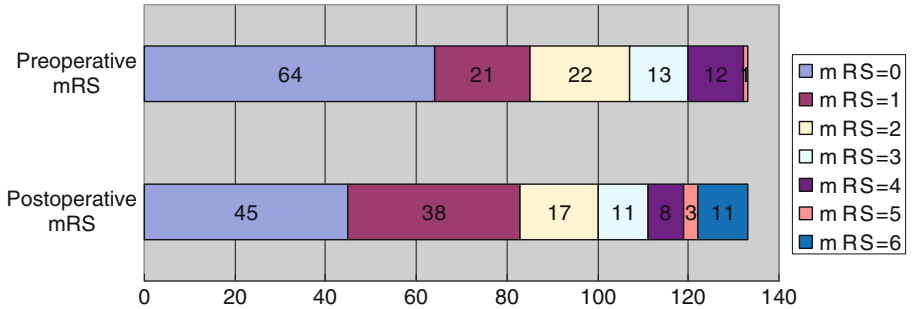

Fig. 2 Perioperative mRS in CAS

Table 2 Causes of death

CEA patients		CAS patients	
Myocardial infarction	2	Myocardial infarction	2
Malignant tumor	2	Stroke	2
Pneumonia	2	Pneumonia	2
Heart failure	1	Heart failure	1
Stroke	1	Subarachnoid hemorrhage	1
Aortic aneurysm rupture	1	Lethal arrhythmia	1
Unknown	2	Unknown	2
Total	11	Total	11

CAS group, but these differences were also non-significant ($P<0.05$).

There were 11 (8.2%) death cases among CEA patients and 11 (5.0%) among CAS patients. Causes of death are shown in Table 2. In the total population, the leading cause of death was heart disease (31.8%), and then it was stroke and pneumonia (18.2 and 18.2%, respectively).

Newly diagnosed strokes after the operation numbered 7 (5.2%) in CEA and 7 (3.2%) in CAS. Heart attacks after the operation comprised 8 (6.0%) in CEA and 7 (3.2%) in CAS.

The average follow-up period was 31.2 months.

Discussion

Carotid disease can be treated with comparably low morbidity and mortality rates by CEA and/or CAS, even in high-risk cases, on condition that each of the characteristics of carotid lesions are considered.

We chose CEA as the first choice for the treatment of severe carotid stenosis, since its efficacy for carotid stenosis has been well confirmed by RCT [7]. On the other hand, we chose CAS for specific cases such as bilateral ICA lesions, distal ICA lesions, higher-level lesions, and other medical risk factors, for which the beneficial effect of CEA is not apparent because of the complication rate [7]. Although the safety and durability associated with CAS have markedly improved, it is still not suitable for the treatment of soft plaques, eccentric or tortuous lesions, and narrow residual lumens. In our experience, atherosclerosis obliterans is another important risk factor in the endovascular procedure.

The stenting and angioplasty with protection in patients at high risk for endarterectomy (SAPPHIRE) trial [8] was the first controlled, prospective randomized trial, published in 2004. In this study, the subjects were high-risk patients such as those with an age greater than 80 years, congestive heart failure, severe COPD, previous endarterectomy with restenosis, and previous radiation therapy. Carotid stenting was compared with endarterectomy. They reported that the perioperative risks of stroke (CAS, 3.1%, CEA, 3.3% , $P=0.94$) and mortality (CAS, 0.6%, CEA 2.0%, $P=0.29$) were similar between CEA and CAS.

In our series of 352 surgeries, CEA or CAS was performed with a comparably low rate of perioperative complications (mortality, 0.75% and 0.46% in CEA, and CAS respectively, at <30 days) [9]. In our study, the preoperative morbidity rates such as for hypertension, diabetes mellitus, coronary heart disease, and hyperlipidemia, were not significantly different between CEA and CAS (data not shown). However, the average age was 4.1 years higher in the CAS group, whereas the average preoperative stenotic rate was 18% higher in the CEA group, and these results showed a significant difference (99% confidence intervals were 4.1 ± 1.93 and 18 ± 0.047 for the average age difference and average preoperative stenotic rate difference, respectively, data not shown). Although the differences were unclear regarding the preoperative medical risk factors, our case assignment seemed to reflect the differences in the stenotic rates and patient ages. These results suggest that our treatment strategies for carotid disease were acceptable.

As for the long-term results of endarterectomy and/or carotid stenting, our results are comparable to those other studies. The average difference between the pre- and postoperative modified Rankin scale was −0.33 in the CEA group and −0.48 in the CAS group, but these differences were not significant ($P<0.05$). For the postoperative stroke, heart attack, or death rate, the differences were also not significant between CEA and CAS groups($P<0.05$).

The CAVATAS study [2], the only randomized trial evaluating the long-term results of carotid stenting, reported the outcomes in 504 patients. They were randomly assigned to undergo CEA or CAS. The investigators did not identify a significant difference regarding the incidence of stroke at 3 years, even though the endovascular patients were not protected against emboli, and almost three quarters of the patients received balloon angioplasty.

There are some points for discussion. The response rate was less than 50%, and the total rate of data collection was 68.8%. Because some patients were referred from other hospitals, operated on in our center, and then referred back to the former hospital after postoperative care, many data on these patients were not available at that time. Moreover, since severely ill or deceased patients cannot respond, mortality and morbidity rates in this study may have been underestimated. As mentioned above, regarding the preoperative medical risks, especially coronary heart disease, the differences in morbidity were not significant between CEA and CAS groups. In our series, we performed CAS for patients with untreated coronary disease, whereas, after coronary disease was treated and became stable, CEA was performed. This might have led to the result that the perioperative and long-term rates of myocardial infarction were not significantly different between CEA and CAS groups.

In conclusion, an appropriate treatment strategy using CEA and/or CAS can be designed when we consider each of the characteristics of carotid stenosis in patients, even in those at high risk. We herein showed one of the treatment strategies for carotid disease, and also suggested that CAS is not inferior to CEA if the cases are properly assigned, although a more complete collection of data and further investigation are necessary.

Conflicts of interest statement We declare that we have no conflict of interest.

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Part V
Stroke Surgery and Management

Chapter 17
Application of Microscope Integrated Indocyanine Green Video-Angiography During Microneurosurgical Treatment of Intracranial Aneurysms: A Review

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Abstract Indocyanine Green Video Angiography (ICG-VA) is recently introduced to the practice of cerebrovascular neurosurgery. This technique is safe and noninvasive and provides reliable real-time information on the patency of blood vessels of any size, as well as residual filling of aneurysms. In this article, a review of the literature and our experience with ICG-VA during microneurosurgery of intracranial aneurysms is presented.

Keywords Indocyanine green · Angiography · Cerebrovascular · Intracranial aneurysm · Subarachnoid hemorrhage · Microneurosurgery

Introduction

Developments in preoperative imaging and improvements in minimally invasive approaches have carried the vascular microneurosurgery to a different level to still compete with the "non-invasiveness" of endovascular therapy [1, 2].

Microneurosurgical clipping is a durable method of treatment for intracranial aneurysms. A perfect clip, around the base of the aneurysm, should occlude the sac totally, preserving the flow in branching and/or perforating arteries. Careful dissection, optimal exposure, temporary occlusion of parent vessels, coagulation and reshaping of the sac, and application of clips of proper length and shape are among the suggested techniques to improve the quality of clipping [1, 3, 4]. However, neck residuals or unexpectedly occluded branches detected in postoperative imaging can be seen even in the most experienced hands [5].

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Postoperative Detection of Improper Clipping

Neck residuals are reported to occur in 4–19% of aneurysm cases in various postoperative studies [6–13], and they may carry a high risk for re-growth and rupture or re-rupture [14–16]. Similarly, inadvertent occlusion of vessels after clipping of an intracranial aneurysm are reported to occur in 0.3–12% of cases in different series [6, 7, 9–11], with the associated morbidity or mortality in more than half of the cases [9].

Recently, we retrospectively analyzed the results of postoperative angiography in 808 clipped aneurysms in 622 patients [5]. Complete occlusion of the aneurysm was achieved in 88% (711) of aneurysms. Neck residuals were detected in 9% and fundus remnants in the remaining 3%. The occlusion was intentionally incomplete in one-third of these cases, either in order to save a major branch or due to calcified, thick aneurysm wall. In the remaining two-thirds, neck or dome residuals were unexpected. Anterior communicating, internal carotid, and pericallosal artery were the most frequent locations for unexpected incomplete occlusions [5]. In the same study, major vessel occlusions were detected in 44 cases, 72% of them unexpected. Internal carotid, middle cerebral and pericallosal artery were the most frequent sites for unexpected occlusions.

Unexpected findings in postoperative imaging studies necessitate re-operation and immediate correction of the clip. The effect of clip repositioning on the outcome is, however, uncertain [5, 17, 18].

Intraoperative Assessment of Clipping

Intraoperative assessment of imperfect clipping can eliminate the need for post-operative studies. Intraoperative angiography, microvascular Doppler, and perivascular flow probe are the methods used to assess the quality of clipping [19–24].

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Intraoperative angiography is believed to be the gold standard method for intraoperative assessment of clipping. Routine or selective use of intraoperative angiography during aneurysm surgery is supported by different studies [5, 21, 24–31]. However, limited routine availability, high cost, false negative findings, and a complication rate of up to 3.5% are the main disadvantages [6, 19, 21, 24, 26, 29–34].

Microvascular Doppler and ultrasonic perivascular flow probe are fast and non-invasive methods, providing real-time information on the patency of major vessels [20, 22, 35–37]. Microvascular Doppler is additionally able to detect aneurysm residuals [36, 37]. However, this is not the case with the perivascular flow probe [19]. None of these methods are able to assess the blood flow in small or perforating vessels.

Indocyanine Green Video Angiography

Microscope-integrated near-infrared (NIR) indocyanine green videoangiography (ICG-VA) is a new technique for intraoperative assessment of blood flow. Principles of the ICG-VA technology are described in detail elsewhere [38–40].

Briefly, after the intravenous injection of indocyanine green (ICG) dye, the field of interest is illuminated with NIR light. Real-time angiographic image with its arterial, capillary, and venous phases is seen on video screen and recorded for further analysis. Playback loops can be repeated as needed. A dose of 0.2–0.5 mg/kg is recommended for ICG-VA, with a maximum daily dose limit of 5 mg/kg.

Microscope-based ICG-VA was first introduced by Raabe et al. in 2003 [38]. In this preliminary study, ICG-VA was found to be a simple and safe method of intra-operative assessment of blood flow. The subsequent study by the same authors [40] compared the findings of ICG-VA with intra- or postoperative digital subtraction angiography (DSA). They reported the findings of ICG-VA to be comparable to both intra and post-operative DSA in 90% of cases [40]. De Oliveira et al. [41] furthermore demonstrated the impressive advantage of ICG-VA in visualization of perforating vessels during the surgery of intracranial aneurysms.

Department of Neurosurgery at Helsinki University Central Hospital serves a population of 2 million in Southern Finland. ICG-VA has been in routine use during cerebrovascular procedures in the department for the last 3 years. During this period there were no procedure related complication recorded.

Recently we retrospectively analyzed the findings of ICG-VA [42] during microneurosurgical clipping of 239 intracranial aneurysms. The results of ICG-VA were compared to postoperative CTA and DSA. There were 6% unexpected neck residuals and 6% unexpected major or minor branch occlusions detected in postoperative imaging. We found unexpected neck residuals to be more frequent in deep seated aneurysms especially in anterior communicating artery location. Unexpected branch occlusion was surprisingly more frequent in middle cerebral artery location, particularly with the giant aneurysms.

The ICG-VA is based on direct visualization of the aneurysm and neighboring vessels in the field of operating microscope. Deep location of the aneurysm in the surgical field is one of the factors limiting the accuracy of ICG-VA findings. Giant size of aneurysms, presence of thick and calcified wall, and arachnoid scarring may also affect the results of ICG-VA. Verification by intraoperative DSA and/or microvascular Doppler should be considered in these instances.

ICG-VA is able to demonstrate the blood flow in large and small vessels including veins. Proper timing of ICG dye injection and repeating video loops may be helpful to verify retrograde flow or residual fluorescence in the vessels. As ICG-VA is not a quantitative technique, any suspicious or delayed filling of branches should be verified by other methods.

In our experience ICG-VA has the unique advantage of assessment of blood flow in perforating vessels. However, it is technically difficult to verify the results in postoperative imaging.

Conclusions

ICG-VA is a simple, fast and reliable method, providing real-time information on blood flow in cerebral vasculature. In selected cases, such as giant, complex, and deep seated aneurysms, the information obtained by this technique should be verified with intraoperative DSA or microvascular Doppler. Visualization of small vessels and perforators is one of the most important advantages of ICG-VA.

Conflicts of interest statement We declare that we have no conflict of interest.

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Chapter 18
Principles of Neuroanesthesia in Stroke Surgery

Tarja Randell

Abstract Subarachnoid hemorrhage (SAH) is a devastating disease with a high incidence of morbidity and mortality. The main aims of therapy are the prevention of rebleeding and the prevention and treatment of delayed cerebral ischemia. SAH is manifested with a variable combination of symptoms and is accompanied by various systemic disturbances, such as cardiac arrhythmias and insufficiency, neurogenic pulmonary edema, and electrolyte disorders.

Successful perioperative treatment – apart from the surgical and endovascular techniques – requires solid knowledge and understanding of the regulation of cerebral hemodynamics, and the effects of subarachnoid hemorrhage and other diseases and various drugs, including the anesthetic agents, on it.

In the following, the basic principles of neuroanesthesia for patients with SAH are reviewed.

Keywords Aneurysm · Neuroanesthesia · Subarachnoid hemorrhage

Subarachnoid hemorrhage (SAH) is most often caused by rupture of a cerebral aneurysm, but it can also be traumatic, or it can originate from an arteriovenous malformation. The characteristic symptoms, varying from mild headache to unconsciousness and death, are mainly caused by the sudden increase in intracranial pressure (ICP), the following cerebral ischemia and the stress reaction with high blood concentrations of catecholamines. Giant aneurysms can cause symptoms related to high ICP also in the absence of hemorrhage.

SAH has a high incidence of morbidity and mortality. Outcome depends not only on the severity of the first bleed, but also on several factors following it, such as re-rupture of the aneurysm with rebleeding, complications during perioperative treatment, including surgical complications, the occurrence of delayed cerebral ischemia, and also on systemic disturbances of physiological homeostasis caused by SAH [1, 2].

The main aims of therapy are the prevention of rebleeding, and the prevention and treatment of cerebral vasospasm. Occasionally also the complications of SAH and associated physiological disorders require medical attention. Prophylactic nimodipine, either orally 60 mg six times a day, or intravenously, is administered to prevent delayed cerebral ischemia [3, 4].

Clinical Manifestations of SAH

The symptoms of SAH vary from mild headache to severe neurological deterioration and death. SAH is also considered a system disease with various clinical manifestations that subside within days or weeks from the bleed [2–7] (Table 1).

SAH impairs both the dynamic and static autoregulation of cerebral circulation, and it may result in either local vasoparalysis, local hyperaemia or the disturbance of whole brain autoregulation. Commonly, the autoregulation curve is switched to the right. The lower limit of cerebral perfusion pressure (CPP) to maintain normal CBF may be as high as 120 mmHg compared to the normal 60 mmHg, which results in the need of maintaining a higher than normal arterial blood pressure. However, this must be balanced against the risk of rebleed before occlusion of the aneurysm: the wall tension of the aneurysm increases more than the tension in cerebral arteries when the blood pressure increases, thus enhancing the risk of aneurysm rupture. An arbitrary upper limit of systolic blood pressure before surgical or endovascular treatment is 160 mmHg, but may be even higher if there is a space occupying intracranial haematoma [3, 8].

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Table 1 Systemic manifestations of SAH

Electrolyte imbalance
Hypokalemia
Hyponatremia
High blood glucose
Cardiopulmonary disorders
Cardiac arrhythmias
Myocardial ischaemia
Cardiac failure
Neurogenic pulmonary edema
Nausea and vomiting

The carbon dioxide reactivity is usually intact after SAH, thus hyperventilation is effective [3, 9].

Prevention of Rebleeding

Rebleeding increases the morbidity and mortality for SAH. To prevent rerupture, the control of blood pressure is of utmost importance: to lower the blood pressure, labetalol in small increments is a feasible choice. Adequate analgesia and anxiolysis provided with small doses of opioids or paracetamol and benzodiazepines, respectively, are also recommended. The doses should be titrated so as not to cause respiratory depression or sedation. However, in unconscious patients, who require tracheal intubation and mechanical ventilation, sedation with propofol is often preferred [3, 4].

Intravenous tranexamic acid 1 g four times a day for 3 days, or until the aneurysm is secured, can be effective in preventing rebleeding [10].

Anesthesia for Stroke Surgery

The aims of neuroanesthesia are presented in Table 2. Most importantly, close co-operation with the neurosurgeon, and the understanding of the surgical procedure are keys to good patient care. Apart from choosing the anesthetic agents, anesthetic considerations include positioning, monitoring, fluid management and immediate planning of postoperative care [3, 4]. The ideal anesthestic agent maintains cerebral autoregulation and carbon dioxide reactivity, does not increase ICP, and does not interfere with brain monitoring. There is no single anesthetic agent to meet the criteria, but in patients with high ICP or an imminent risk for pathological increases in ICP, propofol comes closest to the ideal. Propofol can be used for the induction of anesthesia, but also thiopentone is a feasible choice, having a proven antiepileptic capacity [3, 11]. For maintenance, propofol outweighs inhalation anesthetics because the latter cause vasodilation

Table 2 Aims of neuroanesthesia

Normal or lowest possible ICP
Prevention or treatment of brain swelling
Adequate oxygen and glucose delivery to the brain
Brain protection
Good working conditions for the neurosurgeon
Fast recovery (when not contraindicated)

of the cerebral vasculature followed by an increase in ICP [12]. The use of nitrous oxide is controversial, but if being administered while the neurosurgeon complains of swelling of the brain or a tight brain, it must be discontinued. Opioids, such as fentanyl or remifentanyl can be used for analgesia; also the choice of the muscle relaxant is at the appreciation of the anesthesiologist [3, 4].

Monitoring can be kept as simple as possible: ECG, pulse oximetry, invasive arterial blood pressure monitoring and end-tidal CO_2-monitoring, together with temperature and urine output. During surgery, central venous pressure monitoring is not mandatory, although it is often needed to assess postoperative volume status [3, 4].

Brain relaxation is achieved by osmotic diuresis with mannitol 0.5–1 $g\,kg^{-1}$, and by furosemide. The action mechanism of the latter remains unclear. During surgery, the patients are normoventilated, or mildly hyperventilated if there is need to decrease brain swelling. Other measures to provide optimal operation conditions for the surgeon include discontinuation of all inhaled anesthetics, meticulous positioning in co-operation with the surgeon, and stable hemodynamics. Stable hemodynamic status is maintained with vasoactive drugs, if necessary. The optimal blood pressure should be discussed with the neurosurgeon, and the anesthesiologist should be prepared to manipulate the blood pressure at times [3, 4].

Temporary Clipping

Five minutes of temporary clipping is usually well tolerated without any protective measures. However, to prevent watershed ischemia, increasing the blood pressure with small increments of phenylephrine or norepinephrine is recommended. The level of optimal blood pressure has not been established, but the timing must be planned with the neurosurgeon to avoid an accidental rupture of the aneurysm [3, 4].

Mild or moderate hypothermia may be beneficial, although in the study by Todd et al. hypothermia did not improve the outcome after aneurysm surgery [13]. If a long duration of temporary clipping is planned, profound hypothermia can be considered.

The neuroprotective effect of any presently available drugs remains negligible, although metabolic suppression with thiopentone is sometimes recommended. It is our clinical practice to administer 100% oxygen during temporary clipping [4].

Intraoperative Rupture

Accidental intraoperative rupture of an aneurysm is a hazard that requires rapid and determined decision making. To help the neurosurgeon to place a temporary or a final clip, decreasing the blood pressure or inducing a transient cardiac arrest should be considered if suction fails to clear the field. The off-label administration of adenosine, 12 mg intravenously, is usually followed by 10–15 s cardiac arrest, and normal rhythm returns without any intervention. The neurosurgeon can suction the operative field clear, and place a clip under direct vision. This again requires good co-operation in the team [4].

Postoperative Care

Postoperative care should always be discussed with the neurosurgeon on a case by case basis. Rapid awakening to detect any new or unexpected neurologic defects is feasible only in patients who had been conscious before surgery. While prophylactic employment of triple-H therapy may not be effective in preventing vasospasm, hypotension and hypovolemia are to be avoided. Postoperative analgesia, sedation, prevention and treatment of nausea and vomiting, and maintaining normothermia are usually included in standard local NICU guidelines [3, 4].

Conflicts of interest statement We declare that we have no conflict of interest.

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Chapter 19
Prevention of Symptomatic Vasospasm by Continuous Cisternal Irrigation with Mock-CSF Containing Ascorbic Acid and Mg^{2+}

Akira Satoh, Tatsuya Sugiyama, Hidetoshi Ooigawa, Hiroyuki Nakajima, Takeshi Ogura, Hiroaki Neki, and Eiharu Morikawa

Abstract *Background*: Symptomatic vasospasm (SVS) is still a major cause of poor outcome in cases undergoing early surgical intervention for ruptured intracranial aneurysm. Among the numbers of therapeutic trials to prevent and ameliorate neurological deterioration due to SVS, removal or quenching of oxy-hemoglobin (OxyHb) from subarachnoid colts and administration of Mg^{2+} (Mg) have especially been expected to be effective. In this report the authors investigated the effect of continuous cisternal irrigation (CCI) with mock CSF containing ascorbic acid (ASA) and Mg, performed after early surgery for ruptured aneurysm.

Method: Sixty-three cases which had received CCI were retrospectively compared with 40 control cases as to the incidence of SVS and outcome.

Findings: Incidence of SVS was significantly less frequent ($P < 0.05$) in the CCI group (11%) than in the control group (25%). Severe and definitive SVS requiring additional specific treatment occurred only in 3.2% of the CCI group, while 22.5% in the control ($P < 0.01$). Overall outcome at discharge was significantly better in the CCI group than in the control ($P < 0.01$).

Conclusions: Postoperative CCI with ASA and Mg was definitively effective in preventing SVS and in lessening severity of SVS if it occurs.

Keywords Symptomatic vasospasm · Cisternal irrigation · Ascorbic acid · Oxyhemoglobin · Mg^{2+}

Introduction

Although surgical outcome of ruptured intracranial aneurysm has gradually but steadily been improved, especially after the introduction of early surgical intervention with the advance of pre-, intra- and postoperative management in various aspects [1], symptomatic vasospasm (SVS) is still one of the most serious problems that affects patients' outcome [1–3]. There has been a certain progress in understanding the basic mechanism of vasospasm after subarachnoid hemorrhage (SAH) [4, 5], and a lot of clinical challenges to prevent the incurrence of SVS have been made in many ways in the last decades [1, 6–10]. For all those efforts, the incidence of postoperative SVS as reported recently yet remains almost around 15–30% [1–3, 10]. Among the numbers of substances proposed to provoke spasm, OxyHb released from the subarachnoid clots has been proven to be a major causative factor and needs to be targeted in clinical setting [4, 5, 11–14]. Kodama and his colleagues reported by far much better results with an SVS incidence of 3.2% by using continuous cisternal irrigation (CCI) with Urokinase (UK) and ascorbic acid (ASA), which is acting as an agent reducing and degrading OxyHb [11]. Recently, the effect of Mg administration in preventing and ameliorating SVS has been vigorously studied [8, 9, 15]. We have been adopting CCI with mock cerebrospinal fluid (CSF) containing ASA and Mg^{2+} (Mg) without using UK, which yielded remarkably good results. This report is a case–control retrospective study concerning the efficacy of postoperative CCI with ASA and Mg in preventing SVS.

Patients and Methods

Sixty-three consecutive cases who underwent early direct surgery for ruptured intracranial aneurysm and received CCI with ASA and Mg in 2004–2006 were assigned to the CCI group, and 40 consecutive cases who underwent early

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surgery in 2003–2004 before CCI therapy was started were assigned to a control group. CCI was performed for 10–12 days postoperatively by administering mock-CSF into the lateral ventricle at an infusion rate of 20 ml/h with CSF drainage from the catheter placed in the basal cistern or the lumbar subarachnoid space. Mock CSF was prepared by adding ASA (4 mg/ml) and $MgSO_4$ (3.0 mEq/L) into lactate-Ringer solution, pH of which was adjusted to 7.4 with $NaHCO_3$. The use of mock-CSF was approved by the institutional review board of our hospital. The neurological grade on admission was evaluated by Hunt-Kosnik grading scale, and the outcome by Glasgow Outcome Scale at discharge. Clinical evaluation of SVS was made by a new spasm grading used in our hospital, which is shown in Table 1. Statistical analysis was performed by Fisher's t or Mann-Whitney U test with significance level of $P<0.05$.

Results

Demographic characteristics of the CCI and control groups are shown in Table 2. There were no statistically significant differences between the CCI and control groups regarding age and male to female ratio. Patients' grade on admission and Fisher's CT grading are shown in Figs. 1 and 2, respectively. Nearly 75% of cases were at grade 1 and 2 in both groups, and nearly 80% of cases had thick SAH depicted as Fisher's grade 3.

Incidence of SVS was 11% in the CCI group and 25% in the control with statistically significant difference ($P<0.05$) (Fig. 3). As no additional treatment was given to the cases with spasm grade 2 because the neurological deterioration was very slight with no focal signs like hemiparesis and/or aphasia, these cases were treated safely and easily with CCI only. Regarding SVS that required active and specific antispasm treatment (grades 3 and 4), the incidence was only 3.2% in the CCI group and 22.5% in the control with further significant difference ($P<0.01$) (Fig. 4).

As shown in Fig. 5, the overall outcome at hospital discharge was significantly ($P<0.01$) better in the CCI than in the control group (GR+MD: 92 vs. 75%, SD+V: 8 vs. 13%, D: 0 vs. 12%) (Fig. 3). It is noteworthy that there was no fatal case caused by SVS in the CCI group. No deleterious side effects accompanying CCI with ASA and Mg were observed except for mild to moderate CSF pleocytosis in a few cases, which could be treated without difficulty.

Discussion

It is generally accepted that the amount of subarachnoid clot is well correlated with the incidence and severity of vasospasm after SAH [1, 4, 5, 11]. Consequently, substances released or produced from the clot have been studied energetically to identify the causative factor that provokes vasospasm of the cerebral arteries after SAH. Among those

Table 1 A new grading system used in the authors' institute

Grading of SVS	
Grade	*Clinical manifestation*
1	None
2	Mild and transient neurological deterioration requiring no specific additional treatment for SVS
3	Definitive but reversible neurological deterioration requiring specific additional treatment for SVS
4	Permanent neurological deficit and/or infarction on CT scan

Table 2 Demographic characteristics of CCI and control group. There is no statistically significant difference between the two groups as to age and sex (male to female ratio)

Demographic characteristics			
	CCI (63)	Control (40)	*P*
Age	55.0±11.6	57.4±11.4	ns
Sex (M/F)	29/34 (0.84)	17/23 (0.74)	ns

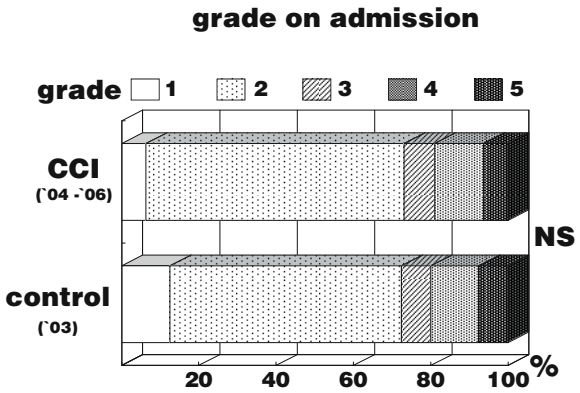

Fig. 1 Neurological grade on admission. Neurological grade is not different in the CCI and control groups. Nearly 75% of the cases in both groups were at grade 1 or 2

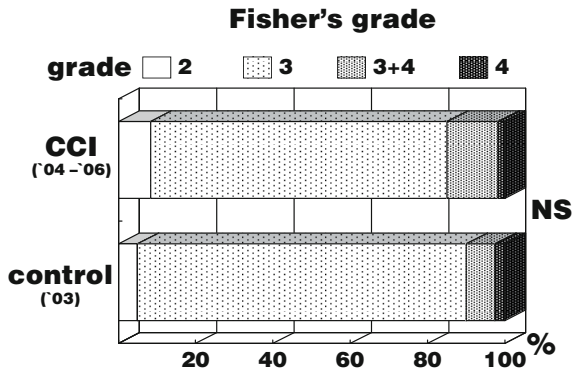

Fig. 2 Fisher's grade on admission (preoperative). "Grades 3+4" represents those having thick SAH with intracerebral or intra-Sylvian hematoma. Fisher's grade is essentially the same in both CCI and control group

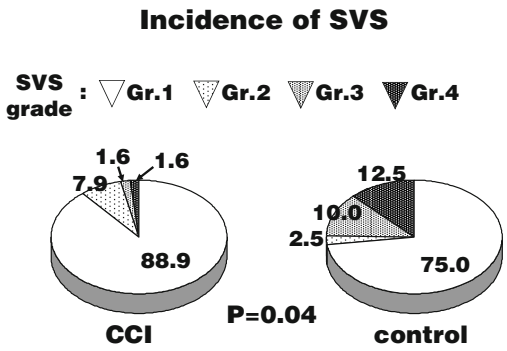

Fig. 3 Incidence of SVS. Incidence of SVS is significantly less frequent in the CCI (11.1%) than in the control group (25.0%), which is significantly different ($P<0.05$)

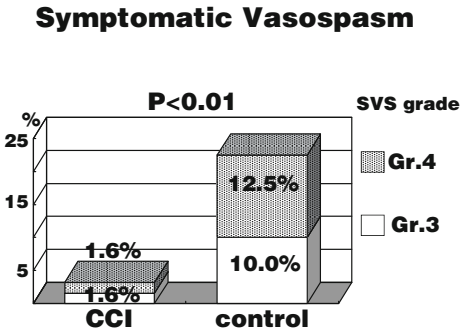

Fig. 4 Incidence of grade 3 and 4 SVS. Incidence of grade 3 and 4 SVS is 3.2% in the CCI group and 22.5% in the control group ($P<0.01$)

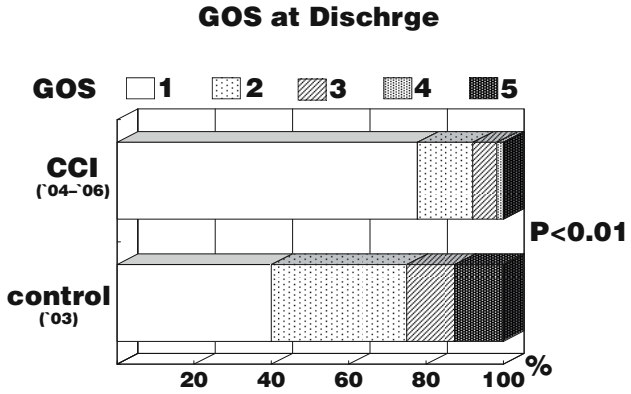

Fig. 5 GOS at discharge. Outcome assessed by GOS is significantly better in the CCI group than in the control group ($P<0.01$). It is noteworthy that there is no fatal case in the CCI group

substances, OxyHb was certified to be the most potent spasmogenic one in a number of experimental studies, and its fate in CSF after SAH in clinical setting is proven to be well corresponding to the development of SVS [4, 5, 11, 14]. Kodama et al. could obtain their excellent results by using CCI with UK and ASA to prevent postoperative SVS [11]. Subarachnoid clot could be removed more quickly when continuously irrigated with UK after chemical lysis of the clot, and OxyHb released from the clot was degraded with ASA [11–13]. The author (A.S.) started using CCI with ASA, with a comparatively low concentration in mock-CSF (1 mg/ml) first which was gradually increased thereafter up to 4 mg/ml to eventually obtain significantly better results (but not as good as Kodama's group) in preventing SVS with an incidence of 33% with 1 mg/ml of ASA, 25% with 2 mg/ml and 12% with 4 mg/ml [16]. In CCI solution, we did not use UK to avoid hemorrhagic complications like postoperative epidural or subdural hematoma or intraparenchymal hemorrhage that may be caused by hemolytic side effect of UK.

Along with the use of ASA we added Mg, adjusted to a little higher concentration (3 mEq/L) than the physiological level (2.2–2.4 mEq/L), to the mock-CSF for CCI. In general, Mg is well known to have a strong vasodilating effect by counteracting to intracellular Ca^{2+} influx in vasoconstricting mechanism [1, 8, 9, 15, 17, 18] Miura et al. reported that Mg concentration in the CSF after SAH dropped below the normal level, and in patients with SVS it was significantly lower than in those without SVS [17]. Besides its direct vasodilatory effect, Mg has polyvalent beneficial effects on the damaged micro-milieu of the central nervous system in spasm stage after SAH. Mg exhibits a range of neuroprotective actions through its antioxidative and/or NMDA receptor-antagonistic functions. It also has anti-platelet aggregation action that is desirable for disrupted intravascular condition in the spastic vessels [1, 15, 18]. A high concentration of Mg in CSF might cause depression of CNS activity. However, the adopted Mg concentration of 3 mEq/L in mock CSF administered into the lateral ventricle at the rate of 20 ml/h is diluted with more than the same amount (500 ml/day) of patient's own CSF, of which Mg concentration is lower than in normal condition (around 2.0 mEq/L or less), making the net concentration be nearly the physiological level which is expected to be clinically safe. Experimentally, Mori et al. reported that in rat SAH model local cerebral blood flow (CBF) is significantly improved in animals that had received administration of Mg into the cisterna magna on day 5 after SAH, while CBF in animals without Mg injection was significantly reduced as compared to control sham rats [18]. A number of clinical trials on the intravenous administration of Mg to patients suffering SAH demonstrated a definite reduction in the incidence of SVS, but failed to constantly yield better outcomes [8, 9, 15]. By administering Mg into the ventricle at a relatively low dose, side effects possibly caused by high dose intravenous administration could be completely avoided in our series.

The incidence of SVS was significantly reduced by CCI with ASA and Mg (Fig. 3), and judging from the spasm grade in both the CCI and control groups, SVS observed in

the CCI group obviously had a much milder degree (Fig. 4). Overall outcome after early surgery was also improved significantly in the CCI group (Fig. 5). It must be stressed that there was no fatal case in the CCI group, which reflects the extreme efficacy of CCI with ASA and Mg in preventing SVS and rendering it less severe if it should occur. We can now considerably simplify the postoperative management just by keeping CCI, and in more than 90% of patients undergoing early surgery for ruptured intracranial aneurysm, we only have to closely observe their neurological condition without adding any further complicated treatments like HHH, albumin administration, intravascular angioplasty or intra-arterial drug infusion etc.

Conclusions

Postoperative CCI with mock-CSF containing ASA and Mg is definitively effective in preventing SVS and in improving the overall outcome of surgically treated cases with ruptured aneurysm.

Conflicts of interest statement We declare that we have no conflict of interest.

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