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Tetsuya Tsukahara
Alberto Pasqualin
Giuseppe Esposito
Luca Regli
Giampietro Pinna *Editors*

Trends in Cerebrovascular Surgery

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Giuseppe Esposito • Luca Regli
Giampietro Pinna
Editors

Trends in Cerebrovascular Surgery

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Editors
Tetsuya Tsukahara
Kyoto Medical Center
National Hospital Organization
Fukakusa, Fushimi-ku,
Kyoto
Japan

Alberto Pasqualin
Institute of Neurosurgery
Verona City Hospital
Verona
Italy

Giuseppe Esposito
Department of Neurosurgery
University Hospital Zurich
Zurich
Switzerland

Luca Regli
Department of Neurosurgery
University Hospital Zurich
Zurich
Switzerland

Giampietro Pinna
Institute of Neurosurgery
Verona City Hospital
Verona
Italy

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Preface

The first European-Japanese Cerebrovascular Congress took place in Zurich in 2001, with Prof. Y. Sakurai and Prof. Y. Yonekawa at the helm; it was called "The Swiss-Japanese Joint Conference." The second meeting was also held in Zurich two years later. The third, under the name of "The European-Japanese Joint Conference for Stroke Surgery," was held in 2006 in conjunction with the 70th anniversary of the Department of Neurosurgery, University Hospital Zurich; the fourth was in Helsinki, Finland, in 2008, with Prof. J. Hernesniemi as the congress president; the fifth European-Japanese Joint Conference for Stroke Surgery was in Düsseldorf, Germany, in 2010; and the sixth meeting, called "The European-Japanese Stroke Surgery Conference (EJSSC)," was held in 2012 in Utrecht, The Netherlands. The seventh EJSSC took place in Verona, from June 25-28, 2014. The main topics of the conference consisted of surgical and endovascular management of intracranial aneurysms and arteriovenous malformations; current concepts in cerebral revascularization; and new developments in cerebrovascular imaging.

The meeting presented an opportunity to gather the latest information on cerebrovascular diseases. The conference also facilitated networking in order to enhance the exchange of clinical and scientific knowledge between researchers and practitioners from different cultures. This volume presents the original papers presented at the meeting.

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Fukakusa, Fushimi-ku, Kyoto, Japan — Tetsuya Tsukahara
Verona, Italy — Alberto Pasqualin
Zurich, Switzerland — Giuseppe Esposito
Zurich, Switzerland — Luca Regli
Verona, Italy — Giampietro Pinna

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Treatment of Intracranial Aneurysms and Intracerebral Hematoma

Surgical Management of Aneurysmal Hematomas: Prognostic Factors and Outcome

P. Meneghelli, F. Cozzi, A. Hasanbelliu, F. Locatelli, and Alberto Pasqualin

Abstract From 1991 until 2013, 304 patients with intracranial hematomas from aneurysmal rupture were managed surgically in our department, constituting 17 % of all patients with aneurysmal rupture. Of them, 242 patents presented with isolated intracerebral hematomas (in 69 cases associated with significant intraventricular hemorrhage), 50 patients presented with combined intracerebral and subdural hematomas (in 11 cases associated with significant intraventricular hemorrhage), and 12 presented with an isolated subdural hematoma. The surgical procedure consisted of simultaneous clipping of the aneurysm and evacuation of the hematoma in all cases. After surgery, 16 patients (5 %) submitted to an additional decompressive hemicraniectomy, and 66 patients (21 %) submitted to a ventriculo-peritoneal shunt. Clinical outcomes were assessed at discharge and at 6 months, using the modified Rankin Scale (mRS); a favorable outcome (mRS 0–2) was observed in 10 % of the cases at discharge, increasing to 31 % at 6 months; 6-month mortality was 40 %. Applying uni- and multivariate analysis, the following risk factors were associated with a significantly worse outcome: age >60; preoperative Hunt-Hess grades IV–V; pupillary mydriasis (only on univariate); midline shift >10 mm; hematoma volume >30 cc; and the presence of hemocephalus (i.e., packed intraventricular hemorrhage). Based on these results, an aggressive surgical treatment should be adopted for most cases with aneurysmal hematomas, excluding patients with bilateral mydriasis persisting after rescue therapy.

P. Meneghelli, MD • F. Cozzi, MD • A. Hasanbelliu, MD
A. Pasqualin, MD (✉)
Section of Vascular Neurosurgery, Institute of Neurosurgery, University and City Hospital, Piazzale Stefani 1, 37128 Verona, Italy
e-mail: alberto.pasqualinvr@gmail.com

F. Locatelli, MD
Unit of Epidemiology and Medical Statistics, Department of Public Health and Community Medicine, University and City Hospital, Verona, Italy

Introduction

Aneurysmal rupture usually results in subarachnoid hemorrhage (SAH), and intracranial hematomas (intracerebral and/or subdural) can complicate aneurysmal rupture, respectively, in up to 42 % of cases, according to various series [10, 12, 22, 26]; this condition heavily affects the clinical outcome. The surgical management of aneurysmal hematomas is still controversial [12], especially since there have been few studies on poor-grade patients with intracranial hematomas, and the results are often conflicting [25].,In recent years, however, prompt surgical treatment has been reported to be associated with reasonably good clinical results [1, 12, 25]; our group previously recognized an early surgical approach as a significant factor positively influencing a patient's outcome [22]. Endovascular modalities have also been reported in the treatment of aneurysmal hematomas [6, 8, 18, 23, 28], even if there is concern over the lapse of time between aneurysm embolization and surgical evacuation of the hematoma.

The aim of this study is to present a 24-year experience in the surgical management of aneurysmal hematomas in order to define the probability of a favorable outcome and the leading prognostic factors that finally affect the outcome.

Materials and Methods

Between 1991 and 2013, 1,754 patients with aneurysmal-SAH were admitted to our department; a total of 1,418 patients (81 %) underwent clipping of the aneurysm, and 336 patients (19 %) underwent endovascular treatment. An intracranial hematoma (intracerebral or subdural) was observed in 304 patients (17 %) who underwent urgent evacuation of the hematoma and exclusion of the aneurysm by clip; they represent the essence of this study. There were 107 males and 197 females, with the mean age 56 (range: 16–82). The

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clinical grade at admission was evaluated with the Hunt-Hess scale (HH), together with the assessment of monolateral or bilateral mydriasis. There were 14 patients in HH grade I, 26 in grade II, 58 in grade III, 62 in grade IV, and 143 in grade V. Unilateral mydriasis was detected in 75 of them (24 %), whereas bilateral mydriasis was detected in 36 of them (12 %).

All of the patients submitted to CT scans on admission; the presence of hydrocephalus and hemocephalus, midline shift (<10 mm, or ≥10 mm), type of the hematoma (intracerebral, subdural, or both), and site and volume of the hematoma were recorded for each patient. A total of 77 patients (25 %) presented with hydrocephalus on admission, and 80 (26 %) presented with hemocephalus (i.e., "packed" intraventricular hemorrhage). A midline shift <10 mm was detected in 128 patients (42 %), and ≥10 mm in 121 patients (40 %); no shift was found on CT scans in 55 patients (18 %). As shown in Table 1, an isolated intracerebral hematoma (ICH) was seen in 242 patients, and in 69 cases the hematomas were associated with significant intraventricular hemorrhage (ICH + IVH); 50 patients presented with a combined intracerebral and subdural hematoma (ICH + SDH) (Fig. 1), and 12 presented with an isolated subdural hematoma (SDH). The observed volume of the ICH was <30 cc in 156 patients, between 30 and 50 cc in 68 patients, and >50 cc in 68 patients. The aneurysmal location was determined with digital subtraction angiography (DSA) or CT angiography (CTA). There were 235 standard-size (<15 mm), 53 large (15–20 mm) and 16 giant aneurysms (>20 mm). The relationship between the location of the aneurysm and type of hematoma is shown in Table 1. The time interval between hemorrhage and surgery was reported for each patient and divided into three groups: <6 h in 118 patients, between 6 and 12 h in 110 patients, and >12 h in 76 patients.

As regards the surgical approach, an enlarged frontopterional craniotomy was adopted for middle cerebral artery (MCA), internal carotid artery (ICA) and anterior communicating artery (ACom) aneurysms, a frontal craniotomy with an interhemispheric approach for distal anterior cerebral artery (ACA) aneurysms, and a retromastoid craniotomy for PICA aneurysms. After careful dural opening, partial evacuation of the hematoma (ICH) was performed in order to relax the brain and decrease the need for brain retraction; partial removal of the hematoma was thought to prevent a dramatic drop in intracranial pressure and consequently decrease the risk of premature aneurysmal rebleeding. Clipping the aneurysm was thereafter performed; intraoperative flowmetry [5] was used since 2001 (Fig. 2). Temporary occlusion of the parent vessel was required in 106 cases in order to safely dissect and finally clip the aneurysm (Fig. 2). The procedure ended with the complete evacuation of the hematoma, which in some cases led to the opening of the lateral ventricle; in other cases a "packed" hemocephalus was evacuated through a third ventriculostomy.

Clinical outcome was evaluated through the modified Rankin Score (mRS) at discharge and at 6 months; it was divided into favorable outcome (mRS 0–2) and unfavorable outcome (mRS 3–6).

Univariate and multivariate analysis were applied to the following risk factors, in order to define their weight on outcome: age (≥60), preoperative HH grade, pupillary reactivity, aneurysmal location, midline shift, hematoma volume, presence of hemocephalus, time to treatment, and temporary occlusion. Crude odds ratio (95 % confidence interval and relative P-value) was calculated using a univariate logistic regression model ($\chi 2$ test and Fisher exact test) in order to evaluate the effect of prognostic factors on clinical outcome. Subsequently, a multivariate logistic exact regression model was used to estimate simultaneously the effect on outcome for significant prognostic factors (according to the previous univariate analysis). Pupillary reactivity was excluded from the multivariate regression model because of disproportion in the distribution of cases. The statistical analysis was performed with STATA software, release 13 (StataCorp LP, College Station, TX, USA) and Statxact software, release 8.0 (Cytel Software Corp., Cambridge, MA, USA).

Results

After the surgical evacuation of the hematoma and clipping of the aneurysm, 16 patients (5 %) needed a decompressive hemicraniectomy to treat intracranial hypertension; a ventriculo-peritoneal shunt was placed in 66 patients (21 %). Other post-surgical complications were meningitis in 1 case,

Table 1 Aneurysmal site and type of hematoma

Site	ICH only	ICH + IVH	ICH + SDH	ICH + SDH + IVH	SDH only
Anterior communicating/distal anterior cerebral	33 (42 %)	32 (41 %)	4 (5 %)	8 (10 %)	2 (2 %)
Middle cerebral	129 (74 %)	24 (14 %)	20 (11 %)	2 (1 %)	–
Internal carotid	10 (21 %)	11 (24 %)	15 (32 %)	1 (2 %)	10 (21 %)
Posterior circulation	1 (33 %)	2 (67 %)	–		–
Total	173	69	39	11	12

ICH intracerebral hemorrhage, *IVH* intraventricular hemorrhage, *SDH* subdural hematoma

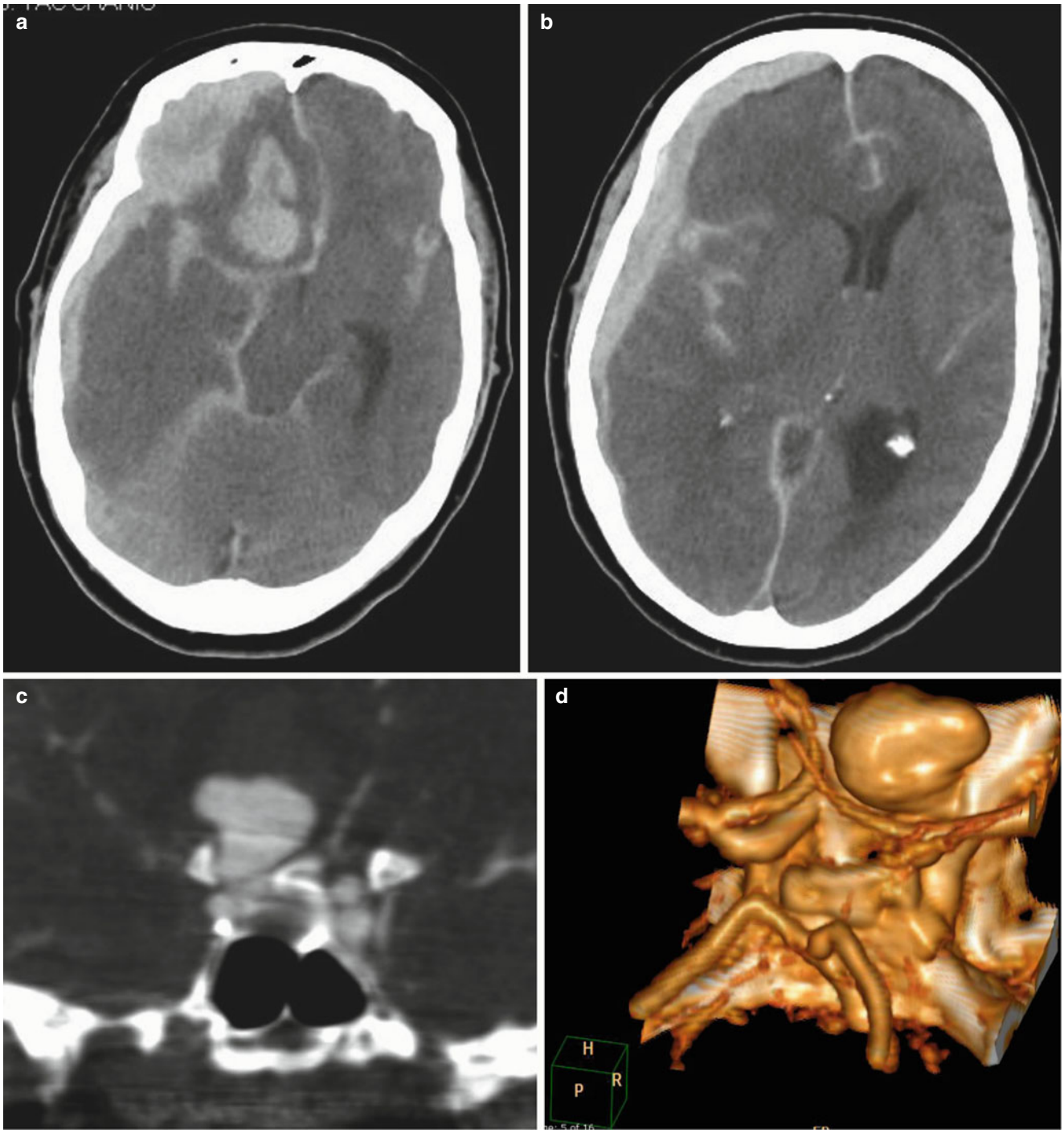

Fig. 1 Seventy-three-year-old woman presenting in coma, with bilaterally areactive pupils (GCS 3) and with right pupil still areactive after mannitol: (**a**, **b**) preop. CT scan, showing a large subdural and frontal hematoma, with marked ventricular shift; (**c**, **d**) angio CT, showing a large paraclinoid aneurysm of the internal carotid artery; (**e**) early postop. CT scan, after simultaneous evacuation of hematomas and exclusion of aneurysm with four clips, through temporary occlusion of internal carotid artery for 30 min (note presence of ventricular hemorrhage); (**f**) CT scan 1 month later, after insertion of a ventriculo-peritoneal shunt. The patient improved after surgery, being able to walk and exhibiting mild cognitive impairment (with paresis of left hand) 1 year after surgery

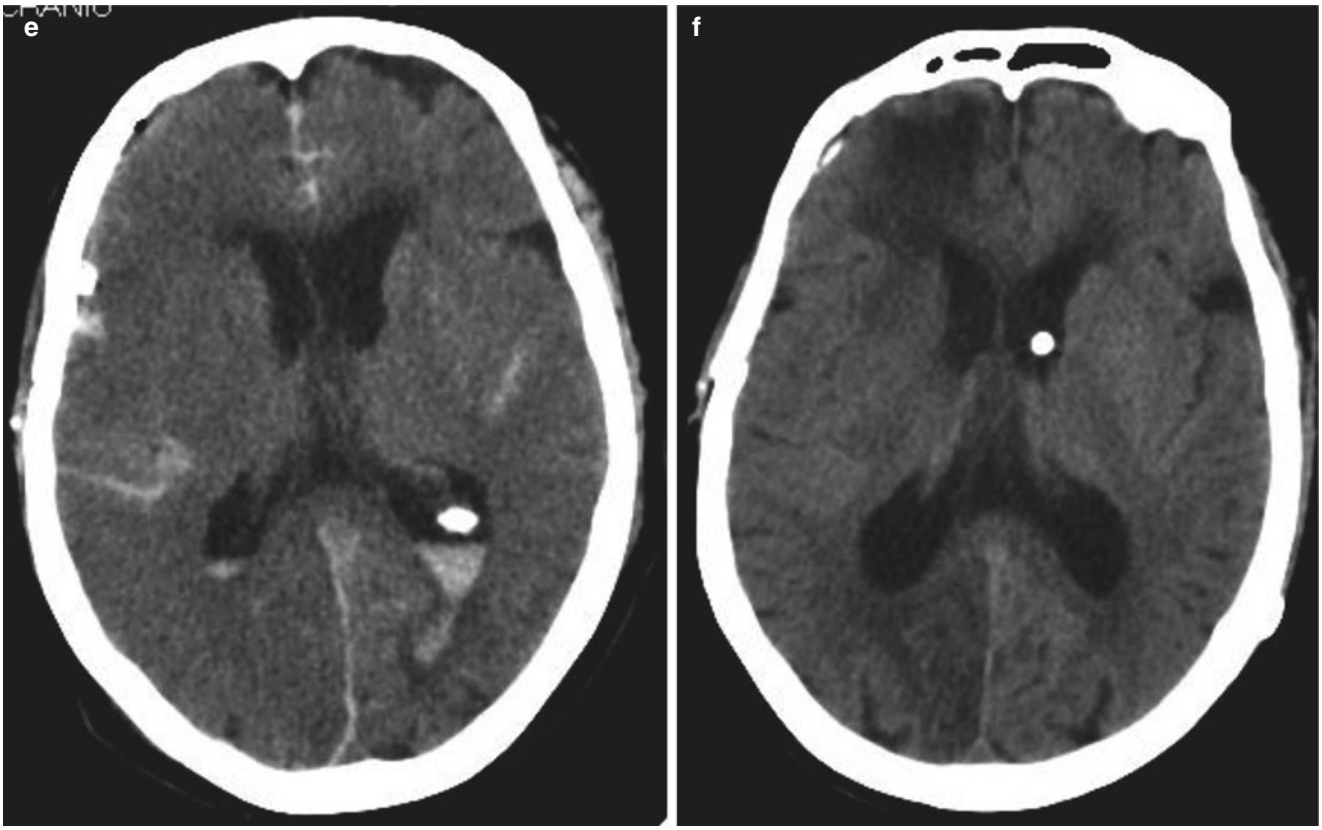

Fig. 1 (continued)

diabetes insipidus in 1 case, pulmonary edema in 2 cases, and pneumonia in 14.

The clinical outcome at discharge and at 6 months is shown in Table 2; a significant improvement in outcome (with favorable results increasing from 10 % at discharge to 31 %) was observed at 6 months post-surgery. The relationship between morbidity (mRS 3–5) and mortality vs. location of the ruptured aneurysm is shown in Table 3; the lowest mortality was observed for patients with ACom and distal ACA aneurysms (23 %).

The following clinical/radiological risk factors showed a significant relation with outcome, as shown in Table 4: preoperative grade (Hunt-Hess classification), pupillary reactivity, midline shift, hematoma volume, and hemocephalus. When plotting time to treatment vs. outcome, a paradoxical increase in favorable outcome was observed in patients operated on more than 12 h from hemorrhage (49 % vs. 29–23 % for patients operated on earlier); this only means that the group operated on later consisted of a higher percentage of patients in better clinical conditions than the group operated on earlier. This conclusion is confirmed by the results of the multivariate analysis, where time to treatment had no significant influence on outcome. As regards pupillary reactivity, a highly significant difference was noted between no mydriasis and monolateral mydriasis on univariate analysis; this prognostic factor was excluded from multivariate analysis, owing to statistical inadequacies.

Discussion

The incidence of an intracranial hematoma from aneurysmal rupture is variably reported in the literature, ranging from 2-42 % according to various series [10, 12, 22, 26]. In our previous study on a consecutive series of 899 patients with ruptured aneurysms admitted between 1971 and 1982, the incidence of intracranial hematomas was 24 % (22); in the present series, the incidence is slightly lower (17 %), possibly due to better treatment of hypertension and/or other factors. The clinical course in these cases can be devastating: in our experience, the only way to reach acceptable results remains an early exclusion of the aneurysm together with total or subtotal evacuation of the hematoma; this is the opinion of other authors as well [1, 12, 25]. In this regard, some anatomical/surgical conditions should be considered. First,

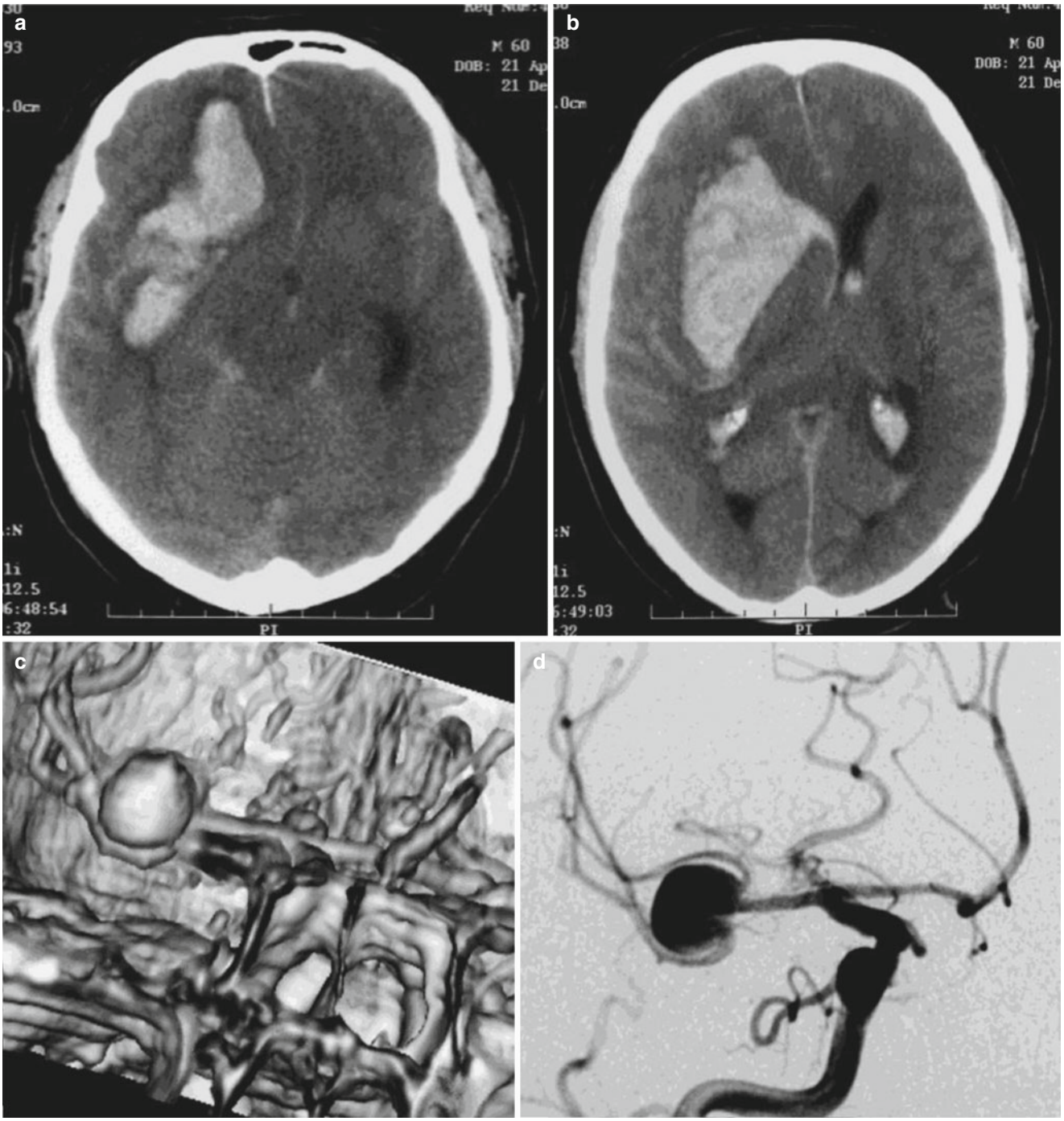

Fig. 2 Sixty-year-old man presenting with stupor and left hemiplegia (GCS 6): (**a**, **b**) preop. CT scan; (**c**, **d**) preop. angio CT and angiography (note aneurysm on arrow-shaped division of right middle cerebral artery); (**e**) early postop. CT scan, after simultaneous evacuation of hematoma and clip exclusion of aneurysm (through temporary clipping of M1 tract for 6+4 min and intraop. flowmetry); (**f**) subsequent CT scan, showing ventricular catheter for monitoring of intracranial pressure; (**g**, **h**) postop. angiography, showing adequate exclusion of the aneurysm. The patient improved after surgery, being able to walk (with mild hemiparesis) 3 months later

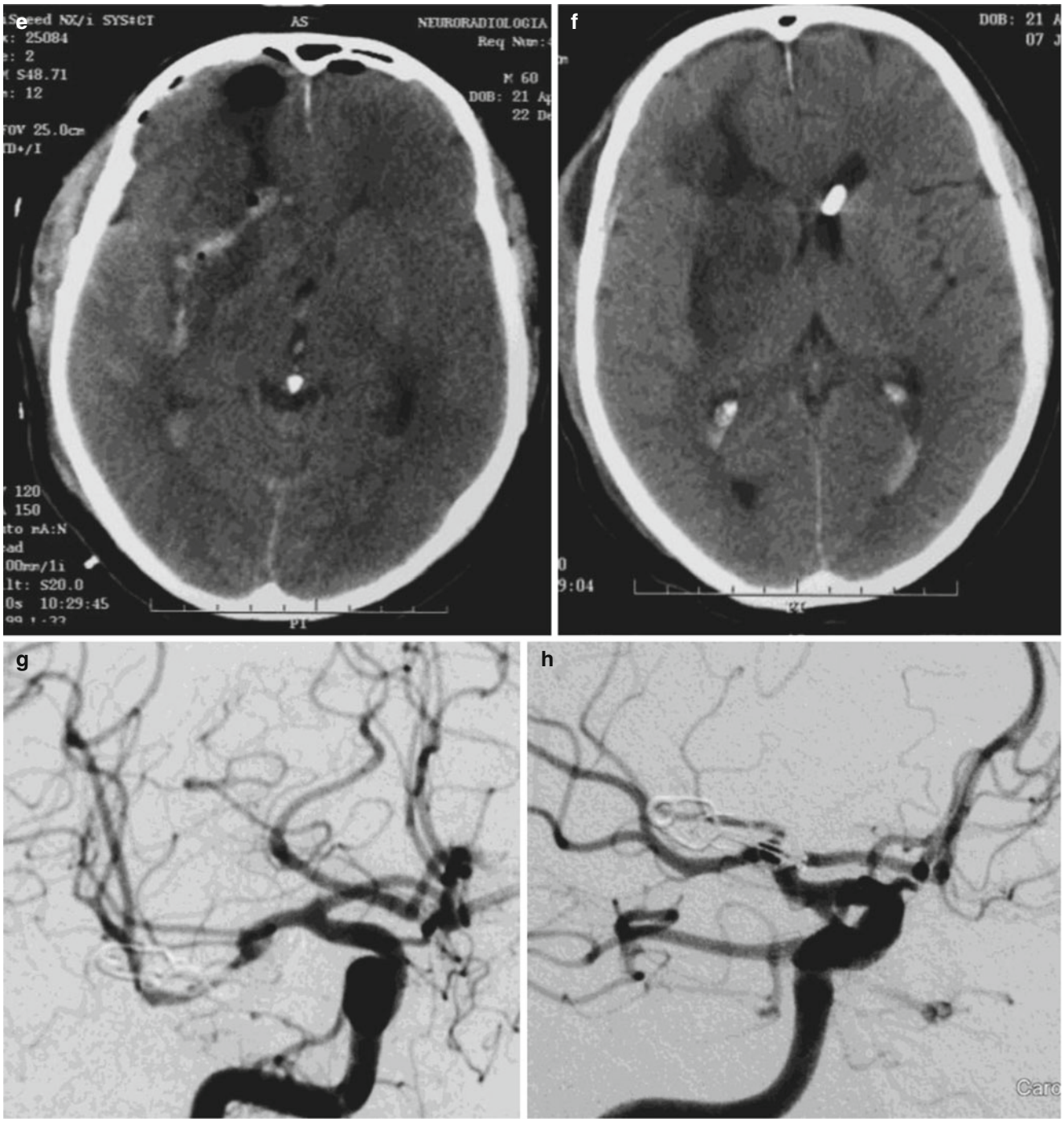

Fig. 2 (continued)

Table 2 Modified Rankin Score (mRS) in 304 patients evaluated at discharge and at 6 months after surgery

mRS	0–1	2	3–4	5	6
At discharge	9 (3%)	20 (7%)	91 (30%)	88 (29%)	96 (31%)
At 6 months	47 (15%)	49 (16%)	71 (23%)	16 (6%)	121 (40%)

Table 3 Six-month morbidity and mortality in patients with aneurysmal hematomas, according to the aneurysmal site

Site	mRS 3–5	Death (mRS 6)
Anterior communicating/distal anterior cerebral (79 cases)	49 (62 %)	18 (23 %)
Middle cerebral (175 cases)	100 (57 %)	59 (34 %)
Internal carotid (47 cases)	28 (59 %)	15 (32 %)
Posterior circulation (3 cases)	2 (66 %)	1 (34 %)

Table 4 Univariate and multivariate analysis on predictors of outcome

	Univariate			Adjusted		
	OR	95 %	*P*-value	OR	95 %	*P*-value
Age (vs. <60 years)	2.13	1.28–3.54	0.003	6.14	2.82–13.34	<0.001
Hunt-Hess (vs. I, II, III)	9.88	5.65–17.28	<0.001	6.19	2.81–13.60	<0.001
Time to treatment (vs. <6 h)						
6–12 h	1.37	0.75–2.50	0.29	1.59	0.71–3.53	0.2
>12 h	0.42	0.23–0.77	0.005	1.00	0.44–2.28	0.9
Pupillary mydriasis (vs. none)						
Monolateral	4.57	2.27–9.22	<0.001	–	–	–
Bilateral	–	–	–			
Midline shift (vs. none)						
<10 mm	2.34	1.22–4.46	0.01	2.07	0.86–4.99	0.1
>10 mm	12.46	5.66–27.42	<0.001	5.79	1.80–18.56	0.003
ICH volume (vs. <30 cc)						
30–50 cc	4	1.98–8.04	<0.001	3.58	1.42–9.01	0.006
>50 cc	6.42	2.88–14.33	<0.001	2.21	0.79–6.14	0.1
IVH (vs. none)	4.36	2.13–8.91	<0.001	4.04	1.65–9.91	0.002
Temporary occlusion (vs. none)	1.27	0.76–2.13	0.35	2.22	1.06–4.63	0.03

OR odds ratio

the infiltration of the fronto-parietal operculum in large hematomas – as well as the possible involvement of the insula or the outer part of the basal ganglia – can limit a complete evacuation; in the opposing view, when the hemorrhage is limited to the temporal or frontal lobe, surgical evacuation is facilitated and brain relaxation is obtained earlier and in a higher percentage of patients. Furthermore, in order to obtain better relaxation of the brain, we have frequently performed – especially in recent years – the fenestration of the lamina terminalis, even in the absence of ventricular hemorrhage. In the presence of large hematomas with ventricular hemorrhage, we have penetrated the ipsilateral ventricle surgically through the hematoma in many cases, in addition to the insertion of an external ventricular drainage.

The rapid occurrence of clinical deterioration in these cases cannot be overemphasized; this is especially true in the presence of an acute subdural hematoma, where evacuation of the clot must be done as soon as possible, due to the early occurrence of ipsilateral mydriasis [3, 9, 14, 20, 26]. In our series, subdural hematomas were observed mostly with ruptured middle cerebral and internal carotid artery aneurysms associated with a parenchymal hematoma in the majority of cases, and observed without parenchymal hematomas in one-fifth of the cases; in the latter situation – observed most frequently with ruptured internal carotid aneurysms – the outcome can be surprisingly good even in the presence of ipsilateral mydriasis, provided that the evacuation is performed as soon as possible [3, 9, 14, 20, 26]. It should be stressed that the occurrence of an isolated subdural hematoma remains an exceptionally rare event after aneurysmal rupture, occurring in 0.6–0.9 % of cases with bleeding aneurysms, according to both the present series and another study [14].

Before considering the possible risk factors for outcome, it is worth mentioning that an alternative way of treatment for these patients is surgical evacuation of the hematoma after endovascular occlusion of the ruptured aneurysm [6, 8, 18, 23, 28]; the largest reported series (30 cases) is from Tawk et al [28]. However, this approach delays the evacuation of the hematoma, while the almost simultaneous evacu-

ation plus clipping maneuver relieves the rise in intracranial pressure earlier than with the combined treatment. This may be a precious advantage for patients with rapid deterioration or who already have ipsilateral mydriasis. Indeed, a few authors have recently reported the use of both approaches (endovascular/surgical, or surgical only) in their patients [8, 23], possibly based on logistic opportunities or other factors.

A troublesome condition that can arise a few days after the surgical evacuation of the hematoma is the occurrence of subacute brain swelling; this may be due to incomplete evacuation of the hematoma, surgery-related stenosis or occlusion of an efferent vessel (leading to localized or more diffuse ischemic damage), lowering of cerebral perfusion due to vasospasm, or the presence of other factors negatively influencing intracranial pressure; in this situation, decompressive hemicraniectomy has been proposed by many authors [4, 7, 11, 21, 24]. In the largest reported series by the Frankfurt Group, a total of 19 patients with intracranial hemorrhage from aneurysmal rupture were submitted to hemicraniectomy, the majority due to delayed infarction [11]. It is undeniable that – in the presence of a large hematoma with raised intracranial pressure – the exclusion of the aneurysm may be problematic, with risk of stenosis of the afferent vessels. In this regard, the introduction of intraoperative flowmetry with Charbel's probe helps to avoid or minimize the risk of ischemia, allowing a complete control of the distal perfusion during and after clipping [5]. The timing of hemicraniectomy remains a controversial point, and there is no doubt that its efficacy decreases when neurological deterioration has already occurred; ideally, the procedure should be done at an earlier step – when intracranial pressure begins to rise and/or midline shift becomes significant – or even done prophylactically, as suggested by some authors [27].

When evaluating possible risk factors for outcome in patients with aneurysmal hematomas, some clinical, radiological and surgical factors have been considered significant by many authors. Among clinical data, *age* is certainly linked with prognosis [10]; however, the turning point has been reported in various series, being 70 years for Nakagawa et al [17], 65 for Oh et al, [19] and 60 for Shimoda et al [25]; from our experience, we agree with this last value. It should be noted that the crucial age is even younger for the Frankfurt Group of (50 for a favorable outcome vs. 57 for an unfavorable one) [10]. The Hunt and Hess grade was reported to be a significant risk factor by our group already in 1986 [22]; more recently, other authors have confirmed this [2, 10, 17]. In the present series, the Hunt and Hess grade has been confirmed as a major determinant of outcome at univariate and multivariate analysis. *Pupillary reactivity* has been previously investigated in two studies [13, 29]. In our experience, the presence of mydriasis played a significant role on prognosis only on univariate analysis.

Among radiological data, the *location of the hematoma* has been reported to play a role on the outcome by Japanese authors [25, 29], with a statistical difference between temporal vs. sylvian vs. diffuse hematomas; we have not considered this factor precisely (*i.e. the location of the ruptured aneurysm*) does not seem to be linked with outcome – at least not in our study. *Midline shift* has already been considered an important factor for outcome; in our previous study – as well as in that of Oh et al – midline shift over 5 mm was linked with a worse outcome [19, 22]. In the present analysis, midline shift over 10 mm is a better predictor of unfavorable outcome. *Hematoma volume* has been previously reported as a determining factor for outcome [10, 19, 25]; however, there is no agreement on the crucial size, which has been reported to vary from 30 to 50 cc, according to various authors. In the present analysis, a significant difference was observed – both on univariate and multivariate analysis (see Table 4) – between patients with hematomas smaller than 30 cc and patients with larger hematomas. *Hemocephalus* (i.e., "packed intraventricular hemorrhage") was recognized as an important risk factor by our group in 1986 [22] and more recently by other authors [15, 16]; in the present study, hemocephalus is confirmed as a powerful predictor of outcome, both on univariate and multivariate analysis.

Among surgical data, *time to treatment* has been previously shown to play a role in outcome; according to Shimoda et al, worse results have been observed for operations performed after 6 h from hemorrhage [25]; according to the Frankfurt Group, the crucial time is even less (3.5 h from hemorrhage) [10]. In our study, we cannot confirm these observations, possibly due to a disproportionate number of patients in better clinical conditions belonging to the group operated on after 12 h from hemorrhage; despite these data, we fervently believe that patients with intracranial hematomas should be operated on as quickly as possible. Finally, *temporary arterial occlusion* appears to have no influence on outcome, both on uni- and multivariate analysis.

Conclusion

Hematomas from aneurysmal rupture constitute a devastating clinical entity, with high postoperative mortality (up to 32–34 % for hematomas caused, respectively, by ruptured ICA or MCA aneurysms). However, even in severe preoperative clinical conditions, a favorable outcome can be achieved in a relatively large number of patients (up to 31 % in our series) by immediate surgery, particularly in the presence of a subdural hematoma. From our statistical analysis, age, preoperative grade, midline shift, hematoma volume, and hemocephalus remain the most significant risk factors for outcome.

Conflict of Interest Statement We confirm that we have no conflict of interest.

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Results of Clipping Surgery for Aneurysmal Subarachnoid Hemorrhage in Elderly Patients Aged 90 or Older

Yota Suzuki, Atsushi Watanabe, Kenji Wakui, Tetsuyoshi Horiuchi, and Kazuhiro Hongo

Abstract

Background

The number of elderly patients with aneurysmal subarachnoid hemorrhage (SAH) is increasing. Although advanced age is one of the recognized risk factors for poor outcome, conservative treatment for aneurysmal subarachnoid hemorrhage cannot provide satisfactory outcome in elderly patients. The aim of this study is to assess the outcome in patients aged 90 or older, for whom ruptured aneurysms were treated by clipping.

Methods

We retrospectively reviewed the medical records of nontraumatic SAH patients who were hospitalized at the Chiba Neurosurgical Clinic between 2004 and 2013. Of the 702 patients, 8 patients (1.1 %) were aged 90 or older. Of them, four underwent clipping surgery and the other four died or were managed conservatively. Their preoperative conditions were evaluated with the World Federation of Neurosurgical Societies Grading Scale of SAH, and the Fisher classification was used to assess the bleeding severity. The location of the ruptured aneurysm was determined by three-dimensional computed tomographic angiography or cerebral angiography. The Glasgow Outcome Scale evaluation was assigned at discharge.

Results

Four patients (four female, all WFNS grade 1), aged 90 or older, underwent clipping surgery. Fisher classification was three in two patients and four in the other two. Location of the ruptured aneurysm was internal carotid artery in two, anterior communicating artery in one, and posterior inferior cerebellar artery in one patient. Two of these four patients had a favorable outcome.

Conclusions

We propose that advanced age alone does not exclude suitable surgical clipping in patients with aneurysmal rupture in the tenth decade of life.

Keywords Cerebral aneurysm • Elderly • Subarachnoid hemorrhage • Surgery

Introduction

In many developed countries, there are many problems associated with the aging populations. In particular, Japan has the highest life expectancy among all World Health Organization (WHO) member states, and women in Japan have the highest life expectancy in the world, at 87.0, according to the WHO World Health Statistics 2014 (http://www.who.int/kobe_centre/mediacentre/whs_2014/en/). Consequently, the number of elderly patients with aneurysmal subarachnoid hemorrhage (SAH) is increasing. Although advanced age is one of the recognized risk factors for poor outcome, conservative treatment of aneurysmal SAH cannot provide a satisfactory outcome in elderly patients. The aim of this study is to assess the outcome in patients aged 90 or older in whom ruptured aneurysms were treated by clipping.

Methods and Materials

From the SAH database, we have performed a retrospective review of 702 patients who were hospitalized at the Chiba Neurosurgical Clinic between 2004 and 2013. We retrieved the data of patients who underwent aneurysm clipping aged 90 or older at the onset of SAH. The preoperative condition

Y. Suzuki, MD • T. Horiuchi, MD (✉) • K. Hongo, MD
Department of Neurosurgery, Shinshu University School of Medicine, 3-1-1 Asahi, Matsumoto 390-8621, Japan
e-mail: tetuyosi@shinshu-u.ac.jp

A. Watanabe, MD • K. Wakui, MD
Chiba Neurosurgical Clinic, Chiba, Japan

T. Tsukahara et al. (eds.), *Trends in Cerebrovascular Surgery*, Acta Neurochirurgica Supplement 123,
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was assessed with the World Federation of Neurosurgical Societies (WFNS) Grading Scale of SAH [1], and the bleeding severity was evaluated using the Fisher classification [2]. The ruptured aneurysm was confirmed with three-dimensional computed tomographic angiography or cerebral angiography. The Glasgow Outcome Scale evaluation was assigned at discharge and classified into "favorable" (good recovery or moderate recovery) and "unfavorable" (severe disability, vegetative state, or dead) outcomes [3].

Results

Of all the patients, 572 (81.5 %) received an intervention (504 open surgery, and 68 endovascular surgery), and 130 (18.5 %) were managed conservatively.

There were eight patients (1.1 %) aged 90 or older. Table 1 shows their characteristics; all were women. Four of them underwent aneurysm clipping (Case Nos. 1, 5, 6, and 8). The other four patients died or were treated conservatively because of poor clinical condition. A clinical summary of the patients who underwent clipping is shown in Table 2. The preoperative condition of all patients was WFNS Grade I. Fisher classification was Group 3 in two patients and Group 4 in the other two. The location of the ruptured aneurysm was the posterior communicating artery (PComA) in two patients, anterior communicating artery (AComA) in one, and posterior inferior cerebellar artery (PICA) in the other. Two of the four patients had a favorable outcome. Preoperative grade was the indicator for surgical treatment. One patient suffered from vasospasm after surgery. Normal pressure hydrocephalus did not occur in all patients, and pneumonia associated with SAH occurred in one case (Case 1).

Illustrated Case (Case 8)

The 90-year-old woman presented with headache, and a CT scan showed an SAH caused by an AComA aneurysm (Fig. 1). Successful aneurysm clipping was performed (Fig. 2), and the postoperative course was uneventful. On Day 22 the patient was discharged without neurological deficits.

Discussion

To the best of our knowledge, this is the first study of SAH patients aged 90 or older. Many previous publications have shown acceptable outcomes with surgical treatment of good grade elderly SAH patients [4–12]. Horiuchi et al reported that 53.2 and 50.6 % of surgically treated patients in their eighth and ninth decades had favorable outcomes [5]. Laidlaw and Siu also reported that an aggressive ultra-early surgical strategy for elderly patients provided favorable independent outcomes in 53 % of good grade patients [8]. Conservative treatment for aneurysmal SAH cannot provide

Table 1 Characteristics of subarachnoid hemorrhage in patients aged 90 or older

Case no.	Age (years)	Gender	WFNS grade	Fisher group	Location	Size (mm)	Clipping	GOS at discharge
1	94	F	I	4	VBA	9	Yes	VS
2	91	F	IV	3	–	–	No	D
3	92	F	IV	3	–	–	No	D
4	91	F	IV	3	ICA	5	No	D
5	90	F	I	4	ICA	6	Yes	SD
6	90	F	I	3	ICA	8	Yes	GR
7	96	F	II	2	ICA	6	No	SD
8	90	F	I	3	ACA	4	Yes	GR

No. number, *WFNS* World Federation of Neurosurgical Societies, *ICA* internal carotid artery, *ACA* anterior cerebral artery, *MCA* middle cerebral artery, *VBA* vertebro-basilar artery, *GOS* Glasgow outcome scale, *GR* good recovery, *SD* severe disability, *VS* vegetative state, *D* dead

Table 2 Clinical results of clipping surgery for aneurysmal subarachnoid hemorrhage in elderly patients aged 90 or older

Case no.	Age (years)	Location of aneurysm	Vasospasm	Hydrocephalus	Complication	GOS at discharge
1	94	VA-PICA	No	No	Pneumonia	VS
5	90	IC-PComA	No	No	No	SD
6	90	IC-PComA	Yes	No	No	GR
8	90	AComA	No	No	No	GR

No. number, *WFNS* World Federation of Neurosurgical Societies, *IC-PComA* internal carotid artery-posterior communicating artery, *AComA* anterior communicating artery, *VA-PICA* vertebral artery-posterior inferior cerebellar artery, *GOS* Glasgow outcome scale, *GR* good recovery, *SD* severe disability, *VS* vegetative state

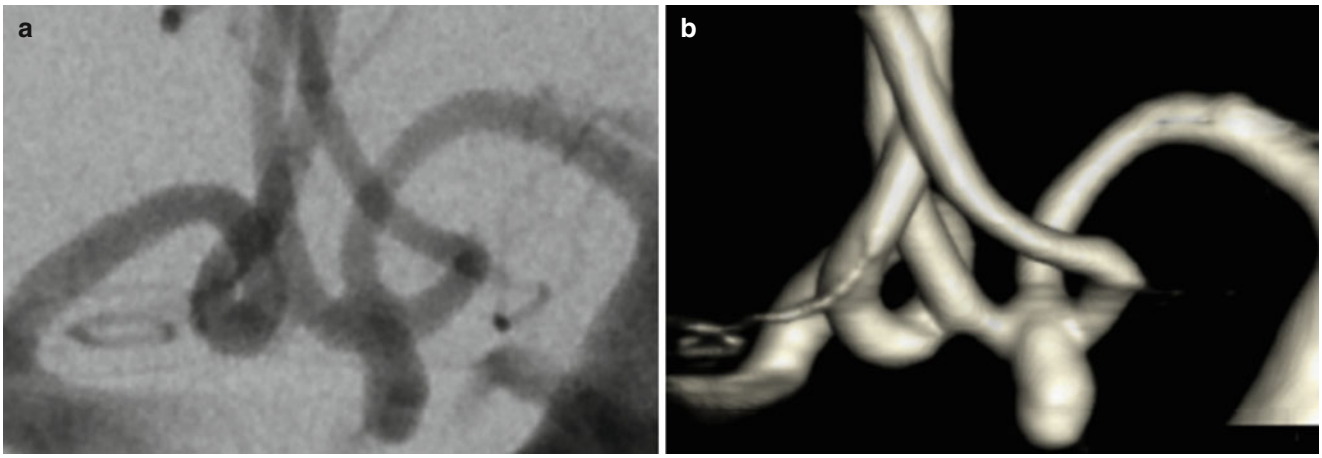

Fig. 1 Anterior-posterior projection of left carotid angiograms (**a** conventional image, **b** three-dimensional image) showing an anterior communicating artery aneurysm projecting inferiorly

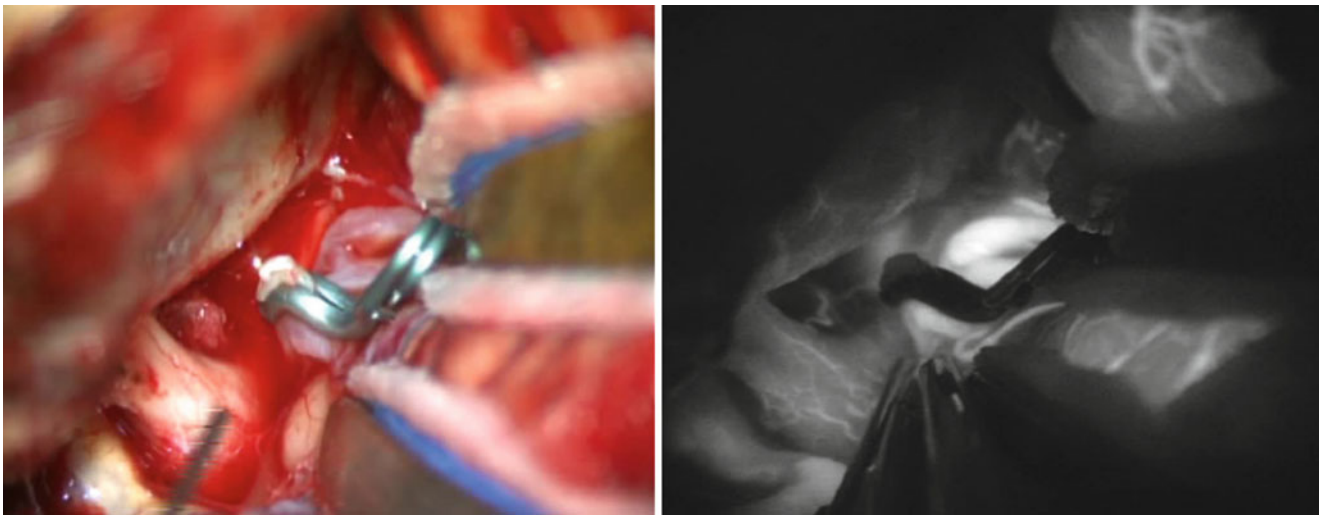

Fig. 2 Intraoperative photograph showing that the aneurysm was obliterated using a crank shaft clip (*left*), and indocyanine green videoangiography demonstrating complete clipping (*right*)

satisfactory outcome in elderly patients [10, 11]. Compared with the natural course of untreated ruptured aneurysms in elderly patients, our treatment outcome may be acceptable.

In this study, clipping was performed on patients who lived independently before ictus, with preoperative WFNS Grade 1 the indicator for surgical treatment. Two out of four patients had a favorable outcome, and so we recommend clipping surgery in selected patients even aged 90 or older.

Elderly patients with an SAH will be more likely to receive endovascular coil embolization, due to recent advances in endovascular devices and techniques [13–18]. However, all ruptured aneurysms cannot be obliterated with the endovascular approach in elderly patients harboring severely tortuous vessels, renal insufficiency, or allergic reaction to the contrast medium. Clipping surgery then still has an important role in treating elderly patients.

Conclusions

Clipping surgery is still a choice for the treatment of ruptured aneurysm in elderly patients even 90 years of age or older with good preoperative clinical condition. We propose that advanced age alone does not exclude adequate clipping in patients with aneurysmal rupture in the tenth decade of life.

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

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Flexible Endoscopic Aspiration for Intraventricular Casting Hematoma

Terushige Toyooka, Hiroshi Kageyama, Nobusuke Tsuzuki, Shoichiro Ishihara, and Kazunari Oka

Abstract

Background

Conventionally, patients suffering a massive intraventricular hemorrhage have undergone external ventricular drainage. However, long-term or repeated drainage increases the risk of complications due to infections or shunt dependency. Neuroendoscopic surgery may offer some advantages over more conventional procedures.

Methods

Thirteen patients suffering intraventricular hematoma associated with intracerebral hemorrhage, treated in our hospital between April 2011 and March 2014, were reviewed retrospectively. Casting hematomas in the ventricles were manually aspirated using a flexible endoscope. The timing of the operation, period of post-endoscopic ventricular drainage, additional internal shunt surgery, 3-month post-surgical outcome, and critical complications were evaluated.

Results

Two patients (treated during our earliest use of endoscope) who underwent surgery on the 7th and 16th day post-onset required subsequent cerebrospinal shunt surgery. In contrast, of the 11 patients who underwent endoscopic surgery on the day of onset, only 1 patient required an additional, third ventriculostomy due to a secondary obstruction of the aqueduct by adhesive fibrous membranes. After 3 months, all six patients with mRS scores of 2–3 satisfied all the following criteria: initial Glasgow Coma Scale scores higher than 8, flexible endoscopic surgeries performed on the day of onset, and period of ventricular drainage of less than 4 days.

Conclusions

Early surgical intervention using a flexible endoscope and short period of post-surgical drainage can be highly effective for patients suffering from casting intraventricular hematomas associated with intracerebral hemorrhage. The advantages of this treatment may be a less invasive procedure, ICP control in the acute phase, breaking away from ventricular drainage in the early stage, and prevention of hydrocephalus or intracranial infectious complications in the long term.

Keywords Neuroendoscope • Flexible endoscope • Intracerebral hemorrhage • Intraventricular hematoma

Introduction

Patients with an intraventricular hemorrhage (IVH) originating from bleeding in the basal ganglia have two critical problems: They develop a neurological focal deficit due to cerebral damage, as well as consciousness impairment as a result of high intracranial pressure due to acute hydrocephalus. The amount of intraventricular blood has been known to become a strong prognostic factor [1]. Its early removal is desirable, because intraventricular hematoma has been reported to be not only a mechanical obturator, but also a chemical exacerbation factor [4]. Conventionally, patients with IVH due to intracerebral hemorrhage (ICH) have received burr-hole surgery with the setting of a ventricular drainage tube. However, sufficient rapid elimination of hematoma is not achieved in many cases because the percentage of clot resolution is 10.8 % per day and is independent of the initial clot volume, type of underlying hemorrhage, and use of ventricular drainage tube [9].

Neuroendoscopic surgery for severe IVH has not been reported in a large-scale study and it has not been established

T. Toyooka, MD (✉) • H. Kageyama, MD • N. Tsuzuki, MD
Department of Neurosurgery, Kuki General Hospital,
418-1 Kamihayami, Kuki, Saitama 346-0021, Japan
e-mail: teru_toy1809@friend.ocn.ne.jp

S. Ishihara, MD
Department of Endovascular Neurosurgery, International Medical Center, Saitama Medical University, Hidaka, Japan

K. Oka, MD
Department of Preventive Medicine, Iizuka Hospital,
Fukuoka, Japan

T. Tsukahara et al. (eds.), *Trends in Cerebrovascular Surgery*, Acta Neurochirurgica Supplement 123,
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as standard. Basaldella et al. [2] showed that flexible neuroendoscopic aspiration plus external drainage reduced subsequent shunt surgery by 34 % when compared with external drainage alone, but it did not significantly affect the outcome of patients.

Oka et al. [11] used a flexible neuroendoscope (videoscope) that realized a safer operation in the ventricles under a high resolution visual field. We used a videoscope in our casting IVH cases.

Methods

Patient Population

This study was a prospective analysis of all patients undergoing endoscopic surgery for casting intraventricular hematoma due to intracerebral hemorrhage between April 2011 and March 2014 at the Department of Neurosurgery, Kuki General Hospital (Kuki, Japan). Thirteen patients (11 males) were diagnosed with hypertensive intracerebral hemorrhage accompanied by clinical warning signs, revealed by computed tomography (CT) scan, that ruptured into the adjacent ventricles and filled the lateral or third ventricle or the aqueduct with hematoma. The age range of the patient cohort was 56–86 (mean: 70.8).

Treatment

All patients underwent endoscopic surgery within 16 days of onset. Under general anesthesia, a burr-hole was placed at the point of the precoronal and 30–35 mm lateral from the midline, which was essentially set at the unilateral side with a lot of hematoma in the lateral ventricle or at the bilateral sides (Fig. 1). A transparent sheath (Neuroport mini®; Olympus Corporation, Tokyo, Japan) with an outer diameter of 6.8 mm and an inner diameter of 5.8 mm was inserted for the endoscopic working tract. Then a flexible endoscope (VISERA Videoscope®; Olympus Corporation, Tokyo, Japan) was

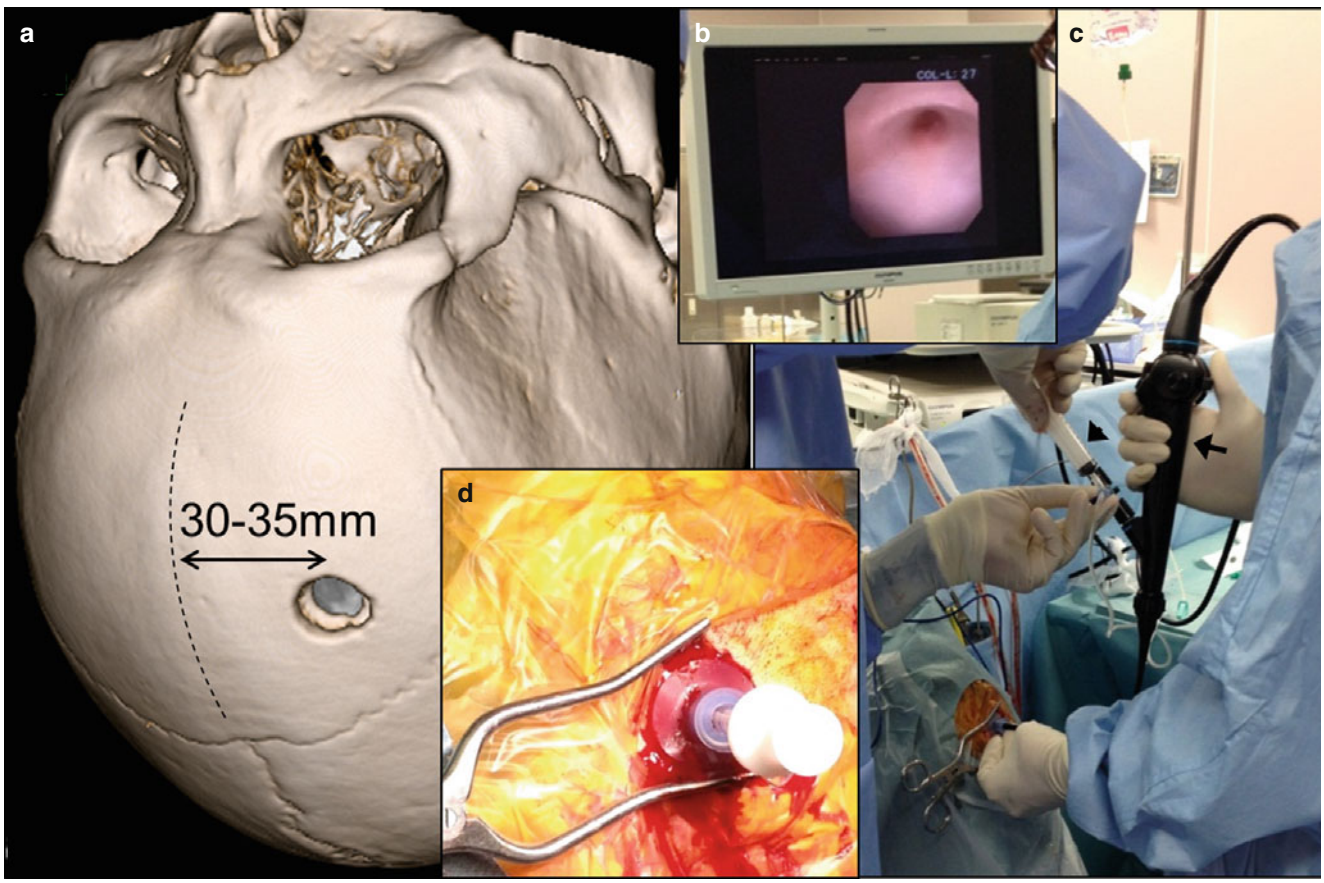

Fig. 1 Surgical procedure of flexible endoscopic hematoma evacuation. (**a**) A burr-hole was placed at the point of the precoronal and 30–35 mm lateral from the midline. (**b**) A transparent sheath was inserted for the endoscopic working tract. (**c**) Videoscope® (*arrow*) was inserted, and ventricular hematomas were manually aspirated with a 10 ml syringe (*arrowhead*). (**d**) Videoscope® gives a high-definition image by a CCD camera implanted at the top of the scope

inserted, and ventricular hematomas were manually aspirated with a 10 ml syringe. The endoscopic procedure was performed under a clear visual field by continuous washing with a perfusion of an artificial cerebrospinal fluid (ARTCEREB®; Otsuka Pharmaceutical Factory, Inc., Tokushima, Japan). Hematoma evacuation was completed when most of the hematomas casting at the foramen of Monro, the third ventricle, the aqueduct and, if possible, the fourth ventricle, were removed (Fig. 2). A drainage tube (Silascon®; Kaneka Medix Corporation, Osaka, Japan) was inserted into the third or the lateral ventricle through the working tract – except in three patients whose ventricular hematomas were removed completely. The ventricular drainage tube was removed as soon as possible after confirmation that clamping of the drainage tube did not cause ventricular dilation.

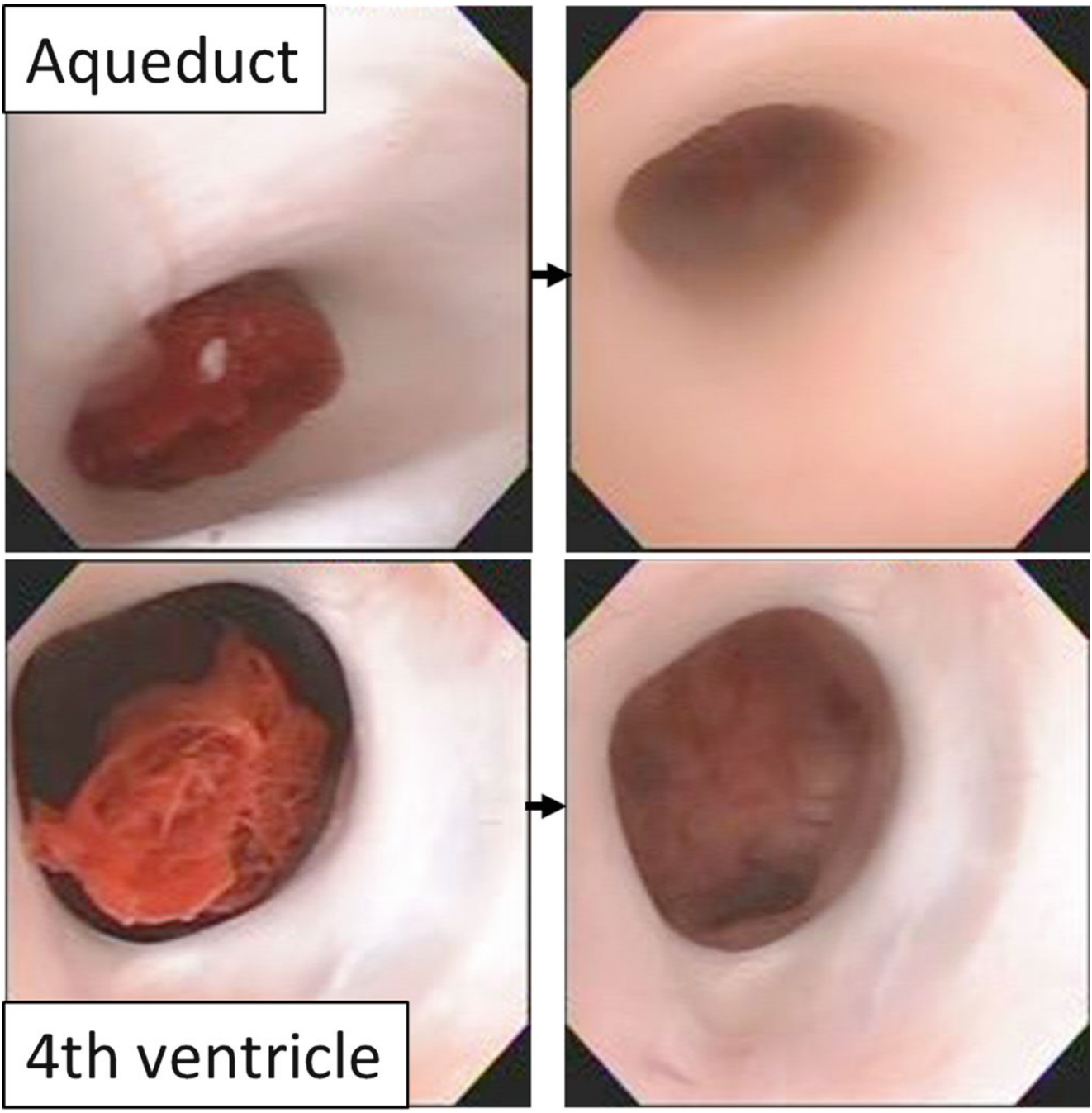

Fig. 2 Hematoma evacuation at the aqueduct (*upper column*) and the fourth ventricle (*lower column*) using a flexible endoscope

Evaluation

The timing of endoscopic surgery, period of post-endoscopic ventricular drainage, additional internal shunt surgery, 3-month post-surgical outcome, and critical complications were evaluated.

Results

Patient Characteristics and the Timing of Endoscopic Surgery

The characteristics of 13 patients with intraventricular casting hematoma due to intracerebral hemorrhage in basal ganglia are summarized in Table 1. Nine patients had hemorrhagic sources in the thalami, three in the putamens, and one in the head of the caudate nucleus. Seven patients had histories of hypertension and were taking medication for it (54 %). One patient took antiplatelet drugs for a previous cerebral infarction, and another had a history of hepatocellular carcinoma and suffered thrombocytopenia. None of the patients had had intracerebral hemorrhage previously. Four patients lapsed into mild impaired consciousness, with initial Glasgow Coma Scale (GCS) scores of 10–14; six patients lapsed into moderate impaired consciousness with GCS scores of 8–9, and three patients lapsed into a comatose or semi-comatose state with GCS scores of 3–6.

In two patients (treated during our earliest use of endoscope), the timing of endoscopic surgery was the 7th and 16th day post-onset, respectively. The first patient received conservative treatment initially and underwent endoscopic hematoma evacuation on the seventh day post-onset, due to subacute hydrocephalus. The second patient underwent a setting of bilateral ventricular drainage on the day of onset and endoscopic hematoma evacuation on the 16th day post-onset. The other 11 patients underwent endoscopic hematoma evacuation on the day of onset.

Ventricular Drainage Periods and Additional Shunt Surgery

The results of the postoperative state are summarized in Table 2. The two patients who underwent delayed endoscopic surgery on the 7th and 16th day of onset required subsequent CSF shunt surgery after all. Only one patient treated on the day of onset required an additional third ventriculostomy due to a secondary obstruction of the aqueduct by adhesive fibrous membranes. The three most critical patients with initial GCS scores of 3–6 required long periods (10–13 days) of ventricular drainage after endoscopic surgery, and two of the three patients required subsequent CSF shunt surgery. A CT scan showed massive hematomas occupying entire ventricles. In contrast, mild and moderately impaired consciousness patients with initial GCS scores of 8–14 who underwent endoscopic surgery on the day of onset required ventricular drainage for fewer than 6 days. All three patients who received an additional procedure of intrathecal injection with urokinase required subsequent CSF shunt surgery.

Table 1 Clinical characteristics of patients with intraventricular casting hematoma due to intracerebral hemorrage

No.	Age	Gender	Hemorrhagic source	Initial GCS	Focal neurological deficit(s)	Past history (medication)
1	56	M	Lt. thalamus	10	Hemiplegia, aphasia	HT
2	76	M	Rt. thalamus	14	Hemiparesis	HT
3	65	M	Lt. thalamus	14	Hemiplegia, aphasia	HT
4	65	M	Rt. caudate	4	Decerebrate	HT
5	76	M	Rt. thalamus	6	Anisocoria	Brain tumor
6	72	F	Lt. thalamus	8	Anisocoria, hemiplegia	–
7	85	M	Lt. thalamus	8	Hemiplegia, aphasia	HT, CI (aspirin)
8	59	M	Lt. thalamus	8	Hemiplegia, aphasia	–
9	86	F	Rt. thalamus	9	Hemiplegia	HT
10	69	F	Lt. putamen	3	Loss of light reflex on both pupil	HCC, thrombocytopenia
11	72	M	Lt. putamen	8	Hemiplegia, aphasia	HT
12	67	F	Rt. putamen	9	Hemiplegia	–
13	73	M	Lt. thalamus	13	Hemiplegia, aphasia	–
Mean 70.8						

GCS Glasgow Coma Scale scores, *M* male, *F* female, *Lt.* left, *Rt.* right, *HT* hypertension, *CI* cerebral infarction, *HCC* hepatocellular carcinoma

Table 2 Postoperative courses after endoscopic surgery in patients with intraventricular casting hematoma due to intracerebral hemorrage

No.	Initial GCS	Day of endoscopic surgery from onset	Drainage[a] period (days)	Additional surgery	Critical complication	mRS after 3 months
1	10	7	6	VP shunt	–	4
2	14	16	0	ETV	–	4
3	14	1	0	–	–	3
4	4	1	13	EVD	Ventriculitis	5
5	6	1	13	ETV	–	5
6	8	1	2	–	–	3
7	8	1	–	–	CPM	5
8	8	1	–	–	–	2
9	9	1	–	–	–	4
10	3	1	10	–	–	5
11	8	1	4	–	–	3
12	9	1	4	–	–	4
13	13	1	3	–	–	2

GCS Glasgow Coma Scale scores, *VP shunt* ventricular peritoneal shunt, *ETV* endoscopic third ventriculostomy, *EVD* external ventricular drainage, *CPM* cerebral pontine myelinolysis

[a]Drainage period means number of days of indwelling of the ventricular drainage tube from the day of endoscopic surgery

After 3 months, the results were that three patients showed good recovery, with modified Rankin Scale (mRS) scores of 2; three patients had mRS scores of 3; and the remaining seven patients had mRS scores of between 4 and 5. All six patients with mRS scores of 2–3 had initial GCS scores over 8 and had undergone endoscopic surgery on the day of onset, with a period of ventricular drainage of fewer than 4 days.

Case

Figure 3 shows a characteristic case with thalamic hemorrhage. The patient was a 72-year-old woman who suddenly became confused and hemiplegic. The initial CT scan showed left thalamic hemorrhage with casting hematoma in the third, fourth, and anterior horns of the lateral ventricle. She underwent emergency endoscopic surgery on the day of onset. Hematomas causing impairment of cerebrospinal fluid circulation were sufficiently evacuated and the ventricular drainage tube was removed on the second post-operative day (POD). She required no additional cerebrospinal fluid shunt surgery and progressed favorably with mRS 3 at 3 months after onset.

Discussion

Hemorrhage complicated with intraventricular hematoma has several difficult problems not seen in patients with ICH alone. There is not only rapid elevation of intracranial pressure due to acute hydrocephalus in the acute stage, but also damage in ventricle-facing structures in the chronic stage that leads to a grave prognosis with high mortality and morbidity [3, 5]. The fibrinolytic system of CSF is limited, and hematomas remain for weeks after a hemorrhage [7, 10]. In the late stage, biochemical changes and blood degradation products such as bilirubin oxidative products are responsible for oxidative stress in the brain tissue surrounding the hematoma and may be responsible for late damage to the ventricle-facing structures [2, 6].

The two patients who underwent delayed endoscopic surgery on the 7th and 16th day of onset required subsequent CSF shunt surgery after all. A second case required an additional third ventriculostomy due to a secondary obstruction of the aqueduct by adhesive fibrous membranes. However, the next nine patients (except for two cases of severe hematomas packed in the whole ventricles who underwent early endoscopic surgery of the day of onset) required no additional CSF shunt surgery. A rapid and sufficient removal of intraventricular hematomas in the hyperacute stage may be essential for preventing secondary damage or additional injury to the brain tissue and lead to a good prognosis for severe IVH patients.

The effectiveness of hematoma evacuation by using a rigid neuroendoscope for intracerebral hemorrage has recently been reported [8]. By using a rigid endoscope, hematomas in the foramen of Monro and the anterior part of the third ventricle are able to be safely removed, but those in the posterior part of the third ventricle and the aqueduct cannot be removed by anatomical restriction. Remnant hematomas in the aqueduct have a high probability of

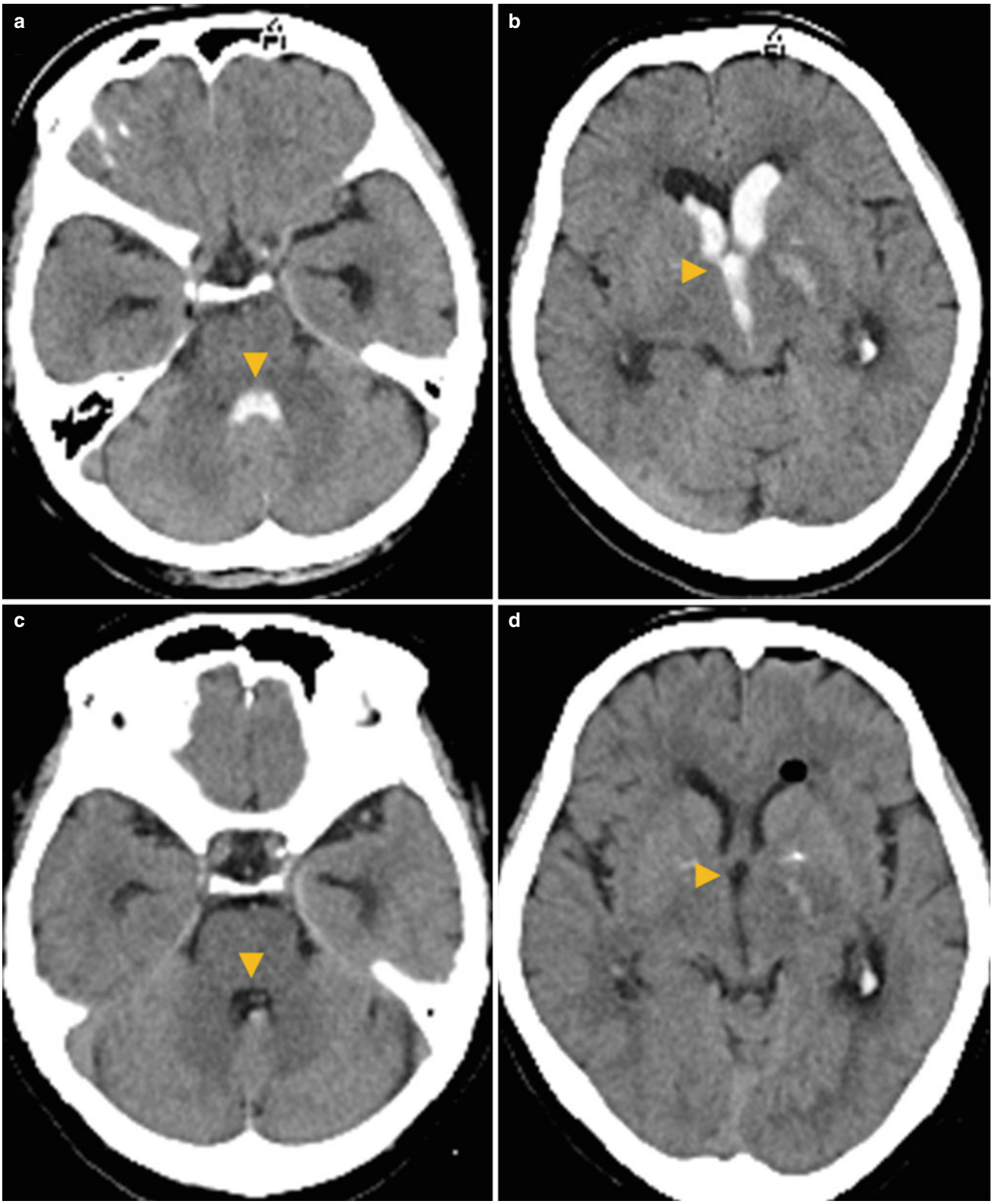

Fig. 3 Representative case of flexible endoscopic surgery for intraventricular hematoma due to thalamic hemorrhage. The initial computed tomography (CT) scan showed left thalamic hemorrhage with casting hematoma in the anterior horn of the lateral ventricle, the third ventricle (**a**, *arrowhead*), and the fourth ventricle (**b**, *arrowhead*). Post-operative CT scan shows that most of the hematomas casting in the ventricles were removed (**c**, **d**, *arrowheads*)

causing non-communicating hydrocephalus due to surrounding adhesive fibrous membranes [12]. A flexible endoscope permits the evacuation of casting hematoma in the aqueduct or the fourth ventricle by careful operation of an experienced surgeon. A videoscope presents a high-definition image by a CCD camera implanted at the top of the scope and might offer high-quality performance for the safe aspiration of IVH [11].

Conclusions

Early surgical intervention using a flexible endoscope and short period of post-surgical drainage can be highly effective for patients suffering from casting intraventricular hematomas associated with intracerebral hemorrhage. The advantages of this treatment may be less invasive procedures, ICP control in the acute phase, breaking away from ventricular drainage in the early stage, and prevention of hydrocephalus or intracranial infectious complication in the long term.

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

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Treatment of Intracranial Aneurysms

Clipping Surgery for Paraclinoid Carotid Aneurysm

Tetsuyoshi Horiuchi, Yasunaga Yamamoto, Yota Suzuki, Masayoshi Kobayashi, Shunsuke Ichinose, and Kazuhiro Hongo

Abstract

Background

Paraclinoid carotid aneurysm is widely treated with coil embolization. However, all paraclinoid carotid aneurysms cannot be obliterated by the endovascular approach.

Methods

Our direct surgical procedure was presented. The clinical data of surgically treated paraclinoid carotid aneurysms were retrospectively reviewed.

Results

One hundred ninety paraclinoid carotid aneurysms in 181 patients were directly obliterated at the Shinshu University Hospital and its affiliated hospitals between 1991 and 2013.

Conclusions

Direct surgical repair of the paraclinoid carotid aneurysm is still useful, even in the era of endovascular treatment.

Keywords Aneurysm • Clipping • Paraclinoid carotid artery • Superior hypophyseal artery

Introduction

The paraclinoid carotid aneurysm includes all intradural proximal carotid aneurysms originating from the internal carotid artery (ICA) between the distal dural ring and the origin of the posterior communicating artery [9, 17]. Two branching arteries of the paraclinoid carotid aneurysm are the ophthalmic artery and the superior hypophyseal artery (SHA). Recently, the paraclinoid carotid aneurysm has often occluded with coil embolization because of its anatomical location. However, all aneurysms cannot be obliterated through the endovascular approach. This paper introduces our clipping techniques for paraclinoid carotid aneurysm.

T. Horiuchi, MD (✉) • Y. Yamamoto • Y. Suzuki • M. Kobayashi
S. Ichinose • K. Hongo
Department of Neurosurgery, Shinshu University School of Medicine, 3-1-1 Asahi, Matsumoto 390-8621, Japan
e-mail: tetuyosi@shinshu-u.ac.jp

Materials and Methods

Operative Technique

Positioning

The patient is positioned in the supine position and the head is fixed in a Sugita head holder with rotation to the side opposite the planned craniotomy. The affected cervical ICA is routinely prepared for possible proximal control despite the contralateral approach. For the retrograde suction decompression technique, the cervical ICA exposure is also useful. Lately, intraoperative catheter angiography has not been used because indocyanine green (ICG) videoangiography and neuroendoscope have been widely applied.

Approach Selection

Ruptured paraclinoid carotid aneurysms are treated via the ipsilateral approach for proximal control. By contrast, in unruptured aneurysms, the ipsilateral or contralateral approach is selected according to preoperative neuroimages. The aneurysm projecting medially or infero-medially can be clipped through contralateral craniotomy. Kakizawa and colleagues presented the parameters of the contralateral approach [12]. The prechiasmatic cistern is the key space, and the relationship between the optic nerve and aneurysm is very important.

Neurophysiological Monitoring

There is no question of the importance for neurophysiological monitoring, especially in the visual evoked potential (VEP). In our institute, VEP has been used as the intraoperative visual function monitoring since December 2004. Our

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colleagues reported the usefulness of VEP in aneurysm surgery [1, 14]. During SHA aneurysm surgery with the contralateral approach, SHA related to aneurysm can be easily found in the prechiasmatic cistern (Fig. 1). Temporary SHA occlusion using a microclip is performed, whether VEP is attenuated or not (Fig. 1).
When no VEP change occurred after temporary SHA occlusion, complete obliteration takes first priority. However, the SHA should be spared if the VEP decreases under temporary SHA occlusion.

Bony Removal and Distal Dural Ring Dissection

We usually perform intradural bony removal with a high-speed drill or bone curette. An advantage of intradural removal includes directly seeing the important neural and vascular structures and minimal, but sufficient, removal can be achieved. Tanaka et al proposed the useful intradural removal as a protective dural method in 2003 [16]. Circumferential dural ring dissection is essential for mobilizing the ICA for safety clipping.

Multiple Clipping Technique

In the Sugita aneurysm clip, there is not much difference in physical characteristics between titanium and cobalt alloys [4, 5, 7, 8]. Therefore, titanium clips should be used to reduce mechanical artifacts on neuroimages. Formation clipping with fenestrated clips – as one of the multiple clipping techniques – provides ICA formation. There are three kinds of formation clipping (tandem, facing, and crosswise combinations). However, formation clipping using fenestrated clips is difficult in some cases because adjustments of fenestrated clips are not easy. Therefore, perpendicular clipping may be safe in some small, paraclinoid carotid artery aneurysms. The technical complication with using multiple fenestrated clip application is known as straightening of the ICA [18]. For a large aneurysm, a retrograde suction decompression technique is also useful for clipping.

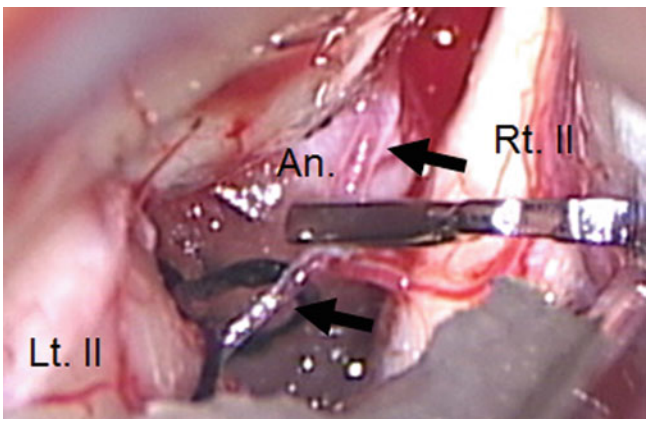

Fig. 1 Intraoperative photograph through the left-sided craniotomy (contralateral approach) showing the temporary occlusion of right superior hypophyseal artery (*arrows*). *An* aneurysm, *Lt* left, *II* optic nerve, *Rt* right

Results

Between 1991 and 2013, 190 paraclinoid carotid aneurysms in 181 patients at the Shinshu University Hospital and its affiliated hospitals were treated using the above-mentioned surgical techniques and under neurophysiological monitoring. Coil embolization cases were excluded. Based on preoperative neuroimages, aneurysms were classified into five groups: carotid-ophthalmic (42 aneurysms), SHA (72), carotid cave (34), dorsal (33), and other aneurysms (9).

Illustrative Case of Carotid-Ophthalmic Aneurysm

A 61-year-old woman presented with headache, and a carotid-ophthalmic aneurysm was found. The ophthalmic artery originated from the aneurysmal dome and the aneurysm was pressing on the optic nerve (Fig. 2a). After the right cervical ICA was secured, a right frontotemporal craniotomy was performed. Under VEP monitoring, the aneurysm was excluded with good preservation of the ophthalmic artery. No visual disturbance developed after surgery. Postoperative three-dimensional computed tomographic angiography showed good obliteration of the aneurysm (Fig. 2b). The patient was discharged without neurological deficits.

Illustrative Case of Dorsal Aneurysm

A 43-year-old woman was referred for a large dorsal aneurysm detected on brain screening (Fig. 3), and the patient underwent clipping surgery. The postoperative course was uneventful.

Illustrative Case of SHA Aneurysm (Contralateral Approach Case)

A 67-year-old woman suffering from Parkinson's disease, was found to have an SHA aneurysm (Fig. 4a). The aneurysm was located in the prechiasmatic cistern and the SHA originated from the aneurysm dome (Fig. 4a). A contralateral approach was selected, an ipsilateral cervical ICA was

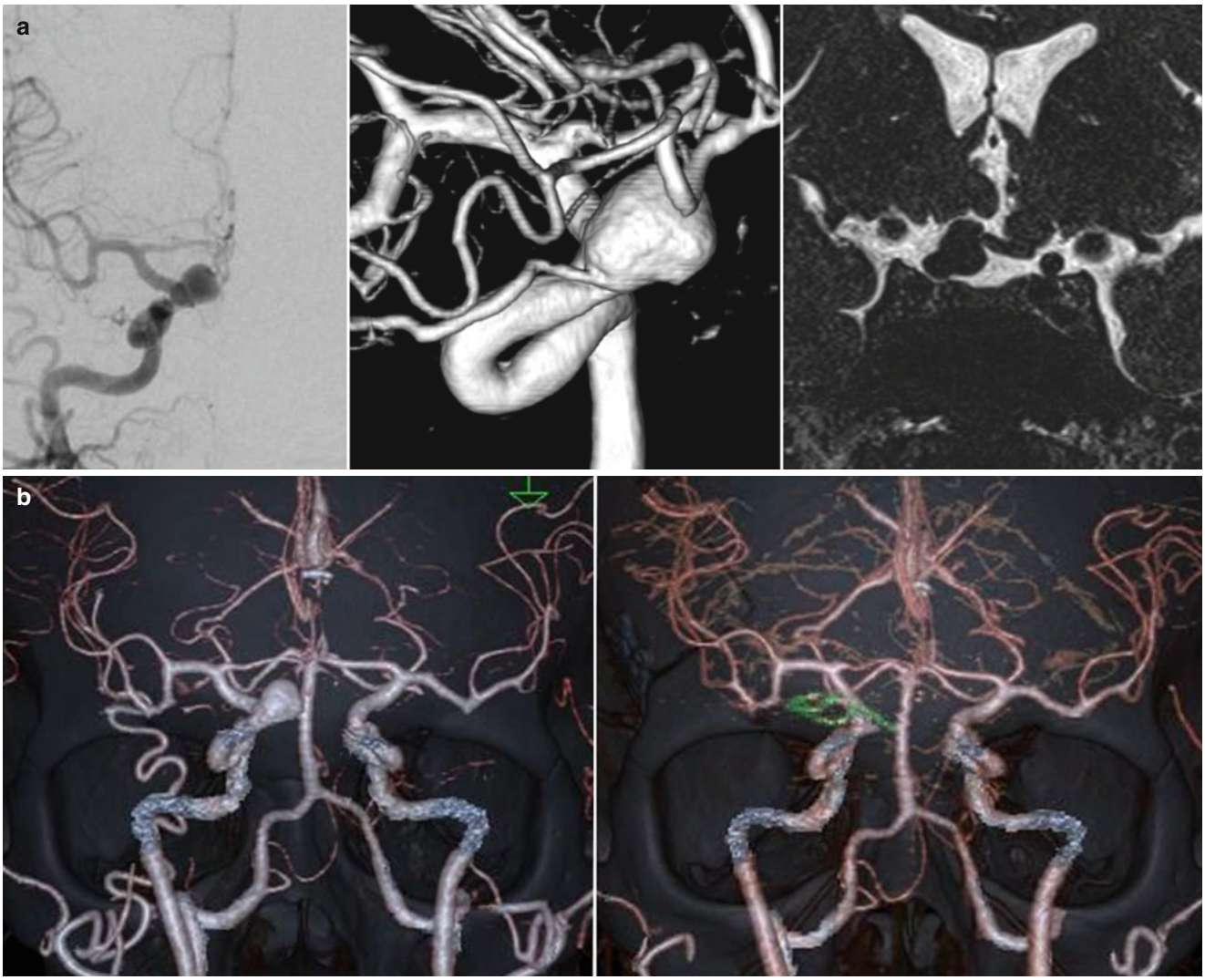

Fig. 2 (**a**) Antero-posterior (*left*) and oblique (*center*) projections of right carotid angiograms showing the aneurysm projecting superomedially and the ophthalmic artery originating from the aneurysmal dome. Coronal section of magnetic resonance imaging (*right*) showing the aneurysm compressing the right optic nerve. (**b**) Antero-posterior projection of preoperative (*left*) and postoperative (*right*) three-dimensional computed tomographic angiograms (3-D CTA) revealing the successful obliteration of the aneurysm

prepared, and a contralateral fronto-temporal craniotomy was performed. The SHA was found in the prechiasmatic cistern and it was temporarily occluded under VEP monitoring. Since no VEP change occurred, the aneurysm with the SHA was clipped (Fig. 4b). Although the SHA was sacrificed, no visual disturbance developed after surgery.

Discussion

Paraclinoid carotid aneurysm is one of the more difficult lesions to treat surgically because there are important neural and vascular structures related to the aneurysm. Therefore, endovascular treatment would be a better option for aneurysm exclusion because of the rapid development of this innovative device as well as endovascular technology. However, there are some concerns related to coil embolization. High recurrence rates after coil embolization were reported in patients with large or giant and partially thrombosed paraclinoid carotid aneurysm [15]. Additionally, endovascular treatment also has a potential risk of visual impairment or worsening of visual function due to mechanical compression and/or ischemia [11].

Clipping surgery for the paraclinoid carotid aneurysm has been refined due to the skull base approach, multiple clipping technique, retrograde suction decompression method, insurance bypass, intraoperative electrophysiological monitoring, ICG videoangiography, and so on [2, 6, 9, 17]. Our group has reported clinical characteristics and surgical tech-

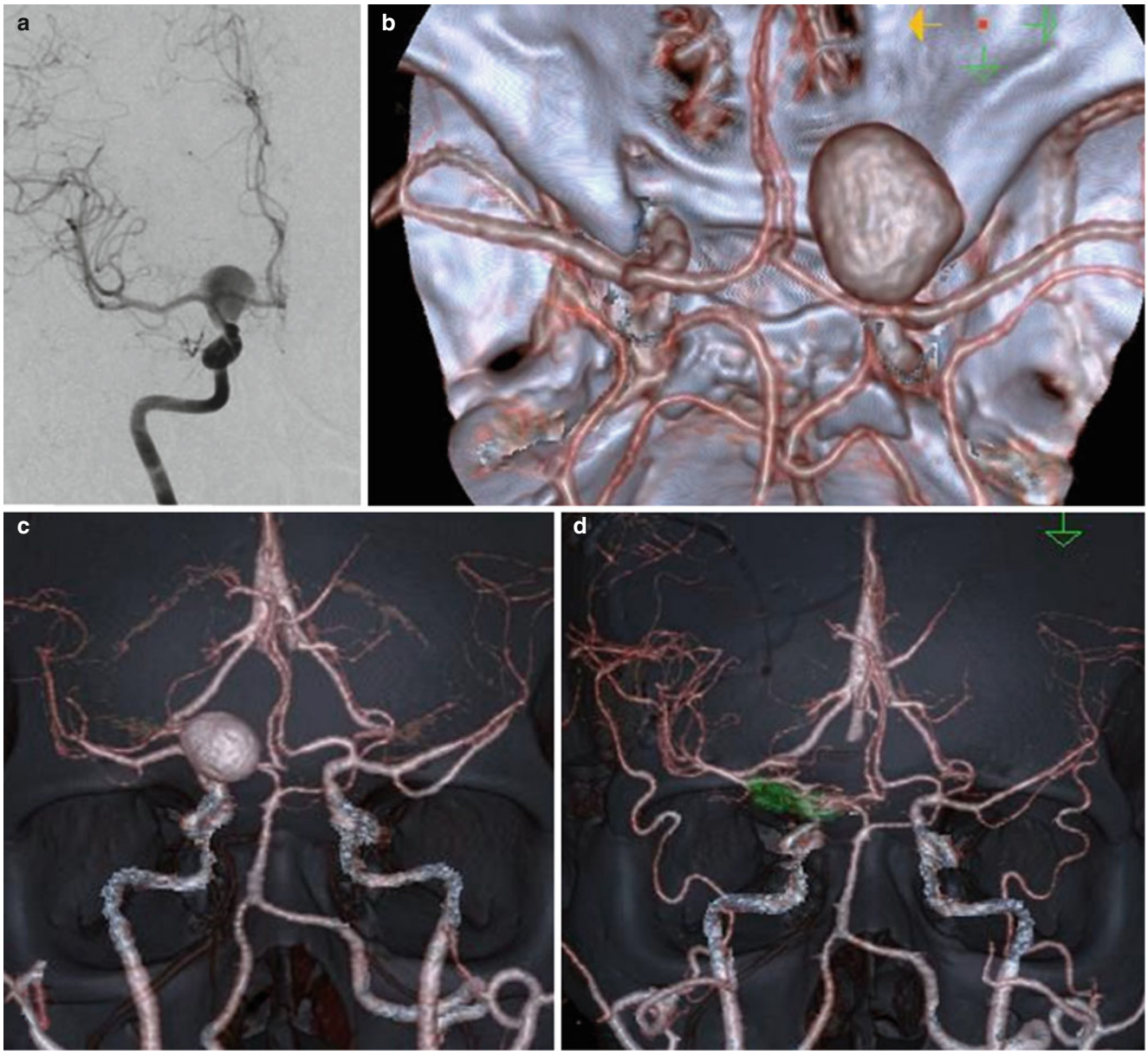

Fig. 3 Preoperative right carotid angiogram (**a**) and 3-D CTA (**b**, **c**) showing the large dorsal aneurysm. Postoperative 3-D CTA (**d**) showing the complete clipping of the aneurysm

niques for paraclinoid carotid aneurysms [2, 3, 6, 9, 12, 13, 17]. In 1989, Kobayashi et al [13] classified the most proximal intradural ICA aneurysm projecting medially or inferomedially as carotid cave aneurysms. After the introduction of the concept of the carotid cave, the paraclinoid carotid aneurysm surgery has been advanced, based on detailed understanding of microsurgical anatomy. Recently, we retrospectively analyzed the postoperative visual impairment in patients with SHA aneurysm [10]. According to our results, unilateral SHA sacrifice during aneurysmal obliteration does not induce postoperative visual disturbance [10]. Further studies from other institutions would be necessary to clarify a role of SHA on the postoperative visual impairment of paraclinoid carotid aneurysm surgery.

Conclusions

We present our surgical techniques and propose the usefulness of direct clipping surgery for the paraclinoid carotid aneurysm in endovascular era.

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

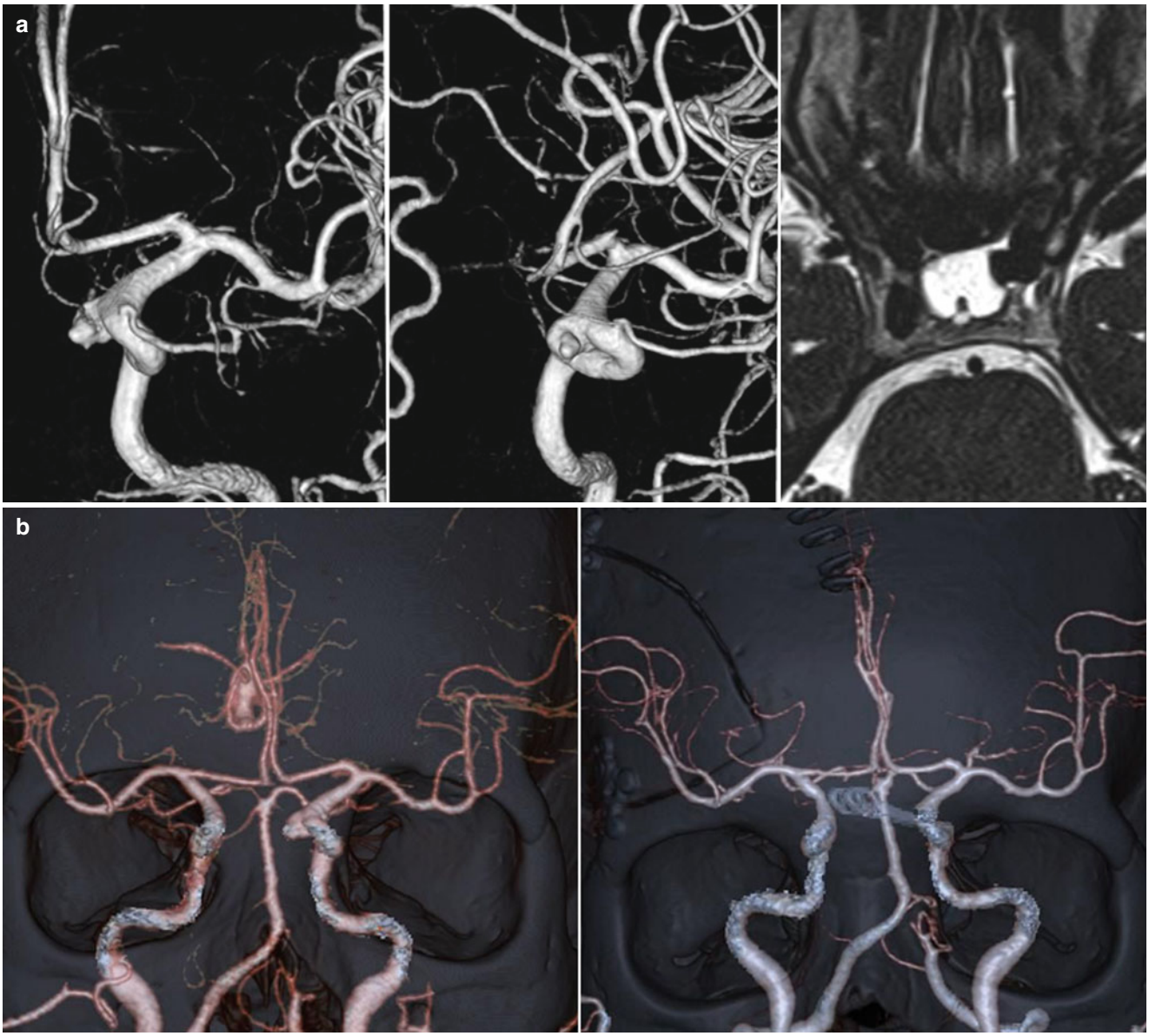

Fig. 4 (**a**) Antero-posterior (*left*) and oblique (*center*) projections of left carotid angiograms showing the superior hypophyseal artery aneurysm. Axial section of magnetic resonance imaging showing the aneurysm located in the prechiasmatic space. (**b**) Antero-posterior projection of preoperative (*left*) and postoperative (*right*) 3-D CTA demonstrating the successful obliteration of the aneurysm

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Outcome After Surgical Treatment of Paraclinoid Carotid Aneurysms

Alberto Pasqualin, Pietro Meneghelli, Francesco Cozzi, and Franco Chioffi

Abstract Surgery on paraclinoid carotid aneurysms is technically demanding and entails considerable risks, especially to visual function. The aim of this study was to evaluate the clinical and visual outcome after surgery in 66 patients with paraclinoid carotid aneurysms (30 ruptured and 36 unruptured) treated between 1990 and 2014. Thirty-six aneurysms were of standard size, and 30 were large (16–20 mm) or giant (>20 mm); the Barami classification was used in every case. During surgery, multiple clips were needed in 25 % of patients with standard, and in 80 % of patients with large-giant aneurysms; temporary carotid occlusion was performed on 11 % of patients with standard and 63 % with large-giant aneurysms. Postoperatively, a cerebrospinal fluid fistula was repaired surgically in two patients. At the 3-month follow-up, the modified Rankin Score (mRS) was favorable (0–2) in 63 % of patients with *ruptured* and in 97 % with *unruptured* aneurysms; four patients presenting with large hematomas died. Postoperative visual impairment (worsening or newly developing deficit) was noted in 25 % of cases with standard and 14 % of cases with large-giant *ruptured* aneurysms, and, respectively, in 10 % with standard and 31 % with large-giant *unruptured* aneurysms. It has been concluded that surgery remains a reasonable choice in the management of patients with paraclinoid carotid aneurysms.

Keywords Paraclinoid carotid aneurysms • Ophthalmic artery • Unruptured aneurysms • Microsurgery • Flowmetry • Visual function

A. Pasqualin, MD (✉) • P. Meneghelli, MD
Section of Vascular Neurosurgery, Insitute of Neurosurgery, Azienda Ospedaliera – Universitaria Integrata di Verona, Piazzale Stefani, 1, Verona 37100, Italy
e-mail: albertopasqualin@tin.it

F. Cozzi, MD
Division of Neurosurgery, Cesena City Hospital, Cesena, Italy

F. Chioffi
Division of Neurosurgery, Trento City Hospital, Trento, Italy

Introduction

Treatment of aneurysms originating from the paraclinoid tract of the internal carotid artery requires special care, owing to the complex anatomy of the region [10, 13, 22–24] and the proximity of vital neural structures, such as the optic nerve. Although microsurgical exclusion has for a long time been considered the best treatment for these lesions [2, 3, 7–11, 16, 21, 25, 28], endovascular modalities of exclusion have also been proposed [14, 15, 27, 29, 31], and a few series of combined surgical and endovascular treatment have been published since 2001 [4, 12, 17, 18, 30, 33]. Aneurysms located in this region are strongly related to the ophthalmic artery and the distal carotid ring; some of them – called "transitional" [1, 2] – may have partial intracavernous extension, which requires a more complex surgical approach. In order to plan surgery more adequately, a few anatomo-radiological classifications have been proposed, based on the projection of the sac, the relative position of the anterior clinoid process and the relation with the ophthalmic and superior hypophyseal arteries [1–3, 6, 7]. A peculiar feature of aneurysms in this location is the frequency of large ones, which adds further difficulties to the surgical exclusion.

The aim of this paper is to report our experience in the surgical treatment of 66 patients submitted to surgery in our institute from 1990 to 2014, all harboring aneurysms located on the paraclinoid segment of the internal carotid artery, 30 of them ruptured and 36 unruptured; special attention has been paid to the aneurysmal size and to the outcome after surgery, particularly regarding visual function.

Materials and Methods

Between 1990 and 2014, 66 patients with paraclinoid carotid aneurysms were subjected to surgery in our institute. The clinical presentation was hemorrhage in 30

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patients (with significant intracranial hematomas in 8 of them) and visual disturbances in 14 patients. In 22 of them, the aneurysm constituted an incidental discovery on MRI or CT scan (done for headache in ten cases, for vertigo in five cases, and for other reasons in seven cases). Thirty-six aneurysms were of standard size (within 15 mm in maximum diameter) and 30 were large or giant; associated aneurysms in other locations were operated at the same time in 12 of these patients. As regards the precise location/projection of the aneurysm, we adopted the Barami classification (Barami); accordingly, 37 patients presented a "Barami type Ia" aneurysm (the most common location, at the origin of the ophthalmic artery and with superior projection) (Fig. 1); 2 patients presented with a "Barami type Ib" aneurysm (distal to the origin of the ophthalmic artery, still with superior projection); 7 presented with a "Barani type II"

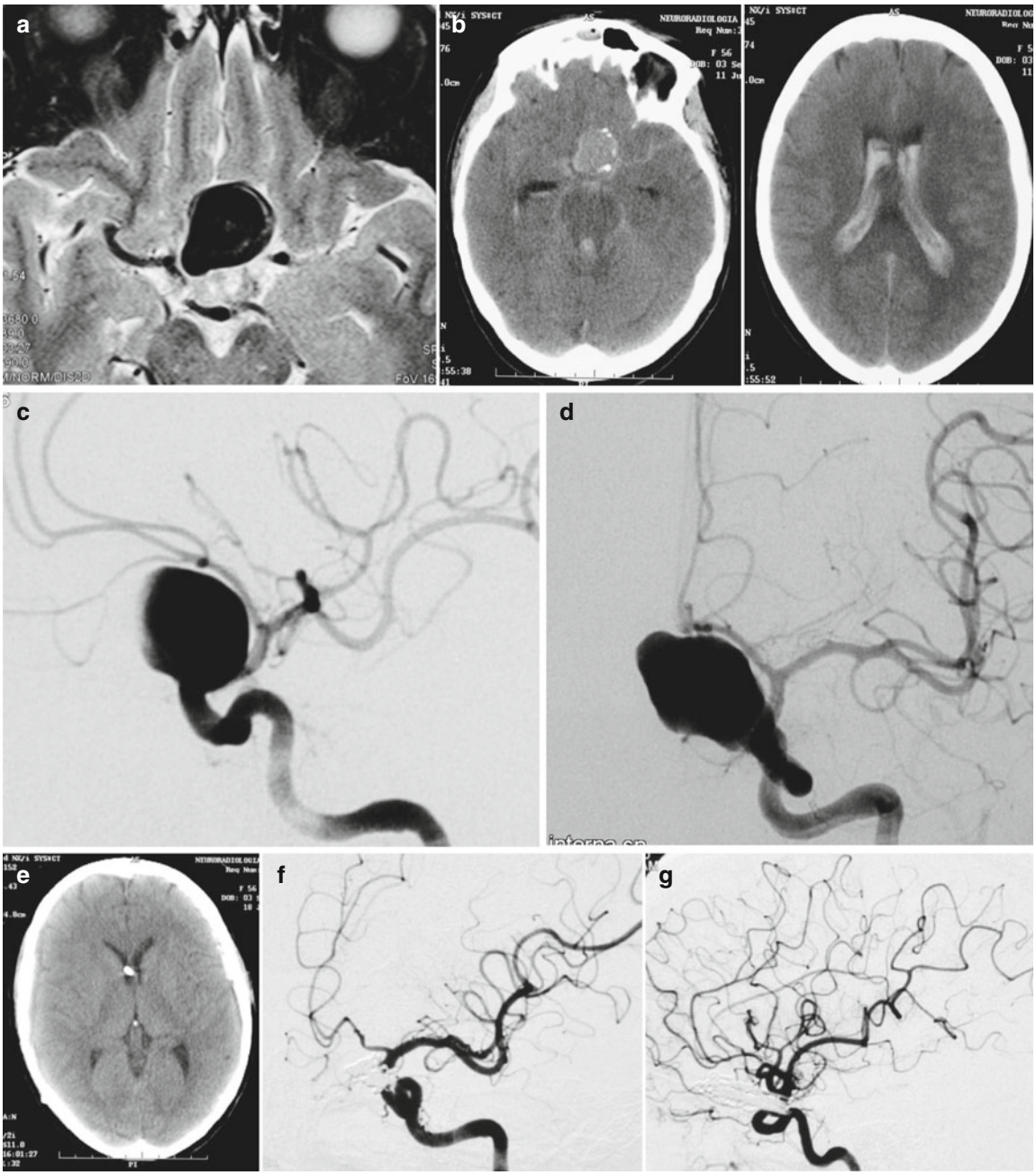

Fig. 1 (**a**) MRI of a 56-year-old woman with marked decrease of vision in her left eye; (**b**) severe subarachnoid and ventricular hemorrhage a few hours after MRI; Glasgow Coma Score 4 on admission; (**c**, **d**) angiography showing a giant left paraclinoid aneurysm (Barami type I a); (**e**) CT scan after ventriculo-peritoneal shunt; (**f**, **g**) post-op angiography showing exclusion of the aneurysm. Complete recovery of neural function 3 months after surgery, except for left amaurosis

aneurysm (originating on the ventral side of the carotid artery) (Fig. 2); 17 with a "Barami type III," an aneurysm at the origin of the superior hypophyseal artery and/or projecting medially under the optic nerve; and 3 presented with a "Barami type IV" aneurysm (a transitional aneurysm, partly located in the cavernous sinus).

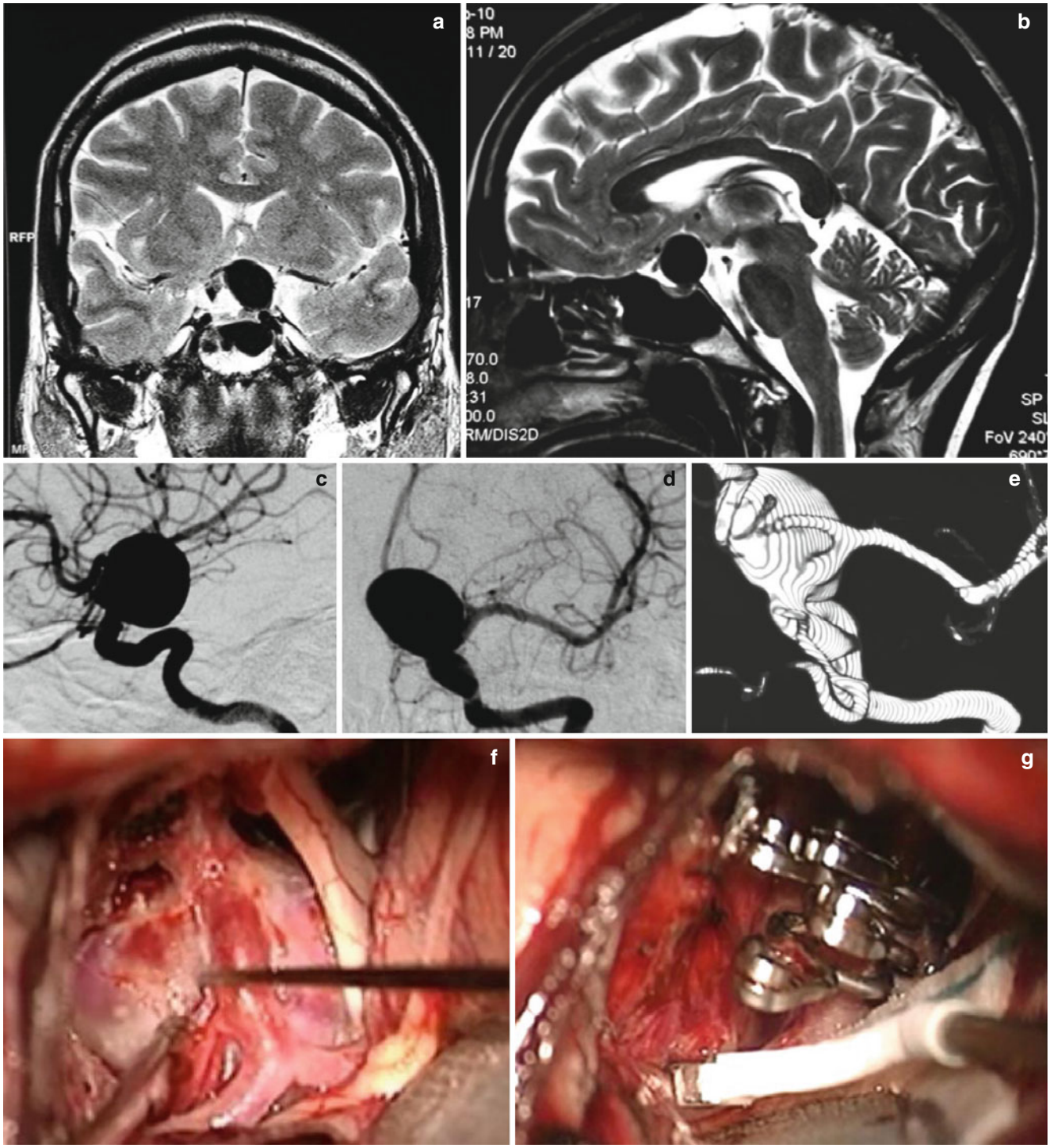

Fig. 2 (**a**, **b**) MRI of a 44-year-old woman with progressive visual impairment in her left eye; (**c**–**e**), large bulbous left paraclinoid aneurysm with postero-medial (ventral) projection at angiography (Barami type II); (**f**) intraop view showing the position of the aneurysm under the internal carotid artery, and the displacement of posterior communicating and anterior choroidal arteries over the dome; (**g**) intra-op view after exclusion with multiple fenestrated clips, showing Charbel's ultrasound probe on the M1 tract for flow measurement; (**h**) post-op CT scan; (**i**, **j**) post-op angiography. Worsening of visual acuity in left eye after surgery; no other deficits

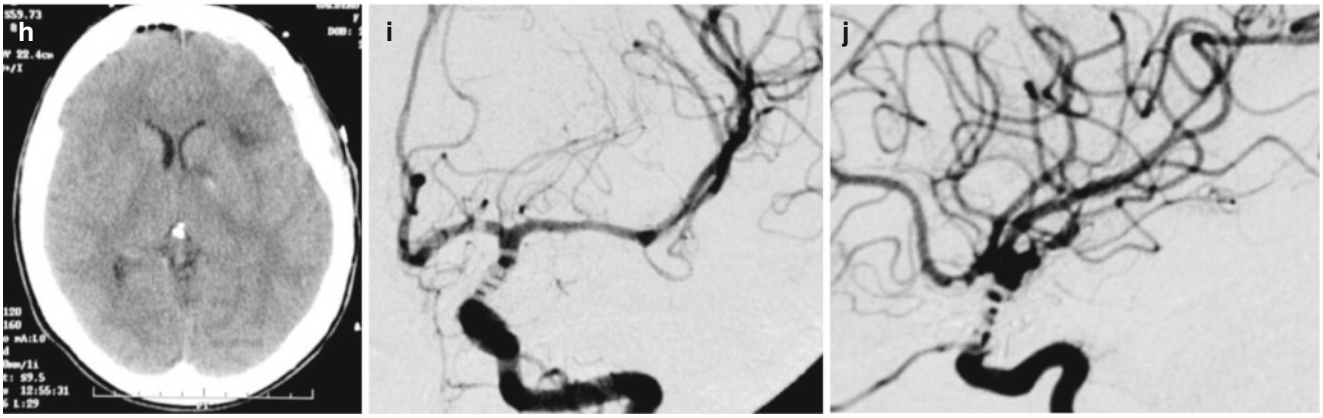

Fig. 2 (continued)

Table 1 Surgical data in 66 patients, according to aneurysmal size (expressed as maximum diameter)

Aneurysmal size	Clinoidectomy	Flowmetry	Temporary ICA occlusion: <10 min	Temporary ICA occlusion: ≥10 min	Evacuation of hematoma	Multiple clip exclusion	Clipping of other aneurysm
≤15 mm (36 cases)	25 (69 %)	4 (11 %)	4 (11 %)	–	3 (8 %)	9 (25 %)	8 (22 %)
>15 mm (30 cases)	24 (80 %)	10 (33 %)	9 (30 %)	10 (33 %)	5 (17 %)	24 (80 %)	4 (13 %)
Total (66 cases)	49 (74 %)	14 (21 %)	13 (20 %)	10 (15 %)	8 (12 %)	33 (50 %)	12 (18 %)

A standard surgical procedure was performed in these cases: an ipsilateral fronto-pterional approach with wide opening of the sylvian fissure before the retraction of the frontal lobe, control of the carotid artery at the neck (through manual compression or direct surgical exposure in patients with complex/large aneurysms), and optic foraminotomy with anterior clinoidectomy, obtaining exposure of the distal carotid ring and of the origin of the ophthalmic artery. While optic foraminotomy was performed in all cases, anterior clinoidectomy was needed in 49 of 66 cases (25 with standard, and 24 with large or giant aneurysms) (Table 1). Furthermore, intraoperative flowmetry with the Charbel ultrasound probe [5] was used before and after clipping in 14 cases (all operated on after 2001). In most cases, the insonated arteries were the ipsilateral A1 and M1 tracts (Fig. 2g). Temporary closure of the internal carotid artery was used in 23 cases – in 13 for less than 10 minutes, and in 10 for longer periods (Table 1). Exclusion of the aneurysm was obtained with a single clip in 33 patients, and with multiple clips in another 33 patients (9 with standard, and 24 with large/giant aneurysms) (Table 1).

Results

After surgery, a ventriculo-peritoneal shunt was inserted in ten patients for the control of hydrocephalus. Two cases required reoperation for the treatment of a cerebrospinal fluid fistula and both had a complete neurological recovery, without visual deficits. Other complications consisted of postoperative hemorrhages in four cases (limited in size in three, and requiring surgical evacuation in one), clinical deterioration from spasm in one case, pulmonary emboli in one case, and scalp infection in one case. All but one of these cases had a favorable outcome at 3 months after surgery.

Postoperative angiography (done in all surviving patients) showed complete exclusion of the aneurysm in 57 patients. In two out of five patients with incomplete exclusion, a stenting procedure was performed thereafter (in one case, also with coils); in a third patient, the remnant was occluded with coils only. In the remaining two patients with incomplete exclusion, the small remnant was left untreated and was not enlarged at a follow-up angiography.

Clinical outcome was evaluated at 3 months from surgery through the modified Rankin score; as shown in Table 2, among the 30 patients with ruptured aneurysms, a favorable result (modified Rankin score 0–2) was observed in 19 patients (63 %) and a significant disability in seven patients (23 %); four patients died (all due to the severity of the initial hemorrhage). Among the 36 patients with unruptured aneurysms, a favorable result was achieved in 35 of them (97 %); only one patient developed a significant disability (due to multiple postoperative hemorrhages caused by an autoimmune coagulopathy). A visual outcome is presented in Table 3 (for ruptured aneurysms) and in Table 4 (for unruptured aneurysms). For patients with ruptured aneurysms, postoperative visual deficits were present in 31 % of patients

Table 2 Clinical outcome 3 months after surgery (modified Rankin Score = mRS), according to clinical presentation (ruptured vs. unruptured) and aneurysmal size (standard ≤15 mm; large/giant >15 mm)

	mRS 0–2	mRS 3–4	mRS 5	mRS 6
Ruptured:				
Standard (16 cases)	10 (62 %)	5 (31 %)	–	1 (6 %)[a]
Large/giant (14 cases)	9 (64 %)	2 (14 %)	–	3 (21 %)[a]
Unruptured:				
Standard (20 cases)	19 (95 %)	1 (5 %)	–	–
Large/giant (16 cases)	16 (100 %)	–	–	–

[a]All deaths due to severity of initial hemorrhage

Table 3 Visual impairment in patients with *ruptured aneurysms,* according to aneurysmal size (standard ≤15 mm; large/giant >15 mm)

	Preoperative visual deficit:		Postoperative visual deficit:		
	Mild	Severe	Unchanged	Worsened	*De novo*
Standard (16 cases)	2 (12 %)	–	1 (6 %)	1 (6 %)	3 (19 %)
Large/giant (14 cases)	1 (7 %)	4 (29 %)	2 (14 %)	2 (14 %)[a]	–
Total (30 cases)	3 (10 %)	4 (13 %)	3 (10 %)	3 (10 %)	3 (10 %)

[a]Amaurosis in one patient

Table 4 Visual impairment in patients with *unruptured aneurysms,* according to aneurysmal size (standard ≤15 mm; large/giant >15 mm)

	Pre-operative visual deficit:		Post-operative visual deficit:		
	Mild	Severe	Unchanged	Worsened	*De novo*
Standard (20 cases)	5 (25 %)	–	2 (10 %)	1 (5 %)	1 (5 %)
Large/giant (16 cases)	3 (19 %)	5 (31 %)[a]	5 (31 %)[a]	3 (19 %)	2 (12 %)
Total (36 cases)	8 (22 %)	5 (14 %)[a]	7 (19 %)[a]	4 (11 %)	3 (8 %)

[a]Amaurosis in two patients

with standard aneurysms (pre-existing in 6 %), and in 28 % of patients with large/giant aneurysms (pre-existing in 14 %); three patients with standard aneurysms presented a *de novo* deficit, vs. none with larger aneurysms (Table 3). For patients with unruptured aneurysms, postoperative visual deficits were present in 20 % of them with standard aneurysms (pre-existing in 10 %) and in 62 % of patients with larger aneurysms (pre-existing in 31 %); one patient with a standard aneurysm had a de novo deficit, vs. two with larger aneurysms (Table 4).

Discussion

The paraclinoid segment of the carotid artery presents a rather complex anatomy when compared to the other sites of origin for aneurysms of the anterior circulation [10, 13, 22–24]. The anatomical space is very narrow and needs to be widened through optic foraminotomy and anterior clinoidectomy. Although in a few cases with unusually highly positioned aneurysms (in regard to the anterior clinoid) clinoidectomy does not need to be extensive; complete exposure of the distal carotid ring is required for safer exclusion of the aneurysm in most cases, performing a generous clinoidectomy. In our experience, we performed an intradural clinoidectomy in all cases, in order to obtain a direct visualization of the aneurysm through high-speed drilling of the clinoid. However, we agree that – especially for unruptured aneurysms – extradural clinoidectomy can be a reasonable alternative in experienced hands [8, 9, 21, 35]. Regarding the extent of bone removal, care must be taken not to open the *membrana mucosa* of the ethmoid sinus, due to the possibility of a cerebrospinal fluid (CSF) fistula. In rare cases with a highly pneumatized anterior clinoid process – where the risk of a fistula is higher – a piece of muscle should be inserted into the bone cavity and sealed with collagen glue at the end of surgery. Regarding the feasibility of a controlateral approach to these aneurysms, as pointed out by Kakizawa et al [19], we have used an ipsilateral approach in all of our cases; we believe that this approach constitutes a safer procedure and that a controlateral approach should be limited to patients with bilateral ophthalmic aneurysms, as already suggested by Yasargil and Abdulrauf [34].

The importance of a preoperative classification cannot be overemphasized. We adopted the Barami classification [2],

although simpler classifications are also adequate to define the variable origin and projection of aneurysms in this location [1, 3, 6, 7]. It is certainly important to differentiate between "true" ophthalmic aneurysms and superior hypophyseal aneurysms that project medially under the optic nerve; in this second situation, a different strategy of clipping must be applied in order to obtain a complete exclusion of the sac (especially of the hidden deeper part of the neck). However, a clear relationship with the origin of the superior hypophyseal artery is difficult to establish in large/giant aneurysms with medial infra-optic projection; this anatomical situation may constitute a limit of the Barami classification. Another problem of classification is constituted by the so-called "transitional" aneurysms (i.e., aneurysms partially located in the cavernous sinus); Barami et al distinguish between type IIIb (aneurysms with infradiaphragmatic extension) and type IV aneurysms (also transitional, but ventrally projecting aneurysms and sometimes enlarging the distal dural ring). In our experience, this distinction is not always possible. There is no doubt that the "transitional" type of paraclinoid aneurysm is difficult to treat surgically. As suggested by Sherif et al [30], an endovascular approach may be safer for these patients. Again, surgeons with expertise in operations inside the cavernous sinus may disagree on this point [8, 9].

The surgical problems are certainly increased by large-sized aneurysms, and this is very common for this aneurysmal location, as shown in our series. Only Lai and Morgan report that 58 % of operated unruptured aneurysms in their series are small (less than 7 mm) [25]. A large size – apart from being an obvious risk factor for visual outcome – requires a particular strategy during surgery, with generous use of temporary carotid occlusion (even for periods of 20–30 minutes in patients with good angiographic filling from the contralateral carotid artery), and a "creative" assembly of multiple clips, with fenestrated clips being preferred for large, ventrally projecting aneurysms. Endoluminar thrombosis or aneurysmal wall calcifications may further complicate the surgical procedure; while in the first case, opening of the sac during temporary carotid occlusion or trapping may be necessary, the use of combined fenestrated/non-fenestrated clips positioned in parallel seems to be a good solution for aneurysms with calcified walls.

A less frequently encountered anatomical feature is the presence of firm adhesions between the aneurysmal wall and the planum ethmoidale, for large aneurysms projecting directly anteriorly. In these cases, early exposure of the proximal part of the neck – very close to the origin of the ophthalmic artery – is recommended before manipulation of the sac.

A very useful adjunct to surgery, especially for complex paraclinoid aneurysms, is constituted by intraoperative flowmetry with a Charbel's ultrasound probe [5]; measurement of the flow on the distal carotid artery and especially on the ipsilateral A1 and M1 tract before and after clipping of the aneurysms gives the best confirmation of adequate flow distal to the site of clipping, thus avoiding the danger of ischemia.

Regarding outcome, the possibility of a visual deficit must always be taken into account when planning surgical exclusion of these aneurysms. All of the published surgical series present a certain percentage of visual deficits, different in each series, possibly depending upon the expertise of the surgeon and the percentage of large/giant aneurysms in that series [6, 17, 20, 26, 28, 32]. In the well-studied and very large surgical series of Lai and Morgan, the percentage of post-op visual impairment has been very low, with 10 % of cases improving from preoperative deficits [25]. The expertise of the senior author and the large number of small aneurysms in this series of unruptured aneurysms must be taken into account.

Conclusions

Direct surgical treatment remains a valid option for paraclinoid aneurysms of the internal carotid artery, with a few possible exceptions. While knowledge of anatomy remains fundamental in the surgical approach to these lesions, the possibility of visual damage should always be considered, especially for larger lesions. It is not yet clear whether alternative endovascular treatments can avoid this risk and still obtain a stable occlusion of the aneurysm.

Conflict of Interest We confirm that we have no conflict of interest.

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Predictive Factors for the Occurrence of Visual and Ischemic Complications After Open Surgery for Paraclinoid Aneurysms of the Internal Carotid Artery

Ken-ichiro Kikuta, Ryuhei Kitai, Toshihiko Kodera, Hidetaka Arishima, Makoto Isozaki, Norichika Hashimoto, Hiroyuki Neishi, Yoshifumi Higashino, Shinsuke Yamada, Munenori Yomo, and Kousuke Awara

Abstract

Objective

To investigate the predictive factors for visual and ischemic complications after open surgery for paraclinoid aneurysms of the internal carotid artery (ICA).

Materials and Methods

Thirty-eight consecutive patients with unruptured paraclinoid aneurysms of ICA operated on between 2009 and 2013 were included in this study. The male:female ratio was 6:32 and the ages ranged from 33 to 81 (mean: 60 ± 2). Twenty cases were asymptomatic and 18 had ophthalmological symptoms. The sizes of the aneurysms ranged from 2 to 35 mm (mean: 10.6 ± 9 mm). Twenty-three patients were treated by clipping and 15 by trapping with bypass (high-flow bypass in 11, and low-flow in 4). Twenty-four patients underwent removal of the anterior clinoid process. Among them, 8 underwent en bloc anterior clinoidectomy with a high-speed drill, and 16 had piecemeal excision with a microrongeur or ultrasonic bone curette. Intraoperative monitoring was performed using motor-evoked potentials (MEP) and visual-evoked potentials (VEP) in 27 and 15 cases, respectively.

Results

Complete obliteration of the aneurysm was achieved in 37 cases (97.4 %). The patency rate of bypass was 100 %. Postoperative worsening of visual acuity, including one case of blindness, was observed in six cases (11 %). Worsening of visual field defects occurred in 14 cases (38 %), but 10 of them were transient. Transient oculomotor nerve palsy occurred in six cases (15 %). Postoperative stroke was detected by diffusion-weighted imaging (DWI) in five cases (13 %), four of which were symptomatic. Statistical analysis showed that piecemeal anterior clinoidectomy was significantly safer than en bloc removal in preserving visual function. Trapping with high-flow bypass had a significantly greater risk of postoperative stroke than direct clipping.

Conclusions

Intraoperative VEP monitoring might be useful for preventing postoperative worsening of visual function. Two-stage treatment with bypass and endovascular trapping might be safer than single-stage trapping alone.

Keywords Paraclinoid aneurysm • Anterior clinoidectomy • Bypass • Visual function

Abbreviations

ACP	Anterior clinoid process
BOT	Balloon occlusion test
DWI	Diffusion-weighted imaging
ICA	Internal carotid artery
MEP	Motor-evoked potential
MRI	Magnetic resonance imaging
OphA	Ophthalmic artery
RAG	Radial artery graft
SHA	Superior hypophyseal artery
STA-MCA	Superficial temporal artery to middle cerebral artery
SVG	Saphenous vein graft
VEP	Visual-evoked potential

K.-i. Kikuta, MD, PhD (✉) • R. Kitai, MD, PhD
T. Kodera, MD, PhD • H. Arishima, MD, PhD
M. Isozaki, MD, PhD • N. Hashimoto, MD • H. Neishi, MD
Y. Higashino, MD • S. Yamada, MD • M. Yomo, MD
Division of Neurosurgery, Department of Sensory and Locomotor Medicine, Faculty of Medical Sciences, University of Fukui, 23-3 Matsuokashimoaizuki, Eiheiji-cho, Yoshida-gun, Fukui 910-1193, Japan
e-mail: kikuta@u-fukui.ac.jp

K. Awara, MD
Section of Operating Theater, University of Fukui Hospital, Fukui, Japan

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Introduction

The treatment of paraclinoid aneurysms of the internal carotid artery (ICA) is difficult [1]. Anterior clinoidectomy, including removal of the roof of the optic canal, the anterior clinoid process (ACP), and the optic strut, is usually necessary for direct clipping. There is evidence of some risk to visual function, especially in anterior clinoidectomy with high-speed drills. Therefore, trapping without anterior clinoidectomy has been an alternative, especially for complicated paraclinoid aneurysms. Cases without adequate collateral circulation in the face of permanent occlusion of the ICA need bypass surgery [1]. We reviewed the surgical results in our series of paraclinoid aneurysms treated by direct clipping or trapping, and investigated the predictive risk factors for visual and ischemic complications after surgery.

Materials and Methods

Patient Characteristics

Thirty-eight consecutive patients with an unruptured paraclinoid aneurysms of ICA who underwent surgery between 2009 and 2013 at the University of Fukui Hospital were included. The male:female ratio was 6:32 and the ages ranged from 33 to 81 (mean: 60+2). Twenty cases were asymptomatic, and 18 had some visual symptoms. Preoperative digital subtraction angiography (DSA) was performed in all cases, and development of the collateral circulation was examined using Matas and Alcock tests with manual occlusion. The size of the aneurysms ranged from 2 to 35 mm (mean: 10.6+9 mm). Under Al-Rodhan's classification, the aneurysm was type Ia in 4 cases, Ib in 7, II in 14, III in 7, and IV in 6. Whether the aneurysm was clippable or not was determined by the size and shape of the aneurysm, the characteristics of the neck, Al-Rodhan's classification, and the development of collateral circulation. Perioperative ischemic complications were evaluated by 3 Tesla MRI studies, including DWI, within 2 weeks after surgery. Postoperative visual complications were evaluated by measuring visual acuity and visual fields by an ophthalmologist before surgery, 2 weeks after surgery, and 6 months after surgery. A Goldmann perimeter was used for evaluating visual field defects.

Removal of Anterior Clinoid Process (Anterior Clinoidectomy)

The method of anterior clinoidectomy in our series was classified into two groups. Early in our series, anterior clinoidectomy was performed en bloc with high-speed drills to avoid direct or heat injury to the optic nerve (Fig. 1a, b). We later switched to piecemeal excision using an ultrasonic bone curette (Fig. 1c) and microrongeur (Fig. 1d).

Intraoperative Electrophysiological Monitoring

Motor-evoked potentials (MEPs) with transcranial stimulation (five continuous short trains, strength: 230–450 V, duration: 200 ms, interstimulus interval: 2 ms) were recorded from both the bilateral upper and lower extremities in all cases. Onset latency and largest peak-to-peak difference for MEPs were evaluated during recordings, and an amplitude decrease exceeding 50 % was defined as deterioration of the MEP. Visual evoked potentials (VEPs) were recorded with a light-stimulating device made of fiberglass adapted to high-luminosity light-emitting diodes (LEDs). After administration of anesthesia, transparent eye patches were placed on the closed eyes. The light-stimulating device was then placed on the eyelids and covered with another transparent eye patch. The recording electrodes were inserted subcutaneously at a point 4 cm above and 4 cm lateral to the external occipital protuberance. The stimulus was decreased from 20,000 Lx to determine supramaximal intensity. The usual luminosity was 5000 Lx. The duration and frequency of the stimuli were 20 ms and 1 Hz, respectively. A signal processor (Neuropack, Nihon Kohden) was used to record the VEPs and the recording was calculated from the arithmetic mean of 100 responses.

Statistical Analysis

The data were analyzed with JMP software (Version 10, SAS Institute Inc., Cary, NC, USA). The variables were estimated by using a chi-square test. Values of $P<0.05$ were considered statistically significant in each comparison.

Results

Eleven aneurysms that were regarded as easy to clip were treated by neck clipping without exposure of the cervical ICA. Four aneurysms that were thought difficult to clip were treated by surgical trapping, or by endovascular trapping with bypass because of poor collateral circulation. Low-flow bypass, superficial temporal artery to middle cerebral artery (STA-MCA), was used in two cases. High-flow bypass from the external carotid artery to the M2 segment of the MCA using a radial artery graft (ECA-RAG-M2) or saphenous

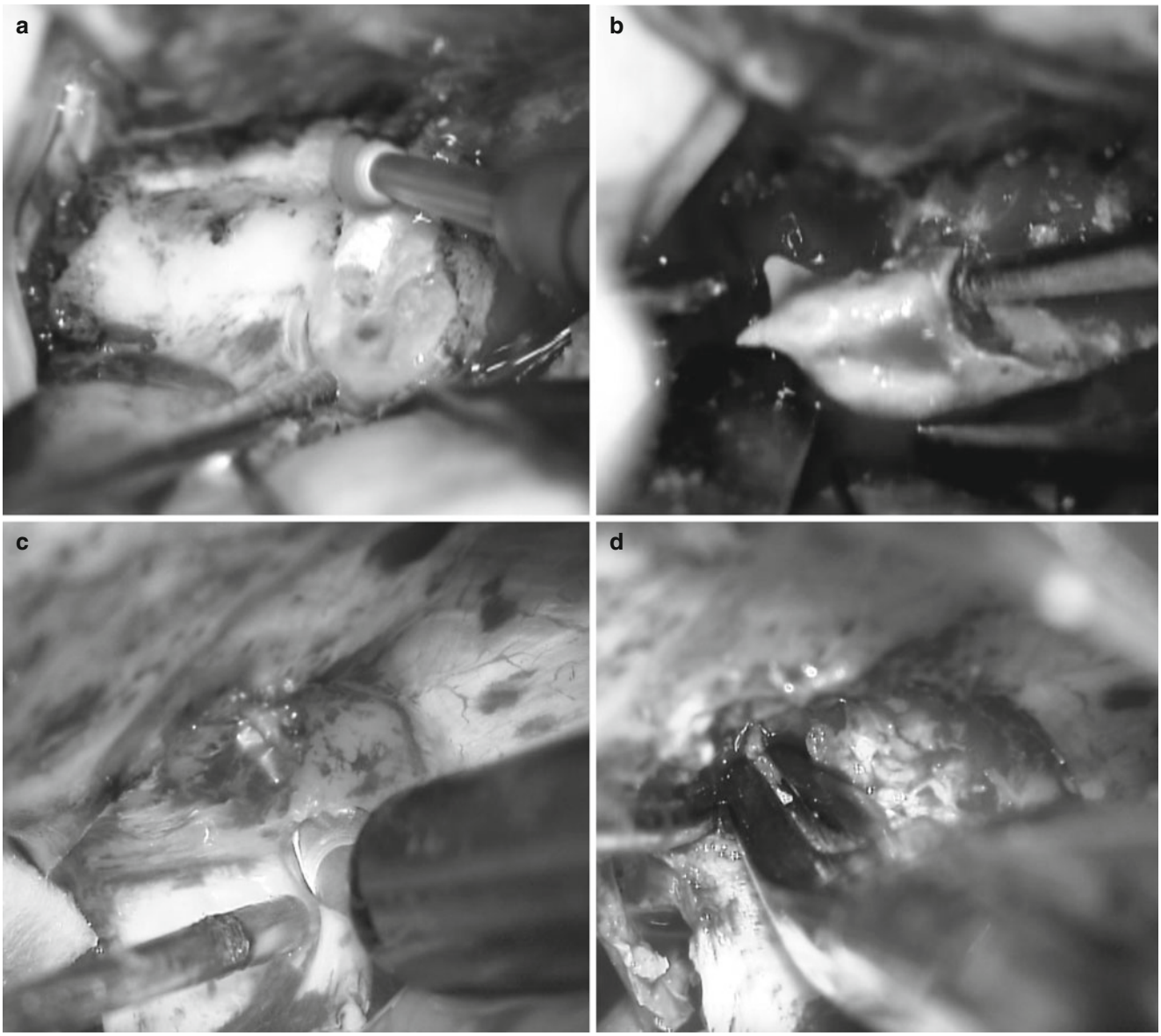

Fig. 1 In the early stage of our series, en bloc anterior clinoidectomy was performed with high-speed drills (**a**, **b**). Anterior clinoidectomy has been converted to a piecemeal method using an ultrasonic bone curette (**c**) and microrongeur (**d**)

vein graft (ECA-SVG-M2) was used in two cases. It was uncertain whether the other 23 aneurysms could be clipped or not. Since they could possibly be treated by trapping, a preoperative balloon occlusion test (BOT) was performed. Thirteen cases tolerated the testing, and ten did not. Eleven of the 13 cases that tolerated BOT were treated by clipping with exposure of the cervical ICA. The remaining two cases were treated by trapping and STA-MCA bypass. Nine of the ten cases that did not tolerate BOT were treated by trapping with high-flow bypass. The remaining case was treated by clipping after placing a high-flow bypass, when it became clear that it could be clipped during surgery.

Anterior clinoidectomy was performed in 24 cases. Twenty-three had direct clipping and one had trapping. Eight of the 24 cases received en bloc anterior clinoidectomy using high-speed drills (Fig. 1a, b), and 16 underwent piecemeal anterior clinoidectomy using an ultrasonic bone curette or microrongeurs (Fig. 1c, d). Intraoperative monitoring with MEP was performed in 27 cases (71%), with temporary occlusion of the parent artery in 10 of them. Two showed reduction of MEP amplitude exceeding 50% of the control value. In these cases, temporary occlusion was immediately terminated to avoid ischemic complications. Ischemic lesions were detected by DWI in five cases (13%), and four were symptomatic. VEP monitoring was performed in 15 cases (39%) and 3 (8%) showed abnormal findings. Worsening visual acuity and visual fields were observed in 6 (15%) and 14 cases (37%), respectively, at 2 weeks after surgery. The worsening visual field defects were completely resolved in 10 of the 14 cases at 6 months after surgery.

Oculomotor nerve palsy was observed in six (15%) cases, and five were transient.

Statistical analysis showed that postoperative worsening of visual acuity occurred significantly more often in patients undergoing anterior clinoidectomy, and in those with abnormal intraoperative VEPs. Postoperative worsening of visual fields occurred significantly more often in patients undergoing direct clipping and anterior clinoidectomy. VEPs could not adequately predict postoperative worsening of visual fields. Postoperative transient oculomotor palsy also occurred considerably more often in patients undergoing direct clipping and anterior clinoidectomy (Table 1). En bloc anterior clinoidectomy with high-speed drills induced postoperative worsening of visual acuity, visual fields, and oculomotor palsy significantly more often than piecemeal excision with an ultrasonic bone curette and microrongeurs (Table 2).

Postoperative stroke occurred significantly more often in patients undergoing trapping and bypass, which were perceived to be significant risk factors. Neither temporary occlusion of the parent artery nor abnormal intraoperative MEPs were related to the occurrence of postoperative stroke (Table 3). The method of trapping could be classified into two types: surgical trapping, and endovascular trapping. Surgical trapping was single-staged and was performed immediately after bypass surgery. Endovascular trapping was performed 1–3 weeks after bypass surgery; this was done after repeated BOT. The risk of postoperative stroke was smaller in cases of endovascular trapping than of surgical trapping. Statistical analysis suggested that postoperative stroke occurred significantly more often in patients undergoing surgical rather than endovascular trapping (Table 4).

Table 1 Postoperative worsening of visual acuity was significantly more frequent in patients undergoing anterior clinoidectomy and in those with abnormal intraoperative VEP

Procedure	*N*	Worsening of visual acuity	*p*	Worsening of visual field	*p*	Oculomotor nerve palsy	*p*
Direct clipping	23	5	0.21	13	0.0018*	6	0.0311*
Trapping	15	1		1		0	
Anterior clinoidectomy	24	6	0.0145*	14	0.0003*	6	0.0415*
Without clinoidectomy	14	0		0		0	
Abnormal findings on VEP	3	2	0.0118*	2	0.2545	0	0.4345
Normal VEP during surgery	35	4		12		6	

Both postoperative worsening of visual fields and oculomotor palsy were significantly more frequent in patients undergoing direct clipping and anterior clinoidectomy

Table 2 En bloc anterior clinoidectomy with high-speed drills induced postoperative worsening of visual acuity, visual fields, and oculomotor palsy significantly more often than piecemeal anterior clinoidectomy with an ultrasonic bone curette and microrongeurs

Anterior clinoidectomy	*N*	Worsening of visual acuity	*p*	Worsening of visual field	*p*	Oculomotor palsy	*p*
En bloc fashion with high-speed drills	8	4	0.0455*	8	0.0034*	5	0.0027*
Piecemeal fashion with ultrasonic bone curette and microrongeurs	16	2		6		1	

Table 3 Postoperative stroke was significantly more frequent in patients treated by trapping or surgery with bypass

	Total number	Number of symptomatic postoperative stroke	*p*
Direct clipping	23	0	0.0088*
Trapping	15	4	
Surgery with bypass	17	4	0.0188*
Surgery without bypass	21	0	
Temporary occlusion of the parent artery	10	0	0.2064
No temporary occlusion	28	4	
Abnormal findings on MEP	2	4	0.6182
Normal MEP during surgery	36	0	

Postoperative stroke was not related to temporary occlusion of the parent artery or to abnormal findings on intraoperative MEP

Table 4 Postoperative stroke was rare with endovascular trapping compared to surgical trapping, and was more frequent with high-flow bypass than low-flow bypass

	N	Postoperative stroke (symptomatic)	*p*
One-staged surgical trapping	11	4	0.0041*
Two-staged internal trapping with repeated BTO	4	0	
High-flow bypass	13	4	0.0136*
Low-flow bypass	4	0	

Postoperative stroke also occurred significantly more often in patients who had high-flow bypass than those with low-flow bypass.

Representative Cases

Case 1

A 54-year-old woman was diagnosed with a left paraclinoid ICA aneurysm by screening MRI for underlying Osler-Weber-Rendu disease (hereditary hemorrhagic telangiectasia). The aneurysm was 5 mm in diameter and Al-Rodhan's type III (Fig. 2a, b). Preoperative BOT showed that she would tolerate ICA occlusion. Successful neck clipping was performed with exposure of the cervical ICA, with en bloc anterior clinoidectomy using high-speed drills (Fig. 2c). Intraoperative VEP showed marked reduction of the amplitude of N70 (Fig. 2d). Ophthalmological studies revealed visual acuity loss in the left eye (0.1 diopter), and left nasal and right upper temporal hemianopsia on a Goldmann perimeter (Fig. 2e).

Case 2

A 63-year-old woman was diagnosed with a left paraclinoid ICA aneurysm by an MRI screening for transient hand tremor. The aneurysm was 9 mm in diameter and Al-Rodhan's type III (Fig. 3a, b). Preoperative BOT showed that she would tolerate CA occlusion. Successful neck clipping was performed with the exposure of the cervical ICA, with piecemeal anterior clinoidectomy using an ultrasonic bone curette and microrongeurs (Fig. 3c). Intraoperative VEP was stable (Fig. 3d). Ophthalmological studies showed no visual acuity loss, no visual field defect, and no oculomotor nerve palsy (Fig. 3e).

Case 3

A 65-year-old woman was diagnosed with a right paraclinoid ICA aneurysm by screening MRI for headache. The aneurysm was 14 mm in diameter and Al-Rodhan's type I b (Fig. 4a). The anterior choroidal artery adhered to the aneurysmal wall (Fig. 4a: white arrows). Preoperative BOT showed that she was intolerant to ICA occlusion, so surgical trapping combined with high-flow bypass with SVG was performed (Fig. 4b, c). The anterior choroidal artery was spared and intraoperative MEP was stable. Although the bypass was patent, she exhibited left hemiparesis after surgery, due to delayed occlusion of the anterior choroidal artery (Fig. 4d).

Discussion

Paraclinoid aneurysms have been perceived as among the most difficult to obliterate [1]. Aneurysms at the origin of the ophthalmic artery (ICA-OphA) and of the superior hypophyseal artery (ICA-SHA) were initially described as clippable [1]. They had marked female predominance, a high incidence of multiple aneurysms, and they presented with subarachnoid hemorrhage or visual deficits; some were identified only incidentally [2]. Carotid cave aneurysms are another subtype of ICA aneurysm in the area of the ophthalmic segment. The aneurysms usually project ventromedially, extend into the cavernous sinus, and can be clipped by using ring clips [3]. Al-Rodhan et al proposed a simple classification of paraclinoid ICA aneurysms: type Ia, ICA-SHA; type Ib, ICA ventral aneurysm proximal to the origin of the posterior communicating artery; type II, ICA-SHA; type III, carotid cave aneurysm; and type IV, intracavernous aneurysm [4].They treated 78 % of the aneurysms by direct clipping and 22 % by bypass. Excellent outcomes were achieved in 87 %, and complications were observed in 13 %, including one death [4]. Another report showed complete obliteration by direct surgery in 80 % of type Ia, 80 % of type Ib, and 71.4 % of type III aneurysms, with transient and permanent morbidity of 8.6 % and 2.9 %, respectively [5]. A recent report showed that permanent morbidity, including complete visual loss and postoperative death related to stroke, occurred in 6.4 %; transient morbidity, such as cerebrospinal fluid (CSF) rhinorrhea or oculomotor nerve palsy, occurred in 10.4 % after direct clipping of unruptured paraclinoid aneurysms [6]. In our series, permanent visual complications and ischemic complications occurred in six (16 %) and four cases (10 %), respectively.

Most paraclinoid aneurysms require removal of the roof of the optic canal, the ACP, and the optic strut, with opening of the dural ring to completely expose the aneurysm [4, 6]. Meticulous skull base techniques are needed for direct clip-

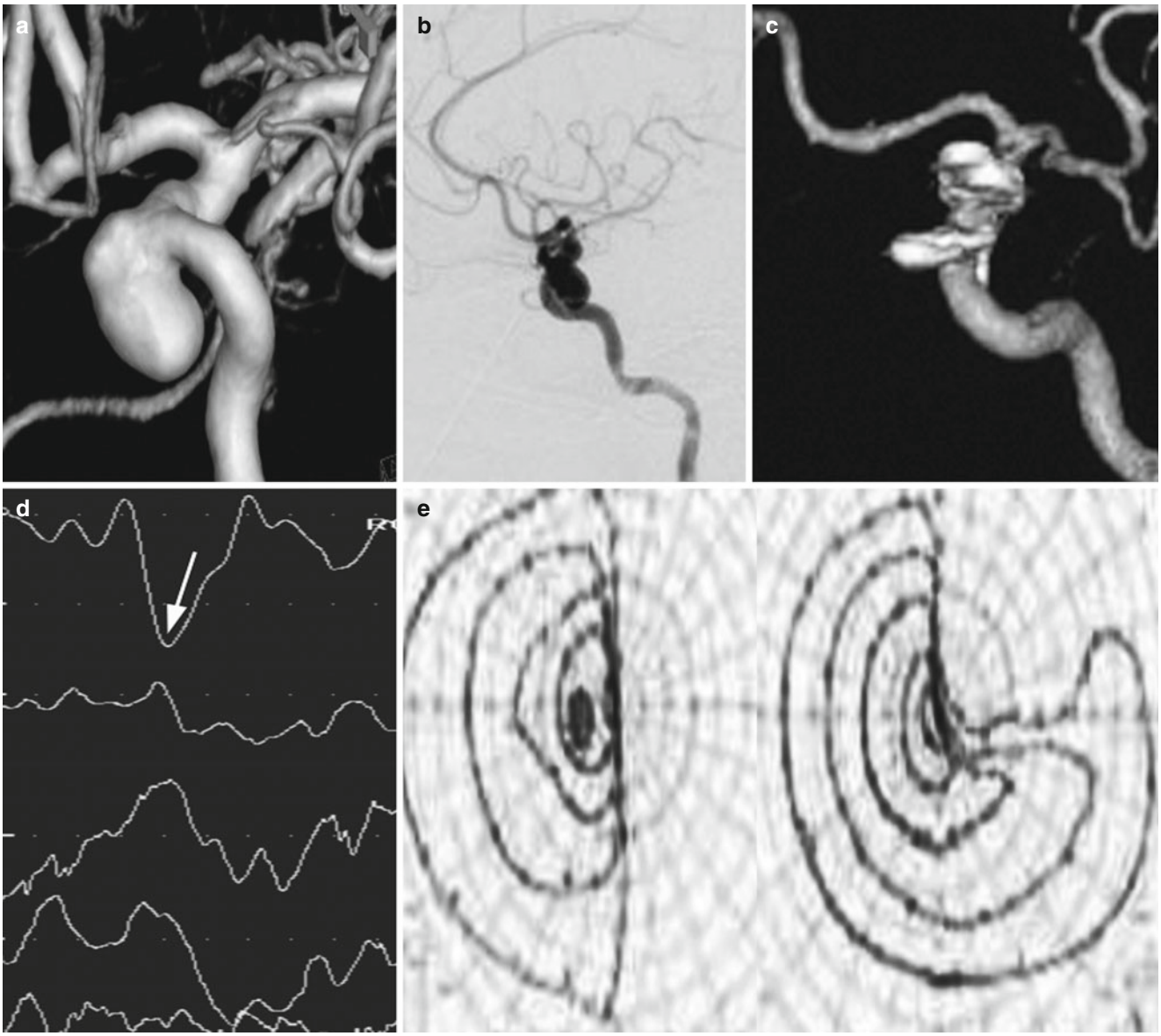

Fig. 2 A 54-year-old woman with Osler-Weber-Rendu disease had a 5-mm Al-Rodhan type III left paraclinoid aneurysm (**a, b**). Successful neck clipping was performed (**c**). Intraoperative VEP showed marked reduction in the amplitude of N70 (**d**: *arrow* indicating N20). She exhibited severe visual acuity loss and visual field defects after surgery (**e**)

ping of the aneurysm. This study showed that worsening visual acuity loss was significantly related to anterior clinoidectomy, and that intraoperative VEP monitoring could provide a warning. Although the worsening of visual field defects was also significantly related to direct clipping and anterior clinoidectomy, VEP was not predictive.

The method of anterior clinoidectomy is important for the avoidance of vision complications. Many neurosurgeons still use high-speed drills for anterior clinoidectomy. However, the drill bit sometimes causes direct or heat injury to the optic nerve and the blood vessels, including the ICA. The drill bit also sometimes catches on cotton pledgets, injuring surrounding brain tissue. To mitigate these risks, en bloc anterior clinoidectomy using high-speed drills has been developed [7, 8], which can reduce the amount of bone removal in clinoidectomy, thereby reducing the risk of direct or heat injury. The "no drill" technique for clinoidectomy has also been developed [9]. This method uses rongeurs or microrongeurs instead of high-speed drills [10]. The use of an ultrasonic bone curette is another option for anterior clinoidectomy [11]. The curette does not induce heat injury, or mechanical injury, by catching on cotton pledgets [12].The best method for anterior clinoidectomy remains uncertain. Our study clearly showed that postoperative visual complications occurred significantly more often in en bloc clinoidectomy with high-speed drills than in piecemeal

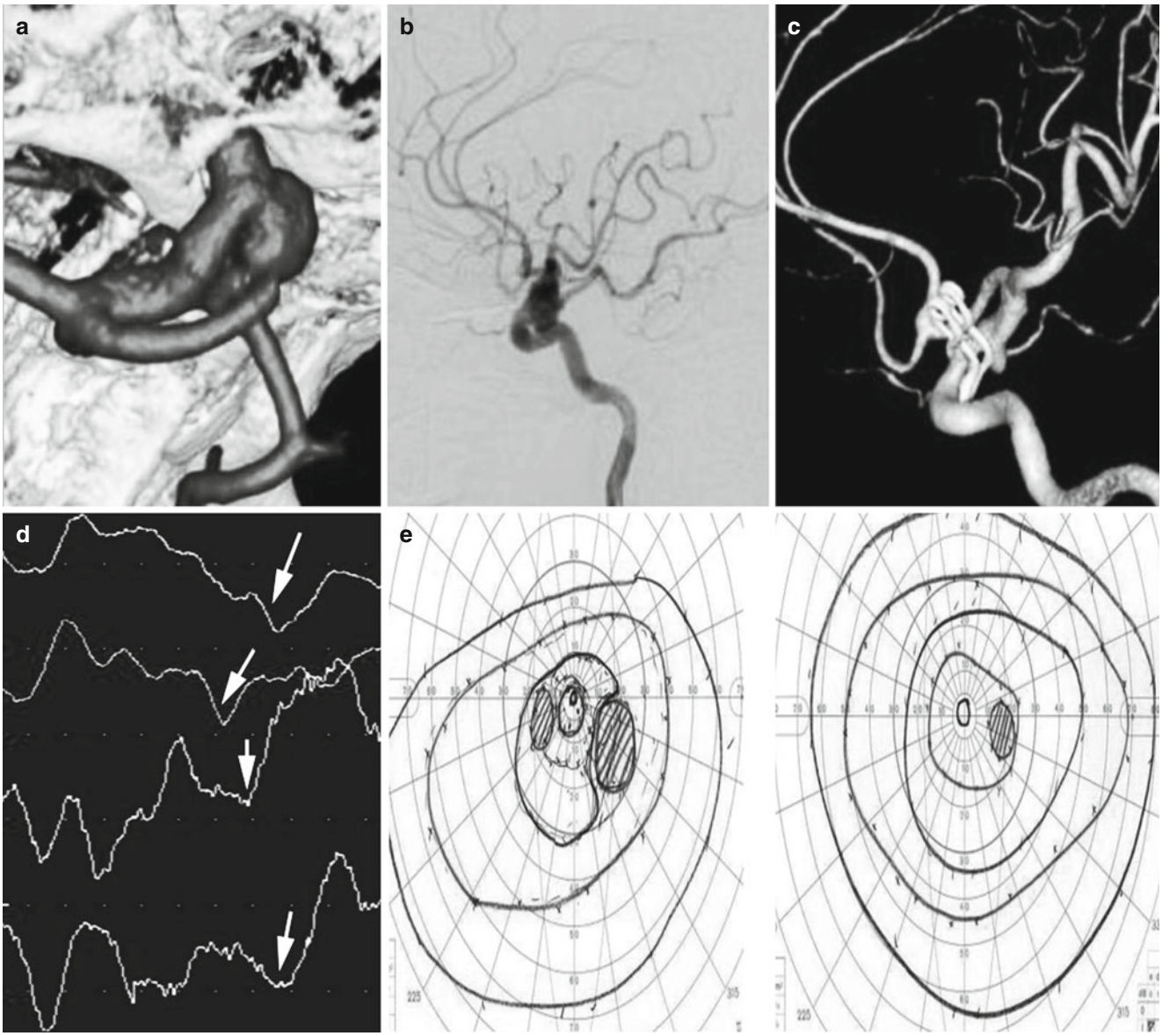

Fig. 3 A 9-mm left paraclinoid ICA aneurysm was Al-Rodhan's type III (**a**, **b**). Successful neck clipping was performed (**c**). Intraoperative VEP was stable (**d**: *arrows* indicating stable N20). No visual acuity loss, visual field defect, or oculomotor nerve palsy was detected after surgery (**e**)

clinoidectomy with an ultrasonic bone curette and microrongeurs.

Another approach to paraclinoid aneurysms is trapping. This method does not require anterior clinoidectomy and rarely induces postoperative visual dysfunction. However, bypass surgery is needed in cases of the inadequate development of collateral circulation in response to parent artery occlusion; this sometimes induces ischemic complications after surgery. Our study showed that treatment using trapping and bypass surgery increases the risk for postoperative stroke. Our data showed that the risk of postoperative stroke was reduced by using a two-stage treatment strategy, consisting of endovascular trapping (with repeated BOT) 2–3 weeks after bypass surgery, as compared to single-stage surgical trapping.

There were significant limitations to our study. The number of cases was too small to provide adequate statistical power. Although we analyzed consecutive cases, this is only a retrospective study with selection bias. The treatment approach to the aneurysms was decided according to subjective factors, such as size, shape, and neck characteristics, which were judged by visual inspection.

Conclusions

In surgery for paraclinoid aneurysms, piecemeal anterior clinoidectomy using an ultrasonic bone curette and microrongeurs may be better for preserving visual function. Intraoperative VEP monitoring is also useful. For trapping of the aneurysms, two-stage treatment with bypass

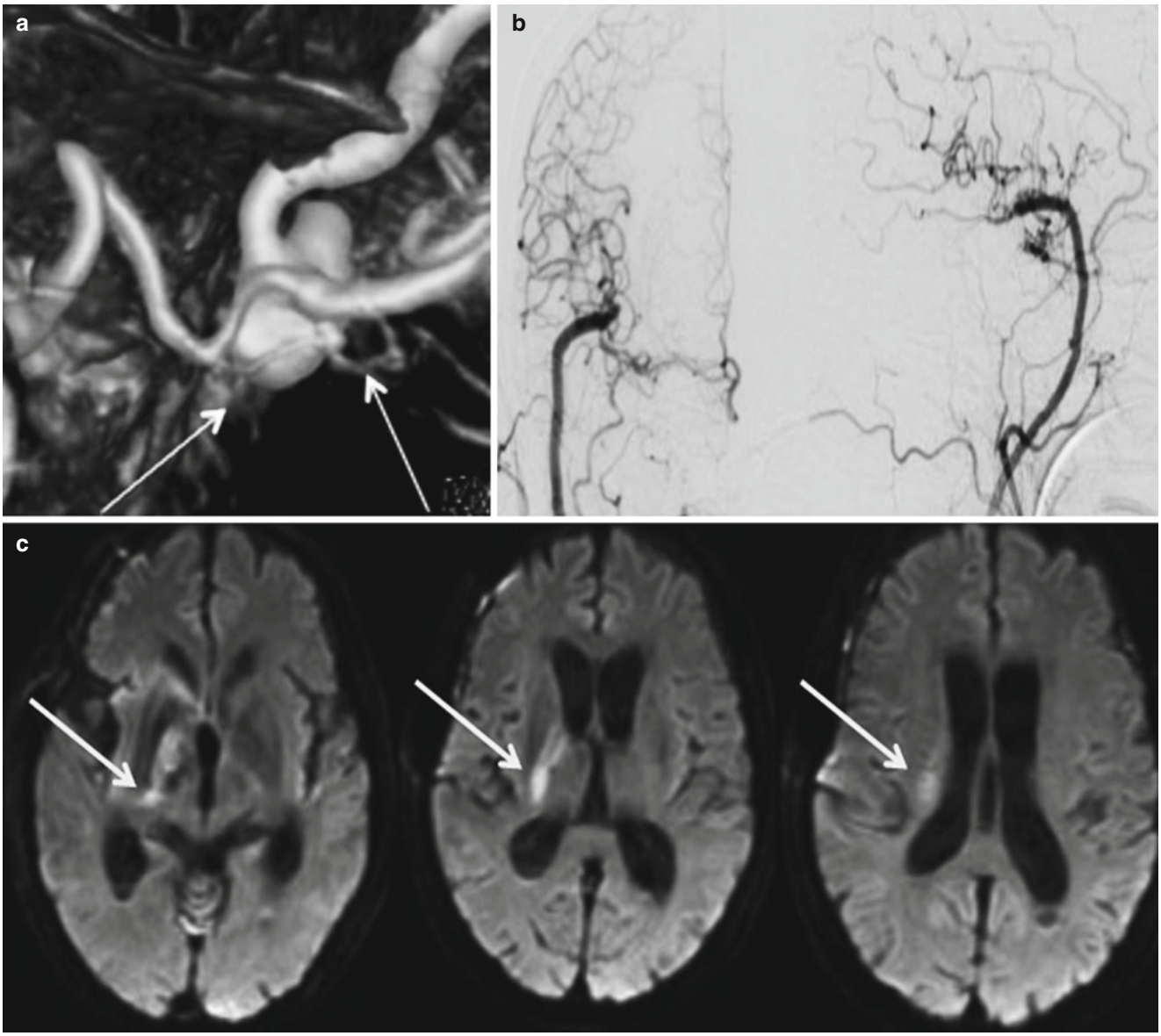

Fig. 4 A 14-mm right paraclinoid ICA aneurysm was Al-Rodhan's type Ib (**a**). The anterior choroidal artery adhered to the aneurysmal wall (**a**: *white arrows* indicating anterior choroidal artery). Successful surgical trapping combined with high-flow bypass using SGA was performed (**b**). Although the bypass was patent, she exhibited left hemiparesis due to delayed occlusion of the anterior choroidal artery (**c**: *arrows* indicating infarct lesions in the area of anterior choroidal artery)

and endovascular trapping with repeated BOT might be safer than single-stage trapping.

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

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Retrograde Suction Decompression Through Direct Puncture of the Common Carotid Artery for Paraclinoid Aneurysm

Naoki Otani, Kojiro Wada, Terushige Toyooka, Kazuya Fujii, Hideaki Ueno, Satoshi Tomura, Arata Tomiyama, Yasuaki Nakao, Takuji Yamamoto, and Kentaro Mori

Abstract

Background

Surgical clipping of paraclinoid aneurysm can be very difficult because strong adhesions may hinder the dissection of the perforators and surrounding anatomical structures from the aneurysm dome. We describe our experience with using retrograde suction decompression during the clipping of paraclinoid aneurysms and discuss the relative advantages and pitfalls.

Materials and Methods

This study included 23 patients with large and giant paraclinoid aneurysms who underwent surgical treatment consisting of direct clipping with suction decompression between March 2004 and August 2014. Direct puncture of the common carotid artery (CCA) was performed with a 20-gauge needle. The aneurysm was temporarily trapped by clamping of the CCA and external carotid artery (ECA), followed by temporary clipping of the intracranial internal carotid artery (ICA) distal to the aneurysm neck. Blood was then gently aspirated through a catheter introduced into the cervical ICA, resulting in collapse of the aneurysm. Therefore, safe aneurysm dissection was feasible during interruption of the blood flow, which could be maintained for up to 5 min. This procedure was repeated until dissection and clipping of the aneurysm were completed.

Results

Seven patients were admitted with SAH, 11 with asymptomatic unruptured aneurysm, and 5 with symptomatic unruptured aneurysm. The aneurysms were located on the paraclinoidal segment of the ICA in 15 cases, on the ICA-posterior communicating artery (PComA) in 6, at the ICA bifurcation in 1, and on the anterior wall of the ICA in 1. None of them suffered complications related to the CCA puncture. Surgical outcome was good recovery in 13 patients, moderate disability in 4, severe disability in 4, and vegetative state in 1.

Conclusion

Retrograde suction decompression through direct puncture of the common carotid artery is a useful adjunct technique for the clipping of paraclinoid ICA aneurysms.

Keywords Paraclinoid aneurysm • Suction decompression • Surgical result • Microneurosurgery • Extradural anterior clinoidectomy

Introduction

Giant or large aneurysms account for only 2–5 % of all intracranial aneurysms [14, 18] and have traditionally been associated with higher morbidity and mortality without treatment [15]. Microsurgical treatment for these aneurysms remains a big challenge. Complete clipping of paraclinoid aneurysms presents great difficulties because of the complicated anatomical location close to the optic structures and internal carotid artery (ICA). In addition, there are great difficulties in achieving proximal control of the parent artery and obtaining adequate visualization of the aneurysmal neck, due to their large sizes and broad necks [12].

Microsurgical treatment of these aneurysms may require the use of retrograde suction decompression (RSD) to facilitate safe and complete clipping [10, 12, 17]. RSD provides adequate relaxation of the aneurysmal dome, enabling the surgeon to fully dissect the ICA and its branches, as well as the aneurysmal dome. We usually clip paraclinoid aneurysms using extradural anterior clinoidectomy via an extra-

N. Otani, MD (✉) • K. Wada • T. Toyooka • K. Fujii • H. Ueno
S. Tomura • A. Tomiyama • K. Mori
Department of Neurosurgery, National Defense Medical College,
3-2 Namiki, Tokorozawa, Saitama 59-8513, Japan
e-mail: naotani@ndmc.ac.jp

Y. Nakao • T. Yamamoto
Department of Neurosurgery, Juntendo University Shizuoka Hospital, Izunokuni, Japan

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dural temporopolar approach (ETA) [6, 7], or RCD through direct puncture of the common carotid artery (CCA).

In this article we present our experience and results with the use of the two above-mentioned strategies for the clipping of large/giant paraclinoid aneurysms.

Patients and Methods

Patient Characteristics

This retrospective analysis included 23 patients, 22 women and 1 man, aged 37–78 (mean age: 66), with large/giant intracranial aneurysms. These patients underwent RSD and direct clipping at the National Defense Medical College Hospital and Juntendo University Shizuoka Hospital between March 2004 and August 2014. Medical charts, radiological findings, surgical techniques, complications, and final clinical results were retrospectively reviewed.

Surgical Procedure

Preoperative Preparation

Three-dimensional CT angiography (3-D CTA) and/or digital subtraction angiography (DSA) were mandatory for investigating paraclinoid angioanatomy. DSA allowed checking the cross-flow from the contralateral side through the anterior (ACom) and/or posterior communicating (PCom) artery. The anterior clinoid process (ACP) size, shape, pneumatization, and relationship with the sphenoid or the ethmoid sinus were assessed on bone CT for safe clinoidectomy. All patients underwent detailed evaluation of the location of the ICA bifurcation and the existence of the carotid stenosis. Cerebral blood flow (CBF) study was used to estimate intraoperative occlusion time risk and to eventually consider the use of cerebral revascularization strategy. To avoid postoperative cerebrospinal fluid (CSF) leakage, and to obtain adequate brain relaxation, patients received pre-operative external spinal drainage. Intraoperative monitoring of the motor-evoked potential was routinely used for a safe clipping procedure. Suction decompression via the CCA was required for large and giant paraclinoid aneurysms to obtain proximal control of the ICA and perform intraoperative angiography, and to allow safe intracranial aneurysm dissection from surrounding anatomical structures (such as the optic nerve). Intraoperative DSA was done to confirm complete clipping and preservation of blood flow in the parent artery. Indocyanine green (ICG) videoangiography and/or microvascular Doppler ultrasonography were regularly used to further assess the patency of the parent and branch vessels.

Retrograde Suction Decompression with Extradural Anterior Clinoidectomy via the Extradural Temporal Approach (ETA)

After administering general anesthesia, the patient is placed in the supine position, and the head is rotated 30° away from the operative side. The neck is slightly extended. A fronto-temporal skin incision is performed, followed by inter-fascial dissection, and the temporal muscle is retracted inferiorly. A standard fronto-temporal craniotomy is performed up to the supra-orbital notch, and the temporal squama is rongeured out until the floor of the middle cranial fossa is exposed; if considered necessary, an orbito-zygomatic osteotomy is performed. The lesser wing of the sphenoid is flattened until the meningo-orbital band is exposed and incised to a length of about 4 mm. The peeling of the dura propria from the lateral wall of the superior orbital fissure (SOF) begins and continues until the ACP is exposed epidurally. Drilling of the ACP with a high-speed drill using cold saline irrigation starts from the lateral part of the ACP. The optic canal is then partially opened in the medial part of the ACP using a micro-punch to avoid heat injury. After removal of ACP, the clinoid segment (C3) of the internal carotid artery can be seen. The remainder of the optic strut can be removed with either a small diamond drill or micro-punch to provide space for the clip blade. The dura mater is then opened along the sylvian fissure, and continued inferomedially to the level of the optic nerve. The additional wide opening of the sylvian fissure is helpful for minimal retraction of the frontal lobe to expose the ICA and the optic nerve. The posterior communicating artery (Pcom) and anterior choroidal artery (Acho), and their branches, are identified. An incision from the falciform ligament to the optic sheath helps to mobilize the optic nerve. An additional incision is made across the distal dural ring to expose and identify the origin of the ophthalmic artery and to mobilize the ICA. Such incisions of the falciform ligament and distal dural ring will facilitate movement of the optic nerve and ICA. CSF leakage is a potential risk if the ethmoid air cells are opened during drilling of the ACP. Therefore, the opened ethmoid air cells should be carefully packed with autologous muscle with fibrin glue sealant.

Simultaneously, the cervical CCA, the ICA, and the external carotid artery (ECA) are routinely exposed for proximal control, suction decompression, intraoperative angiography, and high-flow bypass if necessary. A puncture of CCA is performed using a 20-gauge needle just before suction decompression. The aneurysm is temporarily trapped by temporal clipping of the intracranial ICA distal to the aneurysm neck, with special attention to spare the AchoA, followed by clamping of CCA and ECA. Blood is gently aspirated through the catheter introduced into the cervical ICA, resulting in aneurysmal collapse and therefore enabling

the surgeon to finalize dissection and clipping. The occlusive time lapse is limited to 5 min – even if there are no changes in the electrophysiological monitoring – followed by 5 min of reperfusion. After removing the temporary clips/clamps, control angiography is usually performed. Complete hemostasis at the puncture site is achieved by suturing, and a postoperative 3-D CTA is performed to confirm the efficacy of treatment and to rule out complications.

Results

All patient characteristics and surgical outcomes are summarized in Table 1. Seven patients were admitted with SAH, 11 with asymptomatic unruptured aneurysm, and 5 with symptomatic unruptured aneurysm including visual disturbance in 4 and hypopituitarism in 1. Extradural anterior clinoidectomy via ETA was performed in 20 patients, except for 2 with ICA bifurcation and IC-PCom aneurysms. The aneurysmal sites were ICA-paraclinoid in 15, IC-PCom in 6, ICA bifurcation in 1, and ICA-anterior wall in 1 patient. There were no complications related to the direct puncture of the CCA.

Postoperative outcomes were a good recovery in 13 patients, moderate disability in 4, severe disability in 4, vegetative state in 1, and death in 1 patient. Favorable outcome was 73.9%. One patient with a ruptured large IC-PCom aneurysm died of re-rupture of the remnant aneurysmal neck, secondary to postoperative intensive therapy for cerebral vasospasm. In this case, complete clipping was not possible because of the difficulty in dissecting the PCom from the

Table 1 Clinical characteristics of 23 patients who underwent suction decompression using direct puncture of the common carotid artery between March 2004 and August 2014

Case no.	Age/gender	Side	Site	SAH	Size (mm)	ETA	Complications	SO		
								ADL	KPS	GOS
1	76/F	R	ICA paraclinoid	–	20	+	VD	2	90	GR
2	69/F	L	ICA paraclinoid	Grade IV	12	+	–	4	40	SD
3	66/F	R	ICA paraclinoid	–	13	+	ONP	1	90	GR
4	53/F	L	ICA paraclinoid	–	25	+	–	1	100	GR
5	76/F	L	ICA paraclinoid	Grade III	10	+	Ruptured distal	5	20	VS
										ACA AN
6	62/M	R	ICA-PCom	Grade IV	12	+	Re-ruptured	6	0	D
7	73/F	R	ICA paraclinoid	Symptomatic	12	+	–	3	40	SD
8	73/F	R	ICA paraclinoid	Grade III	18	+	–	4	20	SD
9	42/F	L	ICA paraclinoid	–	15	+	–	1	100	GR
10	73/F	L	ICA paraclinoid	–	13	+	–	1	100	GR
11	66/F	L	ICA-PCom	Grade V	13	+	SV	4	90	MD
12	60/F	R	ICA anterior wall	Grade II	10	+	–	1	90	GR
13	55/F	R	ICA-PCom	–	15	+	–	1	100	GR
14	72/F	L	ICA paraclinoid	Symptomatic	16	+	–	2	80	MD
15	78/F	R	ICA-PCom	–	15	+	–	1	100	GR
16	59/F	L	ICA paraclinoid	Symptomatic	25	+	–	2	80	MD
17	37/F	L	ICA bifurcation	–	8	–	–	1	100	GR
18	65/F	L	ICA paraclinoid	Symptomatic	13	+	–	2	80	MD
19	65/F	L	ICA-PCom	–	12	+	CI (AchA)	4	40	SD
20	56/F	R	ICA paraclinoid	Symptomatic	13	+	–	1	100	GR
21	62/F	R	ICA-PCom	–	18	–	–	1	100	GR
22	71/M	R	ICA paraclinoid	–	6	+	–	1	100	GR
23	68/F	L	ICA paraclinoid	Grade II	20	+	–	1	100	GR

M male, *F* female, *R* right side, *L* left side, *ICA* internal carotid artery, *PC* posterior communicating artery, *SAH* subarachnoid hemorrhage, *ETA* extradural temporopolar approach, *SO* surgical outcome, *VD* visual disturbance, *ONP* oculomotor nerve palsy, *ACA* anterior cerebral artery, *AN* aneurysm, *SV* symptomatic vasospasm, *CI* cerebral infarction, *AchA* anterior choroidal artery, *ADL* activity of daily living, *KPS* Karnofsky performance status, *GOS* Glasgow Outcome Scale, *GR* good recovery, *MD* moderate disability, *SD* severe disability, *D* death

aneurysmal dome; therefore we reinforced the aneurysm wall with Fibrin glue. In the 11 asymptomatic aneurysmal patients, one presented with severe hemiparesis due to an infarction in the anterior choroidal artery territory. In the five symptomatic aneurysmal patients, surgical results showed good recovery in one, moderate disability in three, and severe disability in one. Another patient suffered cerebral infarction due to intra-aneurysmal thrombus, resulting in severe disability. All three of the patients who showed MD suffered cognitive dysfunction or motor hemiparesis caused by old infarction and hypopituitarism, and did not show improvement of cognitive dysfunction postoperatively, resulting in moderate disability. However, at the 3-month follow-up, the patients' muscle strength was restored and their ADL became independent. Except for one patient, all aneurysms were successfully clipped, and postoperative 3D-CTA revealed no major branch occlusion or residual aneurysm.

Case Presentation

Case 1

A 62-year-old female had been diagnosed with a large left posterior communicating artery (PcomA) bifurcation aneurysm 8 years previously. Recent 3-D CTA revealed an unruptured left PcomA bifurcation aneurysm that progressively grew to 18 mm, with a newly developed bleb (Fig. 1a). Intraoperatively, the aneurysm was tightly attached to the tentorial membrane and temporal lobe, so the PcomA bifurcation and the perforators could not be directly dissected (Fig. 1c) and RSD was considered necessary. The aneurysm was therefore detached from the perforators with suction decompression, and clipped after shrinking its dome (Fig. 1d). Postoperative CTA showed no remarkable abnormality (Fig. 1b), and the postoperative course was uneventful.

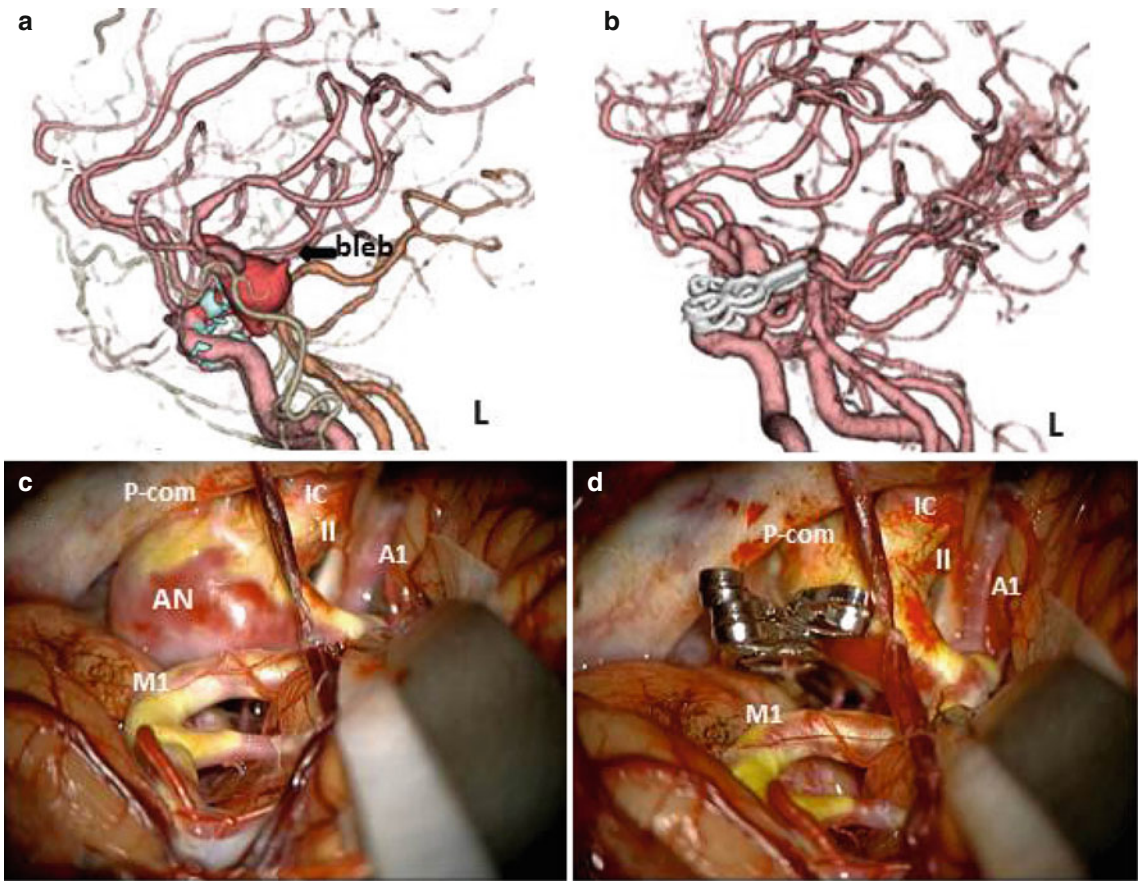

Fig. 1 A 62-year-old female presented with an unruptured left PcomA bifurcation aneurysm that progressively grew to 18 mm, with a newly developed bleb (**a**). Intraoperatively, the aneurysm was found to be tightly attached to the tentorial membrane and temporal lobe, so the PcomA bifurcation and the perforators could not be confirmed (**c**). After RSD, it was possible to shrink the dome, dissect the perforators, and finally successfully clip the aneurysm (**d**). Postoperative 3DCTA showed no remarkable abnormality (**b**)

Table 2 Comparison of surgical outcomes for suction decompression with direct puncture of the CCA as previously reported

	References	Year	No. of pts	Site	Size	Surgical outcome		
						GR + MD	SD + VS	D
Batjer et al.	[3]	1994	22	ICA paraclinoid	G	18 (82.0 %)	3 (14.0 %)	0
Hauck et al.	[14]	2008	62	AC	L/G	42 (68.0 %)	20 (32.0 %)	9 (15.0 %)
Eliava et al.	[8]	2010	83	ICA paraclinoid	G	69 (83.1 %)	11 (13.3 %)	3 (3.6 %)
Present report	–	–	23	ICA paraclinoid	L/G	17 (73.9 %)	5 (21.7 %)	1 (4.3 %)

Ref reference, *pts* patients, *ICA* internal carotid artery, *AC* anterior circulation, *G* giant, *L* large, *GR* good recovery, *MD* moderate disability, *SD* severe disability, *VS* vegetative state, *D* death

Discussion

Paraclinoid aneurysms are categorized as ophthalmic (originating from the superior surface of the ICA), superior hypophyseal (originating from the inferomedial surface of the ICA), and variant aneurysms, which are classified as a "supraclinoid type" (located on the anterior wall of the ICA), or an "infraclinoid type" (located on the posterior wall of the ICA) [5, 13]. Paraclinoid aneurysms are surrounded by many important osseous and neuro-vascular structures, such as ACP, optic nerve, oculomotor nerve, ICA, or ophthalmic artery. Microsurgical treatment of these aneurysms is challenging [12]. RSD is a useful option to facilitate safe and complete clipping [10, 12, 17], and it provides adequate relaxation of the aneurysm enabling the surgeon to fully dissect the ICA and its branches as well as the aneurysmal dome, in order to obtain adequate visualization of the aneurysmal neck and allow safe reconstruction of the parent artery.

Direct puncture of the aneurysm followed by blood suction using a butterfly needle to deflate the aneurysm were first described in 1981 [11]. However, this type of technique was cumbersome and prevented the surgeon from using both hands during dissection. After that, a retrograde suction aspiration through an angiocatheter inserted into the cervical internal carotid artery was reported in 1990 and 1991 [2, 20]. Fan et al. [10] used aspiration through the ECA to minimize the risk of embolization and ICA dissection. RSD using Seldinger's method has been previously reported [1, 4, 9, 12, 17, 19]. This endovascular RSD method remains an effective treatment for the direct clipping of large and giant paraclinoid aneurysm. However, there are some therapeutic problems, namely long-term intra-arterial permanence of the catheter, the necessity of a DSA device, and inadequacy in securing the CCA for premature rupture.

We usually directly clip paraclinoid aneurysms using both of the following strategies: (1) extradural anterior clinoidectomy via an extradural temporopolar approach [6, 7]; and (2) suction decompression through direct puncture of the CCA. Clinical data from this method are described in Table 2. Eliava et al. [8] reported favorable outcome in 83.1 %, poor outcome in 13.3 %, and death in 3.6 %. Hauck et al. [14] reported favorable outcome in 68 %, poor outcome in 32 %, and death in 15 %. Batjer et al. [3] reported favorable outcome in 82 %, poor outcome in 14 %, and death in 0 % in 22 patients who underwent this surgical procedure for treating giant paraclinoidal aneurysms. Recently, Mattingly et al. [16] reported that RSD is useful for improving the visual outcome in symptomatic paraclinoid aneurysms: visual outcome was improved in 79 %, and unchanged in 21 %. In our experience, favorable outcome was reported in 73.9 %, poor outcome in 21.7 %, and death in 4.3 % (including poor-grade ruptured SAH patients). Every report showed acceptable clinical results in comparison with the natural course of giant ICA aneurysms.

Conclusions

In this article, we have presented our experience with direct clipping using retrograde suction decompression (RSD) through direct puncture of the common carotid artery for large/giant paraclinoid aneurysms. RSD provides adequate relaxation of the aneurysm enabling the surgeon to fully dissect the aneurysmal dome in order to adequately see the aneurysmal neck and to allow safe reconstruction of the parent artery.

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

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Bypass Surgeries in the Treatment of Cerebral Aneurysms

Takayuki Hara, Shintaro Arai, Yoshiaki Goto, Tsuguhito Takizawa, and Tatsuya Uchida

Abstract

Background

During surgery for cerebral aneurysm, revascularization techniques are occasionally needed to (1) treat an aneurysm (trapping or flow alteration); (2) preserve blood flow during temporary parent artery occlusion (insurance); and (3) repair accidentally injured vessels (troubleshooting). Herein we present our surgical case experiences.

Methods

Revascularization modalities were employed in 33 (7.6 %) of 452 cases of surgically treated aneurysms. The aneurysm locations and associated required bypass procedures were: (1) 7 middle cerebral artery (MCA) aneurysms with 7 superficial temporal artery (STA)-MCA bypass procedures; (2) 10 internal carotid artery (ICA) aneurysms with 9 high-flow and 1 STA-MCA procedures; (3) 10 vertebro-basilar artery aneurysms with 2 high-flow, 6 occipital artery (OA)-posterior ICA, and 1 STA-superior cerebellar artery (SCA) procedures; (4) 1 posterior cerebral artery (PCA) aneurysm with OA-PCA bypass; and (5) 5 anterior cerebral artery aneurysms with 4 A3-A3 and 1 A3-STA-A3 procedure. Curative bypasses for aneurysmal treatment, temporary bypasses, and troubleshooting procedures were performed in 25, 3, and 5 cases, respectively.

Results

Among the 26 aneurysms treated via curative bypass, 16 aneurysms that were trapped or clipped using revascularization techniques had better outcomes (no aneurysmal rupture and 1 perforator infarction), whereas among the 10 aneurysms that could not be trapped or clipped and were thereby treated via flow alteration (e.g., bypass plus proximal artery clipping), 2 developed symptomatic infarction and 2 exhibited aneurysmal rupture after partial thrombosis. Patients whose bypass procedures were used for temporary parent artery occlusion (insurance) or troubleshooting had no complications.

Conclusion

Complex aneurysm clipping or trapping using bypass techniques yielded good results. In particular, perforator vessel ischemia still requires resolution. Flow alteration techniques leading to aneurismal thrombosis carried the risks of ischemic and hemorrhagic complications when applied to intracranial aneurysms. Bypasses for temporary use or troubleshooting were quite effective.

Keywords Cerebral aneurysm • Bypass • Flow alteration • Clipping • Trapping

Introduction

When treating complex cerebral aneurysms, direct clipping is occasionally difficult because of an irregular shape, perforator involvement, or thrombus formation. Bypass techniques are among the treatment options for these aneurysms [7–9]. Bypasses have three purposes when used during surgery for aneurysm. The first is curative aneurysm treatment. With revascularization, some aneurysms (e.g., branch-involved type) can be cured by clipping or trapping. For non-clippable/trappable aneurysms, a flow control method (flow alteration) involving various bypass techniques can also be used as a curative treatment. The concept of flow alteration relies on the induction of intra-aneurysmal thrombus formation, which prevents aneurysm growth or rupture. A typical example is treatment of an internal carotid artery (ICA) cavernous giant aneurysm with an external carotid (EC)-ICA high-flow bypass plus ICA proximal ligation [2].

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T. Hara, MD, PhD (✉) • S. Arai, MD • Y. Goto, MD
T. Takizawa, MD • T. Uchida, MD
Department of Neurosurgery, Toranomon Hospital,
2-2-2 Toranomon, Minato-ku, Tokyo 105-8470, Japan
e-mail: takayuki_hara@syd.odn.ne.jp

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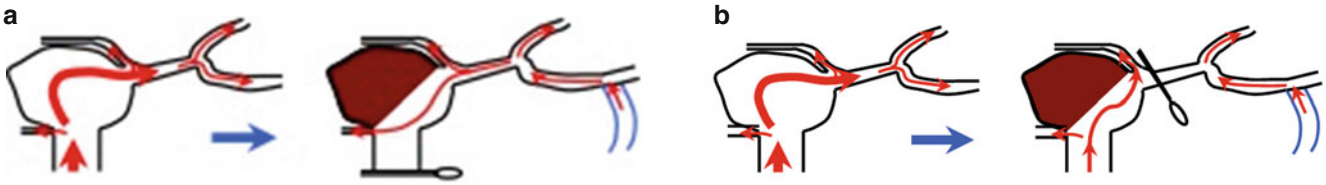


Fig. 1 Types of flow alteration. (**a**) Inflow control (bypass + proximal clip). (**b**) Outflow control (bypass + distal clip)

The details of flow alteration are presented in Fig. 1. The second purpose is to provide a temporary blood supply during direct clipping (prophylactic bypass), which is sometimes combined with a suction decompression method. The third purpose is the repair of an accidentally injured vessel (troubleshooting bypass). Herein we present the authors' experiences.

Methods

Between 2006 and 2013, 35 bypass procedures were used during surgical treatment of 452 aneurysms (7.4%). The locations of the aneurysms and the bypass methods used are listed in Table 1. Seven middle cerebral artery (MCA) aneurysms were treated via superficial temporal artery (STA)-MCA bypass. Furthermore, 10 ICA aneurysms were treated via 9 EC-MCA high-flow and 1 STA-MCA bypasses, 5 anterior cerebral artery (ACA) aneurysms were treated with 4 A3-A3 and 1 A3-STA-A3 bypasses, 10 vertebro-basilar (VA-BA) aneurysms were treated with 2 V3-P2 high-flow, 6 occipital artery (OA)-posterior inferior cerebellar artery (PICA), and 1 STA-superior cerebellar artery (SCA) bypass, and 1 PCA giant aneurysm was treated with an OA-posterior cerebral artery (PCA) bypass. In 26 cases, revascularization was used as a curative treatment (clipping/trapping/flow alteration); the bypass was used for prophylaxis in 4 cases and for troubleshooting in 5 cases.

Bypass for Curative Aneurysm Treatment

Among the 26 curatively treated cases (Nos. 1–26 in Table 1), 1 ACA aneurysm was clipped after an A3-A3 bypass, 15 aneurysms were trapped after various revascularization procedures, and ten cases were treated using flow alteration methods. Flow alteration included proximal inflow control (bypass + proximal parent artery occlusion) and distal outflow control (bypass + distal parent artery occlusion). In our series, proximal control was used in nine cases, and distal control was used in one case (Table 1).

Bypass for Temporary Use (Prophylactic Bypass) (No. 27–30 in Table 1)

Three MCA giant aneurysms were clipped after STA-MCA bypass. Before clipping, the aneurysms were collapsed using suction decompression (two cases) or thrombectomy (one case). The STA-MCA bypasses supplied cortical blood flow during these maneuvers and were no longer necessary after successful clipping. One large, ruptured BA aneurysm was also clipped after V3-P2 high-flow bypass because there was no collateral flow from the posterior communicating artery (P-com) to the upper BA.

Bypass for Troubleshooting (Nos. 31–35 in Table 1)

Three STA-MCA and two A3-A3 bypasses were used for troubleshooting. In cases of parent artery injury, direct suture repair is performed first, although this procedure is occasionally impossible because of atherosclerotic changes in the vessel walls or extensive vessel injury (dissection-like). Two STA-MCA bypasses were applied to MCA aneurysms with parent artery injuries (M2), and one bypass was applied to an MCA aneurysm with neck laceration. All of the A3-A3 bypasses were applied to the anterior communicating artery (A-com) aneurysms with A2 injuries.

Results

Bypass for Curative Aneurysm Treatment

In the 16 cases with aneurysms that were finally clipped or trapped, the patients were cured without aneurysm regrowth or rupture. Three ischemic complications occurred in this group: one from bypass occlusion for an ICA-dissecting aneurysm 1 day after surgery, and two from insufficient bypass flow. These two cases showed watershed infarction 1 day after surgery.

On the other hand, eight of ten aneurysms treated with flow alteration methods were found to have undergone

Table 1 Summary of cases

No.	Age	M/F	Location	Onset	Bypass	Purpose	Surgical complications	Radiological outcome (after surgery/follow- up)	Clinical outcome (after surgery/ follow up)	Follow up
1	58	M	A-com	Ischemia	A3-A3	Clipping	–	Cured/cured	GO/GO	24 months
2	54	F	MCA large	SAH	STA-MCA	Trapping	–	Cured/cured	MD/MD	3 months
3	48	F	VA large	Thrombosed	OA-PICA	Trapping	–	Cured/cured	GO/GO	12 months
4	51	F	PICA dissection	SAH	Transposition	Trapping	–	Cured/cured	SD/SD	3 months
5	81	F	PICA dissection	SAH	OA-PICA	Trapping	–	Cured/cured	SD/SD	3 months
6	48	M	VA dissection	SAH	OA-PICA	Trapping	–	Cured/cured	MD/MD	6 months
7	69	F	PCA giant	Asymptomatic	OA-PCA	Trapping	Infarction	Cured/cured	MD/MD	12 months
8	59	F	IC ant wall	SAH	High flow (EC-M2)	Trapping	Bypass occlusion → infarction (1POD)	Cured/cured	SD/SD	60 month
9	59	F	IC giant	Asymptomatic	STA-MCA	Trapping	Infarction (1POD)	Cured/cured	SD/SD	84 months
10	38	M	ACA bacterial	SAH	A3-STA-A3	Trapping	–	Cured/cured	MD/GO	6 months
11	37	F	IC ant wall	SAH	High flow (EC-M2)	Trapping	–	Cured/cured	MD/GO	60 month
12	47	M	ACA	SAH	A3-A3	Trapping	–	Cured/cured	GO/GO	6 months
13	47	M	VA (thrombosed/giant)	SAH	OA-PICA	Trapping	–	Cured/cured	SD/MD	3 months
14	65	M	VA (thrombosed/giant)	Mass sign	OA-PCA	Trapping	–	Cured/cured	GO/GO	3 months
15	66	F	IC giant	Diplopia	High flow (EC-M2)	Trapping	–	Cured/cured	GO/GO	12 months
16	53	M	MCA (thrombosed/giant)	Ischemia	STA-MCA	Trapping	–	Cured/cured	MD/MD	6 months
17	89	F	IC giant	Asymptomatic	EC-M2	Flow alteration (proximal occlusion)	Bled	Not cured Partially thrombosed/ ruptured	GO/SD	4 months
18	69	F	IC C3	Diplopia	High flow (EC-M2)	flow alteration (proximal occlusion)	–	Cured Thrombosed/ thrombosed	GO/GO	12 months
19	78	F	IC large C2	SAH	High flow (EC-M2)	Flow alteration (proximal occlusion)	–	Cured Thrombosed/ thrombosed	SD/SD	18 months
20	74	F	IC large C2	SAH	High flow (EC-M2)	Flow alteration (proximal occlusion)	–	Cured Thrombosed/ thrombosed	MD/GO	6 months
21	49	M	BA AN	SAH	High flow (V3-P2)	Flow alteration (proximal occlusion)	Re-bled	Not cured Partially thrombosed/ reruptured	SD/D	3 days

(continued)

Table 1 (continued)

No.	Age	M/F	Location	Onset	Bypass	Purpose	Surgical complications	Radiological outcome (after surgery/follow- up)	Clinical outcome (after surgery/ follow up)	Follow up
22	56	F	IC large C2	SAH	High flow (EC-M2)	Flow alteration (proximal occlusion)	–	Cured Thrombosed/ thrombosed	SD/SD	3 months
23	63	F	IC giant	Diplopia	High flow (EC-M2)	flow alteration (proximal occlusion)	–	Cured Thrombosed/ thrombosed	MD/GO	12 months
24	79	M	ACA (thrombosed/large)	Asymptomatic	A3-A3	Flow alteration (distal occlusion)	Infarction (1POD)	Cured Thrombosed/ thrombosed	MD/GO	12 months
25	48	F	BA AN (large)	Asymptomatic	STA-SCA	Flow alteration (distal occlusion)	–	Cured (coiled)	GO/GO	18 months
26	53	M	BA thrombosed	Mass sign	High flow (V3-P2)	Flow alteration (proximal occlusion)	–	Cured Thrombosed/ thrombosed	SD/SD	12 months
27	64	M	MCA giant	Thrombosed	STA-MCA	Temporary use	–	Cured/cured	GO/GO	12 months
28	64	F	MCA giant	Thrombosed	STA-MCA	Temporary use	–	Cured/cured	GO/GO	18 months
29	79	F	BA AN	SAH	High flow (V3-P2)	Temporary use	–	Cured Thrombosed/ thrombosed	SD/SD	3 months
30	73	M	MCA large	Asymptomatic	STA-MCA	Temporary use	–	Cured/cured	GO/GO	6 months
31	65	F	MCA	SAH	STA-MCA	Troubleshoot	–	Cured/cured	GO/GO	18 months
32	54	F	A-com	SAH	A3-A3	Troubleshoot	–	Cured/cured	MD/GO	3 months
33	67	F	MCA large	Asymptomatic	STA-MCA	Troubleshoot	–	Cured/cured	GO/GO	12 months
34	69	F	MCA large	Asymptomatic	STA-MCA	Troubleshoot	–	Cured/cured	GO/GO	12 months
35	60	F	ACA	SAH	A3-A3	Troubleshoot	–	Cured/cured	GO/GO	6 months

Clinical outcome (just after surgery and at follow-up) was assessed according to the Glasgow Outcome Scale (GOS)

thrombosis and shrinkage, although two ruptured after intra-aneurysmal thrombus formation. One case (unruptured ICA giant aneurysm: No. 17 in Table 1) re-bled 4 months after surgery, whereas the other one (ruptured BA trunk aneurysm: No. 21 in Table 1) did so 3 days after surgery.

Two illustrative cases that were treated with flow alteration techniques are presented below.

Case 1 (No. 19)

A 78-year-old female patient was admitted with subarachnoid hemorrhage (Hunt and Kosnik grade 4). Digital subtraction angiography (DSA) demonstrated a large left ICA aneurysm (22 mm) involving the anterior choroidal artery (Acho). Because direct clipping was considered difficult due to perforator vessel involvement and sclerotic changes in the parent artery (ICA), an E2-M2 high-flow bypass plus cervical ICA ligation (proximal flow alteration) was applied. After surgery, the aneurysm had completely thrombosed and the patient was discharged with a modified Rankin scale (mRS) score of 1. Her aneurysm did not recur or re-rupture during the 18-month follow-up period (Fig. 2).

Case 2 (No. 17)

An 89-year-old woman was incidentally diagnosed with a large left ICA aneurysm. After 15 months, the aneurysm increased in size from 15 to 22 mm, indicating rapid growth. This aneurysm was similar to that in Case 1 in terms of Acho involvement and atherosclerotic ICA changes, and therefore a flow alteration was the selected treatment modality. The same type of surgery used in Case 1 (EC-M2 high flow bypass + proximal ICA ligation) was applied to this case. The aneurysm was almost completely thrombosed, and the patient discharged without neurological deficits (GOS: GO). Four months after discharge, however, the patient returned to our institute with a subarachnoid hemorrhage (initial rupture). DSA upon admission revealed that although the aneurysm remained mostly thrombosed, a slight inflow from the bypass artery was present (partial recanalization). The patient, whose medical condition was poor (GOS: SD), refused future treatment and was transferred to an affiliated hospital (Fig. 3).

Bypasses for Temporary Use and Troubleshooting

Patients who underwent bypass procedures for temporary use and troubleshooting did not experience ischemic complications and had good outcomes.

Discussion

When treating complex, large, giant, or thrombosed aneurysms, direct clipping is occasionally difficult to achieve and requires technical assistance. Bypass is among these assistant modalities, particularly when trapping is applied. Trapping via bypass can cure an aneurysm while maintaining blood flow distal to the aneurysm, but it is associated with some difficulties. The existence of perforating arteries near the aneurysm and difficulties associated with simultaneous proximal and distal parent artery occlusion (e.g., ICA cavernous aneurysm) enable trapping. Proximal or distal parent artery occlusion with bypass provides an alternative to trapping [8]. This method is also called flow alteration, and has been used to treat ICA cavernous giant aneurysms. Symptomatic ICA cavernous aneurysms can be cured via EC-M2 high-flow bypass with cervical ICA ligation [5]. This procedure reduces inflow to the aneurysm and thus induces intra-aneurysmal thrombosis. This flow alteration technique has also been applied to intracranial aneurysms with reported efficacy [1, 8]; however, this treatment has some limitations. Firstly, we cannot always maintain blood flow in the surrounding perforator vessels if they become a flow outlet after bypass plus parent artery occlusion (stump occlusion phenomenon). One suspected mechanism underlying this phenomenon is thrombus formation around the orifices of perforator vessels; accordingly, aggressive antiplatelet therapy may be helpful. Secondly, the final treatment outcome is not predictable after applying this flow alteration technique. In our series, the majority of aneurysms were cured using this technique (thrombosis and shrinkage), but some aneurysms ruptured even if they were treated using the same strategy. The presented cases (Figs. 1 and 2) had similar aneurysms and were treated similarly (EC-M2 bypass + ICA ligation), but the outcomes were different. In accordance with Raymond, who reported that thrombus formation and remaining inflow contribute to aneurysm growth and rupture [6], aneurysm thrombosis does not necessarily equal a cure. In fact, aneurysm growth after flow alteration has been reported not only in cavernous ICA giant aneurysms, but also in intracranial aneurysms [4]. Care should be taken after this treatment, and close follow-up is necessary.

Bypasses were used quite successfully for prophylaxis or troubleshooting. Although the necessity of temporary bypass is controversial, we cannot estimate the clamping time during suction decompression or thrombectomy [3]; prophylactic bypass is definitely necessary if a preoperative balloon test is positive for occlusion. Troubleshooting is required when the parent artery or aneurysmal neck is accidentally injured during surgery. Direct suture repair and clip occlusion are among the available options, but these are not always

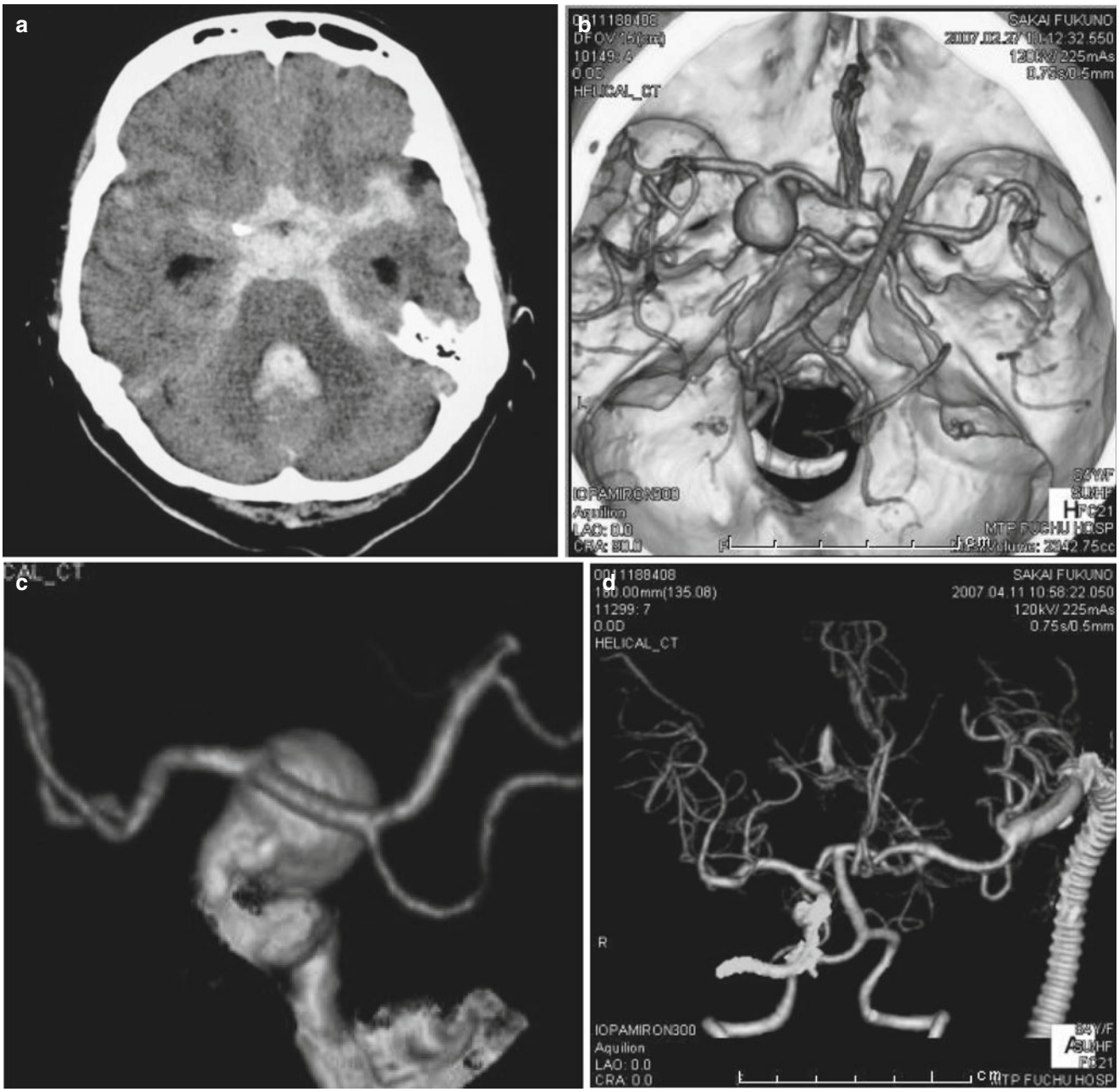


Fig. 2 (**a**) Computed tomography (*CT*) image upon admission indicating thick subarachnoid hemorrhage. (**b**, **c**) CT angiography (*CTA*) upon admission shows a large aneurysm in the left internal carotid artery (*ICA*) with anterior choroidal artery involvement and atherosclerotic left ICA changes. (**d**, **e**) Postoperative CTA shows the completely thrombosed aneurysm after external carotid-M2 high-flow bypass with cervical ICA ligation

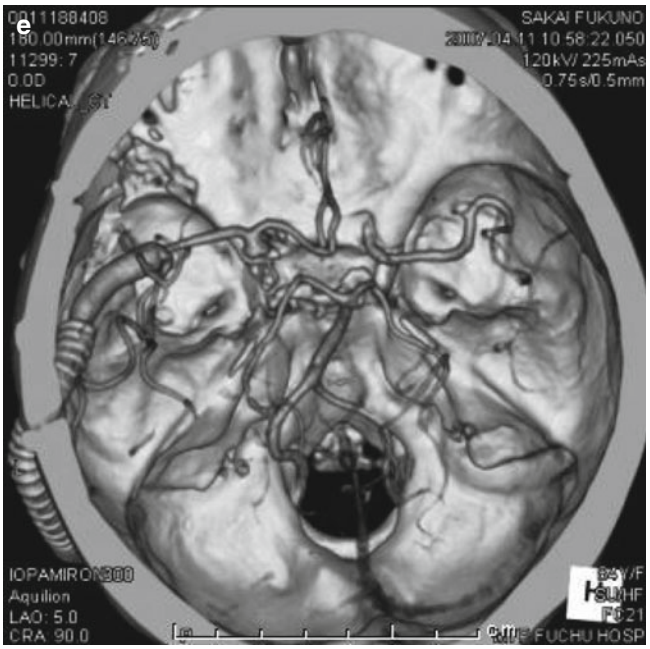


Fig. 2 (continued)

possible because of vessel wall fragility or the risk of vessel occlusion. If achieved within a limited time, repair with bypass is a safe and indisputable method for restoring blood flow to the parent vessels. Surgeons should be familiar with various bypass techniques and implement them as needed soon after vessel injuries.

Conclusions

Complex aneurysms that are clipped or trapped can be treated curatively with various bypass techniques. Flow alteration techniques carry the risk of regrowth/re-rupture even if the aneurysm had initially thrombosed (partial thrombosis is not safe); careful follow-up is therefore necessary. Additionally, bypass techniques are quite useful for providing a temporary blood supply and troubleshooting.

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

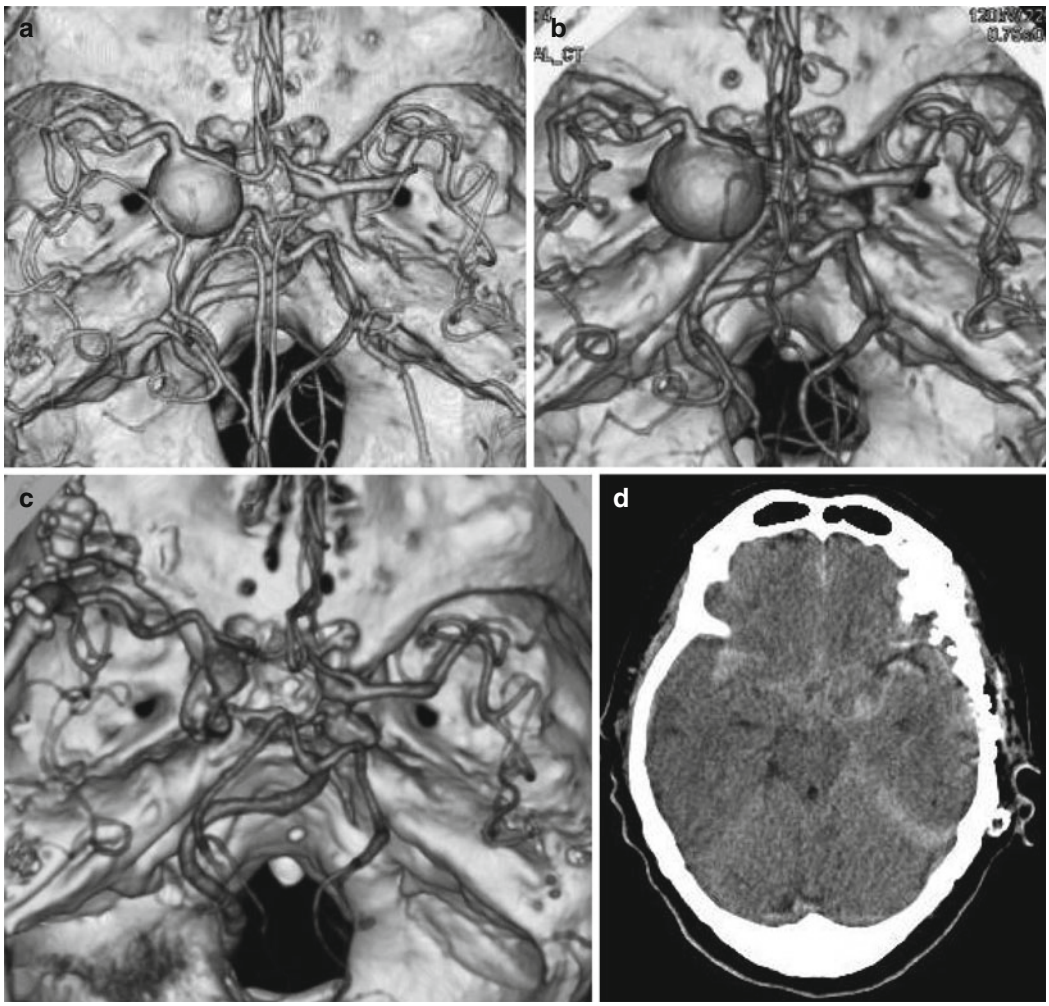
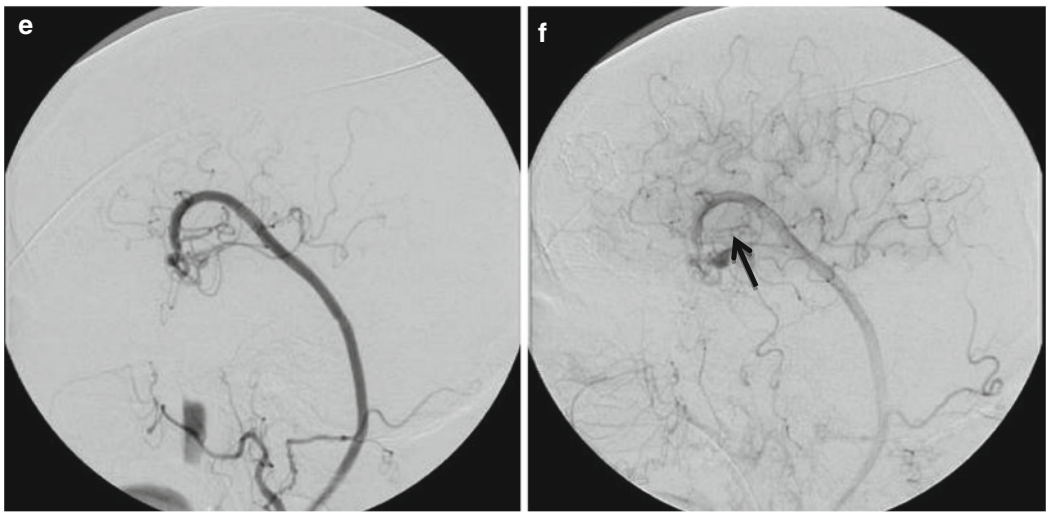


Fig. 3 (**a**, **b**) Computed tomography (*CT*) angiography (*CTA*) shows that the left internal carotid artery aneurysm increased in size (15 mm → 22 mm) over an 18-month period. (**c**) CTA after surgery shows that the aneurysm was mostly thrombosed following external carotid-internal carotid bypass + proximal occlusion (flow alteration). (**d**) CT upon subarachnoid hemorrhage (*SAH*) onset shows bleeding from the aneurysm 4 months after surgery. (**e**, **f**) Digital subtraction angiography upon SAH onset shows a small inflow from the high-flow bypass even though the aneurysm remained thrombosed (*arrow*)

Fig. 3 (continued)



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Surgical Treatment of Complex Cerebral Aneurysms Using Interposition Short Vein Graft

Yasuhiko Kaku, Hiroaki Takei, Masafumi Miyai, Kentarou Yamashita, and Jouji Kokuzawa

Abstract

Background and Aims

Cerebral revascularization strategies may become necessary in select patients who present with challenging cerebral aneurysms. In this study, we present the techniques of a moderate-flow extra-intracranial bypass using a short interposition vein graft and concurrent aneurysm management.

Methods

The short interposition vein graft was used for the reconstruction of complex cerebral aneurysms in nine patients. In eight of them , the superficial temporal artery (STA) main trunk was used as a donor site for the anastomosis of a short interposition vein graft, and an extracranial vertebral artery (VA) was used in one case. The vein grafts were implanted into the M2 of the middle cerebral artery (MCA) for the adjunctive treatment of internal carotid artery (ICA) aneurysms in three patients, into the A3 of the anterior cerebral artery (ACA) in one patient, into the P2 of the posterior cerebral artery (PCA) for the adjunctive treatment of complex PCA aneurysms in three patients, into the P3 of the PCA for the adjunctive treatment of a basilar artery (BA) trunk giant aneurysm in 1 patient, and into the postero-inferior cerebellar artery (PICA) for the adjunctive treatment of the VA dissecting aneurysm in one patient.

Results

All of the bypasses were patent. Intraoperative flow measurements confirmed a moderate flow-carrying capacity of the short interposition short vein graft (30–70 ml; mean: 43 ml/min).

Conclusion

The STA main trunk to proximal MCA/PCA bypass and the extracranial VA to PICA bypass using short interposition vein grafts can provide sufficient blood flow and may be a reasonable alternative to the conventional EC-IC bypass/high-flow bypass.

Keywords Complex cerebral aneurysm • EC-IC bypass • Short vein graft

Introduction

Cerebral revascularization strategies become necessary in selected patients harboring challenging cerebral aneurysms [6, 8]. Bypass techniques should be considered when there is a need for trapping or prolonged temporary occlusion. A superficial temporal artery (STA) is the mainstay of donor vessels for extracranial-intracranial bypass (EC-IC bypass) in cerebral revascularization. However, the typically used STA anterior or posterior branch does not always have an adequate flow-carrying capacity. Conversely, a typical high-flow bypass between the cervical carotid artery and the intracranial vessels also has several disadvantages, including problems resulting from long grafts, hyperperfusion, and the need for additional neck incisions. In this article, we present the techniques of a moderate-flow EC-IC bypass using a short interposition vein graft and concurrent aneurysm management in detail.

Materials and Methods

We report on nine patients on whom a short interposition vein graft was used for bypass construction. The STA main trunk was used as a donor in eight of the nine cases, while the extracranial VA was used in one. The vein grafts were implanted into the M2 of the middle cerebral artery (MCA) for adjunctive treatment of internal carotid artery (ICA) aneurysms in three patients, into the A3 segment of the anterior cerebral artery (ACA) in another one, into the P2 segment

Y. Kaku, MD (✉) • H. Takei, MD • M. Miyai, MD
K. Yamashita, MD • J. Kokuzawa, MD
Department of Neurosurgery, Asahi University Murakami Memorial Hospital, Hashimoto-cho 3-23, Gifu 500-8523, Japan
e-mail: kaku@murakami.asahi-u.ac.jp

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of the posterior cerebral artery (PCA) for the adjunctive treatment of complex PCA aneurysms in three patients, into the P3 segment of the PCA for adjunctive treatment of a BA trunk giant aneurysm in one patient, and into the posterior inferior cerebellar artery (PICA) for the adjunctive treatment of the vertebral artery (VA) dissecting aneurysm in another one. The patients' characteristics are presented in Table 1.

Operative Technique

Saphenous Vein Harvest

The greater saphenous vein begins anteromedial to the tibia at the ankle and then gradually becomes more posterior at the knee. In most adults, the greater saphenous vein will be visible in the ankle area. The vein exposure is begun at the ankle area and traced up at least 10–15 cm superiorly (Fig. 1a). The prominent branches are ligated, while tiny branches are coagulated and divided. The vein is left in situ until extraction (Fig. 1b), when the distal end of the graft is ligated in order to avoid misdirection, and the vein is then sectioned and removed. After extraction, it is flushed through with heparinized saline and distended at moderate pressure (Fig. 1c). The vein should be carefully transferred without reversal.

Bypass Technique

The surgical technique used was as follows: An STA main trunk was dissected over a length of 2 cm, and a frontotemporal or suboccipital craniotomy was made to approach the recipient artery and lesion. The recipient artery (M2 of the MCA or P2/3 of the PCA) was exposed through a transsylvian approach, and the PICA was exposed through a suboccipital trans-tonsillar approach. End-to-end anastomosis between the STA main trunk and the vein graft, or end-to-side anastomosis between the extracranial VA and the vein graft, was created using interrupted 9-0 nylon sutures. A discrepancy in the size between the vein graft (generally 2–2.5 mm in diameter) and the STA main trunk (1.5–2 mm in diameter) can be compensated for by using beveled end-to-end anastomosis with a fishmouthed cut of the STA main trunk. The cut flow of the graft was then measured. End-to-side anastomosis between the short interposition vein graft (ca. 10 cm to the MCA and 15 cm to the PCA) and the intracranial recipient artery was then performed using interrupted sutures or running sutures with 9-0 nylon. After confirming the patency of the bypass, an approach to the lesion was undertaken.

Results

In all cases, successful bypass surgery using short interposition vein grafts and concurrent aneurysm exclusion was achieved. In eight of the nine patients, the perioperative course was uneventful. One patient with a ruptured right PCA (P1) aneurysm died due to the initial damage from a severe subarachnoid hemorrhage. All of the bypasses were patent. The intraoperative flow measurements confirmed the moderate flow-carrying capacity of the STA main trunk-interposition short vein grafts (20–100 ml; mean: 43 ml/min).

Illustrative Case

Case 4

An 84-year-old female patient had rapidly progressing cognitive dysfunction over the previous month. MRI and 3-D CTA showed a left distal ACA giant partially thrombosed

Table 1 Patients' characteristics

Case	Age	Gender	Diagnosis	Donor	Recipient
1	44	F	R IC blood blister aneurysm	STA main	MCA (M2)
2	53	F	L IC blood blister aneurysm	STA main	MCA (M2)
3	68	F	R IC (C3) aneurysm	STA main	MCA (M2)
4	84	F	L distal ACA giant aneurysm	STA main	ACA (A3)
5	65	M	BA trunk giant aneurysm	STA main	PCA (P3)
6	46	M	R PCA (P1) aneurysm	STA main	PCA (P2)
7	30	M	L PCA (P1/2) large aneurysm	STA main	PCA (P2)
8	77	M	L PCA (P1/2) giant aneurysm	STA main	PCA (P2)
9	47	F	Dissecting left VA aneurysm	VA (V3)	PICA

IC internal carotid artery, *ACA* anterior cerebral artery, *MCA* middle cerebral artery, *PCA* posterior cerebral artery, *VA* vertebral artery, *STA main* main trunk of superficial temporal artery, *PICA* posterior inferior cerebellar artery

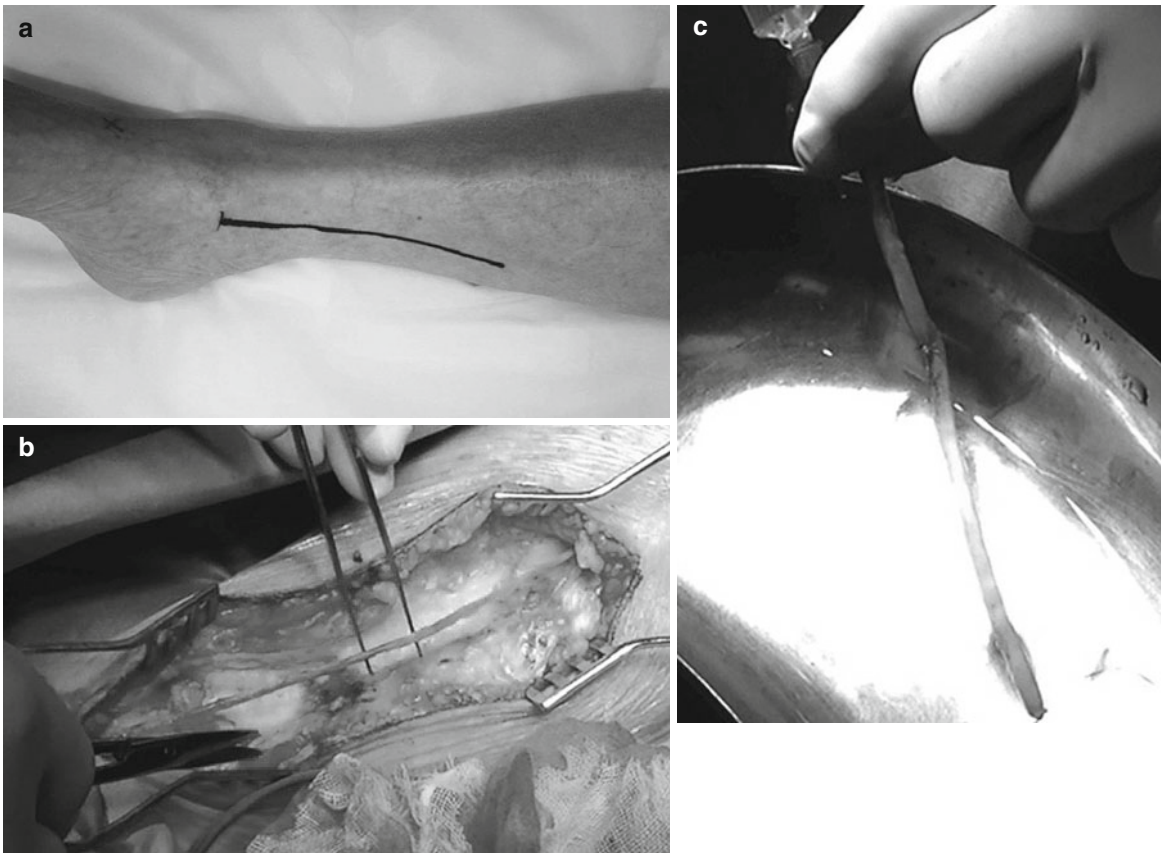

Fig. 1 (**a**) The vein exposure is initiated at the ankle area and traced up at least 10–15 cm superiorly. (**b**) Prominent branches are ligated, while tiny branches are coagulated and divided. The vein is left in situ until extraction. (**c**) After extraction, the vein graft is flushed through with heparinized saline and distended at moderate pressure

aneurysm (Fig. 2a). As a prolonged temporary occlusion of the ACA was suspected during the management of such a complex aneurysm, revascularization techniques using an interposition short vein graft between the STA main trunk and the A3 segment of the ACA became necessary to prevent cerebral ischemia (Fig. 2b, c). The aneurysm was finally eliminated by two clips with the reconstruction of the ACA (Fig. 2d). The patient tolerated the operation well without any neurological deficits, and post-operative 3-D CTA showed good patency of the left ACA with the elimination of the aneurysm (Fig. 2e).

Case 9

A 47-year-old female patient presented with a WFNS grade 2 subarachnoid hemorrhage (SAH). 3-D CTA and 3-D DSA showed that a right VA dissecting aneurysm with aplastic contralateral VA and bilateral P1 were hypoplastic (Fig. 3a). There must be poor collateral vasculization when simple parent artery occlusion undergo. The V3 segment of the right VA to the right PICA bypass using an interposition short vein graft was undertaken (Fig. 3b), and the aneurysm was trapped just proximal to the aneurysmal dilatation and distal to the aneurysmal dilatation just proximal to the PICA. The patient tolerated the operation well. Post-operative 3-D CTA demonstrated a good patency of the short vein graft with the complete elimination of the aneurysm (Fig. 3c).

Discussion

Cerebral revascularization strategies may become necessary in select patients harboring aneurysms that are challenging to treat due to size, shape, location, aneurysm type (e.g., dissecting aneurysms), vessels arising from the dome, or poor collateral vascularization when the parent artery or branch occlusion is required. Cerebral revascularization techniques are used to prevent cerebral ischemia and subsequent clinical sequelae.

The STA is the mainstay of donor vessels for EC-IC bypass in cerebral revascularization. This surgical technique has remained an important tool in the neurosurgeon's armamentarium for the management of complex cerebral aneurysms. Recently, the use of less invasive STA-MCA bypass techniques for the surgical treatment of cerebrovascular

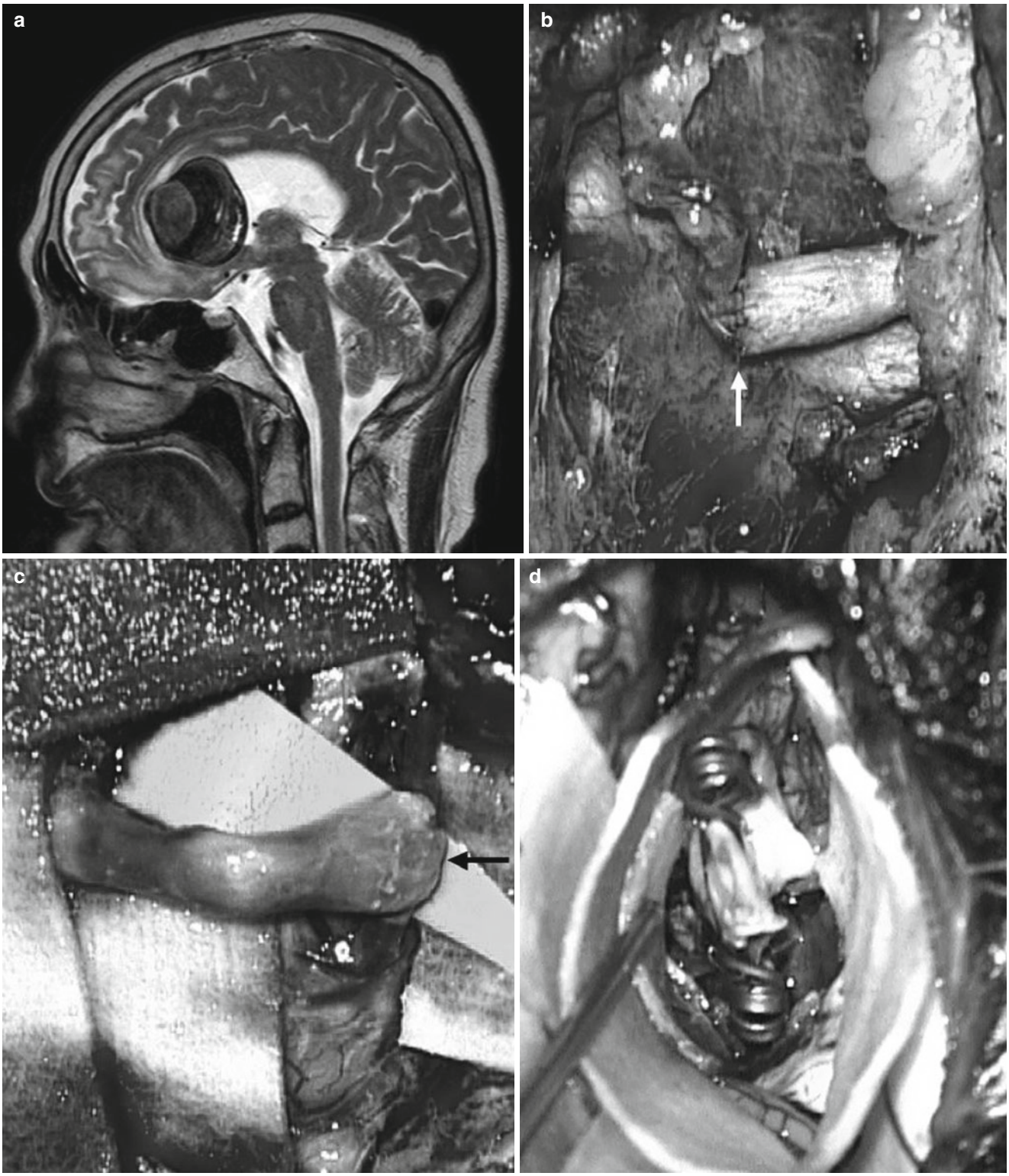

Fig. 2 (**a**) MRI demonstrating a left distal ACA giant, partially thrombosed aneurysm. (**b**) An intra-operative photograph demonstrating the anastomosis between the STA main trunk and the interposition vein graft (*arrow*). (**c**) An intra-operative photograph demonstrating the anastomosis between the interposition vein graft and the A3 segment of the ACA (*arrow*). (**d**) The aneurysm was eliminated by two clips with the reconstruction of the ACA. (**e**) Post-operative 3-D CTA demonstrating a good patency of the left ACA with the elimination of the aneurysm

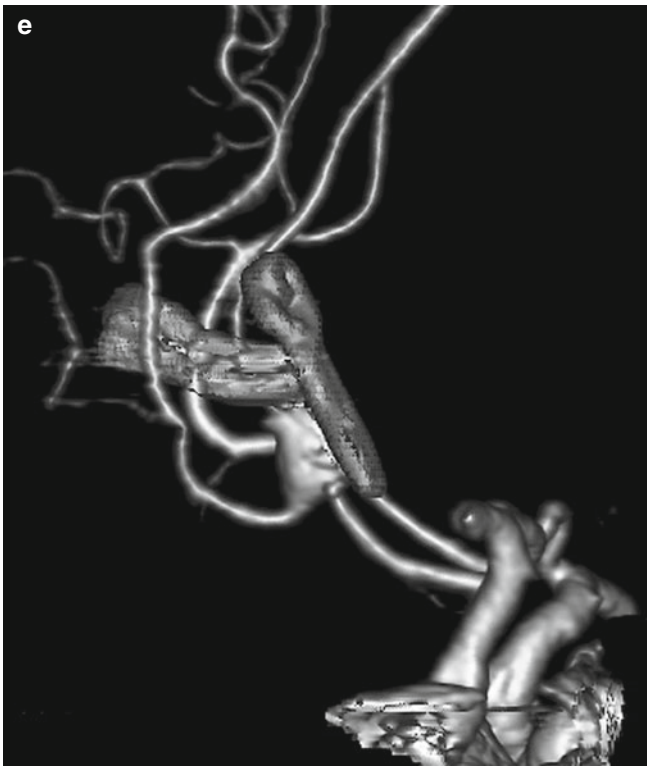

Fig. 2 (continued)

occlusive disease has been gaining favor [3]. However, the typically used STA anterior or posterior branch is not always adequate in its flow-carrying capacity at the time of aneurysm trapping. Conversely, the typical high-flow bypass between the cervical carotid artery and the intracranial vessel also has several disadvantages, including problems resulting from long grafts, hyperperfusion, and the need for additional neck incisions.

The STA main trunk is a valuable donor option for cerebral revascularization [1, 2, 4, 5, 7, 9]; it has a larger diameter than the distal branch, so the STA trunk is expected to have a higher flow capacity than its branches. The STA main trunk provides a moderate and adequate flow. The intraoperative cut flow measurements demonstrated a rate of 30–70 ml/min. The use of the STA trunk allows for the use of short interposition grafts (less than 15 cm in length) rather than vein or arterial grafts from the cervical region. It is well accepted that shorter interposition grafts are desirable for graft longevity and patency. According to Poiseuille's law [$Q = \pi r^4 P/8\eta L$ (r = internal radius, P = pressure at the vessel, η = blood viscosity, L = total length of the vessel)], the radius of the vessel and the length of the graft have an impact on the blood flow. Because the flow is related to the radius raised to the fourth power, a minimal change in the radius of a vessel will have an exponential impact on the rate of blood flow. Additionally, the length of the vessel will also impact the blood flow inversely, i.e., a larger graft diameter and a shorter graft length provide more blood flow. In addition, the procedure can be undertaken in a single operative field without creating an additional neck incision. A proximal STA to proximal PCA/M2 bypass using short interposition vein grafts can provide sufficient blood flow and may be a reasonable alternative to ECA to PCA/M2 bypass using long vein grafts or STA distal branch to PCA/M2 bypass.

Cerebral revascularization in the posterior circulation is well recognized to be a key component in the treatment of complex and giant intracranial aneurysms [4]. Not only giant aneurysms, but often dissecting aneurysms need to be carefully treated in a deconstructive manner (proximal occlusion or trapping), necessitating revascularization in many cases. In cases of posterior circulation aneurysms, if the PCA is chosen for the bypass, the P2 segment of the posterior cerebral artery is selected. The P2 segment is exposed lateral to the midbrain. We used a trans-sylvian trans-choroidal fissure approach via the temporal horn of the lateral ventricle for P2 exposure, because this approach provides an adequate angle of the operative corridor without any excessive retraction of the brain. In some patients, the P2 may be atherosclerotic. In such a case, a non-sclerotic segment should instead be selected for bypass.

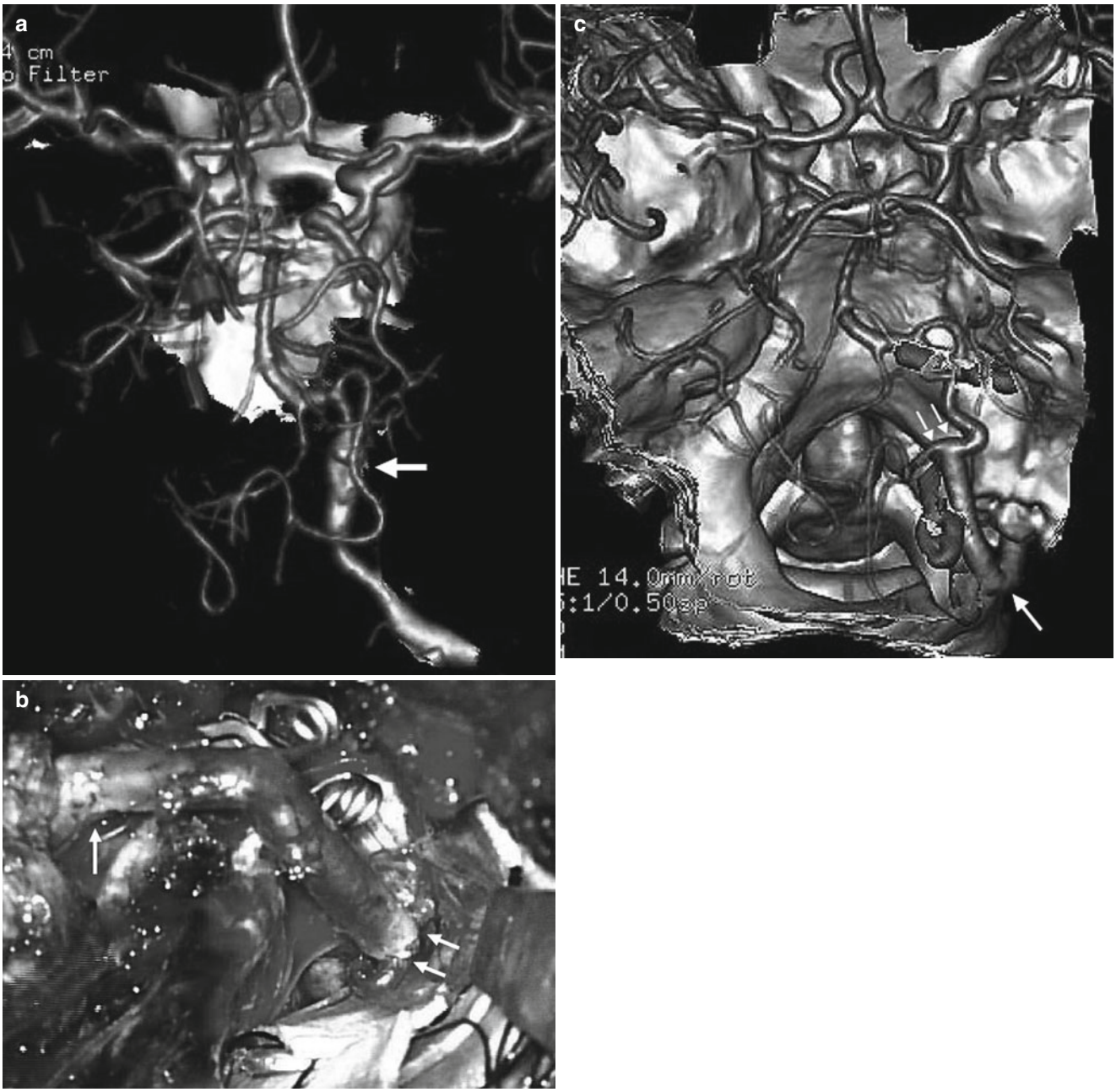

Fig. 3 (**a**) 3D-CTA showing a right VA dissecting aneurysm (*arrow*) with aplastic contralateral VA and bilateral P1 were hypoplastic. (**b**) An intra-operative photograph demonstrating the extracranial VA (*arrow*) to the PICA (*double arrow*) bypass using an interposition short vein graft. (**c**) Post-operative 3-D CTA demonstrated good patency of the graft. The *arrow* indicates the anastomosis between the extracranial VA and the vein graft, and the *double arrow* indicates the anastomosis between the vein graft and the PICA

Conclusions

The use of a short interposition vein graft provides a moderate and adequate flow. The intraoperative cut flow measurements were demonstrated to be 30–70 ml/min, which can provide sufficient blood flow. It is well-accepted that a shorter interposition graft is desirable for both graft longevity and patency. In addition, these surgical procedures could be successfully performed in a single operative field without any additional neck incision. A short interposition vein graft is adequate to enhance the tolerance of prolonged temporary arterial occlusion during clipping of the complex aneurysms or to achieve proximal occlusion or trapping.

Conflict of Interest The authors declare that they have no conflict of interest.

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Partial Trapping Strategies for Managing Complex Intracranial Aneurysms

Giuseppe Esposito, Jorn Fierstra, and Luca Regli

Abstract In this chapter we discuss the rationale of partial trapping strategies and associated flow-replacement bypass surgery for managing complex intracranial aneurysms (IAs).

Keywords Intracranial • Complex aneurysm • Partial trapping • Bypass • Revascularization

A complex intracranial aneurysm (IA) is defined as an aneurysm >2.5 cm or an aneurysm of any size with one of the following features: challenging anatomical accessibility, complex angioanatomy (e.g., non-saccular morphology of the lesion, presence of efferent arteries or small perforating branches arising from the aneurysm), uncommon etiology (i.e., dissecting, infectious, etc.), previous (endo)vascular treatment, as well as factors such as intraluminal thrombosis, atherosclerotic plaques or calcifications of the aneurysm wall and/or neck [1–3].

Surgery still has a predominant role in the treatment of such complex lesions. The treatment goal is both aneurysm exclusion and maintenance of blood flow to the vascular territories [2, 4]. Reconstruction of complex IAs with clips is often possible in giant partially thrombosed aneurysms, for example after thrombectomy [4]. Whenever clip-reconstruction is not feasible, trapping strategies represent invaluable treatment options [2, 4].

Among the various trapping strategies, a first distinction has to be made between *complete* and *partial* trapping. Complete trapping allows direct, complete, and immediate exclusion of the aneurysm from the circulation. We propose further subdividing *complete* trapping strategies into "classic" and "variant" as follows: (a) *complete trapping* "*classic,*" which consists of complete exclusion of the aneurysm by permanent occlusion of all the afferent and efferent arteries, and (b) *complete trapping* "*variant*," which consists of complete exclusion of the aneurysm by means of permanent occlusion of the afferent artery and of one or more – *but not all* – of the efferent arteries [4].

Partial trapping strategies, as opposed to complete trapping strategies, do not completely exclude the aneurysm from the circulation. Their aim is to induce aneurysmal thrombosis by hemodynamic alterations, namely by changing (usually reducing) the flow and by inducing flow-stagnation, thereby decreasing the hemodynamic stress within the aneurysm. Partial trapping strategies can be further subdivided into "*proximal*" *or* "*inflow occlusion*" and "*distal*" *or* "*outflow occlusion*," indicating that the occlusion is done either upstream (proximal) or downstream (distal) to the aneurysm. Therefore the aneurysm continues to be in contact with the blood circulation, filling either through the inflow artery in case of outflow occlusion, or through the outflow artery in case of inflow occlusion.

Among trapping strategies, complete trapping is always favored, since it has the advantage of immediate aneurysm exclusion and it should always be considered as the best treatment option. The choice between "complete" or "partial" trapping depends, however, on the aneurysmal and peri-aneurysmal anatomy [3–5], but there are situations in which complete trapping can be precarious, such as when important perforating arteries arise from the aneurysm sac and contraindicate the use of total trapping procedures, or when the manipulation of the aneurysm sac for careful inspection of all the branches or adjacent neural structures is considered inadvisable and too risky. Here, partial-trapping strategies may provide a sensible alternative [4–7].

G. Esposito, MD, PhD (✉) • J. Fierstra, MD, PhD • L. Regli, MD
Department of Neurosurgery, University Hospital Zurich,
University of Zurich, Frauenklinikstrasse 10,
Zurich CH-8091, Switzerland
e-mail: giuseppe.esposito@usz.ch; jorn.fierstra@usz.ch;
luca.regli@usz.ch

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Complete and partial trapping strategies are in general combined with a flow "replacement" bypass, to permanently supply blood flow to the downstream vascular territories, i.e., the territory supplied by the occluded vessel(s) [2, 4, 8].

Partial Trapping Strategies

The rationale behind partial trapping strategies is the change of the flow within the aneurysmal lesion, inducing a reduction of blood flow (stagnation) and decrease in hemodynamic stress. Such changes may favor induction of aneurysmal thrombosis and reduction of aneurysmal rupture risk [4, 6, 8].

With proximal inflow occlusion, the anterograde inflow to the aneurysm is permanently blocked by application of a microsurgical clip on the afferent (parent) artery. A distally placed bypass will supply both the downstream arterial territory and provide retrograde blood flow into the aneurysm for aneurysmal and perianeurysmal perforators if present [5–7].

Distal outflow occlusion consists of a definitive clip application on the efferent artery/arteries distally to the aneurysm, in order to block the outflow. In these situations, the distally placed bypass supplies the downstream arterial territory only and does not provide flow into the aneurysm. Aneurysmal and perianeurysmal perforators, if present, are perfused anterogradely by the parent artery.

Partial outflow occlusion has been mainly reported for the treatment of complex middle cerebral artery (MCA) and posterior inferior cerebellar artery (PICA) aneurysms [4–11]. The reason for this is that complex aneurysms of both the bifurcation and the M1 segment of the MCA and the proximal segment of the PICA frequently involve important perforators that cannot be sacrificed without major neurological deficits.

With distal outflow occlusion, concerns remain that by blocking the outflow, the risk of rupture might increase due to elevation of intra-aneurysmal pressure. This hypothesis, however, has not yet been proven [4, 7]; rather, hemodynamic changes due to partial trapping lead to intra-aneurysmal thrombosis. Herein lies a potential limitation of the strategy; since there is no control over the extent, speed, and rate of aneurysm thrombosis, aneurysm rupture, or inadequate perfusion of vital perforators might nevertheless occur, due to either partial thrombosis only or, on the contrary, due to complete and too-rapid thrombosis.

The question of whether partial occlusion changes the natural history of the aneurysm by reducing the risk of future rupture without increasing the risk of ischemia can only be answered by monitoring over time. Recent reports, do not assert a higher rupture rate even in the presence of partial thrombosis [4, 6–8, 11]. In the largest "outflow occlusion" clinical series available, Nussbaum et al. [8] reported a good long-term outcome in 16 of 18 patients (mean follow-up period: 6.5 years).

Complementary Flow Replacement Strategies

When applying trapping strategies, flow replacement bypasses play a main role in permanently supplying blood flow to downstream vascular territories [2, 4, 7–9]. For this, a bypass strategy can be selected from a wide array of constructs and techniques available: extra-to-intracranial (EC-IC) vs. intra-to-intracranial (IC-IC), occlusive vs. non-occlusive, high vs. low capacity, single vs. double, end-to-side vs. side-to-side vs. end-to-end microanastomosis. The choice of the ideal bypass depends mainly on the anticipated flow demand – namely, the amount of flow needed. Quantitative volumetric measurements should be performed intra-operatively.

The concept of flow demand differs according to the location of the aneurysms. For proximally located aneurysms (i.e., ICA aneurysms, excluding ICA-termination), the flow demand depends on the presence of collateral compensatory flow. Namely, in complex ICA aneurysms with patent ACom arteries, the flow demand (or flow deficit) is the subtraction of the M1 flow at baseline and after clipping of the ICA. The goal of a bypass is then not necessarily to replace the entire ICA flow, but to replace the flow deficit after ICA occlusion, given that collateral flow will compensate for the remainder. For distally located aneurysms (i.e., ICA-termination, MCA, PICA), the flow demand corresponds entirely to the flow provided by the permanently occluded vessel for final aneurysmal treatment.

Other factors playing a role in the selection of the best revascularization procedure are the availability and morphology of donor and recipient vessels [1–4, 7]. Sometimes even direct vessel reconstruction/reimplantation (by the use of side-to-side, end-to-side, or end-to-end microanastomosis) is a valid option, depending on aneurysmal and peri-aneurysmal angioanatomy [4].

Intraoperative Flow Assessment

In the intraoperative setting, prompt flow changes after partial trapping can be visualized with indocyanine-green video angiography (ICG-VA) [2]. With this technique, one can get direct visual feedback over flow-changes in the aneurysm, the patency of perianeurysmal perforators, and bypass patency.

We also consider quantitatively measuring the flow (ml/min) (Transonic Systems Inc., Ithaca, NY, USA) to be mandatory in the afferent and efferent arteries before and after trapping, as well as flow through the bypass, in order to be able to (1) calculate the flow demand, and (2) verify that the bypass matches the flow demand (as described above).

Post-operative Follow-Up

We routinely perform early post-operative neuroimaging (CTA, MRA and/or digital subtracted angiography – DSA) to assess the onset of aneurysmal thrombosis, the patency of the bypass, and postoperative presence of ischemic lesions. Clinical and neuroradiological monitoring over time plays an important role, in order to monitor aneurysmal changes and reduce the risk of future rupture and the risk of ischemia. Our follow-up protocol (CTA, MRA, DSA) is as follows: (1) at 3-months; (2) annually for the first 3 years after treatment; (3) at 5 years; and (4) finally, every 5 years.

Final Considerations

Trapping strategies represent invaluable treatment options for managing complex intracranial aneurysms. Among trapping strategies, complete trapping is always favored, since it has the advantage of immediate aneurysm exclusion and it should always be considered as the best treatment option.

Partial trapping strategies represent the last resource measure for treating complex IAs and have to be used when clip-reconstruction or total trapping strategy are considered inadvisable or too risky. The combination of hemodynamic change and intra-aneurysmal thrombosis progression constitute a complex biological process that we are, however, neither able to model nor predict. Influences of hemodynamic alterations and thrombosis dynamics on the risk of aneurysmal rupture and ischemia are to be further characterized with mathematical models and long-term follow-up data.

Complete and partial trapping strategies are in general associated with a flow "replacement" bypass, to permanently supply blood flow to the downstream vascular territories.

Conflict of Interest The authors report no personal financial or institutional interest in any of the drugs, materials, or devices mentioned in this article. The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper. The authors state that this article has not been previously published in whole or in part or submitted elsewhere for review.

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Emergency Non-occlusive High Capacity Bypass Surgery for Ruptured Giant Internal Carotid Artery Aneurysms

Jan-Karl Burkhardt, Giuseppe Esposito, Jorn Fierstra, Oliver Bozinov, and Luca Regli

Abstract

Aim

Managing ruptured giant internal carotid artery (ICA) aneurysms in an emergency situation is very challenging. By reporting two cases, we discuss the role of the Excimer Laser-assisted Non-occlusive Anastomosis (ELANA) technique as an armamentarium for cerebrovascular surgeons dealing with giant ICA aneurysms presenting with subarachnoid hemorrhage (SAH).

Materials and Methods

The management of two consecutive patients treated with ELANA bypass during a 6-month period (June- December 2013) for ruptured giant ICA aneurysms in an emergency setting is presented.

Results

The two patients presented with SAH and newly diagnosed giant ICA aneurysms (both Fisher 3; WFNS scores 2 and 4, respectively). Both patients received an emergent high-capacity extra- to intracranial (EC-IC) bypass with interposition of a saphenous vein graft between the external carotid artery (ECA) and the ICA-termination. The intracranial anastomosis was performed by the use of the non-occlusive ELANA technique. The aneurysms were successfully trapped, and there were no major complications and no major persistent morbidity in either patient. A good clinical outcome was obtained with a modified Rankin scale of 2 at the last follow-up in both patients.

Conclusion

Emergency ELANA bypass surgery is a useful instrument for managing patients with giant ICA aneurysms presenting with SAH. In experienced hands, the technique does not seem to carry increased risk and may expand the surgical options due to its non-occlusive nature.

Keywords Emergency bypass • Excimer laser-assisted non-occlusive anastomosis (ELANA) • Giant aneurysm, ruptured aneurysm, complex aneurysm • Subarachnoid hemorrhage

Introduction

The treatment of patients with ruptured giant ICA aneurysms is challenging. Often, selective clipping, clip reconstruction, or endovascular treatment of such lesions is considered too risky. In these cases, aneurysm trapping is recommended for optimal long-term surgical results [3, 4, 6, 7]. Since the goal of any aneurysm treatment is both aneurysm exclusion and blood flow preservation, bypass surgery remains an important management option [2, 3]. The selection of the ideal bypass procedure depends on multiple factors: the amount of flow to the occluded arterial territory, the intracranial vascular angioarchitecture, and the availability of donor and recipient vessels [3].

In cases of ruptured ICA aneurysms, bypass technique should preferably not interrupt for a prolonged time (>30–40 min) the high flow provided by the ICA in a brain that is prone to SAH-related ischemic injury (intracranial hypertension, vasospasm, and delayed cerebral ischemia – DCI). The ELANA technique allows the construction of an end-to-side anastomosis without the need for temporary occlusion of the recipient artery, thus avoiding the transient cerebral ischemia. This technique has been developed for safer treatment of complex intracranial aneurysms [8–10]. Here, we report our experience with the ELANA bypass strategy in the emer-

J.-K. Burkhardt, MD (✉)
Department of Neurosurgery, University Hospital Zürich, Zürich, Switzerland

Department of Neurosurgery, University Hospital Zurich, University of Zurich, Frauenklinikstr.10, Zürich 8091, Switzerland
e-mail: Jan-Karl.Burkhardt@usz.ch

G. Esposito, MD, PhD • J. Fierstra, MD, PhD • O. Bozinov, MD
L. Regli, MD
Department of Neurosurgery, University Hospital Zürich, Zürich CH-8091, Switzerland

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gency setting for treatment of ruptured complex ICA aneurysms during a 6-month period at University Hospital Zurich, Switzerland.

Materials and Methods

Between June and December 2013, two patients underwent surgical treatment of giant ruptured ICA aneurysms in an emergency setting with the use of flow-replacement ELANA bypass surgery at the Department of Neurosurgery, University Hospital Zurich, Switzerland. Both patients were operated on by the senior author (L.R.). Emergency setting was defined as any surgery performed within 48 h from the onset of SAH-symptoms.

Patients underwent preoperative computed tomography angiography (CT-A) and/or digital subtraction angiography (DSA) with 3-D reconstructions to optimally define the anatomy. Control angiography (CT-A or DSA) was performed within the first 48 h after surgery and subsequently, depending on the clinical development. Follow-up CT-angiography was scheduled, depending on the case (routinely 3 months and 1 year after surgery). Pre-op status was assessed according to the "World Federation of Neurological Surgeons" (WFNS) scale. Functional health of patients was assessed after surgery and at follow-up according to the "modified Rankin Scale" (mRS) and the "Glasgow Outcome Scale" (GOS).

ELANA Technique

The ELANA technique permits the construction of a non-occlusive end-to-side anastomosis on intracranial recipient vessels using an interposition graft. The technique for the construction of a high-capacity EC-IC bypass (with graft interposition) is herein described.

In brief, after having harvested a 30 cm graft (saphenous vein or radial artery), a platinum ring (2.6 or 2.8 mm) is attached to the interposition graft by flipping its distal end around the platinum ring and sewing with 8 interrupted sutures to secure it in place; this procedure is performed under microscopic control outside the patient. In order to perform an EC-IC bypass (as performed on the two reported patients), the ipsilateral bifurcation of the common carotid artery (CCA) is exposed in the neck. Intracranially, the supraclinoidal ICA and the aneurysmal anatomy are explored through a pterional craniotomy.

First the venous graft with the attached ring is stitched end-to-side to the intracranial recipient artery using eight microsutures. Then the graft is tunneled from the craniotomy to the cervical incision. The ECA is the preferred donor vessel (as it better tolerates temporary occlusion) for performing a classic occlusive end-to-side anastomosis using the distal part of the saphenous vein graft. The laser catheter, composed of a central suction portion and outer circular fiberoptic array, is then passed through the graft from an opening made on its lateral side near the intracranial anastomosis. The tip of the laser catheter is positioned within the platinum ring of the intracranial anastomosis against the sidewall of the recipient vessel. After 2 min of vacuum suction, the laser is activated to cut out an arteriotomy "flap." The catheter is then withdrawn, and the presence of the arteriotomy wall flap in the central suction portion of the catheter tip is checked and removed [9]. Flow through the bypass is established after suturing the side opening in the graft wall and backward and forward bleeding through the graft.

The key is (1) to correctly orient the vein, because of the presence of venous valves within the saphenous vein. The distal part of the vein graft must be connected with the donor (in our cases, the ECA), the proximal part with the intracranial recipient (in our cases, the ICA-termination); and (2) to avoid twisting and kinking of the graft during tunneling.

Principles of Intraoperative Flow Measurements: To "Match the Flow Demand"

The flow is measured with a flowmeter (Transonic Systems Inc., Ithaca, NY, USA) before (for baseline measurements) and after the bypass in the following arteries: (1) the cervical ICA; (2) the supraclinoidal ICA, when anatomically feasible; (3) the M1 segment of the MCA; and (4) the A1 segment of the ACA. The bypass flow is also measured, before and after ICA occlusion.

The aim of the bypass is not necessarily to replace the entire ICA flow, but to replace the flow deficit after ICA occlusion, given that collateral flow (e.g., through the A1 segment) may compensate for the remainder. The aim is in fact to at least "match the flow demand," where the flow demand is defined as the flow drop after parent (ICA) vessel occlusion. For instance, in ICA aneurysms with a patent ACom artery, the flow demand is the subtraction of the M1 flow at baseline and after clipping of the ICA.

Results

The two patients presented with SAH and newly diagnosed giant ICA aneurysms of the ophthalmic and communicating segments, respectively (both Fisher 3; WFNS scores were 2 and 4, respectively). In both patients EC-IC bypass surgery

was performed by means of interposition of a saphenous vein graft between the ECA and the intracranial ICA bifurcation. The intracranial anastomosis was made using the ELANA technique, and the aneurysms were treated by total trapping. There was no major complication – in particular, no postoperative hemorrhage and no major persistent morbidity in both patients. A good clinical outcome was obtained with an mRS of 2 at the last follow-up (at the 30-day discharge in patient 1, and at 1 year in patient 2).

Case Presentations

Case 1

A 48-year-old man presented with severe headache and right temporal hemianopsia. CT/CTA showed an SAH (Fisher grade 3) with a ruptured giant (25 mm) left supraclinoidal ICA aneurysm of the communicating segment (Fig. 1a). At admission, the patient was stable with a GCS of 14 and WFNS of 2. After digital subtraction angiography (DSA), endovascular strategies and direct surgical clipping of the aneurysm were considered too risky. The patient failed the balloon occlusion test (BOT) of the left ICA. Therefore, EC-IC bypass and aneurysm trapping was considered the best treatment modality. Surgery was performed within 48 h of SAH and consisted of the following steps: (1) harvesting of a 30 cm-saphenous vein graft, exposure of the CCA bifurcation at neck (very important for proximal control) and measurement of the flow of the cervical ICA (50 ml/min); (2) left pterional craniotomy; (3) construction of a high-capacity EC-IC bypass by interposition of a saphenous vein graft between the cervical ECA and the left ICA termination. The intracranial anastomosis was made using the ELANA technique: just before lasering the intracranial arteriotomy, the patient was given 3000 IE heparin and 300 mg aspirin; (4) after temporary cervical ICA occlusion, the flow of the bypass reached 55 ml/min: the bypass matched the flow demand; (5) finally, clinoidectomy was performed to allow microsurgical dissection of the aneurysm (because of the risk of aneurysm rupture during clinoidectomy, we decided to first do the bypass followed by the clinoidectomy); (6) the aneurysm was dissected and completely trapped by a proximal ICA clip (immediately after the origin of the ophthalmic artery – OA) and a distal ICA clip (immediately before the posterior communicating artery – PComA). The OA, the PComA, and the

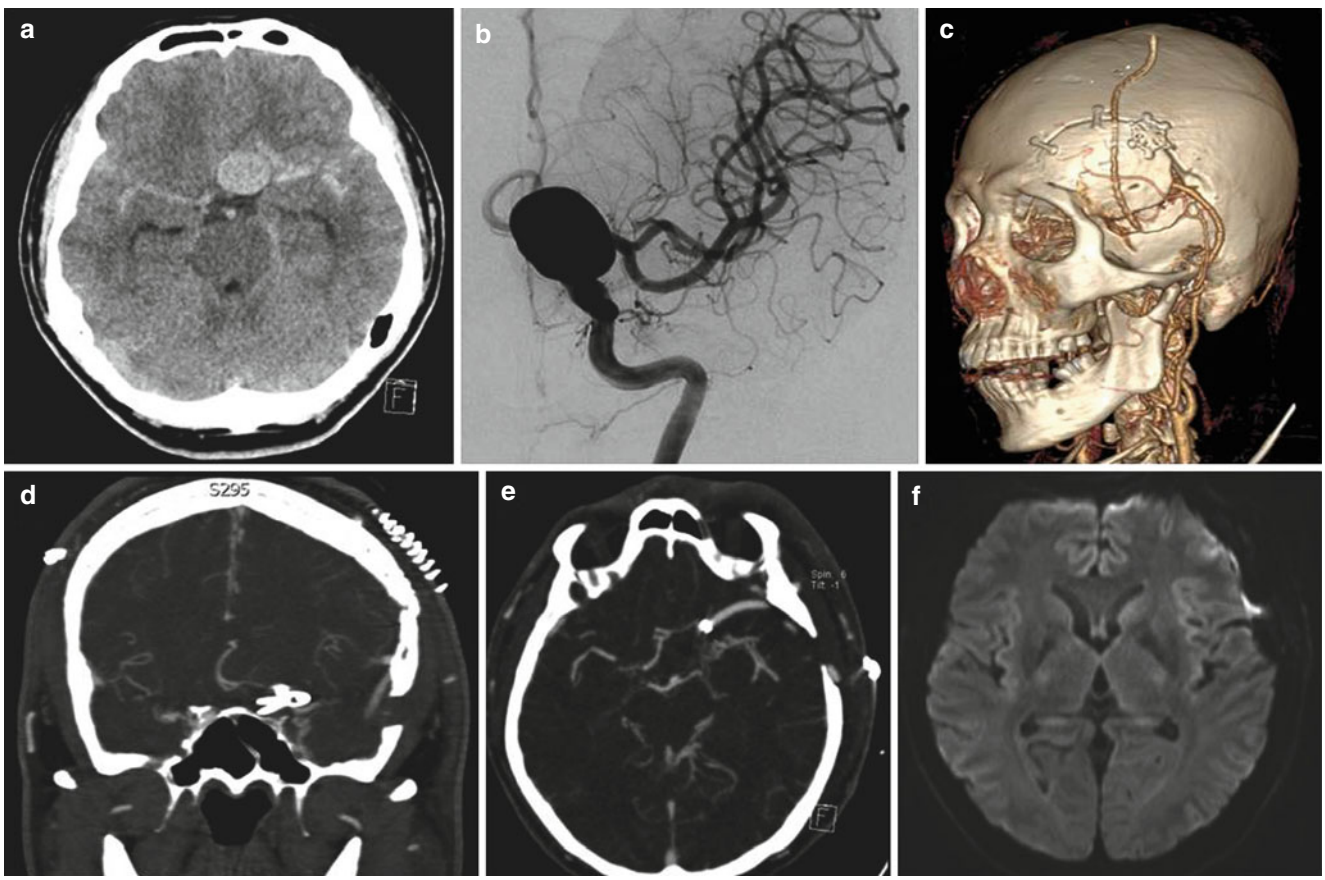

Fig. 1 Axial CT (**a**) and DSA (**b**) showing ruptured ICA aneurysm. Postoperative 3-D reconstruction CTA (**c**) showing ELANA bypass and axial (**d**) and coronal CTA (**e**) indicating trapped aneurysm. Postoperative diffusion MRI (**f**) showed no diffusion restriction

choroidal artery (AChA) were spared from trapping; and (7) finally, aneurysmal decompression with thrombectomy was performed in order to decompress the optic nerve.

The postoperative course was uneventful. Post-operative neuroimaging (CTA) confirmed the exclusion of the aneurysm and the patency of the bypass (Fig. 1d, e). Diffusion MRI showed no ischemic lesions (Fig. 1f). The patient was discharged on day 15 after SAH with a GCS of 15 and improved right-sided temporal hemianopsia. Since the patient was a tourist living in a Far Eastern country, he flew back home on day 30 and long-term follow-up is missing.

Case 2

A 74-year-old woman was admitted with headache, a temporal hemianopia of the right eye, an amaurosis of the left eye and fluctuating vigilance (GCS 7–11), and was diagnosed with SAH (WFNS 4, Fisher grade 3) due to a ruptured giant (32 mm) left-sided supraclinoid ICA aneurysm in the ophthalmic segment. Although the patient passed the occlusion test of the left ICA (sufficient collateral flow through the ACom), the indication for surgery was taken with the aim of decompressing the optic nerve, maintaining optimal blood flow with a high-capacity EC-IC bypass, and diminishing the risk of delayed cerebral ischemia (DCI). Surgery was performed within 48 h of SAH.

Direct exploration of the peri-aneurysmatic angioanatomy was considered too risky because of the aneurysm size and morphology. For this reason, we decided to deflate the aneurysm by temporarily clipping the cervical ICA (preoperative balloon test occlusion indicated tolerance).

The giant aneurysm was then trapped, followed by thrombectomy to decrease the mass effect on the optic structures. The ophthalmic artery, the PComA, and the AChA were seen and spared.

An EC-IC bypass with the interposition of a saphenous vein graft between the left ECA and the left intracranial ICA-bifurcation was performed. The intracranial anastomosis was made using the ELANA technique: just before lasering the intracranial arteriotomy, the patient was given 3000 IE heparin and 300 mg aspirin. The rest of the bypass procedure was performed as described above for case 1. The final bypass flow was 70 ml/min and matched the flow demand (in this case, matching the previously measured baseline flow in the ICA).

After surgery the patient improved clinically without any signs of fresh ischemia or new neurological deficits, and the visual function significantly improved after surgery. Postoperative 48 h CTA documented aneurysmal occlusion and patency of the bypass. The patient was transferred to neurorehabilitation on day 16 with an mRS of 4. A small wound necrosis needing surgical revision occurred 2 months after surgery. At the 3-month follow-up, the patient showed neurological recovery to an mRS of 2, and neuroimaging confirmed patency of the bypass and aneurysm exclusion, without showing any ischemic sequelae. At the 1-year follow-up, the patient showed complete neurological recovery, with an mRS of 1.

Discussion

In these two patients harboring giant ICA aneurysms presenting with SAH, total trapping strategies were applied together with non-occlusive high-capacity flow-replacement bypass surgery [8, 11, 12]. The treatment was performed in an emergency setting, defined as within 48 h after SAH. The aim of this report is to further support the use of ELANA surgery in selected situations, such as treatment of complex ruptured aneurysms in an emergency setting. Both patients had good postoperative clinical outcomes. There were no hyperperfusion complications due to the high-capacity nature of the bypass, and no DCI due to SAH.

The treatment strategy was planned according to the intracranial angioanatomy and patients' conditions; both had visual deficits due to compression of the optic nerve and chiasm by the giant aneurysm. Relieving the mass effect on the optic apparatus was a major goal of surgery and could best be achieved by rapid aneurysm deflation after complete trapping. Endovascular treatment or partial trapping might even worsen visual deficits in giant ICA aneurysms [1].

In patients failing BTO of an ICA harboring a giant unclippable und uncoilable aneurysm, high-capacity bypass is recommended to adequately maintain the ICA flow before trapping the aneurysmal lesion [4, 7, 8]. In patients with ruptured complex ICA aneurysms who tolerate BTO, high-capacity bypass surgery might be helpful to reduce the incidence of DCI [5].

In comparison to conventional occlusive microanastomosis [14], ELANA is a non-occlusive micro-anastomosis technique approved for intracranial use. The use of a non-occlusive technique avoids the prolonged temporary occlusion of a major artery (ICA) with a large downstream territory [13] and may be particularly attractive for patients presenting with acute SAH. This remains, however, a hypothesis that cannot be proven in a series of only two patients. These two also showed that an acute SAH in a good grade patient is not a contraindication for an ELANA microanastomsis on the intracranial ICA bifurcation. The presence of brain swelling represents a contraindication to the performance of a deep microanastomsis.

Conclusions

Emergency ELANA bypass surgery is a useful instrument in the treatment of ruptured giant ICA aneurysms in highly selected patients with good clinical grade. In expe-

rienced hands, the technique does not seem to carry increased risk and may increase the surgical options due to its non-occlusive nature.

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

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Unruptured Aneurysms and Flow Dynamics

Clipping Surgery for Unruptured Middle Cerebral Artery Aneurysms

Tadayoshi Nakagomi, Kazuhide Furuya, Junichi Tanaka, Shigehiko Takanashi, Takehiro Watanabe, Takayuki Shinohara, Akiko Ogawa, and Norio Fujii

Abstract Clipping surgeries for 139 consecutive unruptured middle cerebral aneurysms were performed between April 1991 and March 2014. Left hemiparesis occurred in one case (0.7 %). Transient symptoms arose in six patients due to perforator injury, arterial branch occlusion, damage to the venous system, or chronic subdural hematoma. Neither mortality nor decline in cognitive function was noted in this study. Clipping surgery for unruptured middle cerebral artery aneurysms can be done with minimal morbidity. However, meticulous management during the perioperative period as well as the use of modern technologies during the surgery, such as MEP monitoring and ICG videoangiography, are needed for safe and secure clipping surgery.

Keywords Unruptured cerebral aneurysm • Clipping surgery • Complications

Introduction

Aneurysmal clipping has been the standard method for the treatment of an unruptured intracranial aneurysm (UIA) [1]. However, with the technological advances in devices, endovascular treatment has been used with increasing frequency [2–4]. Aneurysmal clipping has been recommended over endovascular coiling for young patients and for small or anterior circulation aneurysms, i.e., low-risk cases [5]. On the other hand, endovascular treatment may be suitable for high-risk UIA patients (the elderly, or for posterior aneurysms, etc.) [5]. Among the anterior circulation aneurysms, a middle cerebral artery (MCA) aneurysm has been considered to be a better indication for aneurysmal clipping because of low morbidity and mortality during and after the clipping surgery [6]. However, there are many types of possible perioperative complications associated with clipping surgery for unruptured MCA aneurysms, including perforator injury, arterial branch occlusion, damage to the venous system, brain contusion during dissection, and so on. These complications may result in transient or permanent neurological deficits or, rarely, in death (Figs. 1, 2, 3, 4, and 5).

In this study, perioperative events/complications for 139 consecutive patients who underwent clipping for 143 unruptured MCA aneurysms were investigated and are discussed.

Materials and Methods

From April 1991 until March 2014, 296 consecutive patients (312 aneurysms) underwent clipping surgery for ICAs at Teikyo University Hospital. Eighty-six were males and 210 were females, and the mean age was 59.3. Fifty-two patients had previous histories of subarachnoid hemorrhage. MCA aneurysms were the most common (45 % of aneurysms). The size of unruptured aneurysms varied from 3 to 24 mm, with the average size 6.2 mm. The size of unruptured MCA aneurysms were as follows: 3–4 mm in 59 (41.3 %), 5–6 mm in 36 (25.2 %), 7–8 mm in 35 (24.5 %), and > 9 mm in 13 cases (9.1 %). The average size of unruptured MCA aneurysms was 5.5 mm.

One hundred and thirty-nine consecutive patients (143 MCA aneurysms) underwent clipping surgeries. Forty-one patients were males and 98 were females; the mean age was 60.8. The procedure time for aneurysmal clipping was nearly 3 h. The perioperative events/complications for 139 consecutive patients who underwent clipping for 143 unruptured MCA aneurysms have been investigated and are discussed herein.

T. Nakagomi, MD (✉) • K. Furuya, MD • J. Tanaka, MD
S. Takanashi, MD • T. Watanabe, MD • T. Shinohara, MD
A. Ogawa, MD • N. Fujii, MD
Department of Neurosurgery, Teikyo University School of Medicine, Tokyo, Japan
e-mail: nsnaka@med.teikyo-u.ac.jp; nakagomi@aok.bb4u.ne.jp

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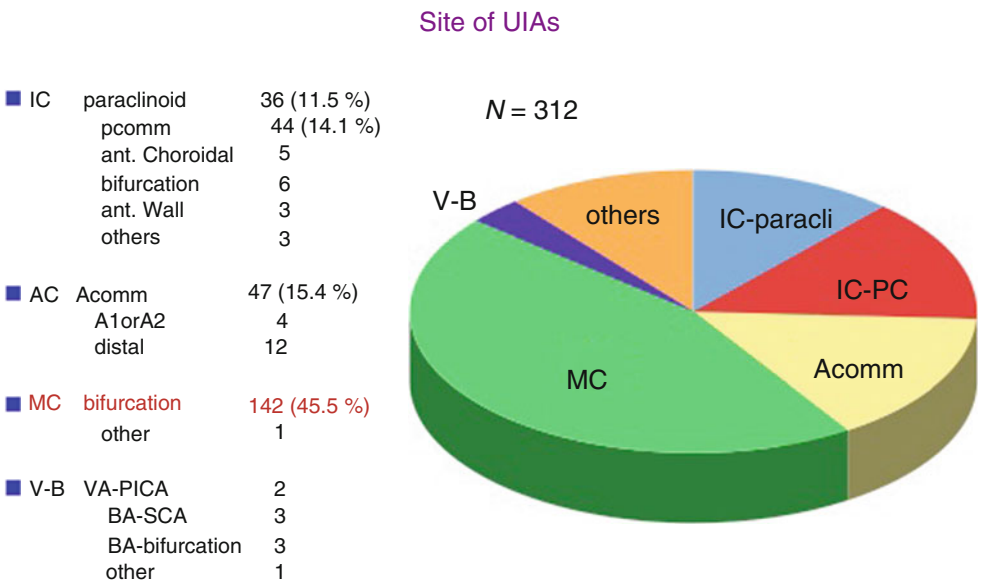

Fig. 1 Location of the unruptured aneurysms reported in this article. MCA was the most common location

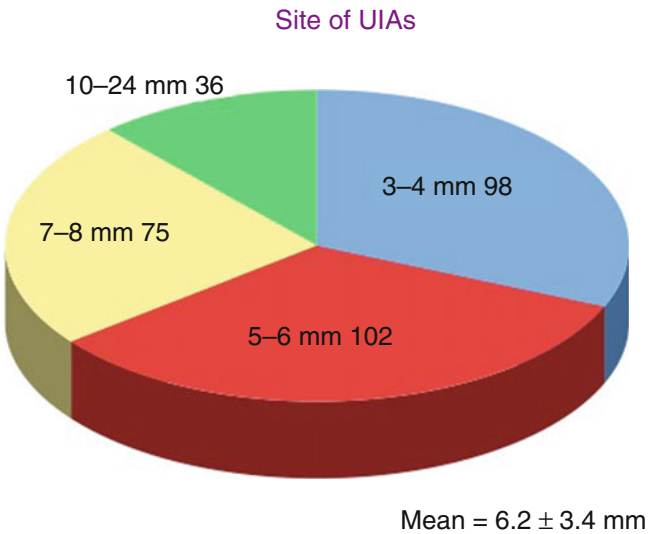

Fig. 2 The size of unruptured aneurysms varied from 3 to 24 mm. Average size was 6.2 mm

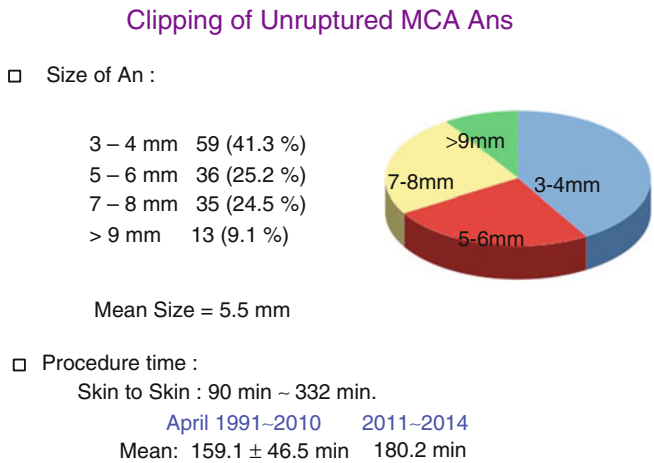

Fig. 3 Size of the MCA aneurysm and procedure time needed for the clipping. Most MCA aneurysms were less than 6 mm. Mean procedure time was approximately 3 h

Results

Perioperative events/complications consisted of perforator injury, arterial branch occlusion, premature rupture, one case of incomplete clipping, damage to the venous system, brain contusion during dissection, and chronic subdural hematomas. Among these complications, perforator injury was the most frequent cause of morbidity in the patients.

Perforator injury occurred in two cases. One case was asymptomatic, but in the other (which seemed to have had a successful clipping), the patient developed left hemiparesis postoperatively (modified Rankin scale 3). In this patient, a pre-operative angiogram showed a short M1 segment. Lacunar infarction in the right centrum semiovale was seen in the post-op CT scan, which was considered due to stenosis or occlusion of a lenticulostriate artery by the placed clip. This case taught us that morphological study combined with micro-Doppler study alone is not enough for the confirmation of the vessel patency. Motor-evoked potential (MEP) monitoring during clipping surgery was done thereafter and the results were definitively useful, in particular for large and giant aneurysms, internal carotid artery (ICA) bifurcation aneurysms, MCA bifurcation aneurysms with short M1, or when temporary clips were supposed to be used. The use of indocyanine green (ICG) videoangiography was begun in 2004 by injecting ICG (0.5 mg/kg) intravenously. ICG videoangiography clearly showed the patency of the perforators, as well as those of

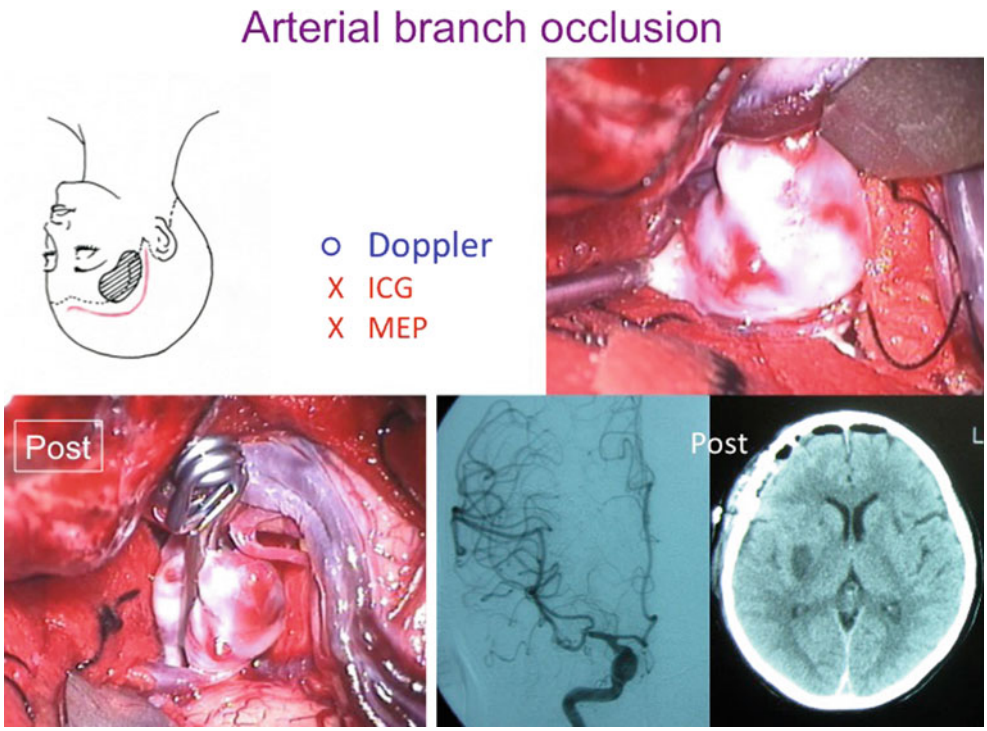

Fig. 4 In this case, clipping seemed to be successful, but right hemiparesis appeared postoperatively. Lacunar infarction in the right putamen to centrum semiovale was noted. It was caused by stenosis or occlusion of the LSA by the placed clip

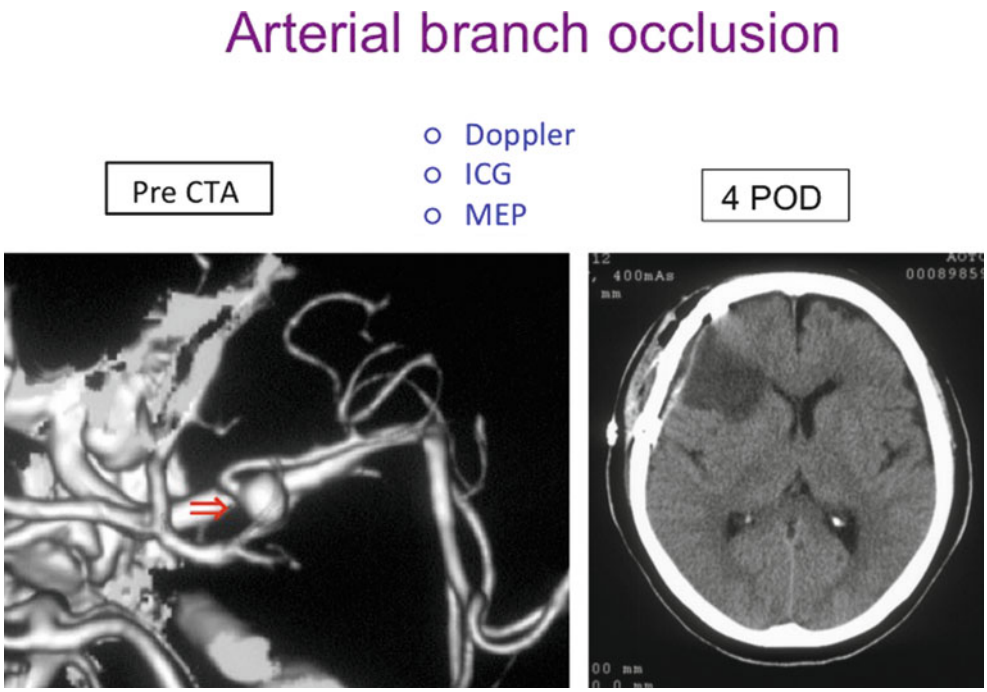

Fig. 5 In this case, cerebral infarction appeared 4 days after clipping. Clip-induced arterial branch stenosis (or vasospasm) was suggested as a cause of the infarction. The patient was discharged without any neurological deficits. *Red arrow* shows aneurysmal neck where a branch became stenotic

the proximal and distal arteries. Since the introduction of both MEP monitoring and ICG videoangiography, major complications (resulting, for instance, in hemiparesis) have not occurred.

Clip-related arterial branch occlusion occurred in one case, when cerebral infarction in the right frontal lobe appeared 4 days after clipping. This patient was discharged without any neurological deficits, however.

Premature rupture occurred in two cases. In one of them, it occurred during dome dissection, and in the other during a clip-movement performed for better clip-placement. In this case, the wall of the aneurysm dome was very thin (the patient was known to have polycystic kidney disease). In both cases, the premature rupture was managed successfully and the patients were discharged without neurological deficits.

Damage to the venous system occurred in one case, resulting in brain edema, although the patient showed no neurological symptoms. Brain contusion during dissection occurred in another patient, who developed epilepsy after surgery and was maintained on an anti-epileptic drug for 1 year. Incomplete clipping occurred in another patient; an additional clip was applied distal to the first clip. In a patient operated on for an MCA aneurysm, chronic subdural hematoma occurred 2 months after clipping. A burr-hole and irrigation were performed on this patient, who was then discharged without neurological deficits.

Discussion

In this study, a major complication (hemiparesis-Modified Rankin score 3) occurred in one case (0.7 %). Neither mortality nor decline in cognitive function was noted in this study. Many studies have examined the management outcomes of UINs, but published clinical outcomes differ considerably between studies. In the ISUIA study, the mortality rate during treatment was 1.5 %, and significant morbidity (Modified Rankin scale score of 3 or less, or a Mini-Mental State Examination score of less than 25) was found in 11.7 % of patients who had open surgeries at the 1-month follow-up [7]. In a UCASII study, 558 UIAs were treated surgically. Major morbidity, which was defined as either a decrease in the Modified Rankin scale score to 2 or less, or a decrease in the Mini-Mental State Examination score to less than 25, was noted in 5.3 % of cases [8]. Morbidity was higher in the aneurysms that were large or located in posterior circulation [7]. Compared to these two reports, our results look acceptable due to the low morbidity.

Unruptured MCA aneurysms can be managed with low mortality and morbidity. However, there are many types of perioperative events/complications associated with clipping surgery, including perforator injury, arterial branch occlusion, damage to the venous system, brain contusion during dissection, and so on. These complications result in transient or permanent neurological deficits or, rarely, in death.

Following are a few tips that can be useful for surgeons operating on unruptured aneurysms:

1. Major veins, such as the superficial Sylvian vein, frontobasal vein, and frontal bridging veins, must be preserved.
2. Premature rupture should be avoided. However, proximal control should be prepared.
3. Patency of the perforators or distal branches must be maintained.

Many kinds of events/complications associated with clipping surgery may, however, occur peri-operatively. MEP monitoring and ICG videoangiography represent very useful intra-operative tools.

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

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Flow Dynamics of Aneurysm Growth and Rupture: Challenges for the Development of Computational Flow Dynamics as a Diagnostic Tool to Detect Rupture-Prone Aneurysms

Juhana Frösen

Abstract Saccular intracranial aneurysm (sIA) is a relatively common disease that can potentially cause a devastating, life-threatening intracranial hemorrhage. Many sIAs never rupture and thus do not necessitate interventions, making the detection of rupture-prone sIAs a very relevant clinical problem. Moreover, because currently available methods to prevent sIA rupture have significant risks of morbidity and mortality, diagnostic tools that can predict imminent rupture and help plan proper timing of prophylactic interventions, can improve patient care. Hemorrhage from an sIA occurs when hemodynamic stress exceeds sIA wall strength. Computational fluid dynamics (CFD) is a tool with which the hemodynamic stress to which the sIA wall is exposed can be determined non-invasively. Studies using CFD in sIAs have demonstrated associations of wall shear stress (WSS) with aneurysm growth, fragile sIA wall, and sIA rupture; these studies show the potential of CFD as a diagnostic tool. This review discusses the limitations of CFD and of the studies performed, and what needs to be done in order to develop CFD into a useful diagnostic tool to determine aneurysm-specific rupture risk.

Keywords Intracranial aneurysms • Computational fluid dynamics • Wall shear stress • Degenerative remodeling • Fragile wall • Rupture • Subarachnoid hemorrhage

Introduction

Saccular intracranial aneurysm (sIA) is a relatively common disease. According to the best estimates, 2–3 % of the population is affected by it, especially the middle-aged population [1, 2]. Compared to their high prevalence, sIA rupture and subsequent intracranial hemorrhage is relatively rare (10–20/100,000 per year, depending on the particular population [3]), and many sIAs never rupture [4]. Due to the devastating consequences of sIA rupture (mortality approximately 40 %, neurological deficits or cognitive impairment common among survivors [5]), and risks associated with rupture preventing therapy (5–7 % permanent morbidity, 1–2 % mortality, [6, 7]), it is of paramount importance to focus therapy on those sIAs that are rupture-prone. Although natural history studies have identified patient-related and aneurysm-related risk factors for rupture [4, 8, 9], a large number of sIA patients suffer devastating ruptures without having any of the patient-related known risk factors or rupture- associated aneurysm characteristics.

Rationale for the Use of Computational Flow Dynamics to Identify a Rupture-Prone sIA

Aneurysms rupture when hemodynamic stress imposed on the aneurysm wall exceeds wall strength. It therefore seems logical that one could predict impending sIA rupture by measuring wall strength and hemodynamic stress. Direct measurement of the mechanical stress imposed by hemodynamic forces on the aneurysm wall is difficult and would require invasive measurements. Computational fluid dynamics (CFD) goes around these limitations by using angiography-derived vessel geometries and laws of fluid physics to calculate the mechanical stress on the aneurysm wall (Fig. 1 and Table 1). The non-invasiveness and apparent exactness (laws of physics) make CFD look like a robust, scientific solution to determine the risk of sIA rupture. CFD is used in the design of airplanes, oil valves, etc. [10, 11]. Despite the robustness of the method, there are several limitations to its applicability for clinical use, and especially to determine the risk of sIA rupture. Furthermore, blood flow and pressure

J. Frösen, MD, PhD
Department of Neurosurgery, Kuopio University Hospital, Puijonlaaksontie 2, Kuopio 00029, Finland
e-mail: juhana.frosen@kuh.fi

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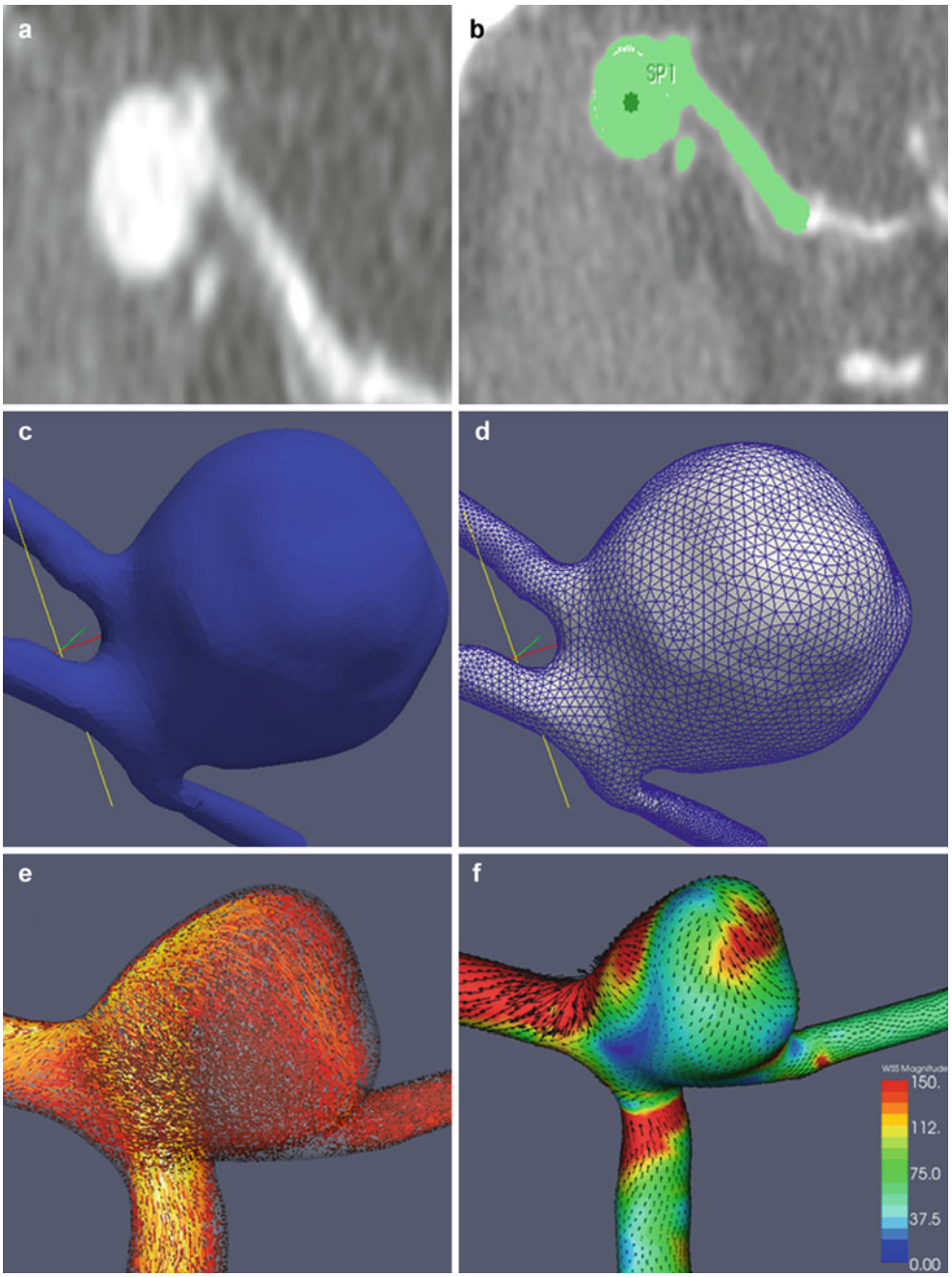

Fig. 1 Building a computational fluid dynamics model of flow and hemodynamic stress in an intracranial aneurysm begins by acquiring 3-D angiography images in dicom format. Suitable imaging methods include 3-D rotational digital subtraction angiography, magnetic resonance angiography, or computer tomography angiography (CTA), provided that the voxel size is small enough (usually requires so-called "raw data"). (**a**) Displays a middle cerebral artery aneurysm in an axial section of CTA raw data. Next step is to extract the geometry of the aneurysm and parent vessels from the CTA. (**b**) Displays this process called segmentation, in which a computer program (in this case Slicer 3.6 using VMTK toolkit, www.spl.harvard.edu) outlines the aneurysm and selected vessels (in *green*) from the CTA data with the help of fiducial markers (*green dot* on the aneurysm) placed by the user. The end result is a 3-D representation of the aneurysm geometry (**c**). This 3-D geometry of the aneurysm is then turned into a wire grid model, in which the surface or the volume of the aneurysm is divided into small geometric cells (**d**). Vectors of flow are calculated using equations of fluid physics in each of these cells (**e**), as well as values for the hemodynamic stress parameters considered relevant. A usual way of presenting the values obtained in each cell is a heat map, in which the magnitude of a hemodynamic stress variable is presented in each cell of the geometric model by a color (**e**). Please note that (**a**–**d**) represent the same middle cerebral artery aneurysm, whereas (**e**–**f**) are from a different middle cerebral artery aneurysm

Table 1 Summary of the studies that associate wall shear stress (WSS) with degeneration or rupture of the intracranial aneurysm (IA) wall

Study	Number of aneurysms	Population	Type of WSS associated with growth, fragile wall, or rupture		References
WSS and aneurysm growth					
Boussel et al.	7	American	Low	Mean 0.76 vs. 2.55 Pa	[28]
WSS and fragile wall					
Fukazawa et al.	12	Japanese	Low	Mean 0.29 vs. 2.27 Pa	[29]
Kadasi et al.	16	American	Low	Mean 0.38 vs. 0.82 Pa	[30]
Cebral et al.	20	American	High	Mean values not given	[31]
WSS and aneurysm rupture					
Cebral et al.	210	American	High	Mean 384 vs. 277 dyn/cm^3	[32]
Xiang et al.	119	American	Low	Mean 2.71 vs. 3.87 Pa	[33]
Lauric et al.	18	American	Low	Mean WSS not significantly different	[34]

Whether higher or lower WSS values were found at sites of aneurysm wall growth, fragile wall, or in ruptured sIAs compared to other regions of the aneurysm wall or to unruptured IAs, is summarized as applicable. The mean WSS at the site of wall growth or degeneration is given, as well as mean WSS at other regions of the aneurysm wall. For studies that associate WSS with IA rupture, the mean WSS is given for ruptured and unruptured sIAs. Please note that units of WSS differ among the studies

induce different kinds of force vectors on the vessel wall, and the biological response of the sIA wall to these mechanical stress forces needs to be elucidated before CFD can be used to determine sIA rupture risk.

Interaction of Hemodynamic Forces with the sIA Wall

The mechanical stress imposed on the vessel wall by blood flow and pressure can be divided into two main components: (1) wall shear stress (WSS) that is tangential to the lumen and caused by friction, and (2) wall tension (WT) caused by circumferential stretch created by pulse pressure wave and transmural pressure difference, which leads to distension and tension of the aneurysm wall. It is the tension of the wall that leads to rupture when it exceeds the tensile strength of the wall matrix. Nevertheless, WSS and other stress vectors also have an effect on vessel wall remodelling, since they affect the function and phenotype of endothelial cells, smooth muscle cells, and fibroblasts, and can induce wall inflammation [12–14].

Endothelial cells and smooth muscle cells (SMCs), the two main cellular components of the sIA wall, react differently to mechanical stress. SMCs are highly sensitive to mechanical stress, but normally are not as exposed to WSS as the endothelial cells – unless the endothelium is lost. SMCs react to increased pressure, wall tension (or WSS when exposed to it) by contraction, change of phenotype, proliferation, and synthesis of new matrix [12, 13]. Endothelial cells are more sensitive to WSS and require a physiological WSS for proper function. Too-high or too-low WSS, or otherwise aberrant WSS, not only leads to dysfunction of endothelial cells but may also cause complete loss of the endothelial layer [15–18]. Endothelial cells act as a barrier between the sIA wall and plasma, and loss of this barrier function and subsequent free diffusion of plasma components into the sIA wall can trigger wall degeneration that eventually leads to rupture [16]. Endothelial cells also interact with SMCs via nitric oxide (NO) production and other chemokines [17], and thus regulate the phenotype and function of SMCs and fibroblasts that are capable of matrix synthesis and adaptive remodeling to hemodynamic stress. In addition, endothelial cells play an important role in the chemotaxis of inflammatory cells into the sIA wall [18] and inhibit thrombosis on the luminal surface. Thrombus formation on the luminal surface of the sIA wall is clearly associated with a degenerated, rupture-prone sIA wall [16, 19, 20] and thrombus-derived cytotoxic compounds and matrix degrading proteases have been implicated as the cause of sIA wall degeneration and rupture [16]. Aberrant flow conditions can also predispose to thrombus formation [21]. Although WSS is not the force that breaks sIA wall matrix and causes rupture, it affects the function of sIA wall endothelial cells and can trigger and modify wall degeneration and rupture via the mechanisms described above.

Technical Limitations and Challenges of CFD Modelling of sIA Hemodynamics

CFD modelling begins with the generation of a 3-D geometric representation of the structure to be modelled, in the case of sIA the parent artery, the main arterial branches, and the aneurysm itself (Fig. 1). Based on this geometry, a 3-D grid model called "mesh" is then generated (Fig. 1). In this model, the volume of the geometry to be modelled is divided into

discrete cells. Next, flow and related mechanical force vectors are determined in each of the cells, using equations of fluid physics. A commonly used method to present the results is a heat map in which the value of each cell in the mesh is represented by a color (Fig. 1).

It is important to understand that the accuracy of how well the 3-D geometry used for modelling represents the true geometry of the related arteries and aneurysm affects the results obtained [22]. Moreover, the size and density of the cells in the 3-D grid model can affect the results [23]. Finally, and most importantly, depending on what is modelled or calculated, the physics equations used can incorporate parameters that are not known for sIAs. This means that those parameters need to be extrapolated or simply guessed in order to enable the calculations. This, of course, has a significant effect on the validity of the calculations and models [24]. A typical example of such a parameter is Young's modulus and other parameters that described the elasticity or mechanical properties of the sIA wall; these parameters are especially necessary to calculate wall tension, the most relevant hemodynamic stress parameter for determining wall rupture [25].

Most literature on CFD modelling in sIAs focuses on WSS and not on wall tension, because the parameters or so-called boundary conditions needed to perform the calculations for WSS are better known than those needed to calculate wall tension. Even in WSS modelling, however, one needs to carefully check that the values selected for the boundary conditions make sense and are within the physiological range.

Hemodynamic Stress and sIA Formation

Non-physiological high WSS has been shown to induce aneurysm-like changes in animal models in which arterial bifurcations were artificially created to produce aberrant WSS [26]. Before that, the formation of intracranial aneurysms had been induced in various species by manipulating cerebral artery flow conditions with the ligation of one or several of the main arteries supplying the brain, sometimes coupled with the induction of hypertension and inhibition of collagen matrix formation [27, 28]. Together these studies show that hemodynamic stress, non-physiological high WSS, and subsequent artery wall remodelling, lead to sIA formation.

Hemodynamic Stress and sIA Growth

Because of its shape, once formed, even the small aneurysm-like dilatation will have flow conditions that differ from normal arteries. These aberrant flow conditions affect the function of cells in the aneurysm wall and can induce endothelial dysfunction, luminal thrombosis, and eventually SMC death and wall inflammation as discussed above and reviewed in detail by Frösen et al. [16, 29]. Mechanical stress can affect SMC cell signalling and proliferation, and may induce aneurysm enlargement via growth of the aneurysm wall in addition to pure mechanical distension. Aneurysm geometry associates with the activation of cell signalling pathways in the sIA wall [30–32]. Whether aberrant flow triggers sIA growth or sIA growth occurs because of wall proliferation, in every case sIA growth leads to change in flow conditions and hemodynamic stress, including WSS, to which endothelial cells are sensitive.

Shojima and colleagues were among the first to study WSS with CFD in a larger series of sIAs. In the 20 middle cerebral artery sIAs that they studied, maximal WSS was found near the sIA neck, whereas at the tip of the sIA fundus, WSS was low [33], suggesting that high WSS would trigger sIA formation and low WSS predisposed to wall degeneration [33]. Boussel et al. studied WSS in seven IAs that were followed for an average of 16 months and underwent two MR-angiography studies [34]. In these aneurysms, growth occurred at sites that were exposed to abnormally low WSS [34], in line with the conclusions of Shojima et al. [33]. It is worth noting, however, that the three ruptured sIAs included in the Shojima series had higher average WSS in their funduses than the unruptured ones [33].

Hemodynamic Stress and sIA Wall Degeneration

In order to use CFD to predict the risk of rupture, it is even more important to understand what kind of hemodynamic stress is associated with wall degeneration and fragility than to look for associations with growth. In 12 aneurysms, Fukazawa et al. studied the association of WSS and sIA wall structure observed during microsurgical clipping [35]. They found that low WSS is associated with thin, translucent, and most likely fragile walls (Table 1, [35]). Kadasi et al. studied WSS and wall structure in surgery in 16 sIAs on 14 American patients [36]. Like in the Japanese series, Kadasi found that low WSS is associated with a thin, translucent wall that had been interpreted as being fragile (Table 1, [36]).

Although the agreement between the Japanese and American studies suggest that low WSS is truly associated with a fragile sIA wall, one needs to remember that the association does not demonstrate causality. There are no data to confirm that the fragile wall was under low WSS when the sIA wall began to degenerate. This is important to note, especially since wall fragility is supposed to predispose to wall

enlargement, which in turn changes the sIA geometry and would change the results of flow simulations. In fact, in a study that looked for associations of WSS with the formation of secondary pouches on the sIA wall, Cebral et al. found that secondary blebs form at sites of high WSS, but after their formation they are subjected to low WSS (Table 1, [37]). Cebral's results are not necessarily contradictory to those of Fukazawa and Kadasi, but they well demonstrate that flow conditions in the aneurysm change during aneurysm growth [37]. As a result, the same part of the sIA wall can be exposed to a completely different kind of hemodynamic stress during the evolution of the sIA. These observations show the need for follow-up studies with hemodynamic models and data of sIA wall structure from different time points during the development of the aneurysm. Although necessary, studies of this kind are difficult to carry out and will inevitably have selection bias.

Hemodynamic Stress and sIA Rupture: Controversy

Studies on the association of WSS and sIA rupture are also controversial (Table 1, refs). Cebral et al. studied 83 ruptured and 127 unruptured sIAs in 128 patients, and found that mean WSS was higher in ruptured sIAs [38]. Xiang et al. compared the geometry and flow dynamics of 38 ruptured and 81 unruptured sIAs, and contrary to Cebral et al, found that mean WSS was lower in ruptured sIAs [39]. Lauric et al. studied WSS in 18 volume-matched internal carotid artery sIAs, and demonstrated that part of the WSS associations with rupture status might be explained by differences in size [40]. The controversial results reported have lead to the validity of CFD for intracranial aneurysms to be questioned [41].

Why CFD Is Not Ready as a Tool for Diagnostic Use in the Clinical Setting

Despite the contradictory results, several studies conclude that the flow dynamics and flow-induced mechanical stress is different in ruptured and unruptured sIAs, and that flow-induced stress is associated with sIA wall degeneration (Table 1). This suggests that CFD can be developed into a clinically useful diagnostic tool. However, before CFD-derived hemodynamic variables can be used as diagnostic markers of a rupture-prone aneurysm, the effect of hemodynamic stress on the sIA wall has to be studied, and the interaction of mechanical forces and aneurysm wall cells elucidated. Aneurysm walls are not inert and are not passively dilating structures, but instead are composed of cells that are capable of synthesizing new matrix and reorganizing the fibers of the existing extracellular matrix [16, 29]. Moreover, cells in the aneurysm wall are sensitive to mechanical stress and respond to it, as discussed above. The sIA wall will therefore remodel when exposed to hemodynamic stress, unless the wall has lost the very cells capable of adaptive remodelling [16, 29]. This has two implications: (1) the structure and the viability of the cells in the sIA wall need to be known in order to understand how the mechanical stress values obtained from the CFD models will affect the sIA wall and rupture risk, and (2) when comparing CFD results of ruptured and unruptured sIAs, it cannot be determined whether wall rupture was caused by the kind of hemodynamic stress observed at the time of the study, or by exposure to a very different hemodynamic environment at an earlier stage during the development of the aneurysm. The observation that many ruptured sIA walls lack the endothelial cells [19, 20] that are sensitive to WSS, suggests that if WSS can really trigger sIA wall degeneration and eventual rupture, it occurs sometime before rupture. At the time of rupture, the aneurysm geometry may have changed so that the WSS at the rupture site is very different from the one that triggered the degeneration. Longitudinal follow-up studies with CFD models of hemodynamic stress during different stages of sIA development are crucial for learning what kind of hemodynamic stress leads to sIA rupture.

What Needs to Be Done to Turn CFD into a Useful Diagnostic Tool for the Detection of sIA Rupture-Risk?

Before hemodynamic variables can be used as diagnostic tools for predicting rupture-risk, the causality between those hemodynamic variables and wall rupture needs to be established. In addition, the pathophysiology of how hemodynamic stress leads to wall degeneration needs to be understood. Studies that collect follow-up data of the evolution of unruptured sIAs after hemodynamic stress in the aneurysm were determined with CFD or other methods, can provide us with knowledge about which hemodynamic stress parameters will predispose to wall degeneration and rupture. Studies that associate hemodynamic stress and sIA wall structure determined by a histological sample, by MRI, or by some other method, can provide us with information on how hemodynamic stress interacts with sIA wall remodelling. Animal models will probably be needed to complement patient-derived data and establish causality, simply because of the difficulty of designing a safe patient follow-up study that collects the data on aneurysm hemodynamics and wall structure at different times. Case-control type comparisons

of ruptured and unruptured sIAs with CFD alone are not enough, as demonstrated by the contradictory results in the literature (Table 1).

In addition to longitudinal studies and studies that determine sIA wall structure in addition to CFD, standardization of the CFD protocols and ranges of values used for boundary conditions (e.g., blood viscosity and whether blood is considered a Newtonian or non-Newtonian fluid) is necessary to reduce confusion. This should be performed by the biomechanical engineering community working with sIAs. The optimal way to determine a range of proper values for those boundary conditions that are physiological variables would be to measure them from a large enough population of sIA patients. This would be particularly useful for the mechanical properties of the aneurysm wall, since little data on it exists in the literature; from histological studies we know that sIA wall structure is very heterogenous – and therefore great variation will also be found in the mechanical properties. Knowledge of the mechanical properties of the sIA wall would enable accurate computational modelling of wall tension, the most important variable of mechanical stress to determine the risk of wall rupture.

Conclusions

Hemodynamic stress affects the cerebral artery and aneurysm wall, predisposes to sIA formation, and might predispose to sIA rupture. Hemodynamic stress in sIAs can be determined non-invasively with CFD, and studies using CFD have already shown differences in the hemodynamics of ruptured and unruptured sIAs. For the time being, CFD should, however, be considered to be a research tool and not a diagnostic tool to be used in the clinical setting. If further research will establish causality and determine how exposure to aberrant hemodynamic stress causes the degenerative remodelling that eventually leads to sIA rupture, CFD will then have the potential to become a diagnostic tool that is able to determine aneurysm-specific rupture-risk and to contribute significantly to the personalized risk assessment that will guide treatment decisions.

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Conflict of Interest The author declares that he has no conflict of interest.

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Cerebral Revascularization for Ischemia and Moya-Moya Disease

Reconsideration of Hemodynamic Cerebral Ischemia Using Recent PET/SPECT Studies

Jyoji Nakagawara

Abstract Hemodynamic cerebral ischemia has been conceptually confirmed by positron emission tomography (PET) imaging, and misery perfusion could be compensated with both vascular and metabolic reserve; however, these compensatory reserve capacities do not always respond in the same manner from short-term to long-term compromise of hemodynamic cerebral ischemia.

In patients with acute misery perfusion, $CMRO_2$ is immediately compensated by a marked increase of OEF combined with a limited increase of CBV. In patients with chronic misery perfusion, a moderate increase of OEF is compatible with a moderate increase of CBV, which could correlate with a moderate decrease of vascular reserve (VR). In moyamoya disease with long-standing misery perfusion, hemodynamic cerebral ischemia is initially compensated with a great deal of vasodilation, and can then be followed with an increased OEF in response to the degree of progression.

The stage of hemodynamic cerebral ischemia has been defined by an increase of OEF, but could be reconsidered from different patterns of the engagement of compensatory reserve capacities, and misery perfusion could be classified into three subtypes, such as acute, chronic, and long-standing misery perfusion.

Keywords Hemodynamic cerebral ischemia • Misery perfusion • Vascular reserve • Metabolic reserve • PET • SPECT

Introduction

Hemodynamic cerebral ischemia [1] has been conceptually confirmed by positron emission tomography (PET) imaging, and its classical stages are shown in Fig. 1. In Stage II ischemia (misery perfusion [2, 3]), decreased cerebral perfusion pressure (CPP) results in the reduction of cerebral blood flow (CBF) due to loss of vascular reserve based on reactive vasodilatory response, but the cerebral metabolic rate of oxygen ($CMRO_2$) is maintained with the elevation of oxygen extraction fraction (OEF) that indicates metabolic reserve [4]. Thus, misery perfusion could be compensated with both vascular and metabolic reserve; however, these compensatory reserve capacities do not always respond in the same manner from short-term to long-term compromise of hemodynamic cerebral ischemia.

In this article we reconsider classifying misery perfusion [2, 3] into acute, chronic, and long-standing subtypes and clarify the differences of compensatory reserve capacities in these three subtypes, using recent PET/SPECT studies.

Recent PET Studies

PET with inhalation of ^{15}O-tracers provides essential information, such as CBF, OEF, and $CMRO_2$, for clarifying the stage of hemodynamic cerebral ischemia in patients with ischemic stroke. We have already established a technique for calculating all functional images only from a single dynamic PET scan during the sequential administration of $H_2{}^{15}O$ and $^{15}O_2$ using the dual-tracer autoradiography (DARG) approach [5]. Recently, the technique was developed up until the dual basis function method (DBFM) as an extension of the previous DARG approach, without an additional $C^{15}O$ scan for compensating cerebral blood volume (CBV) [6]. The DBFM method enables the accurate assessment of CBF and $CMRO_2$ without losing accuracy or statistical certainties within a significantly shortened examination period (<10 min), in

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J. Nakagawara, MD, PhD
Department of Neurosurgery, Integrative Stroke Imaging Center, National Cerebral and Cardiovascular Center,
5-7-1, Fujishiro-dai, Suita, Osaka 565-8565, Japan
e-mail: george@ncvc.go.jp

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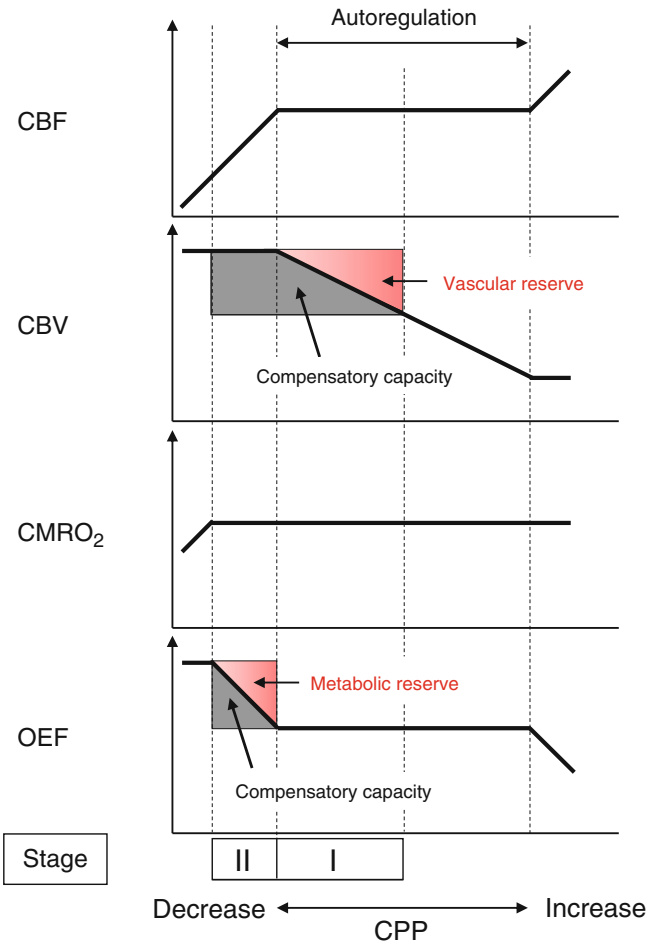


Fig. 1 Stages of hemodynamic cerebral ischemia (concept): in Stage II ischemia (misery perfusion), decreased CPP results in reduction of CBF due to loss of vascular reserve, but $CMRO_2$ is maintained with the elevation of oxygen extraction fraction (OEF), which indicates metabolic reserve

clinical settings. The information on CBV was also obtained from independent short $C^{15}O$ scan on demand.

The PET scanner that we used was Biograph-mCT (Siemens, Knoxville, TN, USA), a hybrid CT/PET tomograph. Following a low-dose x-ray CT acquisition for attenuation coefficient map, a dynamic PET scan was carried out. The scanner provided tomographic PET images for 109 slices for an in-plane FOV diameter of 700 mm and an axial FOV of 218 mm [7]. The spatial resolution was 4.4 mm in full width at half maximum (FWHM) at the center of FOV.

Acute Misery Perfusion

Acute misery perfusion can be observed in progressing stroke due to hemodynamic etiology, and its clinical significance seems to warrant urgent intervention. A recent ^{15}O-gas PET study showed specific findings of acute misery perfusion thus: in the affected area, CBF was decreased to a critical flow level, and $CMRO_2$ was compensated by a marked increase of OEF, but a limited increase of cerebral blood volume (CBV) was observed because reactive vasodilatory response could be limited under the condition with the abrupt reduction of CPP. An ^{15}O-gas PET of a representative case is demonstrated in Fig. 2.

As a new concept, types of hemodynamic cerebral ischemia and its compensatory reserve capacities can be seen in parallel from the viewpoint of a therapeutic time window (TTW), which is shown in Fig. 3. In severe acute misery perfusion, an increase of OEF and limited increase of CBV could be observed as indicators as compensatory reserve capacities associated with critical reduction of CBF. With the abrupt reduction of CBF, $CMRO_2$ could be mainly compensated by a marked increase of OEF, which could be also seen in the ischemic penumbra [8, 9] without a significant increase of CBV.

Chronic Misery Perfusion

In chronic misery perfusion, which is hitherto seen in patients with occlusive disease of major cerebral arteries due to atherothrombosis, cerebral oxygen metabolism can be maintained by the elevation of OEF associated with significant reactive vasodilation, which is a significant increase of CBV. This concept was demonstrated in the classical stage of homodynamic cerebral ischemia (Fig. 1). The clinical significance of chronic misery perfusion could be a marker of recurrent stroke [10, 11]. A recent ^{15}O-gas PET study showed specific findings in chronic misery perfusion: in the affected area, CBF was decreased to a mild to moderate level, and $CMRO_2$ was compensated by a moderate increase of OEF. A moderate increase of CBV was also observed.

^{15}O-gas PET of a representative case is shown in Fig. 4. In patients with chronic misery perfusion, a moderate increase of OEF was compatible with a moderate increase of CBV, which could correlate with a moderate decrease of cerebrovascular reserve (CVR).

Chronic misery perfusion could be equivalent to Stage II hemodynamic cerebral ischemia using quantified CBF-SPECT such as the ^{123}I-Iodoamphetamine (IMP)-Autoradiography (ARG) method [12]. Stage II ischemia is defined by both a resting CBF of less than 80 % of the normal mean CBF and CVR (which are calculated from (DIAMOX-activated CBF/resting CBF – 1) × 100 %), less than 10 % [13]. Imaging of Stage II ischemia using SPECT could be a surrogate marker correlated with stroke recurrence [14, 15]. Figure 5 shows a principle of Dual Table ARG (DTARG) for IMP-SPECT, which could provide a

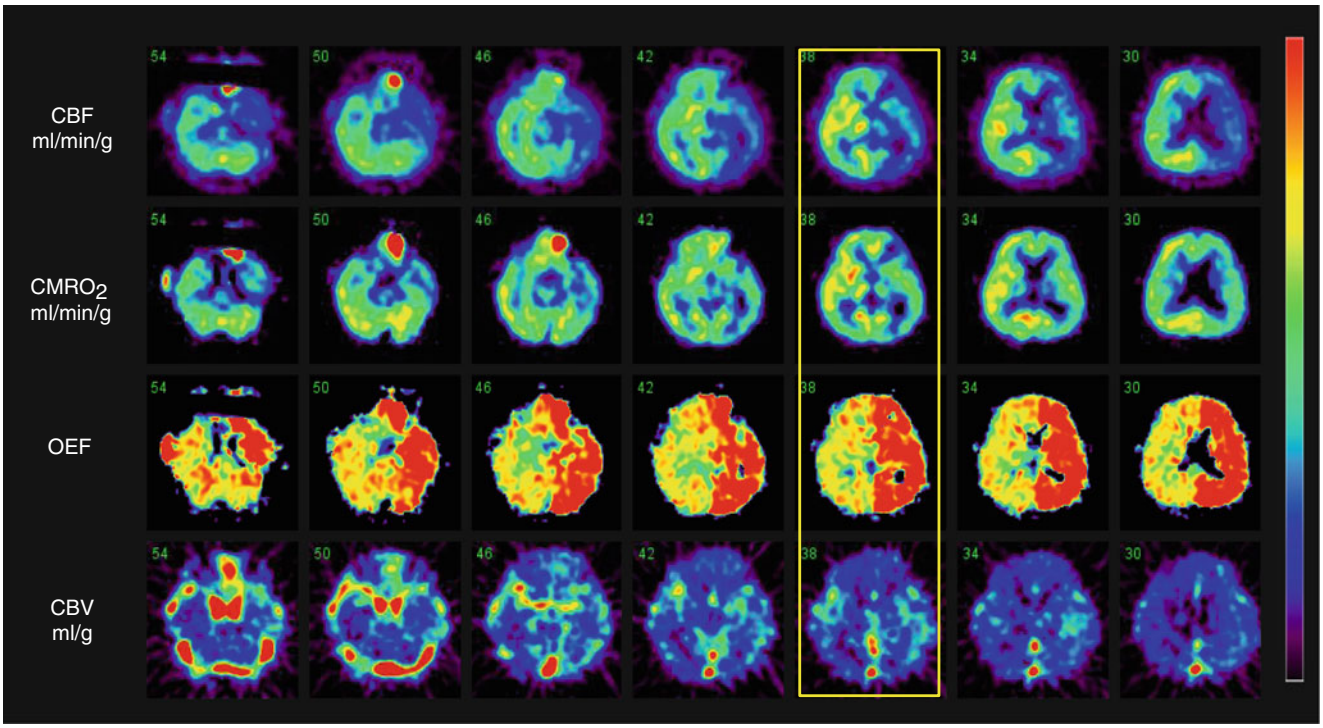


Fig. 2 ^{15}O-gas PET of acute misery perfusion: this 61-year-old male suffered from right hemiplegia in progression. MRA on admission showed occlusion of the left common carotid artery. MRI demonstrated progression of infarction in the left centrum semiovale. ^{15}O-gas PET on day 21 showed a marked decrease of CBF, mild decrease of $CMRO_2$, marked increase of OEF, and limited increase of CBV in the left cerebral hemisphere. Surgical revascularization should have been performed within the first week from stroke onset

1-day protocol of both resting and DIAMOX-activated CBF quantification [16]. Using a split dose of IMP and common arterial input function, an accurate CVR can be obtained. In DTARG, resting CBF was quantified by the conventional IMP-ARG method using look-up table method using 1st table (resting table) for each pixel (Fig 5). Then, DIAMOX-activated CBF was quantified by look-up table method using second table (consisting of resting and DIAMOX-activated tables: dual table), which started from each pixel value at the end of the first SPECT imaging (Fig 5). The accuracy of CVR measurement using SPECT was an important issue in the Japanese EC-IC Bypass trial (JET

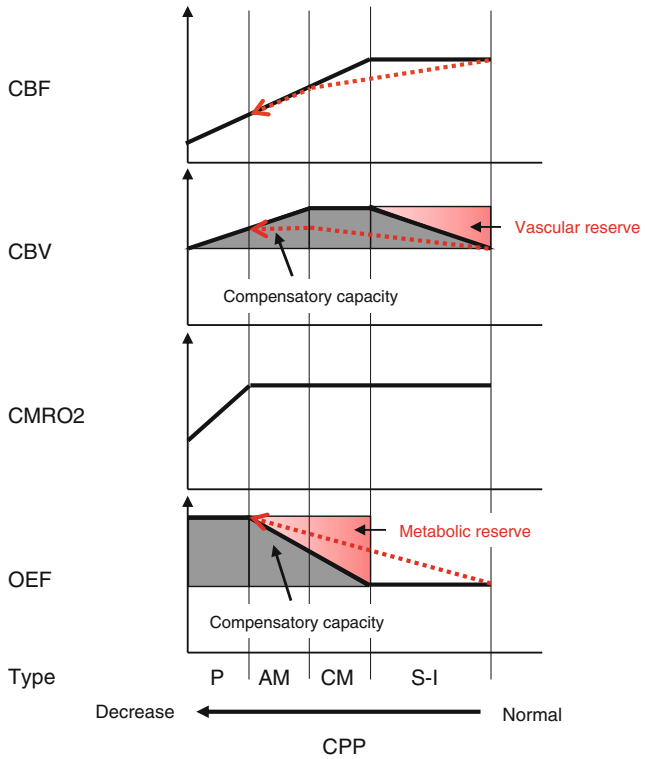


Fig. 3 Types of hemodynamic cerebral ischemia (concept) and acute misery perfusion: types of hemodynamic cerebral ischemia and its compensatory reserve capacities could be put in parallel from the point of view of a therapeutic time window (TTW). In severe acute misery perfusion, a greater increase of OEF and smaller increase of CBV can be observed as indicators of compensatory reserve capacities associated with a critical reduction of CBF. Under the abrupt reduction of CBF, $CMRO_2$ could be mainly compensated by a marked increase of OEF, which can also be seen in the ischemic penumbra without a significant increase of CBV. *P* penumbra, *AM* acute misery, *CM* chronic misery, *S-I* stage I ischemia

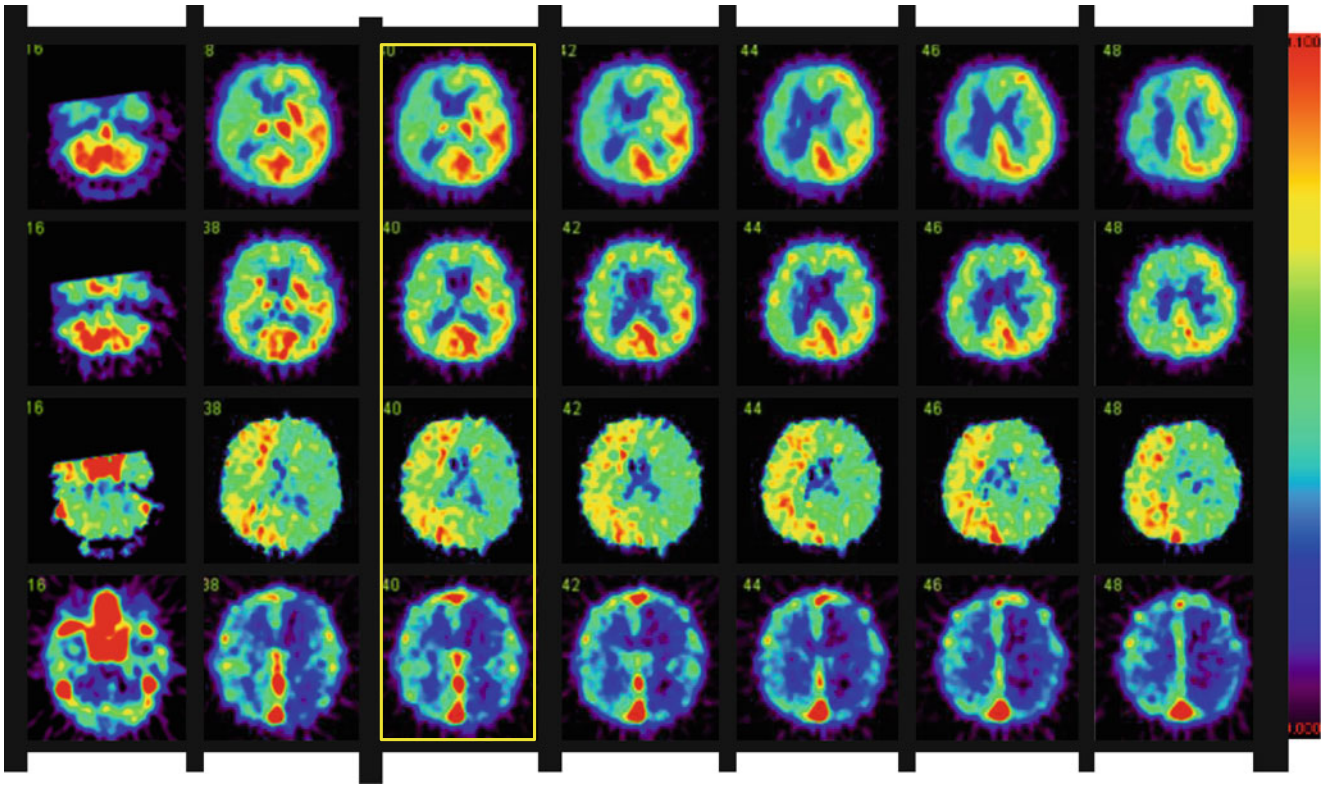


Fig. 4 ^{15}O-gas PET of chronic misery perfusion: this 76-year-old man suffered from TIA with left hemiparesis. CTA 2 days after TIA showed severe stenosis of the right carotid artery. MRI (Flair image) on the same day showed white matter infarction in the right centrum semiovale. ^{15}O-gas PET showed a moderate decrease of resting CBF, mild decrease of $CMRO_2$, moderate increase of OEF, and moderate increase of CBV in the right whole MCA territory

Study) [17]. In addition, stereotactic extraction estimation (SEE) JET analysis using a standardized brain surface template was developed to overcome the limitation of past tomographic ROI assessment in quantified CBF-SPECT [18]. As an advanced application of SEE-JET analysis for a whole-brain cortex, resting CBF, DIAMOX-activated CBF, cerebrovascular reserve, and stage of hemodynamic cerebral ischemia could be estimated pixel by pixel in each cortical vascular territory (Fig. 6). SEE-JET analysis of a representative case, as demonstrated in Fig. 4, is presented in Fig. 6. In patients with chronic misery perfusion, a moderate increase of OEF is compatible with a moderate increase of CBV, which could correlate with a moderate decrease of vascular reserve (Fig. 7).

Long-Standing Misery Perfusion

Long-standing misery perfusion is observed in moyamoya disease, and its clinical significance can also be a marker of recurrent stroke or TIA. In moyamoya disease, slowly-progressing occlusive changes initially occur in bilateral intracranial carotid bifurcation, and then fine cortical and perforating arteries are dilated and developed into moyamoya vessels that function as collateral vessels to directly and indirectly (via medullary vessels) connect with cortical arteries [19, 20]. Therefore, initial vessel dilation in moyamoya disease can be promoted by various mechanisms from compensatory vasodilation associated with the progression of hemodynamic cerebral ischemia.

This new concept was verified in recent PET/SPECT studies on moyamoya disease. The relationships between CVR-SPECT and OEF-PET, or CVR-SPECT and CBV-PET, were estimated in moyamoya disease. In Fig. 8 (*left*), a decrease of CVR-SPECT well correlated with an increase of OEF-PET, and a significant decrease (<0.1) of CVR-SPECT was found in a significant increase (+2SD<) of OEF-PET. However, a smaller decrease (0.1<) of CVR-SPECT was also found in a smaller increase (<+2SD) of OEF-PET. On the other hand, in Fig. 8 (*right*), a decrease of CVR-SPECT also correlated well with an increase of CBV-PET, but a smaller decrease (0.1<, <0.3) of CVR-SPECT was found in a significant increase (+2SD<) of CBV-PET, and significant decrease (<0.1) of CVR-SPECT was constantly indicated in an extreme increase of CBV-PET. These findings suggest that initial vessel dilation in moyamoya can cause a significant increase of CBV without a significant

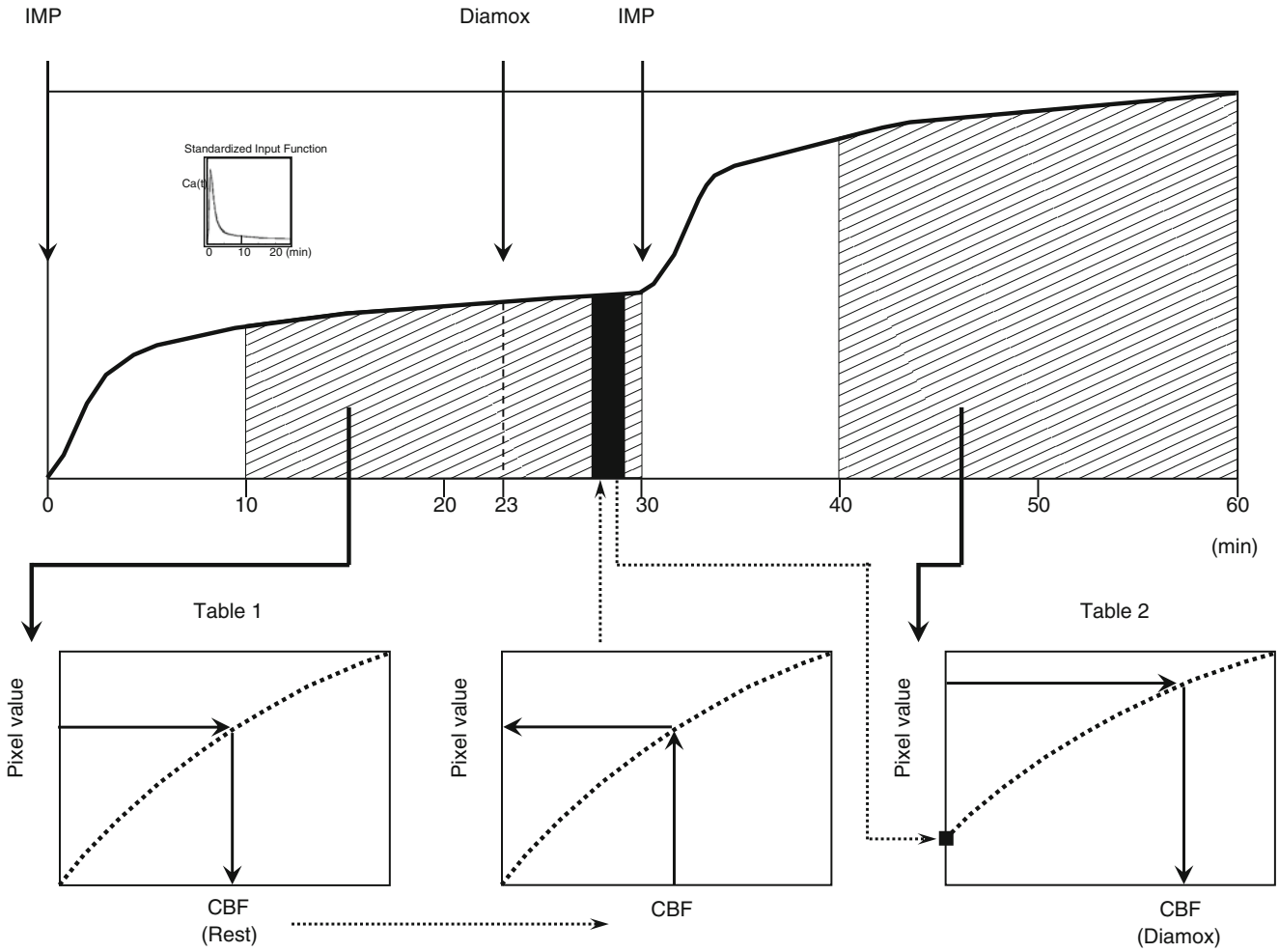


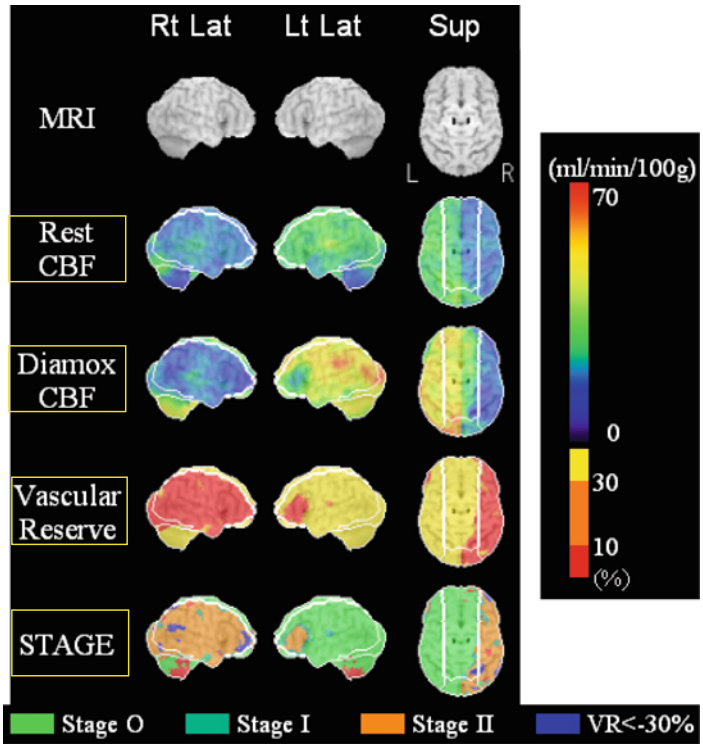
Fig. 5 Principle of dual table ARG: in resting CBF quantification, a relationship between pixel value of first SPECT and resting CBF is calculated based on a two-compartment model to make up table 1, and then first SPECT is transformed to resting CBF map pixel by a pixel using table look-up method in the same manner as the IMP-ARG method [12]. On the other hand, in acetazolamide-activated CBF quantification, the pixel value of the second SPECT is influenced by background radioactivity of the first tracer injection. Therefore, a relationship between the pixel value of the second SPECT and acetazolamide-activated CBF is calculated to make up table 2, which consists of both a resting table and an acetazolamide-activated table (dual table). The table 2 starts from pixel value calculated from resting CBF map and then the second SPECT is transformed to an acetazolamide-activated CBF map pixel by pixel, using the table-look up method

decrease of CVR and significant increase of OEF, and then the progression of hemodynamic cerebral ischemia could cause a further increase of CBV with a significant decrease of CVR and final increase of OEF.

In moyamoya disease with long-standing misery perfusion, hemodynamic cerebral ischemia was initially compensated with large amounts of vasodilation (marked increase of CBV) and then could be followed by a mild to moderate increase of OEF in response to the degree of progression. SEE-JET analysis of DTARG and ^{15}O-gas PET of a representative case is demonstrated in Figs. 9 and 10. In moyamoya disease with long-standing misery perfusion, hemodynamic cerebral ischemia is initially compensated with large quantities of vasodilation and then an increased OEF in response to the degree of progression (Fig. 11).

Compensatory Reserve Capacities in Different Types of Cerebral Ischemia

In this article, different types of hemodynamic cerebral ischemia were estimated using recent PET/SPECT studies, and classical stage hemodynamic cerebral ischemia was reconsidered from the point of view of a therapeutic time window (TTW). In particular, compensatory reserve capacities can respond differently in a different type of cerebral ischemia (Fig. 12). In penumbra, a maximal increase of OEF occurs in response to metabolic demand, but no significant increase of CBV fails to maintain cerebral circulation; the therapeutic time window (TTW) is extremely limited to several hours from stroke onset. In acute misery perfusion, a marked increase of OEF and limited increase of CBV can maintain a



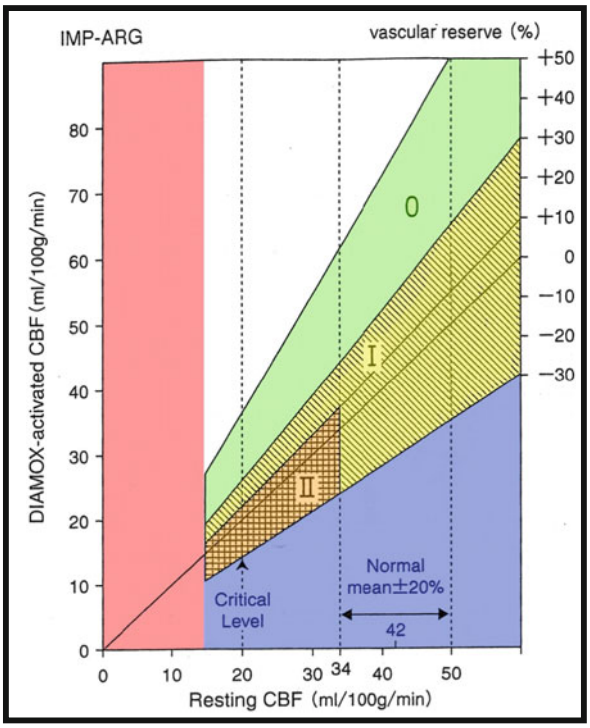


Fig. 6 Stereotactic extraction estimation (SEE) JET analysis and stratification of hemodynamic cerebral ischemia using quantified CBF-SPECT: SEE-JET analysis using standardized brain surface template and DTARG for patient in Fig. 4 showed a moderate decrease of resting CBF, no increase of DIAMOX-activated CBF, loss of vascular reserve, and Stage II ischemia in the right whole MCA territory. Stratification of hemodynamic cerebral ischemia using quantified CBF-SPECT was defined as follows: Stage 0: cerebrovascular reserve: normal (30 % ≤). Stage I: cerebrovascular reserve: reduction (10 %<, <30 %), or cerebrovascular reserve: reduction (≤10 %) and resting CBF within normal range (80 % of normal mean<). Stage II: cerebrovascular reserve: loss (≤10 %) and resting CBF: reduction (≤80 % of normal mean) (slope of oblique line corresponds to cerebrovascular reserve)

critical level of cerebral circulation and oxygen metabolism, so the TTW is limited to several days from onset. In chronic misery perfusion, a moderate increase in both OEF and CBV can maintain Stage II ischemia and the TTW can be opened to several months from the onset. In long-standing misery perfusion, a marked increase of CBV and mild increase of OEF can maintain hemodynamic ischemia, so the TTW can be opened to several years from the onset.

Therefore, in homodynamic cerebral ischemia, CBV-PET, which reflects compensatory vasodilation, could be a measure of endurable reserve, and OEF-PET, which indicates metabolic compensation, might be a measure of instantaneous reserve. Homodynamic cerebral ischemia could be reconsidered from different patterns of the engagement of compensatory reserve capacities and misery perfusion could be classified into three subtypes: acute, chronic, and long-standing misery perfusion.

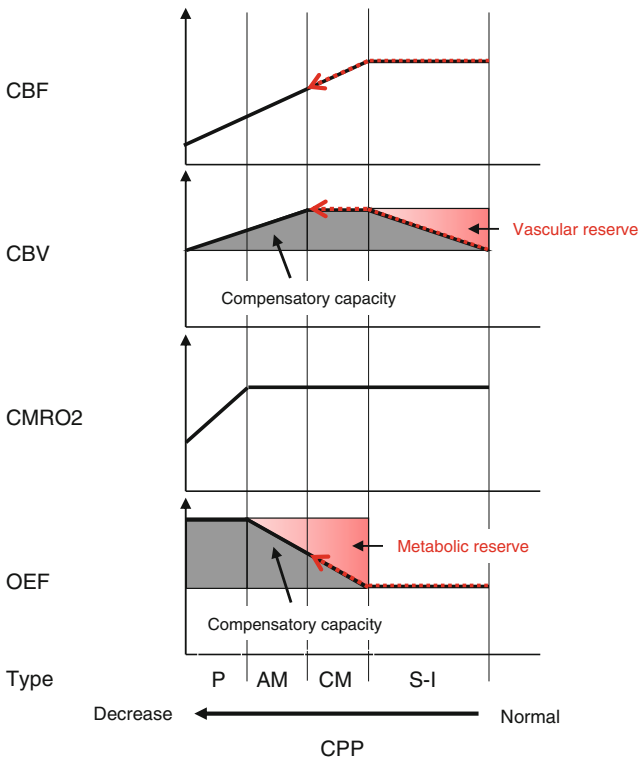


Fig. 7 Types of hemodynamic cerebral ischemia (concept) and chronic misery perfusion: in patients with chronic misery perfusion, a moderate increase of OEF is compatible with a moderate increase of CBV, which could correlate with moderate decrease of vascular reserve. *P* penumbra, *AM* acute misery, *CM* chronic misery, *S-I* stage I ischemia

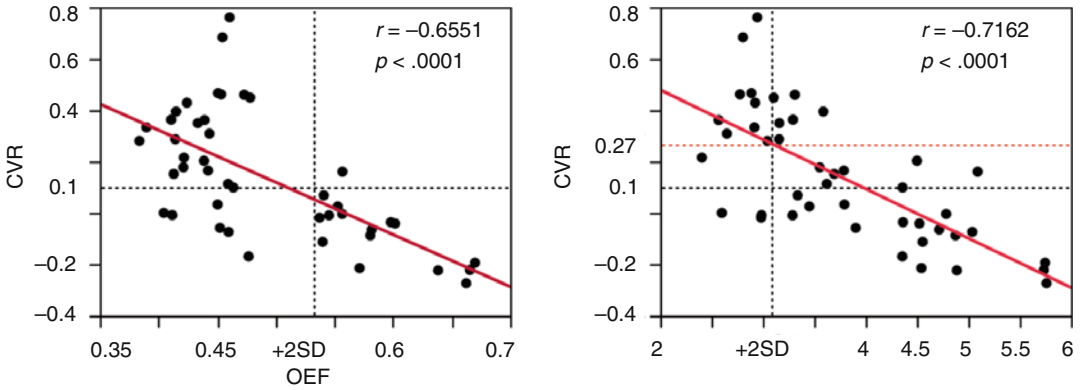


Fig. 8 Regression analysis of relationships between CVR-SPECT and OEF-PET, or CBV-PET in moyamoya disease: decrease of CVR-SPECT correlated well with an increase of OEF-PET, and a significant decrease (<0.1) of CVR-SPECT was found in a significant increase (+2SD<) of OEF-PET. But a smaller decrease (0.1<) of CVR-SPECT was also found in a smaller increase (<+2SD) of OEF-PET. On the other hand, a decrease of CVR-SPECT also correlated well with an increase of CBV-PET. However, a smaller decrease (0.1<, <0.3) of CVR-SPECT was found with a significant increase (+2SD<) of CBV-PET and a significant decrease (<0.1) of CVR-SPECT was constantly indicated in extreme increase of CBV-PET

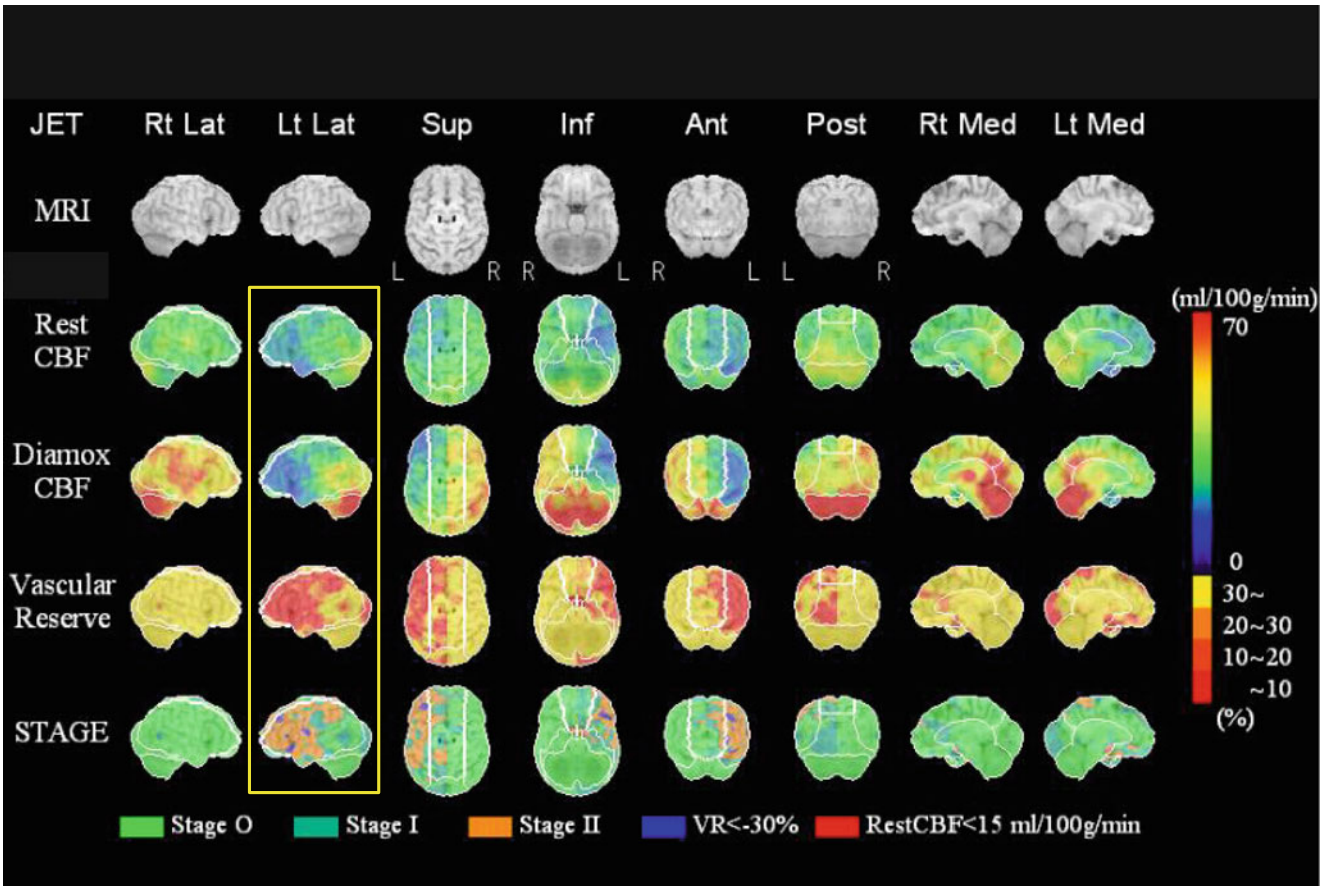


Fig. 9 SEE JET analysis using DTARG of long-standing misery perfusion: in this 55-year-old man, DSA for detail examination of his long-standing TIA episode over 10 years showed *left-sided* moyamoya disease. SEE JET analysis using DTARG showed moderate decrease of CBF, steal phenomenon of DIAMOX-activated CBF, marked decrease of vascular reserve, and Stage II ischemia in the left MCA territories

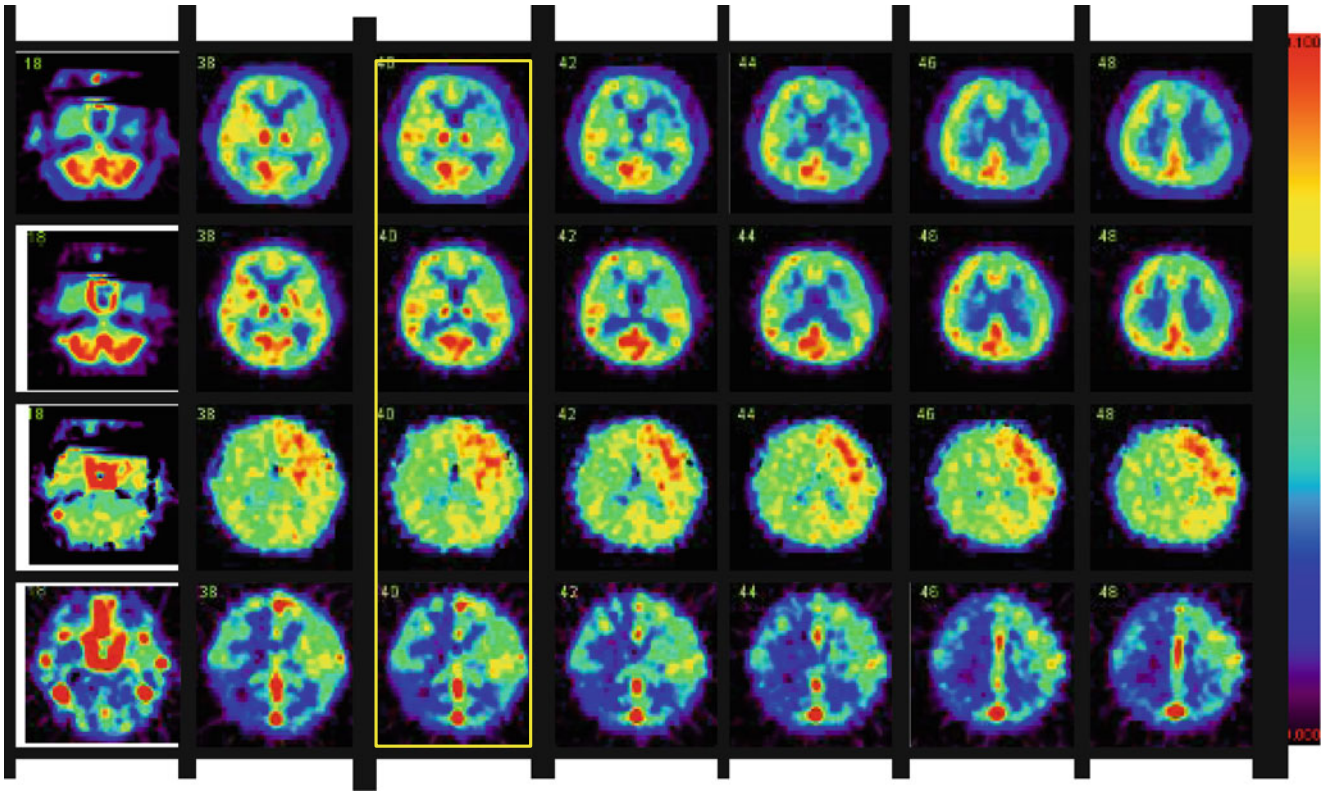


Fig. 10 ^{15}O-gas PET of long-standing misery perfusion: ^{15}O-gas PET for patient in Fig. 9 showed moderate decrease of CBF, mild decrease of $CMRO_2$, marked increase of both OEF and CBV in the left MCA territory

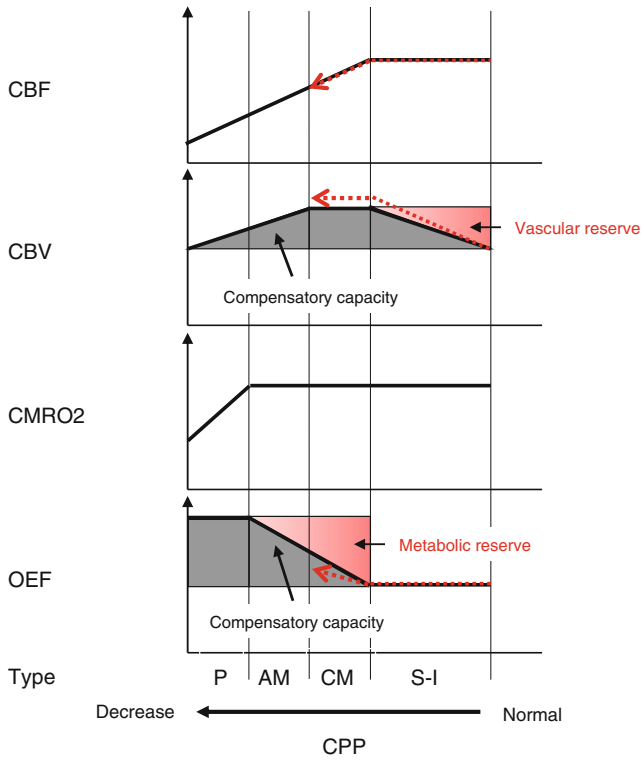


Fig. 11 Types of hemodynamic cerebral ischemia (concept) and long-standing misery perfusion: in moyamoya disease with long-standing misery perfusion, hemodynamic cerebral ischemia is initially compensated with a large amount of vasodilation and can then be followed with an increased OEF in response to the degree of progression. *P* penumbra, *AM* acute misery, *CM* chronic misery, *S-I* stage I ischemia

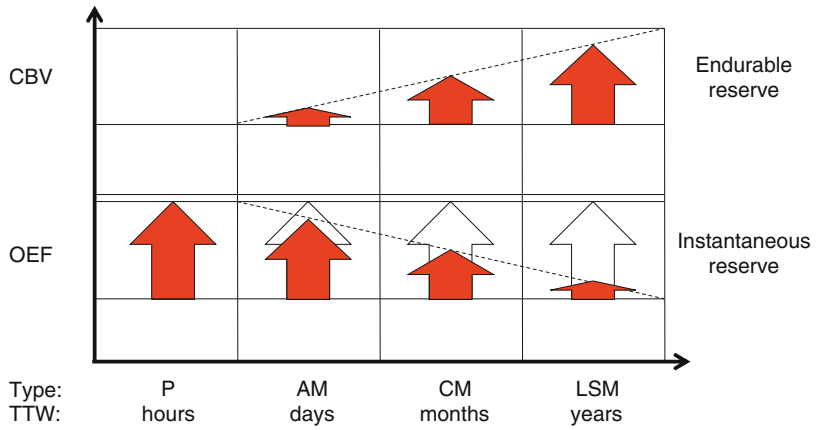


Fig. 12 Compensatory vascular and metabolic reserve in different types of cerebral ischemia and each therapeutic time window (TTW). In penumbra, maximal increase of OEF occurs in response to metabolic demand, but no significant increase of CBV fails to maintain cerebral circulation; TTW is very limited – to several hours from onset. In acute misery perfusion, a marked increase of OEF and limited increase of CBV can maintain critical levels of cerebral circulation and oxygen metabolism, so TTW is limited to several days. In chronic misery perfusion, when a moderate increase of both OEF and CBV can maintain Stage II ischemia, TTW could be opened to several months. In long-standing misery perfusion, a marked increase of CBV and mild increase of OEF can maintain hemodynamic ischemia, so TTW could be opened to several years. *P* penumbra, *AM* acute misery, *CM* chronic misery, *LSM* long-standing misery

Conclusions

In patients with acute misery perfusion, $CMRO_2$ is immediately compensated by a marked increase of OEF combined with a limited increase of CBV. In patients with chronic misery perfusion, a moderate increase of OEF is compatible with a moderate increase of CBV, which can correlate with a moderate decrease of vascular reserve (VR). In moyamoya disease with long-standing misery perfusion, hemodynamic cerebral ischemia is initially compensated with large amounts of vasodilation and can then be followed with an increased OEF in response to the degree of progression.

The stage of hemodynamic cerebral ischemia has been defined by an increase of OEF, but could be reconsidered from different patterns of the engagement of compensatory reserve capacities, and misery perfusion could be reclassified into 3 subtypes: acute, chronic, and long-standing misery perfusion.

Conflict of Interest Statement We confirm that we have no conflict of interest.

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Surgical Treatment of Carotid Artery Stenosis

Tetsuya Tsukahara

Abstract

Background and Purpose

The indications for carotid endarterectomy (CEA) and carotid artery stenting (CAS) have not been established. CEA is more appropriate than CAS if soft atherosclerotic plaques are included in the stenotic lesion, since such soft plaques are associated with a high incidence of ischemic complications during CAS. This report presents our surgical methods and the clinical results of CEA and CAS, and suggests an appropriate treatment strategy using plaque diagnosis, especially for high-risk patients.

Materials and Methods

From January 2001 until December 2013 we surgically treated carotid stenosis in 241 lesions by CEA, and 309 lesions by CAS. The average age of the patients was 70.5 in CEA and 71.4 in CAS. The symptomatic stenosis rate was 67 % and the average stenotic rate was 82 % in CEA; these were 61 % and 66 %, respectively, in CAS.

Results

Stenosis of carotid arteries was relieved in all cases after CEA or CAS. Peri-operative mortality with CEA and CAS was 0.4 % (1/241) and 0.3 % (1/309), respectively. Morbidity by ischemic stroke with CEA and CAS was 2.9 % (7/241) and 1.6 % (5/309), respectively. Surgical morbidity was not high in patients with medical risk factors.

Conclusions

Carotid stenotic lesions can be treated with comparably low morbidity and mortality rates using CEA and/or CAS even with high risks when appropriate surgical methods are selected, considering each characteristic of carotid stenosis using plaque diagnosis.

T. Tsukahara, MD, PhD
Department of Neurosurgery, National Hospital Organization, Kyoto Medical Center, 1-1 Mukaihata-cho, Fushimi-ku, Kyoto 612-8555, Japan
e-mail: ttsukaha@kyotolan.hosp.go.jp

Keywords Carotid endarterectomy (CEA) • Carotid artery stenting (CAS) • Plaque diagnosis

Introduction

The benefit of surgical intervention for severe carotid stenosis has been confirmed by randomized clinical trials (RCT) [5, 9]. Although there are now two surgical therapeutic methods, carotid endarterectomy (CEA) and carotid artery stenting (CAS), indications for CEA and CAS for cervical carotid stenosis, have not been fully established. CEA was considered the first choice of surgical treatment for severe carotid stenosis, especially with eccentric or tortuous lesions, and a narrow residual lumen with massive soft plaque. CAS was considered when CEA was believed to be high-risk because of the presence of one or more of the following: a contralateral ICA lesion, a distal carotid lesion, a cervical lesion higher than the C2 vertebral level, or medical risk factors, such as untreated coronary disease. The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial reported that the stroke-preventing effect was not significantly different between CEA and CAS in high-risk patients [14]. However, to achieve better clinical results, we have to select CEA or CAS, considering not only the patient's condition, but also the characteristics of carotid stenosis and plaque.

We preoperatively examined the characteristics of carotid plaque using carotid ultrasonography (US) and/or BB-MRI. With the combination of these methods, the character of the carotid plaque was clarified, with the diagnostic rate of soft plaque 79 % on carotid US, and 93 % on BB-MRI [1]. This report presents our surgical methods and clinical results of CEA and CAS, and suggests an appropriate treatment strategy, especially for high-risk patients.

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Materials and Methods

From January 2001 until December 2013, we surgically treated carotid stenosis in 241 lesions by CEA, and 309 lesions by CAS. The ages of the patients were not different between the CEA group and the CAS group; the average age was 70.5 in CEA and 71.4 in CAS. The symptomatic stenosis rate was 67 %, the average stenotic rate was 82 % in CEA, and these were 61 % and 66 %, respectively, in CAS (Table 1). Most of the symptomatic patients with severe and unstable plaque were treated by CEA. On the other hand, patients with milder carotid stenosis tended to receive CAS.

Table 1 Characteristics of patients

	CEA	CAS
Cases	241	309
Age (mean)	70.5	71.4
Sympt: asympt	67 %:33 %	61 %:39 %
Stenosis rate (mean)	82 %	66 %

Table 2 Medical risk factors

				CHD
(%)	HT	DM	DL	Untreated (%)
CEA	70	26	28	20/0
CAS	43	22	24	15/8

HT hypertension
DM diabetes mellitus
DL dislipidemia
CHD coronary heart disease

Medical risk factors of the patients are shown in Table 2. Hypertension was more complicated with the CEA group. All the patients who had untreated coronary disease were treated by CAS, not by CEA.

Procedures: CEA and CAS

CEA

CEA Protocol

Antiplatelet drugs are continued during the perioperative stage. CEA is performed with trans-nasal intubation under general anesthesia. The patient is placed in a supine position with head extension. Before skin incision, the level of the carotid bifurcation and the plaque is marked by US sonography. A linear skin incision is made along the anterior border of the sternocleidomastoid muscle (Fig. 1).

After the skin incision, the platisma is incised, and the dissection is continued along the anterior border of the sternocleidomastoid muscle. The common carotid artery is exposed medial to the internal jugular vein in the lower part of the incision, reflecting the descending hypoglossal nerve medially. Then a tape is placed around the artery; after this, we perform the operative procedure under a microscope.

The bifurcation of the common carotid artery is exposed. The carotid sinus is blocked with lidocaine chloride to prevent hypotension and bradycardia. To prevent embolic stroke, an IV bolus of heparin is applied to maintain an activated clotting time (ACT) over 200 s. For most of the

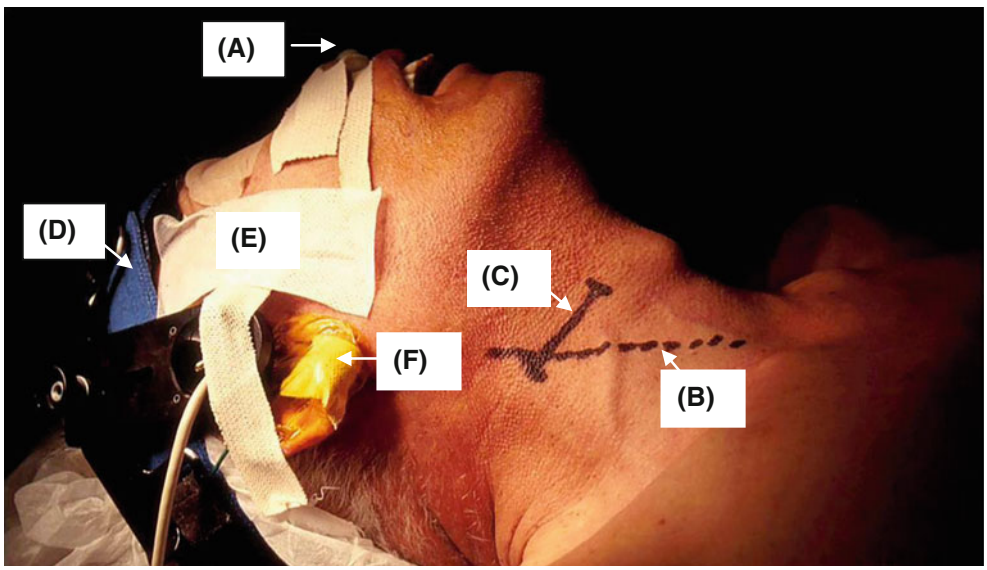

Fig. 1 Position of the patient and intra-operative monitors. Patient is placed in the supine position with trans-nasal intubation (*A*) and head extension. (*B*) The anterior border of sternocleido-mastoid muscle. (*C*) The level of the carotid bifurcation. (*D*) Sensor of INVOS. (*E*) TCD probe. (*F*) SEP electrode

patients, 3,000 units of heparin are first given, then 1,000 units are added when the ACT level is lower than 200 s.

The distal internal carotid artery is carefully exposed. Blunt dissection of the bifurcation and arteries from their posterior side tissue should be avoided. This manipulation sometimes induces stimulation of the carotid sinus, the dislodging of fragile plaques, and injury to the superior laryngeal nerve. The internal carotid artery needs to be dissected distally until we can see the normal arterial wall, since careful inspection enables us to know the sclerotic change of the internal carotid artery and distal end of the plaque. Vessel tape is placed at a more distal portion of the plaque, and tape is also placed around the external carotid artery.

We always estimate the risk of hemodynamic stroke during cross-clamping of the carotid arteries by monitoring CBF with INVOS. An aneurysm clip is placed at the distal portion of the internal carotid artery plaque. When INVOS shows a decrease of oxygen saturation SaO2 of more than 10 %, we consider using an internal shunt. The common carotid artery is occluded with an appropriate vascular clamp, being careful not to injure the vagal nerve.

A longitudinal incision is applied to the common and internal carotid arteries. Arteriotomy is then extended to both the proximal and distal ends of the plaque with Potts scissors. A dissector is used to separate the plane between the plaque and the outer arterial wall (Fig. 2). Usually, the intimal thickness extends proximally in the common carotid artery and we do not look for stenosis too proximally.

The plaque in the common carotid artery is then separated from the outer arterial wall by sharply cutting the inner wall with scissors. After the plaque at the carotid bifurcation has been separated from the lateral side of the arterial wall, the distal end of the plaque in the internal carotid artery is carefully dissected from the outer wall. When the distal end of the plaque is fully removed, there is a very clean dissection plane with a normal vascular intimal layer. Since the remaining piece of the plaque in the internal carotid artery may cause acute occlusion of the artery after CEA, care must be taken to remove the distally extended plaque along the lateral wall of the internal carotid artery. As the plaque is usually most adhesive to the outer layer on the medial side of the bifurcation, we dissect this portion of the plaque after cutting both the proximal and distal ends of the plaque. Then the plaque in the external carotid artery is removed *en bloc*. After irrigation of the arterial wall with heparinized saline, loose fragments adhering to the wall are grasped and pearled off from the inner wall with a fine forceps.

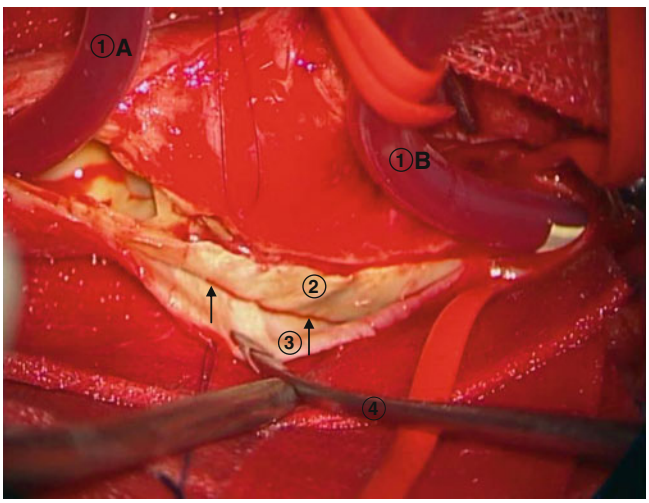

Fig. 2 Dissection of the plaque from the outer arterial wall. A dissector is used to separate the plaque clearly from the outer arterial wall (*arrow*). *1A* Internal shunt of the proximal side. *1B* Internal shunt of the distal side. *2* Plaque. *3* Outer arterial wall. *4* Dissector

The arteriotomy is closed with continuous GORE-TEX CV-7 sutures beginning at each end of the arteriotomy. Just before the sutures are tied, backflow is allowed from the internal, external, and common carotid arteries so that air and debris are flushed out of the arteries. Blood flow is reopened first into the external carotid artery to wash out any remaining debris in the external carotid artery (after having opened the common carotid artery), and then the internal carotid artery is reopened.

We usually do not reverse the intra-operative heparin. When hemostasis has been achieved, the incision is closed.

CEA: Special Technique for a Lesion in a High Position

When the carotid bifurcation is located high in the neck or the distal end of the plaque extends to the C2 vertebral level, the skin incision should be curved over the muscle posteriorly and toward the mastoid process. This procedure allows maximum exposure to the base of the skull and helps avoid injury to the mandibular branch of the facial nerve. After that, it may be necessary to retract the posterior belly of the digastric muscle. At the same time, the occipital artery may be divided (Fig. 3, arrows) and the descending hypoglossal nerve may be dissected to free the hypoglossal nerve medially (Fig. 3, arrow); then we can see the distal internal carotid artery.

Monitoring of CBF During CEA

For monitoring during CEA, we used EEG, the sensory-evoked potential (SEP), transcranial Doppler (TCD), and INVOS (Fig. 1), although we perform CEA with a single monitor of INVOS at present. EEG and SEP can comparably detect dysfunction of the cerebral hemisphere over a wide area – including ischemic event – although they cannot distinguish between embolic stroke and hemodynamic stroke. With TCD we can detect the flow of the middle cerebral artery and high intensity transient signal (HITs) during CEA [7]. However, the sensitivity of TCD is not sufficient to use it for CBF monitoring during CEA. Only INVOS can detect CBF changes in real time when the carotid artery is clamped during CEA, although it detects the changes of the CBF at comparably narrow areas of the frontal cortex (Fig. 4). Its sensitivity is almost one hundred percent [2].

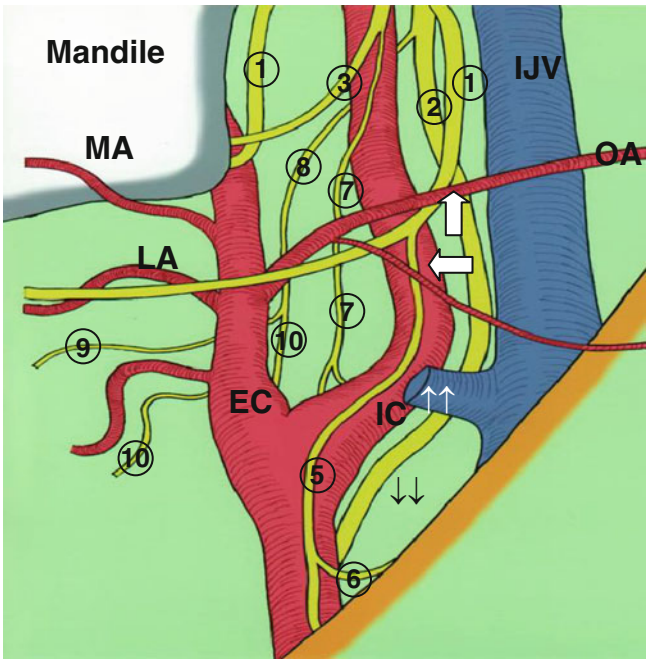

Fig. 3 Schematic drawing of the local anatomy. *1* Hypoglossal nerve. *2* Vagus nerve. *3* Glossopharyngeal nerve. *4* Marginal mandibular nerve (branch of facial nerve). *5* Descending hypoglossal nerve. *6* Ansa hypogrossal nerve. *7* Carotid sinus nerve. *8* Superior laryngeal nerve (branch of vagus nerve). *9* Internal laryngeal nerve. *10* External laryngeal nerve. *EC* external carotid artery, *IC* internal carotid artery, *IJV* internal jugular vein, *LA* lingual artery, *MA* maxillary artery, *OA* occipital artery, *SM* sternocleidomastoid muscle. *SMB* sternocleidomastoid branch of occipital artery, *SThA* superior thyroid artery. (⇦) Dissection of descending hypogrossal nerve. (⇧) Dissection of SMB

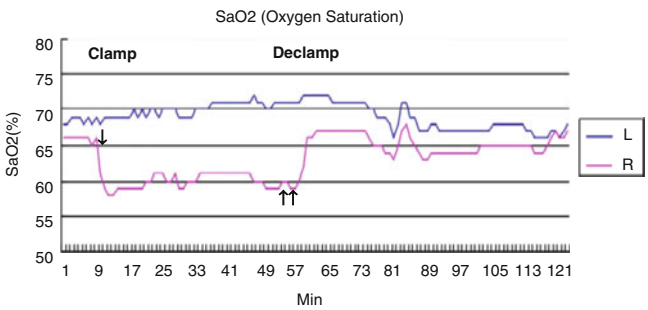

Fig. 4 A typical record of INVOS during CEA. Closing of right internal carotid artery induced a prompt decrease of SaO2 (Oxygen Saturation). (↓). After reopening of the arterial flow, SaO2 level was recovered promptly. (↑↑)

CAS

CAS Protocol

Dual antiplatelet drugs were administered for at least 1 week before treatment and then for 3 months after treatment, followed indefinitely by single or dual antiplatelet drug therapy. Intravenous heparin was administered intraprocedurally to achieve a target ACT of 300 s. CAS was performed under local anesthesia.

We routinely used transient balloon occlusion, and basically used a filter device. After activation of the EPD and evaluation of the plaque using an intravascular ultrasound (IVUS) console, a coaxial angioplasty balloon was used to pre-dilate the carotid lesion. The target lesion was pre-dilated with a balloon selected based on the distal ICA diameter ratio. Next, a self-expanding stent was deployed across the internal carotid stenosis. We mainly used the closed-cell stent, especially in cases with vulnerable plaque on BB-MRI and IVUS, considering the advantages of a closed-cell stent to provide a scaffold for fractured plaque and provide additional stabilization for the plaque. The lesion was post-dilated with a balloon with an ICA ratio of 0.8 to 1.0, if necessary.

Table 3 Surgical results

CEA			
Death;(renal failure, MOF)	1	0.4 %	(1/241)
Major stroke	3	1.2 %	(3/241)
Minor stroke	4	1.6 %	(4/241)
MI	0		
CAS			
Death; (blue toesyndrome, MOF)	1	0.3 %	(1/309)
Major stroke	5	1.6 %	(5/309)
Minor stroke	5	1.6 %	(5/309)
MI	1	0.3 %	(1/309)

MOF multi-organ failure
MI myocardial infarction

Surgical Results

Surgical results are summarized in Table 3. Stenosis of carotid arteries was relieved in all cases after CEA or CAS. Perioperative mortality with CEA and CAS was 0.4 % (1/241) and 0.3 % (1/309), respectively. Morbidity by ischemic stroke with CEA and CAS was 2.9 % (7/241) and 1.6 % (5/309), respectively. Surgical morbidity after CAS was not inferior to that after CEA, even in high-risk patients [9, 10].

Discussion

In Japan, the number of surgical interventions for carotid stenosis has increased by more than three or four times over the last 20 years in proportion to the increase in the number of patients with carotid stenosis. The Japanese Neurosurgical Society estimated that the number of surgical interventions

for carotid stenosis performed throughout Japan was 4,246 cases, including 2,395 cases of CEA and 1,851 cases of CAS in 2003, and 7,445 cases, including 2,839 cases of CEA and 4,606 cases of CAS in 2007, respectively. Twenty years ago, less than 2,000 patients received surgical treatment (CEA) for carotid stenosis. These changes in the situation can be explained by the fact that the development of endovascular treatment has overlapped with the period of increasing carotid stenotic lesions in Japan, and CAS has been widely accepted by the introduction of self-expandable stents and distal embolization blocking systems over the last 10 years. On the other hand, the Japanese Guidelines for the Management of Stroke 2004 and 2009 favored CEA over CAS for the treatment of symptomatic severe carotid stenosis. Thus, there is still some controversy regarding the indication for CEA or CAS for cervical carotid stenosis.

The SAPPHIRE trial was the first completed controlled, prospective, randomized trial in which CEA was compared with the state-of-the-art CAS with cerebral protection [14]. The SAPPHIRE trial only enrolled patients who were considered at high risk for CEA, such as octogenerians, those with carotid reoperation, cervical radiation, contralateral carotid occlusion, severe tandem lesion, high cervical lesion (at least C2), lesion below the clavicle, or contralateral laryngeal palsy. The SAPPHIRE trial reported that the perioperative risks of stroke (CAS, 3.1 %; CEA, 3.3 %) and mortality (CAS, 0.6 %; CEA 2.0 %) were similar; however, more patients suffered from postoperative myocardial infarction (MI) in the CEA group than in the CAS group.

A recent international RCT comparing CAS with CEA in patients with symptomatic carotid stenosis reported that the incidence of stroke, death, or procedural myocardial infarction was 8.5 % in the CAS group compared with 5.2 % in the CEA group [6]. The risks of any stroke and all-cause mortality were higher in the CAS group than in the CEA group. Another recent international RCT also reported the superior stroke-preventing effect of CEA over CAS [3].

Regarding the high medical risk, in our series of treatments we chose CAS for patients with untreated coronary disease. After the coronary disease was treated and stabilized, CEA did not induce MI in the perioperative period. Other high medical risks did not affect the clinical results [12, 13]. Regarding octogenarians, the age of our patients was not different between the groups of CEA and CAS. CEA can be performed safely for aged patients if they do not have other medical risk factors [13]. As for patients with carotid reoperation and cervical radiation, CAS is the first choice, since plaque in these patients sometimes adheres tightly to the medial layer, so it may be difficult to construct a smooth intraluminal wall with CEA.

We chose CAS for specific subgroups of patients, such as those with a distal ICA lesion and a higher-level lesion, for whom the beneficial effect of CEA is not apparent because of the complication rate. The mean cervical level of the lesion in Japanese patients is C3 or C4, and a number of patients have the lesion at the C2 vertebral level, which is at least one vertebral level higher than the lesions of European patients [11]. This situation sometimes complicates the operative procedure of CEA and causes more complications of lower cranial nerve palsy. Clinical outcomes of the patients with bilateral ICA lesions were not poorer when they received combination treatment using CEA and CAS; milder stenosis was first treated by CAS, and then severe stenosis of the contralateral side was treated by CEA [12]. The SAPPHIRE trial and other RCTs did not evaluate the character of the plaque or sclerotic lesion of the aorta and common carotid arteries, which have to be considered to achieve better clinical results [5, 6, 14].

Major ischemic complications of CEA are (1) embolic stroke in the perioperative stage, and (2) hemodynamic stroke during occlusion of the carotid arteries. The most important factor to prevent embolic stroke may be the surgical procedure itself. Precise and stable manipulation of the sclerotic arteries is essential. Although it is necessary to detect the precise dissecting layer and not to leave any plaque at the distal end of ICA, this procedure is sometimes complicated, especially when the lesion is located at a high cervical level [11]. The continuation of the antiplatelet drugs and full heparinization (ACT > 200 s) during cross-clamping of the arteries are also necessary for the prevention of embolic stroke.

For the prevention of hemodynamic stroke during cross-clamping of the arteries, brain protection and an internal shunt are effective. The prevention of excessive hypotension with brain-protective drugs, such as mannitol and propofol, are also effective.

We used an internal shunt in selected cases to prevent hemodynamic stroke. Since it sometimes increases the risk of embolic stroke when inserting a shunt into a distal ICA region, an internal shunt is used in selected cases after examining the cerebral blood flow during closure of the carotid arteries. The internal shunt maintains the brain perfusion pressure during clamping of the carotid arteries. However, on the other hand, it may sometimes increase the risk of embolic stroke by injuring the vessel wall when it is inserted into sclerotic arteries. The decision regarding the use of an internal shunt depends on the experience of the surgeons and clinics [10].

At present, there are three points of view regarding the use of an internal shunt, since its application is not directly linked with a decrease of surgical complications:

1. Using an internal shunt for all CEA cases (Group 1)
2. Not using an internal shunt for all CEA cases (Group 2)
3. Using an internal shunt for selective CEA cases when the closing of arteries induces marked decrease of cerebral blood flow (CBF) with intra-operative monitors (Group 3)

Nakajima et al reported that the complication rate of TIA was 3.5 % and cerebral infarction was 1.8 %, after CEA

without internal shunt (Group 2) when it was performed with medicinal brain protection. These complication rates were not different from those of CEA with an internal shunt (Group 1) or CEA with a selective shunt (Group 3) [8].

At our clinic, we use an internal shunt in selective cases (Group 3), monitoring CBF with INVOS. Since the application of an internal shunt depends on the decrease of CBF during the operation, CBF monitoring plays an important role.

A major complication of CAS is embolic stroke caused by dilatation of the stenotic lesion and plaque. Although the safety and durability of CAS have markedly improved, it is still not suitable for the treatment of soft plaque, eccentric or tortuous lesions, or a narrow residual lumen, as a major complication of CAS is embolic stroke caused by dilatation of the stenotic lesion and plaque. Since the recent developments of MRI and Doppler echography have enabled us to detect the characteristics of carotid plaque, we should select CAS or CEA according to the plaque characteristics. Other major complications of CAS involve embolic complications during the catheterization of eccentric and tortuous sclerotic arteries. We also encountered mortality as a result of catheterization complications, such as blue toe syndrome [13]. When comparing CAS with CEA, the risk of any neurological event is higher, particularly during catheterization and ballooning, despite the use of cerebral- protection devices [4]. We should therefore select CEA for severe carotid stenosis and tortuous lesions after studying the aortic arteries by 3-D CTA or DSA angiography.

Conclusions

Carotid stenotic lesions can be treated with relatively low morbidity and mortality rates using CEA or/and CAS, even for patients with high medical risks or bilateral carotid stenosis, when appropriate surgical methods are selected t the characteristics of the carotid plaque and other sclerotic lesions of each patient.

Conflict of Interest Statement I declare that I have no conflict of interest.

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Lateral Position of the External Carotid Artery: A Rare Variation to Be Recognized During Carotid Endarterectomy

Masaki Ito, Yoshimasa Niiya, Masashi Kojima, Hiroyuki Itosaka, Motoyuki Iwasaki, Ken Kazumata, Shoji Mabuchi, and Kiyohiro Houkin

Abstract

Background

External carotid artery (ECA) positioned laterally to the internal carotid artery (ICA) at the level of the common carotid artery (CCA) bifurcation is occasionally encountered during carotid endarterectomy (CEA). This study aimed to determine the frequency of this phenomenon and provide technical tips for performing CEA.

Methods

The study included 199 consecutive patients (209 carotid arteries) who underwent CEA at Otaru Municipal Medical Center in 2007–2014. The position of the ECA with respect to the ICA at the CCA bifurcation was preoperatively rated as either lateral or normal, using three-dimensional computerized tomographic angiography (3-D CTA) anteroposterior projections. Postoperative diffusion-weighted images (DWIs), and postoperative 3-D CTA images were reviewed.

Results

Among the 209 carotid arteries with atherosclerosis, 11 instances (5.3 %) of lateral position of the ECA were detected in 11 patients. Ten of these arteries (91 %) were right-sided (odds ratio 11.1; 95 % confidence interval 1.38–88.9). Wider longitudinal exposure of the arteries was used during CEA, and the CCA and ECA were rotated clockwise or counter clockwise. The ICA lying behind the ECA along the surgical access route was then pulled out laterally and moved to the shallow surgical field. Cross-clamping, arteriotomy, plaque removal, and wall suturing were performed as usual. No cerebral infarcts were detected on postoperative DWIs, and 3-D CTA revealed no CCA and ICA kinking.

Conclusions

Lateral position of the ECA is not extremely rare in patients undergoing CEA for atherosclerosis and may be a congenital variation, although this is still controversial. CEA can be performed safely if the arteries from the CCA to the ICA are rotated, and the ICA is moved to the shallow surgical field under wider longitudinal exposure. Although no postoperative cerebral infarcts were detected, the risk of artery-to-artery embolism resulting from artery repositioning prior to plaque removal should be taken into consideration.

Keywords Atherosclerosis • Carotid endarterectomy • Carotid artery • External carotid artery abnormalities • Variation

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M. Ito, MD, PhD (✉)
Department of Neurosurgery, Otaru General Hospital, Wakamatsu 1-1-1, Otaru 047-8550, Japan

Department of Neurosurgery, Hokkaido University Graduate School of Medicine, North 15, West 7, Kita-ku, Sapporo 060-8638, Japan
e-mail: masakiitou-nsu@umin.ac.jp

Y. Niiya, MD, PhD • H. Itosaka, MD, PhD • M. Iwasaki, MD, PhD • S. Mabuchi, MD, PhD
Department of Neurosurgery, Otaru General Hospital, Wakamatsu 1-1-1, Otaru 047-8550, Japan

M. Kojima
Department of Radiology, Otaru General Hospital, Wakamatsu 1-1-1, Otaru 047-8550, Japan

K. Kazumata, MD, PhD • K. Houkin, MD, PhD
Department of Neurosurgery, Hokkaido University Graduate School of Medicine, North 15, West 7, Kita-ku, Sapporo 060-8638, Japan

Introduction

A growing number of reports describe instances of anomalous origin, course, and branching of the internal carotid artery (ICA) and the external carotid artery (ECA) of the neck. In light of the importance of the regions supplied by these arteries, the anatomical variants of the carotid arteries are of considerable interest for several medical

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specialties, including neurosurgery, plastic surgery, otorhinolaryngology, ophthalmology, odontostomatology, and vascular surgery. Failure to detect these vascular anomalies preoperatively increases the risk of peri- and postoperative complications.

Atherosclerotic disease in the carotid arteries of the neck is a major cause of ischemic cerebrovascular events. Therefore, comprehensive knowledge of the vascular anatomy is essential for successful neurosurgical and neurovascular interventions associated with carotid artery pathology, including severe atherosclerotic luminal stenosis. A number of articles and textbooks are currently available that present a detailed description of the relevant vascular anatomy for surgeons performing carotid endarterectomy (CEA) [2, 3]. In particular, knowledge of the common variations and anomalies at the bifurcation of the ICA and ECA, including lateral positioning of the ECA, is considered essential for performing CEA safely. In general, the ECA is positioned medially to the ipsilateral ICA at the level of the common carotid artery (CCA) bifurcation. However, the ECA is occasionally positioned laterally to the ipsilateral ICA. Several unbiased diagnostic cerebral angiography studies conducted in Japan and the USA reported the incidence of this inversed configuration of the ECA and ICA to be within 4.3–12.3 %, and most cases were found to be unilateral [1, 8–10]. However, no reports have focused on CEA of the ECA in the lateral position. In this paper, we retrospectively reviewed the data of the patients with atherosclerotic carotid artery luminal stenosis who underwent CEA over the course of 7 years. The incidence of lateral positioning of the ECA was investigated, and technical notes are presented on the treatment of such cases.

Methods and Materials

Study Subjects

This study included 199 consecutive patients with atherosclerotic luminal stenosis and/or ulcer formation in the cervical portion of the ICA who underwent CEA between April 2007 and February 2014 at the Otaru Municipal Medical Center. CEA via the standard anterior sternocleidomastoid (SCM) approach [4] was generally considered appropriate for patients who experienced transient ischemic attack or minor completed stroke due to ipsilateral cervical carotid artery stenosis of >50 %, calculated according to the North American Symptomatic Carotid Endarterectomy Trial method from angiography data. CEA was also indicated for asymptomatic patients with severe carotid artery stenosis (>70 %). When bilateral CEA was required, the two procedures were performed at least 6 weeks apart, and the patient was examined by an otolaryngologist to ensure that no occult cranial nerve or vocal cord dysfunction was present before the second procedure. Three-dimensional computerized tomographic angiography (3-D CTA) was performed on all patients before and after the surgery, except for cases with planned renal replacement therapy because of severe reduction in glomerular filtration rate. A total of 209 carotid arteries treated with CEA were included in this study. We performed carotid artery stenting in about ten patients during the study period.

Protocol for 3-D CTA

All 3-D CTA procedures were performed using a 64-row multislice computed tomography scanner (Aquilion™ TSX-101A; Toshiba Medical Systems, Otawara, Japan). The scanogram included the area between the levels of the aortic arch and the atlas. A total volume of 50–80 mL of iopamidol (Iopamiron 370; Bayer Healthcare, Leverkusen, Germany), a low-osmolarity iodinated contrast material, was administered intravenously using a bolus tracking method via an 18- to 20-gauge catheter positioned in the antecubital vein. A trigger value of 150 Hounsfield units was set in the ascending aorta. The scanning parameters were 120 kV, 300–400 mA, speed: 1 s/cycle, field of view diameter: 240 mm, slice thickness: 0.5 mm, and slice interval: 0.5 mm. The post-processing was conducted using a workstation (Ziostation; Ziosoft, Tokyo, Japan) by an experienced radiology technician (M.K., third author), and 3-D multi-colored images were produced. Volume rendering and maximum-intensity projection were applied as post-processing techniques to aid evaluation.

Determination of the Position of the ECA and ICA at the CCA Bifurcation by 3-D CTA

The common carotid bifurcation and the courses of the ECA and ICA in the neck were clearly discernible in the post-processed 3-D CTA images in all cases. The position of the ECA with respect to the ICA at the CCA bifurcation was rated as either lateral or normal in the anteroposterior projections, as reported previously [9]. ECAs with equivocal positions were presumed to be normal. The degree of carotid bifurcation was measured using 3-D CTA anteroposterior projections with the above-mentioned workstation (Fig. 1). For the purposes of this study, the angle of carotid bifurcation was considered positive when the ECA was positioned

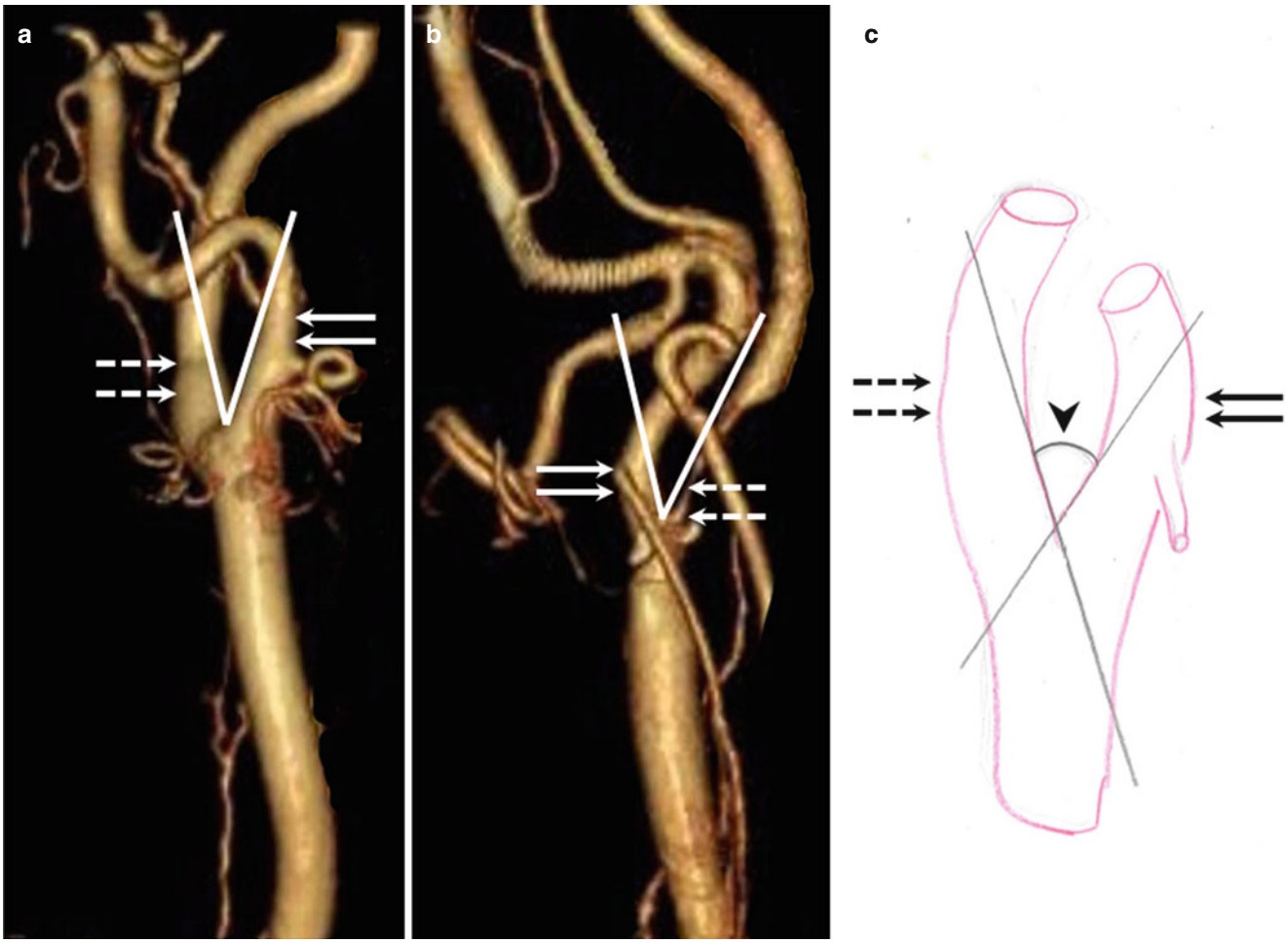

Fig. 1 Three-dimensional computerized tomographic angiography anteroposterior images of the right carotid artery in the neck. The degree of carotid bifurcation was considered positive when the external carotid artery (ECA) was positioned medially with respect to the internal carotid artery (ICA) (Panel **a**) and negative when the ECA was positioned laterally (Panel **b**). (Panel **c**) shows the carotid bifurcation angle (*arrowhead*), which was measured in this study. *Solid and dashed double arrows* indicate the ECA and the ICA arising from the common carotid artery, respectively

medially with respect to the ICA, whereas negative values corresponded to ECAs positioned laterally.

Surgical Procedure

General endotracheal anesthesia was induced after the patient was placed in the supine position. Non-invasive monitoring of the regional frontal lobe oxygenation state during the surgery was performed using near-infrared spectroscopy. Except for patients receiving dual or triple antiplatelet therapy, the dose of antiplatelet agents was not reduced preoperatively. The CCA and its bifurcation were exposed, using a standard approach reported elsewhere [7]. In brief, the head and neck were extended and rotated to the side contralateral to the surgical incision, as appropriate. A curvilinear skin incision along the anterior portion of the SCM muscle was made toward the mastoid tip. The skin and subcutaneous tissue were divided to the level of the platysma. Following sharp cutting of the platysma along the skin incision and proper retraction, the underlying connective tissue, including fat, was dissected to identify the anterior edge of the SCM muscle. The posterior margin of the parotid gland was meticulously dissected without damaging the parotid membrane, so that the anterior border of the SCM muscle was exposed as widely as the longitudinal operative window allowed. After the SCM muscle was retracted dorsally by hooks, dissection was performed in the mid-portion of the operative window until the internal jugular vein (iJV) was identified. Retracting the iJV dorsally permitted the exposure of the carotid sheath overlying the CCA, and the carotid sheath was dissected to expose the carotid artery. At this point, we

gently cut the sheath lineally along the CCA toward the ECA-ICA complex. A clockwise or counterclockwise rotation of the CCA and ECA-ICA was then performed by hitching up the underlying carotid sheath. Finally, the CCA and ICA were drawn out to the shallow surgical field. The completion of this process with satisfactory hemostasis allowed proceeding with the conventional steps, including arterial clamping, arteriotomy, three-way internal shunt tube insertion, meticulous dissection of the carotid plaque, and arteriotomy closure with a running suture under an operative microscope. A routine magnetic resonance imaging scan including diffusion-weighted imaging and magnetic resonance angiography was performed as part of routine postoperative imaging immediately after the surgery or at postoperative day 1. In cases with suspected or predicted postoperative hyperperfusion syndrome [5], single-photon emission computed tomography was performed to measure the regional cerebral blood flow. The surgical procedure is schematically illustrated in Fig. 2, which also shows representative 3-D CTA images before and after the surgery in a patient with lateral position of the ECA.

Analysis of Postoperative Changes in the Degree of Carotid Bifurcation and Surgical Complications

3-D CTA was repeated in all the enrolled patients between postoperative days 1 and 3 to visualize postoperative changes in the operated carotid artery. Pre- and postoperative anteroposterior 3-D CTA images were inspected for all the 209 carotid arteries to compare the degrees of carotid bifurcation. A surgical complication was defined as postoperative death, postoperative stroke, ipsilateral carotid occlusion or carotid artery stenosis of >50%, postoperative hyperperfusion syndrome, myocardial infarction, gastrointestinal bleeding, wound complication, or cranial nerve palsy that occurred within 1 week of the surgery.

Statistical Analysis

All continuous data were expressed as mean ± standard deviation. The 209 carotid arteries were divided into two groups (lateral or normal position of the ECA) according to preopera-

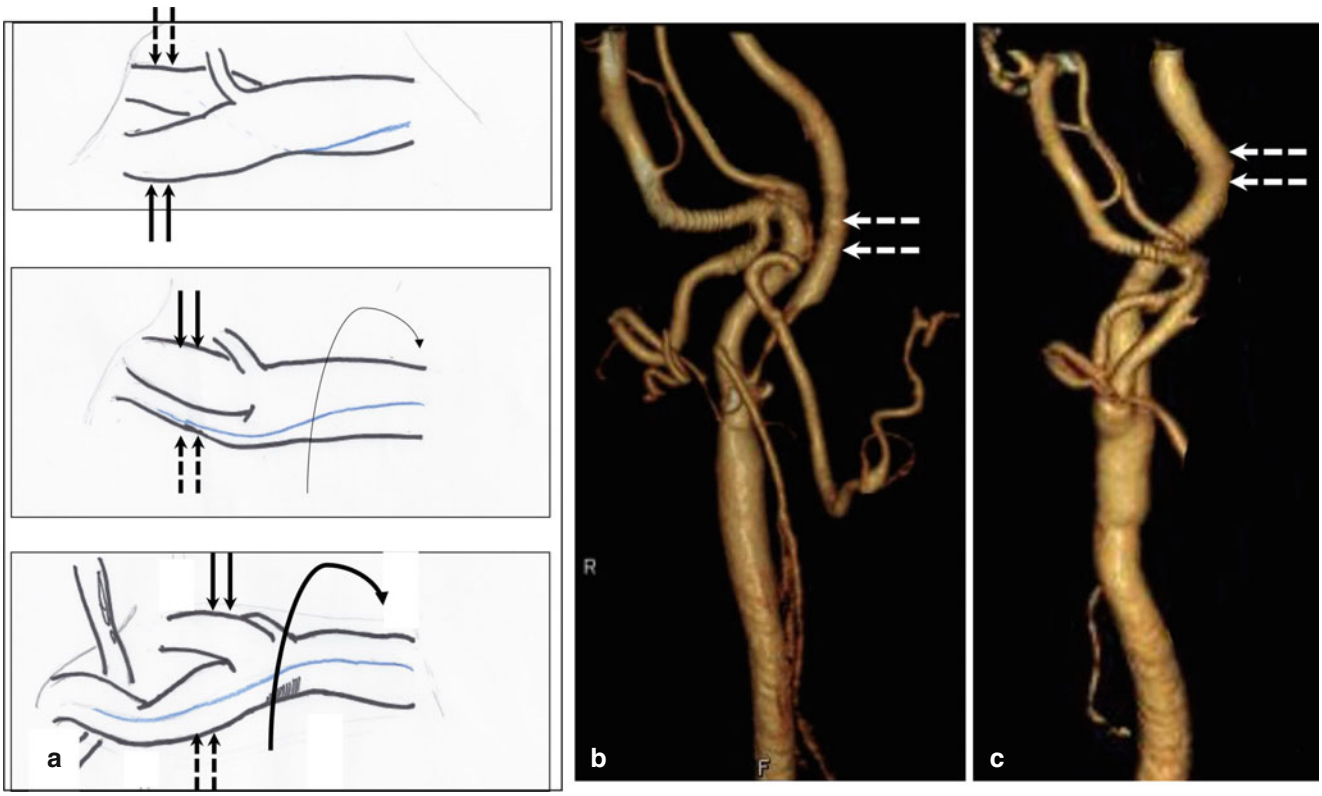

Fig. 2 A schematic illustration of the steps necessary to expose the right internal carotid artery (ICA). Initially, the ICA (*dashed double arrows*) and the proposed arteriotomy line (*blue*) lay behind the external carotid artery (ECA, *double arrows*) (Panel **a**, *top*). The right carotid artery was gently rotated clockwise along the common carotid artery (CCA) toward the ECA-ICA complex by hitching up the underlying carotid sheath (Panel **a**, *middle*). Finally, the CCA and ICA were drawn out to the shallow surgical field, and the proposed arteriotomy line on the ICA was exposed (Panel **a**, *bottom*). (Panels **b** and **c**) show representative anteroposterior three-dimensional computerized tomographic angiography images of the right carotid artery (*dashed double arrows* indicate the ICA) before and after carotid endarterectomy, respectively, in a 79-year-old man with lateral position of the ECA

tive 3-D CTA findings. Comparisons between the two groups were performed using Fisher's *t*-test and the Chi-square, or Fisher's probability test, as appropriate, for continuous and dichotomous variables, respectively. Multivariate logistic regression was used to calculate odds ratios (ORs) and 95 % confidence intervals (CIs) after controlling simultaneously for potential confounders. The continuous and dichotomous variables considered in the model were age and gender, side (right or left), and lesion characteristics (i.e., symptomatic or asymptomatic lesion; severe or moderate stenosis), respectively. The significance level was set at $P<0.05$. Statistical analyses were carried out with Excel (EXCEL-TOUKEI 2012[R], Social Survey Research Information Co., Ltd., Tokyo, Japan).

Results

Baseline Patient Characteristics

Of the 199 consecutive patients with atherosclerotic stenosis of the cervical portion of the ICA, 173 were men and 26 were women, with the mean age of 73.4 (range: 44–88). The baseline characteristics are summarized in Table 1. Unilateral CEA was performed in 189 patients (96 right side, 93 left side), and bilateral-staged CEA was performed in 10 patients. There were 97 patients with asymptomatic carotid stenosis.

Incidence of Lateral Position of the ECA and Characteristics Related to Atherosclerotic Carotid Stenosis

Eleven instances of lateral position of the ECA were observed in 11 patients with atherosclerotic carotid stenosis who underwent CEA over 7 years (5.3 % of the carotid arteries and 5.5 % of the patients). Clinical summaries of these patients before and after CEA are given in Table 2. We compared potential confounding factors between laterally and normally positioned ECAs (106 right and 103 left carotid arteries). As shown in Table 3, lateral positioning of the ECA was much more common for the right-side carotid artery than for the left (right, 10 of the 11 carotid arteries; left, 1 carotid artery) when compared with normal positioning of the ECA (right, 96 of the 198 carotid arteries; left, 102 carotid arteries). Thus, lateral positioning of the ECA was observed much more frequently on the right side than on the left (90.9 % and 48.5 % of laterally and normally positioned ECAs were located on the right, respectively; OR 11.1; 95 % CI 1.38–88.9; $P=0.024$); there were no patients with laterally positioned ECAs on both sides. Atherosclerosis-related factors such as age, gender, and lesion characteristics (i.e., symptomatic lesion and severe carotid stenosis) were not associated with the incidence of lateral position of the ECA.

Postoperative Changes and Surgical Complications After CEA

Preoperatively, the degree of carotid bifurcation was significantly different between the groups with lateral and normal positioning of the ECA when the position of the ECA with respect to the ICA at the CCA bifurcation was rated in the 3-D CTA anteroposterior projections ($-21\pm9.5°$ and $9.5\pm9.2°$, $P<0.001$). The postoperative angles were $-12\pm10°$ and $9.6\pm9.1°$ in these two groups, respectively. The postoperative change of the degree of bifurcation was significant in the group with lateral positioning of the ECA ($9.7\pm11°$, $P=0.02$), but not in the normal group ($0.1\pm7.0°$, $P=0.88$).Surgical results can be summarized as follows: Carotid stenosis was corrected in all the 209 treated carotid arteries. In the group with lateral positioning of the ECA,

Table 1 Baseline characteristics of the enrolled patient

		Unilateral operation		Bilateral operation
	All	Right side CEA	Left side CEA	Staged CEA
Valuable	($n=199$)	($n=96$)	($n=93$)	($n=10$)
Age, y, ± SD	73 ± 7.5	73 ± 8.1	73 ± 7.1	74 ± 5.1
Male gender, *n* (%)	173 (86.9)	86 (89.6)	79 (84.9)	8 (80.0)
Asymptomatic case, *n* (%)	97 (48.7)	46 (47.9)	47 (50.5)	4 (40.0)
Hypertension, *n* (%)	159 (79.9)	80 (83.3)	69 (74.2)	10 (100)
Dyslipidemia, *n* (%)	83 (41.7)	36 (37.5)	43 (46.2)	4 (40.0)
Diabetes mellitus, *n* (%)	59 (29.6)	26 (27.1)	30 (32.3)	3 (30.0)
Ischemic heart disease, *n* (%)	71 (35.7)	28 (29.2)	38 (40.9)	5 (50.0)
Lateral position of ECA, *n* (%)	11 (5.5)	6 (5.9)	5 (5.2)	0

CEA carotid endarterectomy, *SD* standard deviation, *ECA* external carotid artery

Table 2 Clinical data in patients with the lateral position of external carotid artery before and after carotid endarterectomy

Age, y / gender	Side	Clinical diagnosis	NASCET criteria	Degree of carotid bifurcation		Complication	
				Before CEA	After CEA	Postoperative stroke	Others
58/M	Right	Cerebral infarct	Severe	−2.4	1.3	None	None
71/F	Right	Asymptomatic CS	Moderate	−16.8	−5.3	None	None
72/M	Right	Cerebral infarct	Severe	−21.1	−13.4	None	None
73/M	Right	TIA	Moderate	−23.8	−23.6	None	None
78/M	Right	TIA	Moderate	−34.9	0	None	Periauricular numbness
79/M	Right	Cerebral infarct	Severe	−25	−13.8	None	hyperperfusion syndrome
79/M	Right	Cerebral infarct	Severe	−21.4	0	None	None
80/F	Right	Asymptomatic CS	Severe	−11.6	−14.3	None	None
74/M	Right	Asymptomatic CS	Moderate	−14.8	−11.4	None	None
77/M	Right	Asymptomatic CS	Severe	−30.81	−13.76	None	None
72/M	Left	Asymptomatic CS	Moderate	−30.67	−31.96	None	None

M male, *F* female, *CS* carotid stenosis, *TIA* transient ischemic attack, *CEA* carotid endarterectomy

Table 3 Relationship between lateral position of the external carotid artery and potential co-founders in atherosclrerotic carotid stenosis

	Lateral position of ECA		Univariate analysis	Logistic regression analysis	
	Yes	No	*P* value	*P* value	OR (95 % CI)
No. of carotid artery	11	198			
Degree of carotid bifurcation, mean ± SD	−21 ± 9.5	9.5 ± 9.2			
Age, y, mean ± SD	74 ± 6.2	73 ± 7.4	0.812	0.534	
Male gender, *n*	9	172	0.645	0.649	
Right side, *n*	10	96	0.0062	0.024	11.1 (1.38–88.9)
Symptomatic lesion, *n*	6	96	0.696	0.686	
Severe stenosis, *n*	6	141	0.308	0.270	

ECA external carotid artery, *OR* odds ratio, *CI* confidence interval, *SD* standard deviation

one patient experienced transient periauricular numbness caused by injury to the great auricular nerve, and another patient experienced transient postoperative hyperperfusion syndrome (Table 2). No permanent surgical complications, including cranial nerve palsy or postoperative stroke as well as postoperative ipsilateral carotid occlusion, were observed in the lateral position group. In the normal position group, postoperative stroke was observed in two patients, including an ipsilateral cerebral infarct and a brain stem-cerebellar infarct. An asymptomatic ipsilateral petechial thalamic hemorrhage and a myocardial infarct were observed and resolved in two other patients. Eight patients developed transient postoperative hyperperfusion syndrome in the normal group. Taken together, two permanent surgical complications (1.0 %) were observed in the normal position group. Thus, although there was no mortality in either group, the rates of permanent morbidity were 0 % and 1.0 % in the lateral and normal position groups, respectively. The overall morbidity was 6.7 % in this patient series (14 instances of transient and permanent morbidities were observed among 209 procedures).

Discussion

Lateral Position of the ECA in a Series of CEAs

Previous reports used unbiased series of angiograms taken for the purpose of diagnosis of head trauma, intracerebral or subarachnoid hemorrhage, head and neck tumors, and cerebral aneurysms in patients ranging from newborns to the elderly in their 80s, to show that the incidence of lateral position of the ECA in the Japanese population is within 4.3–4.9 % [1, 8, 10]. Thus, lateral position of the ECA is not an uncommon phenomenon, and its occurrence was assumed to result from congenital anomalies (excessive migration of the embryonic external carotid artery trunk) or atherosclerosis (elongation or tortuosity of the carotid arteries). Our 199 consecutive Japanese patients with atherosclerotic carotid stenosis who underwent CEA in a single center in the course of 7 years were mostly men (87 %) with advanced age (73 ± 7.5 years; range: 44–88), and 5.3 %

of the ECAs were positioned laterally. In agreement with the published data, the results of the multivariate logistic regression analysis indicated that laterally positioned ECAs were encountered significantly more often on the right than on the left (90.9 % and 48.5 % of the laterally and normally positioned ECAs were found on the right, respectively; OR 11.1; 95 % CI 1.38–88.9; $P = 0.024$). Based on several reasons, we believe that the etiology of lateral positioning of the ECA is heterogeneous. First, despite controlling for potential confounders, including age, gender, and factors related to carotid atherosclerosis, the predominantly right-side location of the anomaly was still observed in our atherosclerotic patients. If atherosclerosis were the main precipitating factor, we would expect this predominance to be weaker. Second, if this condition resulted purely from atherosclerosis, lateral positioning of the ECA would be observed bilaterally more frequently than in the unbiased series. Third, asymmetry of the carotid atherosclerosis may still be a result of congenital variations or anomalies even in these elderly, atherosclerotic patients, as this ECA position defect may be present and undetected until the treatment for atherosclerosis is carried out. Very recently, Selwaness et al showed that plaque incidence, severity, and composition were not equally distributed between left and right carotid arteries [6]. Based on this result, they proposed that the asymmetry of carotid atherosclerosis might be explained by geometric factors, such as bifurcation angle and configuration of the right and left carotid arteries with respect to the aortic arch. Because the left carotid artery directly connects to the aortic arch and the right carotid artery arises from the brachiocephalic artery, the authors suggested that vessel anatomy might influence the hemodynamic forces, and the left carotid artery might be exposed to higher arterial pressure. Although there is no conclusive evidence on whether lateral position of the ECA has a congenital origin or results from atherosclerosis, we tend to agree with the authors of the above report – that it may be caused by variations or anomalies associated with geometric factors. Irrespective of the origin, knowing about the incidence of this condition in patients with atherosclerosis is essential for surgeons performing CEA.

Technical Notes and Postoperative Changes

We found that the angle of carotid bifurcation was significantly changed in the group with lateral position of the ECA after the surgery (−21 ± 9.5° vs. −12 ± 10°), whereas no such change was observed in the normal position group (9.5 ± 9.2° vs. 9.6 ± 9.1°). CEA may alter the arterial wall stiffness, length, or tortuosity because arterial plaque is removed and the arterial wall is sutured. It can be anticipated that the courses of the ECA and ICA arising from the CCA may change after CEA, resulting in kinks, especially in carotid arteries with unusual anatomical configuration, including lateral position of ECA. Moreover, from the viewpoint of a surgeon performing CEA, the ICA always lies behind the ECA in patients with lateral position of the ECA; therefore, the ICA should be drawn out to the shallow surgical field by rotating the carotid arteries. The steps following this maneuver can be performed in the usual manner, as described in the Methods and Materials section (above). Kinking or occlusion after CEA has not been reported in patients with lateral position of the ECA. In agreement with this, we did not observe carotid occlusion or kinking immediately after CEA, although the position of the ECA was shifted 9.7° medially with respect to the ipsilateral ICA at the CCA bifurcation after the surgery. The incidence of surgical complications was lower in the lateral position group than in the normal position group. However, it should be noted that the number of patients with lateral position of the ECA was quite small. Since this procedure involves mobilization of the ICA, which may carry rupture of vulnerable plaque, surgeons should be aware of the potential risk of intraoperative artery-to-artery embolism. Therefore, CEA with distal protection at an earlier stage or carotid artery stenting should be considered in patients with highly anticipated plaque vulnerability and lateral position of ECA.

ConclusionsThe incidence of lateral positioning of the ECA was 5 % in our single-center, 7-year study of atherosclerotic carotid stenosis patients who underwent CEA. Although there is no conclusive evidence, based on the predominantly unilateral nature and right-side location of the laterally positioned ECAs in the atherosclerotic population, we speculate that this condition is more likely to be a result of congenital variations or anomalies rather than atherosclerosis. Wider longitudinal exposure, rotation of the carotid arteries, and drawing the ICA out to the shallow surgical field are essential for performing CEA safely in such patients. Although no kinking of the CCA and ICA occurred in the cases with laterally positioned ECA, the risk of artery-to-artery embolism resulting from artery repositioning prior to plaque removal should be kept in mind.

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Conflict of Interest The authors declare that they have no conflicts of interest.

Ethical Standards This retrospective study was approved by the Institutional Review Board at Otaru Municipal Medical Center, and informed consent was obtained from all the patients prior to their inclusion in the study.

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Temporary Steno-occlusive Change in the Donor Artery During Mouth Opening (Big Bite Ischemic Phenomenon) After Superficial Temporal Artery to Middle Cerebral Artery Bypass in Adult Patients with Moyamoya Disease and Atherosclerosis

Hiroshi Abe, Toshiro Katsuta, Koichi Miki, Toshio Higashi, and Tooru Inoue

Abstract

Background

Superficial temporal artery (STA) to middle cerebral artery (MCA) bypass is one of the most common surgical procedures performed for direct extracranial (EC) to intracranial (IC) bypasses. We describe a temporary steno-occlusive change in the STA that was caused by mouth opening after the STA-MCA bypass (so-called big bite ischemic phenomenon) in an adult patient with moyamoya disease. The aim of this study was to assess the incidence of this phenomenon in patients with atherosclerosis.

Methods

Adult patients with ischemic cerebrovascular disease who underwent STA-MCA anastomosis were included in this study. Ultrasound examinations were postoperatively performed on 62 sides to determine whether mouth opening affected the blood flow of the donor STA and resulted in any ischemic symptoms within 1 min. Computed tomography angiography was performed during both mouth opening and closing when blood flow changes were recognized in the donor STA.

Results

During wide mouth opening, steno-occlusion of the donor STA occurred in 8 of the 62 affected sides (12.9 %), which included 3 of the 47 sides (6.4 %) in patients with atherosclerosis and 5 of the 15 sides (33.3 %) in patients with moyamoya disease.

Conclusion

Steno-occlusion of the donor STA occurred during wide mouth opening in 12.9 % of the sides of adult patients who had undergone STA-MCA anastomosis. This phenomenon was more common in patients with moyamoya disease than in patients with atherosclerosis.

H. Abe, MD (✉) • T. Katsuta, MD • K. Miki, MD
T. Higashi, MD • T. Inoue, MD
Department of Neurosurgery, Faculty of Medicine, Fukuoka University, Fukuoka, Japan
e-mail: neuroabe1972@gmail.com

Keywords STA-MCA bypass • Mouth opening • Occlusion • Donor artery • Temporal muscle

Background

The use of extracranial (EC) to intracranial (IC) bypass surgery for the treatment of atherosclerotic steno-occlusive disease has been negated in previous reports [13, 14]. However, EC-IC bypasses may be useful in selected cases that present severe hypoperfusion of the brain or progressive stroke during medical therapy. In contrast, the usefulness of direct EC-IC bypasses for the treatment of moyamoya disease has been assumed for a long time [4]. In addition, the results of the Japan Adult Moyamoya Trial suggest that direct EC-IC bypasses prevent rebleeding [8]. Anastomosis of the superficial temporal artery (STA) to the middle cerebral artery (MCA) is one of the most common EC-IC bypass procedures. Because the STA runs superficial to the temporalis muscle, it should be introduced to the cerebral surface by either perforating the muscle layer or by diversion around the muscle (Fig. 1). We observed an interesting phenomenon after STA-MCA bypass: mouth opening caused reversible occlusion of the donor STA, and the patients showed transient symptoms of cerebral ischemia [5]. In the present study, the incidence and mechanism of these occlusions were investigated in a group of patients and compared between patients with atherosclerosis and moyamoya disease.

Methods

Ninety-eight patients with atherosclerotic steno-occlusive disease or moyamoya disease (117 sides, including 62 sides of patients with atherosclerotic disease and 55 sides of patients with moyamoya disease) underwent EC-IC bypass surgeries at Fukuoka University Hospital between August

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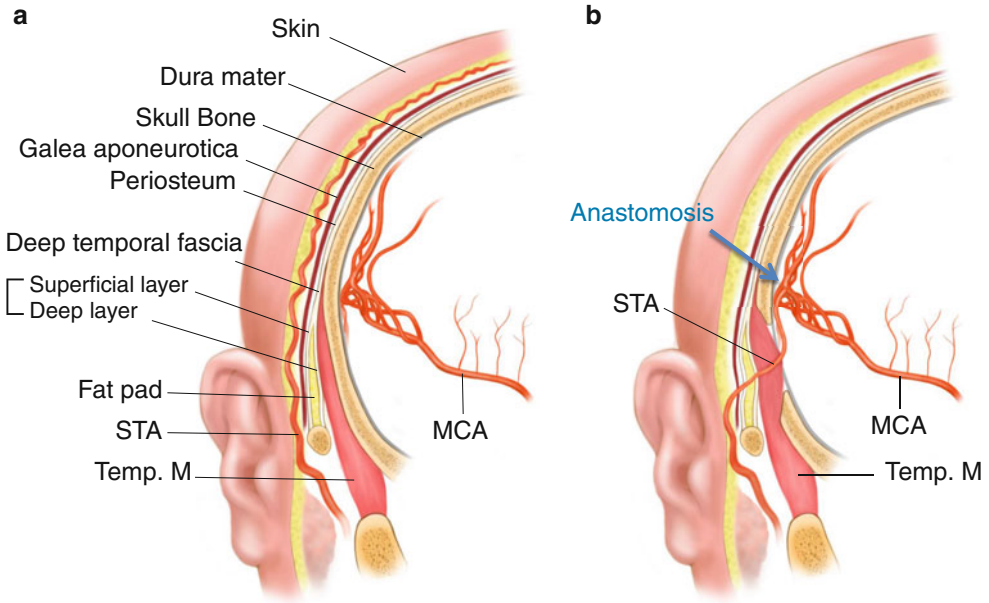

Fig. 1 Drawing of a coronal view of the superficial temporal artery (STA) and surrounding structures. (**a**) Before the STA-middle cerebral artery (MCA) bypass. The STA is located just above the galea aponeurotica. (**b**) After the STA-MCA bypass. The donor STA perforates the temporal fascia and temporal muscle

2008 and July 2013. Among them, the adult patients (>17 years of age) who underwent STA-MCA anastomosis were selected for this investigation. Ultrasound examinations were performed on the 62 sides (47 sides of patients with atherosclerotic disease and 15 sides of patients with moyamoya disease) more than 3 months after the surgery in order to determine whether the mouth-opening movement affected the blood flow of the donor STA. At the same time, the patients were monitored to see whether the mouth-opening movement resulted in any ischemic symptoms within 1 min. The mouths were maximally opened until the mandibular condyle was subluxated anteriorly. A >50 % reduction in the mean flow velocity of the STA was defined as stenosis, and a >90 % reduction was defined as occlusion. Computed tomography angiography (CTA) was performed during both mouth opening and closing conditions when a steno-occlusive change was detected.

Results

The patency of the direct bypass was confirmed before the study in each patient and in the affected side. One side in a patient with moyamoya disease exhibited complete occlusion of the donor STA upon mouth opening, which resulted in ischemic symptoms (Case 1). Decreased bypass flow was observed in seven sides (three sides in patients with atherosclerosis and four sides in patients with moyamoya disease), and none of them was symptomatic. No changes in bypass flow were noted in the other 54 affected sides. As a result, mouth opening affected bypass flow in 8 of the 62 affected sides (12.9 %), which included 3 of the 47 sides (6.4 %) in patients with atherosclerosis and 5 of the 15 sides (33.3 %) in patients with moyamoya disease. The mean ages of the atherosclerosis and moyamoya disease groups were 67.7 and 48.5 years, respectively. In seven of the eight sides in which the bypass flow was affected, both echography and CTA showed that steno-occlusion was caused by compression of the STA against the edge of the bone window. In one side of the patient with moyamoya disease, a redundant STA developed kinking in the muscle layer upon maximal mouth opening.

Representative Cases

Case 1 (symptomatic STA occlusion during mouth opening)
A 40-year-old man underwent a left STA-MCA single bypass and encephalomyosynangiosis (EMS) for symptomatic moyamoya disease. The temporalis muscle was dissected in an inverted-T fashion, and the donor STA was introduced between the two pieces of muscle. Each piece was further split into two layers; the deeper layer was used for the EMS, and the superficial layer was used to cover the bone flap. The postoperative course was uneventful, and the patient was discharged after patency of the STA-MCA anastomosis had been confirmed by ultrasound and angiography. Approximately 2 weeks post-operation, the patient reported

numbness in his right arm when he opened his mouth widely, while eating, and during yawning and brushing his teeth. The numbness developed several seconds after mouth opening and subsided immediately after mouth closing. Continuous mouth opening resulted in shaking of the right hand, which was similar to his initial symptom before the surgery. He experienced shaking of his right arm while he was visiting a dentist, which necessitated frequent pauses during treatment. CTA revealed that the STA was occluded at the edge of the bone window upon mouth opening (Fig. 2). This case was reported in our previous paper [5].

Case 2 (asymptomatic STA stenosis during mouth opening)
A 70-year-old woman underwent a right STA-MCA single anastomosis for an atherosclerotic right internal cerebral artery occlusion with severely low perfusion and decreased

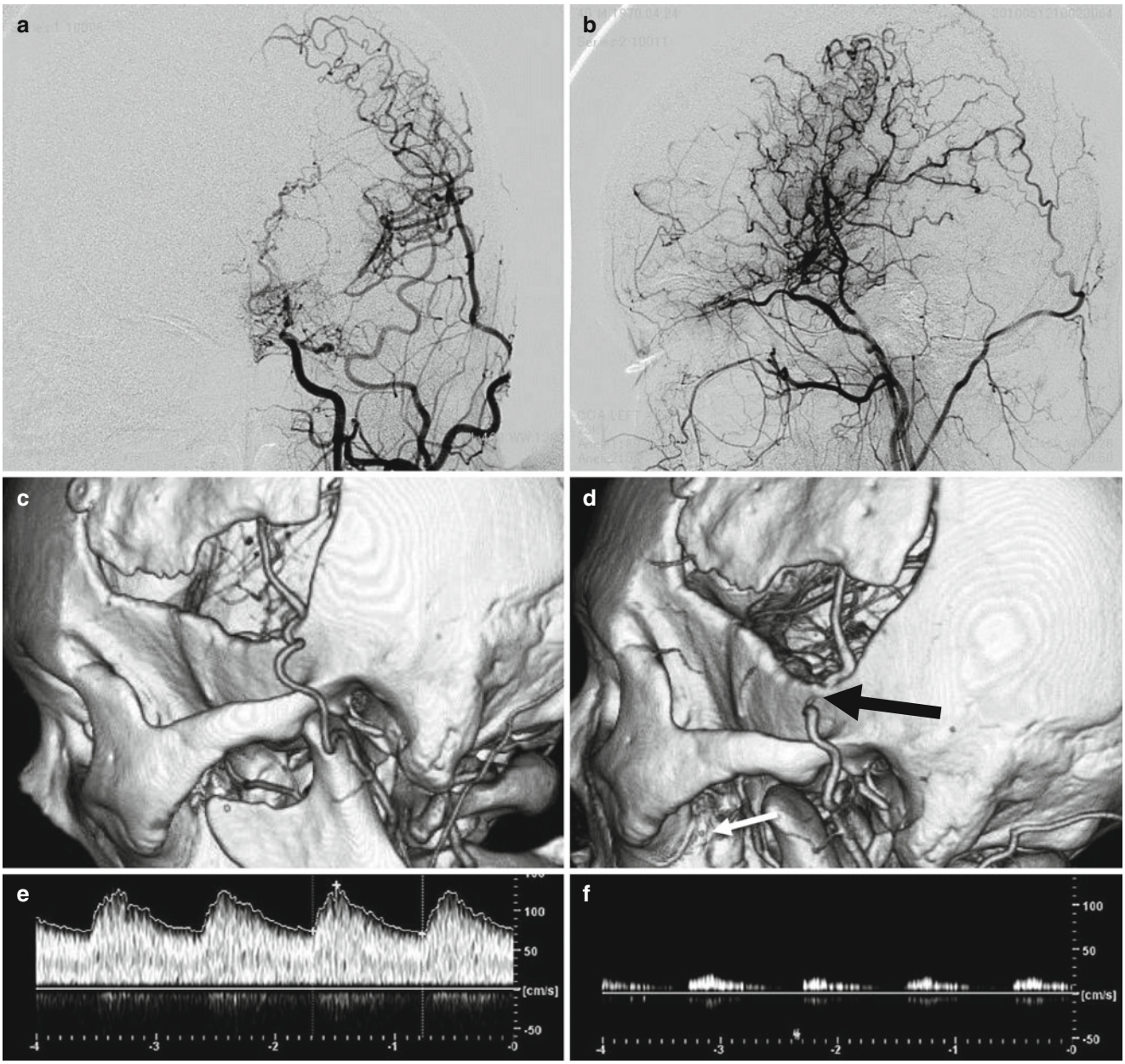

Fig. 2 Angiography and ultrasonic examination of Case 1. (**a**, **b**) Left common carotid angiography after the superficial temporal artery - middle cerebral artery (STA-MCA) bypass (**a**: A–P, **b**: lateral). The MCA territory of the brain receives a blood supply from the STA, especially in the motor-sensory area. (**c**) Computed tomography (CT) angiography that was conducted with the mouth closed showed that the donor STA had good patency. (**d**) CT angiography conducted with the mouth open. The mouth was open until the mandibular condyle subluxated anteriorly (*white arrow*). The donor STA was occluded at the edge of the bone window (*black arrow*). (**e**) Ultrasound examination showing the internal carotid artery (ICA) low pattern of the donor STA when the mouth is closed. (**f**) Ultrasound examination showing the occlusion flow pattern of the donor STA when the mouth is open

vascular reserve in the right MCA territory. The procedure was not combined with an indirect bypass. The postoperative course was uneventful. Ultrasound revealed a reduction in the donor STA flow during mouth opening. The patient was asymptomatic during continuous mouth opening. CTA showed severe stenosis of the donor STA at the lower edge of the bone window upon mouth opening (Fig. 3).

Discussion

The effects of mouth opening on donor vessels after bypass surgery have been described in previous reports. Freyschlag et al described reversible steno-occlusion in three patients with moyamoya disease [2]. We described five patients with moyamoya disease who presented with reversible steno-occlusion of the donor artery after STA-MCA bypasses [5]. Our investigation showed that mouth opening affected bypass flow in 12.9 % of the sides after STA-MCA bypasses, and occlusion that resulted in ischemic symptoms occurred in 1.6 % of the affected sides. Almost all of the patients (seven of eight sides, 87.5 %) in this study exhibited asymptomatic steno-occlusion of the donor STA. Freyschlag et al have suggested that asymptomatic steno-occlusion might occur after a well-developed indirect bypass [2]. Alternatively, according to a number of previous studies [1, 3, 6, 7, 9, 10] in which the occlusion of the donor STA occurred from manual compression after the STA-MCA bypass, ischemic symptoms were rarely seen. Although most patients in these studies seemed to have atherosclerotic steno-occlusion, complete occlusion was not necessarily symptomatic, even if no indirect support was present.

Anterior subluxation of the mandibular condyle from the glenoid fossa, together with the hinge movement, enables the mouth to open as wide as 5 cm [11, 12]. The mean amount of anterior dislocation of the condyle is about 18 mm [11]. The temporalis muscle is fully stretched, and the lower part of the temporal muscle is displaced downward in a passive manner. This movement of the temporalis muscle can cause distortion of the donor STA, which pierces the muscle layer. Freyschlag et al [2] guided the donor artery directly through the fibers of the EMS instead of diverting it around the muscle, and they speculated that an obstruction might be induced by the stretched muscle fibers during mouth opening. In 7 patients, CTA revealed that the steno-occlusion occurred at the lower edge of the bone window. We estimated that the stretched muscle flap pushed the donor STA against the bone edge, regardless of whether or not EMS was adopted. In one case, redundancy of the donor artery led to its kinking when the muscle was stretched. We described at least two different mechanisms of steno-occlusion: (1) compression of the donor STA against the lower edge of the bone window, and (2) kinking of the redundant donor artery, which was caused by displacement of the temporal muscle (Fig. 4). In order to avoid brain ischemia during mouth opening, we recommend maintaining a sufficient distance between the donor STA and the edge of the bone window and adjusting the length of the donor STA in the muscle layer.

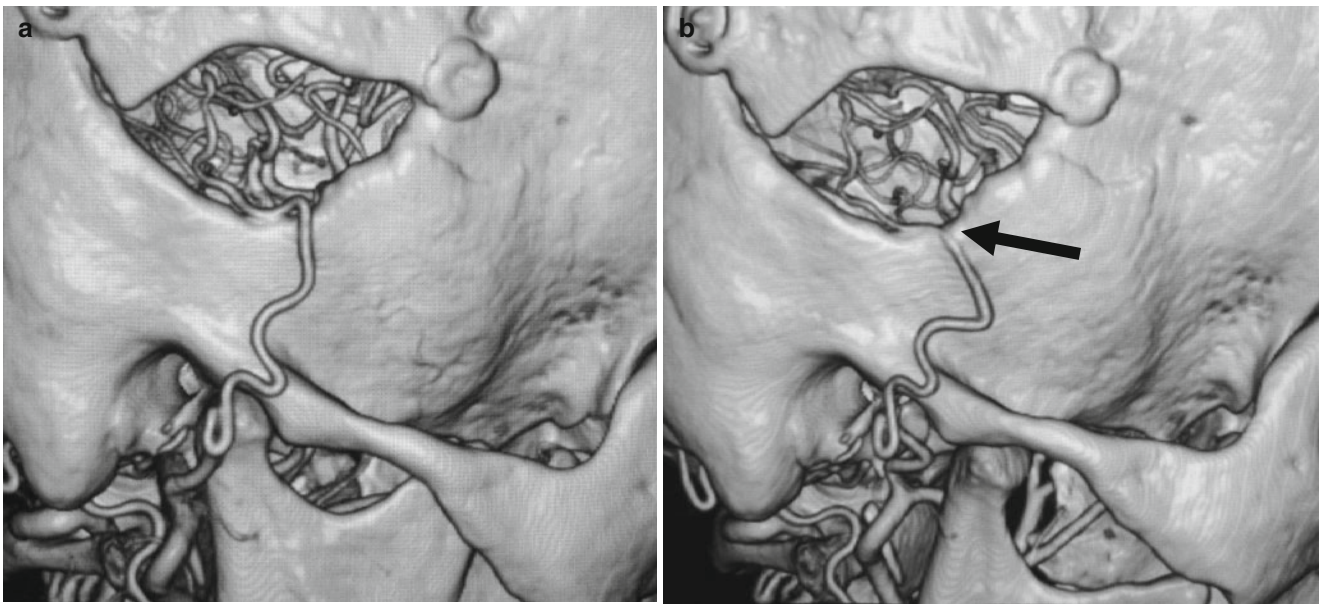

Fig. 3 Computed tomography (CT) angiography of Case 2. (**a**) CT angiography with the mouth closed showing that the donor superficial temporal artery (STA) has good patency. (**b**) CT angiography with the mouth open. The donor STA is narrowing at the edge of the bone window (*black arrow*)

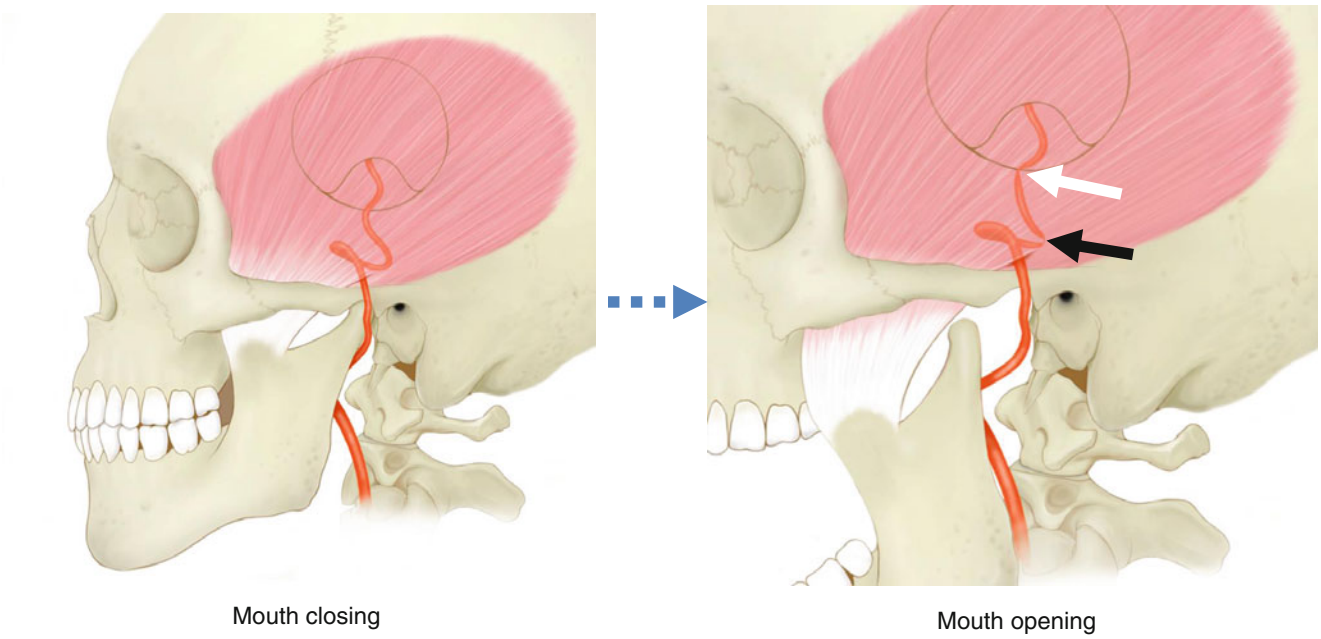

Fig. 4 Artist's rendering of the two types of mechanisms that contribute to the big bite ischemic phenomenon. The donor artery is compressed against the bone edge (*white arrow*), and the redundant donor artery is kinked within the muscle layer (*black arrow*)

In Case 1, complete occlusion during mouth opening led to ischemic symptoms. This patient reported no other difficulties in his daily activities because the symptoms occurred only with wide mouth opening. Other mouth movements, such as eating or speaking, did not bother the patients. However, if continuous wide mouth opening was required, such as undergoing dental treatment, a critical situation might ensue. Furthermore, severe brain ischemia might develop during treatment while the patient is under general anesthesia. We suggest that performing the mouth-opening test during an ultrasound examination is useful for patients with STA-MCA bypasses before they are subjected to general anesthesia in order to avoid brain ischemic complications.

In this study, a steno-occlusive change of the donor artery after STA-MCA bypass that was caused by opening the mouth, which is the so-called "big bite ischemic phenomenon" [5], occurred in 6.4 % of the patients with atherosclerosis ($n=47$) and in 33.3 % of the patients with moyamoya disease ($n=15$); the phenomenon was more common in patients with moyamoya disease than in those with atherosclerosis. These results suggested that the stiffness of the donor artery that depended on the atherosclerotic changes of the STA was implicated in donor arterial compression from the temporal muscle. Furthermore, it is possible that the presence or absence of the indirect bypass is involved in this phenomenon. The EMS is a common procedure that is used for indirect bypasses in patients with moyamoya disease in our institute. The deeper layer of the temporal muscle was used for EMS, and the superficial layer was used to cover the bone flap. The donor STA can be easily stretched or compressed by the temporal muscle because the donor STA passes through both layers of the temporal muscle.

Conclusions

Steno-occlusion of the donor STA occurred during wide mouth opening in 8 of the 62 affected sides (12.9 %) of adult patients with moyamoya disease or atherosclerosis who had undergone STA-MCA anastomosis. Complete occlusion induced ischemic symptoms on one side (1.6 %). This study revealed at least two steno-occlusive mechanisms: (1) the stretched temporalis muscle fibers pushed the donor STA against the lower edge of the bone window, and (2) the redundant donor STA kinked when the muscle was stretched. This phenomenon was more common in patients with moyamoya disease than in those with atherosclerosis.

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Disclosure The authors report no conflicts of interest concerning the materials or methods used in this study or the findings specified in this paper.

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

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Universal Bypass for Treatment of Symptomatic Moyamoya Disease or Moyamoya Syndrome. Analysis of a Personal Case Series on Behalf of the Italian Moyamoya Association

Luigi A. Lanterna, Carlo Brembilla, Paolo Gritti, and Claudio Bernucci

Abstract

Background

Moyamoya (MM) is a very rare cerebrovascular disease, particularly in Caucasians. We describe the results of an Italian case series where the mainstay of treatment was a bypass or a combined approach.

Methods

An analysis of a prospectively collected database was carried out. The main objective was to investigate (1) the risk of perioperative stroke and surgical complications, (2) the risk of new ischemic events, and (3) the risk of new hemorrhages at follow-up (mean follow-up: 2.2 years).

Results

Between January 2011 and January 2015 we carried out 34 bypasses in 23 patients with MM (15 MM disease, 5 unilateral MM, 3 MM syndrome); mean age was 34 (range: 1–57). The mortality and definitive morbidity rates were 0 %. Two patients suffered from transient aphasia and one developed partial palsy of the facial nerve. Five of the 12 patients with preoperative fixed deficits improved. No patient with preoperative ischemia experienced new ischemic symptoms. Rebleeding occurred in 1 of the 11 patients with a hemorrhagic presentation (9 %).

Conclusions

The bypass/combined approach to MM appears to have a favorable risk profile and preventive effectiveness, particularly on TIAs and ischemic stroke.

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L.A. Lanterna, MD, PhD (✉) • C. Brembilla, MD • C. Bernucci
Department of Neuroscience and Surgery of the Nervous System, Papa Giovanni XXIII Hospital, Bergamo, Italy
e-mail: l.lanterna@gmail.com

P. Gritti, MD
Department of Anesthesia – Anesthesia and Intensive Care IV, Ospedale Papa Giovanni XXIII, Bergamo, Italy

Keywords Moyamoya • STA-MCA bypass • STA-ACA bypass • Cerebral bypass

Introduction

Moyamoya (MM) is a very rare cerebrovascular disease, particularly in Caucasians. MM is characterized by the progressive occlusion of the terminal internal carotid artery (ICA) with the secondary development of compensatory collateral networks [15]. Clinically, patients with MM may present with either ischemic or hemorrhagic events. A small subset of patients may have subtle cognitive deficits, headache, epilepsy, or, very rarely, may be asymptomatic. Children more frequently have symptoms related to cerebral ischemia, while adults may be either ischemic or hemorrhagic [2, 15, 16]. Although the natural history of MM is still debated, the disease is usually progressive, with relapsing ischemic or hemorrhagic events. The treatment of MM is surgical revascularization that may be achieved with various methods including direct bypass, different types of synangiosis (indirect revascularization procedures), or a combination of the two approaches [8].

We describe the mid-term results of an Italian case series of patients affected by MM who were treated with either a direct bypass or a combined approach.

Materials and Methods

Methodology and Definitions

An analysis was carried out of a prospectively collected database of patients with MM who underwent surgical revascularization. MM and its variants were defined according to the criteria proposed by the Research Committee on Spontaneous Occlusion of the Circle of Willis [14]. In brief, MM disease (MMD) was diagnosed when there was a stenosis or occlu-

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sion of the terminal ICA on both sides without an underlying cerebrovascular disease being responsible for the pathology. When only one of the ICAs was affected, we made a diagnosis of unilateral moyamoya (uMM), and when there was an underlying disease we classified the case as moyamoya syndrome (MMs).

Data Collection Diagnosis and Treatment

We collected the baseline demographic (e.g., age at presentation, gender, ethnicity, familial occurrence), and clinical data (e.g., type of presentation categorized as hemorrhage or ischemia; type of MM categorized as MMD, uMM or MMs). The angiographic grade was defined according to the Suzuki scale [15]. In addition to angiography and MR, all patients routinely underwent CT or MR perfusion studies with and without the acetazolamide challenge before surgery. For investigative purposes, a subgroup of patients underwent preoperative near-infrared spectroscopy to study cerebral O_2 saturation. The treatment was dichotomized into bypass or combined approach; the latter consisted of a bypass associated with the pan-synangiosis (encephalo-duro-myo-pericranio synangiosis). The bypass was performed using one or both branches of the superficial temporal artery or the occipital artery as donors and, typically, a distal branch of the middle cerebral artery (MCA) as recipient. When the patient had symptoms or hypoperfusion related to the anterior cerebral artery (ACA), we targeted the ACA territory using the middle internal frontal artery as recipient. In the event of symptoms related to the posterior cerebral artery (PCA), the recipient was the parieto-occipital artery coming off the interhemispheric fissure.

Complications and Results

Surgical complications were categorized as (1) cerebral ischemic lesions, (2) intracranial hemorrhages, (3) infections, (4) postoperative seizures, and (5) skin necrosis or delayed wound closure. The patients were followed up and any new ischemic or hemorrhagic event was recorded. For patients with preoperative deficits, we used the Activities of Daily Living (ADL) scale according to Choi et al [3].

Results

From January 2011 to January 2015, at the neurosurgical department of the Papa Giovanni Hospital of Bergamo, 67 bypasses were performed. All the bypasses were carried out by a single surgeon (LAL). Thirty-four bypasses were performed on 23 patients with MM. The remaining procedures were performed for complex aneurysms (17 bypasses), chronic ischemia related to ICA or MCA occlusion (14 bypasses), and skull base tumors (2 cases).

As regards the 23 patients with MM, 15 were affected by MMD, 5 by uMM and 3 by MMs. Two of the three patients with MMs were affected by Recklinghausen's disease and one had MMs associated with an arteriovenous malformation (proliferative angiopathy). There were no familial cases and all patients were Caucasians. These patients had been referred to our department from all over Italy. The mean age was 34 (range: 1–57), with a female-to-male ratio of 3:1. The presentation was hemorrhage in 11 cases (47.8 %), cerebral infarction in 7 cases (30.4 %), and transient ischemic attacks (TIA) in five patients (21.7 %). All pediatric cases (<18 years) presented with either infarctions or TIAs. The Suzuki grade was 3–4 in 7 patients (30 %), 5 in 12 (52 %), and 6 in 4 (17 %).

In 14 patients, we performed a combined approach (e.g., bypass and pan-synangiosis), and in 9 we carried out only a direct bypass. The MCA was the recipient in all but six cases, in whom we targeted the bypass to the ACA (five cases) or the PCA (one case). The procedure-related mortality or definitive morbidity rates were 0 %. Two patients suffered from transient motor aphasia lasting less than 72 h and one developed a partial palsy of the supraorbital branch of the facial nerve. One patient deteriorated because of hydrocephalus and underwent a spino-peritoneal shunt procedure. In three patients there was delayed skin closure without the need for reoperation. There were no post-operative seizures or infections. Five of the 12 patients with preoperative fixed deficits improved within 1 month after surgery (mean preoperative ADL of 3.1 and mean postoperative ADL of 1.9). Postoperative angiographies were performed after 3 months of surgery in 17 patients and demonstrated the function of the bypass in all cases. Six patients are still pending postoperative angiography. During a mean follow-up of 2.2 years, no patient with preoperative ischemia experienced any new ischemic symptoms. Rebleeding occurred in 1 of the 11 patients with a hemorrhagic presentation (9 %).

Discussion

This case series represents one of the largest and and most up-to-date single-center Italian experiences of patients with MM where a direct surgical approach (with single or multiple bypass) was the mainstay of treatment. All patients uniformly underwent at least a bypass that, more recently, was combined with pan-synangiosis. The bypasses were usually targeted to the most hypoperfused brain areas and could be directed to the MCA, ACA, or PCA, according to the symptoms and the perfusion maps. The rationale of a universal bypass approach in MM was that such patients might be refractory to simple synangiosis [10, 11], the peri- and postoperative ischemic risk of pure synangiosis might be higher

as it usually takes several weeks or months to develop effective collaterals and, according to a recent literature review, a direct/combined bypass was more often associated with excellent revascularization than indirect approaches [7]. Furthermore, regarding patients with hemorrhage, the recent randomized trial found a possible long-term benefit of treatment, provided that patients were treated with a bypass [13].

The main finding of this study is that the universal bypass approach may be performed with a low risk of major complications. Indeed, no patient died or remained disabled because of the procedure, and we observed no post-operative strokes. Only two patients had transient deficits. These results are in accordance with the literature. Kazumata and colleagues [7] studied a population of 236 patients and 358 revascularization procedures and found a risk of perioperative stroke of less than 5 %. Similar results have been reported by Guzman and colleagues [4] who reported a surgical morbidity rate of 3.5 % and a mortality rate of 0.7 % in a series of 450 revascularization procedures performed in North America. Bao et al., in a cohort of 288 pediatric MM patients, reported a risk of perioperative complications of 4.2 % [1].

Although most of the published reports on the history of the disease describe Asian populations in whom the pathology may be different from that of Caucasians, the effectiveness of the bypass/combined approach in preventing new strokes seems to compare favorably with the natural history. In our series, regarding the risk of new ischemic strokes or relapsing TIAs, to date no patient has suffered from any new ischemic events after treatment. Although this result may be partially biased by a relatively short follow-up period (2 years), the literature appears to be in line with our data. A recent report that included both adults and children who were followed for more than 10 years, found that 97 % of patients were TIA-free after bypass, with nearly 90 % of patients being able to lead an independent life [12].

The preventive effectiveness of the bypass on rebleeding seems to be lower than that on cerebral ischemia and is still being debated. We found a rebleeding rate of 10 % during a 2-year follow-up, a result that largely corresponds to the recent Japanase and Korean studies. The JAM trial disclosed a risk of recurrence of 11.9 % at 5 years and another observational study found a risk of rebleeding of 7 % with a mean follow-up of 7 years [13]. The recurrence risk without treatment was around 30–37 % and was significantly higher than that of the treated patients. It is noteworthy that all the patients included in the JAM trial underwent a bypass or a combined approach. Furthermore, the Korean study found that the risk of rebleeding was lower in patients treated with a bypass than in those treated with synangioses [9].

Revascularization in patients with misery perfusion may be restorative. Five patients with fixed deficits improved, and the mean ADL shifted from 3.2 to 1.8 within 1 month of surgery. We found similar results in patients with chronic ischemia related to ICA or MCA occlusion. Other authors have supported this observation [5, 6]. In our opinion, these data suggest that treatment may be indicated also in selected patients with fixed and dense deficits related to a condition of misery perfusion, particularly in the event of a discrepancy between the severity of the neurological deficits and the lesions shown on the MRI.

The limitations of this study are its limited statistical power and relatively short follow-up. However, the intention of the study was to investigate only the short- and mid-term results and to compare them with the literature. Although we used the combined approach also for children (three cases, five bypasses), and in each case we performed a direct bypass followed by an uneventful postoperative course, the statistical power of the study is too limited to analyze them as a subgroup. The strength of this study is that it describes a relatively homogeneous population of Italian patients with MM treated with a single technique by a single surgeon.

Conclusions

The bypass/combined approach to MM appears to have a favorable risk profile with preventive effectiveness, particularly on TIAs and ischemic stroke. Treatment in selected patients with misery perfusion may be restorative. The bypass/combined approach may be performed also in children.

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Conflict of Interest Statement All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria, educational grants, participation in speakers' bureaux, membership, employment, consultancies, stock ownership, or other equity interest, and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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Management of Cerebral AVMs

A Prospective and Retrospective Study of Cerebral AVM Treatment Strategies 1990–2014

Atsushi Tsuji and Kazuhiko Nozaki

Abstract Although treatment options for cerebral arteriovenous malformations (AVMs) have changed since the advent of endovascular surgery and radiosurgery, microsurgery is still the major treatment option since it is effective for immediate cure. We proposed, and have applied, a revised treatment strategy to patients at our institution from February 2008 to May 2014, in which the final goal was disappearance of the nidus on angiography in patients who underwent surgical intervention. We followed 67 patients with cerebral AVMs, and in the 59 patients who had surgical intervention, the cure rate was 89.8 % (53 of 59). In all 67 patients, the surgical extirpation rate was 70.1 % (47/67). These rates were significantly higher than those between 1990 and 2008 at our institute. Microsurgical extirpation-related complications were a postoperative fatal hemorrhage in one patient, and visual field defects in two. In the endovascular treatment, two patients experienced hemiparesis, and radiosurgery-related complications were a fatal hemorrhage in one patient. Two patients from the non-surgical intervention group suffered from fatal hemorrhage. To achieve lower morbidity and mortality in AVM microsurgery, complete treatment until disappearance of the lesion, and an effective combination of available treatment modalities, are mandatory.

Keywords Cerebral arteriovenous malformation • Microsurgery • Indication • Risk management

Introduction

Cerebral arteriovenous malformations (AVMs) are still a challenge to treat and are a leading cause of hemorrhagic stroke in young people, with relatively high morbidities and mortalities and annual bleeding rates of about 2–4 % [2, 6, 16,]. Recent advances in microsurgery, radiosurgery, and endovascular surgery have improved AVM management, and multimodal approaches are necessary, particularly for high-grade lesions. Although microsurgery is still the most common treatment owing to its effectiveness for immediate cure, the three modalities should be used in combination in order to reduce overall treatment risks. We proposed, and have applied, a revised treatment strategy for cerebral AVMs at our institute since February 2008; the final goal was complete disappearance of the nidus on angiography in all patients who received surgical intervention. We analyzed clinical data from our institute since 1990 and reassessed our recent treatment policy in order to select appropriate candidates for surgical interventions and reduce surgery-related morbidity and mortality.

Methods

We retrospectively and prospectively followed 132 patients (80 male, 52 female) with cerebral AVMs who were treated at the Department of Neurosurgery, Shiga University of Medical Science (SUMS), between January 1990 and May 2014. The mean age was 37.2 (5–73). Of the 132 patients' initial symptoms were hemorrhage (82), seizure (19), headache (6), incidental (20), and others (5). The number of patients with each Spetzler-Martin (S-M) grade was I 24, II 42, III 45, IV 16, V 5. The applied combinations of treatment modalities included surgical extirpation only (Ex) in 40 patients, transarterial embolization only (TAE) in 7, radiosurgery (Rx) in 13, observation (Ob) in 16, TAE+Ex in 39, TAE+Rx in 8, Ex+Rx in 3, Rx+Ex in 2, and TAE+Ex+Rx in 4. Treatment strategies since February 2008 are shown in Table 1, and the final goal for nidus was set as the complete disappearance on angiography in all patients who received any surgical intervention. To evaluate a revised treatment

Atsushi Tsuji, MD, PhD • K. Nozaki, MD, PhD (✉)
Department of Neurosurgery, Shiga University of Medical Science, Seta Tsukinowa-cho, Otsu, Shiga 520-2192, Japan
e-mail: noz@belle.shiga-med.ac.jp

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strategy since 2008, we determined locations of the lesion, S-M grades, treatment modalities, cure rates, surgical extirpation rates, and surgical morbidities and mortalities in patients treated since February 2008; we also compared them to treatment modalities, cure rates, and surgical extirpation rates from January 1990 to January 2008. The differences in cure rates and surgical extirpation rates were analyzed using Pearson's chi-square test.

Results

Since February 2008, we determined our treatment policy as described in Table 1 and treated 67 patients with cerebral AVMs (43 male, 24 female). We compared patients managed under this treatment policy with the earlier period (between January 1990 and January 2008). The mean age in the 2008–2014 period was 39.7 (7–73). The patients included 39 with hemorrhage as their initial symptom, 9 with seizures, 2 with headache, 14 with incidental detection, and 3 with other symptoms. The number of patients in each S-M grade were 8 in grade I, 23 in grade II, 29 in grade III, 6 in grade IV, and 1 in grade V. Between 1990 and 2008, we treated 65 patients (mean age 34.6; 37 male, 28 female) and the number of patients in each S-M grade was 16 in I, 19 in II, 16 in III, 10 in IV, and 4 in V. The distributions of S-M grades in two time periods were not statistically significant (Mann-Whitney *U* test). Treatment modalities since 2008 included Ex in 24 patients, TAE in 0, Rx in 6, Ob in 8, TAE+Ex in 21, TAE+Rx in 0, Ex+Rx in 3, Rx+Ex in 2, and TAE+Ex+Rx in 3. When comparing treatment modalities before and after 2008, TAE or TAE+Rx were not selected in any patients since February 2008, and Ex+Rx or TAE+Ex+Rx were chosen only since 2008. In 59 patients with any surgical intervention since 2008, complete curative treatment was achieved in 53 of them (89.8 %) overall: 7/7 in grade I, 22/22 in grade II, 20/24 in grade III (2 patients were under follow-up after Rx), 2/6 (4 patients were under follow-up after Rx) in grade IV, and 0/0 in grade V. In the 67 patients since 2008, surgical extirpation rates were 47 (70.1 %) overall: 7/8 in grade I, 21/23 in grade II, 17/29 in grade III, 2/6 in grade IV, and 0/1 in grade V. From January 1990–January 2008, a complete cure was obtained in 28 patients out of 57 (49.1 %), and 32 patients out of 65 (49.2 %) received surgical extirpation. The differences of complete curative rate and surgical extirpation rate between the two time periods were statistically significant, respectively ($p < 0.05$).

The Ex-related complications since included a postoperative fatal hemorrhage in one patient (cerebellum~brainstem, S-M grade IV) and quadrant visual field defects in two patients (both occipital, S-M Grade III). The TAE-related complications were hemiparesis in two patients (both parietal, S-M grade III), and Rx-related complications were a fatal hemorrhage in one patient (basal ganglia, S-M grade IV). Two patients without any surgical intervention suffered from fatal hemorrhage (S-M grade I, V).

Table 1 Treatment strategy since 2008 at the Department of Neurosurgery, Shiga University of Medical Science

Microsurgery	
Candidates	Hemorrhagic case
	Non-hemorrhagic case under age 50
	Asymptomatic case under age 20–30
Indications	With acceptable surgical risks depending on symptoms, size, location, surgeon's skill, etc.
Endovascular	Preoperative TAE for feeders behind
Radiosurgery	Deep and/or adjacent to vital structures

Case Presentation

Case 1 (Fig. 1)

A 37-year-old man with no symptoms was admitted to our institute for microsurgical resection of a right cingulate unruptured AVM (4 × 4 × 3 cm, non-eloquent, no deep drainer) fed by the right internal frontal arteries, right posterior pericallosal artery, and perforators from the right middle cerebral arteries and draining into the ascending cortical veins (S-M grade II). We informed the patient of the relatively high risk of bleeding, considering 40–50 years of life expectancy. The nidus was successfully extirpated via an ipsilateral and contralateral interhemispheric approach after feeder embolization for the internal frontal arteries and posterior pericallosal artery. The patient returned to work in a month and showed no neurological deficits.

Case 2 (Fig. 2)

A 26-year-old woman presented with left hemiparesis due to hemorrhage from a right basal ganglia~paraventricular AVM (1 × 2 × 2 cm, eloquent) fed by perforators from the right middle cerebral artery and draining into the right internal cerebral vein (S-M grade III). Preoperative diffusion tensor imaging showed a 10 mm distance between the nidus and right corticospinal tract. We informed the patient and her family of the high risk of re-hemorrhage and relatively low risk of neurological worsening after microsurgical extirpation through the hematoma cavity, and the nidus was completely extirpated without further neurological deficits. Left hemiparesis improved completely in a few months and she returned to her daily life as a homemaker.

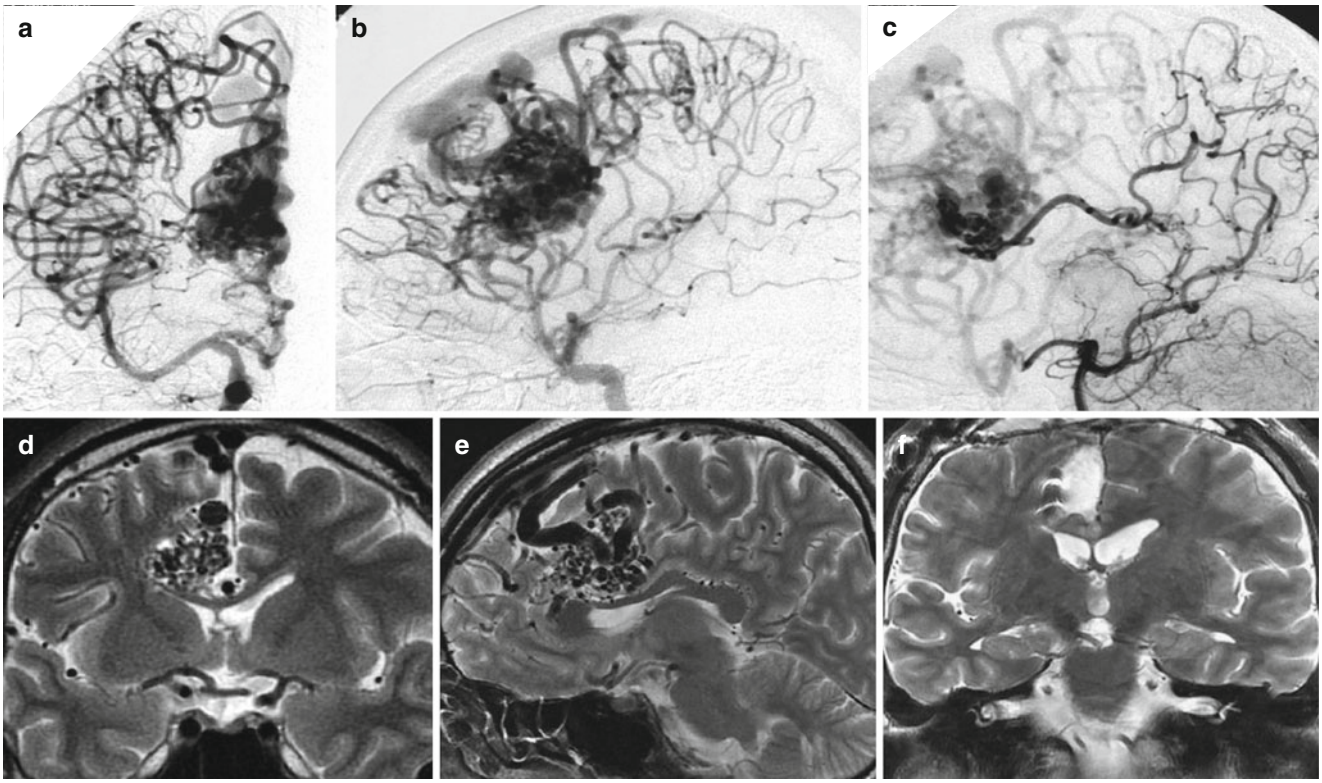

Fig. 1 Right internal carotid angiograms (**a** A–P, **b** lateral), right vertebral angiogram (**c**, lateral), and T2-weighted MR (**d** coronal, **e** sagittal) showing right cingulate AVM of Case 1. Postoperative T2-weighted MR (**f** coronal) showing total removal of the nidus

Discussion

We have applied a revised treatment policy for cerebral AVMs since February 2008, based on the concept that surgical intervention should be chosen after considering the bleeding risk from the lesion over the patient's expected lifetime, that complete cure of the nidus should be achieved using available treatment modalities if any surgical intervention is begun, and that the final goal of any treatment for the nidus should be its complete disappearance on angiography. In this small case study, the surgical extirpation rate was 70.1 % in all patients, and the complete curative rate was 89.8 % (remaining cases were in follow-up after radiosurgery) in patients receiving any surgical intervention, and these rates were significantly high as compared with those before January 2008. Surgical intervention-related severe morbidities were 3 % (endovascular surgery) and mortality was 2 % (microsurgery). These numbers are comparable to the single mortality following radiosurgery and two deaths under observation during the same period. Although Recommendations for the Management of Intracranial AVMs [14] is still the standard guideline for treatment of cerebral AVMs, surgical indication cannot be determined only by S-M grade [15]; other factors should be considered, including the patient's condition: age, comorbidity, social and personal backgrounds, history of hemorrhage and other symptoms, degree of neurological deficits, and the nature of AVMs: shape of nidus (compact, diffuse), location of nidus (sulcal, parenchymal), involvement of perforators, risk of hemorrhage, and presence of a hematoma cavity.

In the revised treatment strategy, hemorrhagic cases, non-hemorrhagic symptomatic cases under age 50, and asymptomatic cases under age 20–30 were considered candidates for microsurgical resection due to the potential bleeding risks during their lifespan. A patient aged 20 or 50 with a lesion having a 2 % annual bleeding rate has a potential lifetime risk of hemorrhage of about 70 % or 50 %, respectively, based on the expected lifespan. The annual bleeding rate is not uniform and differs, depending on location of the lesion, previous hemorrhage or symptoms, and angioarchitectures. In addition, microsurgical treatment risks vary, depending on a patient's age, hemorrhagic presentation, location of the lesion, and its diffuseness [9].

Microsurgical extirpation can be performed with low morbidity in patients with low-grade AVMs but is of limited use in high-grade ones, and the selection of patients influences surgical outcomes particularly in eloquent areas [1, 3, 5]. The identification of classic cortical eloquence is not enough to predict postoperative neurological worsening, and we should assess not only superficial cortical functions but

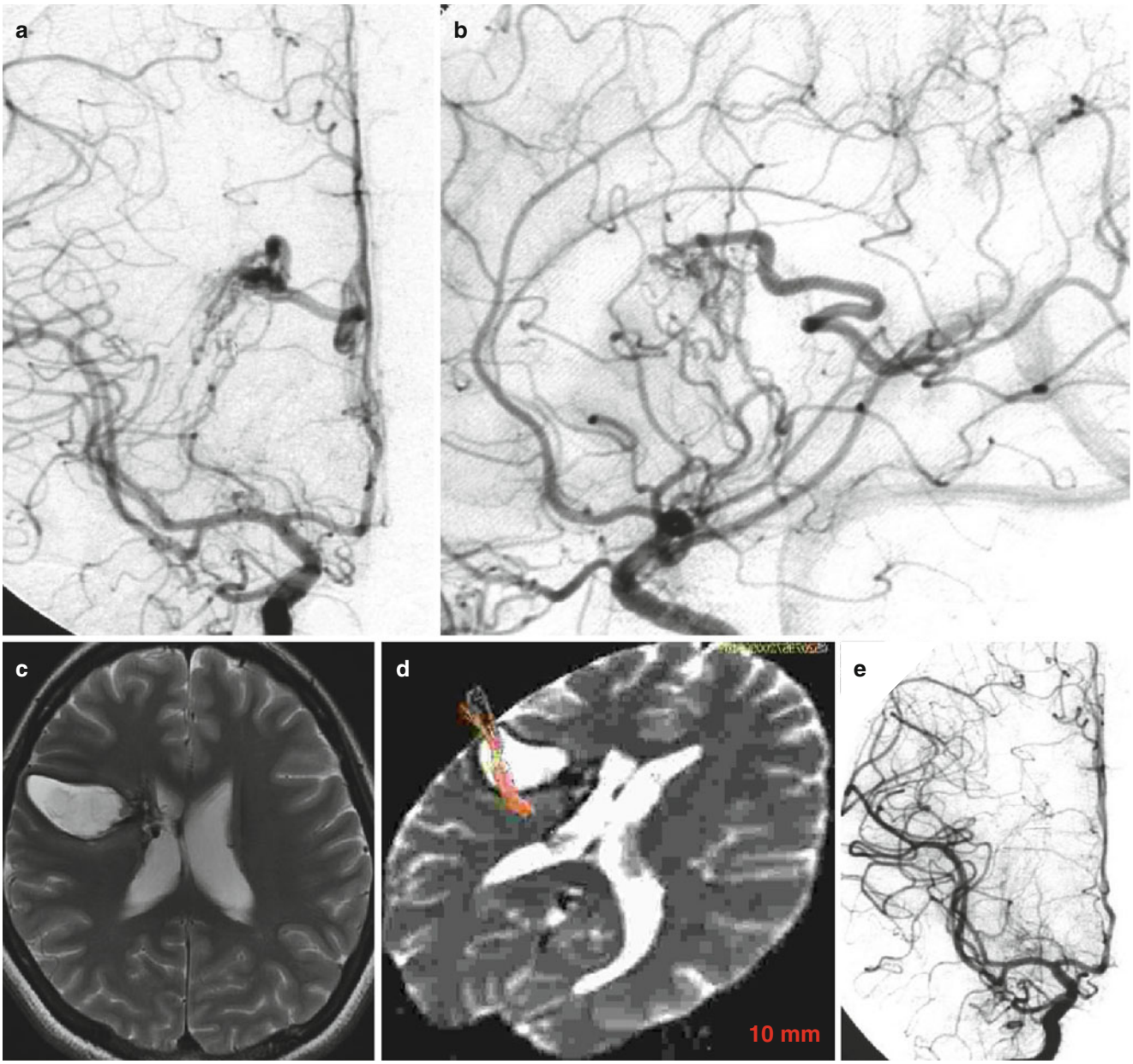

Fig. 2 Right internal carotid angiograms (**a** A–P, **b** lateral) and T2-weighted MR (**c** axial) showing right basal ganglia~paraventricular AVM of Case 2 with a hematoma cavity. Diffusion tensor imaging of right corticospinal tract (**d**) indicates a 10 mm distance between the nidus and the tract (*orange*). Postoperative angiogram (**e**) showing disappearance of the nidus

also subcortical functional fiber tracts [7, 8]. Deep-seated and high-grade AVMs should be treated taking into account previous hemorrhage, and surgical indication for unruptured and asymptomatic cases is limited [12, 13].

Following surgical intervention, complete disappearance of the lesion should be defined as the desired endpoint. Palliative treatments for the nidus should be avoided because of the further risk of hemorrhage [10]. Since 2008 we have combined available treatment modalities in order to obtain a cure defined by angiographical results in all surgical intervention cases. Even after total microsurgical extirpation, the possibility of re-hemorrhage, which may occur (0.1 %/year) even after angiographical confirmation of total extirpation, should be taken into account [4]. Recently, the ARUBA trial showed that medical management alone may be superior to medical management with interventional therapy for preventing mortality or stroke in patients with unruptured cerebral AVMs who were followed for 33 months [11]. These results suggest that unruptured cerebral AVMs should be treated without any surgical intervention. Although the trial will continue with an additional 5 years of follow-up to confirm the results, long-term trials that continue over

20–30 years are necessary in order to study long-term clinical outcomes of patients with cerebral AVMs, since the potential risks of hemorrhage last for a patient's entire life.

Conclusions

Surgical extirpation should be applied in combination with endovascular surgery and/or radiosurgery to patients with cerebral AVMs with consideration of the inherent risks of each lesion and surgery-related risks in order to achieve complete cure.

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

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Multimodal Flow-Assisted Resection of Brain AVMs

Alessandro Della Puppa and Renato Scienza

Abstract

Object

The authors report their personal experience with brain arterio-venous malformations (bAVMs) surgery with a multimodal flow-assisted approach.

Methods

Data from patients who consecutively underwent bAVM resection with the assistance of indocyanine green videoangiography (ICG-VA), micro-flow probe flowmetry, and temporary arterial clipping test under intra-operative monitoring, were retrospectively analyzed.

Results

Twenty seven patients were enrolled in the study. Re-operation for residual nidus was needed in one case (3 %). Average mRS change 1 month after surgery was +0.02. In our experience, the multimodal flow-assisted approach enabled surgeons to shift from one technique to another, according to the stage of resection, AVM location, or specific issues to be addressed. Before resection, the value of ICG-VA and flowmetry in showing AVM angioarchitecture and guiding surgical strategy was related to AVM features. The temporary arterial clipping-test presented a 100 % sensitivity to differentiate between an AVM feeder and a transit artery to the sensi-motor area. At the final stage of resection, flowmetry was more effective than ICG-VA in detecting residual nidus missed at dissection.

Conclusions

Multimodal flow-assisted approach in AVM surgery proved a feasible, safe, and reliable methodology to achieve AVM resection with high radicality and low morbidity rate.

Keywords Brain arterio-venous malformation • Microsurgery • Cerebro-vascular surgery • Flow assessment • Micro-flow probe • Flowmetry: indocyanine green videoangiography (ICG-VA) • Temporary clipping test

Introduction

Intra-operative flow assessment is a validated technique in aneurysm surgery to detect flow reduction during microsurgical clipping; its role is to minimize possible ischemic complications, thus improving the clinical outcome of patients [1, 2, 8, 11, 15]. In brain arterio-venous malformation (bAVM) surgery, experiences on flow-assisted resection including semi-quantitative assessment [12], arterial feeder pressure evaluation [10, 17], and flow velocity recording by Doppler sonography [9, 14] have been reported. Indocyanine green videoangiography (ICG-VA) is an intra-operative technique of flow assessment that has been largely described as a helpful tool in AVM surgery [16] even if a few drawbacks represent a limit on the real impact on patients' outcome [19, 20]. We recently suggested a multimodal intra-operative flow assessment approach to improve ICG-VA during AVM surgery [7]. The purpose of this study is to report the intra-operative findings and the clinical outcomes of this technique in a case series of 27 patients treated for bAVMs.

Materials and Methods

Patients and AVMs

Data were retrospectively analyzed from patients with brain AVMs who underwent surgical resection from January to December 2013 in our department with a

A. Della Puppa, MD (✉) • R. Scienza, MD
Department of Neurosurgery, University Hospital of Padova, Padova, Italy
e-mail: alessandro.dellapuppa@sanita.padova.it

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multimodal flow-assisted approach, based on the assistance of two or more of the following intra-operative low assessment techniques: indocyanine green videoangiography (ICG-VA), micro-flow probe flowmetry, and temporary artery clipping test assisted by intra-operative monitoring. AVM grade was defined according to the Spetzler Martin (SM) scale [18]. Intra-operative data were reviewed in all cases. Preoperative and postoperative (1 month after surgery) modified Rankin Score (mRS) was evaluated in all cases to assess patients' outcome. The result of postoperative resection was assessed in all cases by Digital Subtraction Angiography (DSA) performed immediately after surgery.

Surgical Strategy and Intra-operative Flow Assessment Techniques

The surgery strategy was guided by flow data provided by all the reported techniques, combined in different ways, according to the phase of resection and to the question to be addressed. Indocyanine green video-angiography was performed in all cases before dural opening, and then after dural opening before and at the end of resection. In addition, it was performed when it was deemed necessary during resection. The micro-vascular ultrasonic flow probe (Charbel Micro Flowprobe, Transonic Systems, Inc., Ithaca, NY) [2] was used (1) before resection, after ICG-VA, on both cortical feeders and venous drainages; (2) during dissection on the same vessels or on different vessels (deep vessels); and (3) at the end of surgical resection, on venous drainage before section to check residual flow. In all cases, flow assessment was performed after all arterial feeders and all minor venous drainages were sectioned. The temporary artery clipping test was used to assess the functional importance of a vessel that was involved or was in strict connection with the AVM nidus in order to reduce post-operative neurological deficits. The aim was to distinguish between AVM feeders and transit arteries to the sensi-motor area. The temporary artery clipping was always performed under the assistance of intra-operative neurophysiological monitoring based on MEPs (motor-evoked potentials) and SSEPs (somato-sensory potentials) real-time assessment. After positioning of a clip on the identified artery, MEPs and SEPPs amplitude was monitored for a few minutes (usually 10); if no changes were recorded, the artery was definitively occluded at the exact point where the temporary clip had been previously positioned. Conversely, if a change in amplitude or latency was recorded, the clip was removed and further dissection was carried out.

Results

Patients and AVMs

Data are summarized in Table 1. Twenty-seven patients were enrolled in the study; median age was 45 (range: 23–71). Mean preoperative mRS was 1.64: more in detail, the specific mRS was 0 in 3, 1 in 11, 2 in 14, and 3 in 1 patient. Twenty-one patients presented with a ruptured AVM, and six with an unruptured. In three cases, surgical resection was performed in the acute stage of a bleeding AVM. The AVM was supratentorial in 20 cases, and infratentorial in 7. The SM grade was I in seven patients, II in ten patients, III in nine patients, and IV in one patient [18]. AVMs had been previously embolized in seven cases.

Intra-operative Findings

Data are summarized in Table 2.

ICG-VA

ICG-VA was performed 97 times: 27 before dural opening, 27 before resection, 16 during dissection, and 27 at the end of resection. Before dural opening, the AVM was transdurally visualized in all cases. After transdural ICG-VA, further extension of the craniotomy was necessary in two cases. AVM injury related to dural incision was never reported.

After dural opening, the AVM angio-architecture was clearly shown by ICG-VA in 21 cases before resection: conversely, in 6 cases, ICG-VA did not provide any helpful

Table 1 AVM features and outcome

	n
Patients	27
Median age (range)	45 (23–71)
Gender	12M/15F
Spetzler-Martin grade	
I	7
II	10
III	9
IV	1
Previous bleeding AVMs	21
Pre-operative embolization	7
Mean pre-operative mRS score	1.64
Median post-operative mRS score	1.66
DSA resection rate	97 %

mRS modified Rankin Scale, *DSA* Digital Subtraction Angiography

Table 2 Intra-operative data of multimodal flow-assisted approach

	Flow assessment modality		
Flow assessment stages	ICG-VA	Flowmetry by micro-flow probe	Clipping test
Patients who underwent the procedures			
Before dural opening	27	–	–
Before resection	27	27	1
During resection	16	26	13
At the end of resection	27	22	–
Procedures performed			
Before dural opening	27	–	–
Before resection	27	92	1
During resection	16	104	20
At the end of resection	27	25	–
Total	97	221	21

ICG-VA Indocyanine Green-VideoAngiography

information to the surgical decision-making because of deep location, large size, or presence of an AVM-related hematoma. At the end of resection, ICG-VA did not show a residual nidus in any case. However, in one case (3%) DSA performed immediately after surgery revealed a residual AVM missed at final ICG-VA.

Flowmetry

A total of 221 quantitative flow measurements were performed using a micro-flow probe on 97 vessels: 92 before, 104 during, and 25 at the end of resection. Flowmetry was used in all patients (27 patients) before resection, in 26 patients during resection, and in 22 patients at the end of resection (before permanent venous drainage closure).

Before resection, in all cases flowmetry was able to discriminate between arterial feeders and venous drainages. In all cases, the measurement was helpful for understanding AVM angio-architecture and guiding surgical planning. During dissection, flowmetry was helpful for differentiate between deep arterial feeders and venous drainages not exposed at the beginning of resection whenever present.

At the final stage of resection, before section of the venous drainage, the flow measurement of the venous drainage in five cases showed a residual flow that revealed residual nidus missed at surgical dissection. No major vessel injury occurred from use of the micro-flow probe.

Temporary Artery Clipping Test

Temporary arterious clipping under MEPs and SSEPs monitoring was performed 21 times in 14 patients. In seven cases, clipping induced a MEPs/SSEPs amplitude decrease of >50%. In those cases, a temporary clip was removed and the artery preserved. In all cases, the potentials came back to initial amplitude (i.e., before clipping) by a few seconds (range: 24–78). In 14 cases the temporary occlusion was not followed by MEPs/SSEPs decrease, so it was assumed that the artery could be safely sacrificed.

Patients' Outcome

In one case (3%), an AVM remnant was detected at postoperative DSA; the patient underwent re-operation and resection of residual nidus immediately after DSA. In that patient, a final ICG-VA showed neither residual nidus nor an early venous enhancement; flowmetry by micro-flow probe was not performed at the final stage in that case because of the deep venous drainage location. Average mRS change 1 month after surgery was +0.02: indeed, mean postoperative mRS was 1.66; more in detail mRS was 0 in 3, 1 in 10, 2 in 15, and 3 in 1 patient.

Discussion

Rationale of the Multimodal Flow-Assisted Approach in AVM Resection

The multimodal flow-assisted approach originates in the necessity to further drop the morbidity rate of AVM resection. Understanding of the AVM angio-architecture before and during resection, as well as intra-operative verification of radical resection, are of crucial importance for the surgical patients' outcome, both to improve the resection rate and to reduce intra- or post-operative dangerous bleeding due to residual AVM (unexpected AVM nidus missed at resection) [9, 13, 17]. We undertook a multimodal flow-assisted approach in AVM surgery with the belief that the various flow assessment techniques are complementary, as we already experienced in meningioma and aneurysm surgery [4, 5, 8]. ICG-VA is a well-known technique routinely used in AVM surgery, but it has a few drawbacks that could limit its impact on patients' outcome [19]. Flowmetry by micro-flow probe is a technique that can be synergic to ICG-VA [5, 7, 8]. The temporary artery clipping test is the way we can combine flow with function; indeed, this technique is able to directly evaluate the functional consequence of an arterial sacrifice when operating close to the sensi-motor area [5].

Our Findings

This multimodal approach proved helpful in guiding the surgical strategy. Before resection, ICG-VA and micro-flow

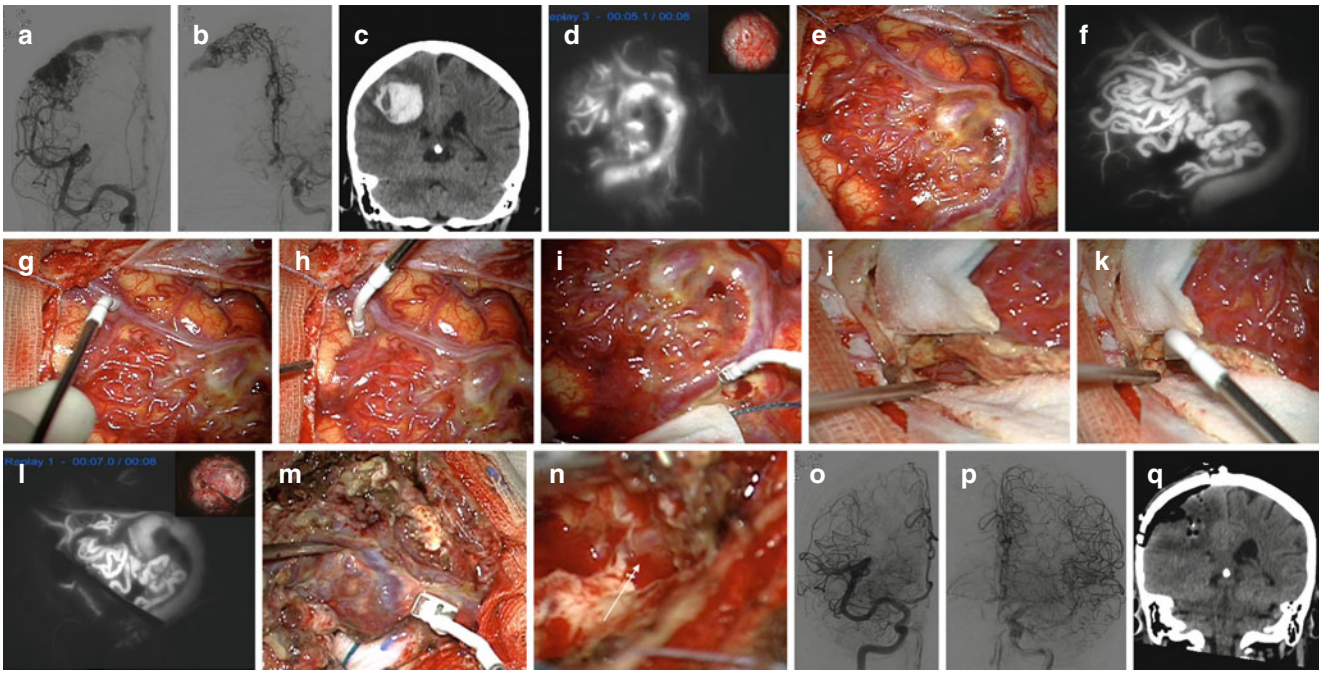

Fig. 1 Sixty-three-year-old female with right fronto-parietal bleeding AVM (SM grade III). (**a**–**c**) Pre-operative images: (**a**, **b**) digital subtraction angiography (DSA) showing a fronto-parietal AVM with main feeders from middle and anterior cerebral arteries and main venous drainage to the superior sagittal sinus; (**c**) CT-scan showing a large intra-nidal hematoma. D-n: intra-operative microscopic images. Before AVM resection: transdural ICG-VA (**d**); after dural opening with pre-resection view (**e**), ICG-VA picture (**f**); flow assessment by micro-flow probe of different vessels before starting dissection in order to clarify ICG-VA data and have a flow baseline value (**g**–**i**). During AVM dissection (**j**–**l**) flowmetry allowed to differentiate between feeder and venous drainage (**j**, **k**); ICG-VA (l) to evaluate current AVM angio-architecture after partial dissection. At the end of AVM resection, flowmetry (**m**) of main venous drainage detected an unexpected high flow (5 ml/min) that allowed detecting a deep residual nidus with an AVM feeder at high magnification (n, *white arrow*): post-operative images (**o**–**q**) DSA (**o**, **p**), and CT scan (**p**)

probe could complement each other resection (Fig. 1). Indeed, in our study, ICG-VA was crucial for understanding AVM angio-architecture; however, in 22 % of cases, flowmetry by micro-flow probe was helpful in making ICG-VA data clearer before resection and thus improving surgical strategy. This happened in deeply located AVMs or in cases in which part of the feeders and venous drainages were subcortical or interhemispheric. ICG-VA played a helpful role before dural opening [6], changing our strategy in 8 % of patients. In the final stage, flowmetry by micro-flow probe proved a more reliable technique than ICG-VA in detecting residual AVM. In fact, in all 22 patients in which the venous drainage was definitively sectioned when no venous flow was detected at flowmetry, no AVM remnants were reported at post-operative DSA. Conversely, in 20 % of cases in which flowmetry was not performed, and even ICG-VA had not shown a residual nidus, a post-operative AVM remnant was registered at post-op DSA. In our study, the temporary arterial clipping presented a 100 % sensitivity to distinguish between an AVM feeder and a transit artery to the sensimotor area, and this enabled avoiding a neurological deficit in all patients affected by fronto-parietal AVMs. Finally, the high radical resection rate (97 %), the low morbidity (mRS average change +0.02), and the lack of intra-operative complications (AVM injury, brain swelling, etc.) show that the present approach is a feasible, safe, and reliable strategy to improve resection rate and surgical outcome of patients. However, the real clinical impact of the present approach must be investigated by larger studies.

Advantages and Main Limitations of the Present Approach

In our experience, the multimodal approach was suitable to different phases of AVM resection. Indeed, the various techniques could complement each other in the different intra-operative stages of AVM treatment, according to the specific issue to be addressed. If AVM features are not suitable for ICG-VA, flowmetry was very reliable in our experience. At the final stage of resection, flowmetry was more reliable than ICG-VA in detecting residual nidus missed at resection. However, some AVM features must be kept in mind because they can reduce the reliability of the approach. The detection of transit arteries by temporary artery clipping is possible

only when a function can be assessed by neuro-physiological monitoring. If a patient undergoes surgery while asleep, only sensi-motor function – and not language function – is evaluable. In our experience, the only patient (3 %) presenting a post-operative worsening was affected by a cerebellar AVM, in which no monitoring was suitable because of the location of the lesion. This issue finally limits the application of the technique to the fronto-parietal area. The very deep location of venous drainage represents a limitation to the flow assessment with micro-flow probe in which the correct measurement is related to a comfortable handling of the vessel. In our experience, the only case in which a re-operation was needed was when flowmetry by micro-flow probe was not suitable for the deep infratentorial location (Fig. 1). Deep subcortical location represents a main limit to ICG-VA. Small vessel size is crucial for micro-flow probe assessment; this is a well-known issue already reported in aneurysm surgery where ICG-VA proved more useful [3]. The very small diameter of deep vessels made most of them unsuitable for the different evaluations.

Conclusions

Our study shows that a multimodal flow-assessment approach can assist AVM surgery in different phases of resection, either exploiting the singular techniques or combining them in different ways, according to the different issues faced during AVM resection. In our experience, the approach was a feasible, safe, and reliable methodology aimed at improving resection rate and surgical outcome of patients. The real clinical impact of the present approach must be investigated by larger studies.

Conflict of interest The authors declare that they have no conflict of interest statement.

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Seizures and Brain Arterovenous Malformation: A Surgical Series

M. Ferlisi, T. Zanoni, G. Moretto, and A. Pasqualin

Abstract Seizures are common symptoms of supratentorial arteriovenous malformations (AVMs). The potential risk factors for epilepsy in patients with AVMs are still controversial. The reported long-term outcome of seizures after surgical treatment of AVMs is variable and the data available are mainly from small retrospective case series.

We identified all consecutive patients between 1990 and 2006 who underwent microsurgical resection of supratentorial AVMs at our institute. Pre-operative risk factors for seizures, intra-operative characteristics, long-term neurological disability, and seizure outcome (Engel's classification) were recorded and analyzed.

During the study period, 110 patients underwent surgical resection of supratentorial AVM. Sixty of them (55 %) were symptomatic for seizures preoperatively. In our series, the absence of preoperative neurological deficits ($p=0.005$), a large AVM size ($p=0.005$), and no history of preoperative AVM hemorrhage ($p<0.001$) were identified as risk factors for preoperative seizures. Following surgical resection, 77 % of patients with preoperative seizures had a modified Engel class I outcome. Among patients without a history of preoperative epilepsy, 56 % had new-onset seizures after surgical resection. None of the risk factors associated with preoperative seizures was associated with post-operative seizures. As there are no reliable factors predicting patients who may benefit from surgical treatment, epilepsy control should not be considered as the primary goal of AVMs surgery.

Keywords Arteriovenous malformation • AVM • Epilepsy • Neurosurgery • Microsurgical resection

M. Ferlisi, MD • T. Zanoni, MD • G. Moretto, MD
Division of Neurology "A", University Hospital of Verona, p.le Stefani 1, Verona 37126, Italy

A. Pasqualin, MD (✉)
Section of Vascular Neurosurgery, Institute of Neurosurgery, University Hospital of Verona, p.le Stefani 1, Verona 37126, Italy
e-mail: albertopasqualin@tin.it

Introduction

Seizures are the second most common manifestation of cerebral arteriovenous malformations (AVMs), and they accounted for the presenting symptom in a third of the patients [11, 17]. Various mechanisms have been hypothesized on the basis of epileptogenicity of the AVMs, including steal phenomena causing local ischemia and gliosis, hemosiderin deposition, and kindling with secondary epileptogenesis [24]. Interventional treatment by neurosurgery, endovascular embolization, or stereotactic radiosurgery can be used alone or in combination, with the aim to obliterate the AVM. The primary endpoint of every therapy is to prevent hemorrhage, but there may be a benefit for secondary epilepsy as well [20]. The aim of this study was to evaluate the characteristics of epilepsy in a group of patients who underwent microsurgical resection of supratentorial AVMs at our institution, in order to characterize risk factors for preoperative seizures. We also aimed to evaluate long-term seizure outcome and possible factors associated with post-operative seizure freedom in patients with surgically resected supratentorial AVMs.

Materials and Methods

We performed a retrospective review of 110 consecutive patients treated between 1990 and 2006 with microsurgical resection for brain AVMs in order to obtain a long-term follow-up after surgery. Inclusion criteria were age 10 to 75 and the supratentorial location of brain AVMs. The patients' clinical records were reviewed, and anagraphic data, clinical presentation, epilepsy history (seizure type, frequency of pre-operative seizures, antiepileptic drug therapy), neurological state before surgery, size and location of brain AVMs, treatments preceding surgery (medical treatment and adjunctive procedures such as endovascular embolization of

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AVMs), and complications were collected. In a subgroup of patients who were available at follow-up, we conducted a prospective review by clinical evaluation in the out-patient epilepsy clinic or by phone interview. In these patients, the neurological state was classified according to the modified Rankin scale [1], and the outcome of seizure was reported according to the Engel Classification (Table 1) [5].

Intervention

The microsurgical resection of the AVMs was performed strictly at the edges of the malformations, closing the main venous drainage only after bipolar coagulation of all feeding vessels. Single or multiple embolization procedures preceded the surgical treatment, depending on the AVM size and microangioarchitectural characteristics of the lesion.

Intravascular embolization was carried out using acrylic glue and, more recently, Onyx. All 110 patients received antiepileptic drug prophylaxis, according to the standard practice in our institute.

Statistical Analysis

Continuous variables are presented as mean ± standard deviation (SD) in normal distributions, or median and range in the skewed data. Categorical variables are presented as whole numbers and percentages. When comparing continuous variables, Student's *t*-test and Mann-Whitney's test were used. The analysis of categorical variables was performed using the Person Chi-square or Fisher exact test. A regression analysis was performed on those variables that showed significance in the univariate analysis. Statistical analysis was conducted using statistical software (IBM SPSS Statistics, version 20).

Table 1 Classification of seizure outcome

Class I: free of disabling seizures
Ia: completely seizure-free since surgery
Ib: non-disabling simple partial seizures since surgery
Ic: some disabling seizures after surgery, but free of disabling seizures for at least 2 years
Id: generalized convulsion with AEDs discontinuation only
Class II: rare disabling seizures ("almost seizure-free")
Class III: noteworthy improvement
Class IV: no noteworthy improvement, or worsened seizures

Modified from Engel Classification (*AED* antiepileptic drugs)

Results

Between 1990 and 2006, 118 patients underwent microsurgical resection of supratentorial AVMs at our institute; eight of them were excluded for insufficient data. The clinical characteristics of the remaining 110 patients are summarized in Table 2.

Sixty patients (55 %) had seizures before surgery, and for most of them (54, i.e., 90 %) seizures were the presenting symptoms of the brain AVMs. Thirty-eight patients had symptomatic intracranial hemorrhage (ICH) at presentation, defined as a symptomatic event (seizure, headache, focal neurological deficit, or alteration of consciousness) that was associated with evidence of intracranial blood on brain imaging; four of them had convulsions (acute symptomatic seizures due to

Table 2 Clinical characteristics of the 110 patients

	No. (%)	
Gender		
Male	69 (63 %)	
Female	41 (37 %)	
Age at time of surgery: median (range)	34.5 (11–75)	
Presenting symptom		
Clinical presentation		Intracerebral hemorrhage at presentation
Seizures	54 (49 %)	4
Headache	34 (31 %)	19
Focal neurological deficits	14 (13 %)	12
Altered state of consciousness	4 (4 %)	2
Incidental diagnosis	3 (3 %)	0
Missing data	1 (1 %)	1
All	110 (100 %)	38 (34 % out of 110)
Pre-operative seizures	60 (55 %)	
1 or 2 seizures	33 (30 %)	
3 or more	27 (25 %)	
Seizure type (of 60 patients)		
Focal	24 (40 %)	
Generalized	36 (60 %)	
Hemorrhage before surgery	38 (35 %)	
Pre-operative neurological deficits	46 (42 %)	
Hemiparesis +/– visual and/or aphasia	14 (13 %)	
Visual only	23 (21 %)	
Aphasia only	4 (4 %)	
Other	5 (5 %)	

ICH); and an additional five with ICH at presentation experienced one or more seizures before surgery.

Among all the patients with preoperative seizures, 33 (55 %) had one or two episodes of seizures before surgery, while in 27 patients (45 %) there was a history of repeated seizures despite therapy. The frequency of the seizures was weekly (2 patients), monthly (12 patients), or yearly (12 patients); for 1 patient, the frequency was unknown.

Prior to surgery, 22 patients received a single-agent antiepileptic treatment and 5 patients received a double- or multiple-agent antiepileptic treatment. The median duration of epilepsy before surgery was 48 months (range 2–360 months) for patients who experienced three or more seizures before surgery, and 11 months (range 1–360) for patients with one or two preoperative seizures. The median volume of the brain AVMs was 11 cc (range 1–62 cc). AVM location is shown in Fig. 1; AVMs were cortical in 67 patients, subcortical in 14, and cortical-subcortical in 29.

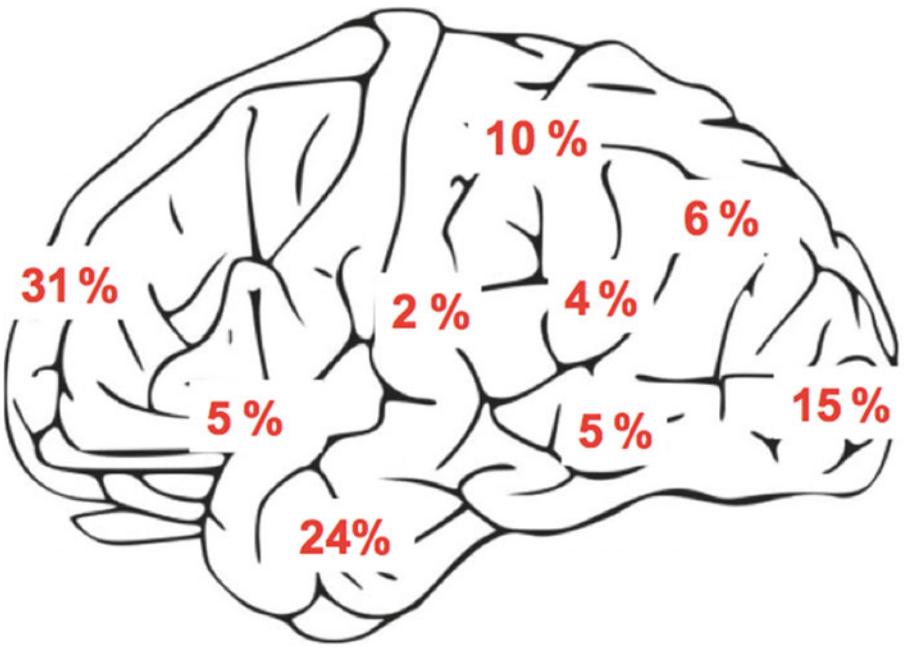
Endovascular embolization of the AVM was performed in 53 patients (48 %) prior to surgical treatment, depending mainly on the AVM size and complexity. Eighteen patients received a single embolization procedure before surgery; multiple embolizations (ranging from 2 to 10) were performed in the remaining 35 patients.

Risk Factors for Pre-operative Seizures

No age or gender differences were observed among patients who did or did not present with a history of seizures. Patients with a normal neurological examination before surgery had more frequent preoperative seizures than patients with neurological deficits (68 % vs. 39 %, respectively, p: 0.003). The median AVM volume was greater in patients with seizures (14 cc, range 1–62) than in patients without seizures (6 cc, range 1–50) (p: 0.03). Patients with a history of AVM hemorrhage had a lower rate of seizures (9/38, 24 %) than those without preoperative hemorrhage (52/72, 72 %) ($p < 0.001$), and a smaller median volume (5 cc, range 1–24) than those without pre-operative bleeding (14 cc, range 1–62) ($p < 0.001$). Conversely, we did not find any association between AVM location and risk of seizures. In the multivariate analysis of risk factors for preoperative seizures, only the absence of pre-operative hemorrhage showed an independent association with preoperative seizures (Table 3).

Long-Term Follow-Up

Sixty-three patients (57 %) were also available for a prospective clinical evaluation after a minimum of 6 years of follow-up (median: 11 years, range: 6–21). Among the 63 patients, 40 had pre-treatment seizures; we assessed seizure outcome with the modified Engel outcome scale in these patients, and the results are shown in Table 4. There was no difference in seizure outcome between patients who experienced one or two seizures before surgery and those who had three or more seizures in the pre-operative period.



Frontal	34 (31 %)
Temporal	26 (24 %)
Parietal	11 (10 %)
Occipital	16 (15 %)
Fronto-temporal	5 (5 %)
Temporo-parietal	2 (2 %)
Temporo-parieto-occipital	4 (4 %)
Temporo-occipital	5 (5 %)
Parieto-occipital	7 (6 %)

Fig. 1 AVM location in the 110 patients

Table 3 Statistically significant risk factors for pre-operative seizures among 110 patients

	Pre-operative seizures	No pre-operative seizures	Univariate *p*	Multivariate *p* (95 % CI)
Normal neurological examination, *n* (%)	42 (68 %)	20 (32 %)	0.003	n.s.
AVMs volume cc, median (range)	14 cc (1–62 cc)	6 cc (1–50 cc)	0.03	n.s.
Pre-operative hemorrhage *n* (%)	9 (24 %)	29 (76 %)	<0.001	0.001 (2.180–18.748)

Table 4 Seizure outcome after treatment in patients with preoperative seizures according to the modified Engel scale

Engel seizure outcome scale	
Class I	77 % (31/40)
Ia	47 % (19/40)
Ib	0
Ic	22 % (9/40)
Id	7 % (3/40)
Class II	7 % (3/40)
Class III	0
Class IV	15 % (6/40)

New-Onset Postoperative Seizures

Of the 23 patients who did not experience seizures before treatment, 13 (56 %) had new-onset of post-operative seizures: 10 patients (43 %) experienced only a few seizures immediately after surgery, and they were seizure-free at the last follow-up, while 3 patients (13 %) developed new-onset epilepsy after surgical treatment. Globally, 87 % (20/23) of patients without pre-operative seizures were seizure-free at the last follow-up, although these figures are not significantly higher than in patients with pre-operative seizures (77 %).

Factors Affecting Seizure Outcome

None of the factors associated with pre-operative seizures were also associated with post-operative seizures (age, gender, AVM size and location, hemorrhage, duration of epilepsy history, frequency of pre-treatment seizures, seizure type). Also, outcomes did not vary significantly according to the pre-operative treatment (surgery alone or preceded by embolization).

Neurological Outcome

At the last follow-up, 45 patients (72 %) were free of significant disability (mRS 0–1), while 18 patients (28 %) presented mild to severe disability. Patients without disability were less affected by post-operative seizures (49 %) than those with neurological disability (67 %), although this difference did not have any statistical significance.

Discussion

In our series, epilepsy was the most common presenting symptom of the brain AVMs. These data, slightly higher than previously reported, probably reflect a bias related to the intrinsic AVM characteristics of a surgical series, where AVMs are usually of a high volume: the median volume of brain AVMs of our patients was significant (median 11 cc, range 1–62). Several factors have been described in association with AVM-related seizures: male gender, nidus location in the temporal lobe, some angioarchitectural characteristics of the nidus, and the size of the lesion [8, 13, 15, 16, 21, 25].

In our series, the size of AVMs, no history of hemorrhage, and a normal neurological examination were positively associated with pre-operative seizures. It is well known that seizures are more common in larger AVMs [6, 11, 12], probably because such lesions have a larger area of contact between the AVM and the neocortical parenchyma. It has been reported that smaller brain AVMs carry a higher risk of hemorrhage, although this could represent a clinical bias [10]. Smaller brain AVMs remain silent or show their presence only when they bleed, while larger AVMs display symptoms more frequently when still unruptured, and usually cause epilepsy in an otherwise healthy patient. As neurological deficits are more common after bleeding of brain AVMs, the three risk factors for seizures can be interpreted as related [4]. Together with location and some angioarchitectural characteristics, brain AVMs at high risk of epilepsy seem to show characteristics (cortical location, large volume, feeding by the middle cerebral artery), somehow in contrast to those of AVMs at high risk for bleeding (deep location, small size, presence of intranidal aneurysms, previous history of hemorrhage) [15, 21].

Surgical treatment of brain AVMs is associated with an overall good seizure outcome: the percentage of seizure-free (Engel class I) patients was 81 %: 77 % in patients with pre-treatment seizure, and 87 % in those patients who did not experience seizures before surgery. It must be clear that these percentages refer to a series of patients surgically treated in order to prevent hemorrhage – not because of epilepsy – and most of them had seizures that were well controlled by antiepileptic drugs. Thus, this cannot be compared with the outcome after epilepsy surgery, which is limited to drug-resistant epileptic patients. It has also been reported that focal epilepsy due to brain AVMs can respond well to antiepileptic drugs – for example, better than temporal lobe epilepsy

related to hippocampal sclerosis [18]. Moreover, while brain AVMs that carry a high risk of seizures seem predictable, thanks to several factors, our data show the absence of reliable predictors of good seizure outcome after surgery.

We found a high risk of new-onset seizures after surgery in patients without epilepsy before treatment. In historical series [3], the risk of developing seizures in untreated brain AVMs was around 18 %, and the most important risk factor for seizures in harboring brain AVMs was surgery [2]. The general incidence of post-operative seizures after craniotomy is estimated to be between 15 and 20 % [7, 23], and it is the personal experience of one of the authors (AP) that the general risk of post-operative seizures after craniotomy is somewhat higher for patients harboring brain AVMs than for all other neurosurgical patients. The evidence base for AED prophylaxis before surgery is poor, current guidelines are not universally accepted [9, 19], and the issue goes beyond the aim of this study. However, our data – together with previous reports in the literature [14, 22] – may suggest that in patients undergoing surgical resection of brain AVMs, prophylactic antiepileptic drugs are recommended. Our findings suggest that the endpoint for AVM surgery should only be the prevention of bleeding [14]. The management of AVM-related epilepsy should not differ from the management of any other form of focal epilepsy, i.e., the best medical treatment, and considering surgery for drug-resistant patients. In these latter cases, the aim of surgery should not be the removal of brain AVM, and the operation should follow the accurate localization and delineation of the extent of the epileptogenic zone through a multimodality approach, thus configuring an "epilepsy surgery".

Conflict of Interest We confirm that we have no conflict of interest.

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Multimodality Management of Cerebral Arteriovenous Malformations with Special Reference to AVM-Related Hemorrhages During Ongoing Staged Treatment

Andreas Gruber, Gerhard Bavinzski, Klaus Kitz, Stephan Barthelmes, Magdalena Mayr, and Engelbert Knosp

Abstract In this study we report and analyze the results of a multimodality management concept for intracranial arteriovenous malformations (AVMs), including microsurgery, embolization, and gamma knife radiosurgery. The study population consists of a consecutive series of 294 patients treated for 304 intracranial AVMs over a 10-year period.

Keywords Arteriovenous malformation • Microsurgery • Embolisation • Radiosurgery • Multimodality Management • Re-hemorrhage

Introduction

Arteriovenous malformations [AVMs] are congenital cerebrovascular pathologies. The underlying defect of a locally deficient capillary bed formation between feeding arterioles and draining veins results in the malformative convolute of pathological vessels, i.e., the AVM nidus, lacking precapillary arteriolar sphincters and thus lacking the characteristic precapillary reduction of arterial to capillary blood pressure. As a result, and in the absence of a functional capillary bed, oxygen-rich blood is shunted under arterial pressure from the arterial to the venous arm of the cerebral circulation, exposing both the malformative intranidal vessels and the draining veins to unphysiologically high blood pressure and thereby increasing the risk of hemorrhage [1, 3]. The annual re-hemorrhage rates of ruptured AVMs are substantially higher and justify invasive treatment. The role of invasive treatment for unruptured intracranial AVMs, however, is still in the process of being defined [10]. Recently, the results of the ARUBA trial have re-demonstrated AVM hemorrhage rates of >2 % per year in unruptured cases [11]. The results of recently published clinical trials [11, 12, 14], however, do not strongly support the notion that all unruptured AVMs should undergo invasive treatment, although low surgical morbidities are indeed achievable in expert hands [13].

Patients and Methods

In view of these findings, the results of a multimodality management concept for intracranial AVMs, including microsurgery, embolization, and gamma knife radiosurgery, have been reviewed and are reported in the current study. The present series is based on a consecutive series of 294 patients treated for 304 intracranial AVMs over a 10-year period. The male:female ratio was 1:1, and the average patient age was 39.3 [± 17.3 SD]. Of these patients, 142 presented with initially unruptured AVMs, whereas the remaining 152 were treated for initially ruptured lesions. Of the patients reported, 62 % underwent monomodality and 38 % underwent multimodality management of their AVMs, respectively. Sixty-six percent of the patients receiving monomodal treatment underwent gamma knife neuroradiosurgery, whereas 77 % of the patients receiving multimodality treatment had a combination of embolization and gamma knife neuroradiosurgery. In this series, all therapeutic modalities available were provided by neurosurgeons trained and cross-experienced in microneurosurgery, endovascular neurosurgery, and gamma knife radiosurgery. Hence, individual treatment plans, including type, number, and sequence of therapeutic procedures delivered were set up by a team of neurosurgeons experienced in the microsurgical, endovascular, and radiosurgical management of cerebrovascular disease. This team was therefore not responsible

A. Gruber, MD • G. Bavinzski, MD • K. Kitz, MD
S. Barthelmes, MD • M. Mayr, MD • E. Knosp, MD (✉)
Department of Neurosurgery, Medical University Vienna, Vienna, Austria
e-mail: engelbert.knosp@meduniwien.ac.at

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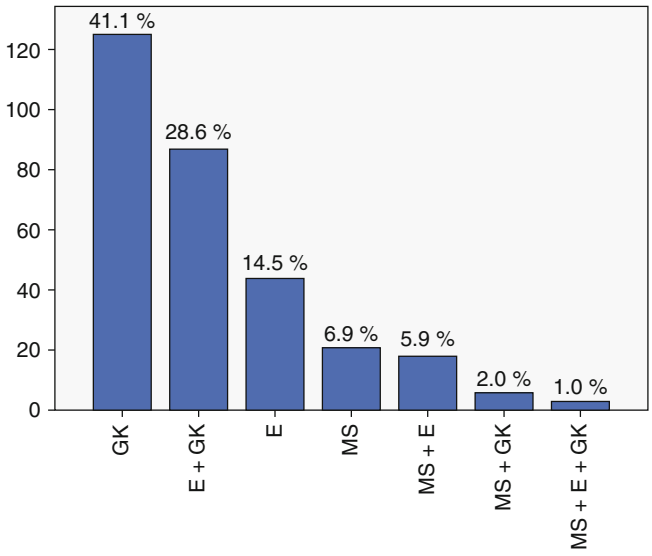

Fig. 1 Therapeutic modalities used in the current series. *E* embolization, *GK* gamma knife radiosurgery, *MS* microsurgery

for individual treatment steps but rather for the overall therapeutic result, i.e., permanent angiographic nidus occlusion. Details on the therapeutic modalities provided in the series are in Figs. 1 and 2.

Results

Among the patients initially presenting with AVM-related intracerebral hemorrhages [ICH], a nidus size of <3 cm and a singular venous drainage pattern were statistically related to an increased AVM hemorrhage risk, as shown in Table 1. The clinical course during ongoing treatment is outlined in Table 2. Of the patients treated, 89.5 % were improved or unchanged throughout the course of treatment, whereas 31 patients [10.5 %] suffered transient or permanent neurological deteriorations during ongoing therapy. In more detail, 9.5 % [4/42] of the patients undergoing embolization, 10.3 % [12/117] of the patients receiving gamma knife radiosurgery, and 13.8 % [12/87] of the patients having multimodality management of their AVMs suffered neurological deteriorations during ongoing treatment.

Among the 294 patients treated, 28 or 9.5 % of the study population suffered non-fatal AVM-related hemorrhages under ongoing, frequently staged treatment (Table 3). In detail and as outlined, 9 % [12/142] of patients with initially unruptured AVMs, and 11 % [16/152] of patients with initially ruptured AVMs suffered ICH during ongoing treatment. Of the 142 patients harboring initially unruptured AVMs, 7 % of those undergoing monomodal therapy and 14 % of those undergoing multimodality management suffered a first ICH during the course of treatment (Table 4). The higher hemorrhage rate under ongoing treatment in the latter group is best explained by the more complex angiomorphology of the AVMs subjected to a multimodality treatment approach, resulting in a longer latency between the initial treatment step and angiographic demonstration of nidus obliteration, thereby leaving more time for AVM-related hemorrhage.

Discussion

In contrast to AVM-related hemorrhages upon admission, where often a small nidus and a single venous drainage were related to hemorrhage [2, 4, 9, 18], among patients suffering ICH undergoing treatment in the present series, a deep nidus location and multiple draining veins were related to an increased hemorrhage risk. It is reasonable to assume that large AVMs with multiple deep and superficial draining veins may present earlier with neurologic symptoms other than hemorrhage, whereas smaller AVMs may only become apparent after rupture and hemorrhage. In contrast, in the present series the AVMs bleeding under ongoing treatment with an average latency of 3.5 years between the initial treatment steps and hemorrhage were larger, often deep-seated or with deep compartments, and with multiple draining veins. This pattern, however, more resembled the characteristics of initially ruptured intracranial AVMs as described in previous long-term follow-,up studies [5–7].

At the time of hemorrhage, the AVMs bleeding under ongoing treatment in the present series were substantially reduced in nidus volume and were often awaiting angiographic closure after a final treatment step using gamma knife neuroradiosurgery. The residual nidus compartments, which ultimately caused the hemorrhage, were usually supplied by deep perforating arteries, i.e., often poor candidates for endovascular treatment, or were situated in eloquent brain parenchyma, i.e., 25 % of the AVMs bleeding under ongoing treatment were located within the brain stem or the basal ganglia (Fig. 3).

A comprehensive description of both treatment efficacy and treatment-related morbidity is provided in a publication by van Beijnum et al [20]. In their meta-analysis of 13,698 AVM patients, permanent angiographic AVM nidus obliteration was on average achieved in 96 % of patients undergoing microsurgical AVM resection, 38 % of patients receiving stereotactic radiosurgery, and 13 % of patients subjected to endovascular treatment. Mortality or permanent treatment-related morbidity occurred on average in 7.4 % of the microsurgical group, 5.1 % of the radiosurgical group, and 6.6 % of the endovascular group, respectively [8, 19]. With regard to multimodality treatment [16], these authors stated that “we were not able to provide reliable estimates on the risk of multimodality treatment. Multimodality treatment may be the safest approach for some brain AVMs, but it may also result

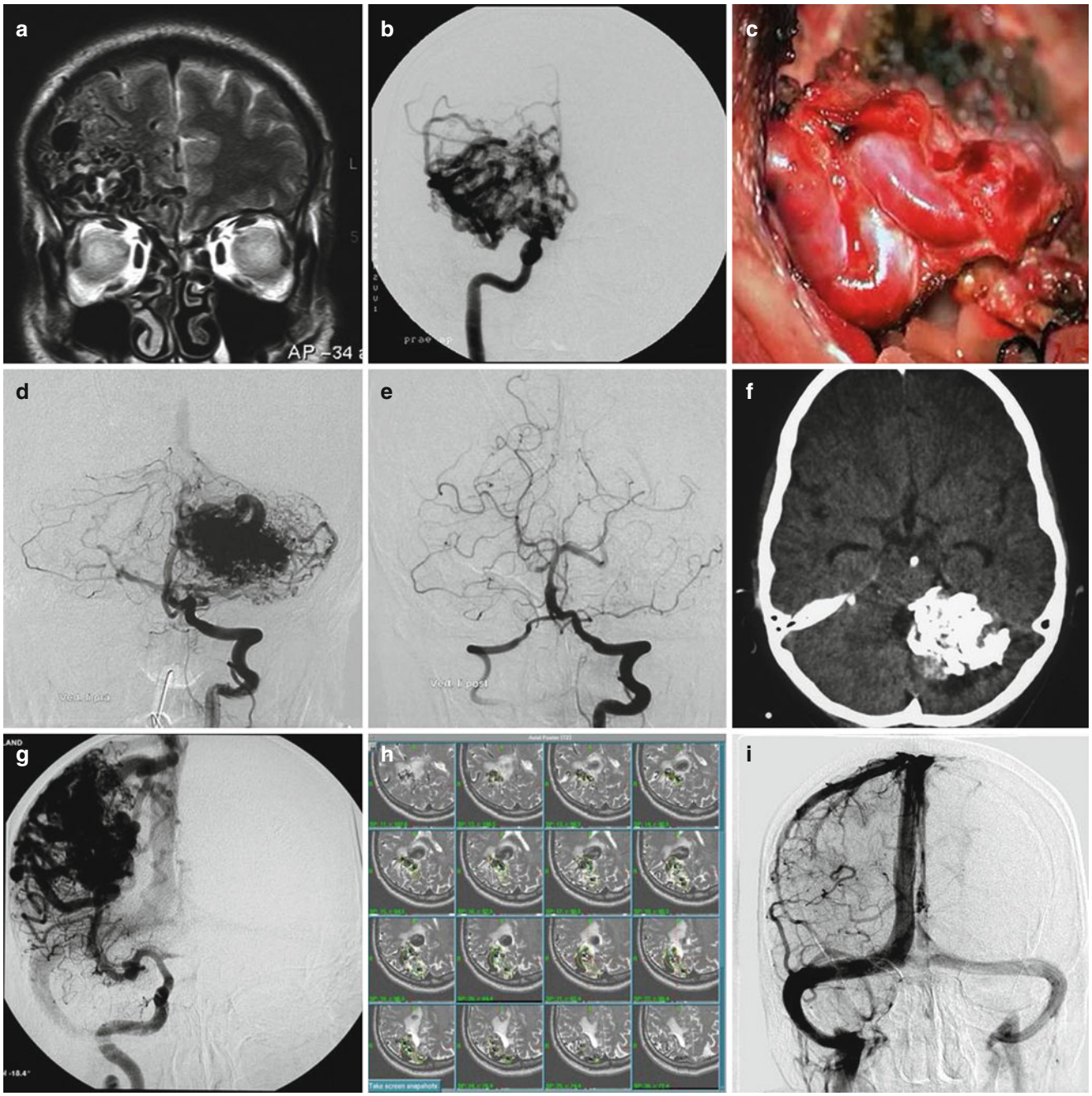

Fig. 2 Therapeutic modalities used in the current series. (**a**–**c**) microsurgical resection of large, unruptured, frontolaterobasal AVM [Spetzler Martin Grade 4] after pre-operative intranidal embolization. The Histoacryl cast does not interfere with surgical dissection and manipulation of the AVM nidus and does not complicate the surgical separation of casted feeding arteries (**d**–**f**), therapeutic embolization of a ruptured cerebellar AVM [Spetzler Marin Grade 3] [15, 17] by solid intranidal Histoacryl casting. The AVM obliteration is obtained by solid intranidal glue embolization rather than proximal feeder occlusion, resulting in permanent angiographic nidus obliteration and thus cure of the malformation (**g**–**i**), staged gamma knife radiosurgery of a large, parieto-occipital AVM [Spetzler Marin Grade 3]

Table 1 AVM-related hemorrhages upon first admission

			no ICH	ICH	Total	
Nidus size	<3 cm	*n*	71	119	190	
		%	37.4 %	62.6	100 %	
	>3 cm	*n*	71	33	104	
		%	68.3 %	31.7 %	100 %	$p < 0.0001$
Drainage	Singular	*n*	21	81	102	
		%	20.6 %	79.1 %	100 %	
	Multiple	*n*	121	71	192	
		%	63.0 %	37.0 %	100 %	$p < 0.0001$
	Superficial	*n*	56	58	114	
		%	49.1 %	50.9 %	100 %	
	Deep	*n*	23	54	77	
		%	29.9 %	70.1 %	100 %	$p = 0.008$

Nidus size <3 cm, as well as singular deep venous drainage patterns, were significantly related to initial AVM-related hemorrhages
ICH intracerebral hemorrhage

Table 2 Clinical course during multimodality management

Asymptomatic	82	27.9 %
Improved	118	40.1 %
Unchanged	63	21.4 %
Worse	31	10.5 %
Total	294	100 %

In the present series, 89.5 % of patients remained clinically unchanged or improved their initially presenting neurological symptoms during ongoing treatment, whereas 10.5 % of patients suffered either aggravation of their presenting symptoms or suffered newly acquired transient or permanent treatment-related deficits

Table 3 Locations of AVMs ruptured during ongoing treatment

Location	Frontal	2	7.1 %
	Frontoparietal	2	7.1 %
	Parietal/central	6	21.4 %
	Sylvian	1	3.6 %
	Occipital	3	10.7 %
	Trigonal/parasplenial	1	3.6 %
	Basal ganglia	7	25 %
	Brain stem	1	3.6 %
	Cerebellar	2	7.1 %
Total		28	100 %

In the present series, 28 patients or 9.5 % of the group suffered AVM-related hemorrhages during ongoing treatment. A significant number of these lesions [8/28 or 28.6 %] were located in the brain stem or the basal ganglia

Table 4 Clinical course during monomodal and multimodality management

	Monomodal (%)	Multimodal (%)
1st hemorrhage	7	14
Seizures	5	12
Neurologic deficits	8	18
Headache	5	14

The incidence of 1st AVM-related hemorrhage during ongoing treatment was 7 % in the group receiving monomodal treatment and 14 % in the group undergoing multimodality management. This difference is explained by the more complex angiomorphology and the longer latency period between the first treatment step and angiographic obliteration in the group subjected to multimodality management. For similar reasons, neurologic deficits, seizures, and headaches, both pre-existing and newly acquired, were seen more frequently in the subgroup receiving multimodality treatment

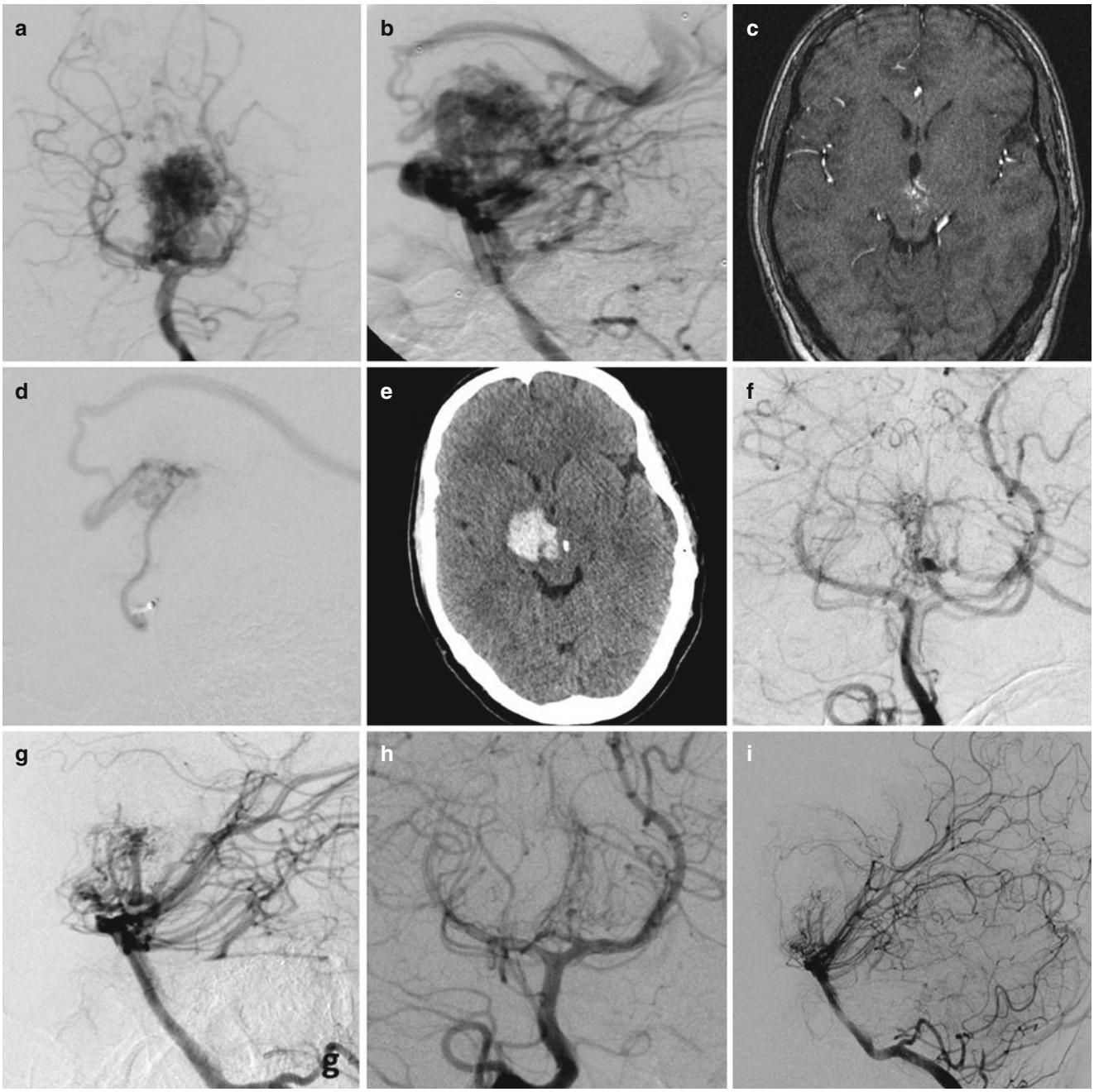

Fig. 3 AVM rupture under ongoing staged multimodality treatment. (**a**–**c**) unruptured mesencephalic AVM with prominent perforating artery supply. (**d**) initial treatment consisted of partial Histoacryl embolization and subsequent gamma knife radiosurgery of the remnant nidus. (**e**) 3 years after the initial treatment, the patient was readmitted with a 1st AVM-related hemorrhage. (**f**, **g**) angiography disclosed a remnant nidus. (**h**, **i**) successful management of the AVM residual by additional gamma knife radiosurgery. The patient's refusal of follow-up explains the undetected remnant AVM nidus 3 years after the initial procedures. The initial radiosurgical dosage planning allowed for additional gamma knife treatment in this particular case

in accumulation of risks of the various treatments involved" [20]. Analysis of our data on both ruptured and unruptured intracranial AVMs showed that efforts to avoid surgical or endovascular morbidities in patients harboring deep-seated AVMs or lesions in eloquent target areas of the brain by using staged multimodality treatment approaches were counterbalanced by a 9.5 % risk of delayed AVM-related hemorrhage and a 10.5 % risk of transient or permanent neurological deterioration during ongoing treatment, i.e., before angiographically proven obliteration of the malformation.

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

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Advances in Embolization of bAVMs

L. Renieri, N. Limbucci, and S. Mangiafico

Abstract Brain AVMs are complex malformations, usually congenital, that need a deep understanding of anatomy and pathophysiology to be safely treated. Nowadays, embolization and radiosurgery are carried out more frequently due to their reduced invasiveness as compared to conventional neurosurgery. This paper aims to describe different and new endovascular approaches that allow the interventionalist to treat almost all the small AVMs and to reduce the nidus of the bigger ones in order to facilitate the surgical or radiosurgical intervention.

Keywords Brain AVM • Embolization techniques • Onyx • Glue

Introduction

Treatment of brain arteriovenous malformations (AVMs) is often a challenge for surgeons and interventionalists because of the high rate of procedural complications. The optimal management of unruptured AVMs in controversial. The recent randomised clinical trial ARUBA [1] concluded that intervention for unruptured brain AVMs carries greater morbidity and mortality than observation, but this trial has been strongly debated and criticized from the neurosurgical community.

Embolization, surgery, or radiosurgery alone are safe and effective for small AVMs, while in the case of larger ones, a multidisciplinary approach [2, 3] might often lead to the cure of the patient (targeted pre-surgical or radiosurgical embolization); Spetzler Martin 4 and 5 AVMs often remain untreatable due to the high morbi-mortality rate of intervention.

L. Renieri, MD • N. Limbucci, MD • S. Mangiafico, MD (✉)
Interventional Neuroradiology, Careggi University Hospital, Florence, Italy
e-mail: mangiax@libero.it

Embolization techniques have really been given a boost after first Onyx (Covidien, Irvine, CA) [4] and then other non-adhesive liquid embolic agents came on the market; nowadays, the interventionalists can achieve the occlusion of an entire nidus in a high percentage of cases.

We report our experience in treating AVMs with a focus on endovascular developments.

Materials and Methods

We retrospectively reviewed from our AVM database data on 205 consecutive patients with bAVMs treated by endovascular embolization in our institute between January 2008 and April 2014, using either Onyx or N-butyl-2-cyanoacrylate (NBCA) glue (Glubran 2, GEM, Viareggio, Italy). The epidemiological data are shown in Table 1.

Overall, 156 of 205 patients (76.1 %) were treated with Onyx alone or in combination with acrylic glue, and 49 of them (23.9 %) with glue only. In 88 cases (43 %), embolization was performed using the Double Arterial Catheterization Technique (DACT), in 104 (51 %) with the Single Arterial Catheterization Technique (SACT), and in 11 cases (5 %) with a trans-venous approach. Only two cases were treated with a combined approach (vein and artery).

Table 1 Epidemiological data on all 205 of the AVMs considered

Mean age	38
Gender	45 % F, 55 % M
Ruptured	56 % (115/205)
Symptomatic	25 % (51/205)
Asymptomatic	19 % (39/205)
Nidus <4 cm (SM 1,2,3)	72.2 % (148/205)
Nidus >4 cm (2,3,4,5)	27.8 % (57/205)

T. Tsukahara et al. (eds.), *Trends in Cerebrovascular Surgery*, Acta Neurochirurgica Supplement 123,
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Protocol

The goal of the endovascular treatment was the complete obliteration in the case of small AVMs and a good devascularization of medium or large ones to make the surgical resection or radio-surgical treatment more feasible and safer. When the AVM was completely occluded endovascularly, angiographic follow-up was scheduled after 6 months and 2 years; if further embolizations were required, they were all performed within 1–3 months. Whenever the AVM was not completely obliterated and a further endovascular procedure was not indicated, patients underwent surgical resection within a few days, or radiosurgery after at least 2 months.

Patient Analysis

We reviewed the occlusion rate of patients treated by embolization alone or by embolization followed by surgical resection or radiosurgery. We also reviewed all complications that occurred during the endovascular treatment or the periprocedural phase (48 h) as well as delayed ischemic or hemorrhagic events (delayed complications were defined as those that occurred 4 weeks from the procedure). The morbidity (defined as mRS >1 at 3 months) and mortality rates were calculated.

Results

Occlusion Rate

The overall multimodal occlusion rate in our series is 87 % (179 of 205). Analyzing the group of AVMs smaller than 4 cm (average volume: 15 cc), curing the patient was achieved in 91.9 % (136 of 148) of cases. The complete obliteration of the AVM was achieved by the following approaches: embolization alone in 62.6 % of the cases (92 of 148); embolization followed by surgery in 16.2 % of cases (24 of 148); embolization followed by radiosurgery in 13.5 % (20 of 148). In the group of AVMs larger than 4 cm (15 cc), the overall occlusion rate was 75.4 % (43 of 57).

The complete obliteration of the AVM was achieved by the following approaches: embolization alone in 8.8 % of the cases (5 of 57); embolization followed by surgery in 28.1 % of cases (16 of 57); embolization followed by radiosurgery in 38.5 % (22 of 57).

Complication Rate of Endovascular Treatment

Overall, various types of periprocedural or delayed adverse events occurred in 29 patients (14.1 %); 11.7 % were hemorrhagic and 2.4 % ischemic. The morbidity and mortality rates were 6.8 % (14 of 205) and 2.9 % (6 of 205), respectively.

In the group of 148 patients with small AVMs, the complication rate was 7.4 % (11): among them, nine were hemorrhagic complications (6 were periprocedural bleedings – 4.1 % – and 3 delayed bleedings – 2 %). Ischemic complications were 1 %. Morbidity and mortality rates were 4.1 % (6) and 1.4 % (2), respectively.

In the group of 57 patients with large AVMs, in 26.3 % (15) of the cases, a complication occurred. Concerning the hemorrhagic risk of the procedure, a periprocedural bleeding was observed in 10 patients (17.5 %), and a delayed bleeding in five of them (8.8 %). The ischemic complication rate was 5.2 %. Morbidity and mortality in this group was 14 % and 8.8 %, respectively.

In our series, high-flow arterio-venous fistulas were present in 70 % (11 of 16) of periprocedural bleedings, and a single venous drainage in 90 % (14 of 16). All the cases (100 %) bled during the last phases of embolization, where 50 % or more of the nidus was already occluded.

Discussion

Nowadays, there are many options (embolization, surgery, radiosurgery, combined approaches) to achieve obliteration of an AVM, but no well-defined guidelines exist and many differences occur among institutes because therapeutic strategies often depend on local expertise. Even the very challenged ARUBA trial [1] does not help find a solution to this critical issue, even if it made clear to the neurosurgical community that good results in this field cannot be attained without a proper selection of patients and detailed operative planning. At our center, the choice of the indication and the modality of treatment are decided on a case-by-case basis in a multidisciplinary context, and all elective patients undergo diagnostic angiography before decisions are made. For small AVMs – in our opinion – the first line of treatment is curative embolization (in one or more sessions), because the results are satisfactory in terms of safety and efficacy and, in the case of residual nidus, treatment can anyway be completed by surgery or radiosurgery, which are usually helped by previous embolization. Another advantage of this strategy is

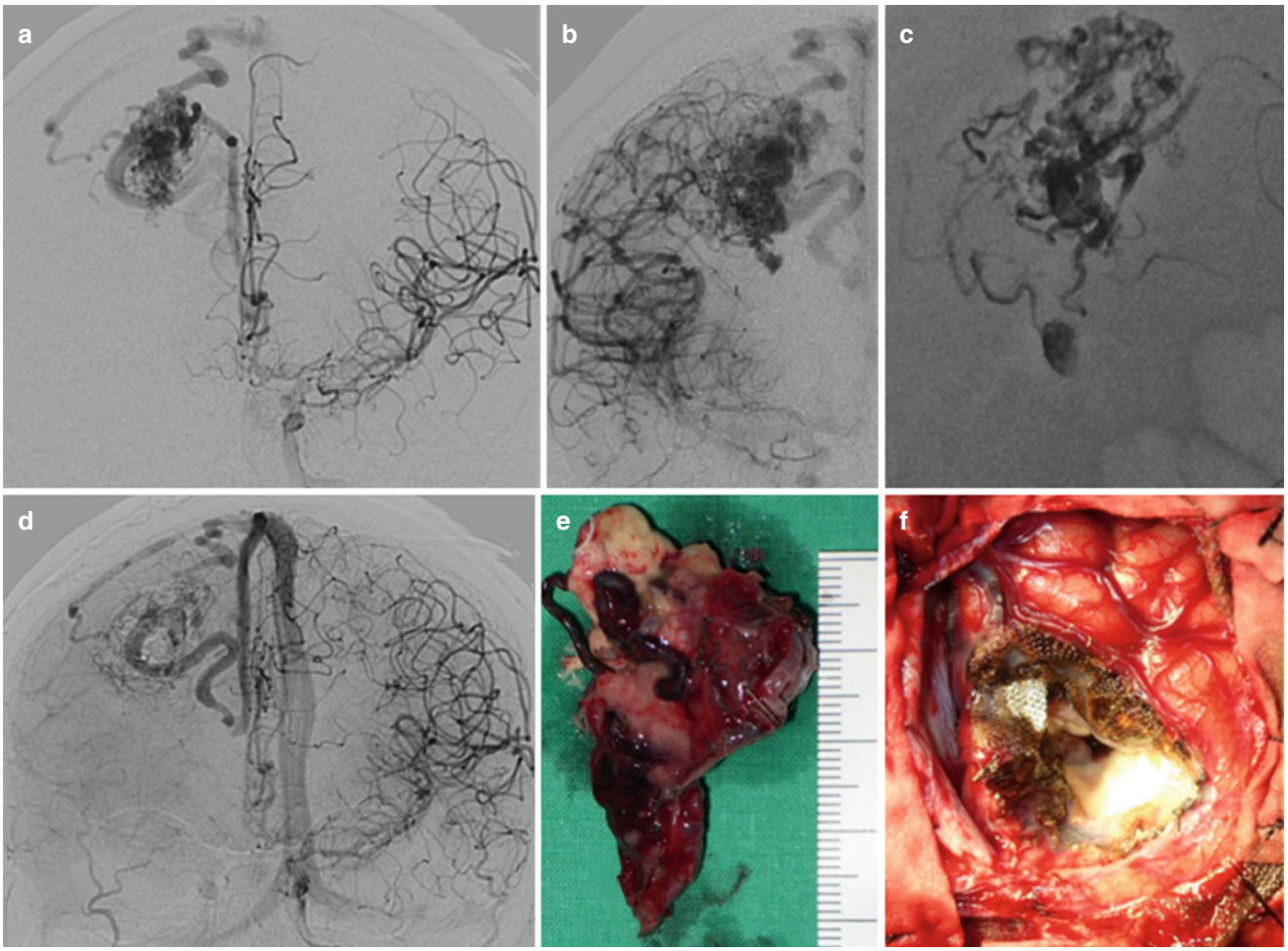

Fig. 1 Pre-central hemorrhagic AVM. (**a**, **b**) Pre-treatment DSA. (**c**) Cast of Onyx with occlusion of one pseudo-aneurysm. (**d**) Final DSA. (**e**, **f**) AVM excision

that the patient usually accepts embolization more than surgery, due mainly to the limited invasiveness. If embolization is considered unfeasible (impossible catheterization of feeding arteries), surgery or radiosurgery are considered to be first options. Obviously, surgery is the first choice when a life-threatening hematoma is present.

Despite the progress of endovascular techniques, large AVMs are definitely a major contraindication for curative embolization due to the high complication rate during their treatment. According to our experience, in the case of large AVMs, once the decision to treat the patient has been made, an interdisciplinary approach is considered. If surgery is feasible, a partial preoperative embolization can lead to a devascularization of the deeper territories, namely the ones that the surgeon may not be able to control adequately, pseudoaneurysms, or macrofistulas. In these cases it is important to avoid narrowing of the venous outlet so that the hemodynamic balance is maintained: entering the nidus is not necessary at all and glue can be safely used to selectively close the feeders one by one. These general principles have to be discussed and planned anyway with the surgeon before every treatment (Fig. 1).

In the case of deep and large AVMs, where surgery may be very complex or even contraindicated, a pre-radiosurgical embolization can be useful to reduce the volume of the nidus or selectively occlude pseudoaneurysms or macrofistulas in case of a hemorrhagic AVM.

Regardless of the aim of the embolization, endovascular techniques have improved tremendously in the last 5 years due to new materials on the market and the operators' increasing confidence and skills. A real boost for brain AVM's treatment has been given by Onyx: it is a non-adhesive liquid embolic agent based on ethylene-vinyl alcohol copolymer. Before Onyx came on the market, NBCA was the main agent for embolizing AVMs, and it is still useful and used to selectively close the pedicles' being curative in well selected cases with a small nidus, or in case of a direct AV

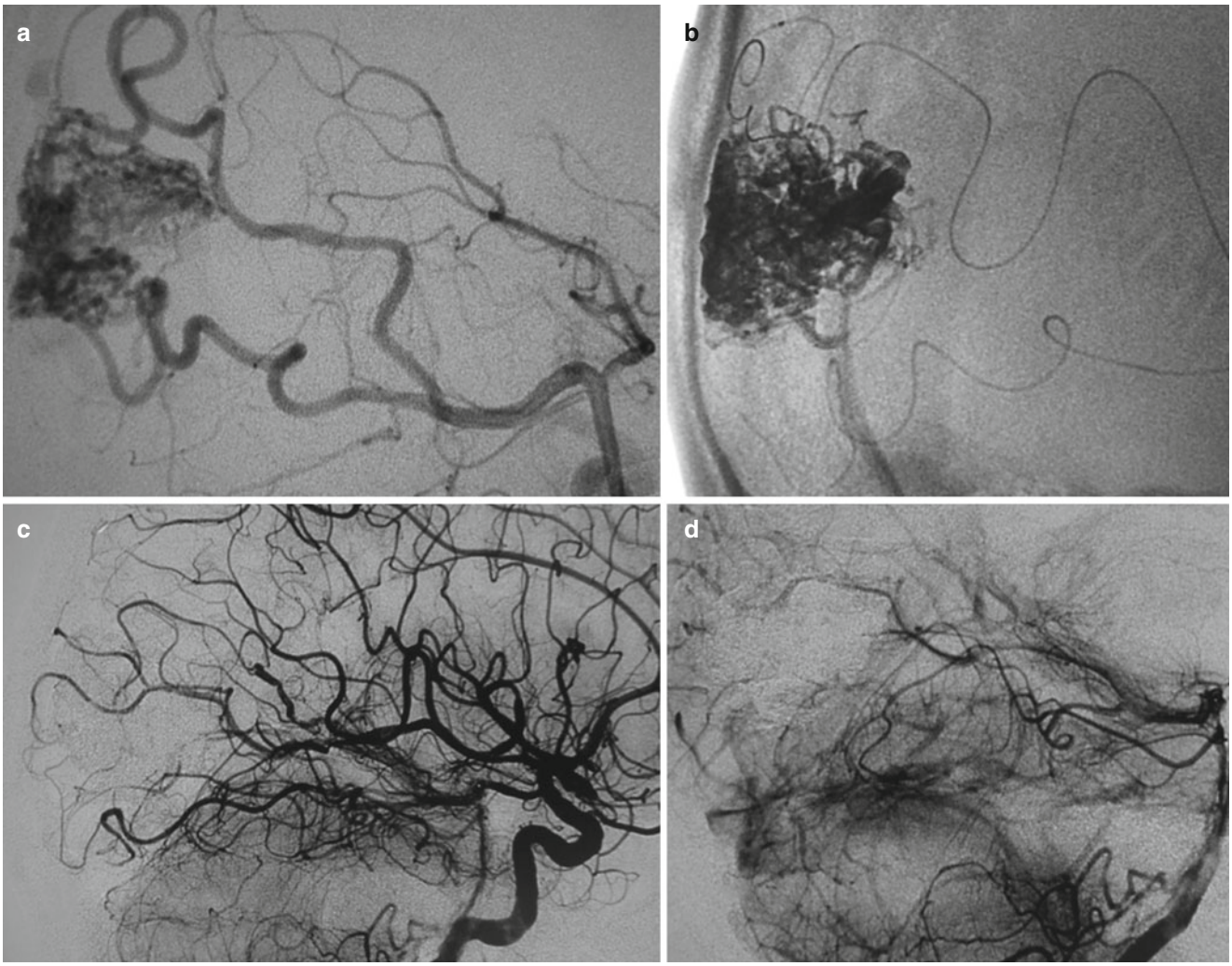

Fig. 2 Double arterial catheterization technique in an occasional parieto-occipital AVM. (**a**) Pre-treatment DSA angio. (**b**) Alternated injections from the two microcatheters in place. (**c**, **d**) Final angiogram and complete occlusion of the AVM

shunt [5, 6]. Nevertheless, it could not properly enter the nidus that devascularizes it – which is exactly one of the major proprieties of Onyx. Since Onyx was introduced [4, 7, 8], interventionalists are becoming increasingly confident with it and they have developed new endovascular approaches to treat brain AVMs, including the complex, deeply located ones that can be very difficult to cure with glue.

Onyx typically makes a plug at the tip of the microcatheter and then proceeds along the feeder, occluding it in a concentric way (from the outside to the inside of the vessel, with a layer-over-layer pattern). This material is flow-independent and progresses toward territories with the lowest gradient of pressure: it means that good managing of injections allows the operator to achieve a progressive occlusion of the compartment with a relatively short retrograde occlusion of the functional artery. The best technique is catheterizing a small feeder (big feeders need a very hard plug and generally lead to long refluxes) and achieving an intra-nidal position; from there, multiple injections can be given (interval from one to another of 30–90: "plug and push technique") until satisfactory occlusion is achieved. Compared to glue, Onyx makes the procedure faster and reduces the number of sessions per patient.

Using a single microcatheter for injections can be ineffective in more complex or multi-compartment cases; as a matter of fact, we experienced some complications due to closing one compartment and continuing injecting to push Onyx into a second compartment while narrowing the interposed venous outlet and leading the AVM to bleed. To avoid such a complication, the dual arterial catheterization technique (DACT) has been developed, i.e., a simultaneous injection from two different points, achieving a gradual, centripetal, exclusion of the nidus. In these cases, the occlusion of the vein is the last step and it is reached after devascularizing most of the arterial feeders. DACT allows the surgeon to achieve better occlusion of the nidus with fewer procedures per patient [9, 10] (Fig. 2).

In the case of a high-flow arterio-venous fistula, a very effective precaution is the use of a balloon catheter proximal to the microcatheter used for injection; blocking the flow,

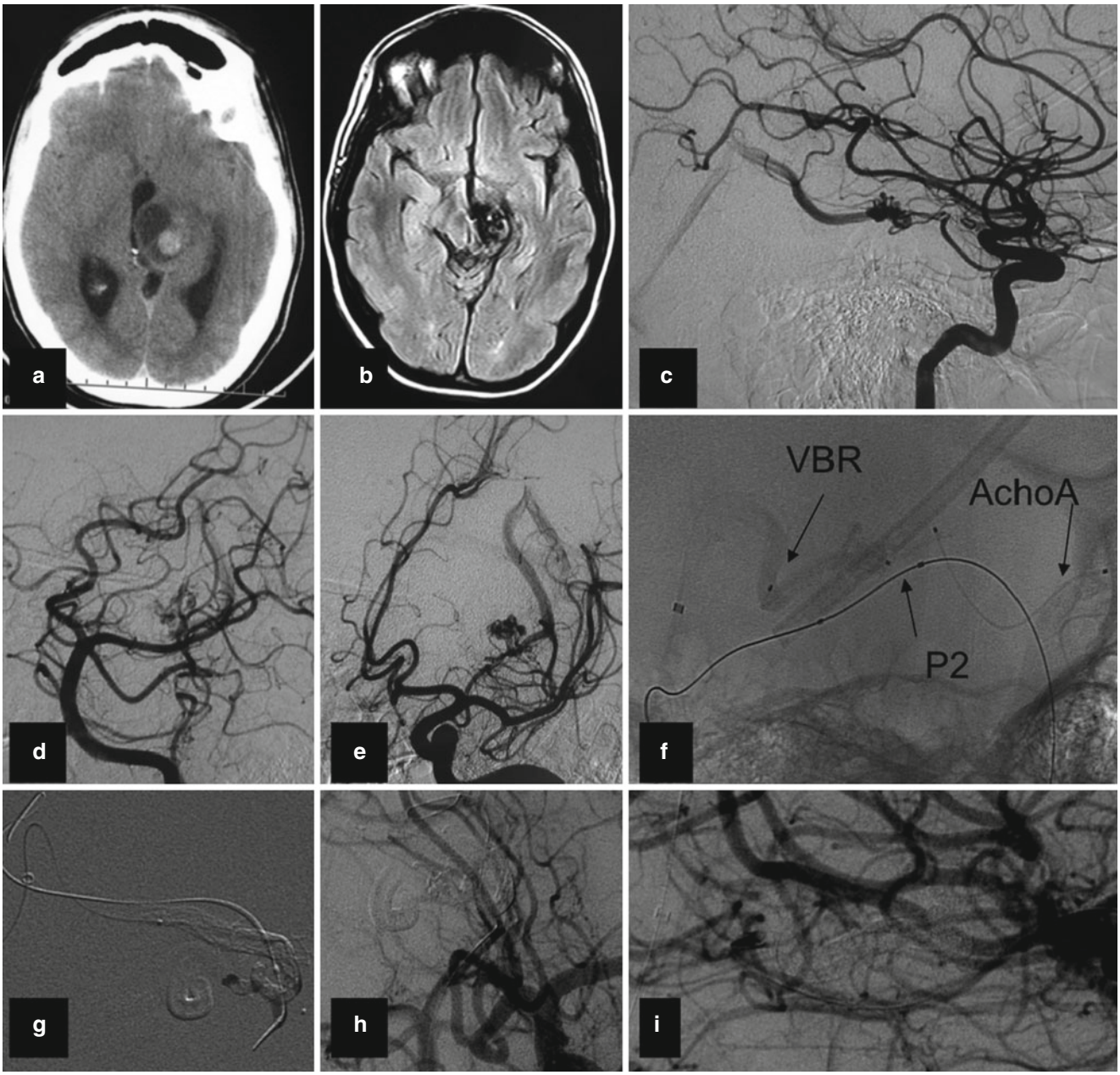

Fig. 3 Left thalamo-mesencephalic AVM. (**a**–**c**) Pre-treatment CT, MR and DSA. (**d**) Thalamogeniculate perforators from P2. (**e**) Thalamic perforators form AChA. (**f**) Positioning of one microcatheter in the Basal Vein of Rosenthal (BVR). (**g**) Onyx injection during inflation of balloon in P2 to avoid reflux in the posterior cerebral artery. (**h**, **i**) Final angiograms

Onyx, or glue progression into the fistula is easier to manage, avoiding a narrowing or definitive occlusion of the venous compartment. A proximal occlusion of the feeder can be achieved even with coils and very concentrated glue; this technique, known as the "pressure cooker technique" is also useful for shortening Onyx reflux, allowing a faster intranidal penetration even in the case of arteriolo-venular shunts [11].

Finally, a new approach is the trans-venous embolization that was recently proposed as an alternative technique for embolization in very select cases [12–14]. In our series, this approach was used in the case of small, usually deeply located AVMs fed by small perforating arteries or with *en-passage* feeders: these features expose patients to high surgical risk and often make the classical trans-arterial embolization unfeasible. In the case of trans-venous embolization, the microcatheter is positioned right inside the head of the vein, close to the convergence of all the feeders; from there, a super-selective injection of Onyx leads to the progressive occlusion of the *core* of the nidus, and then backwards to the arteriolar feeders. When reflux in functional arteries is not allowed, they can be preserved by their temporary occlusion with a balloon during injection (Fig. 3). A concern of trans-venous embolization is the increased hemorrhagic risk in the case of venous outlet

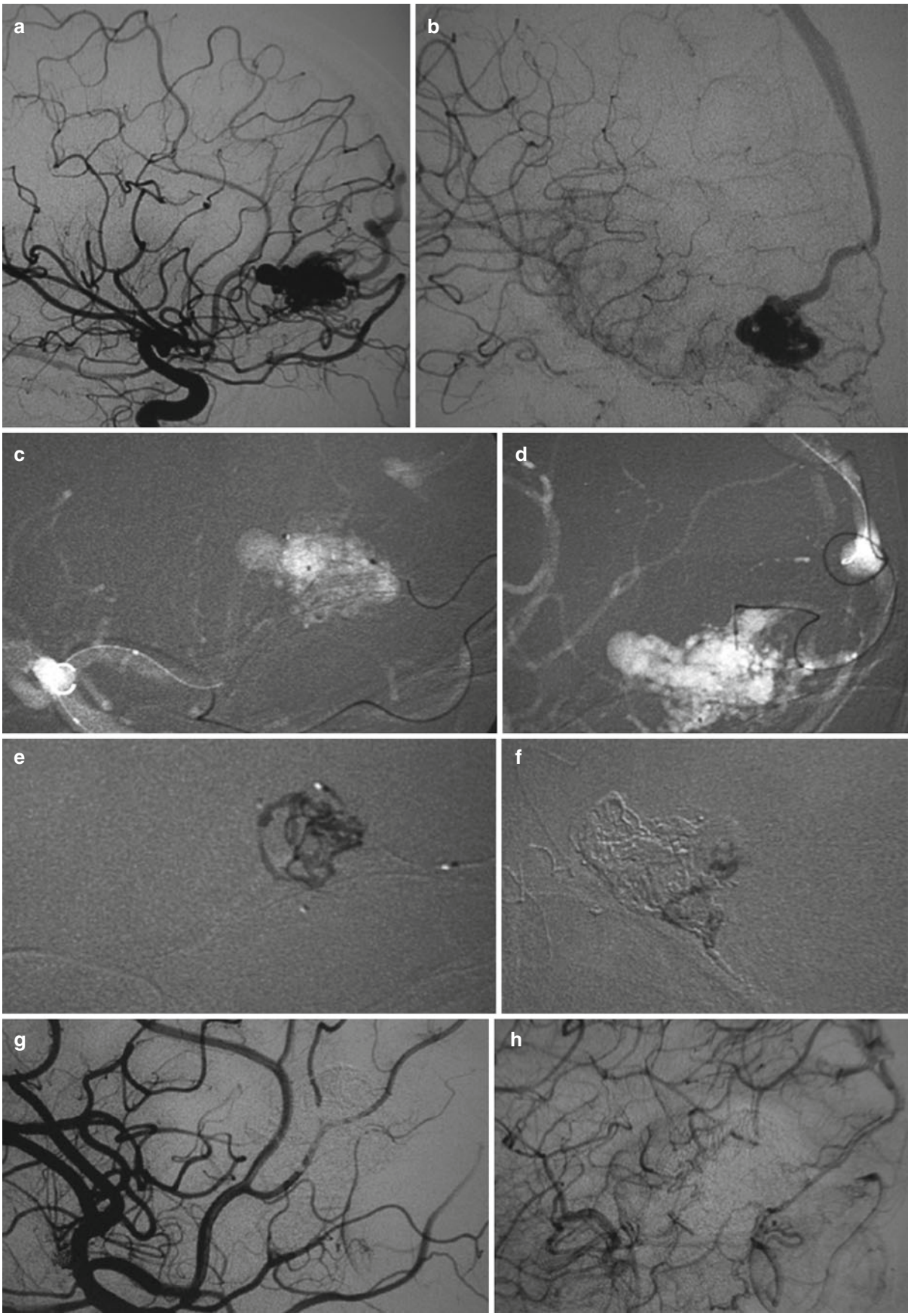

Fig. 4 Fronto-basal AVM (**a**, **b**) pre-treatment DSA. (**c**, **d**) Positioning of the two microcatheters respectively in the artery and in the vein. (**e**) Onyx injection from the vein. (**f**) Onyx injection from the artery. (**g**, **h**) Final angiograms

occlusion with a residual patency of the nidus. For this reason, whenever we are not sure of completely occluding the nidus injecting from the venous side and the pure arterial approach is considered not effective at all, we combine the two techniques, reducing the inflow with classic arterial embolization and then completely occluding the AVM on the venous side (Fig. 4).

Beyond new approaches, there are now new non-adhesive liquid embolics such as Phil (Microvention, Tustin, CA, USA) and Squid (Emboflu, Switzerland) that should theoretically optimize the qualities of Onyx and reduce its critical issues, such as its remarkable radio-opacity and the long time needed to make a stable plug. However, no evidence of the superiority of these new materials is reported in the literature at the moment.

Considering all the techniques and embolic agents, in our series 47.3 % of the patients were cured with embolization alone. These data are similar to those reported, in which the range is 23.1–96 % [15–19] The authors of one of the largest series report an occlusion rate of 51 % in 350 patients with a low complication rate [15]. The disagreement of results depends mainly on the therapeutic strategy chosen by the authors (partial vs, curative embolization) and the anatomical characteristics of the treated AVMs. Based on our database and on the literature, it is clear that a small, compact nidus, a single arterial compartment, and a single venous drainage are important features that could predict the complete occlusion of the AVM by endovascular means. Recently, an endovascular grading scale for AVM embolization was proposed; it incorporates the number of feeding arteries, eloquence, and the presence of an arteriovenous fistula. Authors observed that low grades were associated with endovascular cure and better outcome [20].

Concerning complications, we have an overall hemorrhagic and ischemic rate of 14.1 % (respectively, 11.7 % and 2.4 %). It is important to note that the highest risk is for AVMs larger than 4 cm (15 cc), where we report a hemorrhagic risk of 26.3 % (15 of 57). This can be partially explained by the presence of a complex nidus with various multiple shunts (arteriolo-venular, arterio-venular, arteriolo-venous, and artero-venous), and by the overlapping of the structures that sometimes do not allow the operator to understand the anatomy, especially when a dense cast of Onyx hides the details of the nidus itself. In all these cases, when the bleeding occurred, no angiographic signs of outflow reduction, stenosis of the drainage vein, or anomalies at the post-embolization angiographic control were observed. The reason for these bleedings could be related to an impairment of the intranidal micro-hemodynamic balance.

On the other hand, among small AVMs, all the bleedings could have been forestalled, since a significant flow reduction of the venous outlet was always evident at the end of the embolization; in these cases, the general hemodynamic was compromised. Today, whenever we recognize a contrast stagnation in the venous outlet, we immediately send the patient to surgery while under the same general anesthesia.

In our experience, size is a major risk factor for post-procedural bleedings as the hemodynamic balance of a large AVM is difficult to understand and can apparently lead to unintelligible late bleedings, especially when a conspicuous part of the nidus is already occluded and the Onyx cast could hide the residual angioarchitecture of the nidus, making any venous stasis difficult to detect. Regardless of the size, the presence of a high-flow arterio-venous fistula is another risk factor for intra-procedural bleedings; in our series, it was present in 70 % (11 of 16) of the cases.

Based on our data, a major topic to consider is the venous drainage; a single one is significantly related to higher procedural risk, especially if it is cortical (14 of 16, or 90 %). This can be easily explained, as any impairment of the unique outlet leads to an increase in the intranidal pressure and consequent bleeding.

In all the cases in which we experienced bleeding during the last phases of the embolization, it meant that more than 50 % of the nidus was occluded. In one-third of the cases then, the bleeding occurred while completely closing the nidus. To cure an AVM, the nidus and the head of the vein have to be embolized, and the passage of Onyx in the venous outlet is definitely the riskiest step.

Our findings are confirmed by the current pertinent literature: the largest analysis of complications for endovascular procedures reported a hemorrhagic complication rate of 11 % [21]. In that series, premature venous occlusion was a risk factor in small and midsize AVMs, while in large ones, no variables were risk factors for bleeding. Moreover, the total volume of embolic agents was a hemorrhagic risk factor for small AVMs (for us it was an independent risk factor even in large AVMs).

ConclusionsCurative embolization is safe and effective in small AVMs (less than 4 cm) and can be considered an alternative to surgery (being possibly less invasive) and to radiosurgery (because it may lead to an immediate cure of the patient) in institutes with great endovascular experience. For large AVMs, curative embolization leads to a low obliteration rate with a high risk of complications; therefore, a multidisciplinary approach, with partial embolization followed by surgical resection or radiosurgery, should be considered.

Conflict of Interests Mangiafico S., MD, is proctor for actually he is proctor for codman and Codman

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Treatment of Dural AV Fistulae and Cavernomas

Embryological Consideration of Dural AVF

Michihiro Tanaka

Abstract

Background

The distribution of intracranial dural AVFs (DAVFs) may be affected by the embryological bony structures that consist of membranous bone and endochondral bone.

Methods

We retrospectively analyzed the distribution of the shunt points in 58 consecutive cases of DAVFs. Shunt points were identified with selective digital subtraction angiography, high-resolution cone beam computed tomography (CT), or three-dimensional rotation angiography. All the shunt points were plotted on the map of the skull base in relation to the topography of the endochondral bone and the membranous bone. If the shunt point was localized on the surface of endochondral bone, this was categorized as the endochondral bone group. If it was located on membranous bone, this was categorized as the membranous bone group. If the shunt point was independent from both bony structures, this was categorized as the independent group.

Findings

In 55 of 58 cases, shunt points were identified angiographically. Three cases had multiple shunts. There were 33 shunt points (60 %) belonging to endochondral bone. In this group, 16 cases of sigmoid, 11 of carotid cavernous, 3 of petrosal apex, and 3 of sigmoid DAVF were observed. There were 12 shunt points (22 %) localized on membranous bone; in this group, there were nine cases of transverse sinus, two of superior sagittal sinus, and one case of confluence DAVF. There were ten shunt points (18 %) independent from these two bony structures: four cases of olfactory groove, four . of middle fossa, and two of hypoglossal canal DAVF.

Conclusions

There were correlations between the localization of shunt points of DAVFs and the topography of endochondral bone and the membranous bone. The histological difference of endochondral bone and membranous bone at the level of epidural space might cause the formation of DAVFs.

Keywords Dural AVF • Embryological bony structure • Membranous bone • Endochondral bone • Segmental vulnerability of dural membrane

Abbreviations

CT	Computed tomography
DAVF	Dural AVF

Introduction

The pathoetiology of dural AVFs (DAVFs) is unknown. Intracranial DAVFs account for 10–15 % of all intracranial arteriovenous lesions, but no correlation was observed between age and frequency of aggressive neurologic symptoms [4–7, 16]. However, there is a higher incidence in women of a certain anatomical region on the skull base. There is a peak incidence occurring between 30 and 50 years of age [4, 13]. For example, carotid cavernous DAVFs are often observed in the female population, and the shunt points of carotid cavernous DAVFs are mainly localized on the paramedian aspect of the posterior clinoid processus near the clivus of basilar occipital bone [13]. Therefore, the topographical distribution of DAVFs should be discussed in terms of embryological bony structures.

M. Tanaka, MD, PhD
Department of Neurosurgery, Kameda Medical Center,
Higashi-cho 929, Kamogawa City, Chiba 296-8602, Japan
e-mail: michihiro.tanaka@gmail.com

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Embryonic Development of Bone

Ossification is the term for the formation of bone. There are two ways that bone can ossify during embryonic development [11, 12, 14]; each has its own name: intramembranous ossification, and endochondral ossification. So we vertebrates – except for chondrichthyes (e.g., cartilaginous fish such as sharks) have two types of embryological bony structures (Fig. 1a).

Because of these two ways that bone can develop, there are two types of bone, based on the way they developed embryonically: membranous bones, and endochondral bones. The membranous bones are flat bones, such as spinous process, laminae, clavicle and cranial vault; the other are the endochondral bones, which include the long, short, and irregular bones. On the level of cranium and vertebra, these cartilaginous bones are vertebral bodies, basioccipital, basisphenoid, and the petromastoid bone. Endochondral bone is the structure that develops in and replaces cartilage. During development in the embryological stage, the cartilage is partially or entirely destroyed by the process of calcification. The cartilage is then reabsorbed, leaving bone in its place; therefore, endochondral bone is also called cartilaginous bone. In the human skull base, endochondral bones consist of prechordal, hypophyseal, and parachordal cartilages [11, 14, 15, 18, 22, 23] (Fig. 1b). Based on this embryological architecture, Geibprasert et al. proposed a new classification of craniospinal epidural venous anatomical bases and clinical correlations [13] (Fig. 2). This classification can be interpreted and modified into the concept of embryological bony structures.

Methods and Materials

We consecutively assessed 55 patients with 58 intracranial DAVFs who presented between January 2006 and October 2012. At the time of presentation, the mean age of the patients was 66.4 ± 17.3 (± SD; range 33–85), and the study population was composed of 32 women (58 %) and 23 men (42 %). In all cases, six-vessel study of digital subtraction angiogram, three-dimensional rotation angiography, and high-resolution cone beam CT were performed in order to identify the shunt point. Each shunt point was plotted on the map of the skull base and the distribution was categorized in terms of the embryological bone structure. As a location of shunt formation of DAVFs, it is always on a dural membrane surface and it is beneath the skull bone or free margin of dural membrane, such as a falx or tentorial surface. If the shunt point was localized on the surface of endochondral bone, it was categorized as an endochondral group, and if the shunt point was localized on the surface of membranous bone, it was categorized as a membranous group. In the case where the shunt was located on the surface of falco-tentorial dural membrane or the border zone between endochondral bone and membranous bone, this was considered as independent of both bone structure, so it was categorized as an independent group (Fig. 3).

Results

There were 33 shunt points (60 %) belonging to endochondral bone. In this group, there were 25 women (76 %) and 8 men (24 %) (Table 1). The distribution of shunt points were

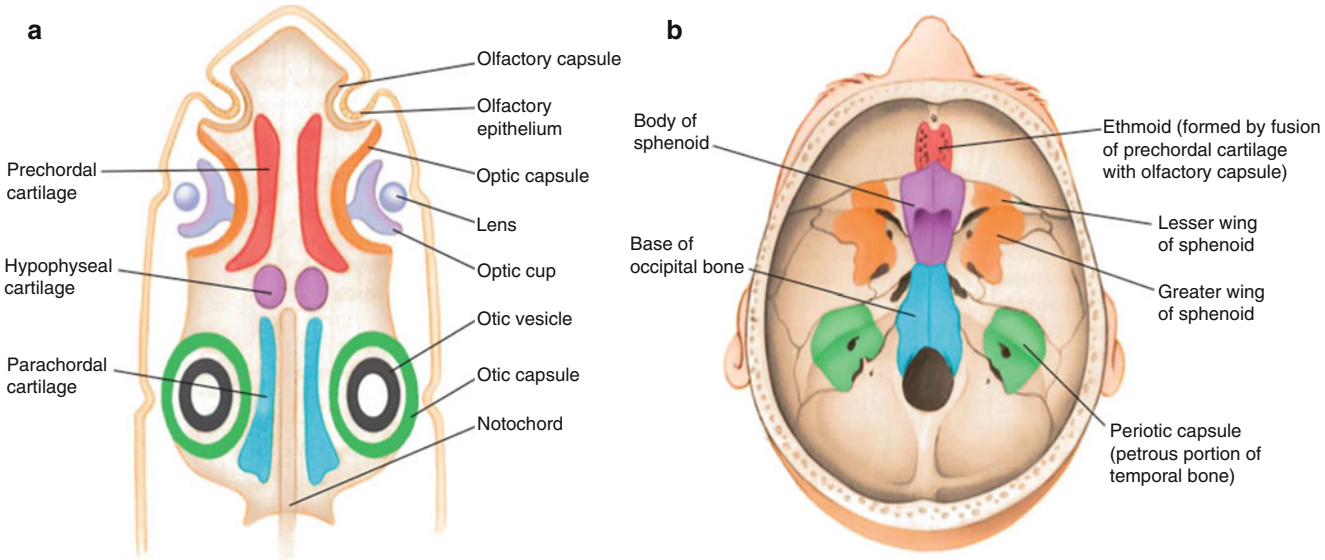

Fig. 1 The base of the skull in humans (**b**) is derived from three pairs of cartilaginous plates formed in early ancestors, (**a**) the prechordal, hypophyseal, and parachordal cartilages. The sensory organs are also protected by sensory capsules

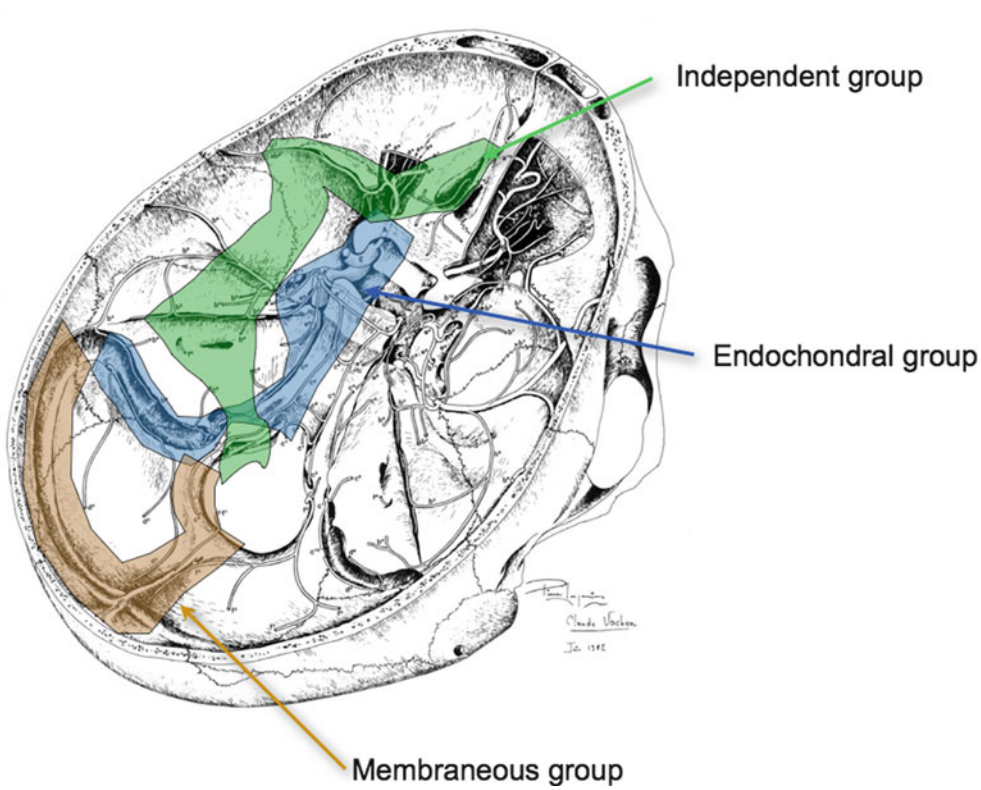

Fig. 2 The *blue* area depicts the endochondral group and the *orange* area relates to the membranous group. The *green* area is independent of these bony structures and the shunt flow of this group drains into emissary-bridging veins of the brainstem; their homologs drain deep cerebral structures such as the anterior condylar vein at the level of hypoglossal canal, the superior petrosal vein, the basal vein of Rosenthal, the vein of Galen, the veins of the olfactory groove, and the orbit (original diagram courtesy of Prof. Pierre Lasjaunias)

16 cases of sigmoid, 11 cases of carotid cavernous, 3 of petrosal apex and 3 of sigmoid sinus (Fig. 4). Clinical manifestation consisted of chemosis in ten patients (30 %), ophthalmoplegia in nine (27 %), bruit in seven . (21 %), headache in five (15 %), intracerebral haemorrhage in three (9 %), and loss of consciousness in two patients (3 %).

There were 12 shunt points (22 %) localized on membranous bone. In this group, there were five women (42 %) and seven men (52 %). There were nine cases of transverse sinus (75 %), two of superior sagittal sinus (17 %), and one of confluence of torcular herophili (8 %). Clinical manifestation consisted of headache in eight patients (67 %), bruit in two patients (16 %) and consciousness disturbance because of intracerebral haemorrhage in one patient (8 %).

There were ten shunt points(18 %) independent of these two bony structures. This group was composed of two women (20 %) and eight men (80 %). There were four patients with olfactory groove, four with faclo-tentorial surface and two with hypoglossal canal (anterior condylar vein). Clinical manifestation consisted of headache in four patients (40 %), tinnitus in three (30 %), intracerebral hemorrhage in two . (20 %), cervical myelopathy in one . (of hypoglossal canal DAVF), and epistaxis in one patient (olfactory groove DAVF) (10 %). The feature of angioarchitecture in this independent group is that it drains primarily into the cortical or spinal veins without reflux into the main dural sinuses, so the independent group was classified as aggressive in terms of the clinical course (Table 2).

There were also three cases of multiple shunt points, but most high-flow shunt was defined and plotted on the map as the original shunt point.

Discussion

Endochondral group

There was an approximately 3:1 female predominance in this group, which is also seen in the cavernous region. The drainage pattern of this group was primarily through the main sinuses, resulting in Types I, IIa, IIb, and II a+b, according to the Cognard classification, and Types 1 and 2 according to the Borden classification, depending on outflow restrictions [5]. The degree of cortical venous reflux varies and depends on the special anatomic variations and compartmentalization of the sinusal space if full coalescence of the venous lumen does not occur, or if there is extensive thrombosis in the main sinuses [5, 6, 9, 10, 19]. The cavernous sinus is bordered by the temporal bone of the skull, the sphenoid bone, lateral to the sella turcica and posterior clinoid processus that belong to the anterior surface of clivus. The shunt points of cavernous DAVFs are mainly localized on the paramedian aspect of posterior clinoid processus near the clivus of basilar occipital bone (Fig. 5). This site of predilection for shunt points corresponds well to the edge of the notochord at the skull base level.

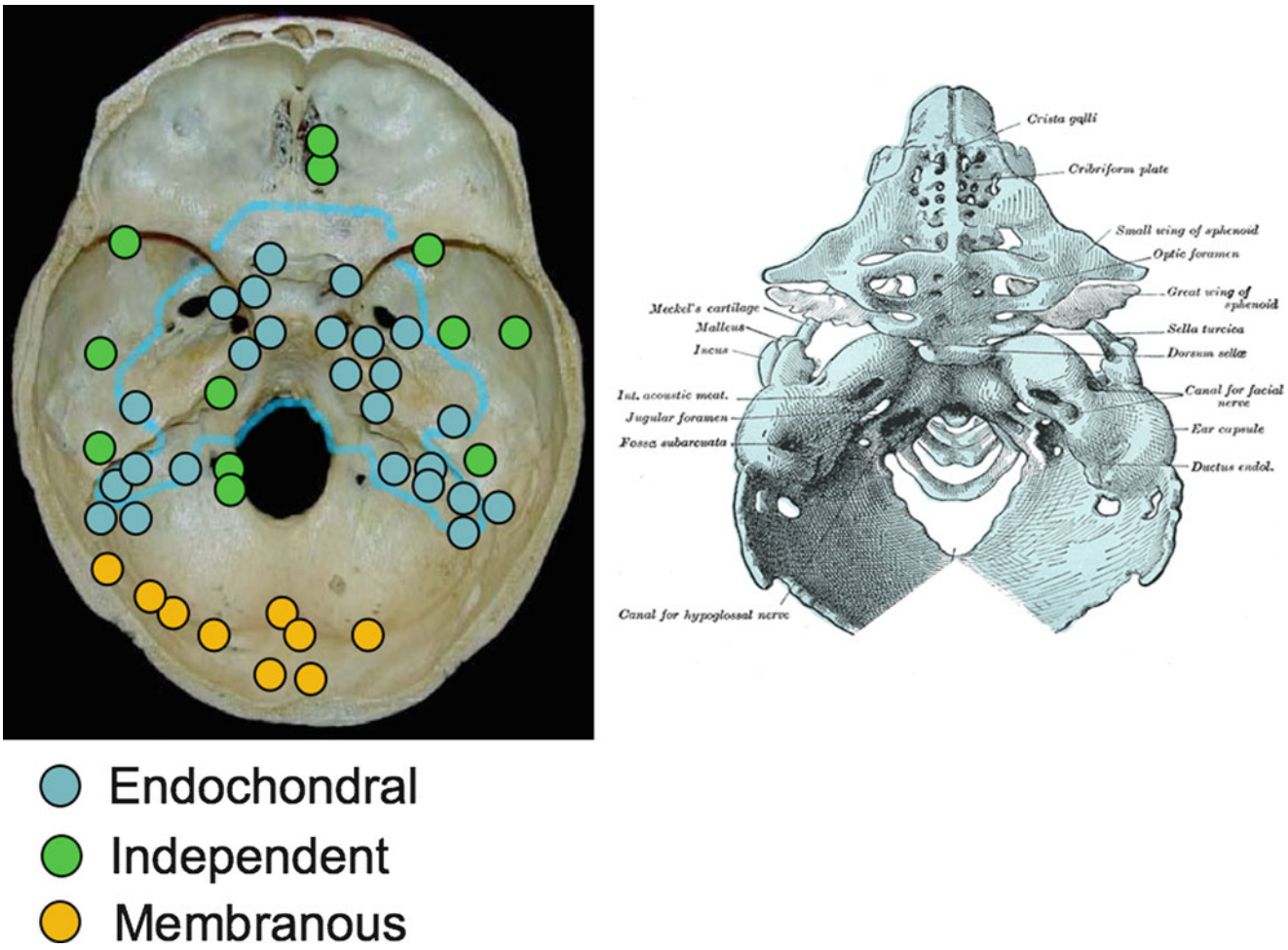

Fig. 3 *(left)* Location of the three groups of DAVFs in relation to the bony structures. The *blue* line delineates the border of endochondral bone at the base of the skull. *Blue* dots are shunting points closely associated with this endochondral bone that includes the cavernous sinus, basioccipital bone, the petrous pyramid, the basisphenoid with its adjacent sphenoid wings, and their related dural structures. *Green* dots indicate the shunt points that are located independent of the surface of either endochondral or membranous bone. One *green* dot plotted in the field of endochondral region at left petrosal apex is not localizing on the endochondral bone, but located on the tentorial surface. *(right)* This is the model of the chondrocranium of a human embryo, 8 cm long (from *Gray's Anatomy*). The membranous bones are not represented. The shape of this model corresponds well to the topography of *blue* lines on the left skull mapping

Table 1 Demography of embryological bone structures and gender predominance

	Female	Male	
Endochondral	25	8	$p<0.01$
Independent	2	8	$p<0.01$
Membranous	5	7	n.s.
	32	23	

Membranous group

There was no significant gender predominance in this group. Confluence of sinuses, transverse sinus, medial occipital sinus, and marginal sinus belonged to themembranous group. In this study, the superior sagittal sinus also categorized to this group (Fig. 6). The venous pressure within the dural sinuses is usually low, thus antegrade, craniofugal flow of the shunts is normally observed. Cortical venous reflux may occur after associated venous outflow restriction or with high-flow shunts. In case of variations of the venous opening into this drainage system such as presence of distal restriction of the sinus and/or the occlusion of the main sinus will rapidly produce cortical venous reflux. These factors should be considered as the aggressive clinical course of dural AVF [4–8].

Independent group

This group had classifications of Types III, IV, and V according to Cognard, and Type 3 according to Borden. These shunts are characterized by male predominance, later age of onset, and the presence of cortical venous reflux. Due to the role played by veins in cranial locations of the independent group, the shunts will involve the subarachnoid portion of the draining cortical vein, causing venous ectasia that may be associated with the hemorrhagic transformation from the venous congestion or rupture of the venous pouches (Fig. 7), especially the olfactory groove (anterior skull base) and tentorial DAVFs, which have aggressive clinical courses because there is no connection with

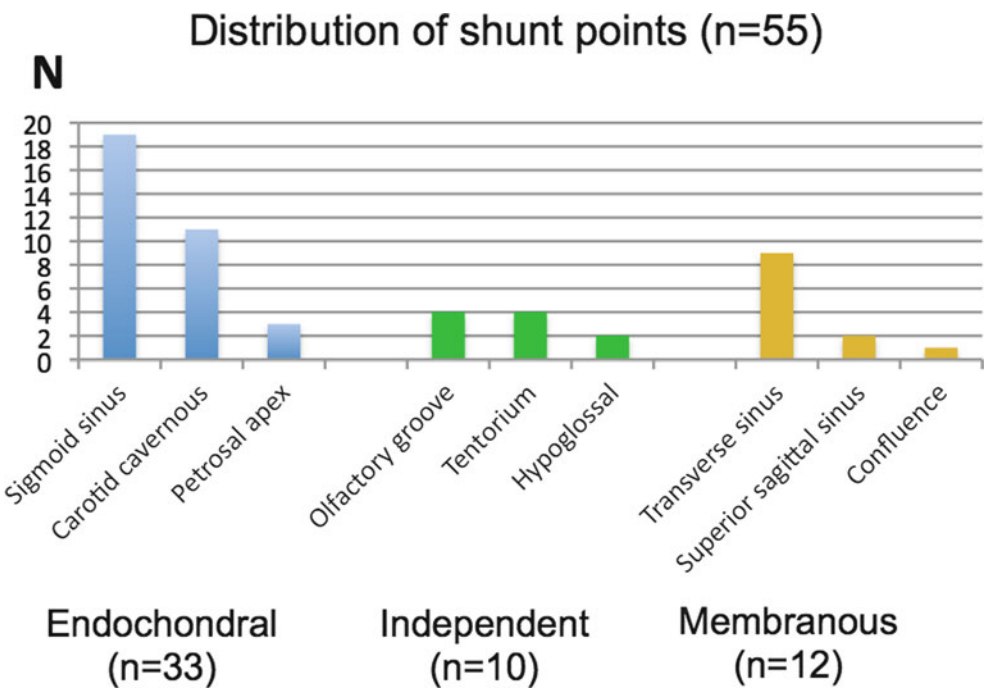

Fig. 4 Graphs show the distribution of shunt points in relation to the three groups

Table 2 Characteristics of grouping DAVFs

	Endochondral	Independent	Membranous
Age and gender distributions	Female dominant, aged 50–80	Male dominant, aged 45–70	No gender predominance
Location of shunt point	Basi sphenoid and adjacent greater wing. Temporal bone. Sigmoid sinus. Basi occipital	Lamina cribriformis. Intra orbital, breschet sinus (lesser wing), superior petrosal sinus, falco-tentorial surface, vein of galen, anterior condylar confluence (hypoglossal canal)	Confluence of sinuses, superior sagittal sinus. Transverse occipital sinus, marginal sinus
Clinical manifestations and angiographical feature	More benign clinical presentations. Lower rate of cortical venous reflux. No cortical venous reflux unless extensive thrombosis of epidural drainage or high-flow shunts	More aggressive clinical presentations, and cortical and spinal venous reflux	Angioarchitecture is multiplicity

the main dural sinuses [1, 9, 17, 19, 20]. In this type of venous outlet, 100% of the shunt flow drains directly into the pial venous system, causing severe venous hypertension even if the shunt is slow and low-flow. From the standpoint of the endovascular approach, most in this group require a trans-arterial approach for embolization. The transvenous approach is not feasible, except for the anterior condylar confluence of DAVFs, because there is no connection to the main dural sinuses.

Segmental Vulnerability of Dural Membrane

As shown in Fig. 8, most DAVFs take place on the border between the neurocranium and viscerocranium; this border zone also corresponds to the boundary between membranous bone and endochondral bone. Membranous bone growth is achieved through bone formation within a periosteum or by bone formation as sutures [11, 12, 14, 15, 21]. Sutures are formed during embryonic development at the sites of the approximation of the membranous bones of the craniofacial skeleton [22, 23]. These dural membranes develop at a relatively later phase of the embryonic stage rather than the development of skull bone and neopallium cortex. The dural membrane is not the single layer structure, but consists of two layers; one is the "dura propria," and the other the "periosteal dura." The dura propria is the inner layer facing the arachnoid membrane that provides the connection to the leptomeningeal venous channel, like bridging veins [2, 3, 21].

The periosteal dura is an outer layer of the dura that is continuous with the outer periosteum, which covers the internal surface of the cranial bone and skull base. This continues through the suture lines and nerve and vessel foramina. Dural sinuses and dural vessel (meningeal arteries and veins) are located in between these two-layer structures. Embryologically, the development of dural membrane is fully affected with the origin and ossification of the bony elements of the head and neck, including the neurocranium, viscerocranium, and cervical vertebrae [15, 23].

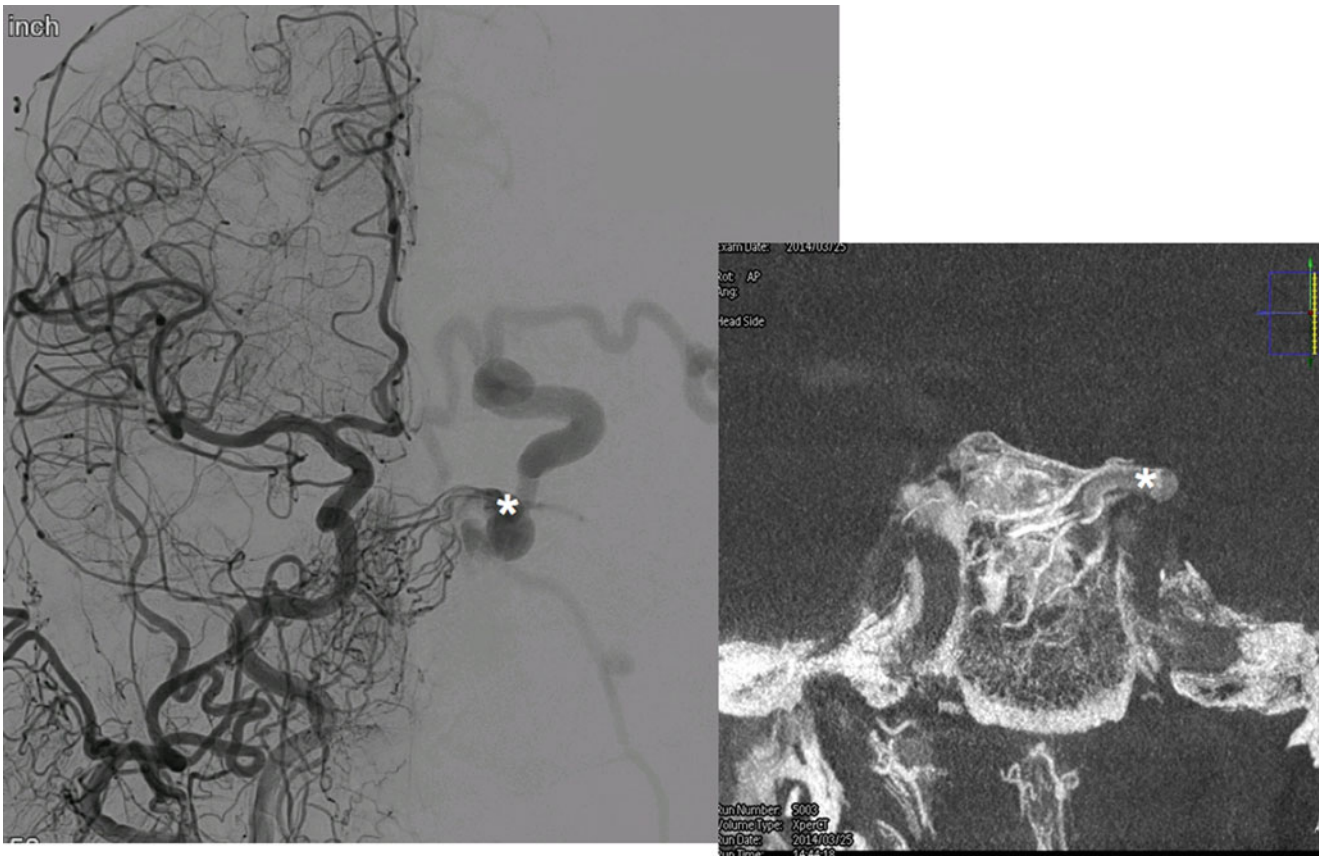

Fig. 5 A 67-year-old woman presented with left chemosis and ophthalmoplegia. Right carotid angiography (AP view) and high-resolution cone beam CT (*left*) showing carotid cavernous DAVF (note the shunt point (*asterisk*) is localized on left paramedian posterior clinoid processus that is categorized as an endochondral group)

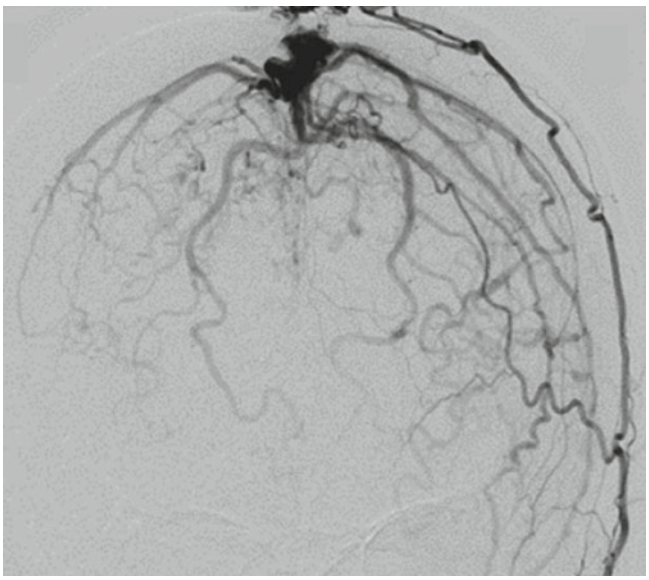

Fig. 6 A 54-year-old man presented with headache and deterioration of cognitive function. Left external carotid angiography showed large extensive cortical venous reflux into the bilateral hemisphere. The shunt point is localized at the superior sagittal sinus that is categorized as a membranous group of DAVF

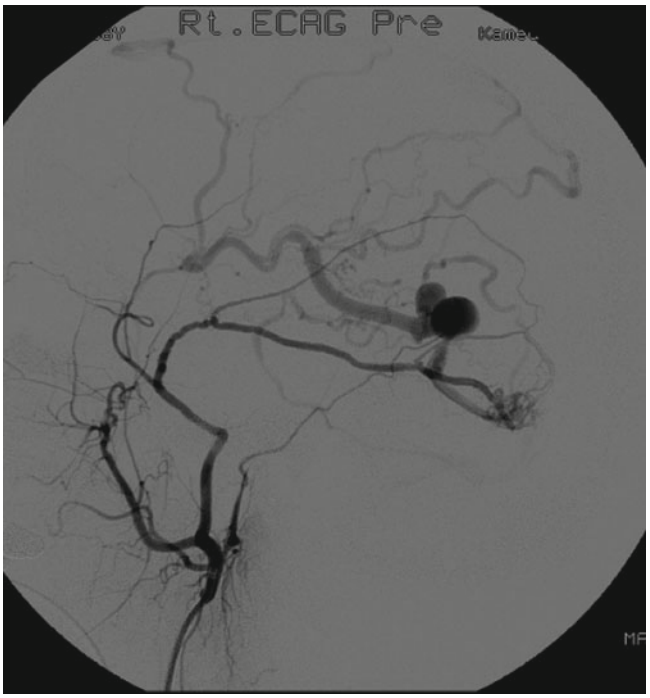

Fig. 7 A 62-year-old man presented with behavior disorder and memory disturbance. External carotid angiography showed a single fistula located on the lateral surface of the tentorium cerebellum. There was no connection with the main dural sinuses, 100% of the shunt flow was directly refluxed into the cortical venous system on the temporal lobe. The entire ipsilateral hemisphere was affected with venous hypertension

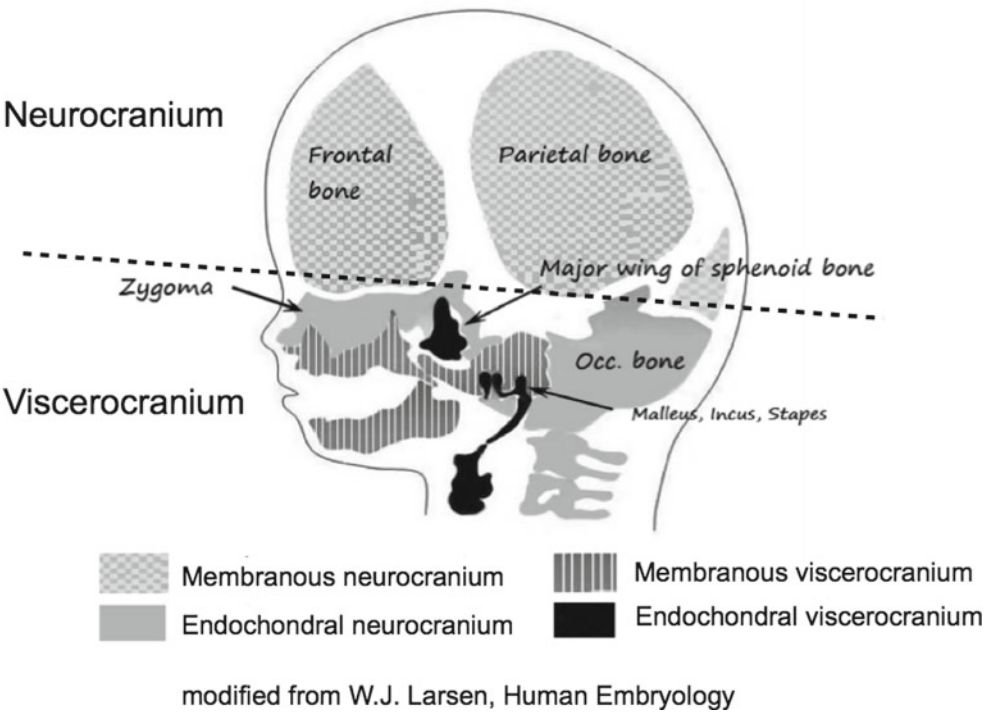

Fig. 8 This diagram shows the anatomical relation of the membranous ossification, endochondral (cartilaginous) ossification, neurocranium, and viscerocranium (note that the *dashed line* indicates the border membranous neurocranium and endochondral neurocranium. Most DAVFs take place in this region.)

Conclusions

There was correlation between the localization of shunt points of DAVFs and the topography of endochondral bone and the membranous bone. The histological differences between endochondral bone and membranous bone at the level of epidural space can induce the segmental vulnerability of the dural membrane and might cause the formation of DAVFs.

To understand the symptomatology of DAVFs, proper analysis of the venous pattern is mandatory. Embryological consideration based on the up-to-date medical imaging facilities may enable us to understand the pathoetiology of the dural AVFs.

Conflict of Interest The author has no conflict of interest and there is no ethical problem with regard to this manuscript.

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Intracranial and Spinal Dural Arterio-Venous Fistula (DAVF): A Surgical Series of 107 Patients

Alessandro Bertuccio, Chiara Robba, Giannantonio Spena, and Pietro Primo Versari†

Abstract

Introduction

Dural arteriovenous fistulas (DAVFs) is a challenging condition in vascular neurosurgery. Development of new endovascular techniques has progressively modified treatment strategies; however, surgery is still considered a valid option of treatment of this pathology.

Materials and Methods

From a retrospective analysis of our database, we selected 107 patients who underwent surgical treatment for DAVFs. Patients were grouped into five categories according to the Borden and Cognard classifications. Patients and treatment characteristics/outcome is reported.

Results

At admission, 30 (28%) patients presented with intracranial hemorrhage. Fifteen (14%) had seizure, whereas nearly half of the patients presented with non-aggressive symptoms, including headache (10, 9.3%), cognitive impairment (8, 7.5%), gait disturbance, and imbalance (8, 7.5%). The majority of patients underwent surgical treatment of fistulas; in some cases, we elected combined surgical-endovascular (obliteration) treatment.

Conclusions

Management of DAVF requires a multidisciplinary assessment and treatment strategies including surgical, endovascular, and radiosurgical treatment. The data reported confirmed that surgical treatment of DAVFs is associated with a good clinical and radiological (complete occlusion of the fistula) outcome in all cases, with a low rate of complications.

Keywords Dural arteriovenous fistulas (DAVF) • Hemorrhage • Spinal dural arteriovenous fistulas

Introduction

Dural arteriovenous fistulas (DAVFs) account for approximately 10–15% of intracranial vascular malformations and are more frequent among older patients [10, 17]. DAVFs can be related to congenital or acquired causes, and they most commonly occur in the cavernous sinus, transverse sinus, sigmoid sinus, and superior sagittal sinus [6, 17].The majority of DAVFs are congenital and related to dural vascular abnormalities. Acquired DAVFs may result from several factors, including traumatic brain injury, venous sinus inflammation, venous sinus thrombosis formation, and brain surgery.

Since DAVFs involve dural and meningeal coverings, clinical presentation is in part determined by anatomical location. Transverse-sigmoid junction and cavernous sinus DAVFs are the two most common locations, and may present with pulsatile tinnitus and/or headache (tranverse-sigmoid sinus), and with cranial nerve deficits and ocular symptoms (cavernous sinus), respectively. Other locations of DAVFs may have various presentations, but in most cases, symptoms are the consequence of spontaneous hemorrhage. The major determinant of hemorrhagic risk is the venous drainage pattern, and in particular the presence of cortical venous reflux. The severity of cortical venous reflux [1, 3, 5, 21] correlates directly with "aggressive clinical presentation," defined as either intracra-

†Author was deceased at the time of publication

A. Bertuccio, MD (✉) • P.P. Versari, MD
Department of Neurosurgery, Civil Hospital, Alessandria, Italy
e-mail: aleberto@hotmail.com; pietroprimo.versari@gmail.com

C. Robba, MD
Department of Neurosciences Critical Care, Addenbrookes Hospital, Cambridge, UK
e-mail: kiarobba@gmail.com

G. Spena, MD
Clinic of Neurosurgery, Spedali Civili and University of Brescia, Brescia, Italy
e-mail: giannantonios@hotmail.com

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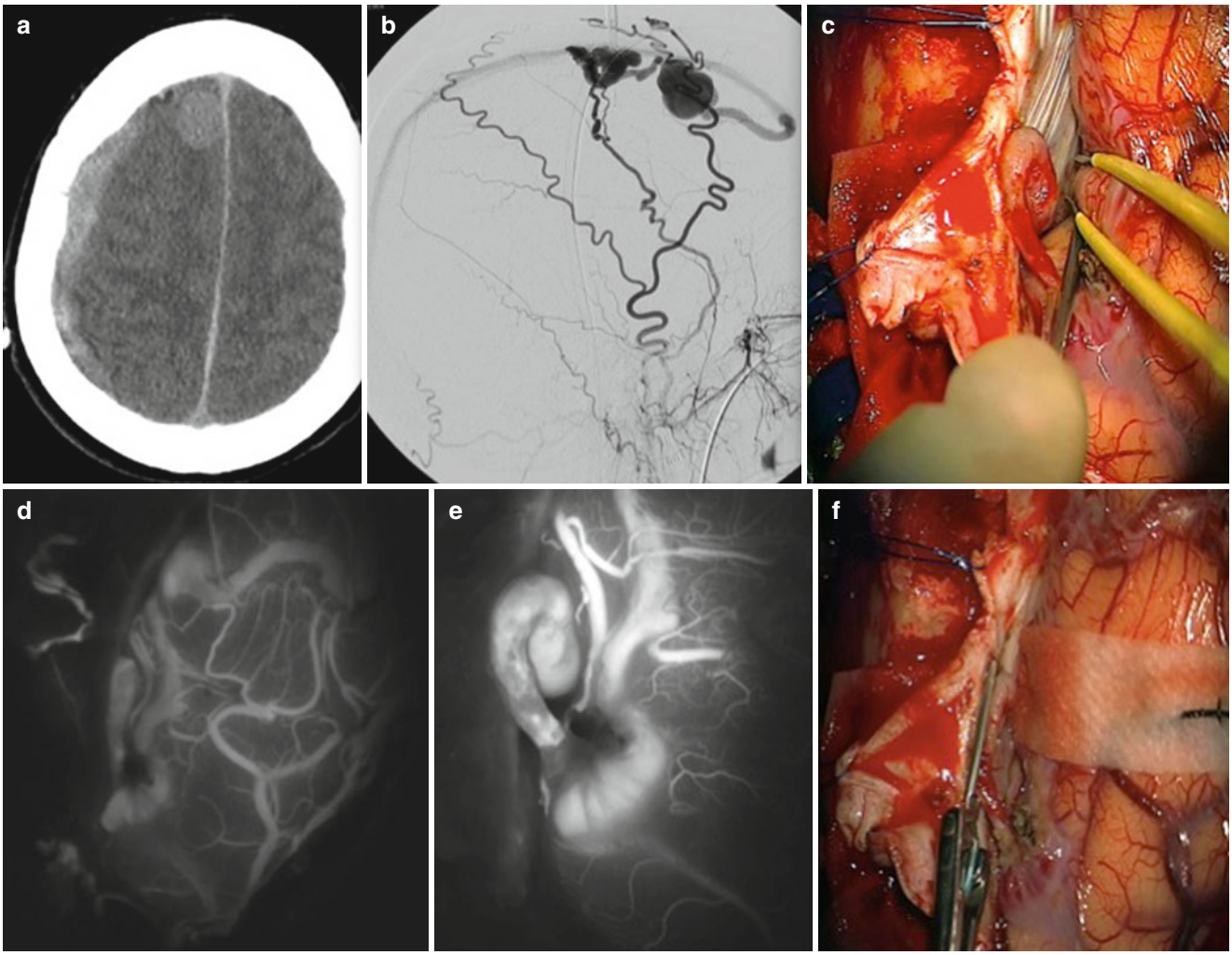

Fig. 1 (**a**) An emergency head CT scan in a patient in a comatose state shows an acute right subdural hematoma. Also evident is a round lesion in the frontal parasagittal area. (**b**) The DSA confirms the presence of a parasagittal dAVF type IV. (**c**) Intraoperative picture shows the isolation of the fistula that is localized in the angle between the falx and the superior sagittal sinus. (**d**, **e**) The use of intraoperative indocyanine green videoangiography defines the DAVF angioanatomy. (**f**) The fistula is surgically excluded

nial hemorrhage or non-hemorrhagic neurological deficit [5]. The risk of hemorrhage fluctuates greatly with various DAVFs and depends mainly by two factors: the venous drainage pattern, particularly cortical venous reflux, and the presence or absence of aggressive symptoms on clinical presentation [25].

The standard of treatment is the interruption of arteriovenous shunting that is traditionally accomplished by open surgery, although endovascular therapy (transvenous and transarterial) has shown to be an efficient alternative to surgery [22] (Figs. 1, 2).

Intracranial DAVFs can be classified according to the type of venous drainage. The classification scheme developed by Cognard et al. and Borden et al. [1, 3] is described in Table 1. All grading systems associate venous drainage pattern with the risk of hemorrhage and neurological deficit. Increased hemorrhagic risk in high-grade lesions is clearly related to retrograde venous drainage into thin-walled cortical veins. In all classifications, low-grade DAVFs (Grade I–IIa Cognard, Grade I Borden) have an annual risk of hemorrhage of 0 %; intermediate lesions (Grade IIb, IIa + b Cognard, Grade II Borden) have a 6 % of hemorrhagic risk, and high-grade lesions (Grade III–V Cognard, Grade III Borden) have an annual risk of hemorrhage of 10 % [1, 3, 24].

In this study, we report data regarding our series of 107 surgically treated intracranial and spinal DAVF.

Materials and Methods

A retrospective analysis of the clinical and radiological findings of patients with DAVFs who underwent surgical treatment between 1990 and 2010 was carried out. We reviewed the hospital records, outpatient clinic charts, and imaging studies of all the patients. The Glasgow Outcome Scale (GOS) was used to assess the clinical outcomes after treatment.

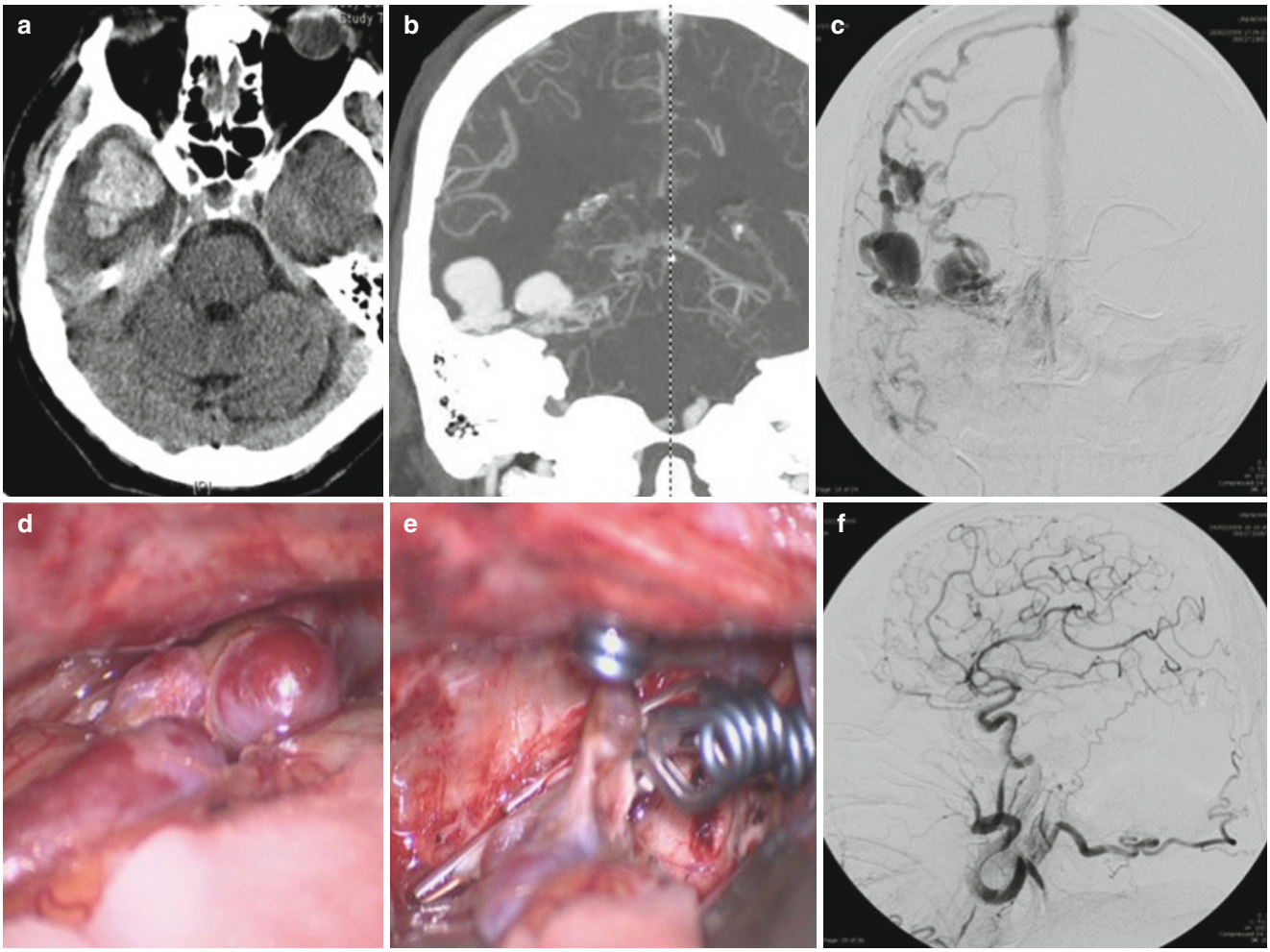

Fig. 2 (**a**) Basal CT scan of a patient suffering from sudden headache shows the presence of a right temporal intraprenchymal hemorrhage. (**b**, **c**) CT-angiography and DSA document the presence of a Type IV temporobasal fistula. (**d**, **e**) Intraoperative picture showing the venous ectasias and the multiple clippings of dilateted veins of the fistula. (**f**) Postoperative DSA confirming the fistula exclusion

Table 1 A comparison between the Cognard [3] and Borden [1] classifications

Type	Cognard	Borden
I	Dural sinus with normal anterograde flow	Anterograde into dural sinus
Ia		Single meningeal feeders
Ib		Multiple meningeal feeders
II	Dural sinus with reflux	Anterograde into dural sinus and retrograde into cortical vein
IIa	Retrograde into dural sinus only	
IIb	Retrograde into cortical veins only	
IIc	Retrograde into dural sinus + cortical vein	
III	Cortical vein only without venous ectasia	Exclusive retrograde into cortical veins that may be dilated
IV	Cortical vein only with venous ectasia (>5 mm and 3 times size of draining vein)	
V	Intracranial DAVF drainage into medullary veins	

Diagnostic imaging was similar in all the patients, with basal CT scans, angio-CT or magnetic resonance imaging (MRI) and MR-angiography (MRA) initially, followed by digital subtraction angiography (DSA) with injection of external carotid arteries for a more precise classification and localization of the fistula. DSA was also repeated immediately after the surgical treatment and at the 1-year follow-up in order to confirm the complete exclusion of the fistula.

Based on preoperative DSA, patients were divided into five groups according to the Borden and Cognard classification:

- Sinusal type I
- Sinusal type II (Cognard Type IIa, IIb, IIa + b; Borden Type II)
- Leptomeningeal (cortical) fistulas (Cognard Type III–IV; Borden Type III)
- Leptomeningeal fistulas Cognard Type V
- Spinal dural av fistulas (sDAVF): These fistulas were classified according to Cognard subtypes (type I: anterograde outflow to spinoradicular (dural) vein or extradural venous plexus; type II: retrograde outflow to extradural venous plexus and pial venous plexus; type III: retrograde outflow to pial venous plexus only).

Surgical interruption and endovascular embolization, alone or in combination, were performed according to clinical setting, lesion location, and venous drainage pattern. The Glasgow Outcome Scale (GOS) at discharge was used to evaluate the clinical outcome.

Results

We found 71 patients with intracranial DAVFs (excluding carotid cavernous fistulas of traumatic origin) and 36 patients with spinal DAVFs, for a total of 107 patients; of these, 57 were males and 50 females, with a mean age of 58.6 (range: 31–82). At admission, 30 (28 %) patients had intracranial hemorrhage; 13 of them (12.1 %) presented in a comatose state. Fifteen patients (14 %) had seizure at onset, whereas nearly half of the patients presented with non-aggressive symptoms, including headache (10, 9.3 %), cognitive impairment (8, 7.5 %), and gait disturbance (8, 7.5 %). Patients with sDAVF were all symptomatic and showed various degrees of myelopathy.

Concerning the location of DAVFs (excluding cavernous sinus DAVFs), 40 patients (37 %) had transverse-sigmoid sinus DAVFs; 9 (8 %) had tentorial DAVFs; 22 (21 %) had anterior cranial fossa DAVFs; and 36 patients (34 %) had spinal DAVFs. Conservative treatment was indicated in all patients harboring a low-grade sinusal type I fistula.

Among the group of sinusal type II (Cognard type IIa, IIb, IIa + b; Borden type II) fistulas, we collected 16 patients; 6 type IIa, 2 type IIb, and 8 type IIa + b. In nine cases, the treatment consisted of sinus resection (with six pre-operation PVA embolization). There was a recurrence in one case, and in eight cases the patients completely recovered. In the remaining seven patients, we performed surgical deafferentation of the leptomeningeal veins.

One patient died because of pulmonary embolism, five patients had a good neurological outcome (GOS 4–5), and one patient had a GOS 3 at discharge.

Among the leptomeningeal (cortical) fistulas (Cognard Type III–IV; Borden Type III) group, a total of 53 patients were assessed. No residual fistulas were observed at postoperative angiography and no cases of clinical recurrence at the 12-month follow-up were recorded. Forty-two patients experienced an improvement in symptoms (GOS = 4–5), nine remained stable (GOS = 4–5), and two died in the immediate postoperative period (one unrelated to treatment).

Two patients with leptomeningeal fistulas Cognard Type V were studied. One presented with progressive myelopathy and experienced neurological improvement after surgical treatment (GOS = 5). The other patient presented with tetraparesis and showed no improvement after surgery (GOS = 2).

A total of 36 patients with sDAVF were classified. sDAVF was detected in 23 patients (64 %) in the thoracic region, and 13 (36 %) in the lumbar region (Fig. 3). All but one patient had single-level sDAVF. Sixteen patients (44.4 %) had a Type I sDAVF according to the Borden classification, while 15 (41.6 %) had type II and 5 (14 %) had type III. In all the patients, a postoperative DSA showed no evidence of residual fistula. Concerning clinical functional status: 15 patients (41.6 %) experienced marked improvement in symptoms, 10 (28 %) had a moderate improvement, 10 (28 %) remained neurologically stable, and 1 patient (2.4 %) worsened neurologically.

Discussion

Patients with DAVF may be asymptomatic or may experience mild to aggressive symptoms, according to the lesion location and pattern of venous drainage [22]. The mean presentation age is generally between 50 and 60 year [3, 4, 12]. Pulsatile tinnitus is a common symptom in patients with transverse-sigmoid sinus DAVFs, which results from increased blood flow through the dural venous sinuses close to the middle ear. Due to their proximity to the orbit, cavernous sinus DAVFs can present with ophthalmoplegia, proptosis, chemosis, retro-orbital pain, and decreased visual acuity [12, 13]. DAVFs that drain into the superior sagittal sinus (SSS) or deep venous system produce symptoms of global venous congestion and persistent intracranial hypertension, leading to intracranial hemorrhage that may manifest with aggressive symptoms, such as hydrocephalus, seizures, and dementia [8, 9].

Specific considerations are provided according to each DAVF subtype:

Sinusal Type I

These malformations are characterized by benign clinical behavior and they have no risk of hemorrhage. In some cases,

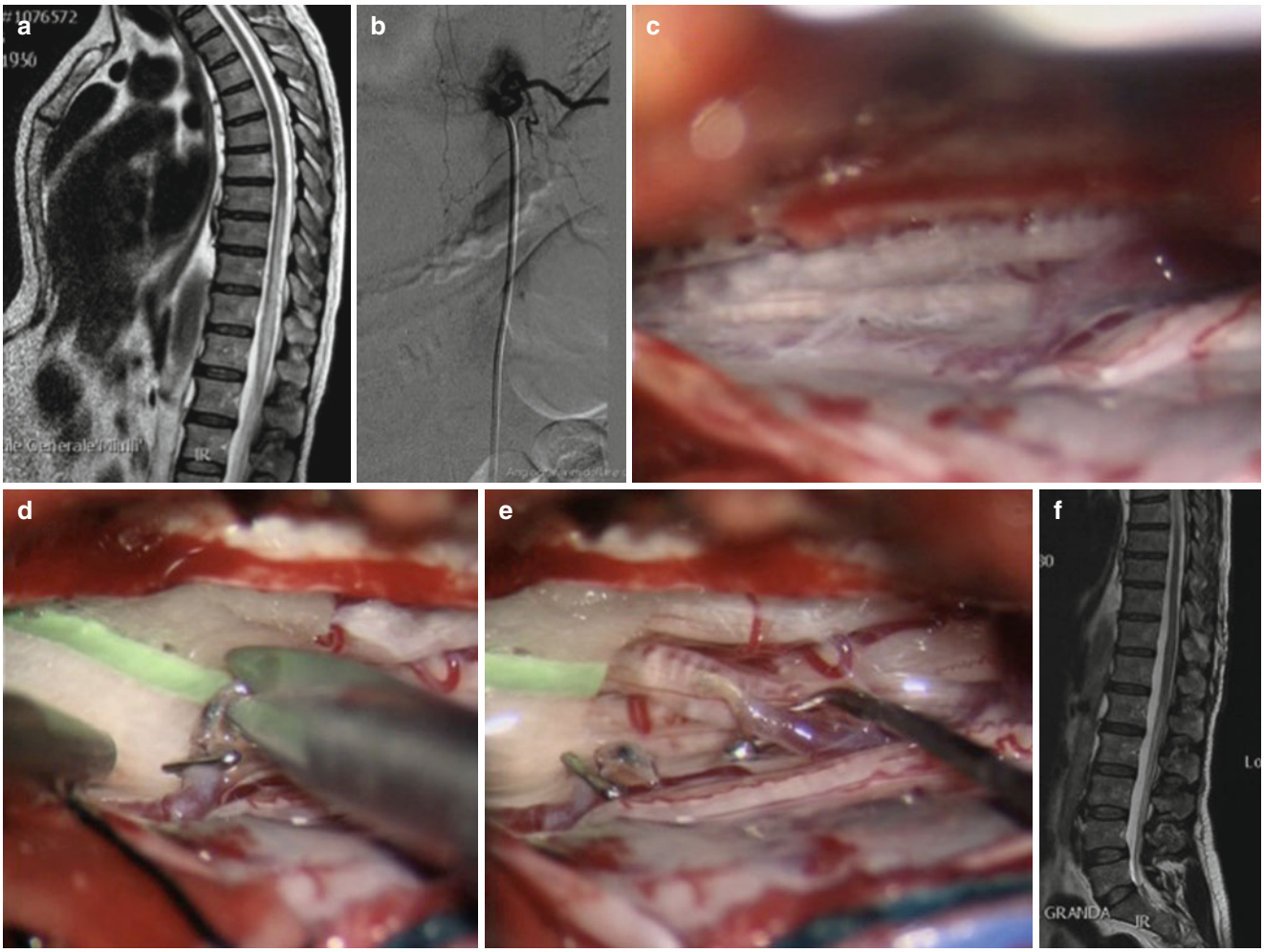

Fig. 3 (**a**) A spinal MRI in a patient with progressive myelopathy showing a hypersignal in the spinal cord due to venous engorgement. Note the little flow void on the posterior aspect of the cord. (**b**) Spinal DSA confirms the suspicion of a type II dorsal sDAVF. (**c**–**e**) Intraoperative pictures showing the stages of the dissection, disconnection, and resection of the fistula. (**f**) Postoperative follow-up MR documents improvement of the myelopathy

a subsequent venous drainage impairment is described [4]. In patients with sinusal type I DAVFs, we suggest clinical and angiographic follow-up. In cases of invalidating symptoms (such as tinnitus), surgical treatment is indicated in order to reduce the drainage outflow and consequently to treat the symptoms [20].

Sinusal Type II (Cognard Type IIa, IIb, IIa + b; Borden Type II)

Patients affected by this DAVF-type II generally present with aggressive clinical behavior caused by intracranial hypertension due to impairment of the venous drainage. The risk of hemorrhage is moderate [21]. The aim of the treatment is the sinus resection/occlusion whenever possible [23]. Among treatment options, we applied tailored strategies, including surgical excision of the fistulous sinus or surgical direct sinus packing, endovascular transvenous embolization, or endovascular embolization with surgical esposure of the sinus.

Leptomeningeal (Cortical) Fistulas (Cognard Type III–IV; Borden Type III)

These DAVFs are associated with a high risk of hemorrhage due to focal venous hypertension. In this group of patients, surgical treatment is imperative. The treatment goal consists of the interruption/disconnection of the venous drainage as close as possible to the point of the fistula [7]. Direct surgical approach represents the most effective and safe method to treat these types of intracranial dAVF, as it is associated with a low procedure-related risk and a high percentage of success [22].

Leptomeningeal Fistulas Cognard Type V

DAVFs with perimedullary drainage are very uncommon [13] and represent a continuum between cortical intracranial fistulas and spinal fistulas. Common presentation symptoms include cervical myelopathy and leg weakness associated with hemorrhage. The treatment strategies are similar to Type III–IV fistulas.

Spinal DAVF (SDAVF)

sDAVF fistulas account for approximately 70 % of all vascular spinal malformations [15, 16]. Spinal dural AVFs generally present with progressive spastic motor weakness [2]: other symptoms include sensory deficits, sphincter disturbances, and back pain, with some patients presenting acutely with hemorrhage or to Foix-Alajouanine syndrome [19].

The pathophysiology of symptoms is typically associated with venous hypertension from shunting of the arterial blood into the valveless venous system of the spinal cord. This causes a decrease in the arterial supply, arterial steal, and ischemia, and consequently leads to progressive necrotizing myelopathy that, if not treated, is irreversible [11, 18].

Even after successful treatment of sDAVF, only two-thirds of all patients show improvement in their motor symptoms and one-third show improvement in other symptoms, such as sensory disturbances, pain, impotence, and sphincter disturbances [2]. The goal of treatment in spinal fistulas is the elimination of the venous congestion, hence giving the spinal cord a chance to recover. This can be achieved by excision, obliteration, or disconnection of the fistula, which can be achieved endovascularly or surgically. Operative treatment of sDAVF can be achieved via a posterior spinal approach, with laminectomy, laminoplasty, or hemilaminectomy with interruption and disconnection of the vein [19]. As for sDAVF, the higher recurrence rate with endovascular embolization makes surgical disconnection the preferred option. The most important causes of failure of endovascular therapy for sDAVF are situations in which the fistula is angiographically occult, and presents multiple small feeders, or failure of the microcatheter to reach the site of the fistula, and failure of the embolic material to hit the draining vein occurs [14]. On the other hand, embolization with glue (Onyx) represent a valid and effective approach, especially if general anesthesia is not required. Failure rate, criterium of cure, and recurrence remain relatively high [18].

Conclusions

Management of DAVF requires a multidisciplinary assessment that includes neurosurgeons and radiologists in order to offer the patients the best treatment strategy. Our data showed that surgical treatment of DAVFs is associated with a good clinical and radiological outcome.

Disclosure Statement The authors declare that they have no personal or institutional financial interest in drugs, materials, or devices.

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

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Epidemiologic Survey of Dural Arteriovenous Fistulas in Japan: Clinical Frequency and Present Status of Treatment

Naoya Kuwayama

Abstract

Background and Purpose

There are few reports describing the prevalence of dural arteriovenous fistulas (dAVFs). We conducted a nation-wide retrograde survey on the clinical frequency and the status of treatment of dAVFs in Japan.

Methods

The first questionnaire was sent to 1,236 certified neurosurgery clinics in Japan to ask about the number of patients treated and the location of dAVF during the 5 years from 1998 to 2002. The second questionnaire was sent to 102 large-volume centers to ask the patients' ages, gender, location of the fistula, clinical presentation, treatment modalities, clinical and radiological results, and recurrence.

Results

In the first survey, 1,815 cases were chosen from 338 clinics, including 826 cavernous sinus, 514 transverse-sigmoid sinus, 105 spinal, and 370 lesions in other places. The estimated detection rate was 0.29 per 100,000 persons per year in Japan. In the second survey, there were 1,490 cases (mean age: 62.7; 628 men and 850 women) that were culled from 68 high-volume centers. The initial clinical presentation was ocular symptoms (45 % of the cases), tinnitus (20 %), intracranial hemorrhage (16 %), and non-hemorrhagic neurological deficits (20 %). Treatment modality was endovascular therapy (76 % of the patients), open surgery (13 %), irradiation (3.4 %), and conservative therapy (11 %). Angiographic results were total obliteration in 59 % of the patients and subtotal obliteration in 16 %. Clinical symptoms disappeared in 54 % of the patients, improved in 16 %, unchanged in 7 %, worsened in 1.5 %, and death occurred in 1.2 %. Recurrence was reported in 5.9 % of the patients.

Conclusions

This survey delineated the clinical frequency and the epidemiologic features of dAVF in Japan.

Keywords Dural arteriovenous fistula • Prevalence • Endovascular treatment

Introduction

Dural arteriovenous fistulas (dAVFs) are a rare but important clinical occurrence causing ocular symptoms, stroke, cognitive dysfunction, and progressing spinal cord symptoms. The diagnostic level of this disease has made remarkable progress due to the development of diagnostic instruments such as digital subtraction angiography (DSA) and magnetic resonance imaging (MRI). The evolution of treatment methods has also been markedly improving the level of treatment of this disease. Epidemiologic features, however, so far remain obscure. In 1969 Newton and Cronqvist [3] described how 15 (11.6 %) of 129 intracranial arteriovenous malformations had a pure dural supply. There have been very few papers since then to investigate the prevalence or incidence of the dAVFs. Recently, the detection rate in Scotland was reported to be 0.16 per 100,000 adults per year, according to the Scottish Intracranial Vascular Malformation Study [1], which is the first report to show regional incidence or detection rates of dAVFs.

We retrospectively investigated the detection rate and current status of the treatment of this disease by sending questionnaires to the all hospitals and clinics certified as training centers for neurosurgeons by The Japan Neurosurgical Society.

N. Kuwayama, MD, PhD
Department of Neurosurgery, Faculty of Medicine,
Toyama University, 2630 Sugitani, Toyama 930-0194, Japan
e-mail: kuwayama@ms.toyama-mpu.ac.jp

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Methods

First Questionnaire

The first questionnaire related to the annual number of patients who came to the respondent's hospital and were diagnosed with a dAVF in any location for the first time. Locations included the cavernous sinus (CS), the transverse-sigmoid sinus (TSS), the superior sagittal sinus (SSS), the tentorium, the craniocervical junction (CCJ), the anterior cranial base (ACB), the spinal cord, and others. The 5-year survey was conducted from 1998 until 2002. It was sent to the departments of neurosurgery of the 1,236 hospitals that were recognized as training centers certified by the Japan Neurosurgical Society. The number of patients detected in 5 years, and the locations of the fistulas, were summed up, and the detection rate was estimated using the population census of Japan in 2000 reported by The Statistic Bureau of The Ministry of Internal Affairs and Communications.

Second Questionnaire

The second questionnaire was sent as an Excel file (Microsoft Corporation) to the hospitals that had responded to the first questionnaire and had reported five or more cases. The content of inquiries was the patients' ages, gender, location of the fistula, clinical presentation, treatment modalities, clinical and radiological results, and recurrence. A single choice was required for the category of "year detected," "radiological outcome," "clinical outcome," and "recurrence." Multiple choices were permitted for "location," "initial clinical presentations," and "treatment modalities." The choice of location was the CS, the TSS (including confluence), the SSS, the superior petrosal sinus (SPS), the inferior petrosal sinus (IPS), the anterior condylar confluence (ACC), the straight sinus (SS), the tentorium, the ACB, the CCJ, the cranial vault, the spinal cord, and others. The data files were collected and analyzed.

Results

First Questionnaire

Three hundred and thirty-eight hospitals responded to the first questionnaire, and 1,815 patients were chosen. The recovery rate was 27.3 %. No patients were detected for 5 years in 94 hospitals, 1–9 patients in 195 hospitals, 10–19 in 26, 20–29 patients in 13, 30–39 in 5, 40–49 in 2, and 50 or more patients in 3 hospitals. The mean number of patients per hospital during those 5 years was 5.4 patients. The location of the fistula was the CS in 826 patients (46 %), the TSS in 514 (28 %), the spinal cord in 105 (5.8 %), the SSS in 97 (5.3 %), the ACB in 79 (4.3 %), the CCJ in 60 (3.3 %), the tentorium in 58 (3.2 %), and other locations in 76 patients (4.2 %).

The detection rate was estimated as 0.29 patients per 100,000 persons per year in Japan. In the regional analysis, it was 0.40 for the Hokkaido and Hotohu area, 0.19 for the Kanto and Koshin-etsu area, 0.35 for the Chubu area, 0.34 for the Kinki area, 0.31 for the Chugoku and Shikoku area, and 0.30 for the Kyushu and Okinawa area.

Second Questionnaire (Table 1)

The second questionnaire was sent to 102 large-volume centers that had detected five or more patients in the first questionnaire. One thousand four hundred and ninety-one (1,491) patients were identified from 68 centers. The recovery rate was 66.7 %. One thousand five hundred and thirty-three (1,533) involved sites (locations) that were recorded in the 1,490 patients.

There were 628 men and 850 women, with a mean age of 62.7 . The proportion of women is 80 % in the CS lesion, 54 % in the ACC lesion, 42 % in the TSS lesion, 32 % in the CCJ lesion, 28 % in the spinal cord lesion, 21 % in the SSS lesion, 20 % in the tentorium lesion, 13 % in the ACB lesion. The mean age was 65.1 in the CS lesion, 63.0 in the TSS, 61.9 in the ACB 61.1 in the ACC, 60.8 in the CCJ, 58.1 in the spinal cord, 57.0 in the tentorium lesion, and 56.7 years in the SSS lesion.

The location of the fistula was the CS in 711 patients (48 %), the TSS in 389 (26 %), the spinal cord in 100 (6.7 %), the SSS in 70 (4.7 %), the tentorium in 54 (3.6 %), the ACB in 53 (3.6 %), the CCJ in 44 (3.0 %), the ACC in 24 (1.6 %), and "others" in 88 patients (5.9 %). Multiple locations were recorded in 104 patients (7.0 %).

The initial clinical presentation of these 1,490 patients was ocular symptoms (45 % of the cases), tinnitus (20 %), intracranial hemorrhage (16 %), and non-hemorrhagic neurological deficits (20 %). The most frequent initial presentation was ocular symptoms (44.9 %) in the patients with a CS lesion, tinnitus (39.3 %) and stroke (38.9 %) with a TSS lesion, sensorimotor disturbance of the legs (99.0 %) with a spinal cord lesion, stroke with the SSS (48.5 %), tentorium (40.7 %), ACB (52.8 %) and CCJ (56.8 %) lesions, and tinnitus (88 %) with an ACC lesion.

Endovascular treatment was given to 1,129 (75.8 %) of the 1,490 patients (91.7 % of the patients with the ACC lesion, 86.5 % with the CS, 83.3 % with the tentorium, 74 %

Table 1 The results of the 1,490 patients with dAVF derived from the second questionnaire

	Total	CS	TS+Cf	SSS	SPS	IPS	ACC	SS	Tent	ACB	CCJ	Vault	Spine	Others
Number of patients	1,490	711	389	70	19	5	24	15	54	53	44	22	100	27
Men	628	139	219	55	12	2	11	11	43	45	30	14	72	13
Women	850	569	164	15	7	3	13	4	11	7	14	8	28	14
Mean age	62.7	65.1	63.0	56.7	56.2	55.2	61.1	58.6	57.0	61.9	60.8	58.0	58.1	50.5
Initial symptoms[a]	**Total**	**CS**	**TS+Cf**	**SSS**	**SPS**	**IPS**	**ACC**	**SS**	**Tent**	**ACB**	**CCJ**	**Vault**	**Spine**	**Others**
Aggressive-1	26.6	4.0	38.9	48.5	36.8	20.0	8.3	53.3	40.7	52.8	56.8	40.9	99.0	22.2
Aggressive-2	9.6	3.9	20.3	35.7	21.0	20.0	0.0	26.6	14.9	9.4	2.3	9.1	0.0	7.4
Ocular symptoms	44.9	90.1	2.8	1.4	15.8	20.0	4.2	13.3	1.9	5.7	6.8	4.5	1.0	37.0
Tinnitus	19.9	12.6	39.3	12.9	15.8	20.0	88	13.3	9.3	3.8	22.7	13.6	3.0	29.6
Others	5.9	2.7	8.0	8.6	31.6	40.0	4.2	6.7	18.5	15.1	2.3	18.2	0.0	14.8
Asymptomatic	6.5	1.7	7.7	7.1	10.5	0.0	0.0	13.3	24.1	26.4	20.5	22.7	2.0	7.4
Treatment[a]	**Total**	**CS**	**TS+Cf**	**SSS**	**SPS**	**IPS**	**ACC**	**SS**	**Tent**	**ACB**	**CCJ**	**Vault**	**Spine**	**Others**
Conservative	11.1	10.1	10.8	8.6	15.8	20.0	4.2	26.7	9.3	20.8	27.3	9.1	6.0	14.8
Endovascular (1)	75.8	86.5	74.0	70.0	73.7	80.0	91.7	73.3	83.3	18.9	47.7	63.6	49.0	74.1
Surgical (2)	13.0	1.4	14.1	25.7	10.5	0.0	8.3	13.3	13.0	67.9	18.2	36.4	51.0	25.9
Combined 1+2	3.4	1.3	9.5	14.3	5.3	0.0	0.0	13.3	1.9	0.0	0.0	0.0	1.0	0.0
Irradiation	3.4	2.5	4.4	2.9	26.3	0.0	0.0	20.0	11.1	0.0	4.5	4.5	0.0	3.7
Others	0.3	0.4	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Obliteration ratio	**Total**	**CS**	**TS+Cf**	**SSS**	**SPS**	**IPS**	**ACC**	**SS**	**Tent**	**ACB**	**CCJ**	**Vault**	**Spine**	**Others**
Total	59.1	66.4	51.4	37.1	10.5	20.0	62.5	33.3	29.6	71.7	45.5	59.1	73.0	51.9
Subtotal	16.4	15.6	20.8	27.1	21.1	40.0	12.5	13.3	27.8	3.8	13.6	9.1	9.0	18.5
Partial	13.0	8.7	18.0	27.1	42.1	20.0	16.7	26.7	25.9	1.9	13.6	22.7	11.0	18.5
Unchanged	7.0	5.3	7.7	5.7	10.5	20.0	4.2	26.7	5.6	15.1	22.7	4.5	3.0	7.4
Clinical results	**Total**	**CS**	**TS+Cf**	**SSS**	**SPS**	**IPS**	**ACC**	**SS**	**Tent**	**ACB**	**CCJ**	**Vault**	**Spine**	**Others**
Cured (1)	53.8	60.9	53.2	50.0	52.6	40.0	66.7	40.0	31.5	54.7	50.0	50.0	21.0	51.9
Improved (2)	16.4	22.5	27.5	31.4	21.1	40.0	20.8	20.0	37.0	13.2	25.0	27.3	52.0	29.6
1+2	70.2	83.4	80.7	81.4	73.7	80.0	87.5	60.0	68.5	67.9	75.0	77.3	73.0	81.5
Unchanged	6.6	4.9	6.4	1.4	5.3	20.0	4.2	33.3	3.7	13.2	11.4	9.1	14.0	7.4
Aggravated	1.5	1.1	0.8	4.3	5.3	0.0	0.0	6.7	7.4	1.9	4.5	4.5	6.0	0.0
Death	1.2	0.4	2.1	1.4	10.5	0.0	0.0	0.0	1.9	1.9	0.0	0.0	2.0	0.0
Recurrence	**Total**	**CS**	**TS+Cf**	**SSS**	**SPS**	**IPS**	**ACC**	**SS**	**Tent**	**ACB**	**CCJ**	**Vault**	**Spine**	**Others**
Positive	5.9	3.7	9.0	15.7	10.5	0.0	16.7	20.0	16.7	0.0	4.5	9.1	7.0	7.4
Negative	73.5	81.1	70.7	61.4	57.9	100	70.8	60.0	42.6	71.7	59.1	68.2	73.0	74.1

Aggressive-1: intracranial hemorrhage, venous infarction, spinal symptoms
Aggressive-2: increased inracranial pressure, seizure, hydrocephalus
CS cavernous sinus, *TS* transverse-sigmoid sinus, *Cf* confluence, *SSS* superior sagittal sinus, *SPS* superior petrosal sinus, *IPS* inferior petrosal sinus, *ACC* anterior condylar comfluence, *SS* straight sinus, *ACB* anterior cranial base, *CCJ* craniocervical junction
[a]Multiple choice

with the TSS, 70.0 % with the SSS, 49.0 % with the spinal cord, 47.7 % with the CCJ lesion, and 18.9 % with the ACB lesion). Surgical treatment was given to 13 % of all the patients (67.9 % with the ACB lesion, 51.0 % with the spinal cord lesion, 25.7 % with the SSS lesion, 18.2 % with the CCJ lesion, 14.1 % with the TSS lesion, 13.0 % with the tentorium lesion, 8.3 % of the patients with the ACC lesion, and 1.4 % with the CS lesion). Conservative treatment was given to 11.1 % of the patients, combined surgical and endovascular treatment in 3.4 %, and irradiation therapy in 3.4 %.

Total and subtotal anatomical obliteration of the fistula was recorded in 59.1 % and 16.4 % of the 1,490 patients at the time of discharge, respectively. The rate of total obliteration was 73.0 % in the patients with a spinal cord lesion,

71.7 % with an ACB lesion, 66.4 % with a CS lesion, 62.5 % with an ACC lesion, 51.4 % with a TSS lesion, 45.5 % with a CCJ lesion, 37.1 % with an SSS lesion, and 29.6 % with a tentorium lesion. Good clinical results (cured and improved) were recorded in 70.2 % of the 1,490 patients (87.5 % of the patients with an ACC lesion, 83.4 % with a CS, 81.4 % with an SSS, 80.7 % with a TSS, 75.0 % with a CCJ, 73.0 % with a spinal cord lesion, 68.5 % with a tentorium lesion, and 67.9 % with an ACB lesion).

Recurrence was recorded in 5.9 % of the 1,490 patients (0 % of the patients with the ACB lesion, 3.7 % with a CS lesion, 4.5 % with CCJ, 7.0 % with spinal cord, 9.0 % with TSS, 15.7 % with SSS, and 16.7 % with a tentorium lesion).

Discussion

This study was the first nation-wide survey on dAVF in the world. The epidemiological features of the intracranial and spinal dAVF were made clear using this large number of cases. The incidence of this disease is not well known and only a few studies [1, 3] have been reported so far. This study also defined the current trend of therapeutic modalities, treatment results, and recurrence rates, which could be supposed the standard condition of the current medical level of Japan.

Detection Rate

The detection rate was 0.29/100,000 person/year, which was higher than previously reported [1, 3]. The improvement of recent diagnostic instruments may contribute to this increasing frequency. This detection rate would be the new landmark study for the epidemiologic features of dAVFs.

Locations of the Fistulas

The cavernous sinus was involved in 46 % of the 1,815 patients in the first questionnaire, and was the most frequent location of the fistulas, considered to be an Asian characteristic. In Europe and North America, the transverse-sigmoid sinus has been reported to be the most frequent site [2, 4].

Treatment

In the majority of cases with sinus-type dAVF (like the CS and TSS), an endovascular procedure was the first modality of the treatment, which is the current trend of therapeutic strategy in the world. The ratio of surgical treatment was higher than 30 % in ACB, spinal cord, and cranial vault lesions, which indicated that surgery still played an important role in these locations.

In the majority of the sinus lesions (CS, TSS, and ACC), the rate of total obliteration and the positive results were high, as expected, yet it was rather low in patients with an SSS lesion, which suggested the difficulty of complete treatment in this lesion. This may be partly because transvenous embolization was not indicated in many cases with SSS lesion to preserve the involved sinus as a route of cerebral venous drainage. The effective transarterial treatment will be one of the major objectives for treating this lesion.

The non-sinus lesion is usually the target of transarterial embolization, using a liquid material like NBCA when treated only endovascularly. Special training is required to use this kind of material effectively and it is generally difficult to treat. Therefore, the rate of surgical intervention was higher in these lesions than in the sinus lesions. The final angio-anatomical results were excellent in ACB and spinal cord lesions, which suggested the good feasibility and efficacy of the surgical treatment. The total obliteration ratio and the favorable clinical results of tentorium lesions, however, remained considerably low (29.6 %), indicating the difficulty of both endovascular and surgical treatment. Treating this kind of lesion may be one of the biggest goals of the future. Another target should be spinal cord lesions, in which the poor clinical results were recorded in contrast to the high anatomical obliteration ratio. We speculate that the reason for this sizeable discrepancy will be the delay of diagnosis and treatment after the onset of the clinical symptoms. Spinal cord lesions mimic both stenosis of the lumbar spinal canal and arteriosclerosis obliterans. The increased knowledge and experience of orthopedic and vascular surgeons may contribute to the early diagnosis of this disease.

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Surgical Approach to Ponto-mesencephalic Cavernoma

Yasuhiko Kaku, Hiroaki Takei, Masafumi Miyai, Kentarou Yamashita, and Jouji Kokuzawa

Abstract

Background and Aims

The surgical treatment of intrinsic brainstem lesions remains a major challenge. In this article we present the results of using an infratentorial-supracerebellar (ITSC) approach for the resection of intrinsic ponto-mesencephalic lesions.

Materials and Methods

The authors reviewed the cases of 16 patients. In seven of them, a paramedian ITSC transcollicular approach was used to resect intrinsic mid-brain lesions, and in the other nine patients, an intermediate or lateral ITSC infra-trochlear approach was used for ponto-mesencephalic lesions.

Results

All 16 lesions were completely removed. There was no recurrence of bleeding during the follow-up period, and no mortality. In seven patients with mid-brain lesions, the preoperative ocular symptoms improved in three of them, and the neurological deficits – other than ocular symptoms improved – in five of them. The preoperative modified Rankin Scale score of 1.8 improved to 1.3 postoperatively. In nine patients with a ponto-mesencephalic lesion, the preoperative ocular symptoms improved in four of nine patients, and the neurological deficits other than ocular symptoms improved in five of them, while one patient exhibited venous infarction in a cerebellar hemisphere that caused neurological deterioration. The preoperative modified Rankin Scale score of 3.75 improved to 2.5 postoperatively in these patients.

Conclusion

The ITSC transcollicular or infra-trochlear approach provide a wide operative entry zone and minimize the functional damage to the surrounding structures for access to ponto-mesencephalic lesions.

Keywords Cavernous malformation • Brainstem • Infratentorial supracerebellar approach • Trochlear nerve

Introduction

The prevalence of cerebral cavernous malformations (CMs) ranges from 0.4 to 0.6 % of the general population, and brainstem CMs account for between 18 and 35 % of cerebral CMs. The hemorrhage rate of patients with brainstem CMs has been reported to range from 2.3 to 21.5 % [1, 4, 7]. Hemorrhagic episodes caused by brainstem CMs can result in serious symptoms due to their precarious locations. The outcomes of untreated brainstem CMs are debatable, but they are commonly considered to be disastrous, with a 20 % mortality rate [9]. The operative treatment of intrinsic brainstem lesions, however, remains a major challenge [2, 3, 5, 6, 8]. In this article, we present results of our using an infratentorial-supracerebellar (ITSC) approach for the resection of intrinsic ponto-mesencephalic CMs.

Case Materials and Methods

We reviewed the cases of 16 patients, 7 in whom a paramedian ITSC transcollicular approach was used to resect an intrinsic mid-brain lesion, and 9 in whom an intermediate or lateral ITSC infra-trochlear approach was used to resect a ponto-mesencephalic lesion.

Y. Kaku, MD (✉) • H. Takei, MD • M. Miyai, MD
K. Yamashita, MD • J. Kokuzawa, MD
Department of Neurosurgery, Asahi University Murakami Memorial Hospital, Gifu, Japan
e-mail: kaku@murakami.asahi-u.ac.jp

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Operative Technique

The ITSC Transcollicular Approach

The transcollicular approach is made through a single superior or inferior colliculus, or both. The rostral limit of the exposure is formed by the posterior commissure above the superior colliculus; its caudal limit, by the trochlear nerve below the inferior colliculus; and its medial limit, by the midline (Fig. 1). The operation was performed with the patient in a three-quarters prone position, and the surgeon sat beside the patient on the opposite side of the lesion (Fig. 2 right). An intermediate linear skin incision was made, and then a small right suboccipital craniotomy was performed with a part of the left transverse sinus exposed (Fig. 2 left). Paramedian bridging veins should be preserved. The arachnoid membrane over the quadrigeminal cistern was then opened and the left trochlear nerve and the superior cerebellar artery came into view (Fig. 3 upper left). A small entry on the supra-trochlear region was made with reference to the preoperative MRI, and the underlying lesion could be approached (Fig. 3 upper right). Both an old hematoma and abnormal vasculature were circumferentially removed (Fig. 3 lower left). The dissection plane should be within the surrounding gliotic layer. Normal brain tissue was finally exposed (Fig. 3 lower right).

The Intermediate or Lateral ITSC Infra-trochlear Approach

The patient was placed in a prone position with the neck tilting to the lesion side. The surgeon sat beside the patient on the opposite side of the lesion (Fig. 4 right). An intermediate linear skin incision was made, and small suboccipital craniotomy was performed with a part of the transverse sinus exposed (Fig. 4 left). Through the intermediate ITSC approach, the trochlear nerve serves as a good surgical landmark. The trajectory of the ITSC infratrochlear approach is more lateral than that of the ITSC transcollicular supratrochlear approach. The dissection followed the downward slope of the anterior lobe of cerebellum beyond the lateral margin of the quadrigeminal plate to the posterolateral mid-brain (Fig. 5). Surgical entry was made inferior to the trochlear nerve and medial to the trigeminal nerve with reference to the preoperative MRI (Fig. 6 left). An old hematoma and abnormal vasculatures were circumferentially extirpated (Fig. 6 right). Normal brain tissue was finally exposed.

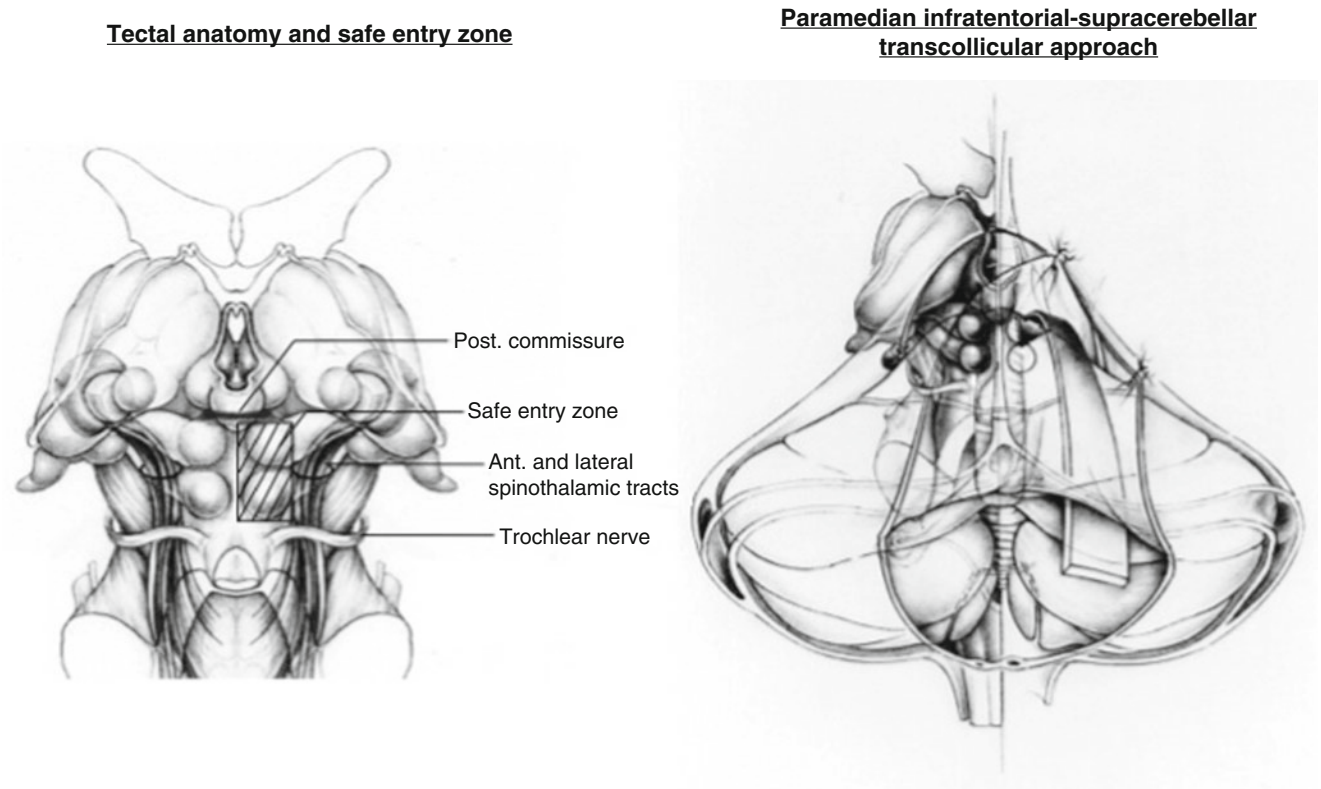

Fig. 1 The ITSC transcollicular approach is made through a single superior or inferior colliculus, or both. The rostral limit of the exposure is formed by the posterior commissure above the superior colliculus; its caudal limit, by the trochlear nerve below the inferior colliculus, and its medial limit, by the midline

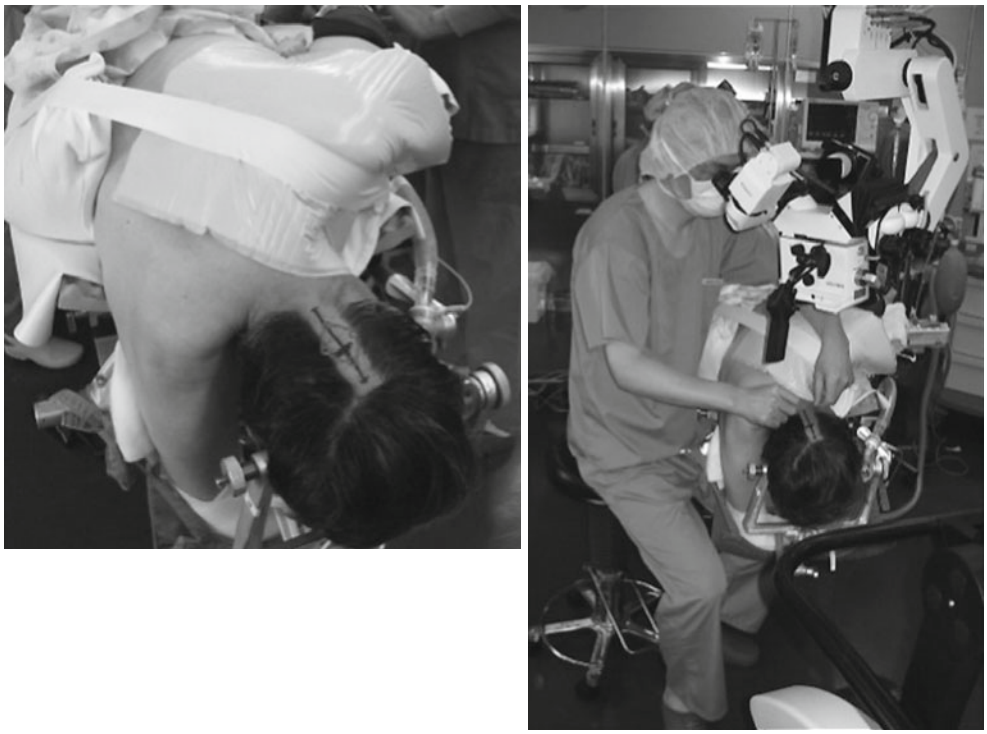

Fig. 2 The ITSC transcollicular approach; the operation was performed with the patient in a quarter-prone position, and the surgeon sat beside the patient on the opposite side of the lesion. An intermediate linear skin incision was made, and a small right suboccipital craniotomy was performed with a part of the left transverse sinus exposed

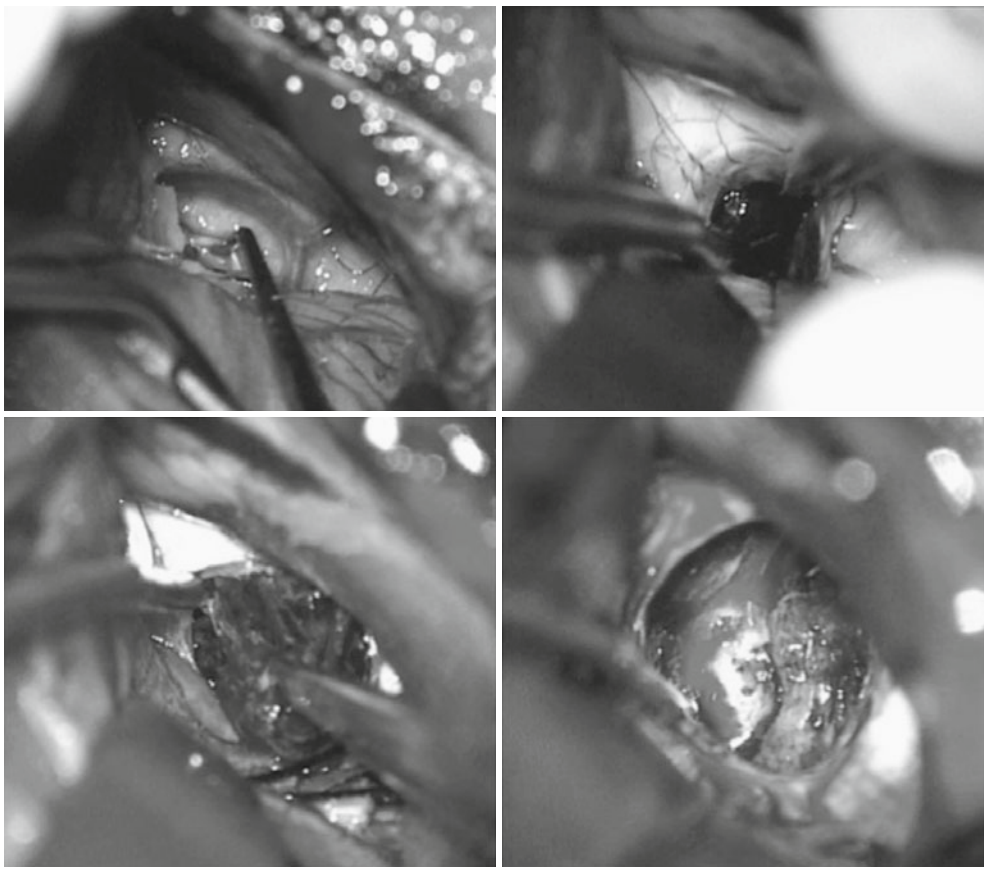

Fig. 3 The operative views through the ITSC transcollicular approach

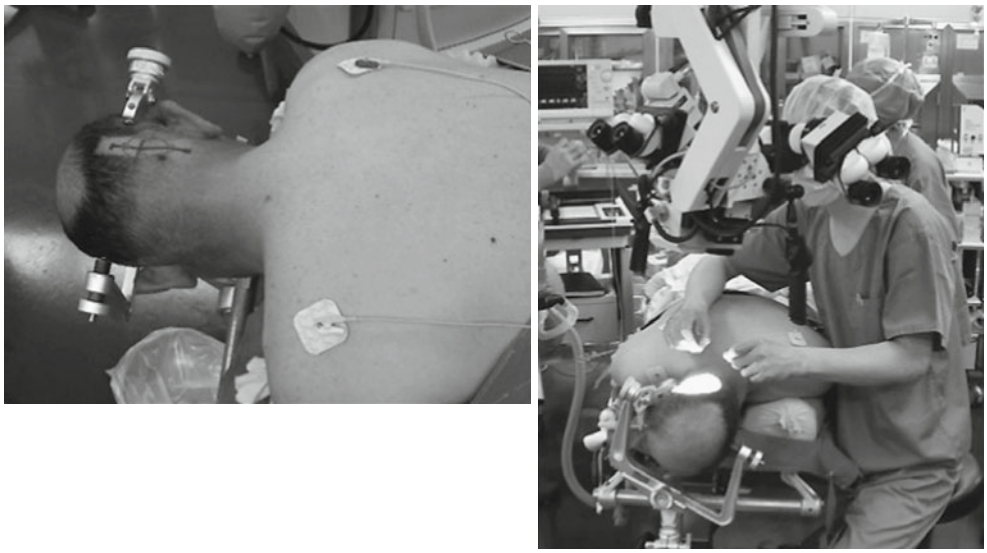

Fig. 4 The intermediate or lateral ITSC infra-trochlear approach; the patient was placed in a prone position with the neck tilting to the lesion side. The surgeon sat beside the patient on the opposite side of the lesion. An intermediate linear skin incision was made, and small suboccipital craniotomy was performed with a part of the transverse sinus exposed

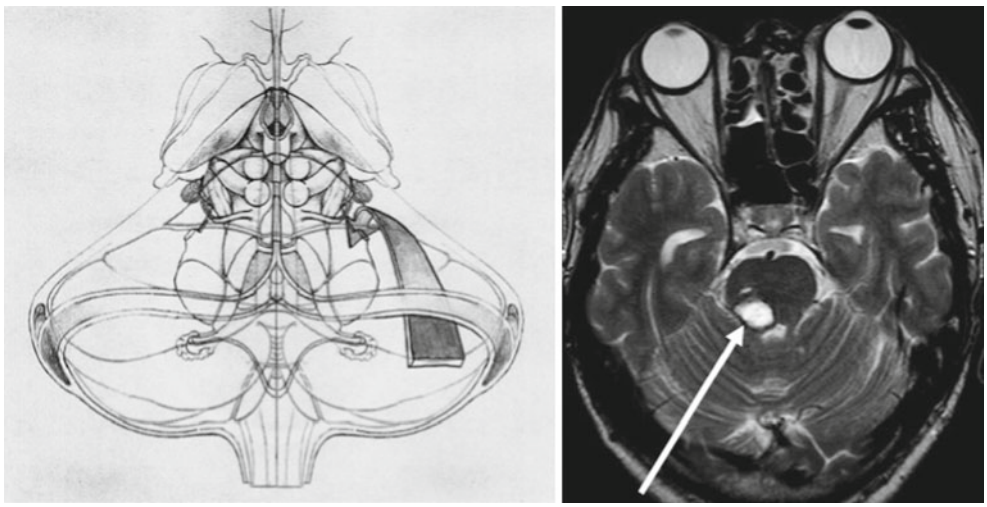

Fig. 5 Through an intermediate ITSC approach, the dissection followed the downward slope of the anterior lobe of the cerebellum beyond the lateral margin of the quadrigeminal plate to the posterolateral mid-brain. *Arrow* indicates the surgical corridor

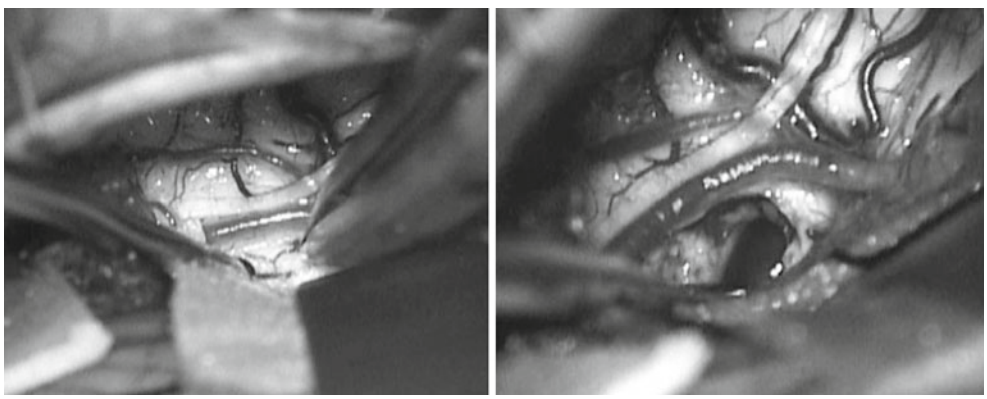

Fig. 6 The operative views through the ITSC infra-trochlear approach

Results

All 16 lesions were completely removed. There was no recurrence of bleeding during the follow-up period and no mortality. In the patients with a mid-brain lesion, the preoperative ocular symptoms improved in three of seven patients, and the neurological deficits other than ocular symptoms improved in five of seven patients. The pre-operative modified Rankin Scale score of 1.8 improved to 1.3 postoperatively.

In the patients with a ponto-mesencephalic lesion, there was also no recurrence of bleeding during the follow-up

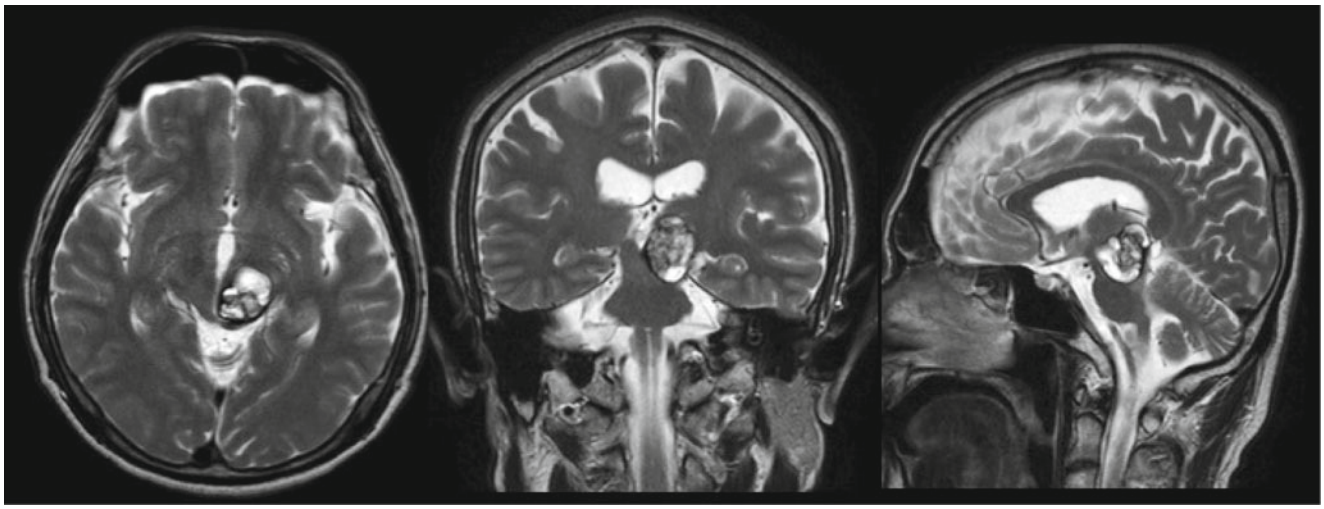

Fig. 7 MRI showing a mixed intensity mass in the left mid-brain extending to the thalamus

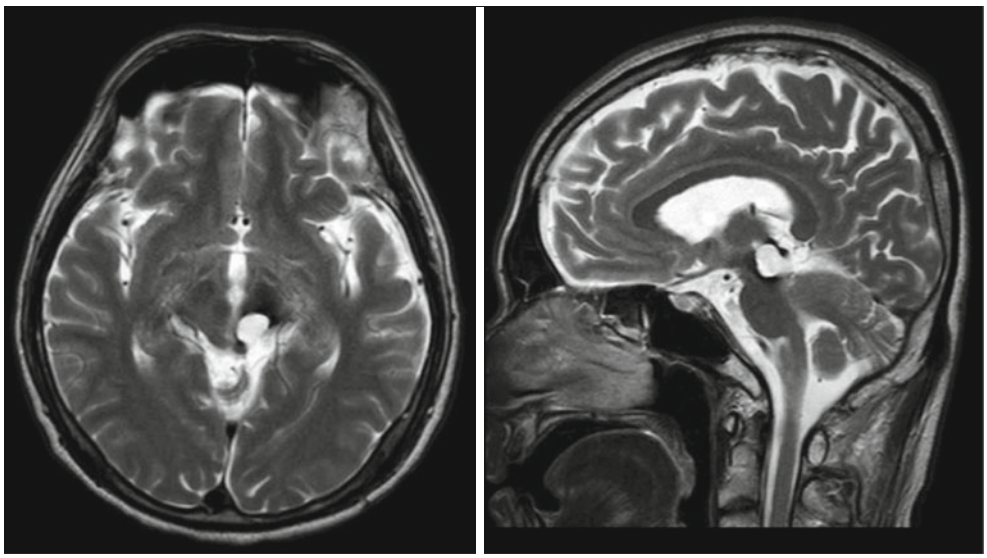

Fig. 8 Post-operative MRI showing a total removal of the lesion

period. The preoperative ocular symptoms improved in four of nine patients, and the neurological deficits – other than ocular symptoms – improved in five of them, while one patient experienced a venous infarction in the cerebellar hemisphere that caused neurological deterioration. The preoperative modified Rankin Scale score of these patients improved from 3.75 to 2.5 postoperatively.

Illustrative Cases

Case 1

A 59-year-old man developed right hemiparesis and diplopia. Neurological examination revealed a horizontal gaze paresis and a right motor and sensory disturbance. MRI showed a mixed intensity mass in the left mid-brain extending to the thalamus (Fig. 7). The lesion was extirpated through a left paramedian ITSC transcollicular approach. Total removal of the lesion was confirmed by a postoperative MRI (Fig. 8). His neurological symptoms other than ocular movement improved.

Case 2

A 56-year-old man developed left hemiparesis and diplopia. MRI showed an irregular small hematoma in the ponto-mesencephalon (Fig. 9). The lesion was extirpated through a right intermediate ITSC infra-trochlear approach. Total removal of the lesion was confirmed by a postoperative MRI (Fig. 10). His neurological symptoms improved.

Discussion

Intrinsic brain stem lesions are surrounded by functionally important tissue that leaves little room for a safe surgical approach [2, 3, 5, 6, 8]. Surgeons should approach lesions

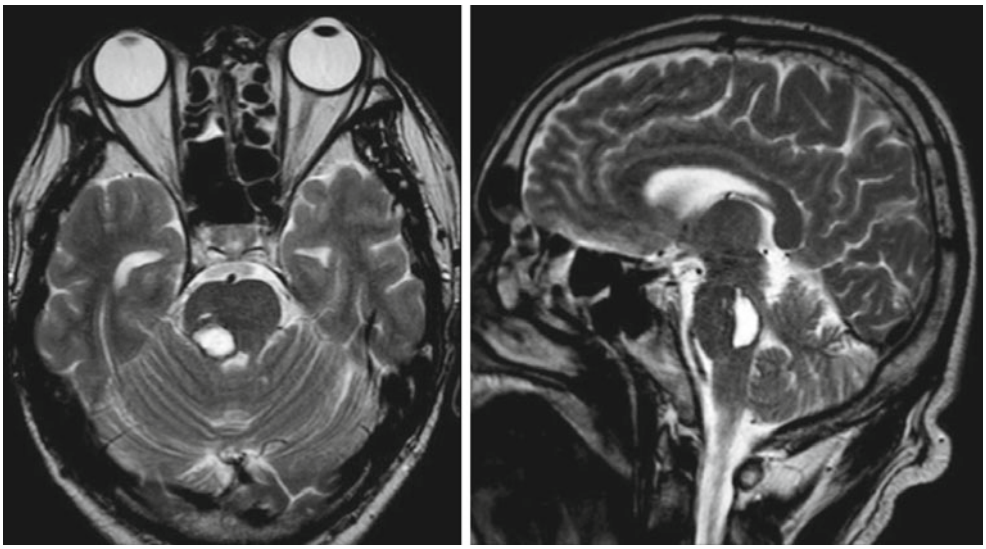

Fig. 9 MRI showing an irregular small hematoma in the ponto-mesencephalon

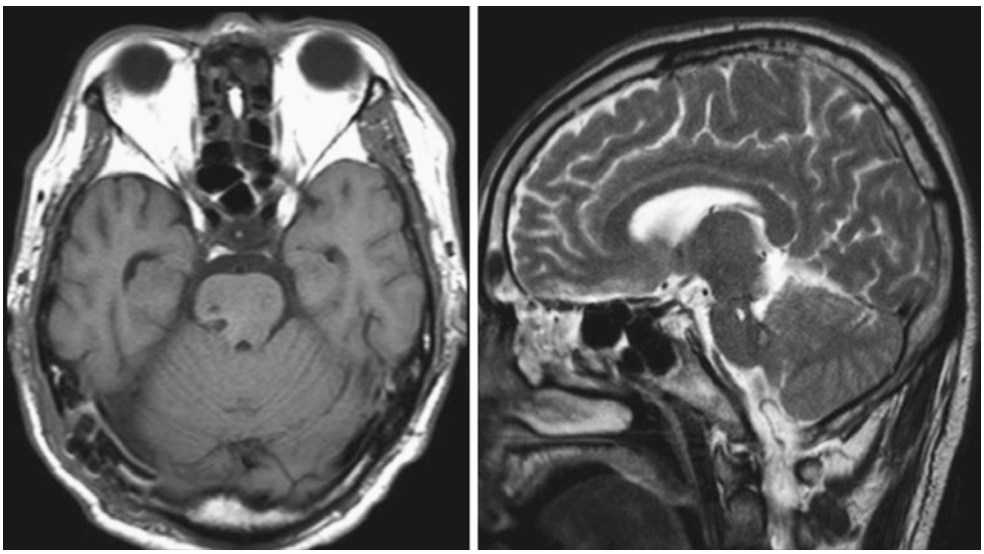

Fig. 10 Post-operative MRI showing total removal of the lesion

through a safe entry zone and closest point to lesions. The direction of the approach is also important. There are some useful surgical landmarks for the surgical approach to ponto-mesencephalic lesions, such as the trochlear nerve and the trigeminal nerve. The trochlear nerve originates beneath the inferior colliculus and courses through the cerebellomesencephalic fissure. It exits the anterior part of the cerebellomesencephalic fissure, continues through the middle incisural space, and enters the lower margin of the free edge of tentorium at the posterior edge of the cerebral peduncle. Deep to the trochlear nerve and branches of the superior cerebellar artery is the posterolateral mid-brain, composed of the superior cerebellar peduncle and the posterior aspect of the cerebral peduncle. A plane of dissection was developed above or below the trochlear nerve, depending on where the lesion came to the surface of the brain stem.

The supra-trochlear transcollicular approach is made through a single superior or inferior colliculus, or both [3]. The rostral limit of the exposure is formed by the posterior commissure above the superior colliculus; its caudal limit, by the trochlear nerve below the inferior colliculus; and its medial limit, by the midline. In this approach, the trochlear nerve is a good surgical landmark, because the inferior and superior colliculi are extended and often could not be identified during surgery. The supra-trochlear transcollicular approach is made through a single superior or inferior colliculus, or both, providing a relatively large safe entry zone to intrinsic mid-brain lesions. The superior colliculi are related to visually triggered saccades. If the superior colliculi are surgically removed, however, accurate visually triggered saccades return during the postoperative recovery period. Regarding the inferior colliculus, because the ascending auditory pathways have several commissural and decussating

connections within the brain stem, a lesion strictly limited to one colliculus results in no alteration of hearing [3]. The presence of some restriction in the approach to the caudal direction and a risk of injury to the bridging veins between the cerebellar surface and the tentorium are drawbacks associated with this approach.

The intermediate or lateral ITSC infra-trochlear approach uses the trochlear nerve and trigeminal nerve as surgical landmarks. The intermediate or lateral ITSC infratentorial-infratrochlear approach opens the cerebello-mesencephalic fissure to expose the superior cerebellar peduncle, interpeduncular sulcus between superior and middle cerebellar peduncles, and the rostral portion of the middle cerebellar peduncle [8]. The intermediate or lateral ITSC infra-trochlear approach provides a wide surgical entry to intrinsic ponto-mesencephalic lesions. The trajectory of the infratrochlear approach should be more lateral than that of the supra-trochlear transcollicular approach. The dissection follows the downward slope of the anterior lobe of cerebellum beyond the lateral margin of the quadrigeminal plate to the posterolateral mid-brain. Excessive retraction of the cerebellum in the caudal direction could also cause injury to the bridging veins.

Conclusion

The ITSC transcollicular or infra-trochlear approach provides a wide operative entry zone for accessing ponto-mesencephalic lesions while minimizing the functional damage to the surrounding structures.

Conflict of Interest The authors declare that they have no conflict of interest.

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