

Y. Yonekawa, T. Tsukahara
A. Valavanis, N. Khan
Editors

Changing Aspects in Stroke Surgery: Aneurysms, Dissections, Moyamoya Angiopathy and EC-IC Bypass

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Edited by
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Prof. Dr. Yasuhiro Yonekawa
Neurochirurgie FMH, Zurich, Switzerland

Dr. Tetsuya Tsukahara
Department of Neurosurgery, Kyoto National Hospital, Kyoto, Japan

Prof. Dr. Anton Valavanis
Institut für Neuroradiologie, Universitätsspital Zurich, Zurich, Switzerland

Dr. Nadia Khan
Neurochirurgische Klinik, Universitätsspital Zurich, Zurich, Switzerland

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Preface

This Supplement is an outline of the proceedings of the 3rd European-Japanese Joint Conference for Cerebral Stroke Surgery which was held in conjunction with the 70th Anniversary of the Neurochirurgische Universitätsklinik Zürich founded by Prof. Krayenbühl.

This meeting has been held twice until now under the name of Swiss-Japanese Joint conference with the aim to exchange recent knowledge and technical advances in the field of stroke surgery and its perioperative management.

This time we have focused especially on dissecting aneurysms, where their epidemiology, pathophysiology, and management are still to be elucidated. In Japan, a nationwide survey on this topic is ongoing, and part of the results are presented in this issue.

Also, one will find some local differences in the incidence and pathophysiology of various vascular diseases like in the case of Moyamoya angiopathy, which presently also has a 50-year history since its initial discovery

in Japan. Neurosurgical advances in this type of angiopathy are discussed in detail in this issue.

The role of EC-IC bypass surgery, with a history of now just 40 years since the pioneer work of Professors Yasargil and Donaghy in 1967, with its extensive availability in the field of stroke surgery to date, is also elucidated.

Last but not least, ongoing developments of endovascular surgery in the treatment of stroke surgery along with the introduction of the current randomised study of unruptured brain AVM (ARUBA) by Prof. Mohr is included.

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*Yasuhiro Yonekawa
Tetsuya Tsukahara
Anton Valavanis
Nadia Khan*

Contents

Part 1: Aneurysms, arteriovenous malformations and fistulas

<i>Mohr, J. P.:</i> A randomized trial of unruptured brain arteriovenous malformations (ARUBA)	3
<i>Manabe, H.:</i> Ruptured cerebral aneurysms treated by stent-assisted GDC embolization – two case reports with long-term follow-up	5
<i>Takahashi, T., Suzaki, N., Tsugane, S., Yamauchi, K., Takada, S.:</i> Suction decompression methods for giant internal carotid ophthalmic aneurysms by using revised double lumen balloon catheters	9
<i>Kikuta, K., Takagi, Y., Nozaki, K., Hashimoto, N.:</i> Introduction to tractography-guided navigation: using 3-tesla magnetic resonance tractography in surgery for cerebral arteriovenous malformations	11
<i>Orakcioglu, B., Becker, K., Sakowitz, O. W., Unterberg, A., Schellinger, P. D.:</i> Serial diffusion and perfusion MRI analysis of the perihemorrhagic zone in a rat ICH model	15
<i>Baumann, F., Khan, N., Yonekawa, Y.:</i> Patient and aneurysm characteristics in multiple intracranial aneurysms	19
<i>Otani, N., Fujioka, M., Oracioglu, B., Muroi, C., Khan, N., Roth, P., Yonekawa, Y.:</i> Thalamic cavernous angioma: paraculminar supracerebellar infratentorial transtentorial approach for the safe and complete surgical removal	29
<i>El Beltagy, M., Muroi, C., Imhof, H.-G., Yonekawa, Y.:</i> Peripheral large or giant fusiform middle cerebral artery aneurysm: report of our experience and review of literature	37

Part 2: Dissection of cerebral arteries

<i>Baumgartner, R. W.:</i> Stroke prevention and treatment in patients with spontaneous carotid dissection.	47
<i>Satoh, A., Sugiyama, T., Hongo, K., Kakizawa, Y., Ishihara, S., Matsutani, M.:</i> Nationwide surveillance of IC anterior (or dorsal) wall aneurysm: with special reference to its dissecting nature.	51
<i>Nishino, A., Suzuki, I., Utsunomiya, A., Suzuki, S., Uenohara, H., Sakurai, Y.:</i> Clinical manifestation and treatment strategy for non hemorrhagic cerebral arterial dissection	57

<i>Yonekawa, Y., Zumofen, D., Imhof, H.-G., Roth, P., Khan, N.:</i> Hemorrhagic cerebral dissecting aneurysms: surgical treatment and results	61
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Part 3: Revascularisation procedures, EC–IC bypass revisited

<i>Mehdorn, H. M.:</i> Cerebral revascularisation by EC-IC bypass–present status	73
<i>Inoue, T., Jinnouchi, J.:</i> Changes in brain volume after EC-IC bypass surgery	79
<i>Kaku, Y., Watarai, H., Kokuzawa, J., Tanaka, T., Andoh, T.:</i> Less invasive technique for EC-IC bypass	83
<i>Alferi, A., Bregy, A., Constantinescu, M., Stucker, F., Schaffner, T., Frenz, M., Banic, A., Reinert, M.:</i> Tight contact technique during side-to-side laser tissue soldering of rabbit aortas improves tensile strength. . .	87
<i>Krayenbühl, N., Khan, N., Cesnulis, E., Imhof, H.-G., Yonekawa, Y.:</i> Emergency extra–intracranial bypass surgery in the treatment of cerebral aneurysms	93
<i>Zumofen, D., Khan, N., Roth, P., Samma, A., Yonekawa, Y.:</i> Bonnet bypass in multiple cerebrovascular occlusive disease	103
<i>Tsukahara, T., Hatano, T., Nakakuki, T., Tsuji, Y., Aoyama, T., Ogata, H.:</i> Combined treatment using CEA and CAS for carotid arterial stenosis.	109

Part 4: Moyamoya angiopathy, history

<i>Iwama, T., Yoshimura, S.:</i> Present status of Moyamoya disease in Japan.	115
<i>Hänggi, D., Mehrkens, J. H., Schmid-Elsaesser, R., Steiger, H.-J.:</i> Results of direct and indirect revascularisation for adult European patients with Moyamoya angiopathy	119
<i>Kikuta, K.:</i> Experiences using 3-tesla magnetic resonance imaging in the treatment of Moyamoya disease	123
<i>Khan, N., Yonekawa, Y.:</i> Moyamoya angiopathy in Europe: the beginnings in Zurich, practical lessons learned, increasing awareness and future perspectives.	127
<i>Hernesniemi, J., Dashti, R., Mateo, O., Cancela, P., Karatas, A., Niemelä, M.:</i> Historical landmarks in vascular Neurosurgery “On July 10 th 2006, at the 70 th Anniversary of the Department of Neurosurgery of Zürich Medical School”	131
Author index	139
Index of keyword	141

Listed in Current Contents

Part 1:

Aneurysms, arteriovenous malformations and fistulas

A randomized trial of unruptured brain arteriovenous malformations (ARUBA)

J. P. Mohr

Doris and Stanley Tananbaum Stroke Center, Neurological Institute Columbia Medical Center, New York, NY, U.S.A.

Summary

Despite almost a century of efforts in the treatment of brain arteriovenous malformations (BAVMs) no clinical trial has yet been performed to demonstrate the benefits of intervention versus conservative (medical) management for those not yet bled. Only insufficient information on the natural history of unbled BAVMs exists to certify that intervention is needed and that such intervention produces a better long-term functional outcome.

Keywords: Brain arteriovenous malformations; natural history.

Introduction

Effective from January 2006, the NINDS awarded Grant 1U01 NS051483 for an international prospective, internet-based randomized (1:1) trial of 800 patients to evaluate the difference, if any, in the incidence of stroke, hemorrhage, death, and functional status over a period of five years for patients with brain arteriovenous malformation (BAVM), which is deemed treatable by the local center, and to whom randomization is offered with regard to conservative (medical management for non-hemorrhage symptoms) vs. any type, number, or sequence of intervention intended to eradicate the BAVM including surgery, endovascular, or radiotherapy treatment(s). Subjects randomized to the conservative management arm are eligible for interventional treatment should hemorrhage occur during the 5-year course of follow-up.

Patients to whom randomization should be offered are those for whom the local treating team has “ethical

equipoise” concerning whether to treat or not. Patients whose BAVM is deemed too daunting for eradication efforts are thus not subject to ethical equipoise. Patients with evidence of having bled are not eligible.

The trial offers the opportunity to assess hemorrhagic predictability for biomarkers such as TNF- α -238G > A and MMP-9 [1, 4, 5, 12]. Support of this testing was applied for at NIH under a grant proposal entitled “BioMarkers for Hemorrhagic Risk “BARUBA” (WL Young, PI), review of which is currently in process. An application to evaluate the use of Minocycline or comparable agent in a parallel clinical trial for the currently untreatable, very large lesions is in preparation as is a proposal for a registry of cases eligible for ARUBA, but who do not accept or are not approached for randomization.

Material and methods

To date 87 centers in the U.S., Europe, Canada, Australia, Brazil and Puerto Rico have enrolled to participate in the trial. The trial has its clinical center at the Neurological Institute in New York (JP Mohr, PI), the European Coordinating Center at the Laraboisiere in Paris (C Stapf, Co-I, M-G Boussier, Service Chief), and the Statistical Center at the International center for Health Outcomes and Innovation Research (InCHOIR – www.inchoir.org) (A Moskowitz and A Gelijns, Co-PIs).

When BAVMs came to attention because of hemorrhage and diagnosis was based on angiogram, it was no surprise that clinicians came to regard BAVMs as lethal a lesion as an aneurysm. Disappointing experiences with individual cases fully justified this view [14]. Little wonder that those discovered prior to hemorrhage were considered suitable for intervention. Such assumed suitability may explain the failure of all but the most recent case series in the literature to have segregated treatment outcomes based on whether patients had bled or not prior to treatment [3, 13, 15].

Based on the literature from the beginning of this field, it seems clear that hemorrhage sets in motion a process that raises the risk of recurrent hemorrhage in the near future, and all workers, including those formulating and planning participation in ARUBA [9, 16] are committed to intervention for BAVMs once hemorrhage has occurred.

Correspondence: J. P. Mohr, Doris and Stanley Tananbaum Stroke Center, Neurological Institute Columbia Medical Center, 710 West 168th Street, New York, NY 10032, U.S.A.
e-mail: JPM10@Columbia.edu

But what of those discovered prior to hemorrhage? With the increasing use of non-invasive techniques, such as magnetic resonance imaging (MR), more and more patients are being discovered to harbor a BAVM prior to having bled: our population-based study in New York demonstrated roughly 2 to 1 non-bleed vs. bleed [18].

Removal by surgery, occlusion of the vessels *via* catheter-delivered intravascular occlusive material, or radiotherapy to the BAVM are time-honored treatments, and can be carried out with a low risk of mortality. But such treatments necessarily involve vasculature embedded in brain parenchyma and carry a risk of injury to adjacent healthy brain tissue [10, 11]. None of such outcomes are intended and all are regrettable, when they occur. Some recent evidence argues that intervention prior to hemorrhage may activate the lesion [21], possibly leading to the very up-regulation of hemorrhagic risk factors that would best be avoided. Furthermore, adjudicating the untoward events of intervention has proved difficult, since early adverse post-treatment effects can always be hoped to fade toward normal. Persistent, undeniable adverse effects have been reported from 3–13% [3, 10, 13]. Post-treatment symptoms of functional importance to the patient have proved even more frequent [10]. Against these outcomes there are some studies showing that clinical effects of first hemorrhage can be quite benign [9, 7], especially when compared with parenchymal hemorrhage of other cause [6, 16]. The costs of intervention are high, as are the long-term costs of post-injury care for all those patients who suffer complications of bleeding or treatment [2].

Prior efforts, well-conducted but not strictly segregating the course followed by those unbled from bleed, have bundled together these two groups [17]. They have yielded hemorrhage and death rates that more accurately reflect the course followed by those that have previously bled but been untreated, leaving unsettled the course of those not having bled. Case series which have separated the two groups suggest a more benign course followed by those unbled [19].

What has been lacking heretofore is a controlled clinical trial which can provide some insights into the true natural history versus the outcomes of intervention for the unbled BAVMs. We expect some of these ambiguities to be resolved from the results of ARUBA. We would be happy indeed to discover the unbled cohort that clearly benefits from intervention and leave aside those whose natural history does not justify such efforts. The literature, including our work, already contains some indicators for hemorrhage risk, which are subject to prospective evaluation [19]. In the absence of such data we have taken the position that intervention for those unbled is experimental therapy [20].

Details of ARUBA, including rationale, frequently asked questions, protocol, lists of participants (sites, committees, adjudicators) and invitations for participation are posted on our website (www.ARUBAstudy.org)

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Ruptured cerebral aneurysms treated by stent-assisted GDC embolization – two case reports with long-term follow-up

H. Manabe

Department of Neurosurgery and Clinical Research, Hakodate National Hospital, Hokkaido, Japan

Summary

Two cases of acutely ruptured cerebral aneurysm of low dome/neck ratio treated by stent-assisted GDC embolization using balloon-expandable coronary stent, and also their long-term follow-up results are reported. After embolization, the basilar trunk aneurysm was completely occluded, and partial occlusion was obtained for the internal carotid (IC)-paraclinoid aneurysm. Oral ticlopidine (200 mg/day) was given after the embolization, and no neurological events were seen during long-term follow-up (64–68 months). Follow-up angiograms of the basilar trunk aneurysm at 20 months showed complete occlusion and no in-stent stenosis. Follow-up angiograms of the IC-paraclinoid aneurysm at 52 months showed complete occlusion of the aneurysm, but mild stenosis at the distal end of the stent graft. These cases suggested that stent-assisted GDC embolization is effective for prevention of rebleeding from ruptured aneurysm during long-term observation even with sufficient dose of antiplatelets therapy. Caution should be taken on aneurysmal recanalization and parent artery stenosis due to stent deployment during long-term period.

Keywords: Cerebral aneurysm; GDC embolization; stent; long-term observation; in-stent stenosis.

Introduction

Guglielmi's detachable coil (GDC) embolization has been established as the major treatment option for cerebral aneurysm, thanks to the development of endovascular technologies and a steady accumulation of outcome data from this treatment over the last decade. However, it is still difficult to obtain the favorite outcome in cases of wide-necked aneurysm due to difficulty in gaining complete occlusion and the possibility of recanalization over the long-term.

A stent-assisted technique is developing as one solution for the problems seen in GDC embolization of

wide-necked aneurysm. In the late 1990s, balloon-expandable coronary stents were used for this technique; in many cases, navigation of this type of stent into the intracranial arteries was challenging due to the non-flexible nature of the stent system. For this reason, only a small number of aneurysms could be treated using this technique. In 2002, the self-expandable flexible stent, which could be easily navigated into intracranial arteries, became available for clinical use to treat cerebral aneurysm. Several reports have detailed the preliminary clinical experience with the stent-assisted GDC embolization [1, 4, 7], but long-term results are still unclear.

In this report, we present two cases of acutely ruptured aneurysm treated by stent-assisted GDC embolization with 20- and 52-month angiographic follow-up. Complications and long-term clinical and angiographic results of this treatment are discussed.

Case reports

Case 1: A 36-year-old man diagnosed with a ruptured small aneurysm (4 mm) with relatively wide neck (3 mm) on the basilar trunk was brought to our hospital. Endovascular occlusion was chosen because of presumed surgical difficulties in manipulation for mid-portion of the basilar artery. Embolization was performed under general anesthesia with systemic heparinization. After failure of insertion of GDC 10 due to coil protrusion into the parent artery, a 9 mm-long balloon-expandable coronary stent (NIR PRIMO coronary stent; Boston Scientific, Natick MA, U.S.A.) was navigated into the basilar artery and was expanded to a 3 mm diameter to cover the aneurysm orifice. The origins of bilateral anterior inferior cerebellar arteries (AICA) were also covered by the stent. Using the scaffold effect by the stent placement on the basilar artery, three GDCs were successfully put into the aneurysm to gain the complete occlusion. Immediate post-embolization angiograms showed complete occlusion of the aneurysm and good filling of the basilar artery and bilateral AICAs. The patient's postoperative course was uneventful. Systemic heparinization was discontinued 48 h after embolization and oral ticlopidine (200 mg/day) was then initiated. The patient got out of

Correspondence: Hiroshi Manabe, M.D., Department of Neurosurgery, Hakodate National Hospital, 18-16 Kawahara-cho Hakodate, 041-8512 Hokkaido, Japan. e-mail: hmanabe@hnh.hosp.go.jp

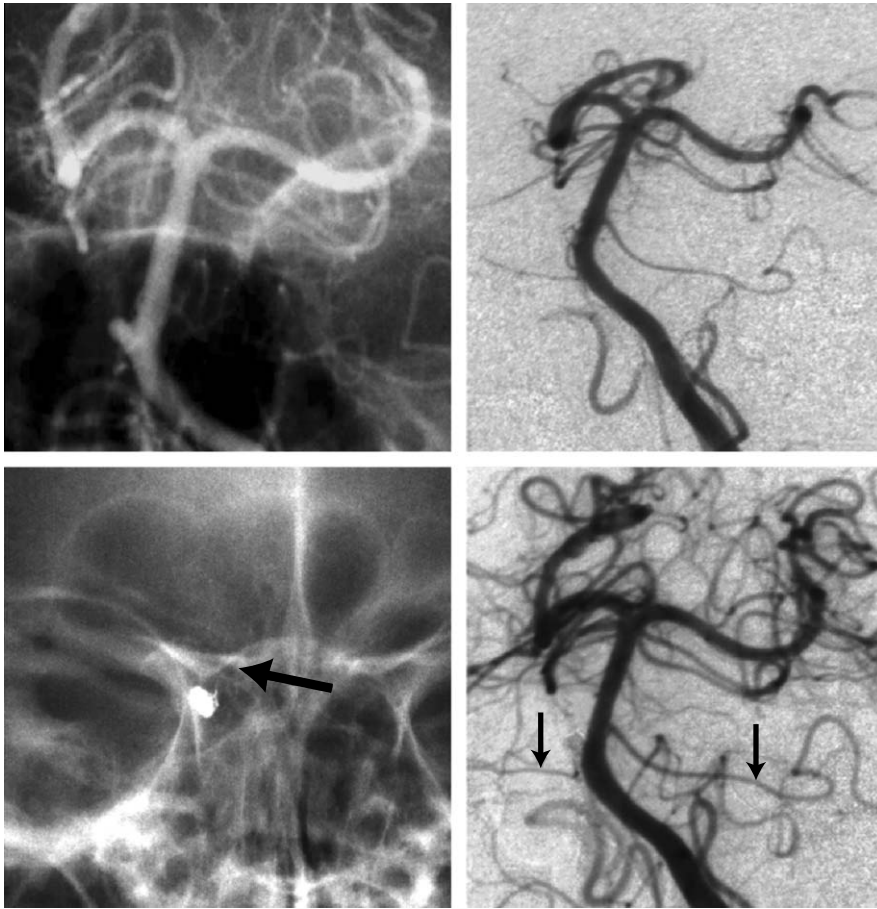


Fig. 1. Films from Case 1. *Upper left* Angiogram on admission showing basilar trunk small aneurysm. *Upper right* Complete occlusion of the aneurysm is seen on immediate post-embolization angiogram. *Lower left* Simple craniogram showing coils and stent (arrow). *Lower right* Follow-up angiogram taken 20 months after embolization revealed good filling of the bilateral anterior inferior cerebellar arteries (arrows) and no in-stent stenosis of the basilar artery



Fig. 2. Films from Case 2. *Upper left* Angiogram showed large aneurysm with wide neck on paraclinoid portion of the internal carotid artery. *Upper right* Immediate post-embolization angiogram showing partial occlusion of the aneurysm. *Lower left* Simple craniogram indicates coil mass and stent (arrows). *Lower right* Angiogram taken 52 months after embolization, showing complete occlusion of the aneurysm and mild stenosis of parent artery (arrow)

hospital 18 days after embolization with no neurological deficit. Follow-up angiograms taken 20 months after embolization revealed complete occlusion of the aneurysm, good filling of the bilateral AICAs and no in-stent stenosis. No neurological events were seen during the 68 months follow-up period.

Case 2: This 65-year-old woman was admitted to our hospital suffering from an aneurysmal subarachnoid hemorrhage. Angiograms revealed a large aneurysm (12 mm) with wide neck (7.5 mm) on the paraclinoid portion of the left internal carotid artery (ICA). Surgical clipping was thought to be difficult because of aneurysm size and location, and conventional GDC embolization (even with the use of balloon-assisted technique) was difficult because of the width of the aneurysm neck, stent-assisted GDC embolization was performed under general anesthesia with systemic heparinization. A 9-mm-long balloon-expandable coronary stent (NIR PRIMO, Boston Scientific) was navigated into the ICA and expanded to a 4-mm diameter to cover the aneurysm orifice. The origin of the left ophthalmic artery was also covered by the stent. The aneurysm was partially occluded with GDCs (total length: 117 cm) delivered through the stent mesh. Systemic heparinization was discontinued 48 h after the procedure, and oral ticlopidine (200 mg/day) was initiated. No complications related to embolization were seen. Follow-up angiograms taken 52 months after embolization showed complete occlusion of the aneurysm and good filling of the ophthalmic artery, however, mild stenosis (less than 30%) of the ICA at the distal end of the stent was also noted. This stenosis had not been seen on the 9-month follow-up angiograms. No neurological events were reported during the 64-months follow-up period.

Discussion

Endovascular treatment for wide-necked aneurysms is still technically challenging, even if performed with the balloon remodeling technique or use of a three-dimensional Guglielmi's detachable coil (3D-GDC). These techniques and this device do not always ensure satisfactory coil packing of the aneurysm with low dome/neck ratio because of coil protrusion. Stent placement into the parent artery to cover the aneurysm orifice is an adjuvant technique in GDC embolization of wide-necked aneurysm, preventing the coil protrusion into the parent artery by acting as a scaffold. With this technique, tighter coil packing into wide-necked aneurysm would be possible compared to that seen with the balloon remodeling technique or use of 3D-GDC.

Although short-term clinical and angiographic results of cerebral aneurysm treated by the stent-assisted GDC embolization are cleared [1, 4, 7], long-term angiographic changes and clinical outcomes are not known. Of the 74 aneurysms treated by stent and coils in Fiorella's report [1], 46% of the treated aneurysms were completely or nearly completely occluded, and 54% were partially occluded on immediate post-procedure angiograms. Initial angiographic follow-up results (1.5–13 months, average 4.6 months) were described for 43 aneurysms treated by stent with GDC (Matrix and/or Hydro Coil in 34 aneurysms, non-bioactive in 9 aneurysms) and for five dissecting aneurysms treated by stent alone.

Follow-up angiograms demonstrated progressive thrombosis in 52% of the aneurysms treated by stent with coils, recanalization in 23%, and no change in 25%. Progressive thrombosis was seen in all dissecting aneurysms treated by stent alone. These initial follow-up results suggested that recanalization may follow GDC embolization, even with the use of stent and bioactive coil combination procedures, but rupture from stent-assisted GDC embolized aneurysms has not been reported. In our Case 1, the small aneurysm remained completely occluded in follow-up angiograms at 20 months post-embolization. In Case 2, the partially occluded large aneurysm may have recanalized; however, progressive thrombosis occurred and completely occluded it. Generally, wide-necked large aneurysm have significant incidence of recanalization, even in cases of complete occlusion immediately after embolization. The progressive thrombosis in Case 2 may be due to stent deployment, which altered the direction of blood flow into the aneurysmal dome, resulting in intra-aneurysm blood stasis. The degree of change in blood flow direction into the aneurysm caused by stent placement should depend on the strut size and metal-to-artery ratio. However, in the current situation, recanalization may follow the partially occluded aneurysm even with stent placement into the parent artery, so that careful observation is needed.

Knowledge about in-stent stenosis following stent-assisted GDC embolization is lacking, because the pathological changes associated with stent placement into a non-atherosclerotic intracranial artery are not well known. In the literature, only three cases of in-stent stenosis after stent-assisted GDC embolization has been reported (the Neuroform stent was used in all stenosed vessels) [1, 2]. We found no other reports of similar complications in the literature, suggesting that the in-stent stenosis after stent-assisted GDC embolization may be rare [2]. In our Case 2, mild stenosis of the parent artery at the distal edge of the stent was seen on 52-month follow-up angiograms; this had not been seen on 9-month follow-up angiograms. Angiograms and simple craniograms of the anterior-posterior projection suggest that the stent mesh does not have contact to the curved arterial wall at the distal edge, leaving space between the stent mesh and arterial wall; however, this late stenosis does not appear to be similar to the "in-stent" situations, as it might occur between the stent mesh and the curved arterial wall. It is well known that in-stent stenosis in coronary artery is caused by neointimal proliferation as a result of intimal injury, and the peak of which is thought to be at 3–6 months after initial

stent deployment [3, 6]. In Case 2, a distal part of the stent graft which did not contact the vascular wall would cause irregular blood flow, which could injure the intima slightly but continuously, leading to late neointimal proliferation. This type of stenosis of the intracranial artery after stent deployment has not been reported in the literature.

Changes to the perforating artery, when the origin is covered by a stent, are still undefined. An experimental study by Masuo *et al.* [9] showed angiographic and histological patency of the perforating artery branching from the stent-covered normal artery. Other clinical and experimental results suggest that the perforating artery could be kept patent after stent deployment if the parent artery is not atherosclerotic [5, 8]. In our cases, the branches from the stent-covered parent artery (i.e., ophthalmic artery and bilateral AICAs) maintained flow.

In conclusion, stent-assisted GDC embolization is one treatment option for the aneurysms that are not amenable for direct surgery or conventional endovascular surgery, and this method could prevent aneurysm from future rupture. Caution should be taken on possible recanalization of the aneurysm and stenosis of the parent artery in long-term angiographic and clinical observation.

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Suction decompression methods for giant internal carotid ophthalmic aneurysms by using revised double lumen balloon catheters

T. Takahashi, N. Suzuki, S. Tsugane, K. Yamauchi, S. Takada

Nagoya Medical Center, Department of Neurosurgery, National Hospital Organization, Nagoya, Japan

Summary

In giant, large internal carotid ophthalmic artery aneurysms, revised double lumen balloon catheters introduced directly into the cervical carotid arteries were used successfully to perform suction decompression methods. No general heparinization was used during these maneuvers except for continuous intraluminal irrigation of heparin contained saline. Intraoperative multi-directional portable DSA ascertained complete neck clippings and patency of parent vessels. These methods were tried for 8 cases of large, giant IC ophthalmic aneurysms. Among these 5 patients who complained of incomplete visual failures, visual acuity improved in 3 cases. Postoperative transient hemiparesis were seen in two cases which had partially thrombosed, calcified giant aneurysm and the other was due to prolonged proximal ICA occlusion at its cavernous portion. Neither dead nor severely disabled cases were seen, fortunately. Delayed postoperative conventional angiography disclosed complete neck clippings sparing parent arteries except for only one case. This revised direct carotid puncture method is simple and acceptable because of minimal morbidity.

Keywords: Suction decompression; giant aneurysm; balloon catheter.

Introduction

To handle giant aneurysms without complications is still technically difficult even if rapid technical developments in endovascular treatment modalities may occur. The most desirable methods to treat giant aneurysms are to occlude the neck completely with patency of parent artery and perforators. In giant paraclinoid, ophthalmic artery aneurysms, softening the neck and dome by trapping the aneurysms is indispensable for complete neck clippings or neck reconstructions. For this purpose, suc-

tion decompression methods were performed via the direct common carotid sheath introducer by double lumen balloon catheters (5.2 F, Selekon balloon catheter, Clinical Supply Inc., Japan).

Clinical material and methods

Under general endotracheal anesthesia, the obligatory common carotid artery was punctured and 5.0 F, 60 mm catheter sheath was inserted under lateral fluoroscopic control, into the internal carotid artery. Then 5.2 F, 70 cm double lumen balloon catheter (Selekon catheter, Clinical Supply Inc., Japan) was introduced through this sheath to the skull base. In this stage after evacuation of the air of balloon system replaced by diluted contrast agents, test occlusion of internal carotid artery by inflating the balloon was done to opacify the internal carotid artery aneurysm and dilated balloon. The diameters of inflated balloons were from 5.0 mm to 6.0 mm by 0.4–0.7 ml contrast agents. Then patients' heads were fixed to carbon-made radiolucent Mayfield head frame by disposable small head pins. After ordinary frontotemporal craniotomy, the Sylvian fissure was separated widely and aspirating the CSF, the optic nerve and proximal internal carotid artery were also identified. Then the optic canal and anterior clinoid process were meticulously drilled away as much as possible. The ophthalmic artery, aneurysmal neck, and distal ICA were also identified, if necessary, after removing the distal fibrous ring. The shape of aneurysmal neck and parent artery were identified before temporary proximal occlusion of internal carotid artery by inflation of double lumen balloon. Brain protecting agents (mannitol, phenytoin, dexamethazone) were also added before occlusion. Ascertaining the diminution of the aneurysmal dome pulsation, after clipping the distal internal carotid artery, the entire space of the aneurysmal dome was isolated by meticulous maneuver in order not to induce premature rupture. At this stage, if the decrease of aneurysmal pulsation and hardness were not enough, suction decompression method was applied by aspirating the blood through the indwelling double lumen balloon catheter. After shrinking the dome, the parent artery was reconstructed by multiple tandem fenestrated ring clips to interrupt the flow of aneurysmal dome sparing the patency of parent artery. Finally after release of all the temporary occlusive clips, the occluding balloon was deflated. Under portable DSA system (Siremobile system, Siemens Inc.), bi-directional cerebral angiography was done to identify the completion of aneurysmal neck clippings.

Correspondence: Tatsuo Takahashi, M.D., Nagoya Medical Center, Department of Neurosurgery, National Hospital Organization, 4-1-1 Sanno-maru, Naka-ku, Nagoya City, Japan.
e-mail: ttatsuo@md.ccnw.ne.jp

Results

By these maneuvers, 8 cases of large-giant IC-ophthalmic aneurysms were treated. Six cases of eight were non-ruptured but symptomatic, found by headache, visual failures and TIAs. In two of these 8 cases, visual acuity of the diseased side had already been blind for a long time. Postoperative improvements of visual acuity were gained in 3 cases of 5 incomplete visual failures. Postoperative transient hemiparesis were found in 2 cases due to embolic accident from partially thrombosed aneurysm and delayed proximal internal carotid artery occlusion at the cavernous portion in spite of intra-operative certification of the ICA patency by angiography. Fortunately, no operative mortality and no subarachnoid hemorrhage were encountered during the postoperative 15 year-follow-up period.

Discussion

Because of their broad-based necks, anatomically difficult access to proximal ICA, and mass effect, surgical treatment of giant IC-ophthalmic aneurysms can be challenging. The technique of open suction decompression of large and giant para-clinoid aneurysms has been reported by surgical exposure of the ICA in the patient's

neck and cannulation of the proximal ICA by Batjer [1] and Flamm [2]. Thereafter, balloon occlusive methods were described by Scott [4] and Shucart [5]. The technique described in this article includes using an NO.5.2 French double lumen balloon catheter through the catheter sheath indwelled into the common carotid artery.

In addition to intra-operative angiography and suction decompression, no general heparinization was needed [3], and no specialized neuroradiological staff was required in this revised new method.

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Introduction to tractography-guided navigation: using 3-tesla magnetic resonance tractography in surgery for cerebral arteriovenous malformations

K. Kikuta, Y. Takagi, K. Nozaki, N. Hashimoto

Department of Neurosurgery, Kyoto University Graduate School of Medicine, Shogoin, Sakyo-ku, Kyoto, Japan

Summary

Objective. To examine the effectiveness of magnetic resonance (MR) tractography in surgery for cerebral arteriovenous malformations (AVMs).

Methods. A preoperative evaluation of major neural tracts around the nidus was carried out with 3-tesla (3 T) MR tractography in 25 consecutive patients with cerebral AVMs. The patients were 12 men and 13 women ranging in age from 4 to 60 years of age (mean age: 31.2 ± 14.1 years). Twelve presented with hemorrhage. Images were obtained with T2-weighted turbo spin echo sequences, axial T1-weighted three-dimensional magnetization-prepared rapid acquisition gradient-echo (MPRAGE) sequences, three-dimensional time-of-flight MR angiography (3D TOF MRA), and thin-section diffusion-tensor imaging (DTI).

Results. The AVMs were obliterated in 22 of the 25 patients. A postoperative study of the MR tractography was carried out in 24 patients. In 21 patients, tracts were preserved and no postoperative neurological worsening was observed. Disruption of the tracts was found in 3 patients, and postoperative worsening was observed in 2 patients. However, no deterioration occurred in 1 patient with cerebellar AVM.

Conclusions. Notwithstanding the limitations of this method, MR tractography can be considered useful for confirming the integrity of deviated tracts, for localizing deviated tracts, and for evaluating surgical risk, especially in cases of non-hemorrhagic AVM.

Keywords: Arteriovenous malformation; magnetic resonance imaging; diffusion tensor imaging; tractography; navigation.

Abbreviations

AVM	arteriovenous malformation
CST	corticospinal tract
3D TOF MRA	three-dimensional time-of-flight MR angiography
IoDSA	intraoperative subtraction angiography
MCP	middle cerebellar peduncle
MPRAGE	magnetization-prepared rapid acquisition gradient-echo

MR	magnetic resonance
OR	optic radiation
SCP	superior cerebellar peduncle
S-M grade	Spetzler-Martin grade
3 T	3-tesla

Introduction

In surgery for arteriovenous malformations (AVMs), complete resection of the nidus is essential. Therefore, the surgical indication for an AVM is usually determined according to the risk for postoperative deficits following a complete resection [1]. Recent advances in MR technology have made it possible to outline major neural tracts in white matter by diffusion tensor imaging (DTI) [2]. We previously reported that a 3 T MR unit can describe most neural tracts more clearly than is possible with a 1.5 T unit [6] and that integration of the location of the corticospinal tract (CST) by 3 T MR tractography was correlated to electrophysiological white matter stimulation mapping [7]. We recently reported our early experiences with 3 T MR tractography applied to 10 patients with AVMs in and around the visual pathway [3]. In this article, we present our early experiences with 3 T MR tractography and tractography-guided navigation in surgery for cerebral AVMs.

Materials and methods

Patients

Between 1978 and 2005, we employed 3-tesla MR tractography to perform preoperative evaluation of major neural tracts around the nidus in 25 consecutive patients with cerebral AVMs. The patients were 12 men and 13 women ranging in age from 4 to 60 years (mean age:

Correspondence: Ken-ichiro Kikuta, M.D., Ph.D., Department of Neurosurgery, Kyoto University Graduate School of Medicine, 54 Kawaharacho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan.
e-mail: kikuta@kuhp.kyoto-u.ac.jp

Table 1. Summary of the 25 patients with AVM who underwent evaluation of major neural tracts with 3 T MR tractography. Indicated are the age, sex, location, Spetzler-Martin grade of the lesion, size (mm), episode of hemorrhage, type of onset, findings of preoperative tractography, preoperative embolization, residue of the nidus on postoperative angiography, findings of postoperative tractography, and postoperative deterioration

Case	Sex	Age	Location	S-M grade	Size (mm)	Symptom	MRT before surgery	Preoperative embolization	Residual nidus	Disruption of the tracts on MRT after surgery	Permanent neurological worsening after surgery
1	F	22	parietal	1	20	hemorrhage	CST	–	–	–	–
2	F	38	occipital	2	20	asymptomatic	OR	–	–	–	–
3	M	45	frontal	2	30	epilepsy	CST	–	–	–	–
4	F	27	temporal	3	30	hemorrhage	CST	–	–	–	–
5	M	44	frontal	2	27	ischemia	CST	–	–	+	hemiparesis
6	F	56	brainstem	3	10	hemorrhage	CST/MCP	–	+	±	cranial n. palsy
7	F	27	parietal	1	20	hemorrhage	CST	–	–	–	–
8	M	49	sylvian	2	25	asymptomatic	CST	–	–	–	–
9	M	48	parietal	3	40	epilepsy	CST	+	–	–	–
10	M	31	frontal	1	20	hemorrhage	CST	+	–	–	–
11	M	44	parietal	2	35	hemorrhage	CST	–	+	N.E.	cognitive dysfunction
12	M	28	frontal	2	35	epilepsy	CST	–	–	–	–
13	F	29	occipital	3	40	headache	OR	–	–	+	hemianopsia
14	F	6	insular	3	28	hemorrhage	CST	–	+	–	–
15	F	17	cerebellar	4	30	ischemia	MCP/SCP	+	–	+/+	–
16	F	29	temporal	1	5	hemorrhage	OR	–	–	–	–
17	M	21	sylvian	3	45	asymptomatic	CST	–	–	–	–
18	F	21	occipital	3	15	hemorrhage	OR	–	–	–	–
19	M	38	parietal	1	25	hemorrhage	CST	–	–	–	–
20	F	4	parietal	1	20	epilepsy	CST	–	–	–	–
21	F	23	frontal	2	30	hemorrhage	CST	–	–	–	–
22	M	26	temporoparietal	3	40	headache	CST/OR	+	–	–	–
23	M	25	occipital	2	25	hemorrhage	OR	–	–	–	–
24	M	60	occipital	2	27	headache	OR	–	–	–	–
25	F	22	temporal	2	30	headache	CST/OR	–	–	–	–

CST Corticospinal tract, OR optic radiation, MCP tracts through middle cerebellar peduncle, SCP tracts through superior cerebellar peduncle, N.E. not examined.

31.2 ± 14.1 years). Twelve presented with hemorrhage, 4 with epilepsy, 2 with ischemia, 4 with headache, and 3 with no symptoms. The AVMs were located in the frontal lobe in 5 patients, the parietal in 6, the temporal in 3, the occipital in 5, the temporoparietal in 1, the periinsular region in 3, and the posterior fossa in 2. The Spetzler-Martin grades of the AVMs were I in 6 patients, II in 10, III in 8, and IV in 1. The characteristics of the patients are presented in the accompanying Table 1. All patients underwent surgical resection of the nidus with intraoperative digital subtraction angiography (IoDSA). Preoperative embolization was performed in 4 patients (cases 9, 10, 15 and 2) without neurological worsening.

Imaging methods

All patients were studied with the same 3-tesla MR scanner (Magnetom Trio; Siemens, Erlangen, Germany) before and one month after surgery without 1 patient. Images were obtained with axial T2-weighted turbo spin echo sequences, with axial T1-weighted three-dimensional magnetization-prepared rapid acquisition gradient-echo (MPRAGE) sequences, with three-dimensional time-of-flight MR angiography (3D TOF MRA), and with thin-section diffusion-tensor imaging. Detailed information on the sequences was presented in our previous paper [3, 6, 7]. MR tractography of such major tracts around the nidi was carried out with DTI Studio version 2.03 software, focusing on the corticospinal tract (CST), optic radiation (OR), fibers through the superior cerebellar peduncle (SCP), and the middle cerebellar peduncle (MCP).

The state of the tracts was evaluated with inspective visualization of MR tractography [3]. When the tracts could not be described as continuous bands, they were judged as “disrupted” [3].

Results

AVMs were completely obliterated in 23 of the 25 patients in this study. In case 11, residual shunt was fairly demonstrated on the IoDSA that was expected to be spontaneously occlusion. However, postoperative bleeding occurred at 3 days after surgery and a second surgery was needed. In the remaining 2 patients, the nidi had migrated within the brainstem or insular cortex near the major neural tracts. Intentional partial resection or feeder clipping combined with stereotactic radiosurgery was performed in the patients.

Postoperative study of MR tractography was carried out in 24 patients. In 21 patients, tracts were preserved and no postoperative neurological worsening was observed. Disruption of the tracts was found in 3 patients and postoperative worsening was observed in 2. However, no deterioration occurred in 1 patient with cerebellar AVM (case 15; Table 1).

Case presentation: tractography-guided navigation in surgery for an occipital AVM (Case 18)

A 21-year-old female presenting with hemorrhage in the right occipital lobe was admitted to our institution with slight quadrant hemianopsia (Fig. 1a). Preoperative

vertebral angiograms demonstrated a small AVM in the right occipital lobe (Fig. 1b and 1c). Three tessa MR tractography revealed the OR ran just outside to the nidus (Fig. 1d). The nidus was resected through bilateral occipital craniotomy. During surgery, data sets of MPRAGE

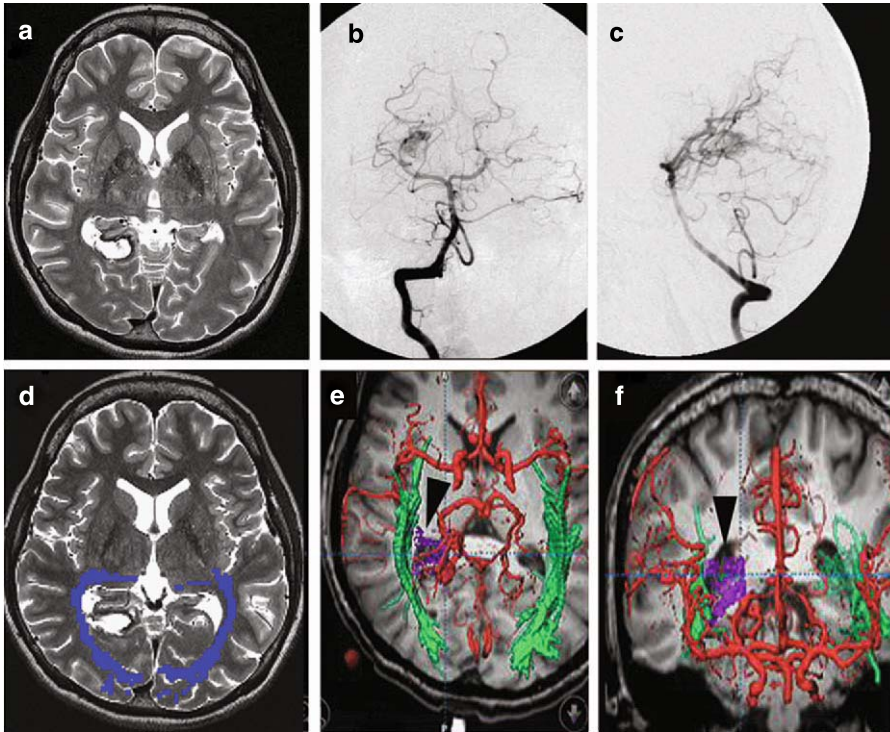


Fig. 1. This 21-year-old female presented with hemorrhage in the right occipital lobe and was admitted to our institution with slight quadrant hemianopsia (a). Preoperative vertebral angiograms demonstrated a small AVM in the right occipital lobe (b and c). Three tessa MR tractography revealed the OR ran just outside to the nidus (d, *blue bundle*: OR). At surgery, data sets from MPRAGE imaging, T2-weighted imaging, MRA, and MR tractography were applied to the neuronavigation system (Vector Vision, BrainLAB, Heimstetten, Germany or Stealth Station) to enable intraoperative monitoring (e and f, *green bundles*: OR, *arrowhead*: nidus)

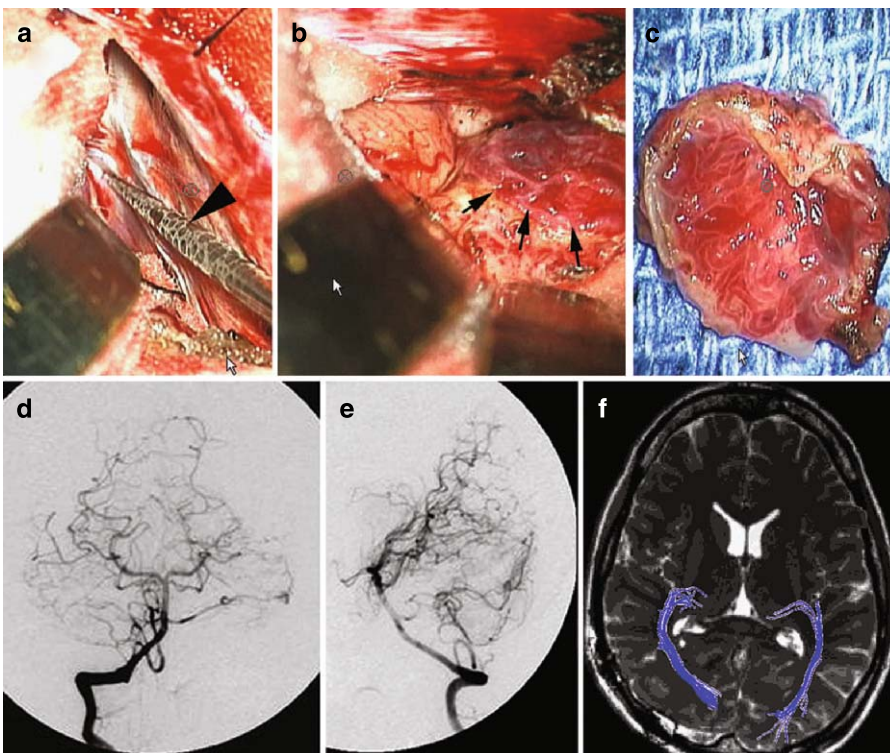


Fig. 2. Navigation informed the operator of the location of the nidus (a, *arrowhead*: probe of navigator) and preserved the OR during the dissection procedures of the nidus within the white matter (b, *arrows*: nidus). The nidus was resected en bloc (c). Postoperative vertebral angiograms revealed complete obliteration of the nidus (d and e) and postoperative MR tractography revealed preservation of the OR (f)

imaging, T2-weighted imaging, MRA, and MR tractography were applied to the neuronavigation system (Vector Vision, BrainLAB, Heimstetten, Germany or Stealth Station) and a fusion process was performed to match these image sets with each other to enable intraoperative monitoring (Fig. 1e). Through navigation, the operator could determine the location of the nidus (Fig. 2a) and preserve the OR during the dissection procedures of the nidus within the white matter (Fig. 2b). The nidus was resected en bloc (Fig. 2c). Postoperative vertebral angiograms demonstrated complete obliteration of the nidus (Fig. 2d and 2e) and postoperative MR tractography showed preservation of the OR (Fig. 2f). The patient was discharged with no deterioration of the visual symptoms.

Discussion

We previously reported that a dissection technique with minimal coagulation that preserves the intranidal venous drainage and the use of IoDSA are important for avoiding postoperative neurological deterioration [1, 5]. MR tractography by diffusion tensor imaging (DTI) has made possible visualization of the major neural tracts in the white matter both in physiological and pathological conditions [2, 3]. Sensorimotor fibers in patients with AVMs situated near sensorimotor cortices could be visualized with DTI [8]. We previously reported that both pre- and postoperative visual symptoms were roughly correlated with the state of the OR as revealed with 3 T MR tractography [3]. In our institution, 3-tesla MR units are routinely used for evaluation of the surgical risk of AVMs, as a 3-tesla unit can describe most neural tracts more clearly than does a 1.5-tesla unit [6].

In this study, pre- and postoperative motor functions also seemed to be roughly correlated to the state of the CST as determined from the 3 T MR tractography. This method might be practical for determining surgical indication of supratentorial AVMs. The limitations of MR tractography in the evaluation of neural tracts were described in our previous paper [3]. The integration of MR tractography is sometimes incorrect in cases of hematoma and in severely tortuous tracts, and the evaluation of tracts by inspective visualization is sometimes less reliable [3]. In addition, one patient in this series with a cerebellar AVM – in whom lobectomy of a cerebellar hemisphere was intentionally performed, sacrificing the spinocerebellar tracts through MCP or SCP – exhibited no deterioration of neurological functions because the cerebellum had high functional plasticity. Although further investigation is necessary, the effectiveness and limitations of 3 T MR tractography in

surgery for AVMs should be clarified. Moreover, the compiling of data on the surgical outcomes of such cases might also reveal whether MR tractography can indicate whether functions remain in the neural tissue within the nidus.

In this paper, we introduce one patient who underwent surgery performed with a 3 T MR tractography-guided neuronavigation system. The use of MR tractography-guided navigation and the evaluation of neural tracts by MR tractography with intraoperative MR units have already been reported in tumor [2, 4]. We believe that tractography-guided navigation seems useful for surgery on moderate or large AVMs and for surgery on small AVMs situated close to the major neural tracts.

Conclusions

In summary, notwithstanding the limitations of this method, MR tractography can be considered useful for confirming the integrity of deviated tracts, for localizing deviated tracts, and for evaluating surgical risk, especially in cases of non-hemorrhagic AVMs.

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Serial diffusion and perfusion MRI analysis of the perihemorrhagic zone in a rat ICH model

B. Orakcioglu¹, K. Becker², O. W. Sakowitz¹, A. Unterberg¹, P. D. Schellinger³

¹Department of Neurosurgery, University Hospital Heidelberg, Heidelberg, Germany

²Department of Neurology, University Hospital Heidelberg, Heidelberg, Germany

³Department of Neurology, University Hospital Erlangen, Erlangen, Germany

Summary

Objectives. Cerebral ischemia has been proposed as a contributing mechanism to secondary neuronal injury after intracranial hemorrhage (ICH). We aimed to examine perihemorrhagic changes with an animal experimental MRI study using a stroke-MRI protocol. In a subset of animals the feasibility and effects of stereotactic hematoma evacuation was investigated.

Methods. An MRI compatible setup for rats was established using a double injection model. ICH was stereotactically placed into the right basal ganglia of 49 Wistar rats. Coronal T2-WI, T2*-WI, DWI and PWI were generated with a 2.35 T animal MRI scanner at 3 time points. Clot volumes, normalized ADC and relative MTT values were analysed in 3 hematoma regions (periphery, outer rim, healthy ipsilateral tissue) in all sequences.

Results. There were no perihemorrhagic ADC decreases consistent with ischemic cytotoxic edema but a mild vasogenic edema surrounding the ICH could be observed. This improved partially with evacuation. Reduced perfusion was seen in the periphery and outer rim. This disappeared with lysis and evacuation of the clot.

Conclusion. No evidence for the existence of a perihemorrhagic ischemic area was found. But, reversible perfusion reduction in this model indicates that early evacuation may help reducing secondary neuronal changes.

Keywords: MRI; PWI; DWI; ischemia; rats; ICH.

Introduction

Many pathophysiological changes in the surrounding of ICH remain unclear. Experimental and clinical studies which highlight the question whether hematoma evacuation can positively influence metabolism and perfusion in order to limit secondary neuronal damage in healthy tissue are rare [1, 3, 6, 10, 16].

Recent studies proclaim less evidence for the existence of perihematomal ischemia in ICH both in experimental and clinical studies [4, 11, 14]. The STICH-investigators could not show a benefit of surgical hematoma evacuation in a large randomised trial [10]. However, this does not exclude the possibility of immediate perfusion benefit after minimal invasive hematoma evacuation. In order to evaluate MRI signal characteristics, the diagnostic accuracy of MRI for ICH as well as eventual perihemorrhagic diffusion and perfusion changes we conducted a serial study using a double injection rat model [6]. We also examined MRI characteristics (DWI/PWI) after rt-PA induced stereotactic hematoma evacuation within 3.5 h after onset.

Methods

Animal preparation

Animal protocols for these studies were approved by the institutional animal care and use committee. A standardized operative setup was followed as previously described [6]. In brief, after anaesthesia was applied all animals remained spontaneously breathing. Monitoring of physiological parameters was performed permanently. Twenty-seven rats were examined in the control group (gr1). The treatment group consisted of 22 animals (gr2).

Operative procedure

Arterial blood volumes of 15 μ l and 35 μ l each were injected sequentially. Neither the catheters nor the syringes were flushed with heparin. Thirty minutes after hematoma placement 12 μ l of rt-PA were injected through the intracerebral catheter into the core of the hematoma. Another 30 min later the lysed blood was aspirated. It was intended to reduce hematoma size by at least 30% [6].

In vivo magnetic resonance imaging (MRI) protocol

All animals were examined in a 2.35 T animal scanner (BRUKER Medizintechnik, Ettlingen, Germany). Planned imaging time points for

Correspondence: Berk Orakcioglu, M.D., Department of Neurosurgery, University Hospital Heidelberg, Im Neuenheimer Feld 400, Heidelberg, Germany. e-mail: berk.orakcioglu@med.uni-heidelberg.de

group 1 were 15 min (TP1), 60 min (TP2), and 210 min (TP3) and for group 2 15 min (TP1), 120 min (TP2) and 210 min (TP3) after intracerebral injection of 35 μ l arterial blood. TP2 at group 2 was delayed, as the evacuation procedure was undertaken between TP1 and TP2.

Three areas were manually outlined to define regions of interest (ROI's) [11], namely the periphery of the hematoma (ROI1), the outer rim of the hematoma (ROI2) and the healthy ipsilateral tissue (ROI3).

MR image-analysis

Hematoma volume (all sequences), apparent diffusion coefficient (ADC) and mean transit time (MTT) values were evaluated serially. Relative ADC maps (rADC) in DWI and relative mean transit times (rMTT) of the perfusion images were examined (Matlab 5.3.1). ADC maps and rMTT were measured in all ROI's. The ADC ratio between a ROI and its contralateral mirror ROI was calculated. As absolute MTT measures vary considerably in rats we calculated the relative MTT (rMTT) of the hematoma side against the healthy corresponding side.

Statistical analysis

For statistical analysis we used a standard software package (SPSS 13.0). All data were normally distributed. A multifactorial ANOVA was used to determine whether there was a significant difference in volume sizes, in ADC values between the hematoma side and corresponding contralateral brain tissue, and the MTT values of each side before and after evacuation of the hematoma. The 95% confidence interval was calculated for the mean difference of both parameters. The $p < 0.05$ level was used to assess statistical significance.

Results

A baseline MRI before ICH injection was performed at time point 1 after 15 min (TP1). Physiological variables were stable through the monitoring period of 3.5 h and are not displayed separately. All animals were sacrificed at the end of the experiment.

Mortality

Surgery and MRI at TP1 were successfully completed in all animals. In group one 4 animals (15%) died before performing the 2nd scan at TP2. In group 2, after evacuation of the hematoma, only 1 rat (4.5%) died before TP2 was reached. Eventually another 15 animals (44%) died in gr1 leaving 8 animals (30%) for a final scan at TP3. In gr2, 12 animals (59%) died prior to TP3 leaving 9 (41%) for the final scan. There was no significant difference in mortality between both groups ($p = 0.64$).

ADC maps in DWI

Mean rADC values for ROI 1 and 2 are shown in Table 1. Mean rADC values in ROI3 did not change over time.

Table 1. Serial mean relative ADC values in ROI 1 and 2 at different time points in both groups

		Evacuation with rt-PA	
		No	Yes
ROI1	TP1	1.09 (± 0.3)	1.09 (± 0.23)
ROI1	TP2	1.08 (± 0.23)	1.05 (± 0.23)*
ROI1	TP3	1.11 (± 0.23)	1.18 (± 0.1)
ROI2	TP1	1.08 (± 0.21)	1.07 (± 0.22)
ROI2	TP2	1.14 (± 0.24)	1.09 (± 0.23)
ROI2	TP3	1.15 (± 0.32)	1.15 (± 0.11)

* Indicates significant decrease of rADC after evacuation at TP2.

Statistical testing to compare changes of rADC within and between groups revealed significant differences in mean rADC between groups at TP2 in the periphery [gr1 = 1.08 ($n = 23$) vs. gr2 = 1.05 ($n = 21$); $p = 0.035$]. There was no ischemia of the outer rim at TP2, but in fact vasogenic edema. Hematoma evacuation did not reduce edema extent (gr1 = 1.14 vs. gr2 = 1.09; $p = 0.118$) at TP2.

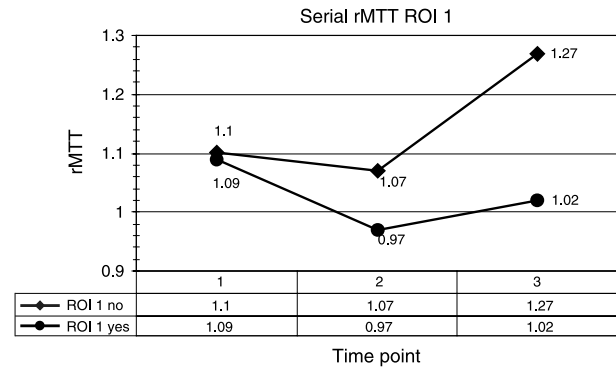


Fig. 1. Progressive relative MTT increase in the periphery (ROI1) of the hematoma; after evacuation of the hematoma a normalization of perfusion (rMTT) is achieved; at TP3 rMTT was normalized ($p = 0.061$)

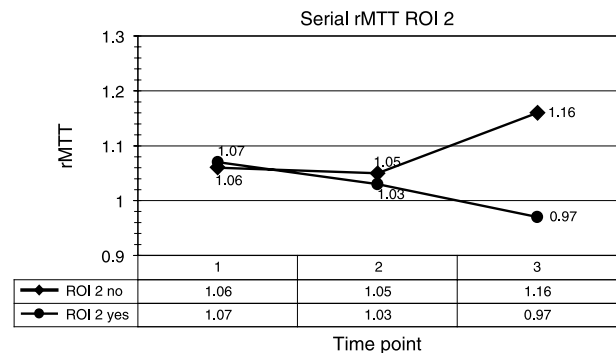


Fig. 2. Moderate relative MTT increase in the outer rim (ROI2); perfusion normalization after stereotactic evacuation

MTT analysis of PWI

Analysis showed that perfusion as indicated by an increased rMTT was reduced in ROI1 and ROI2 at all time points in gr1 and could be normalized in gr2 (Figs. 1 and 2). Relative MTT did not change in both groups in ROI3 at any time point. From TP1 to TP3 rMTT at ROI1 increased from 1.1 ± 0.13 to 1.27 ± 0.4 (Fig. 1). Within-group analysis revealed a trend for reduced perfusion (gr1 (ROI1): $F = 3.882$; $p = 0.068$). Between group analysis likewise showed a trend for a difference between gr1 and gr2 at ROI1 ($F = 3.910$; $p = 0.067$). Relative MTT at ROI2 increased from 1.06 ± 0.11 at TP1 to 1.16 ± 0.11 at TP3 in gr1 (Fig. 2). Within subject effects were not significant ($p = 0.703$). Gr2 showed decreasing rMTT values over time: 1.07 ± 0.14 at TP1 to 0.97 ± 0.1 at TP3. The within subjects effects in this group 2 were not significant ($p = 0.101$). Between group analysis revealed a trend in terms of treatment effect ($F = 4.01$; $p = 0.061$). In conclusion there appears to be a difference in rMTT in favour for gr2; this did not reach statistical significance.

Discussion

Cerebral ischemia has been proposed as a mechanism contributing to secondary neuronal injury after ICH, but the results of different groups are inconsistent and there is an ongoing debate about the existence of a “perihemorrhagic penumbra” [5, 6, 11, 13–15]. As the debate continues we tried to evaluate the MRI characteristics in a rat model before and after hematoma evacuation. Clinical routine MRI is progressing as a primary diagnostic tool in the setting of stroke [7]. Therefore, this study was performed on the basis of a MRI stroke protocol.

The double injection method has been introduced by Deinsberger *et al.* and has achieved acceptance as the most accurate method to mimic spontaneous ICH in rats [2, 6, 11]. Using this model some groups were able to find ischemic tissue or substantially reduced cerebral perfusion around the hematoma core. These findings were based on autoradiographic and histological findings. However, Deinsberger *et al.* found that autoradiographically measured perfusion reduction (CBF) could be significantly reduced by stereotactic evacuation of the hematoma with rt-PA [6]. Recently, Belayev *et al.* performed a combined study of perfusion monitoring by Laser-Doppler-Flow and neurobehavioral tests in mice after ICH. A significantly reduced perfusion (35–50%) was sustained over 90 min and went along with substantial neurological deficits in these animals [3]. The

authors also reported brain swelling without highlighting its etiology. Our findings go along well with these results.

In contradiction to recent experimental and clinical reports our results suggest that there is no relevant ischemic tissue in the immediate surrounding of the hematoma as measured by DWI [3, 6, 9]. We were able to show that perfusion is reduced on the affected side (5–27%) in comparison to the healthy side, but this reduction never reached significance along the time course of 3 h. Comparing the 27% decrease of perfusion in the perihemorrhagic zone PHZ with the range of perfusion decrease in ischemic brain tissue (up to 8-fold) we feel confident to argue that perfusion reduction indicated by MTT in this model is not sufficient to produce a consistent ischemic lesion. This assumption once again is underlined by our findings that rADC values were larger 1.05 at all times and in all ROI's. In a clinical study it was demonstrated that hypoperfusion in the PHZ did not lead to ischemia and it was argued whether these changes might indicate diaschisis [17].

Larger groups or minimal invasive neuromonitoring methods may be able to prove relevant perfusion changes with their impact to metabolic effects. Future studies of the PHZ in ICH should focus on a minimal invasive experimental setup in combination with serial MRI as demonstrated here (Laser-Doppler-Flow, pBrO₂, microdialysis) [8, 12]. The identification of yet unknown pathophysiological changes should help to define parameters that will lead to individual therapeutic decisions such as surgery or medical regimes.

There are limitations to our study. When high-field MRI as a diagnostic tool is used susceptibility artefacts may limit the analysis. Positive effects on functional recovery can not be proved as neurological assessments were not performed.

In conclusion we examined serial MRI characteristics of ICH in rats in the hyperacute phase. Perfusion measured by MTT is mildly reduced in the PHZ of ICH and does not result in ischemia as shown by DWI. Stereotactic evacuation of the hematoma may reverse perfusion reduction.

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Patient and aneurysm characteristics in multiple intracranial aneurysms

F. Baumann, N. Khan, Y. Yonekawa

Department of Neurosurgery, University Hospital Zurich, Zurich, Switzerland

Summary

Introduction. Multiple aneurysms occur in up to one-third of people with intracranial aneurysms. Of such patients, epidemiological data, clinical information, and aneurysm characteristics (of both unruptured and ruptured aneurysms in the same patients) were gathered in this retrospective review.

Patients and methods. Ninety-nine patients operated on for multiple intracranial aneurysms at the Department of Neurosurgery, University Hospital Zurich, Switzerland, between 1994 and 2003 were assessed, 90% with subarachnoid hemorrhage (SAH), 10% with incidental aneurysms.

Results. The female to male ratio was 3:1, median age was 53 years. SAH symptoms included acute headache (74%), decrease of consciousness (54%), nausea and vomiting (40%), epileptic seizure (11%). Neurological signs were meningism (40%), cranial nerve paresis (12%), none (28%). Chronic headache was the major complaint (40%) in patients with incidental aneurysms, 20% had paresis of extraocular muscles. History of smoking and hypertension was present in 47% and 35%. There were 265 aneurysms (median number per patient, 2; range, 2–8), 95% were small (≤ 10 mm), 4.5% large, 0.5% giant (>25 mm); 34% were ruptured, 66% unruptured (median size, 7 mm vs. 4 mm; $p < 0.0001$). Most aneurysms (27%) were on the middle cerebral artery bifurcation. Most ruptured aneurysms (18%) were on the anterior communicating artery and were 10 mm or smaller. Eighty-one percent of patients had (non-surgery related) SAH complications: cerebral vasospasm (44%), post-SAH hydrocephalus (36%), cerebral infarction (36%), intracerebral (25%) and intraventricular (21%) bleeding. Glasgow Outcome Scale score at 3 months was 4 or 5 in 73%.

Discussion. Ruptured aneurysms were significantly larger than unruptured ones. Although discussed controversially, most of our population's ruptured aneurysms were 10 mm or smaller in size. Considering this, our study may contribute to improve the management of patients with intracranial aneurysms.

Keywords: Aneurysm; characteristics; epidemiology; intracranial; multiple aneurysms; review; stroke.

Introduction

The high overall aneurysmal subarachnoid hemorrhage (SAH) mortality rate of about 40–50% as well the high

morbidity rate [4, 9, 43] are ascribed to the event of bleeding itself (i.e. initial bleeding and early rebleeding) on the one hand [31] and to concomitant cerebral ischemia (i.e. vasospasm of the large cerebral arteries) as well as increased intracranial pressure on the other [22, 32]. Due to improved management of patients, the case-fatality rate of aneurysmal SAH has decreased during the past decades [13] despite the constant incidence rates during this time [37].

Epidemiological data

Aneurysmal SAH, accounting for 5–10% of all strokes [43], has an incidence of 10 in 100,000 yearly in the general population [29], with an overall female preponderance of 1.5:1 [22, 35], which even increases in the later decades of life [24]. The prevalence of intracranial aneurysms in the general population lies around 2% [15, 20, 27]. Approximately one-fourth to one-third of these patients has more than one aneurysm [34, 39, 40]. Results differ whether this proportion of multiplicity is higher in patients with unruptured aneurysms [16, 38]. Most authors agree that multiple aneurysms tend to occur in somewhat older patients [1, 30].

Risk factors

Among the factors associated with a higher risk for subarachnoid hemorrhage are cigarette smoking, which appears to be most important (current smoking containing a higher risk than previous smoking), history of hypertension, and heavy daily caffeine intake (demonstrated in a Scandinavian population) [17, 18]. It has been found that the antiprotease activity of alpha 1-antitrypsin was markedly reduced in patients with SAH, and

Correspondence: PD Dr. med. Nadia Khan, Department of Neurosurgery, University Hospital Zurich, Frauenklinikstrasse 10, CH-8091 Zurich, Switzerland. e-mail: nadia.khan@usz.ch

the same finding is true in cigarette smokers [11]. The influence of alcohol is discussed controversially [5, 7, 12, 19, 23, 26]. Important risk factors for atherosclerosis, such as serum cholesterol concentrations and obesity, do not show significant impacts on the risk of SAH. The prevalence of hypertension in SAH patients is only slightly higher than in the general population, therefore as a risk factor for SAH, it seems to be less crucial than for other stroke subtypes, such as intracerebral bleeding [18]. Risk factors for multiple intracranial aneurysms are female gender and smoking at any time, both correlating positively with increasing number of aneurysms [38]. In contrast to single aneurysms, hypertension and family history of cerebrovascular disease were also found to be associated more with multiplicity [8].

Location and rupture

One recent large study [21] demonstrated that in patients with single aneurysms, the most common site in men was the anterior communicating artery (Acomm) with over 40% of aneurysms; in women, it was the internal carotid artery (ICA) with almost one third of aneurysms. As for multiple aneurysms, the most common site in women was still the ICA (for both ruptured [over one third of aneurysms] and unruptured aneurysms [almost 40% of aneurysms]); in men however, it was the middle cerebral artery (MCA) for both ruptured (one third of aneurysms) and unruptured aneurysms (one third of aneurysms). The rate of aneurysm rupture in the Acomm was significantly higher in both men and women than that in other locations.

Studies comparing aneurysm size and rupture rate have come to equivocal results. In 1998, the large International Study of Unruptured Intracranial Aneurysms Investigators reported that aneurysms less than 10 mm in diameter had an annual rupture rate of less than 0.05%, whereas aneurysms of 10 mm or greater size ruptured at 1% per year [16]. In contrast, previously conducted studies with smaller patient numbers concluded that aneurysms were prone to rupture at much smaller sizes [6, 33, 45]. A more recent study concluded that almost 90% of all ruptured aneurysms of the circle of Willis were less than 10 mm in diameter, this being true for anterior circulation as well as for posterior circulation locations [10]. Therefore, although large aneurysms (greater 10 mm in size) are more prone to rupture – possibly due to an increase of aneurysm size over time [36] –, smaller aneurysms do not primarily show benign behavior. When those aneurysms rupture, they in fact

tend to produce more extensive SAH as well as more extensive intraparenchymal hemorrhage [41].

Outcome

Despite excellent neurological recovery, most survivors of SAH never fully regain their pre-morbid status due to cognitive and psychosocial deficits, especially memory problems and attention disorders [42], which can lead to difficulty in social reintegration [2, 3, 14, 25].

Factors associated with poorer outcome after intervention are older age (especially over 50 years), location of the aneurysm on the posterior circulation, large aneurysm size (greater than 10 mm in diameter), worse clinical grade, history of hypertension, history of ischemic cerebrovascular disease, and multiplicity of aneurysms [28, 44].

Study goals

This study reports on patient and aneurysm characteristics in patients with multiple intracranial aneurysms. Thus, in patients with subarachnoid hemorrhage with a ruptured aneurysm and one or more unruptured aneurysms, data (such as location, size, and distribution) of these condition-wise very different aneurysms could be obtained from the same patient, and direct comparison of these aneurysm characteristics was possible.

Patients and methods

A retrospective study of all patients operated on for multiple aneurysms at the Department of Neurosurgery, University Hospital Zurich, Switzerland, between mid 1994 and mid 2003 was performed. Patients were identified using a computerized registry containing all operations of the department. The hospital's vascular neurosurgical unit serves the greater Zurich area with about two million people.

The eligible patients' medical records were analyzed, and information was collected on age, sex, risk factors (presumed absent if there was no documentation), family history of aneurysms, initiating event, initial symptoms, initial neurology, initial blood pressure, complications of SAH, and outcome. The neurological status of patients on admission was graded according to three grading scales: Glasgow Coma Scale (GCS), World Federation of Neurological Surgeons (WFNS) SAH grades, and Hunt & Hess (H&H) SAH classification. H&H grades 1, 2, and 3 were considered low-grade SAHs.

In cases of suspected SAH, the procedure according to the SAH protocol was to first perform CT scanning of the head with Fisher grade (F) assessment, followed by conventional two-dimensional four-vessel intra-arterial digital subtraction angiography (IA-DSA). Incidental aneurysm findings, defined as diagnosed during the investigation of phenomena unrelated to SAH, were followed by IA-DSA as well. The angiograms were reviewed for number, location, type (assumed saccular if not otherwise documented), condition, and size of aneurysms (when ever available).

Classification of aneurysm location was as follows: anterior cerebral circulation comprised of internal carotid artery (ICA), anterior cere-

bral artery (ACA), and middle cerebral artery (MCA). Posterior cerebral circulation comprised of vertebral artery (VA), basilar artery (BA), and posterior cerebral artery (PCA). ICA was further divided into cavernous segment (ICA-CS), ophthalmic artery (Ophtha), paraclinoid segment (ICA-PS), posterior communicating artery (Pcomm), anterior choroidal artery (Acho), and ICA bifurcation (ICA-bif). MCA was further divided into M1 segment (MCA-M1), MCA bifurcation (MCA-bif), and distal MCA (MCA-dist). ACA was further divided into A1 segment (ACA-A1), anterior communicating artery (Acomm), and distal ACA (ACA-dist). VA was further divided into VA trunc (VA-trunc), VA/posterior inferior cerebellar artery junction (VA-PICA), and distal PICA (PICA-dist). BA was further divided into BA/anterior inferior cerebellar artery junction (BA-AICA), BA/superior cerebellar artery junction (BA-SCA), BA trunk (BA-trunk), and BA tip (BA-tip). PCA was further divided into P1 segment (PCA-P1), P2 segment (PCA-P2), and distal PCA (PCA-dist).

The location of the ruptured aneurysm was determined by integration of the preoperative CT scan and IA-DSA as well as intraoperative findings. Criteria were distribution of subarachnoid blood and location of intracerebral bleeding (if applicable) on CT scans, irregular multilobular aneurysm appearance, associated vasospasm, and direct extravasation of contrast media on angiograms, as well as intraoperative location of clot at the aneurysm's rupture site.

The size of the aneurysm was determined by its greatest diameter measured in standard angiographic projections, taking into account the magnification, and the aneurysms were classified as small (10 mm and less), large (between 11 and 25 mm), and giant (more than 25 mm).

All patients were treated microneurosurgically. Postoperatively, all patients received at least one CT scan and at least one DSA. Follow-up was performed at least twice, at three months and at one year after SAH or elective treatment, respectively, at our clinic. It allowed clinical evaluation and neurological examination with assessment of the patient using the Glasgow Outcome Scale (GOS). GOS scores 5 and 4 were considered favorable outcomes.

Statistical methods

For binary variables, we used Fisher's exact test. Comparison of continuous variables was done using a Mann-Whitney test. Throughout the analysis, *p*-values smaller than 0.05 were considered significant. The StatView statistical software was used (version 5.0, 1998; SAS Institute Inc., Cary, NC, U.S.A.).

Results

Patient characteristics (Table 1)

Twenty percent of all patients operated on for aneurysms during the nine years' study time had multiple aneurysms (117 patients). Of these, 99 were assessable (85%). There were 74 women (75%) and 25 men (25%), thus the female to male ratio was 3:1. Median age at diagnosis was 53 years for all patients (range, 24–80 years), 53 years for women (range, 24–80 years), and 53 years for men (range, 33–67 years). There was no significant difference for age between the sexes. Eighty-nine patients (90%) presented with SAH (69 women, 20 men), and ten patients (10%) had incidental detection of their aneurysms (five women, five men).

Table 1. Patient characteristics (*n* = 99 patients)

Sex	
Female	74 (75)
Male	25 (25)
Female:male ratio	3:1
Age at diagnosis	
Median (all patients/women/men)	53/53/53
Range (all patients/women/men)	24–80/24–80/33–67
Diagnosis	
Subarachnoid hemorrhage	89 (90)
Incidental aneurysms	10 (10)
Risk factors (more than one per patient possible)	
Smoking (at any time)	47 (47)
History of hypertension	35 (35)
Alcohol abuse	10 (10)
Family history	4 (4)
Alpha 1-antitrypsin deficiency	1 (1)
Polycystic kidney disease	1 (1)
None	14 (14)
Not available	2 (2)

Figures in parentheses are percentages.

Initiating event and immediate symptoms (Table 2)

In thirteen patients (13%), an initiating event could be recognized. Ten patients (10%) presented with an SAH on exertion (two of them during sexual intercourse). Two patients (2%) had accidents with trauma to the head, which led to the diagnosis of incidental

Table 2. Initiating event and symptoms

Initiating event in SAH patients	13
Exertion	10 (10)
Trauma to the head	2 (2)
Anticoagulation	1 (1)
Symptoms of SAH (more than one per patient possible)	89 (100)
Acute headache	66 (74)
Decrease of state of consciousness (temporary or permanent)	48 (54)
Nausea/vomiting	36 (40)
Epileptic seizure	10 (11)
Loss of urine/loss of stool	5 (6)
Disorientation	3 (3)
Tinnitus	3 (3)
Muscular weakness	2 (2)
Vertigo	2 (2)
Neck pain	1 (1)
Double vision	1 (1)
Paresthesia	1 (1)
Photophobia	1 (1)
Hypoacusis	1 (1)
Symptoms of patients with incidentally detected aneurysms	10 (100)
Chronic headache	4 (40)
Unconsciousness	1 (10)
None	5 (50)

Figures in parentheses are percentages. SAH Subarachnoid hemorrhage.

aneurysms in one patient. One patient (1%) was on anticoagulation.

The majority of patients with SAH, 66 individuals (74%), presented with acute headache. In 48 patients (54%), there was a (temporary or permanent) decrease of the state of consciousness. Nausea and vomiting were present in 36 patients (40%). Ten patients (11%) experienced an epileptic seizure. Five patients (6%) lost urine or stool. Three patients each (3% each) were disoriented or had tinnitus. Two patients each (2% each) had muscular weakness or vertigo. One patient each (1% each) presented with neck pain, double vision, paresthesia, photophobia, or hypoacusis.

Table 3. Patient presentation on admission

Neurological signs (more than one per patient possible)	
SAH patients	89 (100)
Meningism	36 (40)
Paresis/paralysis	11 (12)
Positive Babinski sign	8 (9)
Pupillary dysfunction (anisocoria, missing light reaction)	7 (8)
Missing reflexes	4 (5)
Dysmetria	2 (2)
None	25 (28)
Patients with incidentally detected aneurysms	10 (100)
Paresis/paralysis (extraocular muscles)	2 (20)
Neuropsychological disorder	1 (10)
Ataxia	1 (10)
None	7 (70)
SAH scores	
Glasgow coma scale (excluding intubated patients)	69 (100)
Median	15
Range	4–15
Below 10	9 (13)
WFNS (excluding intubated patients)	69 (100)
Median	1
Range	1–5
Hunt&Hess	89 (100)
Median	2
Range	1–5
Low-grade	64 (72)
High-grade	25 (28)
Fisher	89 (100)
Median	3
Range	1–4
Blood pressure in mmHg	
Mean (systole/diastole)	145/81
Median (systole/diastole)	140/80
Range of systole	90–245
Range of diastole	40–140
In hypertensive patients	59 (60)
Mean	162/87
Median	160/90

Figures in parentheses are percentages. SAH Subarachnoid hemorrhage; WFNS World Federation of Neurological Surgeons.

Of the ten patients with incidentally detected aneurysms, chronic headache was a complaint in four patients (40%). One patient (10%) was found unconscious. Five patients (50%) did not have any symptoms.

Presentation on admission (Table 3)

The most common neurological sign of patients with SAH, present in 36 patients (40%), was meningism. Paresis or paralysis of a cranial nerve was found in 11 patients (12%). Eight patients (9%) had a positive Babinski sign, while four patients (5%) did not have any reflexes. Seven patients (8%) had pupillary dysfunction (including anisocoria and missing light reaction). Dysmetria was present in two patients (2%). Twenty-five patients (28%) did not have any neurological sign. Twenty of the SAH patients (22%) were intubated on admission to the emergency unit.

Of the patients with incidentally detected aneurysms, two (20%) had paresis of extraocular muscles, one patient each (10% each) had a neuropsychologic disorder or ataxia, and seven patients (70%) did not have any neurological sign.

Median GCS score (excluding the intubated 20 patients and the ten patients without SAH) was 15 (range, 4–15), and nine of those 69 patients (13%) had a GCS score below 10. Accordingly, median WFNS score (excluding the intubated 20 patients and the ten patients without SAH) was 1 (range, 1–5).

For all patients excluding the ten patients without SAH, median H&H score was 2 (range, 1–5), and median F score was 3 (range, 1–4). Sixty-four patients (72%) had a low-grade SAH, while 25 patients (28%) had a high-grade SAH.

Mean initial blood pressure was 145/81 mmHg (median, 140/80 mmHg). The systolic blood pressure ranged from 90 to 245 mmHg, while the diastolic blood pressure ranged from 40 to 140 mmHg. Of all admitted patients, fifty-nine (60%) were hypertensive, and their mean blood pressure was 162/87 mmHg (median, 160/90 mmHg).

Risk factors (Table 1)

Smoking at any time was the most prevalent risk factor for subarachnoid hemorrhage and multiple aneurysms in our population. Forty-seven patients (47%) were current or previous smokers. A history of hypertension was present in 35 patients (35%). Ten patients (10%) were alcohol abusers. Family history of aneurysms was pres-

ent in four patients (4%), of which two have lost relatives due to aneurysm rupture. One patient each (1% each) had alpha 1-antitrypsin deficiency or polycystic kidney disease. Fourteen patients (14%) did not have any risk factor. It was not possible to gain information on the risk factors in two patients (2%).

Aneurysms' characteristics

General characteristics (Table 4)

The 99 patients had a total number of 265 aneurysms, with a mean number of 2.7 aneurysms per patient (median, 2; range, 2–8); mean number in women, 2.8 (median, 2; range, 2–8); mean number in men, 2.4 (median, 2; range, 2–4). There was no statistically significant difference between the number of aneurysms and gender, patient age, systolic and diastolic blood pressure on admission, GCS score, H&H score, Fisher score, and WFNS score.

Of the 265 aneurysms, 240 (91%) were assessable for size and shape (in addition to condition). The mean diameter of these aneurysms was 5.4 mm (median, 5 mm; range 1–25 mm). Two hundred and twenty-eight aneurysms (95%) were small, 11 (5%) were large, and one (0.5%) was a giant aneurysm. Two hundred and fifty-two

aneurysms (95%) were saccular and 13 (5%) were fusiform in shape.

Eighty-nine aneurysms (34%) were ruptured (mean size, 7.5 mm; median, 7 mm; range, 2–25 mm), and 176 aneurysms (66%) were unruptured (mean size, 4.2 mm; median, 4 mm; range, 1–18 mm). The difference in size between the ruptured and the unruptured aneurysms was statistically highly significant ($p < 0.0001$).

Location, distribution, size, condition (Table 5 and Figs. 1, 2)

Aneurysms were over 12 times more likely to appear on the anterior cerebral circulation (245 vs. 20 aneurysms). Twenty-seven percent of all aneurysms were located on MCA-bif, which was the highest percentage, 18% were on Acomm, 11% on Pcomm, and 6.5% on MCA-M1. Most ruptured aneurysms were located on Acomm (35% of all ruptured aneurysms), followed by MCA-bif (22%), Pcomm (13%), and MCA-M1 (7%). Sixty-five percent of all Acomm aneurysms, 40% of all Pcomm aneurysms, and 28% of all MCA-bif aneurysms were ruptured (only locations with more than 10 ruptured aneurysms considered).

There were statistically significant differences in size for ruptured aneurysms compared to their unruptured counterparts (ruptured aneurysms larger) in the following locations: anterior cerebral circulation ($p < 0.0001$), MCA ($p < 0.0001$), MCA-bif ($p = 0.0002$), ICA ($p = 0.0068$), Pcomm ($p = 0.0039$), ACA ($p = 0.0004$), and Acomm ($p = 0.0015$).

Complications (Table 6)

A total number of 72 patients (81%) had complications of their SAH (excluding complications associated directly to operative intervention). Thirty-nine patients (44%) had cerebral vasospasm. Post-SAH hydrocephalus was seen in 32 patients (36%). Thirty-two patients (36%) had a cerebral infarction. Intracerebral or intraventricular bleeding occurred in 22 (25%) and in 19 patients (21%), respectively. Seventeen patients (19%) showed neuropsychologic deficits. Elevated intracranial pressure due to cerebral edema with possible consecutive herniation was seen in 11 patients (12%). Six patients (7%) had an epileptic seizure during the course of their disease. Five patients (6%) developed occlusive hydrocephalus.

Outcome

For SAH patients, median GOS score at three months was 5 (range, 1–5); 65 patients (73%) had a favorable

Table 4. *General aneurysm characteristics*

Total number of aneurysms	265 (100)
Number per patient	
Mean (all patients/women/men)	2.7/2.8/2.4
Median (all patients/women/men)	2/2/2
Range (all patients/women/men)	2–8/2–8/2–4
Size (assessable) in mm	240 (100)
Mean diameter	5.4
Median diameter	5
Diameter range	1–25
Small (≤ 10)	228 (95)
Large ($>10 \leq 25$)	11 (4.5)
Giant (>25)	1 (0.5)
Shape (assessable)	265 (100)
Saccular	252 (95)
Fusiform	13 (5)
Condition (assessable)	265 (100)
Ruptured	89 (34)
Mean size in mm	7.5
Median size in mm	7*
Range in mm	2–25
Unruptured	176 (66)
Mean size in mm	4.2
Median size in mm	4*
Range in mm	1–18

Figures in parentheses are percentages. * $p < 0.0001$.

Table 5. Location, side-specific distribution (total number and percentage), and size in mm (median/range) of all aneurysms, unruptured aneurysms, and ruptured aneurysms

	All	Unruptured	Ruptured
Anterior circulation	245 (92)/4/1–25	159 (65)/4/1–18	86 (35)/7/2–25
Right side (excluding Acomm)	109 (44)/5/1–25	77 (48)/4/1–18	32 (37)/7/3–25
Left side (excluding Acomm)	88 (36)/4/1–15	65 (41)/3.5/1–9	23 (27)/7/4–15
Posterior circulation	20 (8)/6/1–9	17 (85)/4.5/1–9	3 (15)/6/6–7
Right side (excluding BA-tip)	8 (40)/5/2–7	5 (30)/3/2–4	3 (100)/6/6–7
Left side (excluding BA-tip)	6 (30)/6/4–9	6 (35)/6/4–9	0
MCA	98 (37.5)/4/1–25	71 (72)/4/1–10	27 (28)/8/3–25
Right side	63 (64)/4/1–25	44 (62)/4/1–10	19 (70)/7/3–25
Left side	35 (36)/4/1–15	27 (38)/3.5/1–9	8 (30)/10/5–15
MCA-M1	17 (6.5)/6/1–15	11 (65)/3/1–10	6 (35)/9/7–15
Right side	12 (71)/5/1–10	8 (73)/3/1–10	4 (67)/8.5/7–10
Left side	5 (29)/7/2–15	3 (27)/3/2–7	2 (33)/11.5/8–15
MCA-bif	71 (27)/5/1–25	51 (72)/4/1–10	20 (28)/7.5/3–25
Right side	43 (61)/4/1–25	29 (57)/4/1–10	14 (70)/7/3–25
Left side	28 (39)/4/1–12	22 (43)/4/1–9	6 (30)/10/5–12
MCA-dist	10 (4)/3/1–15	9 (90)/3/1–5	1 (10)/15/–
Right side	8 (80)/3/1–15	7 (78)/3/1–3	1 (100)/15/–
Left side	2 (20)/?/?	2 (22)/?/?	0
ICA	84 (30.5)/4/1–18	65 (77)/4/1–18	19 (23)/6/4–15
Right side	40 (48)/5/1–18	30 (46)/5/1–18	10 (53)/6.5/4–8
Left side	44 (52)/4/1–15	35 (54)/3/1–7	9 (47)/6/4–15
ICA-CS	14 (5)/5/2–18	12 (86)/4/2–18	2 (14)/11.5/8–15
Right side	9 (64)/5.5/2–18	8 (67)/5/2–18	1 (50)/8/–
Left side	5 (36)/4/3–15	4 (33)/4/3–4	1 (50)/15/–
Ophtha	11 (4)/4.5/1–15	10 (91)/4/1–15	1 (9)/15/–
Right side	5 (45)/3/1–15	5 (50)/3/1–15	1 (100)/15/–
Left side	6 (55)/5/3–15	5 (50)/4.5/3–6	0
ICA-PS	6 (2)/4/1–12	4 (67)/2/1–4	2 (33)/8/4–12
Right side	1 (17)/4/–	0	1 (50)/4/–
Left side	5 (83)/3/1–12	4 (100)/2/1–4	1 (50)/12/–
Pcomm	30 (11)/5/2–10	18 (60)/4/2–6	12 (40)/6/4–10
Right side	18 (60)/5.5/2–8	11 (61)/4/2–6	7 (58)/7/5–8
Left side	12 (40)/4/2–10	7 (39)/3/2–4	5 (42)/5/4–10
Acho	11 (4)/4/2–7	9 (82)/4/2–7	2 (18)/5/4–6
Right side	4 (36)/4/4–5	3 (33)/4.5/4–5	1 (50)/4/–
Left side	7 (64)/4.5/2–7	6 (67)/4/2–7	1 (50)/6/–
ICA-bif	12 (4.5)/3/2–8	12 (100)/3/2–8	0
Right side	3 (25)/5/4–8	3 (25)/5/4–8	–
Left side	9 (75)/3/2–5	9 (75)/3/2–5	–
ACA	63 (24)/5/2–20	23 (37)/4/2–8	40 (63)/6/2–20
Right side (excluding Acomm)	6 (10)/4.5/3–6	3 (13)/4/3–4	3 (8)/6/5–6
Left side (excluding Acomm)	9 (14)/5/4–8	3 (13)/5/–	6 (15)/5/4–8
ACA-A1	2 (1)/6.5/5–8	0	2 (100)/6.5/5–8
Right side	1 (50)/5/–	–	1 (50)/5/–
Left side	1 (50)/8/–	–	1 (50)/8/–
Acomm	48 (18)/5/2–20	17 (35)/4/2–8	31 (65)/6/2–20
ACA-dist	13 (5)/4/3–7	6 (46)/4/3–5	7 (54)/6/4–7
Right side	5 (38)/4/3–6	3 (50)/4/3–4	2 (29)/6/–
Left side	8 (62)/4.5/4–7	3 (50)/5/–	5 (71)/4/4–7
PCA	6 (2.5)/4/2–6	5 (83)/3.5/2–6	1 (17)/6/–
Right side	4 (67)/3/2–6	3 (60)/4/3–4	1 (100)/6/–
Left side	2 (33)/5/4–6	2 (40)/5/–	0
PCA-P1	3 (1.5)/2.5/2–3	3 (100)/2.5/2–3	0
Right side	3 (100)/2.5/2–3	3 (100)/2.5/2–3	–
Left side	0	0	–
PCA-P2	3 (1)/6/4–6	2 (67)/5/4–6	1 (33)/6/–
Right side	1 (33)/6/–	0	1 (100)/6/–
Left side	2 (67)/5/4–6	2 (100)/5/4–6	0

(continued)

Table 5 (continued)

	All	Unruptured	Ruptured
BA	11 (4)/5.5/1.7	10 (91)/5.5/1-7	1 (9)/6/-
Right side (excluding BA-tip)	3 (27)/5/4-6	2 (20)/4/-	1 (100)/6/-
Left side (excluding BA-tip)	2 (18)/?/?	2 (20)/?/?	0
BA-tip	6 (2)/5.5/1-7	6 (100)/5.5/1-7	0
BA-SCA	5 (2)/5/4-6	4 (80)/4/-	1 (20)/6/-
Right side	3 (60)/5/4-6	2 (50)/4/-	1 (100)/6/-
Left side	2 (40)/?/?	2 (50)/?/?	0
VA	3 (1.5)/8/7-9	2 (67)/9/-	1 (33)/7/-
Right side	1 (33)/7/-	0	1 (100)/7/-
Left side	2 (67)/9/-	2 (100)/9/-	0
VA-PICA	2 (1)/8/7-9	1 (50)/9/-	1 (50)/7/-
Right side	1 (50)/7/-	0	1 (100)/7/-
Left side	1 (50)/9/-	1 (100)/9/-	0
VA-trunk	1 (0.5)/?/-	1 (100)/?/-	0
Right side	0	0	-
Left side	1 (100)/?/-	1 (100)/?/-	-

Figures in parentheses are percentages (location on main vessels is in relation to total aneurysm number in the first column). *Acomm* Anterior communicating artery; *BA-tip* tip of basilar artery; *MCA-M1* M1-segment of middle cerebral artery; *MCA-bif* middle cerebral artery bifurcation; *MCA-dist* distal middle cerebral artery; *ICA* internal carotid artery; *ICA-CS* cavernous segment of internal carotid artery; *Ophtha* ophthalmic artery; *ICA-PS* paraclinoid segment of internal carotid artery; *Pcomm* posterior communicating artery; *Acho* anterior choroidal artery; *ICA-bif* internal carotid artery bifurcation; *ACA* anterior cerebral artery; *ACA-A1* A1-segment of anterior cerebral artery; *ACA-A2* A2-segment of anterior cerebral artery; *ACA-dist* distal anterior cerebral artery; *PCA* posterior cerebral artery; *PCA-P1* P1-segment of posterior cerebral artery; *PCA-P2* P2-segment of posterior cerebral artery; *BA* basilar artery; *BA-SCA* basilar artery/superior cerebellar artery junction; *VA* vertebral artery; *VA-PICA* vertebral artery/posterior inferior cerebellar artery junction; *VA-trunk* trunk of vertebral artery.

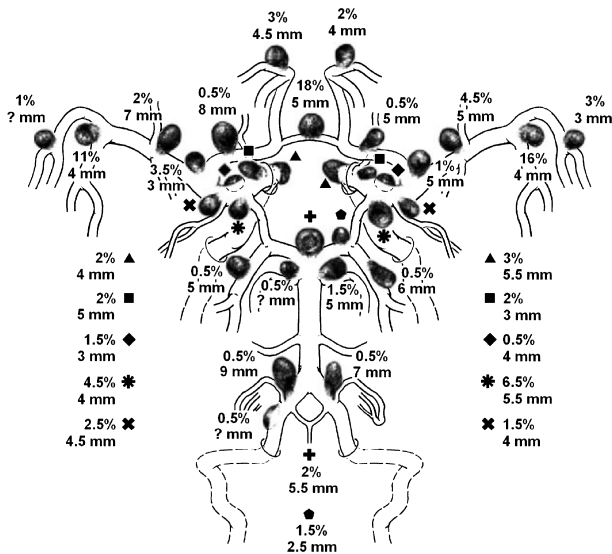


Fig. 1. Location, distribution (side-specific), and median size of all aneurysms. View from above

GOS, and 24 patients (27%) did not, four of which had died (4%). Patients with favorable GOS had significantly ($p = 0.0451$) smaller ruptured aneurysms (mean diameter, 6.8 mm; median, 6 mm; range 3–20 mm) than patients with unfavorable GOS (mean diameter, 9.6 mm; median, 8 mm; range 2–25 mm). At one year after intervention, follow-up information could not be obtained for 24 patients (24%). Median GOS score was still 5 (range,

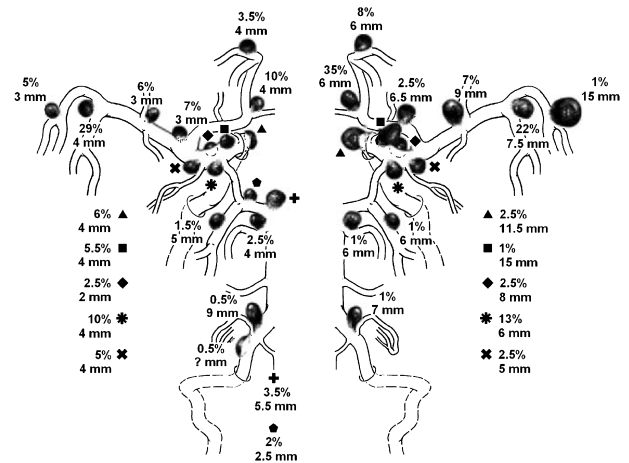


Fig. 2. Location, distribution, and median size of unruptured aneurysms (left) and ruptured aneurysms (right)

Table 6. Non-surgery related SAH complications ($n = 89$, more than one per patient possible)

Cerebral vasospasm	39 (44)
Post-SAH hydrocephalus	32 (36)
Cerebral infarction	32 (36)
Intracerebral bleeding	22 (25)
Intraventricular bleeding	19 (21)
Neuropsychologic deficits	17 (19)
Elevated intracranial pressure/cerebral edema/herniation	11 (12)
Epileptic seizure	6 (7)
Occlusive hydrocephalus	5 (6)

Figures in parentheses are percentages. *SAH* Subarachnoid hemorrhage.

1–5), 50 patients (57%) had a favorable GOS. There were significant statistical associations between GOS score at three months and initial GCS score ($p = 0.0003$), WFNS score ($p < 0.007$), H&H score ($p = 0.006$), and F grading ($p < 0.05$). There was no statistical association between number of aneurysms and worse outcome.

Discussion

About 2% of the general population have intracranial aneurysms [15, 20, 27], and about one-fourth to one-third thereof more than one [34, 39, 40]. Risk factors for such multiplicity are female gender, smoking at any time, hypertension, and family history of cerebrovascular disease [8, 38]. There is an ongoing debate whether there is a critical size – which has been set at 10 mm by some investigators [16] – at which aneurysms rupture [6, 10, 33, 45]. The annual rupture rate for patients with multiple aneurysms was found to be about 7% and thus is three to five times higher than for single aneurysm patients [46]. Worse initial clinical grade, larger size of the ruptured aneurysm, and greater number of aneurysms correlate all with poorer patient outcome [28, 44].

A review of medical records and imaging material of patients operated on for multiple aneurysms at the University Hospital Zurich, Switzerland, over nine years was conducted. Focus was set on epidemiological and clinical data and on radiological evaluation of the aneurysms. Characterisation of both ruptured and unruptured aneurysms was thus possible in the same patients. Follow-up was at three months and at one year after neurosurgical intervention.

Ninety-nine patients with a total of 265 aneurysms (median, 2 aneurysms per patient) were included in this study. There were three times more women than men, and median age for both sexes was 53 years. Ninety percent of patients presented with acute SAH, while the rest had incidentally detected aneurysms.

The most prevalent symptom was acute headache (74%), followed by alteration of consciousness (54%), and nausea and vomiting (40%). One-fourth of patients did not have any symptom. The number one complaint of incidental aneurysm patients was chronic headache (40%). On admission of SAH patients, meningism was the most common neurological sign, present in 40%. Paresis or paralysis of a cranial nerve was found in 12%. A little over one-fourth did not have any neurological sign.

Hypertension was noted in 60% on admission, 35% had a history of hypertension. Almost half of the study population was smoking at one time.

Excluding the intubated patients and the patients without SAH, median GCS score was 15 and median WFNS score was 1, respectively. The SAH patients had a median H&H score of 2 and median F grade of 3.

Median diameter of all aneurysms was 5 mm, 95% of aneurysms were ten millimeters or smaller in size, and 95% of aneurysms were saccular in shape. The median size of the ruptured aneurysm in the 89 patients with SAH was 7 mm. The unruptured aneurysms had a median size of just 4 mm. Ruptured aneurysms were significantly larger than unruptured ones, be it the cause of rupture or its consequence – a question that cannot be answered here. So if the larger aneurysms were the origin of subarachnoid hemorrhage, then the study could aid in decision making as to which aneurysm or aneurysms should be approached in patients with multiple incidental intracranial aneurysms – for prevention of morbidity and mortality from rupture. We are not aware of any other work in the English literature comparing ruptured and unruptured aneurysms in the same patient in this way. The great majority of ruptured aneurysms were of sizes smaller than 10 mm in diameter. In addition, this study emphasizes thus the importance of securing small unruptured aneurysms – especially if located at sites with higher rupture incidence – as these aneurysms do not show benign behavior per se. It may also contribute to clarify ongoing controversy in treatment strategy for such patients.

The most prevalent location was MCA-bif with 27% of all aneurysms, followed by Acomm with 18%, Pcomm with 11%, and MCA-M1 with 6.5%. The most prevalent location for rupture was Acomm (35% of all ruptured aneurysms), followed by MCA-bif (22%), Pcomm (13%), and MCA-M1 (7%). Rupture rates were 65% for Acomm aneurysms, 40% for Pcomm aneurysms, and 28% for MCA-bif aneurysms.

SAH complications included cerebral vasospasm (44%), post-SAH hydrocephalus (36%), intraventricular bleeding and cerebrovascular insult (22% each), and neuropsychologic deficits (19%). Nevertheless, almost three-fourths of patients had a favorable GOS at three months, and significant predictors for this were smaller aneurysms size (median of 6 mm vs. 8 mm), higher initial GCS score and lower initial WFNS score, H&H score, and F grading. We were not able to demonstrate that patients with higher number of aneurysms had a more serious course of SAH.

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Thalamic cavernous angioma: paraculminar supracerebellar infratentorial transtentorial approach for the safe and complete surgical removal

N. Otani*, M. Fujioka*, B. Oracioglu, C. Muroi, N. Khan, P. Roth, Y. Yonekawa

Department of Neurosurgery, Zurich University Hospital, Zurich, Switzerland

Summary

Background. The thalamic cavernous angioma (CA) represents a neurosurgical challenge because of the critical neurologic functions of the thalamus and its surrounding structures and of their deep location inside the brain. Although the natural history of the thalamic CA remains undefined, several studies suggest the poor outcome of those patients especially if the symptomatic thalamic CA is treated conservatively. We describe the advantage of the paraculminar supracerebellar approach to the lesions in the brainstem.

Objective. We studied the usefulness and the safety of the paraculminar supracerebellar infratentorial transtentorial approach for the patients with thalamic CA.

Methods. One hundred and ninety two consecutive patients with CA were treated at the Department of Neurosurgery in the Zurich University Hospital between 1993 and 2003. Among these patients, we analyzed six patients (four female, mean age 43) with thalamic CA who underwent surgical removal with the paraculminar supracerebellar transtentorial approach. We retrospectively reviewed their medical charts, the neuroradiological images, and the operative notes/video records.

Results. Four patients of the six presented with thalamic hemorrhage. CA existed in the left thalamus in four patients and in the right in two. Preoperative symptoms included sensorimotor disturbance (three cases), double vision (three cases), Parinaud syndrome (one case), and thalamic pain (one case). All patients had the thalamic CA completely removed without any postoperative deterioration.

Conclusions. This study suggests that for the removal of thalamic cavernous angioma the paraculminar supracerebellar infratentorial transtentorial approach provides the spacious surgical field with reduced risks of damaging and sacrificing surrounding vascular and neuronal system. This approach could proffer one of the best and safest surgical routes for the radical removal of thalamic cavernous angioma.

Keywords: Cavernous angioma; surgical approach; infratentorial supracerebellar approach; surgical outcome; cerebrovascular disease.

Introduction

Cavernous angiomas (CA) develop in 0.1–4.0% of the general population [5]. CA seem to be relatively benign lesions. However, CA is potentially hazardous due to its nature of repeated occult bleeding, progressive growth, and recurrence/regrowth [3, 19, 21, 23, 25]. CA commonly arises in the cerebral subcortex, the cerebral white matter, and the basal ganglia [6], however, rarely in the thalamus [2, 18, 22].

Thalamic CA represents a neurosurgical challenge because of the critical neurological functions of the thalamus and its surrounding structures that could be exposed only in a restricted surgical field. Recently, however, several reports have suggested a feasibility of surgical treatment of thalamic CA [11, 28].

The natural history of thalamic CA remains undefined. An early study [9] reported a subsequent annual hemorrhage rate of 2.9%. This study points out that the outcomes of patients are poor if the symptomatic thalamic CA is treated conservatively. In addition, the rate of recurrence/rebleeding of the lesions is relatively high if the CAs are not totally removed [17]. Therefore, thalamic CAs, especially if symptomatic, should be removed totally.

We have reported the safety and the usefulness of the supracerebellar approaches to the lesions localized in the tectum, the cerebellar peduncles and/or the posterior parahippocampus [7, 12, 29]. The paraculminar supracerebellar approach could be used for the lesions localized in the pineal region, the thalamus, and the posterior third ventricle. The paraculminar approach provides excellent operative exposure without need to sacrifice the bridging veins or the precentral cerebellar vein, and to retract the culmen downward.

* These authors equally contributed to this work.

Correspondence: Prof. Dr. med. Yasuhiro Yonekawa, Neurochirurgie FMH, Haldenbachstrasse 18, CH-8091 Zurich, Switzerland.
e-mail: yasuhiro.yonekawa@usz.ch

We herein present the feasibility and the efficacy of the paraculminar supracerebellar infratentorial transtentorial approach to the thalamic CA. We suggest that this paraculminar supracerebellar transtentorial route is one of the best surgical approaches to the thalamic CA to preserve intact neuronal structures and to achieve a spacious and excellent operative field.

Subjects and methods

One-hundred-and-ninety-two consecutive patients with CA were treated at the Zurich University Hospital Neurosurgical Department between 1993 and 2003. Of these 192 patients, seven had thalamic CA. Six patients out of seven underwent surgical removal. The remaining one patient was not operated on because of the high surgical risks as opposed to the benefits expected. One patient (Case 1) of the six underwent surgical removal twice in eight years because of CA regrowth even after its neuroradiological total resection in the first operation. Therefore, we analyzed the seven surgical sessions of the paraculminar supracerebellar transtentorial approach for the removal of thalamic CA in the six patients.

The clinical features of the six patients with thalamic CA are shown in Table 1. The patients' age ranged from 20 to 60 years old with a mean of 43. There were two male patients (33%) and four females (67%). Four CAs (67%) were situated in the left thalamus and two (33%) in the right. The two patients (33%) out of six had additional CAs in the superior

colliculus. The size of the thalamic CA ranged from 1.5 to 5.0 cm (mean, 2.5 cm in the maximum length). The four patients (67%) presented with cerebral hemorrhage. The preoperative symptoms included sensorimotor disturbance observed in three patients, diplopia in three, parinaud syndrome in two, Horner syndrome in one, thalamic pain syndrome in one, and dysarthria in one. Those patients with thalamic CA were retrospectively analyzed for their clinical profiles and the outcomes. The feasibility and utility of the paraculminar supracerebellar infratentorial transtentorial approach was evaluated in these patients.

Operative technique

The paraculminar supracerebellar transtentorial approach is performed in the following manner. Patients are placed in the sitting position. The skin is incised vertically in the occipital midline. The occipital squama is dissected and the burr holes are placed. The bone flap is sawed out. A burr hole in the midline over the superior sagittal sinus, just superior to the confluens sinus, is crucial to obtain the sufficient exposure. The opening of the foramen magnum is not necessary. However, the upper portion of the cisterna magna should be exposed and opened for continuous drainage of cerebrospinal fluid (CSF). This procedure could yield an additional space between the superior surface of the cerebellum and the tentorium. The dural incision is made in V-shape, and the dura mater is reflected upward over the bilateral transverse sinuses. To expose the posterior portion of the thalamus, the microsurgical approach is advanced in the paraculminar space between the cerebellar hemisphere and the tentorium with or without dividing the bridging veins that run from the cerebellar hemisphere into the tentorium and/or the transverse sinus. The paraculminar approach could be performed either unilaterally

Table 1. *Clinical characteristics in 6 patients*

Patient no.	Age/sex	Site	Location	Size (cm)	Hemorrhage	IVH	Preoperative symptom
1	20/F	L	THA (pulvinar)	2.0	+	-	sensorimotor disturbance, Horner syndrome, double vision
		L	THA (pulvinar)	2.5	+	-	sensorimotor disturbance, vertical gaze paresis
2	56/M	R	SC and THA, partially	2.0	+	+	Parinaud syndrome, double vision, vertigo
3	43/F	L	THA	1.5	-	-	double vision, gait ataxia, hemiparesis right, dysarthria
4	54/M	L	THA	3.0	-	-	sensorimotor disturbance, thalamic pain syndrome
5	60/F	R	THA	2.5	+	+	sensorimotor disturbance, Parinaud syndrome
6	56/F	L	THA and SC, partially	5.0	+	+	oculomotor paresis

THA Thalamus; SC superior colliculus; REC recurrence.

Table 2. *Surgical outcome for thalamic cavernoma in 6 patients*

Patient no.	Surgical approach	Tentorial incision	Extension of removal	Postoperative symptom	Complications	Operative time (min) (approach to removal)	Surgical outcome	Follow-up period
1	PTSA	-	total	unchanged	-	83	REC	7Y
1 (REC)	PTSA	+	total	unchanged	-	28	GR	3M
2	PTSA	+	total	improved	homonymous hemianopia left (transient)	57	independent	NA
3	PTSA	-	total	improved	vertical gaze paresis (transient)	31	independent	NA
4	PTSA	+	total	unchanged	-	34	GR	NA
5	PTSA	NA	total	improved	-	NA	independent	NA
6	PTSA	+	total	improved	-	48	SD	2Y

PTSA Paraculminar transtentorial supracerebellar approach; REC recurrence; GR good recovery; SD severe disability; NA not available; Y years; M month.

or bilaterally if needed, for lesions localized in the thalamus. To extend the operative field laterally and superiorly, the tentorium is cut and opened from the infratentorial side. This paraculminar approach allows excellent operative exposure of the thalamic lesions without sacrificing the bridging veins or the precentral cerebellar vein, or without retracting the culmen downward.

Results

The surgical results and the postoperative clinical course are shown in Table 2. In all patients successful and total removal of the thalamic CA was achieved. No

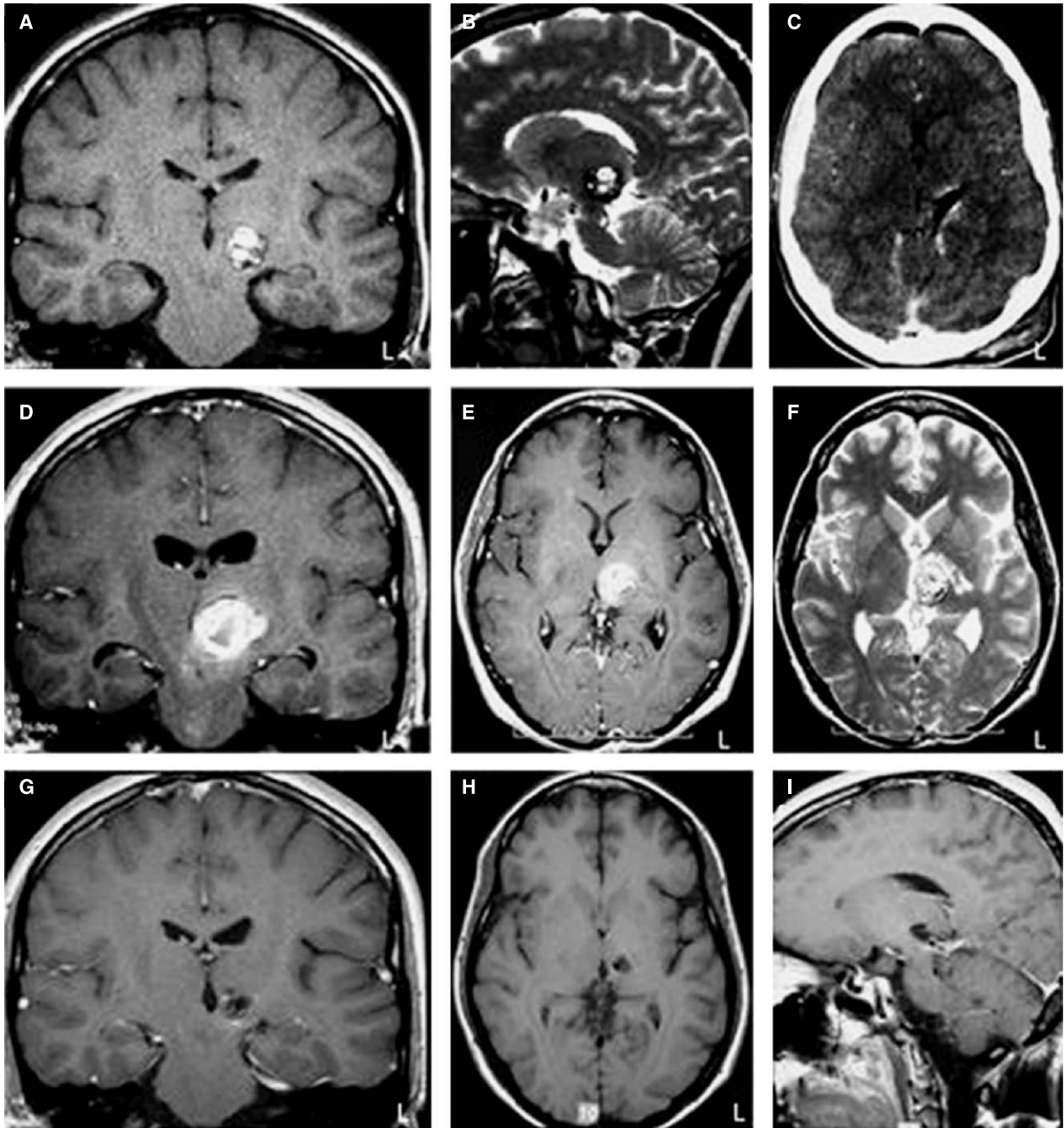


Fig. 1. *Case 1* Coronal T1-weighted (A) and sagittal T2-weighted (B) MR images of a 20-year-old woman, who presented with right sensorimotor disturbance and double vision, showing a cavernous malformation of 2 cm in size in the left thalamus (pulvinar). The CT scan obtained 2 days after surgery (C) showing the total removal of the thalamic CA. The follow-up MRI showing the recurrence of thalamic CA seven years later (D–F: T1, T1 and T2 weighted images). The postoperative MRIs showing the total removal of the thalamic CA (G–I: coronal, axial, and sagittal T1WIs)

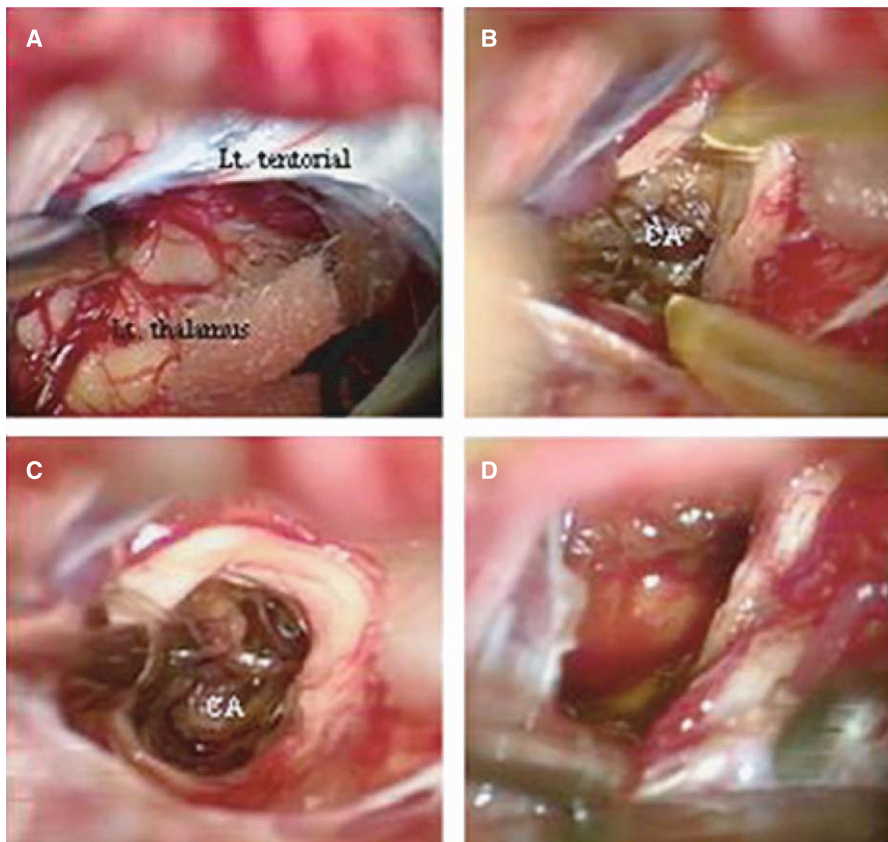


Fig. 2. *Case 1* Intraoperative microsurgical photographs showing the surgical fields of the paraculinar supracerebellar transtentorial approach to the left thalamic cavernoma. Having applied the cerebellar tentorial incision, the pulvinar came sufficiently into view (A). A corticotomy was performed and the thalamic CA was exposed (B). The cleavage plane between the lesion and the brain was clear and was incised and dissected meticulously (C). Finally, the CA was totally removed (D)

patients had neurological and systemic deteriorations after surgery. The preexisting neurological deficits subsequently improved in four surgical sessions out of seven (57%) and remained unchanged in three (43%). One patient (Case 1) had suffered re-growth of the thalamic CA seven years after the first surgery. No other patients had recurrence during the follow-up period. One patient (Case 2) had a transient homonymous hemianopia and another (Case 3) transient vertical gaze palsy after the removal of the CA. The paraculinar approach produced no permanent complications. The microsurgical time required for the removal of the thalamic cavernoma ranged from 31 to 83 min (mean 47 min) in this study.

Case presentation

Case 1

A 20-year-old female with thalamic CA suffered from a sensorimotor disturbance on the right side. She also complained of double vision. The thalamic CA of 2 cm was surgically removed (Figs. 1A–C and 2A–D). She recovered well from the original neurological deficits.

However, seven years later she presented with a vertical gaze paresis and with deterioration of her pre-existing sensory disturbance on the right side. The follow-up magnetic resonance imaging (MRI) study revealed recurrence/regrowth of the thalamic CA (Fig. 1D–F). The paraculinar supracerebellar approach was performed again in the same fashion as during the first operation. The thalamic CA of 2.5 cm was totally removed surgically (Fig. 1G–I). At one year after the second surgery, she showed a very good recovery in her daily life without double vision and had a marked improvement of her right-sided sensory hemisyndrome.

Case 4

A 54-year-old male presented with right hemiparesis and thalamic pain on the right side. The preoperative MRI showed a left thalamic CA of 3.0 cm in size (Fig. 3A–C). The CA was totally removed using the paraculinar supracerebellar transtentorial approach (Figs. 3D–F and 4A–F). The surgery was performed without any operative complication. Postoperatively, the right motor dysfunction improved slightly, however, without remarkable improvement of the thalamic pain.

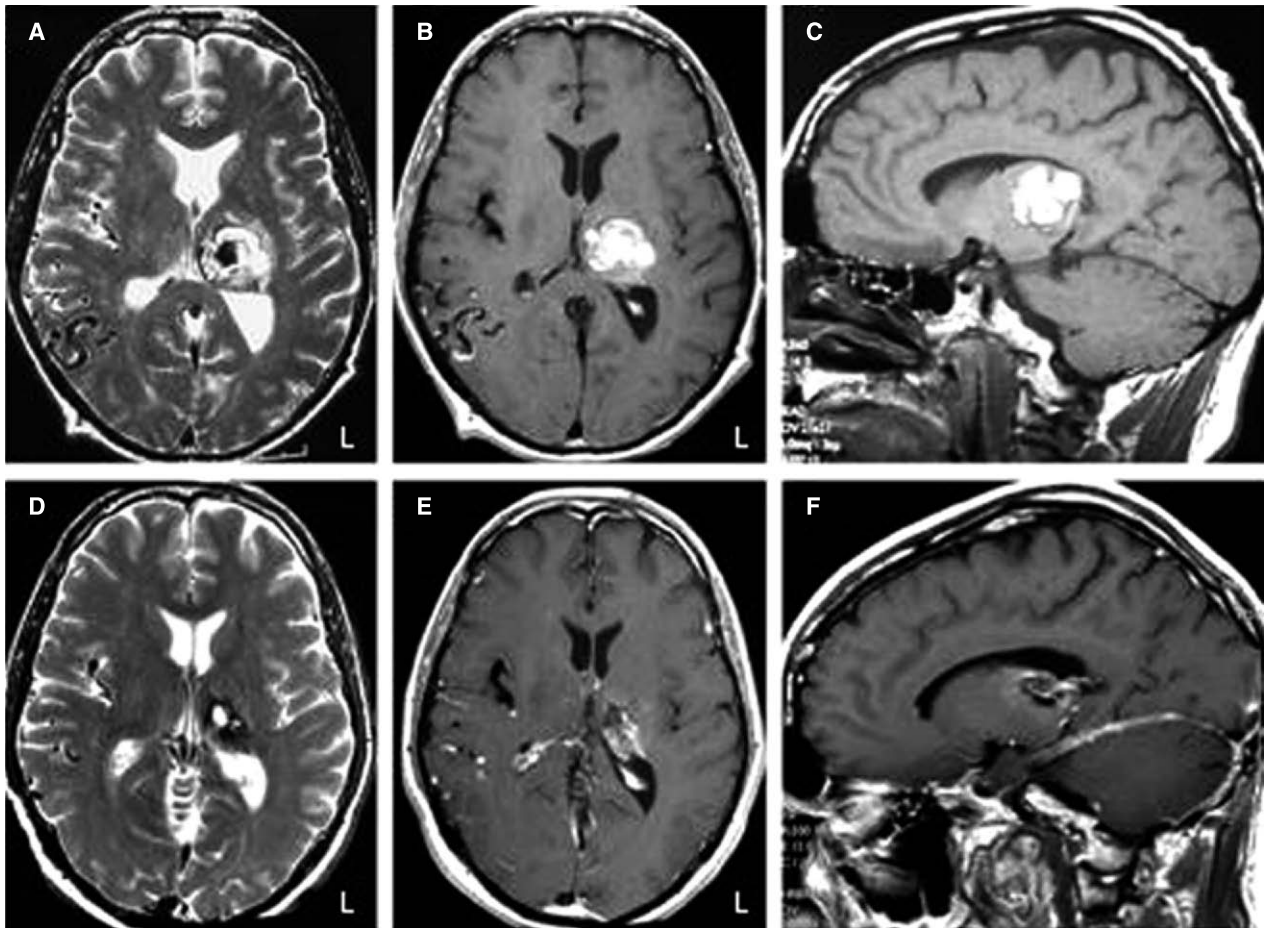


Fig. 3. *Case 4* Axial T2- (A), Gd-enhanced T1-weighted axial (B) and sagittal (C) MR images showing a cavernous malformation of 1.5-cm diameter in the left thalamus. The postoperative MRI showing the thalamic CA was surgically removed totally (D–F: T2 axial, Gd-T1 axial and Gd-T1 sagittal MRIs). Postoperatively, there was a slight improvement in sensorimotor function of the right side without any operative complication

Discussion

Cavernous angiomas have several unique characteristics including the tendency for repeated occult bleedings and progressive growth. The hemorrhage rate seemingly increases after the initial hemorrhage. Pozzati [16] reported 12 cases of CA. In this study, 66% of 12 cases experienced intracerebral hemorrhage, 33% had multiple hemorrhages, and the recurrent bleeding rate was 6.1%. They suggested that recurrent bleeding occurred preferentially during the first two years after the initial hemorrhage. In addition, another report suggested that the annual hemorrhage rate for thalamic CA was 2.9% [9]. The reported annual hemorrhage rate of the thalamic CA is higher than that generally attributed to CAs [3, 21]. This may result from the high neurologic sensitivity of the thalamus and the surrounding anatomical structures even to small hemorrhage or mass effect.

In this study, four patients presented with cerebral hemorrhage and two (29%) patients suffered from pro-

gressive neurological disorders without hemorrhage. In all patients (six patients/seven operations) successful and total removal of the thalamic CA was achieved without additional clinical and/or neurological impairments. The preoperative neurological deficits improved after the removal of thalamic CA in four operative sessions (out of seven, 57%) and remained unchanged in three sessions (43%). One patient (Case 1) had re-bleeding of the thalamic CA in the 7th year after the first surgery. The first surgical removal in this patient was considered complete according to the repeated imaging studies during the follow-up period of two years. We suspect that this is an example case for CA regrowth/regeneration deriving from small amounts of CA cells or tissue. No other patients had CA recurrence during the follow-up periods.

No patients had permanent postoperative complications. Two patients had transient neurological deteriorations; homonymous hemianopia in Case 2 and vertical

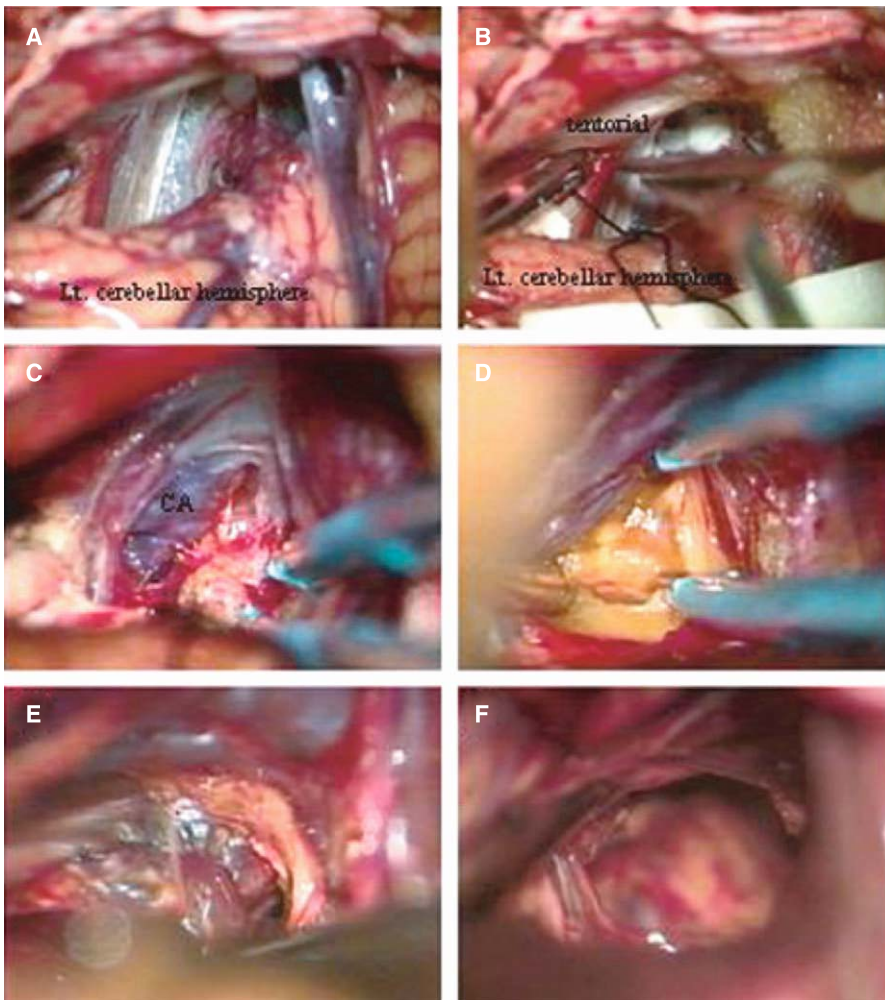


Fig. 4. *Case 4* Microsurgical pictures showing the paraculinar supracerebellar transtentorial approach for the removal of the left thalamic cavernoma. The cerebellar tentorial incision was performed (A and B) and the cortex over the pulvinar came into view (C). The corticotomy revealed the thalamic CA with the old hematoma (D and E). The CA was totally removed by a 34-minutes' microsurgery (F)

gaze palsy in Case 3. Time requirement for microsurgery using the paraculinar supracerebellar transtentorial approach and removal of the thalamic CA ranged from 31 to 83 min (mean 47 min). We suggest that this approach could be one of the best procedural options for thalamic CA with regard to feasibility and safety.

Radiosurgery represents an alternative method for the treatment of thalamic CA [8–10, 16]. Kondziolka *et al.* [9] reported the results of radiosurgically treated thalamic CA in nine patients. They described that reduction of hemorrhagic risk was observed after 2 years' latency. In their study, however, radiosurgical complications developed in 26% of patients, such as rebleeding, radionecrosis, and prolonged cerebral edema. Pozzati [16] suggested an early increase of bleeding risk after radiosurgery for thalamic CA. A recent study [10] reported the outcome following gamma knife surgery (GKS) for brain CAs. According to this study, the rebleeding rate was 1.6% and perilesional edema occurred in 27% of patients which caused a transient morbidity rate of 20.5%

and a permanent morbidity rate of 4.5%. In addition, Karlsson *et al.* [8] do not support GKS for CAs because of the relatively high risk of complications. Therefore, we suggest that surgical resection should be performed in symptomatic patients with thalamic CA, especially if the lesion is located at the thalamic surface close to the CSF space.

On the other hand, deep-seated lesions inside the thalamus are considered unfavourable for microsurgical removal since the circumferential critical structure limits radical resection. The thalamus is anatomically subdivided into anterior, central, and ventricular complexes as well as the pulvinar. The anterior and central nuclei are connected to the frontal cortical area [4, 20]. Lesions in these areas lead to delirium and frontal syndromes [1]. The ventral nuclei are subdivided into motor and sensory components and reciprocally connected to the motor – sensory cortex and the globus pallidus [14, 27]. The pulvinar is connected to the temporal and the parietal association areas and considered important for language

functions [15]. In addition, the ventrolateral border of the thalamus consists of critical structures such as internal capsule and vital subthalamic structures.

The surgical route for the resection of thalamic CA depends on the size of the lesion and on its detailed localization, especially in relation to the ependymal or pial surfaces: the dorsal thalamus abutting the lateral ventricle, the medial thalamus bulging into the third ventricle, the pulvinar protruding into the posterior incisural space, and the deep location away from any CSF space. The surgical route for the thalamic CA includes the midline posterior parietal interhemispheric or transcortical approaches, the transcallosal route through the lateral ventricle and the route inferior to the splenium of the corpus callosum [24]. The ventricular surface of the dorsal thalamic CA may be approached through an ipsilateral or contralateral interhemispheric transcallosal route. However, the transcallosal and transventricular approach harbors the risk of major complications including injury to the fornices leading to memory disturbance. On the other hand, the transcortical approach could involve direct injury to the optic radiation causing homonymous hemianopia. However, the paraculminar supracerebellar infratentorial transtentorial approach theoretically carries no risk of anatomical damage to the cerebral cortex, the corpus callosum, the fornix, the cerebellar hemisphere and the cerebellar vermis. This approach enables the surgeons to obtain a good operative field without damaging vital brain structures. Accordingly, the paraculminar supracerebellar infratentorial transtentorial approach should be considered the method of first choice for the surgical removal of thalamic CA especially if the CA is mainly located in the posterior portion of the thalamus.

The operative window for the thalamus between the bilateral basal veins of Rosenthal is relatively narrow. The lateral extension of the surgical field is limited in the paraculminar approach without the transtentorial method.

However, the infratentorial supracerebellar paraculminar pathway for thalamic CA is completely extra-axial, therefore, is less invasive to the brain. This approach was designed to minimize anatomic and functional damages to critical structures. The infratentorial supracerebellar approach was first described by Oppenheim and Krause in 1917 for the removal of a tumor of the quadrigeminal plate [13]. It was later refined by Zapletal [30] and by Stein [26] for access to the pineal region and the posterior portion of the third ventricle. Median infratentorial supracerebellar approach could be classified

into two groups: the culminar approach [13, 26, 30] and the paraculminar approach (shown in this study). We have described the safety and the usefulness of these supracerebellar approaches to lesions localized in the tectum, cerebellar peduncles and/or posterior parahippocampus [7, 12, 29]. In particular, the paraculminar approach can be used for lesions localized in the pineal region, the thalamus, and the posterior third ventricle. This method offers a good operative exposure without the need to sacrifice the bridging veins or the precentral cerebellar vein, and to retract the culmen downward. The paraculminar supracerebellar infratentorial approach may be modified by adding the tentorial incision. This transtentorial approach widens the surgical field toward the superior and lateral directions still without damaging the normal brain structure. This variation seems to be effective for thalamic CAs of larger size and of more lateral location.

Conclusions

Deep-seated, basal ganglion, thalamus and/or brainstem lesions in the neurosurgical settings require well-designed and less invasive anatomical approaches since these areas seem highly vulnerable to slight mechanical damage in terms of morbidity and mortality. From this point of view, we have suggested several surgical strategies to the lesions in the tectum, superior and inferior colliculus and cerebellar peduncles by using the paramedian supracerebellar approach, and in the posterior temporomedial structures choosing the supracerebellar transtentorial approach [7, 12, 29]. In the present study, we investigated and confirmed the usefulness and safety of the paraculminar supracerebellar infratentorial transtentorial approach to thalamic cavernous angiomas in our consecutive 11-year series of 6 patients. The paraculminar supracerebellar infratentorial transtentorial approach appears to be a very effective way to obtain good surgical view without damaging intact brain structures. Outcomes of our patients with thalamic cavernous angioma were considered favourable. Because this approach exerts less stress to the surrounding normal neuronal tissue, postoperative neurological deterioration, if any, would be transient and the degree of deficits could be mild. This was observed in our study (Cases 2 and 3).

From the present study it is deduced that the paraculminar supracerebellar infratentorial transtentorial approach is one of the best options for the total resection of thalamic CA with less operative complications.

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Peripheral large or giant fusiform middle cerebral artery aneurysms: report of our experience and review of literature

M. El Beltagy, C. Muroi, H.-G. Imhof, Y. Yonekawa

Department of Neurosurgery, University Hospital Zurich, Zurich, Switzerland

Summary

Peripheral large and giant middle cerebral artery (MCA) aneurysms are rare and difficult to treat. We report our and others' experience with different possible modalities used to treat such lesions. Three patients were treated differently at our institution. One harboured a giant fusiform aneurysm on a peripheral branch of the superior trunk of the left MCA, and was treated by extracranial-intracranial (EC-IC) bypass and trapping of the aneurysm. The second patient was harbouring a large fusiform aneurysm on a peripheral branch of the inferior trunk of the right MCA, which was treated by trapping and excision without the need of an EC-IC bypass as assessed pre- and intraoperatively, while the last case was harbouring a giant fusiform aneurysm at the junction of M2-M3 and was treated by EC-IC bypass and end-to-end anastomosis after resection of the aneurysm. The aneurysms proved to be neither mycotic nor dissecting. The patients were clinically intact during their perioperative course without any postoperative complications and required no further treatment. Follow-up angiography demonstrated a functioning EC-IC bypass. Based on the surgical experience in these 3 cases and a review of the reported literature, the authors propose that when considering surgical treatment for such rarely encountered aneurysms, careful pre- and intraoperative evaluation including aneurysm trapping with or without EC-IC bypass when possible should be performed to obtain a satisfactory result without complication.

Keywords: Intracranial aneurysm; middle cerebral artery; EC-IC bypass; fusiform; trapping.

Introduction

Approximately 25% of all clinically significant intracranial aneurysms arise from the middle cerebral artery (MCA). The majority of these are saccular and typically originate as a direct extension of the main MCA trunk (M1 segment) between and beyond its two major branches near the genu [36]. Some MCA aneurysms, however, exhibit a fusiform (spindle-shaped) appear-

ance, at least when they are small and when viewed externally. Fusiform aneurysms have different underlying pathological features, haemodynamics, anatomical distributions, natural histories and treatments than the saccular variety [6]. Aneurysms of the peripheral middle cerebral artery are considered an unusual site [13, 23]. Such distal aneurysms were first described by Poppen in 1951 involving the angular branch and by Stenvers and Verbiest in 1963 arising from the parietal branch [31, 34]. The first to describe an aneurysm involving the posterior temporal branch of middle cerebral artery was Janny *et al.* in 1962 [22]. The largest series to date included nine distal MCA aneurysms [19], eight out of these nine were saccular and one was mycotic with no dissecting lesion observed in this series. When these aneurysms are encountered, the most common aetiology is infection due to mycotic emboli with secondary aneurysm formation [2]. The first case of a peripheral aneurysm resulting from intracranial dissection was reported in 1994 which was treated by excision and revascularization and proved not to be of mycotic origin [30]. Direct microsurgical repair remains the most common method used to treat distal MCA aneurysms, although endovascular surgery has been favoured recently [19].

The purpose of this report is to describe our experience with distal MCA aneurysms, which were fusiform in shape and not amenable to ordinary clipping, owing to their shape and peripheral location. Two cases were on the dominant hemisphere, one was encountered in the left angular artery and required revascularization followed by trapping and excision of the aneurysm, while the other was at the junction of M2-M3 and was treated by excision and revascularization. By contrast, the last case was on the non-dominant hemisphere and could only be trapped

Correspondence: Prof. Dr. med. Yasuhiro Yonekawa, Neurochirurgie FMH, Haldenbachstrasse 18, CH-8091 Zurich, Switzerland.
e-mail: yasuhiro.yonekawa@usz.ch

and excised without need for revascularization with a smooth postoperative course. Interestingly, all aneurysms proved not to be due to bacterial infection after histopathological examination. By reviewing the English literature there was no clear information pointing to the most satisfactory method of treating such rare type of spontaneous peripheral fusiform MCA aneurysms with a good outcome. Thereby we intended to report our experience and review others regarding the available methods of surgical treatment of peripherally situated large or giant fusiform spontaneous MCA aneurysms when encountered on either side of the cerebral hemispheres.

Illustrative cases

Case 1

Patient history: The first patient was a right handed 58-year-old male complaining of a sudden attack of right arm paraesthesia, dysarthria and dizziness. The patient did not experience a history of headache, nausea nor

vomiting. When the patient was admitted to a peripheral hospital, a computerized tomography (CT) was performed with the diagnosis of a suspected left temporal lobe cavernoma (Fig. 1a and b). The next day, he was transferred to the Department of Neurosurgery, University Hospital Zurich, where a magnetic resonance imaging (MRI) of the brain was performed diagnosing a suspected peripheral thrombosed giant aneurysm in the left Sylvian fissure (Fig. 1c and d), thereafter confirmed by cerebral 4-vessel angiography, which showed a fusiform aneurysm arising from a peripheral branch of the superior trunk of the left MCA (Fig. 2a and b). At that time, it was not clear if the aneurysm was dissecting or not. *Examination:* On admission, the patient's Glasgow coma scale (GCS) was 15, with no signs of meningism, no papilloedema nor field defect, no motor deficit with normal coordination and gait, with hypaesthesia in the right shoulder down along the whole right upper limb. *Operation:* The operation was planned on the next day through a left sided question mark incision extending behind the left ear, followed by an extended pterional

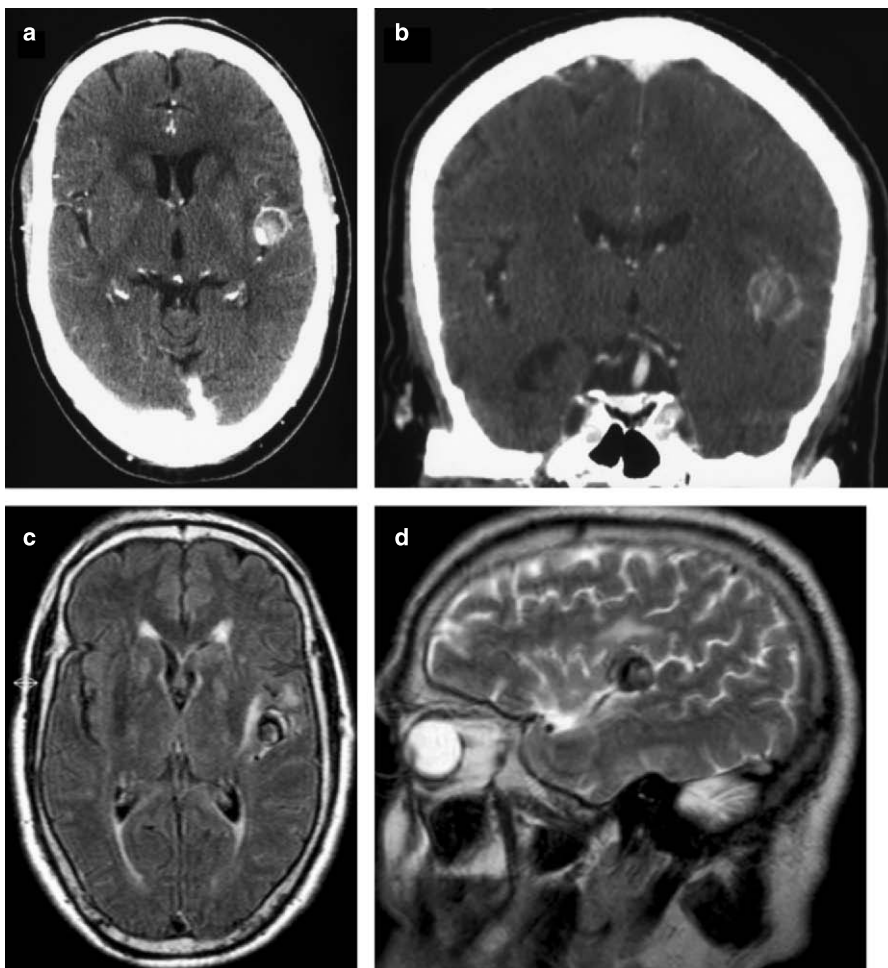


Fig. 1. Case 1. Contrast-enhanced axial (a) and coronal view (b) CT demonstrating a 3 cm hyperdense lesion in the left Sylvian fissure. Noncontrast-enhanced FLAIR axial view (c) and T2-weighted sagittal view (d) MRI showing a giant left MCA aneurysm

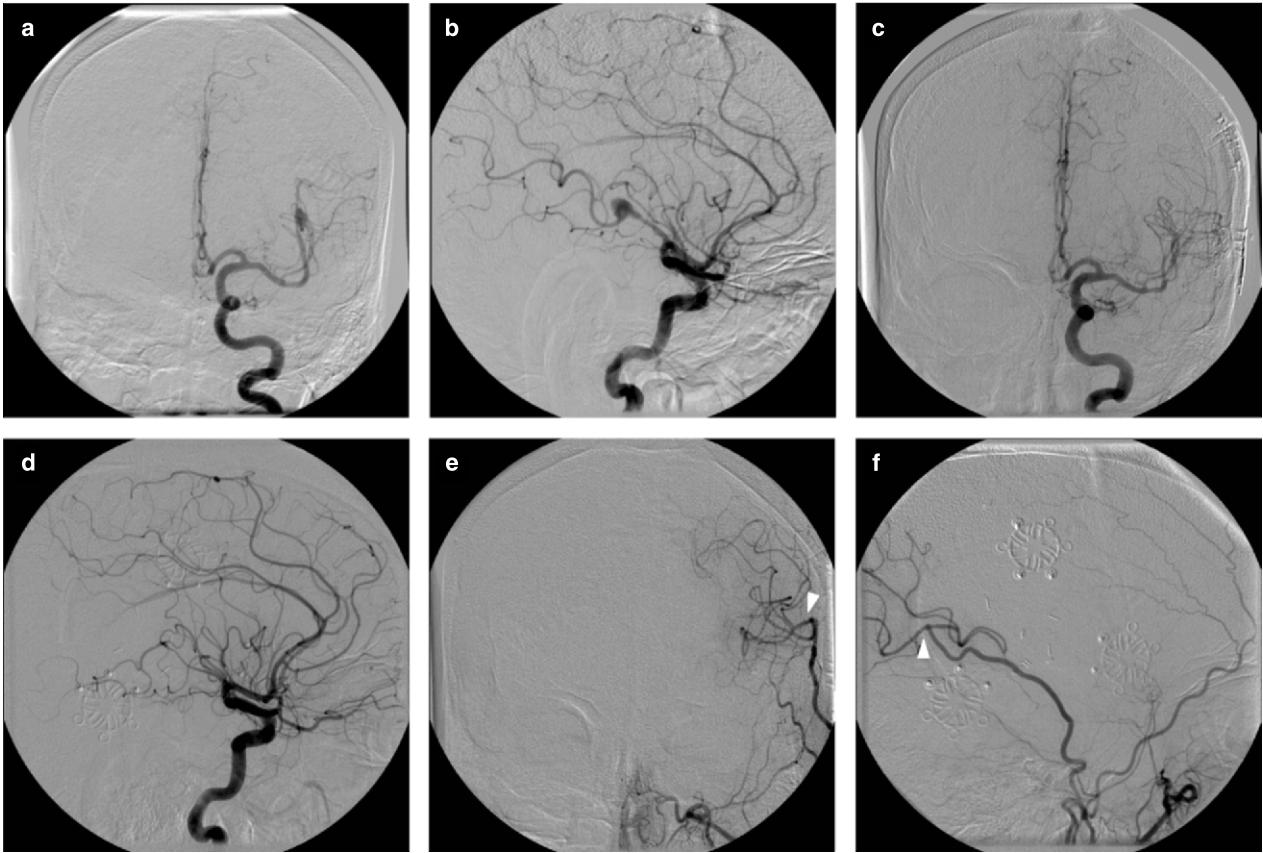


Fig. 2. Case 1. Anteroposterior (a) and lateral (b) left internal carotid artery (ICA) angiograms obtained before surgery, showing the aneurysm. Anteroposterior (c) and lateral (d) left ICA angiograms obtained after surgery. Anteroposterior (e) and lateral (f) selective external carotid angiograms showing functional anastomosis (*arrow heads*)

craniotomy and transSylvian dissection up to identifying a giant (2.5 cm) thrombosed fusiform aneurysm on a peripheral branch of the superior trunk of the left MCA. Preparation of the parietal branch of the superficial temporal artery (STA) on the left side was performed, followed by preparation of the aneurysm and the adjacent vessels to find an open branch to which an EC-IC bypass could be performed, aided by Doppler

identification of a 1.3 mm open branch (superior trunk) from which the aneurysm arose and which showed to be feeding into the angular artery, indicating that trapping without EC-IC bypass would eventually lead to complications from defective flow in the angular artery on the left hemisphere. The decision to perform an EC-IC bypass followed by trapping of the aneurysm was thus confirmed. Preparation of 1 cm length of the desired

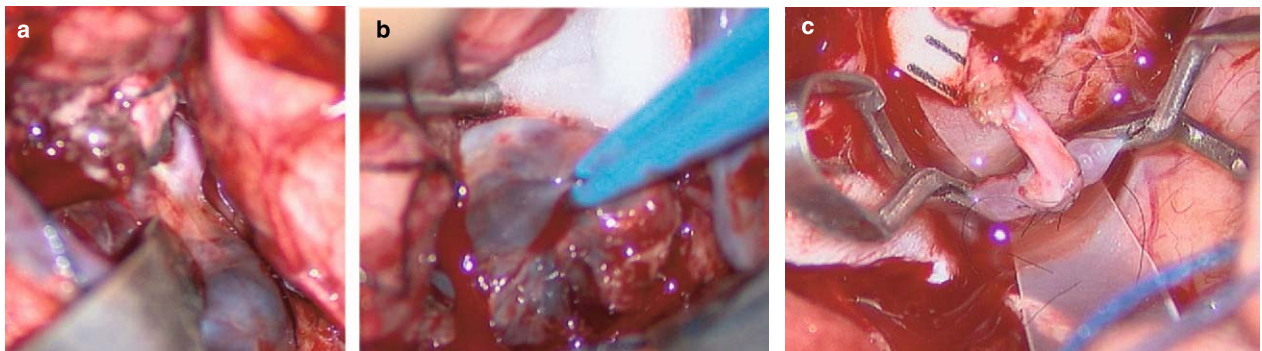


Fig. 3. Case 1. Intraoperative photographs showing the giant thrombosed aneurysm arising from peripheral MCA superior trunk (a), extrusion of the thrombus (b) and the EC-IC bypass (c)

vessel was carried out cautiously to which an end-to-side anastomosis with the previously prepared 1 mm STA branch was performed using 10-0 monofilament sutures. Following the anastomosis, the aneurysm was trapped with two clips and the thrombus was extruded (Fig. 3).

Postoperative course: The patient was transferred to the intensive care unit (ICU) on the day of operation; intubated, and on the next day he was extubated and was moving all four limbs, agitated and with slight dysarthria. Postoperative angiography was performed and showed

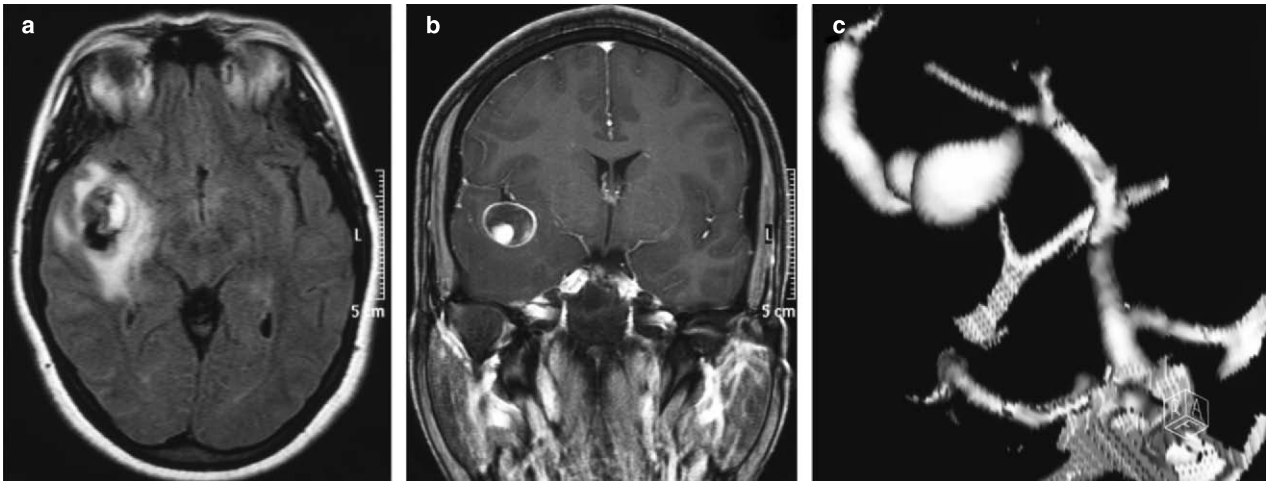


Fig. 4. Case 2. FLAIR axial view (a) and T1-weighted coronal view (b) MRI showing a giant right MCA aneurysm. Reconstructed 3-dimensional CT angiogram showing the aneurysm



Fig. 5. Case 2. Anteroposterior (a) and lateral (b) right ICA angiograms obtained before surgery, showing the aneurysm. Anteroposterior (c) and lateral (d) right ICA angiograms obtained after the operation, showing the 2 clips (arrow heads) and absence of the aneurysm

both the STA branch sutured to the angular artery with patent blood flow in the anastomosis (Fig. 2c–f). CT and MRI examinations were performed showing no detectable abnormality, and the patient was discharged from hospital in a satisfactory medical condition.

Case 2

Patient history: A right handed 29-year-old female patient who was admitted to the Department of Neurosurgery complaining of headache since 14 days with new recent superimposed attacks of vomiting, dizziness, tingling and visual disturbances. *Examination:* On admission to the hospital, the patient had a GCS of 15, with no speech disorders, no signs of meningism, no papilloedema nor field defect, no symptoms or signs of cranial nerve deficit, no motor or sensory deficit with normal coordination and gait. CT, MRI (Fig. 4a–c) and cerebral 4-vessel angiography were performed on the same day revealing a large (2 cm) thrombosed fusiform aneurysm of the right temporo-occipital branch of the inferior trunk of the MCA (Fig. 5a and b). *Operation:* The operation was planned for the next day through a right sided fronto-temporo-lateral craniotomy, followed by trans-Sylvian dissection following the internal carotid artery from proximal to distal up to the bifurcation following the MCA till the aneurysm was visualized and prepared, where temporary clip on the M1 segment of MCA was applied, and the aneurysm was punctured with extrusion of the thrombus through a cortical incision in the distal insular semicircular sulcus, followed by trapping of the aneurysm and excision, without the need for performing an EC-IC bypass. Intraoperative ultrasound showed normal flow in the main arteries. *Postoperative course:* The patient was transferred to the ICU on the day of surgery; she was then extubated on the next postoperative day without any observed neurological deficit. Postoperative CT and 4-vessel angiography were performed with absence of aneurysmal dilatation (Fig. 5c and d). The patient was discharged from the hospital on the 7th day after operation.

Case 3

Patient history: A right handed 37-year-old female patient admitted to our department complaining of gait disturbance, right sided hemisindrome, dysarthria and minimal motor aphasia. *Past history:* Right atrial myxoma which was resected 13, 8 and 3 years ago; the patient had a history of cardio-embolic manifestation 13 years ago with motor aphasia and right sided hemisindrome.

Examination: The patient's GCS was 15, no symptoms or signs of cranial nerve affection other than motor aphasia, right sided hypaesthesia and grade IV hemiparesis with positive Babinski sign. MRI of the brain and 4-vessel cerebral angiography were performed on the same day revealing a 2.5 cm thrombosed fusiform aneurysm at the junction of M2–M3 (between inferior trunk of MCA proximally and posterior parietal and temporo-occipital arteries distally). *Operation:* The operation was performed on the next day through a left sided pterional craniotomy, the STA was prepared for a bypass and the aneurysm was identified. An end-to-side anastomosis was performed between the posterior parietal artery and STA followed by resection of the aneurysm and end-to-end anastomosis between the inferior trunk of M2 and the temporo-occipital artery. Intraoperative ultrasound revealed a normal blood flow in the parent arteries and both anastomoses were apparently functioning. *Postoperative course:* The patient was transferred to the ICU after the operation. She was then extubated on the next postoperative day with no new neurological deficit observed. Three days later the patient suffered an attack of grand mal seizure, which was controlled by carbamazepine. EEG showed no recorded abnormality. Postoperative angiography was performed and showed both anastomoses to be functioning with complete absence of the aneurysm. CT and MRI of the brain revealed no abnormality detected. The patient was discharged on the 13th postoperative day.

Discussion and review of literature

The dilemma in treating intracranial aneurysms that cannot be clipped or adequately and safely occluded with coils is that the lesion can involve the entire circumference of the parent vessel wall incorporating vital perforating arteries or distal vessel branches, this fusiform aneurysms have no true neck, in addition to their complex irregular shape and size making them unamenable to traditional clipping or endovascular coil embolisation. We report our experience and that of others in treating these lesions when incorporating the peripheral branches of the MCA and being either large or giant which further adds to the complexity of management.

We believe that these cases represent a rare review of peripheral MCA fusiform aneurysms that are neither secondary to arterial dissection nor infectious in origin. A literature review for data published on treating peripheral fusiform MCA aneurysms is shown in Table 1. In this largest series to date of distal MCA aneurysms, pub-

Table 1. Review of literature on treating peripheral fusiform MCA aneurysms

Ref.	Aneurysm location	Aneurysm size (mm)	Treatment modality	Outcome
Dolenc <i>et al.</i> [8]	left angular artery	15	excision with STA interposition graft	good recovery
	left temporal artery	10	excision with end to end anastomosis	good recovery
	left temporal artery	4	excision with STA interposition graft	good recovery
Borzzone <i>et al.</i> [3]	left prefrontal branch	45	isolated and clipped	temporary deficit followed by recovery
	distal left MCA branch	25	not treated	no change in the aneurysm dilatation
Al-Yamany [1]	left inferior trunk	4	Hunterian ligation	ischemic stroke with speech difficulties
Ceylan <i>et al.</i> [4]	left inferior trunk	>25	excised with end to end anastomosis	good recovery
Hoh <i>et al.</i> [16]	distal left MCA branch	–	trapping with clips	patient died

lished by Horiuchi *et al.* [19], who reported nine peripheral MCA aneurysms, eight were saccular and were clipped and the remaining one was a mycotic aneurysm that was trapped without revascularization. We focus on cases where the aneurysms are large or giant fusiform in shape and located on the M3 segment of MCA in addition to being neither mycotic nor dissecting and occurring in relatively young patients, which renders decision-making and choice of treatment method more difficult. As most distal intracranial aneurysms occur as a result of bacterial infection, usually associated with endocarditis [2], they have also been reported in conjunction with disseminated fungal infections [20]. Furthermore, histopathological studies and intra-operative assessment of the cases showed that they are not dissecting in nature nor infectious, although it was difficult to evaluate the exact nature solely from preoperative angiograms. Aneurysms secondary to dissection of intracranial cerebral arteries tend to occur more proximally, also within the internal carotid, basilar artery, MCA, and posterior cerebral artery trunks. In most cases of intracranial arterial dissection no specific cause can be identified [14]. Neurosurgeons consider fusiform and dissecting aneurysms to be different entities and believe that distinguishing between them is very important to determine their course of treatment and prognosis. Nevertheless, some authors have reported that fusiform lesions correlate with dissecting aneurysms clinicopathologically [27, 35]. The surgical approach to or endovascular treatment of large and giant fusiform aneurysms in the MCA is technically difficult, so some patients are treated conservatively [18]. Giant fusiform aneurysms are rare, accounting for 5 to 17.6% of giant aneurysms, which themselves represent – depending on literature – 3 to 13% of all intracranial aneurysms [1]. These types of aneurysms are reported to be more common in the vertebrobasilar circulation [18]. In our patients the giant fusiform aneurysms were located on a

peripheral branch of a trunk of the MCA which makes the decision for surgical or endovascular treatment difficult especially in the light of the good clinical condition in which the patients presented and the insufficient literature on the clinical course following conservative treatment of such lesions especially when not being secondary to dissection nor bacterial infection.

Large or giant fusiform aneurysms, when present, are frequently multiple [24, 26], but our patients had no other lesions. Management of these aneurysms must be individualized, but should include: 1) exclusion of the vascular lesion from the native circulation with maintenance of cerebral blood flow; 2) treatment of the mass effect; 3) treatment of subarachnoid haemorrhage and 4) treatment and prevention of positive and negative neurological signs and symptoms. One surgical option is the reconstruction of the vessel wall using multiple clips. This technique was introduced by Drake and improved by Sugita [28], it is technically difficult in such peripherally located aneurysms of too small an arterial calibre. Resection of the aneurysm and end-to-end anastomosis is another treatment option, which was technically feasible in our cases but would have carried a certain risk of occlusion due to the size of the aneurysms. Dolenc [8] treated one case of peripheral fusiform aneurysm by resection and end-to-end anastomosis and although the aneurysm was 4 mm in diameter, the reconstructed artery was narrow and funnel shaped. Other authors [4] have treated a case of giant peripheral left MCA fusiform aneurysm with the same technique (resection with end-to-end anastomosis) and with postoperative follow-up angiography made two years latter showing only a slight flow of blood through the anastomosed vessels, which carries a high risk of occlusion later on. Thus it would always be safer to perform end-to-end anastomosis with an interposition graft to avoid such complication although it is not always technically feasible. Proximal clipping or aneurysm trapping with vascular bypass dis-

tally is probably the most popular option. This latter technique has been successful in most series [7, 9, 29], but although it seems to be effective, regrowth after proximal ligation and STA-MCA bypass has been reported [21] and ischemic complications have occurred even when the vascular bypasses were patent [17, 32]. Wrapping the aneurysm with muslin gauze has been described, but is generally thought to be ineffective due to the high risk of rupture [5]. Conservative treatment is not an option especially not in young and otherwise healthy patients who present with SAH. When Steinberg *et al.* [33] reviewed six reports in the literature of giant unclipable aneurysms, he found that approximately 80% of untreated patients were either dead or severely disabled at the 5-year follow-up evaluation due to brainstem compression, thrombosis of critical arteries, or SAH.

Some authors presented a left M2 segment giant fusiform aneurysm treated with Hunterian ligation of the parent vessel even without distal EC-IC bypass [1], with the patient suffering from a radiologically confirmed stroke and speech difficulties as a result of their treatment. We emphasize that this would be an option only if the aneurysm is located on the M3 in the non-dominant hemisphere and if intra-operative Doppler ultrasound shows normal flow velocity in the main vessels, or alternatively, if the cerebral blood flow measurement by thermal diffusion method is not impaired. On the other hand, it is mandatory to perform revascularization to preserve the blood flow in the peripheral MCA branches in the dominant hemisphere, even when the aneurysm is located on the M3 segment to obtain an optimal, satisfactory outcome.

Endovascular techniques such as parent vessel balloon or coil occlusion and placement of intra-aneurysmal coils have also been used to treat such aneurysms, aiming at the occlusion of the main artery, but this might sometimes be associated with significant risks [10, 12, 15] as approximately 20% of patients do not tolerate acute occlusion of one carotid artery [25].

In the first case the patient had already been suffering from hypaesthesia in the right upper limb and dysarthria, which could be attributed to defective blood flow in the peripheral branches of the left MCA. So a preoperative decision of an EC-IC bypass was made to preserve the flow in the angular artery after trapping of the aneurysm. In this case trapping alone would have interfered with the distal flow in the angular artery with serious infarction. In the second case trapping alone without EC-IC bypass was the optimal treatment option since we were of the opinion that trapping alone at that site of the non-

dominant hemisphere will not lead to serious complications from interference with the blood flow as assessed intraoperatively by means of ultrasound, beside avoiding an extension of the operative time for an unnecessary procedure which might add to an increased morbidity in such a young patient. Conservative management alone was not an option as the patient was young and presented already with mass effect symptoms due to the site and the size of the aneurysm. In case 3 the aneurysm developed later after extirpation of an atrial myxoma which is a well documented event following the removal of such tumours [11]. In this patient the aneurysmal dilatation was located at the junction of the inferior trunk of the left MCA proximally and 2 other important peripheral branches (posterior parietal and temporo-occipital arteries) distally which makes the decision more difficult as the performance of an end to side anastomosis only as in case 1 would establish the flow in only one of the two distal branches while sacrificing the other which would still lead to a certain degree of neurological deficit, therefore the decision of end-to-side anastomosis with the STA and posterior parietal artery together with end-to-end anastomosis between the inferior trunk and temporo-occipital artery after aneurysmal resection was chosen. Collectively the treatment of distal fusiform giant or large MCA aneurysm would entail different methods of surgical procedures ranging from trapping only, which could be easily performed, to trapping or excision with bypass which requires an experienced neurosurgeon. Prediction of the most suitable surgical modality could be made by adequate careful assessment of the preoperative angiography and patient's clinical condition and based on the intraoperative situation, which might be individually variable in different patients, the final decision could be made.

Conclusions

We believe that although many management modalities, including conservative follow-up, could be an option in treating such a rare type of aneurysm but trapping with or without the performance of an EC-IC bypass offers the most satisfactory and technically feasible method that could be performed by neurosurgeons facing this type of aneurysm. Importantly, careful preoperative assessment of the site, size and shape of the aneurysms situated on the peripheral MCA branches together with evaluation of the patients' clinical condition and age would lead to identifying the optimal method for treatment with a satisfactory good outcome for the patient.

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Part 2:
Dissection of cerebral arteries

Stroke prevention and treatment in patients with spontaneous carotid dissection

R. W. Baumgartner

Department of Neurology, University Hospital Zurich, Zurich, Switzerland

Summary

This review on spontaneous dissection of the internal carotid artery (sICAD) will discuss in the first part stroke prevention and focus on vascular risk factors, antithrombotic therapy, and treatment of severe stenosis or occlusion, and dissecting aneurysm. The second part of the review will summarize the treatment of acute ischemic stroke due to sICAD.

Keywords: Stroke prevention; dissection; internal carotid artery; aneurysm; antithrombotic treatment.

Stroke prevention

Vascular risk factors

Hypertension is the main risk factor for aortic dissection and might thus play a role in the pathogenesis of spontaneous cervical artery dissection (sCAD). A multi-center case-control study performed in 153 Italian patients with sCAD reported a trend towards a significant association between the prevalence of hypertension and sCAD [1]. In a multi-center observation study examining gender differences in 696 Swiss and French patients with sCAD and a mean age of 45 years, men more often had a history of hypertension compared to women (31% vs. 15%; $p < 0.0001$) [2]. The Bundesamt für Statistik of Switzerland performed an enquiry about the prevalence of vascular risk factors and other parameters in healthy volunteers who were 35–55 years old in 1997 [3]. Hypertension was observed in 748 (17%) of 4401 volunteers, and was equally frequent in both genders [3].

These findings suggest that arterial hypertension might be more prevalent in male patients with sCAD than in healthy men. In the aforementioned Italian case-control study hypertension was associated with sCAD (odds ratio (OR), 1.94; 95% confidence interval (CI), 1.01–3.70; $p = 0.045$) and spontaneous vertebral artery dissection (OR, 2.69; 95% CI, 1.20–6.04; $p = 0.017$) causing cerebral infarction [1].

Hypercholesterolemia defined as a serum cholesterol level >5 mmol/L was found in 301 (53%) of 570 patients with sCAD [2]. The frequency of hypercholesterolemia was about 60% in the Swiss MONICA center Vaud/Fribourg [4], Swiss military personnel [5] and 61'108 French subjects over 15 years of age who volunteered for a systematic medical check-up [6]. These populations had about the same age compared to the patients with sCAD mentioned above, which suggests that the prevalence of hypercholesterolemia might be similar in patients with sCAD and the Swiss and French population. A bi-centre observational study found that hypercholesterolemia occurs more often in sICAD causing ischemic events compared to those causing just local symptoms and signs on the side of dissection (head- and neck pain, pulsatile tinnitus, Horner syndrome or cranial nerve palsy) or remained clinically asymptomatic [7].

The prevalence of cigarette smoking and diabetes was similar to the findings observed in the normal Swiss population [3] and a population-based, cross sectional study performed in 28'409 French volunteers [8].

In conclusion, hypertension might be a risk factor for sICAD, in particular in men, and antihypertensive treatment may thus also prevent sICAD. Furthermore, anti-hypertensive and lipid lowering therapy might prevent the development of strokes in patients suffering sICAD.

Correspondence: Ralf W. Baumgartner, Department of Neurology, University Hospital of Zurich, Frauenklinikstrasse 26, CH-8091 Zurich, Switzerland. e-mail: ralf.baumgartner@usz.ch

Antithrombotic treatment

Brain imaging studies performed in patients with sICAD suggest that the essential mechanism of stroke is cerebral embolism [9], and transcranial Doppler sonography investigations reported microembolic signals in the middle cerebral arteries that were irrigated by dissected carotid arteries [10]. These findings suggest that the main goal of antithrombotic treatment in sICAD is the prevention of embolic stroke.

No controlled randomised or non-controlled study has compared the safety and efficacy of an antithrombotic treatment with placebo or different antithrombotic treatments (e.g. aspirin with anticoagulation) in patients with sICAD [11]. A systematic meta-analysis investigated in patients with sICAD whether the outcomes “death from all causes” and “dead or disabled” are different after treatment with antiplatelet agents or anticoagulation [11]. There was no difference for the outcome “death of all causes” as 2 (2%) of 109 patients (1.8%) treated with antiplatelets and 4 (2%) of 218 (1.8%) patients treated with anticoagulation died. The endpoint “dead or disabled” occurred in 14 (24%) of 59 patients who underwent antiplatelet treatment, and in 17 (14%) of 119 patients treated with anticoagulants, but did not differ between both groups (Peto OR, 1.94; 95% CI, 0.76–4.91). These data suggest that a randomized controlled trial comparing aspirin with anticoagulation is justified.

Treatment of severe stenosis or occlusion

In a non-controlled observational study, the rate of ischemic events and intracranial hemorrhage was compared in patients with persistent ($n=46$) and transient ($n=46$) severe stenosis or occlusion of the internal carotid artery (ICA) due to unilateral sICAD [12]. Although antithrombotic therapy was given at the discretion of the treating physician, it was similar in both groups. Patients with transient ICA obstruction were age-matched and had the same length of follow-up (7.2 ± 4.3 years) as patients with permanent ICA obstruction (6.2 ± 3.4 years). Patients with permanent carotid obstruction showed annual rates of 0.7% for ipsilateral carotid territory stroke and of 1.4% for any stroke, whereas patients with transient carotid obstruction showed annual rates of 0.3% for ipsilateral carotid territory stroke and of 0.6% for any stroke. These observations suggest that sICAD has a benign long-term prognosis with low rates of ipsilateral carotid territory and that the stroke rate in ICAD is not related to the persistence of severe carotid stenosis or occlusion. Conse-

quently, conservative treatment with antithrombotic agents is sufficient in most patients with sICAD causing severe stenosis or occlusion.

Treatment of dissecting aneurysm

Two monocenter, non randomized observational studies evaluated the clinical and radiological course of cervical aneurysms caused by sICAD during mean follow-up periods ranging from 3 to 4 years [13, 14]. Both studies included 44 patients with 49 aneurysms of the cervical ICA. Antithrombotic treatment included mainly aspirin; a few patients had no antithrombotics. During follow-up, aneurysms persisted in 64–99% with a decreasing size in 15–30%, whereas the remaining aneurysms resolved completely [13, 14]. No ischemia in the territory supplied by the ICA containing the aneurysm, carotid rupture or new local symptoms or signs on the side of the former dissection was observed during follow-up. These findings suggest that conservative management of cervical aneurysms caused by sICAD is associated with a benign long-term outcome.

Treatment of acute ischemic stroke

No controlled randomized trial has yet investigated the safety and efficacy of intravenous (IVT), intraarterial or mechanical thrombolysis in acute ischemic stroke caused by sICAD [15]. Therefore, all currently available data on this issue are derived from observational studies or case reports.

Intravenous thrombolysis

Ischemic stroke caused by sICAD was not an exclusion criterion in the placebo-controlled, randomized IVT trials in patients with acute ischemic stroke [16–19]. Furthermore, patients with sICAD were neither identified prior to thrombolysis nor retrospectively analyzed. SICAD is associated with a false lumen containing the wall haematoma and an intraluminal thrombus. An extension of the mural haematoma may cause local signs on the side of dissection or progression of luminal narrowing. Other potential complications include the development of a dissecting aneurysm, carotid rupture causing cervical or subarachnoid haemorrhage (SAH), and arterio-arterial embolism. Georgiadis *et al.* [15] reviewed 4 studies reporting about 50 patients with sICAD causing ischemic stroke treated with IVT [20–22]. No new or worsened local signs, rupture of the

dissected artery or SAH were observed [20–22]. One patient deteriorated during IVT, probably due to the displacement of a thrombus located at the site of dissection [21]. Mortality was 8%, while 40% of patients had a good outcome defined by a modified Rankin scale score of 0–2 points.

Intraarterial and mechanical thrombolysis

Arterial dissection was an exclusion criterion in the prolyse for acute cerebral thromboembolism (PROACT) II study [23]. The potential adverse effects of intraarterial (IAT) and mechanical thrombolysis, in addition to those mentioned for IVT, include the risk of catheter angiography including iatrogenic thrombo-embolism and catheterisation of the false lumen with rupture of the dissected artery. In the reported 6 patients with sICAD who underwent IAT, no rupture of the dissected vessel, cervical, subarachnoid or intracranial haemorrhage, or peri-interventional arterial embolism was described [24–27]. Patients with sICAD were not excluded from the mechanical embolus removal in cerebral ischemia (MERCi) trial [28]. Nedeltchev *et al.* [29] reported a patient with sICAD causing symptomatic occlusion of the middle cerebral artery who underwent mechanical thrombolysis without adverse events. These limited data indicate that intraarterial and mechanical thrombolysis can be performed safely and successfully in selected patients.

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Nationwide surveillance of IC anterior (or dorsal) wall aneurysm: with special reference to its dissecting nature

A. Satoh¹, T. Sugiyama¹, K. Hongo², Y. Kakizawa², S. Ishihara¹, M. Matsutani¹

¹Department of Neurosurgery, Faculty of Medicine, Saitama Medical University, Moroyama, Japan

²Department of Neurosurgery, School of Medicine, Shinsyu University, Matsumoto, Japan

Summary

Two hundred and twenty-one cases of IC dorsal aneurysm (ICDA) with subarachnoid hemorrhage (SAH) from 365 cases in the nationwide surveillance of ICDA (NSICDA) data bank were studied with special reference to the dissecting type. Dissection of the internal carotid artery (ICA) was confirmed in 50 out of 221 SAH cases. In 193 surgically treated cases, 40 were of the certified dissecting type. Including those with clinical features which strongly suggests the existence of dissecting changes in the ICA wall, 97 cases (55.6% of operated) were thought to be a dissecting type. Incidence of intraoperative bleeding is significantly higher and surgical outcome is significantly worse in the dissecting type than in the non-dissecting type. Treatment options for this peculiar and formidable aneurysm (An) are described.

Keywords: IC dorsal aneurysm; arterial dissection; nationwide surveillance.

Introduction

Aneurysms arising from the superior (or anterior) wall of the C1-C2 portion of the ICA have been known as an ICDA [6, 11–13] or, in Japan, IC anterior wall aneurysm [9, 13]. The term “blood blister-like aneurysm” has been widely used for the non-saccular and wide-based type as well [1, 2, 4, 7, 13, 14, 16–18]. ICDA has also been well known as a strange and dangerous aneurysm that easily ruptures at the neck during surgery [1, 3, 5, 7, 8, 10–14, 17, 18]. In addition, it often regrows and reruptures even after seemingly successful clipping [1, 3, 6, 8, 9, 11–15]. The reason why this peculiar An shows these strange clinical manifestations has not yet been fully clarified. In this report, we will show the data obtained from the nationwide surveillance on the ICDA in

Japan with special reference to its dissecting nature and present some illustrative cases from our own series.

Materials and methods

NSICDA was conducted in 2004 by retrograde registration of cases with ICDA treated in the period between 2001 and 2003 in hospitals approved by board committee of Japan Neurosurgical Society. ICDA was defined simply as an aneurysm on the superior (or anterior) wall of C1-C2 portion of the ICA without any branch artery around the neck. Four hundred and ninety-nine out of 1237 board-approved institutes (40.3%) responded to the surveillance. Eventually 365 cases with ICDA, of which 144 were incidentally found as an unruptured An, and 221 (comprising 60.5% of the total) found with SAH, were registered from 181 hospitals. In this report, 221 SAH cases were studied in detail especially with regard to its dissecting nature. Neurological grade on admission to hospital was assessed by Hunt-Kosnik's grading, and outcome at discharge by Glasgow Outcome Scale (GOS). Statistical analysis was made by Student's *t*-test, Chi-square test or Mann-Whitney *U*-test.

Angiographical characteristics of ICDA

ICDA arises exclusively from the superior (or anterior) wall of the C1-C2 portion of the ICA without any branching artery and often shows unusual and peculiar features on angiogram. It may look as a saucer-like bulging without any neck portion (Fig. 1A), a broad based and double contoured bulging (Fig. 1B) or a quite irregularly ragged shaped dome like a bunch of grapes (Fig. 1C). Abnormal narrowing of the ICA, proximal or distal to the dome, may frequently be associated with the ICDA (Fig. 1B). These peculiar figures of ICDA strongly suggest that it is different from the ordinary aneurysm with which neurosurgeons are facing in their daily practice, and the possibility is implied that many of these unique An might be dissecting in nature.

Cases with dissection in NSICDA

Fifty-six cases, comprising 15.5% of the 361 total cases, were registered to NSICDA as clinically confirmed dissecting aneurysm. Restricted to 221 cases manifested with SAH, 50 (22.5%) were dissecting. Postoperative mortality rate of dissecting aneurysm is 25% and that of the non-dissecting type is 17.8%; hence the overall surgical outcome of

Correspondence: Akira Satoh, Department of Neurosurgery, Faculty of Medicine, Saitama Medical University, 38 Moro-hongo, Moroyama, Iruma-gun, Saitama 350-0495, Japan. e-mail: satohak@saitama-med.ac.jp

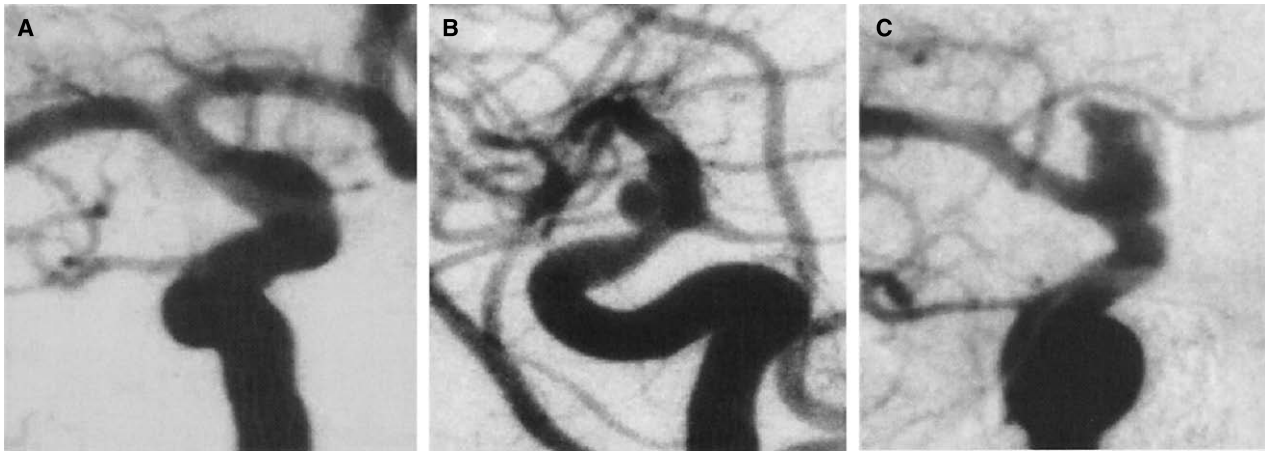


Fig. 1. Abnormal angiographic figures of ICDA: ICDA appears as various abnormal figures on angiogram. A) a saucer-like bulging without any neck portion, B) a broad based and double contoured bulging with abnormal narrowing of the ICA proximal (*or distal*) to the dome, C) an irregularly ragged shaped dome like a bunch of grape

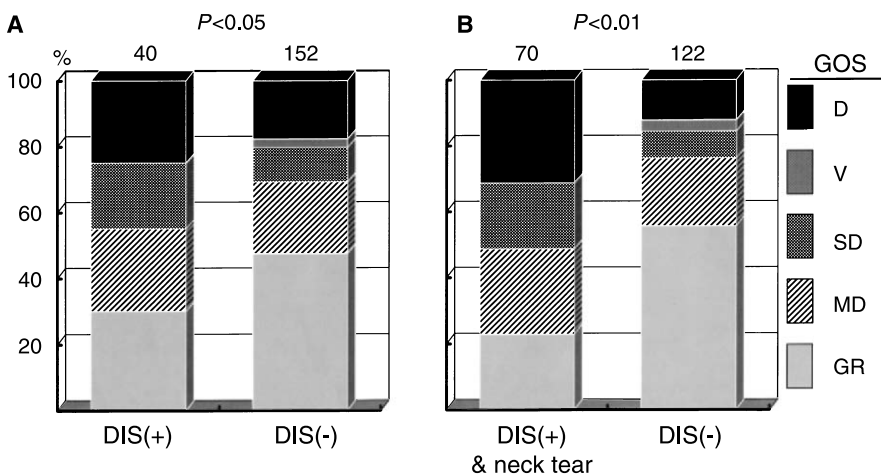


Fig. 2. Surgical outcome of dissecting and non-dissecting type ICDA: A) In 221 ruptured ICDA, 193 cases were surgically treated, of which 40 were reported to be a certified dissecting type. Surgical outcome of dissecting type is significantly ($P < 0.05$) worse than that of non-dissecting type. B) Adding 30 cases of non-dissecting type, in which intraoperative neck tear took place, to the dissecting group, surgical outcome is more significantly ($P < 0.01$) worse in the group than the group of remainders

the first type is significantly worse ($P < 0.05$) than that of the latter one (Fig. 2A). There were 30 cases out of 153 operated non-dissecting aneurysms in which serious intraoperative bleeding occurred in a way that the aneurysmal neck tore off from the parent ICA wall instead of bleeding from the dome. Since this kind of wall disruption (direct neck tear) is quite unusual in normal berry-type An, this type may well be regarded as dissecting in nature. Including cases with intraoperative neck tear definitely into the dissecting group, the postoperative mortality rate becomes 31.4%, and overall outcome is essentially the same as that of pure dissecting group (Fig. 2B).

Illustrative case

Case 1

A 45-year-old housewife was admitted with severe headache which had suddenly occurred 2 h earlier. She was awake and showed no neurological abnormality other than headache. Brain CT scan on admission

revealed SAH restricted within the right side of the basal and ambient cisterns (Fig. 3A). Cerebral angiogram on the day of admission demonstrated no An on the right side, while ICDA was present on the left C2 portion (Fig. 3B and C). Since no An was found on the right side where the blood clot was exclusively present, early surgical exposure was abandoned. The patient suddenly became semicomatose (grade 4) on day 5, and immediate angiogram revealed a newly developed round bulging on the superior wall of the right C2 portion (Fig. 3D). She died of brain damage caused by the rebleeding, and permission for autopsy was given by her family.

Histopathological finding of the right ICA disclosed dissection of the wall at the ruptured site (Fig. 4A), and dissection of the left ICA where unruptured ICDA was present (Fig. 4B).

Case 2

A 55-year-old female was transferred from a local hospital where she suffered the second SAH and had become semicomatose. Brain CT scan

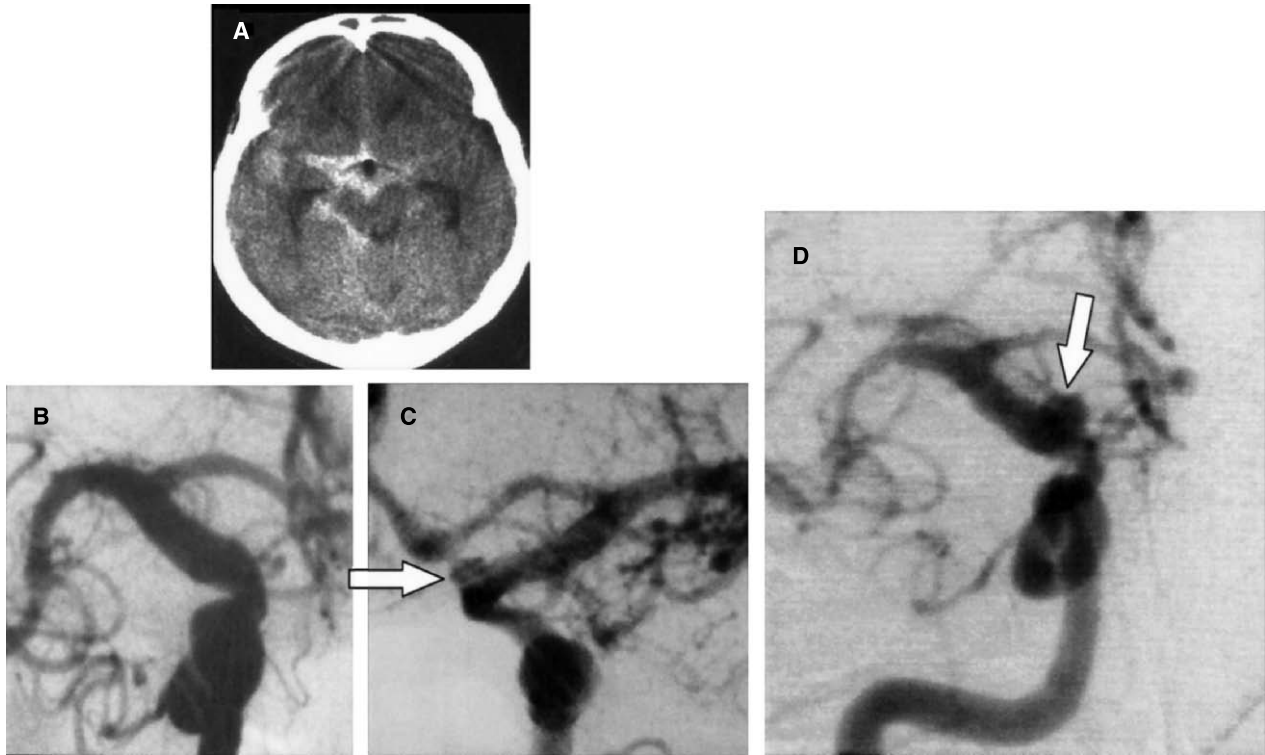


Fig. 3. Case 1; 45-year-old housewife with bilateral ICDA: A) Brain CT scan on admission revealed SAH restricted within the right side of the basal and ambient cisterns. B) Right carotid angiogram on the day of admission demonstrated no aneurysm. C) An aneurysmal bulging, which was definable as ICDA, was present on the left C2 portion (*arrow*). D) Right carotid angiogram taken immediately after the rebleeding on the day 5 revealed a newly developed ICDA in the C2 portion (*arrow*). See the text for the details

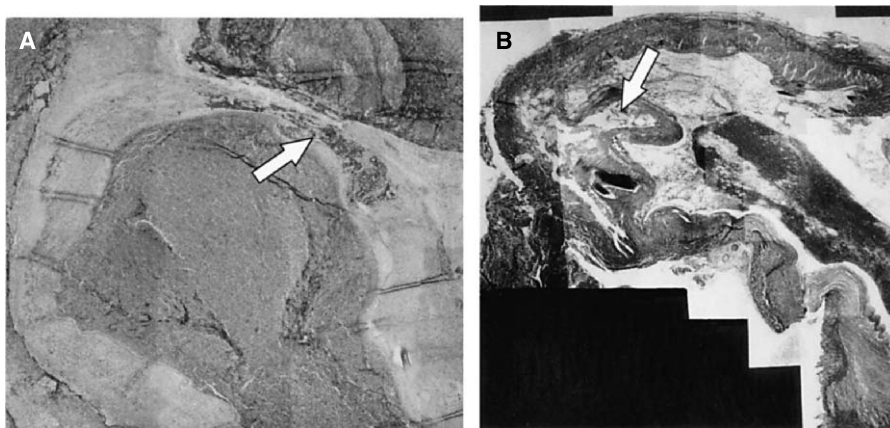


Fig. 4. Case 1; Histological findings of ICDA: A) A dissecting change of the right ICA wall at the ruptured site is shown (*arrow*). B) Dissection of the ICA wall (*arrow*) is present on the left side, where an unruptured ICDA was present. Elastica-Van Gieson stain; $\times 10$ magnification

demonstrated SAH with perifocal edema around the right Sylvian fissure and intraventricular hemorrhage (Fig. 5A). An angiogram taken at the previous hospital disclosed a fusiform bulging of the superior wall of the right C1–C2 (Fig. 5B). She died 5 days after admission, and autopsy revealed a definite dissection at the bulging site (Fig. 5C).

Discussion

ICDA is quite a peculiar type of An exhibiting unique features on angiogram as demonstrated in illustrative

cases and shows unusual clinical manifestations such as preoperative rapid growth of the dome, intraoperative neck tear, postoperative rebleeding or regrowth of dome, or postoperative ICA narrowing or obstruction [1, 3, 5, 7, 8, 10–15, 17, 18]. What sort of pathogenetic condition could produce these abnormal clinical characteristics of ICDA? In 1993 the authors suggested that many of the ICDAs might be dissecting in nature and aneurysmal bulging be a pseudo-An like fragile lump without any

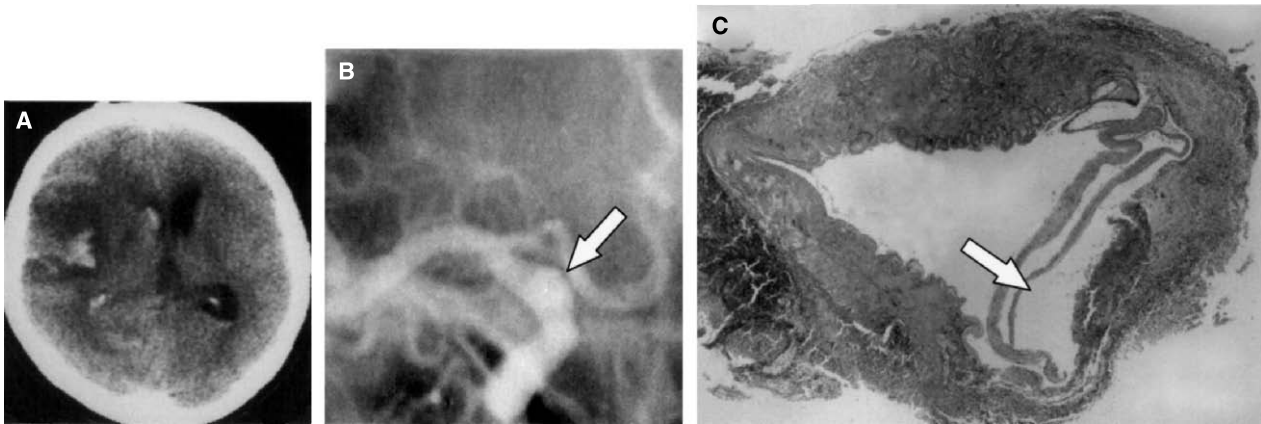


Fig. 5. Case 2; 55-year-old female with right ICDA: A) Brain CT scan on admission demonstrated SAH and intraventricular hemorrhage with perifocal edema around the right Sylvian fissure. B) Right carotid angiogram taken at the previous hospital disclosed a fusiform bulging of the superior wall of the right C1–C2 portion (*arrow*). C) Histology of the right ICA revealed a definite dissection at the bulging site (*arrow*). See the text for details. Elastica-Van Gieson stain; $\times 10$ magnification

definite histological evidence [10]. Soon after that proposal, we happened to have an autopsy case in which the ICA wall dissection was histologically confirmed (illustrative cases 1 and 2) [11]. Numerous reports have been published thereafter describing the dissecting change of the ICA wall found in cases with ICDA [1, 2, 6–8, 10, 11, 15]. Many of the ICDA can be regarded as usual berry type An because the wall and the neck of the dome seem to be as firm and thick as in the ordinary An and to which clipping can be done safely. On the other hand, many of the ICDA have undoubtedly an abnormally thin and fragile wall, where the clipping procedure may possibly cause disastrous neck tear leading very often to fatal outcome. The NSICDA study undertaken in Japan confirmed the inference that a dangerous and abnormally shaped ICDA is dissecting in nature since more than 20% of the registered SAH cases were reported to be definitely dissecting. Probably the true incidence of dissecting An is by far beyond this range because there are many that present abnormal clinical features like postoperative re-rupture or regrowth of the dome, extremely thinned wall of the neck, or intraoperative neck tear besides those registered as dissecting type. Including these abnormal type An into the dissecting group, at least 97 out of 193 operated SAH cases (50.3%) are suspected to be of the dissecting type. Incidence of intraoperative bleeding was significantly more frequent ($P < 0.01$) in the suspected dissecting group (55.6%) than in the remaining 96 cases (17.7%).

The overall surgical outcome was also significantly worse ($P < 0.01$) in the suspected dissecting group than in remaining cases (Fig. 6). Mortality of the former group is 28.9% while that of the latter is 17.7%.

It is well known that clipping is not safe and reliable treatment for arterial dissection. Since we can confirm that many ICDA are dissecting in nature, we have to warn that any attempt for simple clipping must be avoided if the facing ICDA shows any clinical or angiographic signs different from ordinary An. In an analysis of NSICDA data bank which we have published elsewhere [14], the postoperative outcome of early surgery within 96 h after the onset of SAH is significantly worse than that of delayed one ($P < 0.02$; data not shown in this report). At the chronic stage, healing processes of the dissecting site may set in and make the fragile tissue much firmer and tight, and this will allow the neck to be clipped in the ordinary way in most cases.

Judging from the data described here, we recommend the following option for the treatment of ICDA suspected to be of the dissecting type.

1. In case of early surgery, sufficient preparations for dangerous hemorrhage during the surgical procedure is required including securing the cervical ICA before opening the dura, drilling off the anterior skull base in order to secure wide surgical space and the proximal C2 portion, and to be ready for emergency EC-IC bypass.
2. A high-flow bypass and trapping of the ICA instead of attempting to obliterate the dome by clipping is probably the best option for early surgery at the present.
3. If self-expandable stent is available, stenting the C1–C2 portion with or without additional coil packing to the dome might be the optimal treatment [4, 16].
4. If patient's condition permits without rebleeding at the acute stage, delayed surgery should be considered.

Conclusions

Precise analysis of the NSICDA data base disclosed a high incidence of dissecting type An in ICDA manifested by SAH, of which surgical outcome is significantly worse than those without dissecting features. As the outcome of early surgery is significantly worse than that of delayed one, an attempt of simple clipping at acute stage without sufficient preparations is to be avoided in order to cope effectively with hazardous intraoperative bleeding.

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Clinical manifestation and treatment strategy for non hemorrhagic cerebral arterial dissection

A. Nishino, I. Suzuki, A. Utsunomiya, S. Suzuki, H. Uenohara, Y. Sakurai

Stroke Center, Department of Neurosurgery, Sendai Medical Center, Sendai, Japan

Summary

Spontaneous dissections of cerebral and cervical artery are relatively uncommon lesions in Japan. Although reported cases of cerebral and cervical arterial dissection are gradually increasing, natural history and optimal treatment remain unclear. The purpose of this study was to clarify the clinical features, natural history, and optimal treatment for patients suffering from non-hemorrhagic cerebral arterial dissection.

Fifty-four males and 14 females with cerebral or cervical arterial dissection were treated between January 1998 and December 2003 at the Stroke Center, Sendai Medical Center in Japan.

Although most patients suffering from non-hemorrhagic cerebral arterial dissection recover well by conservative treatments, some cases require surgical treatment if they are complicated by enlargement of aneurysms, cerebral ischemia due to bilateral vertebral arterial dissection.

Keywords: Arterial dissection; cerebral; non-hemorrhagic.

Introduction

Spontaneous dissections of cerebral and cervical artery are relatively uncommon lesions in Japan. There are two types of dissection: 1) the hemorrhagic type and 2) the non-hemorrhagic type. Although reported cases of cerebral and cervical arterial dissection are gradually increasing, natural history and optimal treatment remain unclear. The purpose of this study was to clarify the clinical features, natural history, and optimal treatment for patients suffering from non-hemorrhagic cerebral arterial dissection.

Subjects and methods

Fifty-four males and 14 females with cerebral or cervical arterial dissection were treated between January 1998 and December 2003 at the

Stroke Center, Sendai Medical Center in Japan. Patients mean age was 55.1 years (range 20–80 years). All patients in this study had a diagnosis of dissection based on the following angiographical or MRI findings: (1) double lumen, (2) pearl and string sign, (3) string sign, (4) intimal flap. The clinical manifestations and treatment were analyzed.

Results

The diagnostic clue provided 57 patients (76.5%) with cerebral ischemia, 7 (10.3%) with headache, 4 (4.4%) with neck mass, and 5 (8.3%) with brain routine check-up. Of the 68 patients, modified Rankin Scale on admission were 0–2 in 55 (80.8%) patients and 3–5 in 13 (19.2%) patients. As for the anatomic sites of the arterial dissection, 51 (74.7%) patients were observed in the vertebro-basilar system (vertebral artery in 40, basilar artery in 10 posterior cerebral artery in 5 and posterior inferior cerebral artery in 1) and 17 (25.3%) were in the carotid systems (cervical portion of internal carotid artery in 7, intracranial internal carotid artery in 3, middle cerebral artery in 3, anterior cerebral artery in (4). All patients in the acute stage were treated conservatively, however, seven (10.1%) patients showed symptomatic aggravations. Six out of the 7 patients exhibited cerebral ischemic symptoms and another suffered from subarachnoid hemorrhage followed by cerebral infarction (Case 1). Nine patients underwent surgeries. Of the 9 patients, we performed trapping of the dissecting aneurysms in 4 patients due to a tendency of aneurysmal enlargement after being confirmed by a follow-up angiography (Case 2). To prevent further cerebral embolism, dissecting aneurysm in 1 patient at the cervical internal carotid arterial portion was treated surgically by resection. STA-SCA bypass surgery was performed in

Correspondence: Akiko Nishino, Stroke Center, Department of Neurosurgery, Sendai Medical Center, 2-8-8 Miyagino, Miyagino-ku, Sendai, Japan. e-mail: anishino@jun.ncvc.go.jp

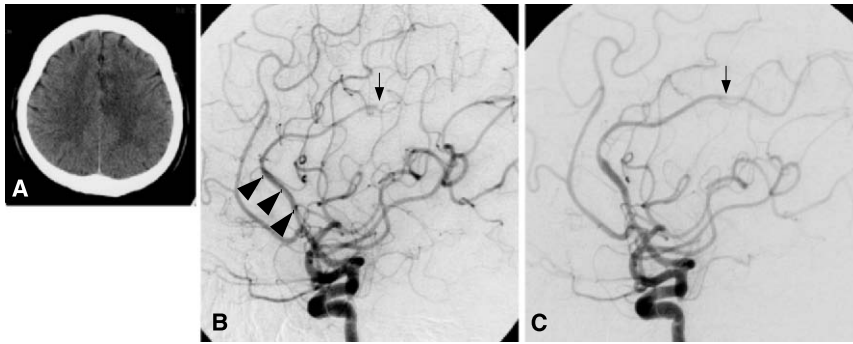


Fig. 1. Case 1 (A) CT scan on admission showing small infarction at the territory of the left anterior cerebral artery. (B) Left carotid angiogram on admission showing fusiform dilatation at the A2 segment. (C) Left carotid angiogram taken 14 days after the onset showing progressive dilatation at the lesion (see text)

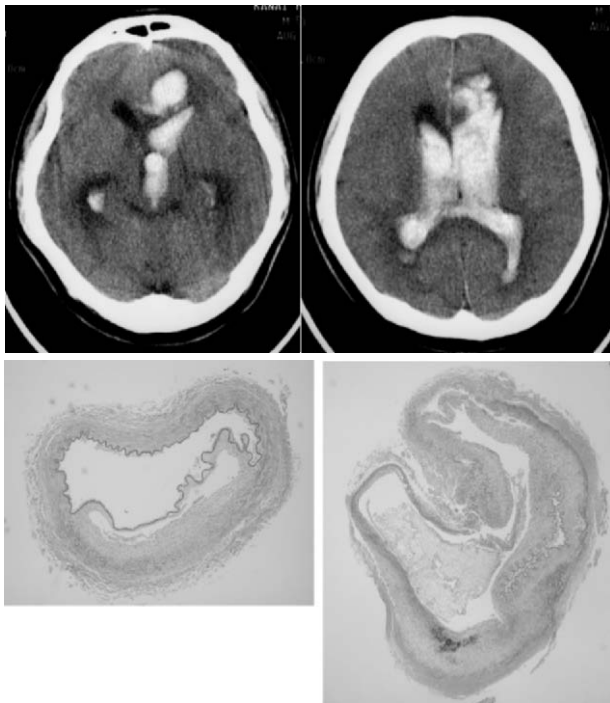


Fig. 2. Case 1 Upper: CT scan taken 21 days after the onset showing massive hematoma. Lower: photomicrographs showing histology of the left A2 segment. Intramural hematoma is observed

4 patients for hemodynamic stress due to the bilateral vertebral arterial dissection (Case 3). Clinical outcomes of the 68 patients at discharge of hospital were excellent or good in 40 patients (58.8%).

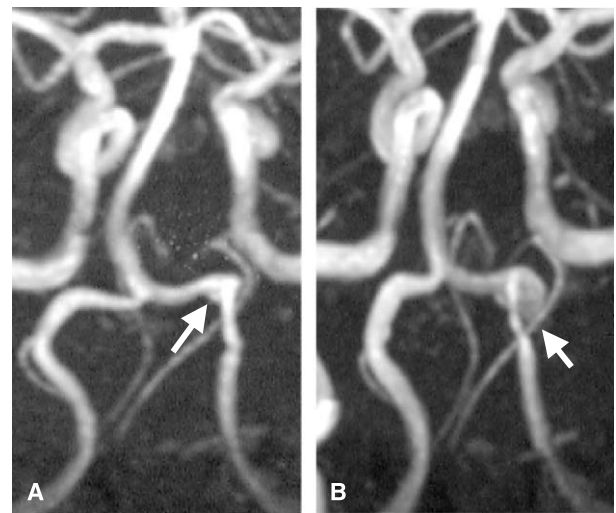


Fig. 3. Case 2 (A) MRA on admission showing fusiform dilatation of the intracranial left vertebral artery. (B) Follow-up MRA taken two months later showing progressive dilatation of the lesion

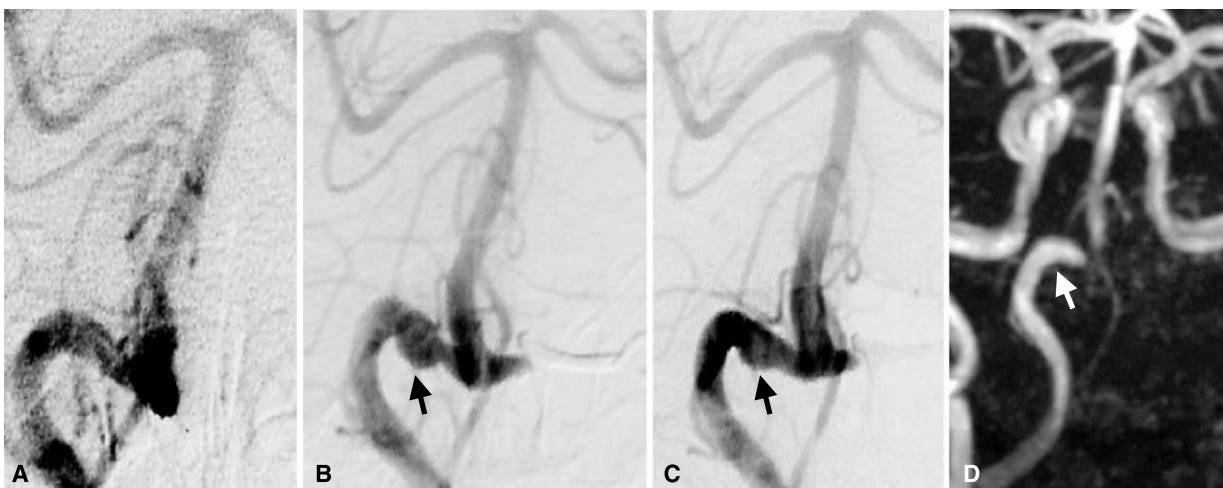


Fig. 4. Case 2 postoperative MRA. (A) Just after the operation. (B–D) One month, two months, six months after the operation

Case 1

A 41-year-old man experienced severe headache and right hemiparesis. CT scan on admission revealed small infarction at the territory of the left anterior cerebral artery (Fig. 1A). Left carotid angiogram showed fusiform dilatation at the A2 segment and occlusion at the distal portion (Fig. 1B). Follow-up angiography at day 14 revealed progressive dilatation at A2 segment and recanalization at the distal portion (Fig. 1C). Twenty-one days after the onset, he fell into cardiac arrest suddenly. CT scan indicated rupture of the dissecting aneurysm after the ischemic onset (Fig. 2 upper). Histology of the left A2 segment showed intramural hematoma (Fig. 2 lower).

Case 2

A 43-year-old man suffered sudden onset of severe headache. MRA showed pearl and string sign at the left intracranial vertebral artery (Fig. 3A). Follow-up MRA two months later indicated enlargement of the dissecting aneurysm (Fig. 3B). We performed trapping of the dissecting aneurysm to prevent rupture. Post-operative angiogram showed disappearance of the dissecting aneurysm. One month later follow-up MRA revealed newly formed pearl and string sign on the contralateral vertebral artery. Fortunately, this dissecting lesion seemed to stabilize on the following angiography (Fig. 4A–D).

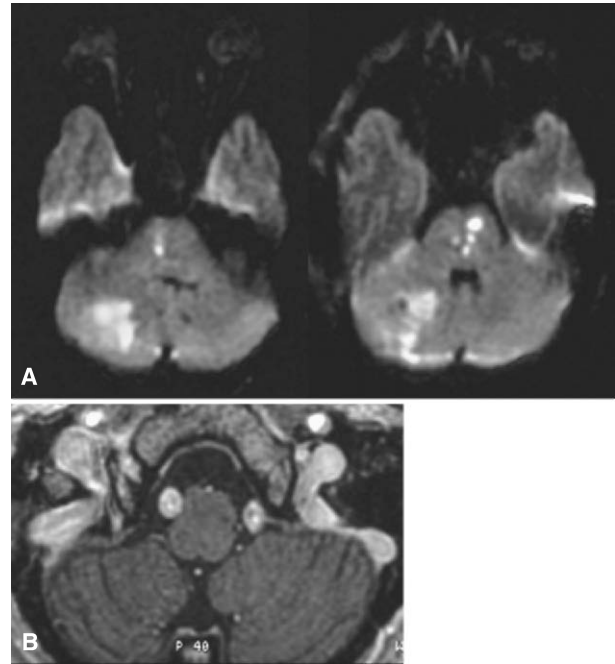


Fig. 5. Case 3 MRI on admission showing pontine and cerebellar infarction and double lumen sign on both vertebral arteries

Case 3

A 45-year-old woman experienced vertigo, nausea and gradually became unconscious. MRI performed 7 days after the onset showed pons and cerebellar infarction (Fig. 5A). Enhanced MRI showed double lumen sign (Fig. 5B). Angiography revealed string signs of the bilateral vertebral arteries (Fig. 6A, B). There was poor

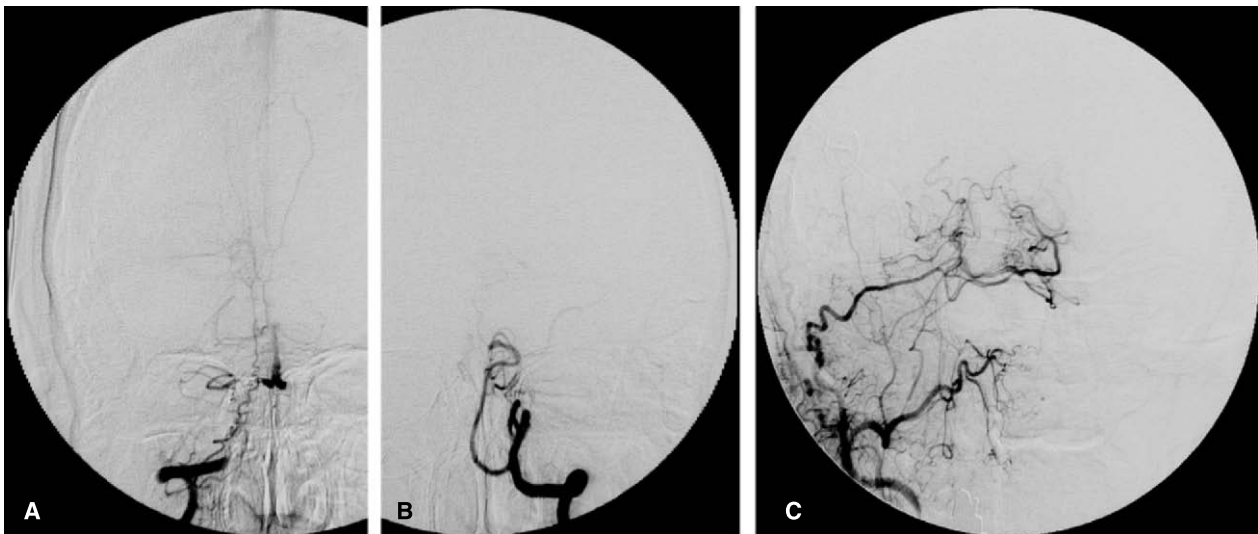


Fig. 6. Case 3(A, B) Preoperative angiography showing the string sign of the bilateral vertebral artery. (C) Postoperative angiography showing patency of STA

collateral flow. As she presented with progressive stroke, STA-SCA bypass was performed emergently. Post-operative angiogram showed patency of STA (Fig. 6C) and her consciousness had recovered.

Discussion

Recently reported cases of cerebral and cervical arterial dissection are gradually increasing [3–5]. Intracranial and posterior circulation tended to be common locations for arterial dissection in Japan, while cervical carotid artery are common in Europe or U.S. [1, 2, 4, 5].

Although most patients suffering from non-hemorrhagic cerebral arterial dissection recover well by conservative treatments, some cases require surgical treatment if they are complicated by enlargement of

aneurysms, cerebral ischemia due to the bilateral vertebral arterial dissection.

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Hemorrhagic cerebral dissecting aneurysms: surgical treatments and results

Y. Yonekawa, D. Zumofen, H.-G. Imhof, P. Roth, N. Khan

Department of Neurosurgery, University Hospital Zurich, Zurich, Switzerland

Summary

Introduction. Cerebral dissecting aneurysms are an increasingly recognized etiology of subarachnoid hemorrhage SAH and cerebral stroke. Hemorrhagic dissecting aneurysms of the anterior circulation have been considered to be somewhat different to those of the posterior circulation not only in terms of their pathophysiology, but also in terms of their management. Herewith our series of hemorrhagic dissecting aneurysms of the internal carotid artery ICA, vertebral artery VA, basilar artery BA and some of those of distal cerebral arteries is presented and compared to the series reported in the literature. Therapeutic consideration in the light of our experiences emphasizing the significance of aneurysm entrapment in combination with bypass surgery is presented.

Material and methods. During the last 13 years over 1000 patients with cerebral aneurysms were treated surgically in our department. Hemorrhagic dissecting aneurysms were diagnosed in 26 patients. Diagnosis was based on neuroradiological findings as well as intraoperative findings. All patients underwent surgical intervention. Clinical findings of these patients were analysed retrospectively. Follow-up outcomes were evaluated according to the Glasgow Outcome Scale GOS at 3 months after treatments.

Results. Location of 26 dissecting aneurysms was: ICA 11 cases (42%), VA 9 cases (35%), BA 3 cases, MCA 2 cases and PCA (P1 segment) one case. Primary surgical treatments were performed on day 3.7 of SAH on average. Clinical manifestation of dissecting aneurysms of the ICA and their outcome was more severe compared with those of the VA ($p < 0.01$): WNFS grade 3.1 vs 2.4 and GOS score 3.4 vs 4.3. As a conventional neck clipping procedure was problematic or impossible (aneurysm recurrence after clipping, premature rupture at the time of exposure or clipping), entrapment (or proximal ligation) plus EC–IC bypass procedure was the most frequent final definitive method of surgical treatment (9/26 35%: ICA 6/11, VA 1/9 and MCA 2/2) followed by proximal ligation or trapping only 7/26, neck clipping 7/26 and coating 4/26.

Conclusions. Hemorrhagic dissecting aneurysms still remain problematic in their diagnosis and treatment. One has to be aware of the diagnostic possibility of dissecting aneurysms as an etiology of SAH. Neurosurgeons have to be prepared to be able to manage complex surgical situations also by the use of EC–IC bypass, as its combination with entrapment procedure can be the final treatment of choice. Less invasive endovascular technique is in evolution but its availability and superiority are still to be settled.

Keywords: Dissecting aneurysms; aneurysm clipping; ligation; entrapment; bypass surgery.

Introduction

Intracranial dissecting aneurysms remain a diagnostic and therapeutic challenge. Their occurrence in various locations of the anterior circulation and posterior circulation has been reported to date [1–7, 9–11, 14–24]. Terminal portion of the internal carotid artery ICA, V4 portion of the vertebral artery VA and the basilar artery BA trunk seem to be the frequent locations. Hemorrhagic dissecting aneurysms have been reported to be different from usual saccular aneurysms in their pathophysiology and clinical presentations. Those of the anterior circulation have been reported to be different from those of the posterior circulation not only in the clinical presentation but also in their management [20]. Intracranial dissecting aneurysms of the posterior circulation presenting with SAH have been reported to have a high incidence of recurrent bleeding within the first days after the ictus (30% to 69%) and to have a mortality of 46.7% in case of a second bleeding [4, 18]. Ongoing treatment options vary in conventional microsurgical treatment and recently also in endovascular treatment. Surgical treatment include radical neck clipping, proximal ligation, trapping with or without bypass combination [6, 14, 15, 24, 26]. Experiences in endovascular proximal ligation by balloon occlusion, stenting with coiling have all been recently reported [3, 21]. The purpose of this communication is to present our experience on 26 patients of hemorrhagic dissecting aneurysms with clinical presentation, conventional microsurgical treatments and their results. Our strategies and their rationale are also reported and discussed comparing with those of literature reported to date.

Correspondence: Prof. Dr. med. Yasuhiro Yonekawa, Neurochirurgie FMH, Haldenbachstrasse 18, CH-8091 Zurich, Switzerland.
e-mail: yasuhiro.yonekawa@usz.ch

Patients and methods

Out of over 1000 patients with cerebral aneurysms surgically treated during the last 13 years (1993–2006) in our institution, a total of 26 patients were diagnosed as having hemorrhagic dissecting aneurysms. On admission, clinical documentation including history and neurological assessment was done along with CT scanning and digital subtraction angiography DSA prior to surgical treatment in the acute stage of SAH. The dissecting character of the aneurysms was diagnosed together with our neuroradiologists by pre-operative DSA, and confirmed during surgery. The following DSA findings are considered to be representative criteria for hemorrhagic dissecting aneurysms: 1. (fusiform) aneurysmal outpouching 2. string sign or pearl and string sign 3. false lumen and/or intimal flap [27]. Dissecting nature of aneurysms were always confirmed at the time of surgery: Peculiar findings of dissecting nature of discoloured aneurysm wall covered with thick clots of tough and extensive adherence. Post-operatively, DSA was performed between 1 week and the 10th post-operative day. Follow-up neurological examination was done routinely after 3 months usually on outpatient basis along with neuroradiology including DSA at need.

Results

The series consisted of 26 patients (7 males and 19 females) with the age ranging from 25 to 71 year-old (51 year-old on average). Primary surgical treatment took place from day 0 to day 13 (day 3.7 on the average) (Table 1).

Location of aneurysms

ICA in 11 cases (42%), VA in 9 cases (35%) and BA in 3 cases (12%) and others (M1 1, M3 1, P1 1). Eleven ICA dissecting aneurysms originated in 9 cases from the anterior(-medial) wall of the distal ICA segment (C1 6, C1-2 3) and in 2 cases from the inferior wall of the C1 segment. The 9 vertebral dissecting aneurysms consisted of 7 cases (75%) at the V4 segment (with PICA origin inclusion in 4 cases and no inclusion in 3 cases) and 2 cases (25%) at the V3 extradural segment. Additionally, aneurysm opacification after a primary “negative” angiography or remarkable increase in size took place in 4 cases (2 basilar trunk aneurysms, one ICA aneurysm and one P1 aneurysm).

Clinical presentation: Fisher score, WFNS grade and GOS

Mean Fisher grade was 3.1 (ICA 3.3, MCA 2.5, VA 2.9 and BA + P1 3.3). Mean WFNS grade of the whole series before surgery was 3 (ICA 3.1, MCA 3, VA 2.4 and BA + P1 4), and mean GOS at 3 months was 3.7 (ICA 3.5, MCA 4, VA 4.3, BA + P1 and 2.5).

Surgical treatment

Primary surgical treatment was performed on day 3.7 on average. Second surgical treatment was necessary in 6 out of 26 cases (VA 1 due to rebleeding with aneurysm enlargement in 4 days in spite of proximal ligation, BA 1 due to rebleeding corresponded with coil compaction, ICA 3 due to aneurysm recurrence in 11, 12 days and 7 months in spite of wrapping plus neck clipping and MCA 1 due to rebleeding associated aneurysm enlargement in 36 days in spite of proximal ligation plus EC–IC bypass. Interval from the first surgery to second one was usually within a month (4, 11, 11, 18, 36 days and 7 months). Definitive surgical treatment procedure of the series was entrapment (or proximal ligation) plus EC–IC bypass in 9 cases (VA 1, ICA 6 and MCA 2) followed by trapping (or proximal ligation) only in 7 cases (VA 6 and P1), neck clipping in 7 cases (BA 1 and ICA 6) and coating in 3 cases (VA 2, BA 1).

Significant profuse bleeding due to premature rupture at the time of aneurysmal exposure or neck clipping necessitating temporary or permanent occluding procedure of the parent artery took place in 8 cases (ICA 7 and P1 1).

Illustrative case 1 (Fig. 1)

RA 58 year-old-female (#16) presented with initial symptoms of sudden headache, meningism, nausea and vomiting. In the emergency room, she had a GCS 14 without any focal neurological deficits. Initial CT scan revealed SAH with Fisher 3. She then suffered from a single generalized seizure with GCS falling down to 8. After sedation and intubation, she was transferred to our intensive care unit with WFNS 4. On DSA, a medially directed “blister” dissecting aneurysm of 4 mm was found on the anteromedial wall at the C1–C2 transitional portion (Fig. 1a). Premature rupture with profuse bleeding took place during exposure of the aneurysm neck in which dissecting nature of the discoloured aneurysm wall was confirmed. This was covered and coated with thick clot extending from the anteromedial wall to the right optic nerve (Fig. 1e). The aneurysm had to be trapped by cross clamping of the ICA placing a proximal clip just distal to the origin of the ophthalmic artery and a distal clip at the transitional zone of C1 and C2 obliquely so that the back flow from the posterior communicating artery PcomA to the C1 portion hence also the flow to the anterior choroidal artery AChoA was warranted. Finally, an EC–IC bypass was constructed between the frontal branch of the STA and the middle temporal artery M3 (Fig. 1f). On day 6 after SAH,

Table 1. *Our cases of dissecting aneurysms (1993–2006)*

Name, M/F, Age	Location	Procedure	WFNS/ Fisher	GOS (3 Ms)	Comments	
1. HK, F, 48	Rt V4, PICA origin included, 5 mm	Day 3, 1. Proximal ligation Day 7, 2. Trapping + STA-PICA bypass	II	3	5	Rebleed with aneurysm enlargement in 5 days
2. BJ, F, 60	Rt V4, PICA origin included	Day 3, Proximal ligation, OA-PICA bypass	I	2	5	Non patent OA-PICA bypass
3. HH, M, 51	Rt V4, PICA origin intact, 4 × 5 mm	Day 1, Trapping	IV	3	3	Multiple small infarctions
4. SH, F, 71	Rt V4, PICA origin intact, 1 cm	Day 2, Proximal ligation	IV	3	3	Partially thrombosed, Postoperative Wallenberg syndrome
5. NM, F, 46	Lt V4, PICA origin included, 4 mm	Day 4, Proximal ligation	III	3	5	
6. MH, M, 51	Lt V4, PICA origin included, 1 cm	Day 2, Incomplete trapping to keep PICA patent	III	3	5	Unruptured aneurysm on the right V4
7. WA, F, 36	Lt V4, PICA origin intact, 4 mm	Day 2, Trapping	III	3	5	
8. VH, F, 63	Lt V3	Day 13, Coating	I	4	5	Posterior fossa SDH
9. FM, M, 47	Lt V3	Day 12, Coating	I	2	5	SAH, Aneurysm V3
10. GH, F, 52	Basilar trunk, 7 mm	Day 7, Coating	V	4	3	Enlargement within a week
11. KP, M, 54	Basilar trunk, 5 mm	Day 8, Coiling Day 19, Neck clipping	III	3	1 (died of vasospasm)	Small overlooked on prim angiogr., enlarged in a week, Coil compact + rebleeding
12. DE, F, 51	Basilar trunk, 1 × 1.5 mm	Day 5, Coating	IV	3	5	
13. CA, F, 33	Rt P1, fusiform, 1 cm	Day 4, Basilar trunk ligation	IV	3	1	3 Ms before ICH with no angiographic abnormality
14. WH, F, 68	Lt C1, posterior-medial, 5 mm	Day 0, Neck clipping, Angled fenestrated clip	V	4	1	SDH, Prem. rupture
15. KA, M, 60	Rt C1, anterior wall, 3 mm	Day 7, 1. Wrapping + Neck clipping Day 25, 2. Trapping + STA-M2 bypass	IV	3	5	Aneurysm recurrence in 18 days
16. RM, F, 52	Rt C1, anterior medial wall, 4 mm	Day 2, Trapping + STA-M3 bypass	IV	3	5	Prem. rupture
17. IA, F, 62	Lt C1, anterior wall, 4 mm	Day 0, Trapping + STA-M3 bypass	IV	3	1	Prem. rupture
18. LM, M, 25	Lt C1, anterior wall, 1.3 cm	Day 3, Ligation (at C2) + STA-M3 bypass	I	2	5	
19. BS, F, 48	Rt C1, inferior wall, 5 mm	Day 3, Neck clipping together with Pcom origin, Angled fenestrated clip	II	3	5	EC–IC bypass against vasospasm
20. HI, F, 51	Rt C1, anterior medial wall, 8 mm	Day 7, 1. Neck clipping + Coating 7 Ms later, 2. Neck clipping	I	4	5	Prem. rupture, Recurrent aneurysm, EC–IC bypass non patent, Multisaccular aneurysms
21. LM, F, 65	Rt C1, posterior medial wall, 3 mm	Day 5, Neck clipping	IV	3	2	Primary angiogram negative, four days later angiogram positive
22. GR, F, 59	Rt C1–C2, anterior medial wall, 1 cm	Day 4, Trapping + STA-M3 bypass	II	4	4	Prem. rupt., EC–IC bypass non patent
23. SB, F, 70	Lt C1–C2, anterior medial wall, 1 cm	Day 1, Neck clipping	III	3	2	Prem. rupture
24. BA, F, 27	Rt C1, anterior wall, 1 cm	Day 1, 1. Wrapping + Neck, clipping Day 12, 2. Reclipping at neck	IV	4	1	Prem. rupture, Rebleeding and recurrent aneurysm in 11 days
25. KS, M, 43	Rt MCA, M1 segment, 1 × 2 cm	Day 1, 1. C1 ligation + STA-M3 bypass Day 37, 2. M1 ligation	IV	3	3	Partially thrombosed, Recurrent bleeding and aneurysm enlargement after C1 ligation
26. RF, M, 34	Rt MCA, M3 segment, 1 cm	Day 5, Trapping + STA-M4 bypass	II	2	5	

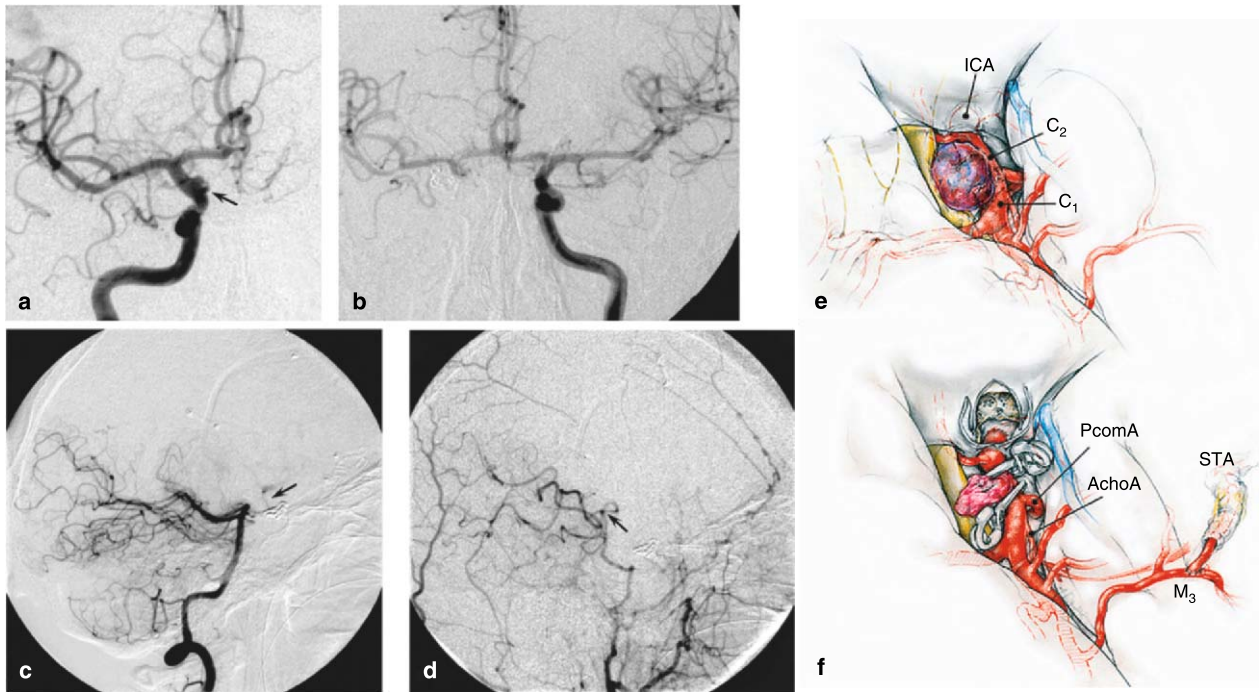


Fig. 1. Illustrative case 1 (#16): A case of typical blister-dissecting aneurysm located anteromedial wall of the ICA at C1–C2 transitional portion. Surgical treatment with aneurysm entrapment combined with STA–MCA bypass. Notice the oblique placement of the distal clip in order to warrant the retrograde flow through the PcomA (See text)

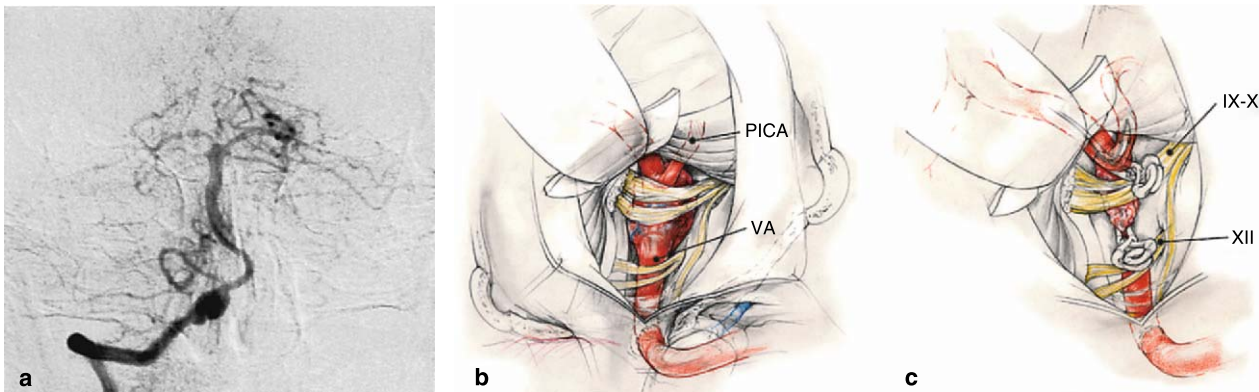


Fig. 2. Illustrative case 2 (#3): A case of dissecting aneurysm of the VA at V4 segment. Surgical treatment with its entrapment preserving the PICA flow via the contralateral VA (See text)

super-selective Papaverine spasmolysis at the time of follow-up angiography had to be performed against symptomatic vasospasm. This DSA showed a good collateral circulation to the distal part of the entrapped right ICA via the anterior communicating artery AcomA, the PcomA and the EC–IC bypass (Fig. 1b–d). Clinically, no new neurological deficits were encountered except for diplopia due to right VI nerve paresis which recovered promptly during admission. Final GOS was 5 also after 14 months of follow-up.

Comment: This case is a typical ICA blister-dissecting aneurysm at the anteromedial wall of the C1–C2 transitional portion, in which also a typical premature rupture took place at the time of exposure, so that entrapment of the aneurysm plus EC–IC bypass procedure was necessary. Direct flow connection between the PcomA–AchoA and the distal part of ICA trapping is considered to be of cardinal importance in order to have collateral circulation as much as possible, so that the distal cross clamping clip should have to be placed

obliquely. An EC–IC bypass was constructed for further augmentation of the collateral flow.

Illustrative case 2 (Fig. 2)

HH 51-year-old male (#3) suffered from intense and constant headache since 3 days. Sudden increase of the headache originating in the occipital region accompanied by nausea/vomiting was followed by loss of consciousness and cardio-pulmonary resuscitation. The patient had history of intermittent atrial fibrillation. On admission to a regional hospital, GCS was 12 associated with motor weakness of both lower extremities. CT scan showed SAH of Fisher 3 and fresh multiple and bilateral small infarctions in the territory of posterior circulation. DSA performed after transfer to our clinic revealed a ruptured aneurysm at the non-dominant right V4 segment just proximal to origin of the posterior inferior cerebellar artery PICA (Fig. 2a). Just prior to surgery on day 1, WFNS was 4. A right sided lateral suboccipital craniotomy combined with a partial condylectomy was performed in the sitting position followed by exposure of the aneurysm which revealed to be a typical dissecting aneurysm of an eccentric fusiform type with wall discoloration at the V4 segment. The PICA originated just from the distal portion of the VA having the distal

end of dissecting aneurysm (Fig. 2b). The aneurysm was trapped as the Fig. 2c shows after removal of a tough hematoma around it. Placement of the distal clip was problematic due to obscure delineation between the distal end of the dissection and the origin of the PICA. Two small medullary perforators originating from the entrapped segment had to be sacrificed. Bypass surgery was not performed, as the PICA filling was well from the dominant left side VA via the retrograde flow. This could be confirmed by micro-Doppler sonography. Post-operatively, the patient was conscious and able to follow basic orders and recovered gradually. Loss of motor strength on both lower extremities was however persistent correlating to the multiple small infarctions. Post-operative hydrocephalus had to be treated with a ventriculo-peritoneal shunt. Follow-up angiography displayed regular findings without aneurysm opacification and the right PICA was filled by the left VA. GOS remained 3 at the time of the 6 month follow-up.

Comment: This typical dissecting VA aneurysm on the non dominant side was trapped with preservation of flow to the PICA via the contralateral dominant VA. flow. Only proximal ligation of the VA might have induced its enlargement eventually with rebleeding due to the retrograde flow as in our case #1. Inclusion of the origin of the PICA in the aneurysm segment would

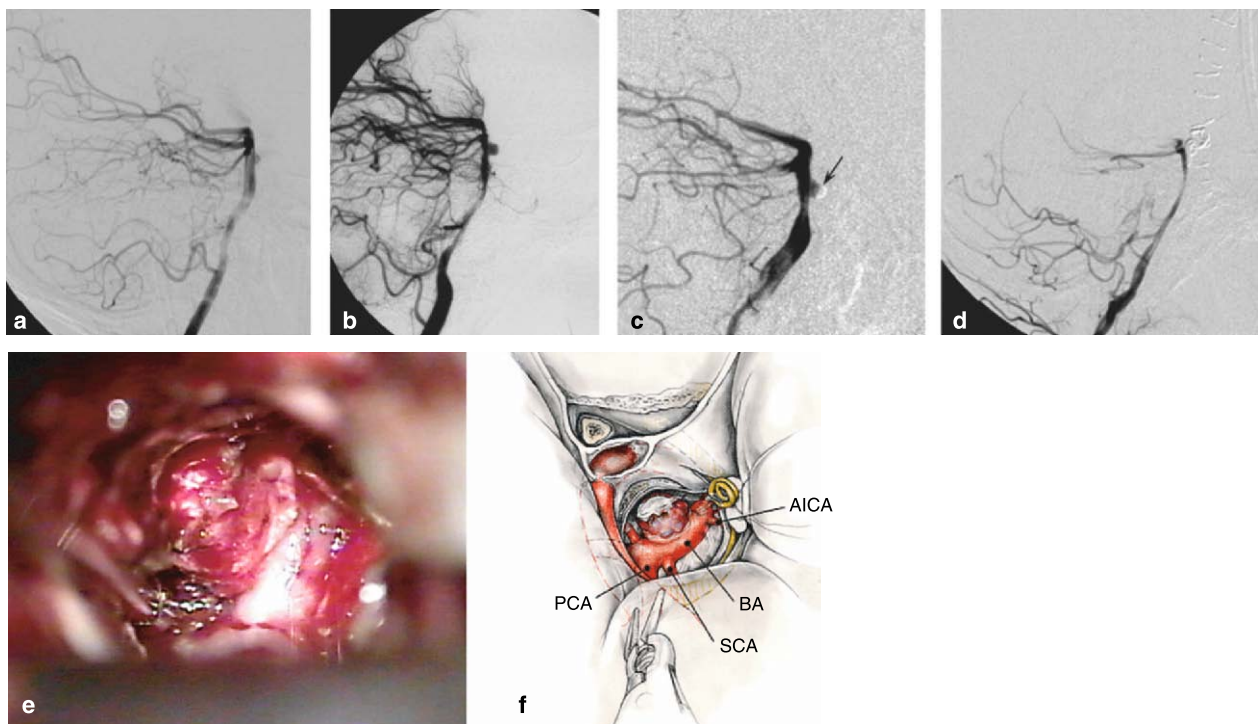


Fig. 3. Illustrative case 3 (#11): A case of basilar trunk dissecting aneurysm. Finally clipped by transcavernous approach after SEAC and extended posterior clinoidectomy (See text)

have necessitated simultaneous construction of an EC–IC bypass, OA-PICA or STA- PICA bypass as in our case #1.

Multiple small infarctions in the territory of posterior circulation having caused motor weakness of both lower extremities might have been induced at the time of cardiopulmonary resuscitation in the presence of a history of intermittent atrial fibrillation.

Illustrative case 3 (Fig. 3)

KP 46 year-old male (#11) with mental retardation felt sudden dizziness and blacked out at the time of sitting after having played foot ball. This was soon followed by nausea vomiting and increasing headache. On admission to our clinic GCS was 13, WFNS II and Fischer 3 of SAH and DSA thereafter displayed “no” origin of the hemorrhage. A small outpouching at the basilar trunk was overlooked (Fig. 3a). A follow-up angiography 5 days later disclosed a enlarged dissecting aneurysms of 5 mm at the basilar trunk (Fig. 3b), so that this was coiled with endovascular method successfully on day 8. Repeated DSA on neurological deterioration showed a remarkable vasospasm, so that Papaverin spasmolysis followed by the treatment of barbiturate-coma therapy and hypothermia in our intensive care unit. Follow-up CT scan on day 17 displayed unexpectedly rebleeding associated with aneurysm refilling with coil compaction as shown on DSA (Fig. 3c), so that aneurysm clipping by craniotomy (with the use of selective extradural anterior clinoidectomy SEAC, posterior clinoidectomy and transcavernous approach in order to expose the aneurysm at the basilar trunk) was performed on day 19 and with WFNS III (Fig. 3e, f). After having an unremarkable regular finding on follow-up CT on the day after surgery, the ICP started to rise. CT scans thereafter showed newly developed multiple infarctions in the territory of all cerebral arteries corresponding with severe vasospasm along with the successfully occluded aneurysm on DSA on day 22 (Fig. 3d). The increase in ICP could not be brought under control in spite of all possible therapeutic means and the patient expired late at night on day 22.

Comment: This is a typical case in which an small aneurysm with unexpected localization was overlooked at the time of the first DSA soon after a SAH, but recognized on its enlargement on reangiography performed after a while. The aneurysm was coiled successfully with endovascular procedure at first considering its technically difficult location by direct surgery. Refilling of the aneurysm might have took place due to neck width

of the aneurysm and not due to its dissecting nature. At the time of surgery, the findings of aneurysm were corresponding to those of dissecting aneurysm: typical discoloration of the wall covered with thick clots stuck tightly (Fig. 3f). The aneurysm could be occluded by neck clipping including part of adjacent healthy parent vessel (basilar artery) wall into the blades by using the transcavernous approach preceded by SEAC and posterior clinoidectomy after a right pterional craniotomy [30].

Discussion

Early reports on hemorrhagic intracerebral dissecting aneurysms including its treatment strategies are represented by the work of Friedman *et al.* in 1984 [7]. Thereafter, a number of reports on dissecting aneurysms at various locations along with proposed treatment strategies have been published especially for those of the posterior circulation [2, 4, 6, 12–15, 17–21, 23–26]. Anxionnat *et al.* published on endovascular and/or on conservative strategies for their series of hemorrhagic dissecting aneurysms of different locations of the posterior circulation in 2003 [3]. In regard to the anterior circulation, Ohkuma *et al.* published in 2002 an extended series of 40 dissecting aneurysms in a Japanese population, in which 32 were hemorrhagic ones [17]. These were located either on the ICA (18 cases), MCA (9 cases), and on the ACA (5 cases). We compared our present series with those reported by Ohkuma *et al.* (hemorrhagic group), Anxionnat *et al.* [3] and by Yamaura *et al.* on nation wide survey of Japan NWSJ in 1998 [25, 26] (Table 2).

Hemorrhagic dissecting aneurysms in the Caucasian population seem to occur with similar frequency in the anterior and the posterior circulation (50% vs 50%) by contrast to the results of NWSJ (2% vs 90%). One has to be careful, however, about cursory interpretation in regard to this distribution difference. Inclusion criteria of some special types of aneurysms of the ICA especially “blister” ICA aneurysms in the classification of dissecting aneurysms is considered to be problematic [10, 12, 19]. Our cases were diagnosed not only on angiographic findings but also on intraoperative findings as has been mentioned above. Thus we could differentiate blister-dissecting aneurysms from so called paraclinoid aneurysms, anterior wall aneurysms and/or posterior wall aneurysms [13, 19, 21, 29]. The diagnosis of dissection aneurysms of the ICA itself has to be questioned and discussed, as their frequency seems to be, in the authors’

Table 2. Comparison of our cases with those of literature: clinical presentation and treatment

	Present series	Ohkuma <i>et al.</i> [20]	Anxionnat <i>et al.</i> [3]	NWSJ [28]
Cases	26 (VA 9, BA 3, PCA 1, ICA 11, MCA 2)	32 (ICA 19, MCA 12, ACA 5)	27 (ACA 1, VA 19, BA 2, PICA 2, SCA 2, PCA 1)	191 (VA 160, BA 10, ICA 4, others 15)
Ant circul AC	13 (50%)	100%	3.7%	2 + α %
Post circul PC	13 (50%)	0%	96.3%	89 + α %
Clinical presentation				
Mean Fisher score	3.1: AC 3.2 PC 2.8	3.0	3.1	
WFNS grade	3.0: AC 3.1 PC 2.9	3.0	2.0	
GOS	3.7: AC 3.6 VA 4.3 PC 3.7	2.8	VA 4.1	4.2 (Cran) 3.9 (EV) 4.0 (Total)
Treatment				
Trapping + Bypass	34.6%			
Trapping	26.9%	28.1%*		12.1%*
Pro Lig only	(8%)			24.3%*
Neck clipping	26.9%	15.6%		1.2%
Coating – wrapping	11.5%	25.0%	3.4%	6.1%
Endovascular	(4%)	3.1%	58.6%	15.2%
Conservative		28.0%	37.9%	38.8%

AC anterior circulation, PC posterior circulation, *Cran* craniotomy, *EV* endovascular. *Indicates (combination of bypass % not known).

opinion, too low when compared to that of other cerebral arteries. In the anterior circulation, the terminal portion of ICA (44% in the present series), and more precisely, the superior medial wall of the C1 segment is a common site of dissecting aneurysms. Dissection seems to take place also at the posterior wall and any other segment of the ICA as shown in our series. In the posterior circulation, the VA (36% in present series) especially the V4 segment including the origin of the PICA appears to be the most common location.

We know that MRI is an important diagnostic tool of arterial dissection but this was not taken into consideration in our series as surgery took place in the acute stage of SAH on day 3.7 on the average.

Clinical presentation of SAH of our patients in terms of Fisher score, WFNS grade was usually more severe in cases of the ICA dissection than in those of the VA dissection but without statistical significance and so was the GOS but with statistical significance, as for the ICA, surgical treatment had a mean clinical outcome of 2.8 [20] vs 3.5 (present series), while for the VA a mean clinical outcome was 4.1 [3], 4.2 (NWSJ) vs 4.3 (present series) (Table 2).

In terms of surgical treatment (Table 2), entrapment or ligation (39% Ohkuma *et al.*; 54% present series) was the most frequent surgical option in the anterior circulation: In the former series it is not clear what percentage was combined with bypass procedure but in the latter it

was always combined with EC–IC bypass procedure. Furthermore the differences in radical neck clipping (22% Ohkuma *et al.*; 46% present series) and wrapping (35% Ohkuma *et al.*, 0% present series) were observed. By contrast, in the posterior circulation, surgical procedures for vertebral artery dissection included proximal ligation (33.3% especially in the early cases) or trapping (44.4%) in our series. The latter was combined with EC–IC bypass as the origin of the PICA was included in the dissection segment. In the NWSJ the proximal ligation was seen in 39% and entrapment in 21%, while their combination with bypass procedure is unknown. Coating was performed in two cases of V3 extradural segment dissection causing intradural bleeding. One of them has been published elsewhere for its peculiar bleeding form of SAH [5]. Alternative procedures described in the series of Anxionnat *et al.* focusing mainly on endovascular treatment are; conservative treatment (37.9%), proximal occlusion by ballooning (31%) and coiling/stenting (27.6%). Finally, in the basilar artery territory, coating and wrapping was done in two of our three cases while conservative treatment (100% Anxionnat *et al.*) was the exclusive strategy in BA locations. Neck clipping was performed only in one case in our series after recanalization and rebleeding from the coiled aneurysm.

With due consideration for pathophysiology of dissecting aneurysms, proximal ligation and/or entrapment has been considered to be the choice of treatment be-

sides neck clipping [6, 26]. Various type of neck clipping procedure (wrapping and clipping procedure or clipping procedure including adjacent healthy wall of the parent artery) has been reported for dissecting aneurysms of the ICA [21, 24, 26], and these seems to be successful in the subacute or chronic stage of SAH as in our cases #20 and #24. But the technique tends to fail in the acute stage giving rise to aneurysm recurrence which was observed in three out of our six cases with primary neck clipping procedure. Furthermore premature rupture was encountered in more than 50% of cases in our series at the time of aneurysm exposure or clipping procedure due to fragility of aneurysm wall stuck and covered with thick clots, while this took place only up to around 10% in our routine saccular aneurysm surgery, which corresponds well with literature [8, 27]. So one is forced to resort to trapping or ligation procedure in combination with EC–IC bypass, in which intrinsic collateral circulation through the PcomA should be secured by putting the clip blade obliquely to the carotid artery. In this way, the origin orifice of the PcomA should be distal to the distal clip blades (Fig. 1f). In order to warrant additional collateral circulation, construction of an EC–IC bypass using usually the frontal branch of the STA to M3 portion of the MCA was done in combination with trapping procedure in 7 anterior circulation dissecting aneurysms (5 ICA cases and 2 MCA cases). Significance of selective extradural anterior clinoidectomy SEAC in surgical management of such technically demanding ICA aneurysms for obtaining proximal control at the time of aneurysm exposure, premature rupture and/or permanent occluding procedure cannot be overemphasized [29, 30]. Necessity and type of bypass procedures could be assessed after various sophisticated methods reported to date in the chronic stage [12] but above mentioned measures to obtain sufficient cerebral blood flow at the time of therapeutic occlusion in the acute stage are to be strived. We thus do not have any cases of serious cerebral ischemia in our series due to therapeutic ICA occlusion.

The same is also for the vertebral artery dissection. Proximal ligation only has long been thought to be the appropriate procedure as its treatment [6], although neck clipping is feasible in some cases from senior authors experience as has been reported by Sano *et al.* [22]. But aneurysm recurrence with or without rebleeding in spite of proximal ligation procedure [6] like in our case #1 justifies the trapping procedure. Complication of Wallenberg syndrome due to VA ligation is considered to take places, however, in the range of around 10%

(11% in our series case and 13% in the NWSJ [26]) so that construction of an EC–IC bypass (OA-PICA, STA-PICA or PICA-PICA bypass) in case of PICA origin inclusion at the segment of VA dissection should be seriously taken into consideration.

Coating or wrapping reported sometimes to be effective was performed also in special cases of our series in which trapping or neck clipping could not be performed and is considered to be of some help as in the case #12 of basilar trunk dissection and in the V3 dissection.

Conclusions

Awareness of possibilities of intracranial dissecting aneurysms in the diagnosis of SAH brings appropriate strategies in planning of surgical treatment. Dissecting aneurysms of the ICA are considered to have more severe clinical presentation and hence outcome than those of the VA. As appropriate treatment consists in elimination of blood flow into the dissection, ligation or trapping of the parent artery is thus the treatment of choice, as a radical neck clipping is dangerous or not feasible in the acute stage especially when located at ICA. The latter is considered to be more possible in the subacute or chronic stage of SAH. At the time of ligation and/or trapping, sufficient collateral circulation into the distal part of the brain has to be warranted, so that an oblique placement of clamp at the time of cross clamping occlusion for preservation of collateral flow via the PcomA and simultaneous construction of an EC–IC bypass should be taken into consideration. As these conventional microsurgical treatments are rather invasive, development and refinement of less invasive endovascular treatments should be strived for.

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Part 3:

Revascularisation procedures, EC-IC bypass revisited

Cerebral revascularization by EC–IC bypass – present status

H. M. Mehdorn

Department of Neurosurgery, University of Kiel Hospitals, Kiel, Germany

Summary

The Extra–Intracranial (EC–IC) arterial Bypass = EIAB has been proposed by Yasargil and Donaghy in 1967 to bypass an occlusive process in the arteries supplying the brain that is not accessible surgically in another way. Following a rise in the number of procedures performed annually worldwide, a sharp decline followed after the International EC–IC Bypass Study had shown that the addition of EIAB did not improve the long-term results in the study population compared to best medical therapy by aspirin alone.

On the basis of a better understanding of the origin of cerebral ischemic events, more precise indications have been developed targeting to improve hemodynamic insufficiency, by surgically adding an extracranial arterial supply. Furthermore, technical improvements of the procedure allow more deliberate indication for EIAB, e.g. using high-flow bypass while performing an “occlusion-free” anastomosis. Also, variations of the technique of encephalo-myo-synangiosis for Moya-Moya disease patients allow additional blood supply to the brain hemispheres.

Keywords: Extra–intracranial arterial bypass; cerebral hemodynamic insufficiency; moya-moya; transcranial Doppler sonography; positron emission tomography; cerebral reserve capacity.

Introduction

The idea of an extra–intracranial arterial bypass (EC–IC Bypass or EIAB) to bypass an occluded internal carotid artery as suggested by C.M. Fisher in 1951 was realized by Yasargil and Donaghy in 1967 with the introduction of microvascular surgery into neurosurgery [26]. Similar to carotid endarterectomy for stenosed extracranial carotid artery, EIAB became an operation very popular among neurosurgeons and neurologists alike, and many variations of technical aspects have been published. The initial EIAB between a branch of the superficial temporal artery (STA) and a cortical branch of the middle

cerebral artery territory (MCA), usually adjacent to the sylvian fissure, joining the 2 arteries with an internal diameter in the range of 1 mm by means of a microsurgical end-to-side anastomosis, rapidly gained popularity to improve symptoms of cerebral ischemia in the carotid artery territory. It soon became obvious that the technique could also be used to improve the much rarer symptoms attributable to occlusive lesions of the posterior circulation, by performing end-to-side anastomoses between the occipital artery and intracranial branches of the vertebro-basilar circulation, e.g. the posterior inferior cerebellar artery (PICA), or between the STA and the superior cerebellar artery (SCA) to bypass e.g. occlusive lesions in the middle of the basilar artery trunk. The latter operations naturally were much more seldom than the EIAB to the anterior circulation, due to the rarity of the symptoms but also due to the technical demands when performing an anastomosis in a deep location.

As was shown in a large number of published reports, EIAB was able to improve symptoms of cerebral ischemia in a number of patients; however, a clear scientific proof of the concept was missing until a large international multi-center trial was instituted in 1978 to evaluate the surgical procedure in a randomized fashion against best medical treatment, using the indication criteria of that time. According to the indication at that time, EIAB was suggested to patients with symptoms of cerebral ischemia attributable to occlusion or stenosis of the internal carotid artery (ICA) or the MCA. Patients were randomized to either medical treatment using aspirin or surgical therapy in addition to aspirin. They were closely followed for the next years, and the results of the study were published in 1985 [2]. It became clear that EIAB was of no additional benefit for the group of patients under study, as the slightly better long-term course in these patients did not overcome the surgical

Correspondence: H. Maximilian Mehdorn, M.D., Ph.D. Professor & Chairman, Department of Neurosurgery, University of Kiel Hospitals, Schittenhelmstr. 10, D-24105 Kiel, Germany.
e-mail: mehdorn@nch.uni-kiel.de

risk occurring in the beginning of each surgical patient's career. The most important finding – which should not have been astounding from previous experience – was that cerebral ischemia of embolic origin could not be prevented by EIAB, rather the territories where the emboli would go to were altered. This meant that particularly patients with ICA or MCA stenoses could not benefit from EIAB, while patients with a good intracranial collateral circulation might not need EIAB [16].

Numerous criticisms have been voiced against the study, particularly bias of selection in various centers, not including patients into the study who in the opinion of the referring neurologist or the operating surgeon “needed the bypass”, too liberal inclusion criteria by not differentiating the origin of ischemia – hemodynamic vs. embolic, and high surgical complication rates. Nevertheless, the results of the study were accepted particularly in the neurological community and, in the USA, also by the insurance companies, thus bringing the patient referral virtually to an end. In the authors former working place, for instance, only 18 EIABs were performed between 1985 and 1990, compared to more than 400 patients operated upon between 1978 and 1985.

Hemodynamic indication for EIAB

On the other hand, it was clear that still patients existed with what was called intracranial hemodynamic insufficiency, or cerebral misery perfusion syndrome, i.e. continuing symptoms of cerebral ischemia despite best

medical treatment with aspirin or even anticoagulation. These patients presented e.g with symptoms attributable to steal phenomena like retinal ischemia or vertebrobasilar insufficiency on the basis of (bilateral) ICA occlusion [14]. Careful studies by Widder and others [9, 17, 24] and Yonas *et al.* [27] have shown that these patients could be evaluated in a non-invasive fashion by transcranial Doppler sonography resp. SPECT studies applied to define the status of hemodynamic capacity. CO₂ inhalation or application of a acetacolamide after obtaining a baseline measurement of the blood flow velocity in the MCA main trunk should result in a “normal” response with rise of the flow velocity by 20% compared to baseline. They showed that patients who had a lower increase of flow velocity would have a higher risk of stroke in the cerebral territory.

On the basis of these findings, the indication for conventional EIAB could be defined anew, and many opera-

Table 1. Protocol for selection of candidates for EIAB

History of cerebral ischemic events
Clinical evaluation incl. Cardiac evaluation (source of emboli to be excluded)
Cranial imaging by CT or (better) MRI incl. DWI
Extracranial and Transcranial Doppler (TCD) sonography
No stenotic lesion – anti-platelet-aggregation medication (ASS)
Stenotic lesion > TCD – reserve capacity testing
> normal –> no angiography
> pathological –> transfemoral angiography
if a suitable candidate for EIAB – further workup and operation, otherwise ASS

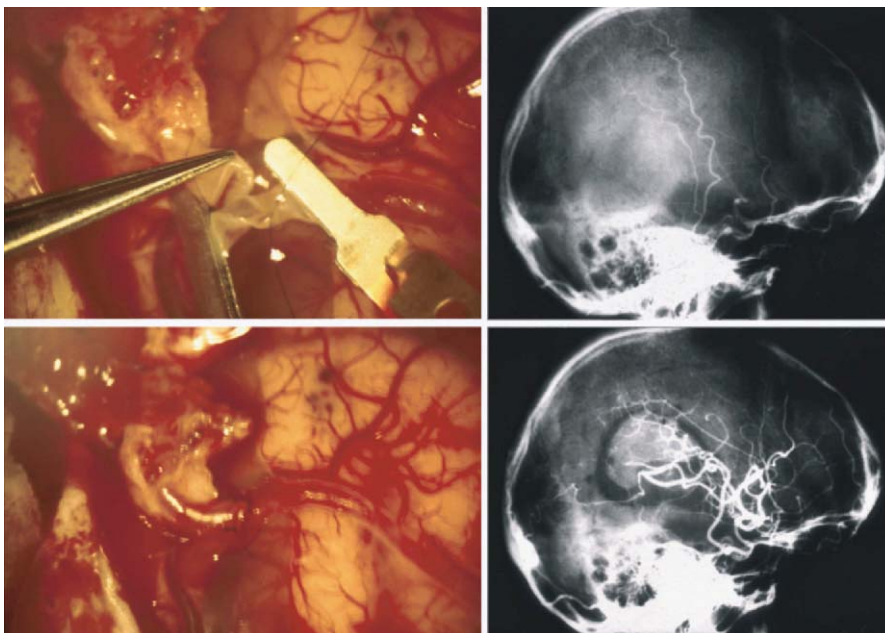


Fig. 1. Conventional EIAB in a patient with ICA occlusion. Note the increase in size of the donor STA 3 months after surgery

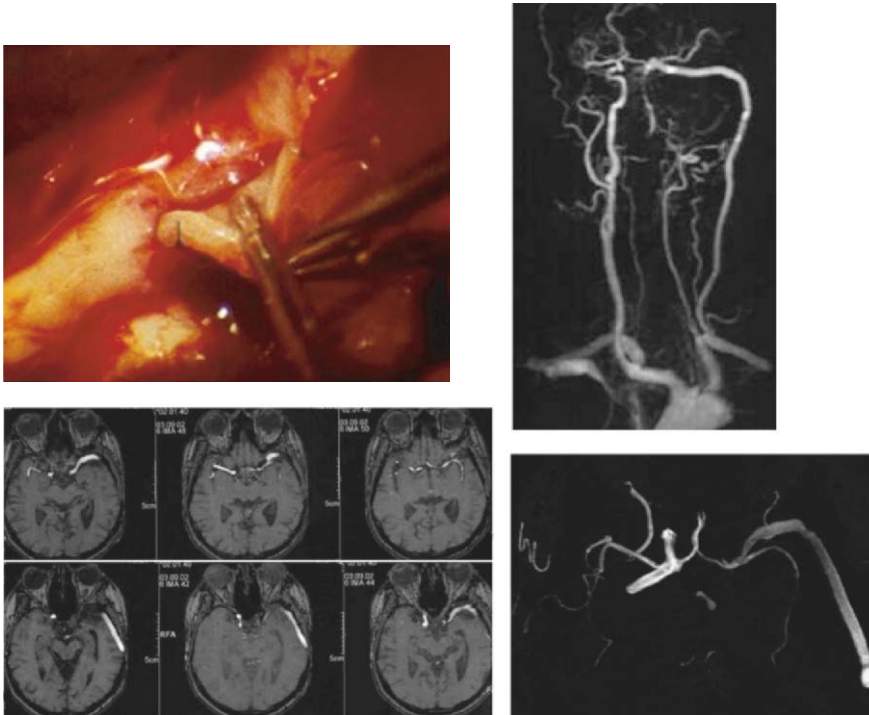


Fig. 2. EIAB using extraanatomic vein graft between the left subclavian artery and the left intracranial ICA. Note the first part of the intracranial anastomosis is performed leaving the recipient artery open. MRI followup 7 years later shows patent bypass corresponding to stable clinical situation

tions have been performed in a few centers around the world [5, 13, 19]. In the author's experience, the algorithm given in Table 1 helped, in a non-invasive manner, to select patients as adequate candidates for EIAB. In a joint data analysis among neurosurgeons who continued to perform EIAB in Germany after 1985, it could be shown that patients who underwent the operation on the basis of a rigid evaluation of cerebral reserve capacity, fared much better in the long-term follow-up than a similar group studied by Widder and followed conservatively [15, 19]. Similar results have been published recently by Japanese colleagues who gave special attention to brain volume development and cognitive functions [6, 18].

High-flow Bypass

As the STA is an artery of an internal diameter of approx. 1 mm that is anastomosed to a cortical artery of approx. the same size, the immediate postoperative additional flow provided to the brain is limited and increases only over time as the diameter of both arteries involved in the anastomosis increases "according to the demand". However, there may be situations when a patient would require additional blood supply either in the absence of a suitable extracranial donor artery or arteries or would require a high volume of blood in an urgent situation, e.g. in the case of a planned or even inadvertent ICA

occlusion during operation of a (giant) intracranial aneurysm. In these instances use of the saphenous vein or the radial artery for extra-anatomic EIAB has been advocated [20, 21, 25]. The recipient site should be of a diameter similar to that of the donor artery; therefore, the anastomosis should be located on the intracranial part of the ICA or the proximal part of the MCA. The technical difficulties in performing such a deep anastomosis are obvious, leading to a critical occlusion time of the recipient artery. Two techniques have been advocated: First, to perform the distal part of the anastomosis while the recipient vessel is not yet occluded, and then occluding the artery only to longitudinally incise it and complete the anastomosis, reducing the occlusion time to one half of the time traditionally required, or to perform a "non-occlusion" anastomosis using an intraarterially introduced laser beam to perform the hole in the recipient artery once the anastomosis is completed [4, 10, 23]. In both instances, one has to be aware that the use of an extra-anatomic graft carries a higher early and late occlusion rate than a STA used as donor artery.

Moya-Moya

While previously thought to be a rather exclusively Asian disease, it has been recognized that Moya-Moya may be more relevant also in the Caucasian population [8, 11]. A variety of techniques have been suggested to improve

cerebral perfusion; most use the combination of direct arterial STA-MCA anastomosis and the myo-synangiosis technique, placing the temporal muscle over the cerebral hemisphere, suturing it to the dura and opening the arachnoid membrane particularly over the sulci, thereby exposing the cortical arteries to the muscular vasculature. It has been shown e.g. by positron emission tomography or MRI perfusion studies that the synangiosis indeed improves markedly the cerebral perfusion [12].

Microsurgical anastomosis as adjunct in aneurysm and skull base surgery

Microsurgically bypassing an intracranial aneurysm [3, 7, 22, 25] can help to allow for its clipping or be sufficient to occlude it by flow alterations in the intracerebral vasculature. This may also be true for the basal intracranial artery territory in a patient harboring a skull base meningioma involving the carotid artery when a collateral circulation insufficient to tolerate carotid artery occlusion may be supported by a proximal extracranial ICA-intracranial ICA bypass or a distal STA-MCA bypass; it may also be necessary to perform, e.g. in the case of a serpentine ACA aneurysm, a side-to-end anastomosis between the distal healthy A2 segment and the aneurysm bearing A2 segment after excision of the aneurysm thus allowing normal circulation in both distal ACA territories, similarly for the MCA territory [1].

Other indications for revascularization

While the indications described so far represent the “classical” indications for “stand-alone” neurosurgical cerebral revascularization, modern neuro-interventional techniques often enough require cooperation between the interventionalist and the neurosurgeon, not only in exceptional emergency cases when a coil has been displaced distally and cannot be retrieved by interventional techniques, but also for creating access for the neuro-interventional, e.g. in severe bilateral vertebral occlusive disease. Also, carotid endarterectomy performed microsurgically in experienced neurosurgical hands should have its place in the team approach of optimizing cerebral circulation.

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Changes in brain volume after EC–IC bypass surgery

T. Inoue¹, J. Jinnouchi²

¹ Department of Neurosurgery, Cerebrovascular Center and Clinical Research Institute, National Hospital Organization Kyushu Medical Center, Fukuoka, Japan

² Department of Cerebrovascular Disease, Cerebrovascular Center and Clinical Research Institute, National Hospital Organization Kyushu Medical Center, Fukuoka, Japan

Summary

We studied changes in brain volume on magnetic resonance imaging in 10 patients with and without EC–IC bypass surgery who met the inclusion criteria for the Japanese EC–IC bypass trial, a multicenter, randomized, double-blind, prospective study of patients with hemodynamic brain ischemia due to cerebral artery occlusive disease. We also examined the association of cerebral hemodynamics on single photon emission computed tomography with the changes in brain volume. As a result, the affected/unaffected ratio of the % brain volume declined in patients without EC–IC bypass surgery ($p < 0.02$, $n = 4$), and the affected/unaffected % rCBF ratio increased in patients with the surgery ($p < 0.03$, $n = 6$). Acetazolamide reactivity increased in the affected hemisphere of patients with surgery ($p < 0.01$). And also two-year increase (decrease) in acetazolamide reactivity of the affected hemisphere showed a significant positive correlation with 2-year changes in the affected/unaffected % brain volume ratio ($R^2 = 0.737$, $p = 0.0007$). Change in acetazolamide reactivity might be a good predictor for brain atrophy in cerebral artery occlusive disease.

Keywords: Stroke; brain infarction; brain atrophy; cerebral blood flow; vascular reactivity; stroke outcome; EC–IC bypass surgery.

Introduction

Brain atrophy has been found to occur with advanced age and several risk factors including hypertension, diabetes mellitus, hyperlipidemia, cigarette smoking and alcohol consumption [1]. Neurological complications, such as Alzheimer's disease also accelerate the evolution of brain atrophy [9]. As well, changes in cerebral blood flow (CBF) may be associated with brain atrophy, especially in patients with cerebral artery occlusive disease that causes a reduction in CBF. However, previous stud-

ies have failed to find a significant relationship between CBF and brain atrophy in patients with dementia [7]. In patients with cerebral artery occlusive disease, a relationship between changes in CBF and brain parenchymal volume was shown in small population studies, where atrophy of the corpus callosum progressed in concert with the deterioration of cerebral cortical oxygen metabolism [10].

The Japanese EC–IC bypass trial (JET) [4] is a randomized, double-blind trial of 206 selected patients with severe hemispheric hemodynamic failure caused by cerebral artery occlusive disease. JET has recently shown that extracranial-intracranial (EC–IC) bypass surgery reduces the incidence of major stroke or death in the 2-year period after the surgery (JET study group, personal communication). We are starting a sub-analysis of the changes in brain volume on magnetic resonance imaging (MRI) for patients enrolled in the JET study to clarify the effect of the bypass surgery on longitudinal changes in brain parenchymal volume. In the present study, we compared the changes in brain volume and cerebral hemodynamics in a small number of patients with and without EC–IC bypass surgery from our institute.

Subjects and methods

We registered 11 Japanese patients with mild ischemic stroke for the JET study between November 1998 and March 2001. One patient of them died suddenly of undetermined cause within 2 years after the registration and was excluded from the study, which left 10 patients in the study. The entry criteria of the JET study [4] are listed in Table 1. The 206 enrolled patients randomly underwent EC–IC bypass surgery (surgical group) or did not undergo surgery (medical group), and continued medical management for 2 years.

Correspondence: Tooru Inoue, M.D., Department of Neurosurgery and Clinical Research Institute, National Hospital Organization Kyushu Medical Center, 1-8-1 Jigyohama, Chuo-ku, Fukuoka 810-8563, Japan. e-mail: itkkr@ qmed.hosp.go.jp

Table 1. Inclusion criteria of JET study

a) TIA or minor stroke
b) Age; less than 73 years
c) symptomatic internal carotid artery (ICA) or middle cerebral artery (MCA) stenosis $\geq 70\%$ in diameter or an occlusion
d) fair activities of daily life corresponding to modified Rankin Scale ≤ 2
e) regional cerebral blood flow (rCBF) of the ipsilateral MCA territory $< 80\%$ of the averaged value for control subjects and acetazolamide reactivity $< 10\%$ in single photon emission computed tomography (SPECT)

Intracranial imaging was evaluated using 1.5-tesla MRI (Siemens) on registration (before surgery), 1 and 2 years later. Brain atrophy was assessed quantitatively using a computer assisted processing system by the staff who were blinded to patients' data according to a method previously described [5]. Measurements were performed on the 3 axial sections of T2-weighted sequence (repetition time 4400 msec, echo time 96 msec) on and above the level of the pineal body (5 mm slice thickness). The area of cerebral parenchyma was quantitatively measured using a semiautomatic method to count the pixels with a given intensity, and was divided by the area inside the skull. The mean value of the calculation on 3 sections was defined as "% brain volume".

Cerebral hemodynamics was evaluated using SPECT (the PRISM 2000X, two-head SPECT system, Picker, USA) according to a method previously described [2]. *N*-isopropyl-*p*-[¹²³I]-iodoamphetamine (IMP) was used as the tracer for 9 patients and ^{99m}Tc-ethyl cysteinate dimer (ECD) was used for another patient. An elliptical region of interest (ROI), $\approx 16 \text{ cm}^2$ in size, was located in the cortical area in the MCA territory of each side on axial sections at the level of the body of the lateral ventricle, corresponding to the level of middle section of MRI. Areas of infarct, if present, were carefully excluded from the ROI. The resting rCBF values were measured quantitatively using the IMP autoradiography method or the ECD Patlack plot method on registration, 1 and 2 years later, and were divided by the averaged value for control subjects in our institute (40.0 ml/100 mg/min for the IMP autoradiography method and 48.0 ml/100 mg/min the ECD Patlack plot method). The results of the division were defined as "% rCBF". The rCBF values were also measured after the acetazolamide challenge test. Data collection began 10 min after the intravenous administration of acetazolamide

(0.17 g/kg). Vasodilatory capacity (acetazolamide reactivity) was expressed using the following equation: acetazolamide reactivity = [(post-acetazolamide CBF – resting rCBF)/resting rCBF] $\times 100$ (%).

Values are expressed as mean \pm SD. Baseline clinical characteristics were compared between patients with surgical and medical groups using chi square and Mann–Whitney's *U*-test as appropriate. Baseline radiological variables were compared between 2 groups using Student's unpaired *t* test. In comparison of 2-year changes in % brain volume and % rCBF between the groups, we used their ratio in the affected to unaffected hemisphere to correct the influence of individual factors other than the arterial stenosis/occlusion. To investigate the time course of variables, we performed one-way repeated-measures analysis of variance (ANOVA) for the comparison within a group, and two-way repeated-measures ANOVA for the comparison between groups. Finally, using changes in the affected/unaffected ratio of % brain volume and % rCBF between registration and two years later and differences in acetazolamide reactivity between the same time points; we evaluated the correlation of these 2-year changes by linear-regression analysis and the Pearson Correlation Coefficient. A *p* value < 0.05 was considered to be significant.

Results

Of 10 patients studied, 6 belonged to the surgical group and 4 belonged to the medical group. Baseline clinical characteristics or baseline radiological variables did not differ significantly between the two groups (Table 2).

Percent brain volume of the affected hemisphere declined in both surgical ($p < 0.001$) and medical ($p < 0.005$) groups, while that of the unaffected hemisphere did not (Fig. 1A). The affected/unaffected ratio of % brain volume declined only in the medical group ($p < 0.02$, Fig. 1B). There was no significant group \times time interaction of % brain volume ratio between the two groups.

Percent rCBF, both in the affected ($p < 0.005$) and unaffected hemispheres ($p < 0.05$), in the surgical group

Table 2. Baseline characteristics of patients at registration

	Surgical group (<i>n</i> = 6)	Medical group (<i>n</i> = 4)
Clinical characteristics		
Age, y	51–69	51–59
Male/female (<i>n</i>)	5/1	3/1
Stenosis (occlusion) of ICA/MCA (<i>n</i>)	3/3	0/4
Modified Rankin scale 0/1/2 (<i>n</i>)	1/3/2	1/2/1
Days after stroke onset, d	42–86	34–81
Radiological values		
% Brain volume, affected hemisphere (%)	80.7 \pm 7.5	83.4 \pm 3.9
% Brain volume, unaffected hemisphere (%)	82.9 \pm 4.4	83.7 \pm 5.0
Regional cerebral blood flow (divided by the control value), affected hemisphere (%)	62.2 \pm 14.6	66.6 \pm 13.9
Regional cerebral blood flow (divided by the control value), unaffected hemisphere (%)	80.2 \pm 12.3	81.2 \pm 9.0
Acetazolamide reactivity, affected hemisphere (%)	1.7 \pm 18.0	–6.1 \pm 13.5
Acetazolamide reactivity, unaffected hemisphere (%)	23.5 \pm 17.2	26.7 \pm 11.1

No variables differ significantly between the groups.

ICA Internal carotid artery, MCA middle cerebral artery.

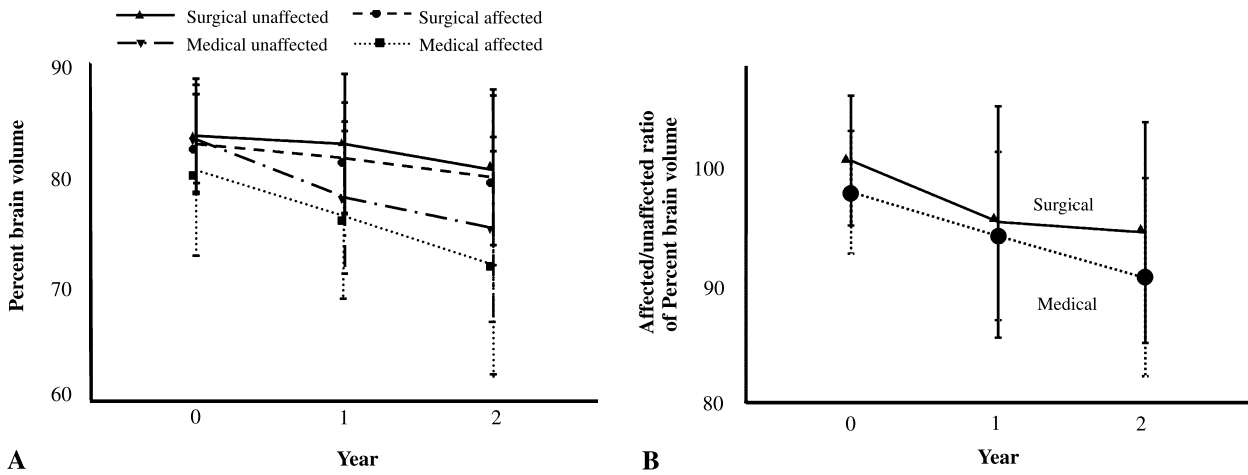


Fig. 1. Changes in % brain volume. (A) One-way repeated-measures ANOVA shows a significant decrease in % brain volume in the affected hemisphere of surgical ($p < 0.001$) and medical ($p < 0.005$) groups. Two-way repeated-measures ANOVA does not show a significant group \times time interaction among groups (B) One-way repeated-measures ANOVA shows a significant decrease in affected/unaffected ratio of % brain volume in the medical ($p < 0.02$) group. Two-way repeated-measures ANOVA does not show a significant group \times time interaction between groups

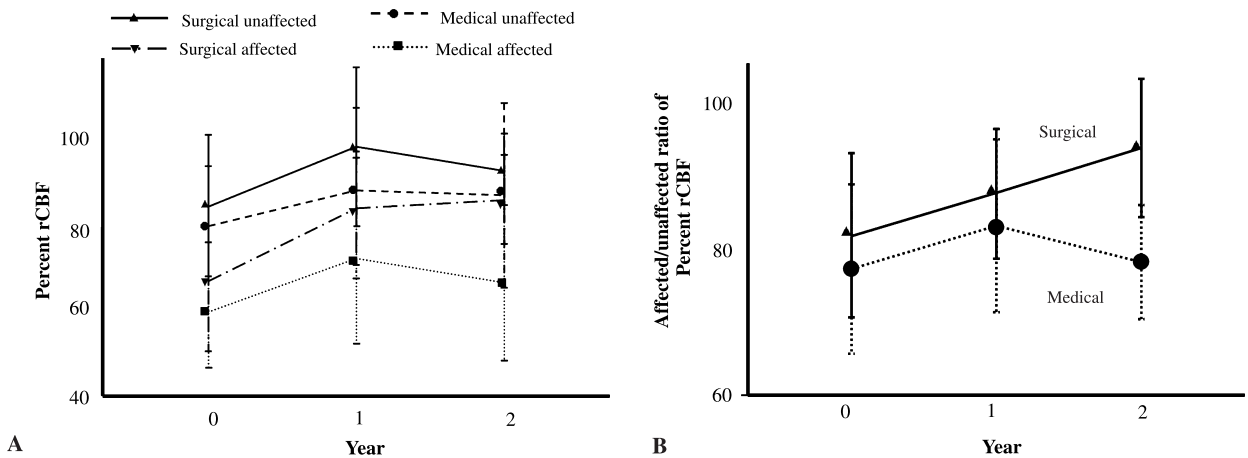


Fig. 2. Changes in % regional cerebral blood flow (rCBF) (A) One-way repeated-measures ANOVA shows a significant increase in % rCBF in the affected ($p < 0.005$) and unaffected hemisphere ($p < 0.05$) of the surgical group. Two-way repeated-measures ANOVA shows a significant group \times time interaction among groups ($p < 0.05$). (B) One-way repeated-measures ANOVA shows a significant increase in affected/unaffected ratio of % rCBF in the surgical group ($p < 0.03$). Two-way repeated-measures ANOVA does not show a significant group \times time interaction between groups

increased while that in the medical group did not in either hemisphere (Fig. 2A). The affected/unaffected % rCBF ratio increased only in the surgical group ($p < 0.03$, Fig. 2B). There was no significant group \times time interaction of rCBF ratio between 2 groups.

2-year increase (decrease) in acetazolamide reactivity of the affected hemisphere showed significant correlation with 2-year changes in % brain volume ratio ($R^2 = 0.737$, $p = 0.0007$, Fig. 3).

Discussion

In the present study, we assessed long-term changes in the brain volume and cerebral hemodynamics for pa-

tients with severe hemispheric hemodynamic failure due to cerebral artery occlusive disease, some of who underwent EC-IC bypass surgery, for preliminary analysis of JET-associated study. The major finding was that the 2-year changes in the affected hemispheric volume on MRI after minor stroke, corrected by the unaffected one, showed meaningful correlation with increase (decrease) in vascular reactivity of the affected hemisphere quantified by acetazolamide test on SPECT.

Measurement of cerebral hemodynamics is essential for choice of the therapeutic strategy and chronic management of the patients with cerebral artery occlusive disease. The current tools for the measurement including SPECT and positron emission tomography are expen-

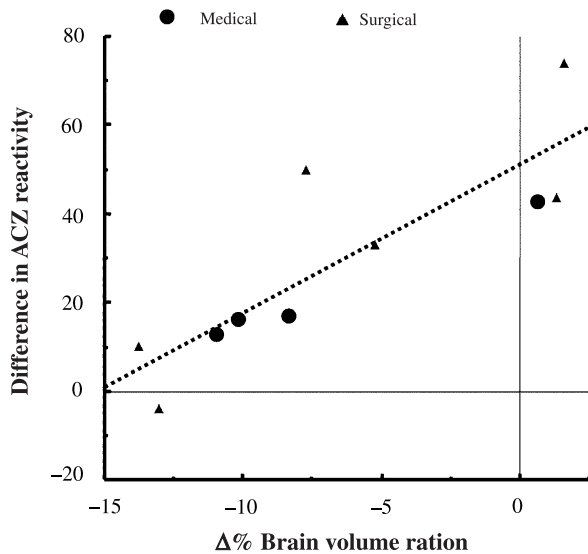


Fig. 3. Correlation of 2-year changes between % brain volume and hemodynamic variables. X axis shows changes in the affected/unaffected ratio of % brain volume and Y axis shows differences in ACZ reactivity of the affected hemisphere between registration and 24 months later. $Y = 50.99 + 3.35 \times X$; $R^2 = 0.737$, $p = 0.0007$

sive, complicated, and time consuming, however. As suggested in the previous study [10], if MRI findings on changes in brain volume can be an indicator for cerebral hemodynamics, they are of great help for the management of chronic patients.

An increase in oxygen extraction fraction seems to increase the risk of ischemic stroke in cerebral artery occlusive disease, and an increase in cortical ischemia would enhance brain atrophy [11]. Acetazolamide reactivity on SPECT was indicative of cerebral hemodynamic reserve, and correlated with oxygen extraction fraction [3]. Decreased acetazolamide reactivity may identify a subgroup of patients who have a higher risk of subsequent ischemic stroke [6]. Thus, brain parenchymal volume might decrease responding to cerebral hemodynamic reserve, not to absolute CBF value, and change in acetazolamide reactivity might be a good predictor for brain atrophy. Another possible explanation is that decreased acetazolamide reactivity indicates decreased cerebral blood volume which might lead to brain atrophy [8].

A limitation of this study is the small number of subjects. A possible difference in progress of brain atrophy

between the surgical and medical groups does not come to a definite finding unless it is still present after analysis using all 206 patients registered in the JET study. It is also important for us to determine whether the present positive correlation between change in acetazolamide reactivity and change in brain volume is reproducible after analysis using all the patients in the JET study.

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Less invasive technique for EC-IC bypass

Y. Kaku, H. Watarai, J. Kokuzawa, T. Tanaka, T. Andoh

Department of Neurosurgery, Asahi University Murakami Memorial Hospital, Gifu, Japan

Summary

Background. We introduce less invasive technique for superficial temporal to middle cerebral artery (STA-MCA) anastomosis, and also described an innovative technique to preoperatively identify the recipient artery using three dimensional CT angiography (3D CTA).

Objective. In a period of 28 months between January 2004 and April 2006, 39 EC-IC bypass were performed for hemodynamic compromised patients (including 9 patients with Moyamoya disease) using less invasive technique.

Methods. Operative technique is as follows: 1) A parietal or frontal branch of STA and cortical arteries could be identified on the original images of 3D CTA. The most suitable segment of both the artery provided as donor and recipient arteries for EC-IC bypass. The distance between the afore-mentioned segment of donor artery (STA) and the superior border of the helix were calculated. 2) A 5 cm linear skin incision on the STA, the center of which was the point measured on preoperative 3D CTA, was made. The temporal muscle was divided in the same fashion, and a 3 cm small craniotomy was made. The recipient artery could be identified on the center of the craniotomy. End-to-side anastomosis was performed in the usual way.

Results. Operation times were 115–172 min (mean 154 min) and intraoperative blood loss was 20–60 ml (mean 38 ml). All bypasses were patent on the post-operative 3D CTA.

Conclusions. This technique for EC-IC bypass was less invasive and cosmetically excellent. 3D CTA provides useful information for planning of the less invasive EC-IC bypass.

Keywords: EC-IC bypass; less invasive technique; 3D CT angiography.

Introduction

We introduce a less invasive technique for superficial temporal to middle cerebral artery (STA-MCA) anastomosis, and also describe an innovative technique to preoperatively identify the recipient artery using three dimensional CT angiography (3D CTA). This method

can provide preoperative identification of the proper recipient artery in STA-MCA anastomosis through a small craniotomy.

Methods

Preoperative examinations

Preoperative examinations also should be considered in the light of less invasiveness. We usually selected patients as a candidate of extracranial to intracranial (EC-IC) bypass with MRI/A, 3D CTA and SPECT with acetazolamide challenge. In most patients conventional angiography is usually not necessary for preoperative evaluation.

We performed 3D CTA with a 16-channel multi-detector row spiral CT scanner (Ultra Light Speed: GE medical systems, Milwaukee, WI, U.S.A.) and slice thickness of 0.6 mm to target a recipient and donor arteries. The original images of 3DCTA principally describe only arteries because timing of scanning was determined to demonstrate specifically for arteries in each individual patient. On the original images of 3D CTA, a parietal or frontal branch of superficial temporal artery and cortical arteries having a diameter of approximately 1mm could be identified on the brain surface or within the scalp. The most suitable segment of both the artery provided as donor (Fig. 2A gray arrow) and recipient arteries (Fig. 2A white arrow) for EC-IC bypass. The afore-mentioned segment could be considered as center of craniotomy, and the distance between the afore-mentioned segment of donor artery (Fig. 2B asterisk) and the superior border of the helix (Fig. 2A arrowhead) were calculated.

Operative technique

Operative technique is as follows; a 5 cm linear skin incision on the parietal or frontal branch of STA, center of which was the point measured on preoperative 3D CTA, was made (Fig. 3A, B). The temporal muscle was divided in the same fashion, and a 3 cm small craniotomy was made (Fig. 3C). The dura was opened as small as possible according to the cruciate method in the center of craniotomy (Fig. 3D). The recipient artery could be identified in the center of the craniotomy (Fig. 3E). End-to-side anastomosis was performed as usual (Fig. 3F). Two anchoring sutures at the apices of the incision and additional 10 interrupted sutures were placed with 10-0 nylon suture. The dura was loosely closed, and bone flap was replaced with 3 titanium plates. The temporal muscle and subcutaneous tissue were closed with absorbable suture, and skin was reapproximated with surgical tapes without any suture for cosmetic reason.

Correspondence: Yasuhiko Kaku, M.D., Department of Neurosurgery, Asahi University Murakami Memorial Hospital, Hashimotocho 3-23, Gifu 500-8523, Japan. e-mail: kaku@murakami.asahi-u.ac.jp



Fig. 1. Intracranial vessels of Moyamoya patient on MRA (A) and 3D CT angiography (B). 3D CTA also demonstrated the right superficial temporal artery (C)

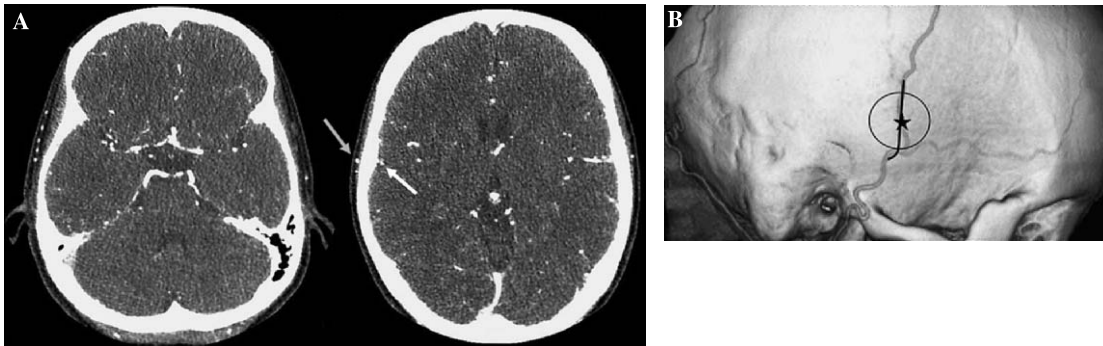


Fig. 2. (A) Original image of 3D CTA demonstrates a parietal branch of STA within the scalp and a cortical artery on the brain surface. The most suitable segment of both the artery provided as donor (*gray arrow*) and recipient arteries (*white arrow*) for EC-IC bypass. The distance between the afore-mentioned segment of donor artery (*gray arrow*) and the superior border of the helix (*arrowhead*) were calculated. (B) Image of craniotomy superimposed on the skull image of preoperative 3D CTA, *asterisk* indicates the afore-mentioned segment of donor artery (center of craniotomy)

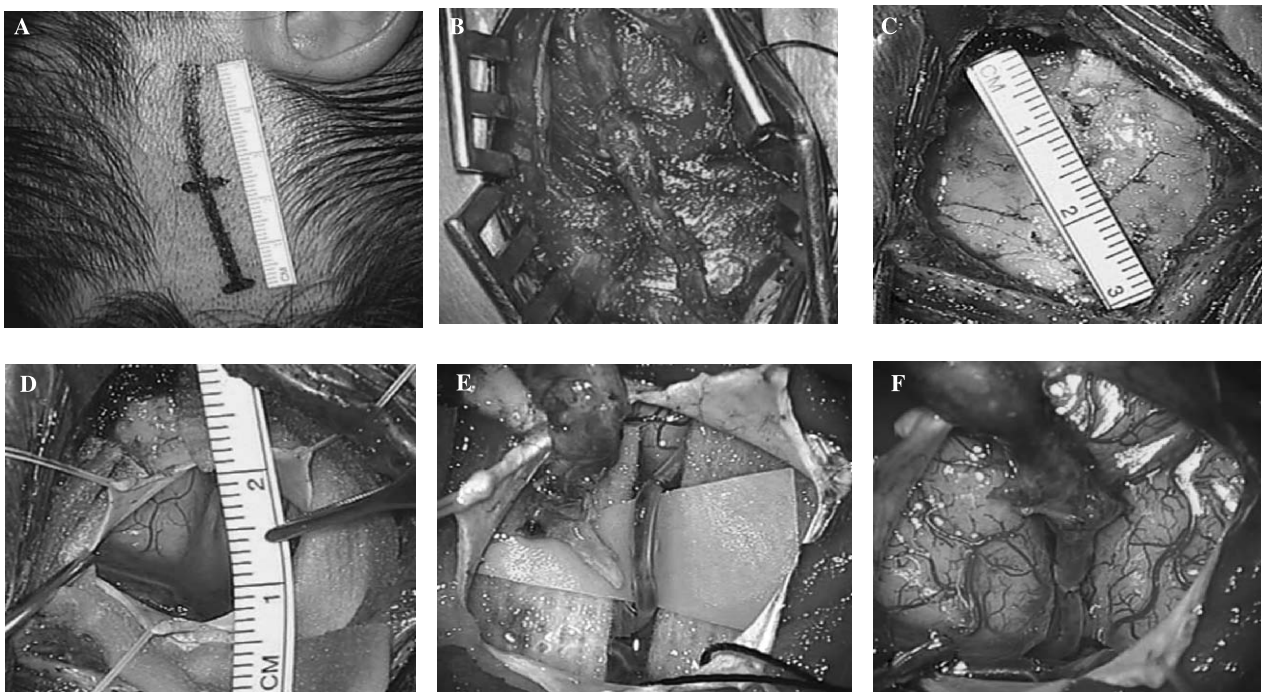


Fig. 3. (A) 5 cm linear skin incision on the parietal or frontal branch of STA, the center of which was the point measured on preoperative 3D CTA. (B) Dissection of parietal branch of STA. (C) 3 cm of small craniotomy. (D) Small opening of the dura in the center of craniotomy. (E) The recipient artery could be identified on the center of the craniotomy. (F) End-to-side anastomosis was completed with interrupted sutures

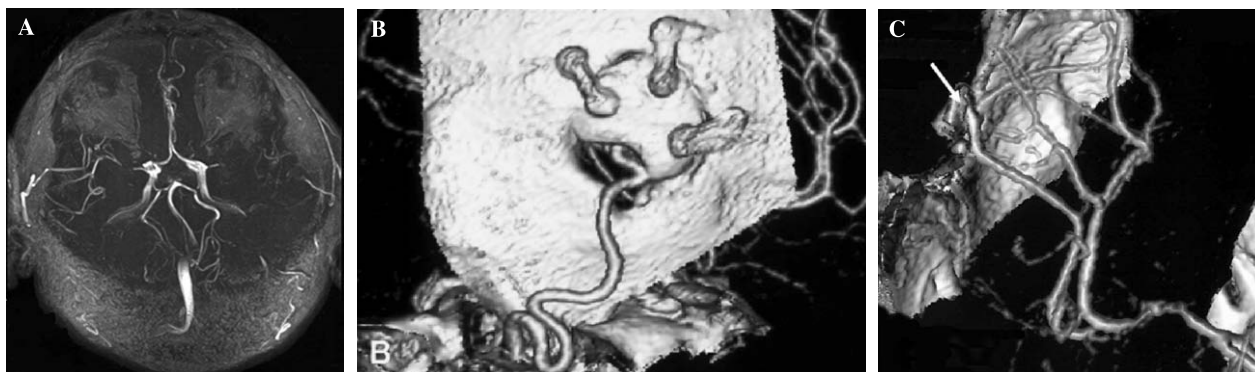


Fig. 4. (A) Postoperative MRA shows the patency of the EC-IC bypass. (B) Postoperative 3D CTA from the view of outside the skull shows the patency of the EC-IC bypass. (C) Postoperative 3D CTA from the view of inside the skull shows the patency of the EC-IC bypass. Arrow indicates the site of anastomosis

Postoperative examinations

We conducted postoperative examinations with MRI/A, 3D CTA and SPECT with acetazolamide challenge. Figure 4 shows the patency of the EC-IC bypass on the MRA (Fig. 4A) and 3D CTA (Fig. 4B, C). Postoperative angiography was usually not necessary for confirmation of the patency of bypass.

Results

During a period of 28 months between January 2004 and April 2006, 39 EC-IC bypass were performed for hemodynamic compromised patients (including 9 patients with Moyamoya disease) using less invasive technique. Candidates for EC-IC bypass were selected according to the criteria of the Japanese extracranial-intracranial bypass trial (JET study), including CBF criteria on SPECT, resting CBF was below 80% of normal value and less than 10% of cerebrovascular reserve capacity for acetazolamide.

In 39 EC-IC bypass procedures using this less invasive technique, operation times were 115–172 min (mean 154 min), and intraoperative blood loss was 20–60 ml (mean 38 ml). There were no mortality and morbidity. The patency of EC-IC bypass and the improvement of regional cerebral blood flow were confirmed in all cases on post operative MRA, 3D CTA and SPECT.

Discussion

STA-MCA anastomosis was first reported by Yasargil in 1969 [7]. Although the international trial in 1985 failed to prove this surgery's prophylactic effects against recurrent stroke, recent studies, such as the Japanese extracranial-intracranial bypass trial (JET study), suggest the validity of STA-MCA anastomosis in intracranial arterial occlusive disease in preventing hemodynamic stroke.

The validity of STA-MCA anastomosis, however, could only be secured under the condition of high patency rate and low morbidity of the bypass procedure. Therefore, the EC-IC bypass procedure must be as less invasive as possible especially for patients with systemic disease [1, 2, 6].

The concept of less invasive neurosurgery considers all steps of procedure: beginning with hair shaving and skin incision, continuing with the approach to the target area. This concept comprises not only the minimum size of craniotomy but also minimum traumatization of all layers encountered in the course of the procedure, and such a method must achieve the maximum efficiency for each individual patients. Therefore, the exact position of the craniotomy should be determined so as to approach the lesion with minimum damage to all layers of structures.

We apply 3D CTA to target the donor STA and an appropriate sized MCA recipient branch in occlusive cerebrovascular disease [3–5]. One of the advantages of this method is the identification of the recipient artery with pinpoint accuracy before scalp incision. An appropriate recipient artery can be exposed at the center of craniotomy with this method. It allows for a smaller craniotomy, which may reduce operative time, intraoperative blood loss and possibly morbidity. This technique may be useful especially in STA-MCA anastomosis for patients with systemic disease, such as heart dysfunction.

Conclusions

We have demonstrated an innovative technique for identification of a suitable recipient vessel for EC-IC bypass in a highly reproducible manner. Afore-mentioned EC-IC bypass was less invasive and cosmetically excellent,

while the surgeon needs the skill of microvascular anastomosis in the narrow and relatively deep operative field. 3D CTA provides useful information for planning of the less invasive EC-IC bypass.

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Tight contact technique during side-to-side laser tissue soldering of rabbit aortas improves tensile strength

A. Alfieri¹, A. Bregy¹, M. Constantinescu², F. Stuker³, T. Schaffner⁴, M. Frenz³, A. Banic², M. Reinert¹

¹Department of Neurosurgery, Inselspital Bern, University of Bern, Bern, Switzerland

²Department of Plastic Surgery, Inselspital Bern, University of Bern, Bern, Switzerland

³Institute of Applied Physics, University of Bern, Bern, Switzerland

⁴Institute for Pathology, University of Bern, Bern, Switzerland

Summary

Background. Cerebral revascularization may be indicated either for blood flow preservation or flow augmentation, often in clinical situations where neither endovascular nor standard surgical intervention can be performed. Cerebral revascularization can be performed by using a temporary occlusive or a non-occlusive technique. Both of these possibilities have their specific range of feasibility. Therefore non-occlusive revascularization techniques have been developed. To further reduce the risks for patients, less time consuming, sutureless techniques such as laser tissue soldering are currently being investigated.

Method. In the present study, a new technique for side-to-side anastomosis was developed. Using a “sandwich technique”, two vessels are kept in close contact during the laser soldering. Thoraco-abdominal aortas from 24 different rabbits were analyzed for laser irradiation induced tensile strength. Two different irradiation modes (continuous and pulsed) were used. The results were compared to conventional, non-contact laser soldering. Histology was performed using HE, Mason’s Trichrome staining.

Findings. The achieved tensile strengths were significantly higher using the close contact “sandwich technique” as compared to the conventional adaptation technique. Furthermore, tensile strength was higher in the continuously irradiated specimen as compared to the specimen undergoing pulsed laser irradiation. The histology showed similar denaturation areas in both groups. The addition of a collagen membrane between vessel components reduced the tensile strength.

Conclusion. These first results proved the importance of close and tight contact during the laser soldering procedure thus enabling the development of a “sandwich laser irradiation device” for in vivo application in the rabbit.

Keywords: Contact; laser tissue soldering; sandwich technique; side-to-side anastomosis.

Introduction

Cerebral revascularization procedures are surgical procedures often performed where there is no alternative

treatment possibility. A bypass may be performed either for flow augmentation such as in Moyamoya angiopathy or flow preservation where the bypass is necessitated for the exclusion of a pathological structure such as a giant aneurysm otherwise untreatable or tumor. Principally there are two techniques for revascularization, either a primary low flow extracranial to intracranial bypass performed on cortical vessels, or a primary high flow bypass on larger vessels more proximal to the circle of Willis. Furthermore cerebral revascularization may also be considered a security operation prior to primary endovascular or combined endovascular open surgical procedure. [1, 2, 4, 5, 11, 18, 20, 30, 35]. Neurosurgical research in this field is then focused on alternative methods leading to a simplification of the anastomosis technique and thus finally to a reduction in morbidity and mortality [9, 28, 49, 51–53]. Currently in the field of neurovascular surgery the Excimer Laser assisted non Occlusive Anastomosis technique (ELANA) is in use for flow preservation revascularization procedure, especially for patients with giant cerebral aneurysms otherwise untreatable [40, 44]. Although the ELANA technique is non-occlusive, meaning that there is no temporary occlusion of the cerebral host blood vessel, it still necessitates a microsuture technique for fixation of a graft vessel to the host, together with a platinum ring for stabilization [44–48]. Furthermore, the applicability of this technique is more suitable to vessels larger than 3 mm in diameter [45]. A technique with a larger degree of freedom in terms of suitability of the vessel size, nature of the vessel (veins or arteries) for anastomosis would be a substantial improvement for the applicability of cerebral revascularization. The re-

Correspondence: Michael Reinert, M.D., Department of Neurosurgery, Inselspital Bern, University of Bern, Bern 3010, Switzerland. e-mail: michael.reinert@neurochirurgie-bern.ch

search on tissue welding using the thermal effect on biological tissue has demonstrated an improvement by the addition of biological glue induced by heat, such as the protein albumin and is referred to as laser tissue soldering [7, 25, 29, 31–33, 38, 39]. Even though the exact nature of the bonding forces are not known, the addition of a protein containing solder is necessary as the tissue can be connected at lower temperatures than without [32]. Several reports using laser tissue soldering for blood vessels have reported a successful short-term in vivo end-to-end anastomosis technique with the aid of intravascular balloon technique [36]. Although positive results for laser tissue soldering with impressive leaking and bursting pressures have been achieved in an end-to-end soldering technique and intraluminal laser irradiation, the reproducibility is still lacking [36]. Thus the area of tissue interaction is larger and therefore has possibly an increased potential for laser tissue soldering. Furthermore, as tissue has the tendency to shrink and curl, during the laser irradiation procedure, a tight contact of the vessels during the laser tissue soldering procedure would lead to more reproducible and stronger tensile strength values. Aim of the present study was to lead reproducible and stronger tensile strength by tight contact of vessels during laser tissue soldering, and compare the results with those of the loose soldering technique.

Methods

Animal vessel model

The abdominal aorta rabbit model was chosen for studying the in vitro tensile strength basically for two reasons. First, the size of the abdominal aorta of the rabbit measuring 3–3.5 mm corresponds to the larger human intracerebral arteries (middle cerebral artery, internal carotid artery), our first target for cerebral revascularization procedures [10]. The second reason was the suitability for future cross correlation of the long-term results using the rabbit animal model. A total of 24 rabbit aortas (Soltermann, Thörigen, Bern, Switzerland) were used. The vessels were kept in sterile saline imbued gauze at 4°C. All experiments were performed in the first 24 h after withdrawal of the rabbit aorta. The vessel thickness was constant over the aorta used in the experiments as previously shown. For the laser soldering experiments all vessels were prepared identically by dissecting the peri-adventitial tissue from the vessel.

Loose and tight contact soldering technique

The loose soldering of vessels consisted in overlaying the vessel using no compression with the custom-designed approximator (Fig. 1A). For the tight contact soldering, the vessels were additionally embedded between two glasses and inserted into the custom-designed device to approximate the tissue under a constant pressure (Fig. 1B).

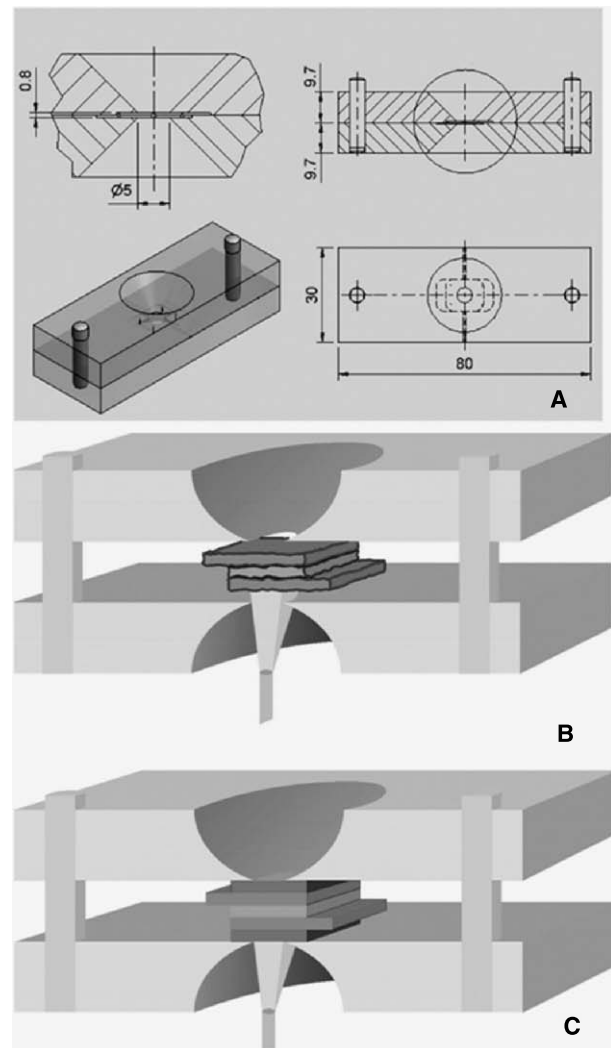


Fig. 1. Experimental set-up of the 3D-overview of the vessel piece adapter (A) with the loose contact (B) and the tight contact (C) vessel tissue soldering technique. In the tight contact technique the vessel pieces are tightly adapted with two glass pieces

Laser specification and temperature registration

As laser source a GaAlAs (gallium aluminum arsenide) diode laser system DL50 (FISBA Optik, St. Gallen, Switzerland) emitting near infrared radiation at 808 nm and for temperature registration, an infrared camera Radiance HS (Raytheon, Waltham, MA, U.S.A.) was used [42]. The images were processed using the accompanying ImagePro software package (Raytheon, Waltham, MA, U.S.A.). Temperature correlations between the loose and tight contact laser soldering techniques are complicated by the fact that the surface of the vessel is not directly exposed to the thermo camera in the tight contact soldering technique as a thin glass is over the vessel. The emissive patterns of the glass and vessel are thus different.

Solder specification

Two different solder application modes were studied for both the tight and the loose soldering technique. First solder application mode was a conventional liquid solder consisting of a 0.1% per weight solution of Indocyanine Green (ICG) (Acros Organics-Janssen Pharmaceuticals,

Table 1.

Irradiation Mode	Tight contact soldering		Loose contact soldering	
	Without collagen	With collagen	Without collagen	With collagen
30 sec continuous	1810	740	280	320
15 sec on – 15 sec off – 15 sec on	730	1120	340	150
	1120	1040	320	170
15 sec on – 15 sec off – 15 sec on	530	710	220	60
	550	660	220	350
	910	470	160	180

Belgium) doped with 25% per weight bovine serum albumin (Sigma-Aldrich Chemie GmbH, Steinheim, Germany) in distilled water. The second solder application mode was a collagen membrane (Tissudura, Baxter GmbH, Heidelberg, Germany) soaked in the conventional solder for 12 h.

Irradiation mode

An irradiation time of totally 30 sec was chosen, based upon previous investigations [8, 17, 22, 23, 31–33, 42]. In one series a continuous irradiation (30 sec on) and in a second series a pulsed irradiation (15 sec on- 15 sec off- 15 sec on) was performed.

Tensile strength assessment

To measure the tensile strength, we used a test stand with a fixed force gauge BFG50 (Mecmesin Limited, Slinfold, West Sussex, U.K.) and a moving table to pull the two soldered tissue samples apart using fixed surgical clamps.

Experimental design

For the tight contact laser soldering procedure 4 series (2 solder types and 2 irradiation modes) were performed. For the loose contact laser soldering procedure, similarly 4 series (2 solder types and 2 irradiation modes) were analyzed. The exact layouts including the results are outlined in Table 1.

Statistical analysis

The statistical analyses were performed using InStat (GraphPad Software, IncSan Diego, CA, U.S.A.). The non-paired two-tailed *t*-test was used for calculation of the significance. The level of significance was set at $p < 0.05$. The values are given as mean \pm standard deviation (SD).

Results

Tight versus loose soldering procedure

The overall tensile strength in the tight (1093.3 mN \pm 160.7) versus loose (235.7 mN \pm 39.7) contact soldering procedure was significantly higher ($p < 0.0005$) using the 30 sec continuous irradiation. In the pulsed irradiation series the overall tensile strength values for the tight

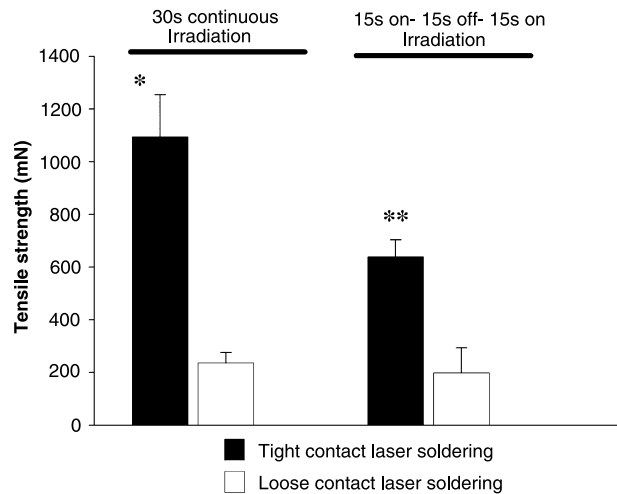


Fig. 2. Tensile strength was assessed with the tensile strength stand in Newton (mN). In the group with the tight contact soldering technique the tensile strength were significantly ($p < 0.0005$) higher than in the loose contact technique and this for either continuous or interrupted irradiation mode

(638.3 mN \pm 65.1) versus loose (198.3 mN \pm 38.6) contact soldering procedure were significantly higher ($p < 0.0005$), however the absolute values were lower (Fig. 2).

Solder type

Overall tensile strength in the additional collagen membrane solder type was lower, but not significantly.

Irradiation time

Overall tensile strength in the continuous irradiation mode was higher, also not significantly.

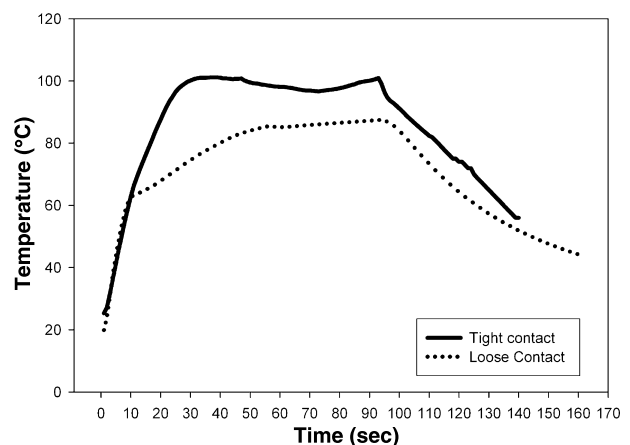


Fig. 3. The diagram indicates the temperature curves for the loose (dotted line) and tight contact (continued line) laser-soldering procedures, in percent of the maximal temperature achieved

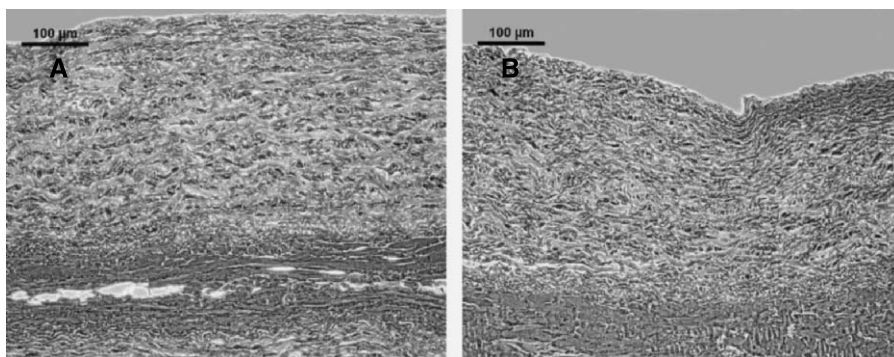


Fig. 4. (A) tight contact sandwich technique (20 \times) HE with phasecontrast (B) loose contact sandwich technique (20 \times) HE with phasecontrast

Temperature

Temperature curves for the loose and tight contact laser-soldering procedures are shown in Fig. 3. A direct correlation between the curves using the same thermo camera parameter settings is not possible as transmissivity and emissivity of the tight sandwich technique with a glass surface is different compared to the loose sandwich technique with a vessel tissue surface.

Histological analysis

The histological analyses of the samples with the tight contact sandwich technique have shown no apparent difference compared to loose technique using a 30 sec irradiation mode. In Fig. 4 the hematoxylin eosin (HE) histological section of a tight (A) and a loose (B) vessel soldering using the phase contrast mode (PH2) (Zeiss Microscope, Carl Zeiss Jena GmbH, Jena, Germany) is shown. Collagen matrix – Cell density is comparable in both specimens.

Discussion

Revascularization can be performed either by using an end-to-end, an end-to-side or a side-to-side anastomosis technique. The target of surgical application for each specific procedure type is different and dependent of the organ to be revascularized or the structure to be bypassed. An end-to-end anastomosis is more suitable for revascularization of a free flap [3, 12, 21, 26], whereas a cerebral aneurysm is bypassed by an end-to-side or side-to-side anastomosis technique [24, 41, 54]. Laser tissue soldering using the side-to-side anastomosis technique permits an increased soldering surface interface interaction as compared to the end-to-end anastomosis technique, and therefore may be suitable for laser tissue soldering techniques.

A perfect alignment of blood vessels such as by putting the vessel ends over a balloon catheter in an end-to-end anastomosis technique using a laser tissue soldering

procedure has shown to improve the reproducibility of the leaking and bursting pressure of the vessel [27, 34, 37, 43, 50]. The stabilization of the tissue thus seems important for improvement of the tensile strength [31]. Our hypothesis of stabilization of the vessel such as pressing them in close contact, always in conjunction with the use of a tissue solder, using a side-to-side anastomosis technique, has proven to be efficient in terms of increasing the tensile strength. The exact reasons for this significant increase in tensile strength can be speculated upon. Increase in bonding can be a result of either frank heat induced tissue destruction such as coagulation, leading to an increase in tensile strength, or be the consequence of a true tissue soldering using forces not related to simple coagulation. These forces are yet to be defined and are controversially discussed in the literature [6, 8, 19, 22, 23, 42]. Histological analysis of the tissue sections of the tight and loose sandwich laser soldering techniques have shown no differences for heat induced tissue destruction as the matrix, such as birefringence distribution in the phase contrast microscopy, and cellular appearance. Furthermore, the laser power parameters were identical. The direct temperature correlations between the two techniques are however difficult using the same thermo camera settings as the emissivity and transmissivity are different. The comparison of the percent temperature curves show that the tight contact sandwich technique has a steadier curve and no fluctuations. These temperature fluctuations are probably related to the stronger tissue distortion resulting from an unopposed tissue alignment such as in the loose contact sandwich technique.

Clinical implications

Gennaro *et al.* found in the histological analysis of CO₂ laser welded venous anastomoses an early full thickness coagulation necrosis of the wall with re-endothelialization by 7 days and complete healing by 30 days after the

procedure [16]. The patency rate was 87% for the laser welded venous anastomoses. Nakata *et al.* in a CO₂ laser carotid artery anastomosis welding found less intimal injury for the laser-welded vessel than for the microsurgically sutured anastomosis [16]. Also, the 1-year patency rates were better for the laser welded group, namely 98% versus 79% for the microsurgical sutured group. From these findings it may be deduced that the healing potential of lasers-welded and -soldered vessels is good even though thermal injuries may be considered high. Good apposition for an end-to-end laser soldering technique was found to be of great importance for a good patency rate [13–15, 36]. The most crucial moment is thus to endure the arterial blood pressure for the time the healing process takes over. In a side-to-side anastomosis technique the wound healing process may be viewed as more complex, as all histological vessel layers are exposed to the blood circulation. In an end-to-side anastomosis study, Tulleken *et al.* has reported a complete endothelialization after 10 days of a microsutured anastomosis with an NdYag laser for vessel perforation [49]. In a later report, the patency rate of an improved end-to-side anastomosis technique using a platinum ring for the laser perforation procedure was shown to be 92% [46]. Using a similar anastomosis technique even in conjunction with expanded polytetrafluoroethylene vessels there was no intimal hyperplasia and an excellent patency rate [40]. These findings demonstrate that an end-to-side anastomosis for high flow revascularization procedure has a favorable long-term profile in regard to local intimal hyperplasia and thus patency rate. These findings of good long-term profile of a side branching anastomosis technique encourage us to further proceed with the development of an end-to-side and side-to-side laser soldering technique of whole vessels using a tight contact technique.

Conclusion

Tight contact laser tissue soldering of rabbit's abdominal aorta has shown to produce significantly higher tensile strength than when using conventional loose technique, while histological post laser soldering appearance is unchanged.

These findings encourage further developments for side-to-side or end-to-side anastomosis techniques with enhanced tissue interface for the soldering procedures.

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Emergency extra–intracranial bypass surgery in the treatment of cerebral aneurysms

N. Krayenbühl, N. Khan, E. Cesnulis, H.-G. Imhof, Y. Yonekawa

Department of Neurosurgery, University Hospital Zurich, Zurich, Switzerland

Summary

The need of an emergency bypass in hazardous situations during treatment of intracranial aneurysms has rarely been addressed in the literature. We report our 10 year experience with emergency bypass for aneurysm treatment.

We retrospectively analyzed the data of patients who underwent emergency bypass surgery for the treatment of an intracranial aneurysm and compared the results with patients treated with bypass as a planned procedure during the same time period. Three groups were formed: group I, emergency bypass during clipping procedure; group II, emergency bypass for therapy refractory vasospasm; group III, planned bypass surgery.

Sixteen patients (35%) out of 46 were treated with emergency bypass. In group I (11 patients) mortality was 37% and a good outcome (GOS 4 & 5) was achieved in 36%. In group II (5 patients) mortality was 20% and good outcome was reached in 60%. In group III (30 patients) mortality was 10% and good outcome was achieved in 86.6%. Outcome was worse in patients with additional SAH.

An emergency bypass procedure as part of the aneurysm treatment should be considered in risky situations. Accurate timely decision-making is crucial combined with a fast and secure bypass technique. Treatment of refractory vasospasm with emergency bypasses may help to improve outcome in selected patients.

Keywords: Aneurysm; cerebral revascularization; extra–intracranial bypass; ischemia; vasospasm.

Introduction

Despite the results of the international EC-IC bypass study in 1985 [54], cerebral revascularization remains an important component in the surgical and endovascular treatment of intracranial aneurysms.

Its goal remains maintaining or improving cerebral blood flow when a major vessel has to be sacrificed. To date, a lot of different techniques of bypass surgery to treat cerebral aneurysms have been published [3, 4, 9,

10, 12, 14–17, 19, 20, 27, 30, 36, 37, 40–42, 44–46, 52, 53]. Most of them address unruptured complex or giant aneurysms of the internal carotid artery (ICA) or middle cerebral artery (MCA), symptomatic due to local mass effect [5, 9, 13–15, 19, 20, 41, 43, 45, 47, 48, 55, 59]. Some bypass procedures although may be required to be performed as emergency procedures in case of intraoperative aneurysm rupture at the neck of aneurysm, where direct clipping or reconstruction of the vessel is not possible or in case of acute intraoperative thromboembolic occlusion of a major vessel by displacement of a plaque or thrombus from the aneurysm lumen into the neck or parent artery during the clipping procedure. These situations are discussed in the daily clinical work but have rarely been addressed yet in the literature.

In the eighties there were some reports of bypass surgery to treat cerebral vasospasm after subarachnoid hemorrhage [6, 7, 25, 39]. Even today with aggressive treatment including calcium antagonists, triple-H therapy, endovascular treatment with angioplasty or selective intra-arterial infusion of papaverine hydrochloride, barbiturate therapy or hypothermia, there are patients who continue to deteriorate in their neurological status. An emergency bypass may be helpful to improve cerebral blood flow in these selected cases.

In this article we retrospectively analyze our 10 year experience with emergency bypass surgery in the treatment of intracranial aneurysms and compare the results and outcome with patients who underwent planned bypass surgery during the same time period.

Methods

We performed a review of the medical records, operating reports and radiological files of all patients operated at the University hospital of

Correspondence: Niklaus Krayenbühl, M.D., Department of Neurosurgery, University Hospital Zurich, Frauenklinikstr. 10, 8091 Zurich, Switzerland. e-mail: nkrayenbuehl@bluewin.ch

Zurich for an intracranial aneurysm from January 1994 to December 2004, who received an additional cerebral revascularization procedure. For the study only patients with standard extra-intracranial EC-IC bypasses were selected. Patients with direct vessel reconstruction or the use of interposing grafts were excluded. The records were studied for the indication and location of the bypass and whether the bypass was planned or done as an emergency procedure. All patients were evaluated regarding their preoperative symptoms, location of the aneurysm, the functioning of the bypass and exclusion of the aneurysm. The patients were divided in three groups: Group I; patients with emergency bypass during clipping procedure, group II; emergency bypass for vasospasm and group III; patients with planned bypass. All groups were analyzed regarding their outcome 3 and 12 months after surgery using the Glasgow Outcome Scale (GOS).

Group I and III were then compared. Further subgroups were made in these two groups for patients with subarachnoid hemorrhage, because of the additional impact of the bleeding on the outcome. Therefore additional data with influence on outcome like the Hunt & Hess and Fisher scores on admission and the occurrence of vasospasm during hospitalization were also collected.

For patients with planned bypass evaluation was performed according to a standard protocol including balloon test occlusion in combination with assessment of cerebral hemodynamics using either SPECT or PET studies. Bypass patency was confirmed in all patients by intraoperative Doppler sonography before closure of the craniotomy. Angiographic follow-up was performed during the hospitalization or at least 3 months after surgery to evaluate the result of clipping and the bypass patency.

Results

During the 10 year period from January 1994 to December 2004 46 patients were treated with a bypass for cerebral aneurysms at our institution. This represents

around 5% of our patients with ruptured aneurysms submitted to surgical treatment during the same period of time. The patient characteristics, distribution of the aneurysms and for patients with SAH the Hunt & Hess and Fisher Scores as well as the incidence of vasospasm are shown in Table 1. From the 23 patients not presenting with hemorrhage, 11 (48%) showed cranial nerve deficits, 3 (13%) ischemic cerebrovascular events, 3 (13%) headache, 3 (13%) unspecific symptoms and 3 (13%) a prior history of SAH with an attempt or partial surgical or endovascular treatment of the aneurysm at an other institution.

All of the 46 bypasses except one were low flow bypasses using the superficial temporal [42] or occipital [3] artery. Sixteen bypasses (35%) were done as an emergency procedure. For all of them, the superficial temporal artery was used and either anastomosed with a branch of the middle cerebral artery (preferably M2 branch) or a branch of the anterior cerebral artery (preferably middle internal frontal artery). During temporary occlusion barbiturate and mannitol was given for brain protection. Seven patients had an intraoperative aneurysm rupture with involvement of the base of the aneurysm, so that direct clipping or vessel reconstruction was not possible anymore. Four patients received a bypass because of intraoperative thromboembolic occlusion of either an A2 or M2 branch.

Table 1. Patients characteristic, aneurysm distribution, Vasospasm, Hunt & Hess and Fisher score

	SAH or ICH (N = 17 + 1 = 39%)	Other symptoms (N = 23 = 50%)	Refractory vasospasm (N = 5 = 11%)	Total (N = 46 = 100%)
Sex	M = 9 (50%) F = 8 + 1 (50%)	M = 7 (30%) F = 16 (70%)	M = 3 (60%) F = 2 (40%)	M = 19 (41%) F = 27 (59%)
Age (y)	25–73	24–78	48–76	24–78
Aneurysm site				
Internal carotid A.	9 (50%)	17 (74%)	2 (40%)	28 (61%)
Anterior cerebral A.	5 (28%)	1 (4%)	2 (40%)	8 (18%)
Middle cerebral A.	1 (5.5%)	4 (18%)	1 (20%)	6 (13%)
Posterior cerebral A.	1 (5.5%)	1 (4%)	0	2 (4%)
Basilar A.	1 (5.5%)	0	0	1 (2%)
Vertebral A.	1 (5.5%)	0	0	1 (2%)
Vasospasm	6 (35%)	0	5 (100%)	11
Hunt & Hess score				
1	4 (24%)		0	4 (18%)
2	6 (35%)		3 (60%)	9 (41%)
3	4 (23%)		2 (40%)	6 (27%)
4	2 (12%)		0	2 (9%)
5	1 (6%)		0	1 (5%)
Fisher score				
1	1 (6%)		0	1 (5%)
2	4 (24%)		0	4 (18%)
3	5 (29%)		4 (80%)	9 (41%)
4	7 (41%)		1 (20%)	8 (36%)

Five patients were treated with an emergency bypass for therapy refractory vasospasm. These patients primarily received standard treatment with calcium antagonist and aggressive triple-H therapy with monitoring of cardiac output, extravascular lung water and intrathoracic blood volume. Superselective intra-arterial instillation of papaverine was performed one or two times in 3 patients and was not possible in 2 patients as selective catheterization failed due to preexisting carotid occlusion or severe stenosis. In the group with no response to papaverine, a bypass was performed as further endovascular treatment like angioplasty was not considered by interventional neuroradiologists. Other treatment modalities like hypothermia or barbiturate therapy were also not considered due to the high risks and the clinical condition of the patient. The indications for the patients with vasospasm are listed in Table 2. All emergency bypasses for vasospasm were done immediately after failure of papaverine instillation or when there was no response to this treatment within 30 min.

Table 2. Overview of indications for emergency bypass surgery

Indications for emergency bypass surgery during clipping	Patients (N = 11)
Intraoperative rupture (5 × ICA, 1 × Pcom, 1 × Acom)	7 (15%)
Intraoperative thromboembolic occlusion of a major vessel (2 × A2 segment, 1 × M2 segment)	3 (7%)
Stenosis after Clip application (MCA)	1 (2%)
Indications for emergency bypass for vasospasm Patients (N = 5)	
No response to papaverine treatment, Proximal MCA spasm Clinical condition, medical history or age not allowing further intensive care treatment	2
No response to papaverine treatment and ICA stenosis due to clip application in a dissecting ICA Aneurysm	1
Failure of catheterization for papaverine treatment due to ICA stenosis of occlusion	2

Outcome

In 40 cases (87%) follow-up angiography, usually performed within one week after surgery to know the aneurysm occlusion status, could be obtained. Complete aneurysm occlusion was confirmed in 36 patients (90%). There was a remnant in 3 patients (7.5%), and one case (2.5%) showed an unchanged, mostly thrombosed giant MCA aneurysm, where a bypass was done with the attempt to reverse blood flow and with no attempt to exclude the aneurysm. In the other 6 patients (13%) follow-up angiography was not performed due to early death or other medical reasons.

External carotid artery injection was obtained in 37 patients (80%) due to the reasons mentioned above, with confirmation of bypass patency in 32 cases (86%).

Clinical follow-up of group I showed a mortality rate of 37%. One patient (9%) was lost to follow-up. Two patients (18%) were severely disabled, one of them lost at one year follow-up, and 4 patients (36%) showed a good outcome (GOS 4 & 5). In group II the mortality rate was 20%, and a good outcome could be achieved in 60% of patients. In group III, 3 patients died (10%) in the first 3 months and one patient died of a major hemorrhage due to an additional AVM during the first year. There was 1 patient with GOS 3 and the rest of the group (86.6%) reached a GOS of 4 and 5 (Table 3). When looked at the subgroup of patients with SAH, the mortality in the group with emergency bypass (group I) was 57% and 20% in the group III. Good outcome (GOS 4 & 5) was reached in 14% of group I and in 80% of group III. Due to the small number of patients in the group with emergency bypass no statistical statement could be made.

The occurrence of vasospasm did not play an important role in the outcome of patients with SAH in the overall view. In group I 3 patients had vasospasm: 1 died, 1 was lost to follow-up and one had a GOS of 5.

Table 3. Outcome of patients with emergency and planned bypass surgery for aneurysms

GOS	Group I patient with emergency bypass (N = 11)		Group II patients with emergency bypass for vasospasm (N = 5)		Group III patients with planned bypass (N = 30)	
	3 Months	1 Year	3 Months	1 Year	3 Months	1 Year
1	4 (37%)	4 (37%)	1 (20%)	1 (20%)	3 (10%)	4 (13.3%)
2	0	0	0	0	0	0
3	2 (18%)	1 (9%)	1 (20%)	1 (20%)	1 (3.3%)	1 (3.3%)
4	1 (9%)	1 (9%)	1 (20%)	1 (20%)	4 (13.3%)*	3 (10%)*
5	3 (27%)	3 (27%)	2 (40%)	2 (40%)	22 (73.3%)	22 (73.3%)
unknown	1 (9%)	2 (18%)	0	0	0	0

* 2 Patients who became symptomatic with thromboembolic event, with already a GOS of 4 preoperatively.

The 3 patients in group III who suffered from vasospasm reached all the GOS 5. The grading of the SAH had no influence on outcome in the patients with emergency bypass. In the group with a planned bypass the patients with a better grade had in general a better outcome although two patients with an initial H&H grade 1 died after surgery. In both of them the bypass was occluded in control angiography resulting in a major infarction.

Illustrative cases

Case 1

A 52-year-old female patient presented with subarachnoid hemorrhage H&H Grade II, Fisher Grade 2 with a small ruptured right sided ICA (pcom) aneurysm (Fig. 1). She underwent craniotomy and clipping of the aneurysm. Intraoperatively it presented as a blister-like aneurysm that ruptured at its base during preparation. Direct clipping and vessel reconstruction was not possible so that the aneurysm had to be trapped and an emergency bypass was performed. Postoperatively she showed no neurological deficits.

Case 2

A 39-year-old male was transferred from a foreign country after clipping of a small, broad based ruptured left sided MCA bifurcation aneurysm (Fig. 2). Control angiography showed a residual aneurysm, therefore he underwent recraniotomy. Intraoperative findings showed that there was probably a rupture of the aneurysm at its neck in the previous operation. The aneurysm base had been supported additionally with a piece of muscle, leading to a pseudoaneurysm, which was diagnosed as a residual aneurysm on angiography. The opening of the neck could be closed by direct suturing and the aneurysm was clipped. Unfortunately due to an intraoperative thrombotic occlusion of the inferior trunk of the MCA, an emergency STA-MCA bypass had to be performed. The patient had no postoperative neurological deficits.

Case 3

A 48-year old female presented with a SAH H&H Grade 2 with a small, right blister type ICA aneurysm (Fig. 3).

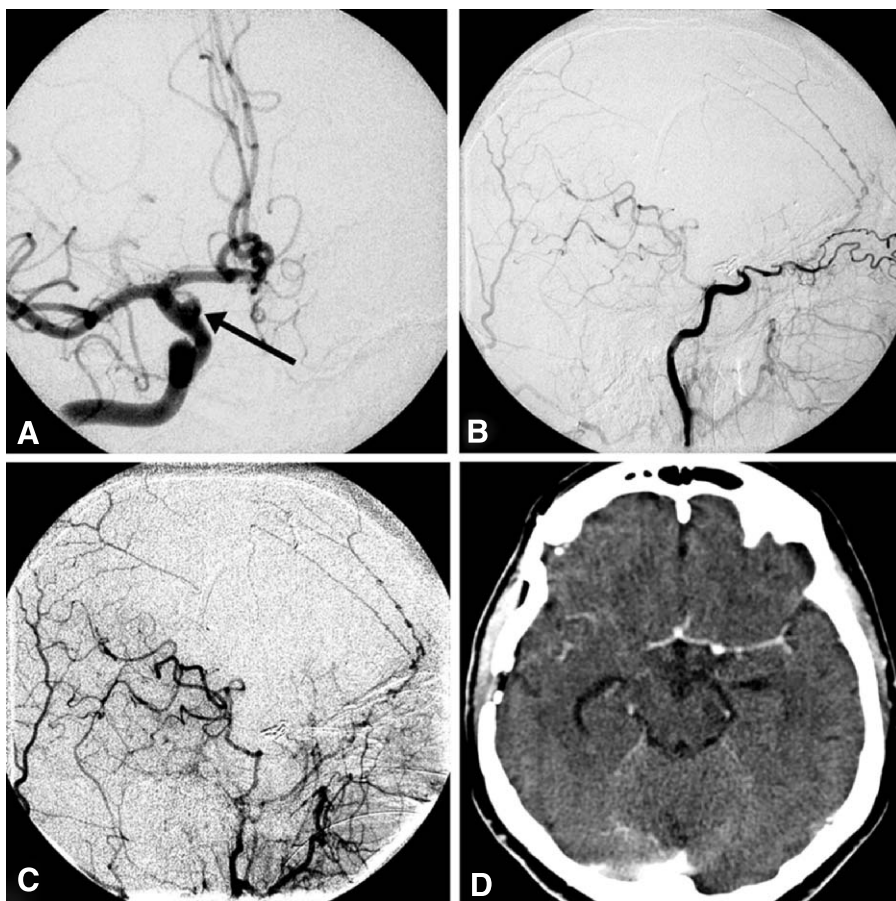


Fig. 1. *Case 1* Angiography before surgery (A) showing a blister-like aneurysm of the right ICA (arrow). Angiography after surgery showing a functioning bypass (C) and the trapped carotid artery distal to the origin of the ophthalmic artery (B). CT after surgery (D) with no signs of ischemia

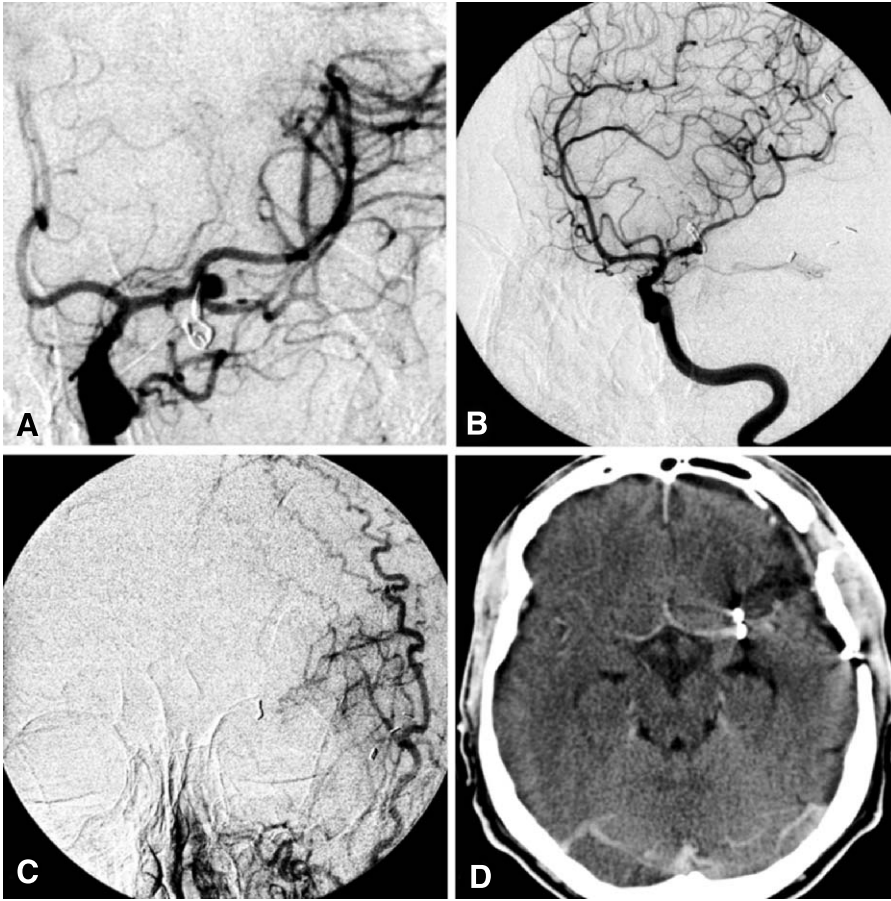


Fig. 2. Case 2 Angiography showing the previously operated MCA aneurysm with filling of the pseudoaneurysm (A). Angiography showing the functioning bypass (C) and occlusion of the inferior MCA trunk (B). CT scan after surgery (D) with slight hypodensity in the area of the sylvian fissure but no other signs of ischemia

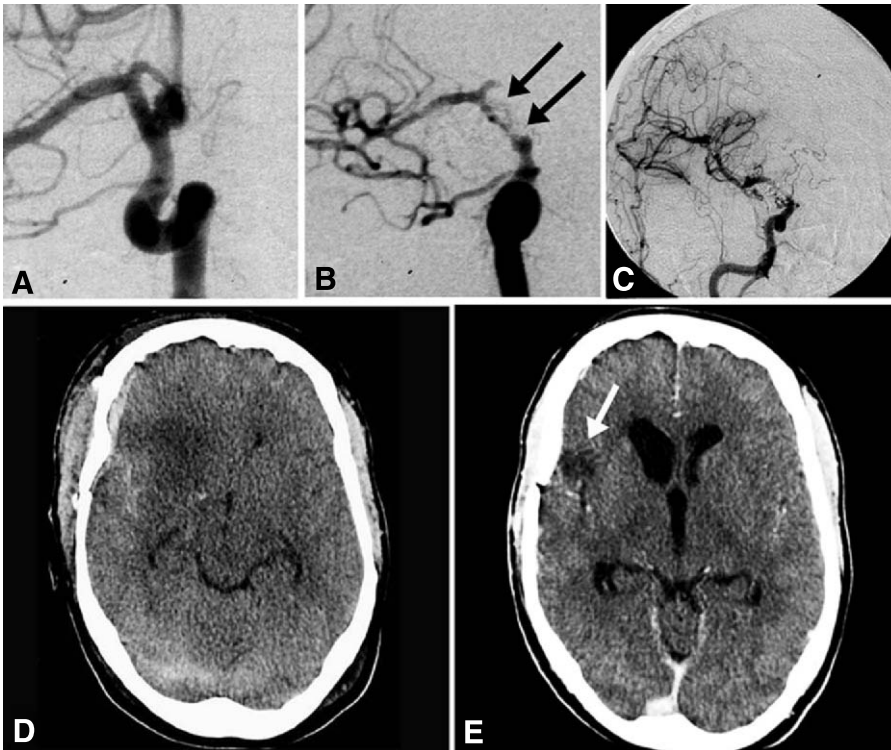


Fig. 3. Case 3 Angiography showing the blister-like ICA aneurysm (A) and the narrowing of the ICA segment due to the clip application (*double arrow*) during first papaverine application (B). (C) Angiography with functioning EC-IC bypass. CT scan just before the first papaverine application with hypodensity in the right basal ganglia (D) and after 3 months (E) showing a small infarction in the right fronto-opercular region (*arrow*)

Surgery was performed on day one. To radically clip the dissecting aneurysm part of the ICA wall had to be included in the clip leading to a partial stenosis of the ICA. Immediate postoperative course was uneventful. The patient developed clinically vasospasm with left sided hemiparesis and additional decreased level of consciousness five days after surgery. She responded well to triple-H therapy and selective papaverine application, but continued to deteriorate 48 h later, with no response to papaverine this time. CT scan showed a hypodensity in the insular and basal ganglia region. To improve cerebral blood flow STA-MCA bypass was performed within 3 h after onset of neurological deterioration, leading to full recovery from the deficits immediately after surgery. Follow-up CT scan showed a small residual ischemia in the right frontoopercular region.

Discussion

The risk of an acute stroke during and after aneurysm surgery remains to be an unavoidable scenario in selected cases where the parent artery is or has to be occluded. Cerebral revascularization is hence an important armamentarium in the management of cerebral aneurysms to augment blood flow in these selected cases. Since the first extra-intracranial bypass, done by Yasargil and Donaghy in 1967 independently, different variants of bypasses have been published for revascularization of the anterior as well as for posterior circulation, showing the evolution of microsurgical and skull base techniques [2, 3, 12, 16, 19–22, 27, 28, 31, 32, 37, 41, 48, 49, 51–53, 56, 58]. Nowadays, bypasses can also be performed without temporary occlusion of the parent artery, using the ELANA technique [10, 18, 24]. Most of the bypasses in aneurysm surgery are performed for complex, giant or fusiform aneurysms where the parent artery has to be sacrificed to completely exclude the aneurysm [3–5, 12, 14, 15, 19, 20, 28, 36, 37, 40–42, 45, 52, 53]. In this paper we present 16 patients, where an extra-intracranial bypass was done as an emergency procedure. For all bypasses we used the frontal branch of the superficial temporal artery as donor vessel, as it is the branch preserved, when doing a pterional craniotomy. Moreover, in our experience, it is easily and relatively quickly available, normally within 15 to 20 min. For sure, the use of radial artery or saphenous vein bypass either with conventional or ELANA technique may be preferred in cases where the internal carotid artery has to be sacrificed, but especially in emergency cases their application is too time consuming.

Our bypass technique and results for cerebrovascular occlusive disease has been published earlier [60]. Nevertheless the time of temporary occlusion during preparation of the donor vessel and performing the anastomosis, although not exactly measured in our study, was often too long resulting in a major infarction. A good outcome (GOS 4 & 5) could only be achieved in 36% of these patients, when compared with the 86.6% achieved when the bypass was planned. The mortality was up to 37%.

One major limitation in our study is the fact that some patients probably were just saved by good collateral blood supply rather than by the bypass itself. But hemodynamic assessment can not be performed in an adequate and quick way in emergency situations and collateral flow can only be estimated according to preoperative angiography studies or by Doppler sonography of cortical vessels. Intraoperative monitoring with SSEP or MEP would have given information about neurophysiological changes during occlusion time, but are not performed at our institution on a routine basis during aneurysm surgery. The reliability of intraoperative hemodynamic or electrophysiological assessment in predicting outcome under these circumstances remains questionable.

In the absence of good collateral flow, part of the tissue in the ischemic penumbra might have been saved by the bypass, but its extent can not be defined. It is known from the NINDS trial that patients treated with intravenous r-PA therapy for ischemic stroke within 3 h were at least 30 percent more likely to have minimal or no disability at three months follow-up than patients treated with placebo [33]. This shows that the timing of performing emergency bypass is important and no time has to be lost. In our study, it also seems that the additional impact of subarachnoid hemorrhage is making the brain tissue more vulnerable for ischemia resulting in a worse outcome in this group of patients.

The need for faster bypasses under these circumstances is obvious. One of the possibilities is direct side to side anastomosis with adjacent vessels like a M2/M2 anastomosis in a M2 occlusion [49] or an A3/A3 anastomosis in occlusion of an A2 segment [29]. Also PICA/PICA anastomoses have been reported [28, 34]. But all these methods have the risk of ischemia in the donor and recipient vascular territories and the feasibility depends on the individual anatomical configuration of the vessels and the location where the revascularization is needed. A second possibility would be the use of an artificial graft like a polytetrafluoroethylene graft which

has been used for external carotid artery to MCA anastomosis [8, 50] or a Dacron graft which is used for carotid artery bypass procedures [3]. The problem with artificial grafts is the small size of the intracranial vessels and the need for anticoagulation to prevent graft occlusion with the risk of hemorrhage. Moreover the need of two suture lines, even in experienced hands, takes more than 30 min, which bears the risk of ischemia, despite brain protection with mannitol, barbiturate or mild hypothermia.

Most of our patients with aneurysm rupture resulting in an irreparable defect at the neck of the aneurysm were blister-like aneurysms of the internal carotid artery. It is known that these aneurysms are difficult to treat [1, 57]. Even with newer imaging techniques like CT- or MR-angiography, the characteristics of the aneurysm wall and the hemodynamics can not be predicted preoperatively. Due to our experience, we believe that whenever there is a doubt of a blister-like aneurysm one should be prepared for a bypass before doing the craniotomy. It should also be considered for giant, partially thrombosed ICA, MCA or anterior communicating artery aneurysms, which bear the risk of thromboembolic occlusion of a major vessel.

Bypass and vasospasm

Although advances in intensive care and interventional endovascular management of cerebral vasospasm after SAH have been made in the last decade, there are still patients who suffer from permanent neurological deficits after symptomatic vasospasm. We performed EC-IC bypass revascularization procedures as a last resort in 5 selected patients, who were refractory to conventional triple-H therapy and treatment with calcium antagonists in combination with selective intra-arterial papaverine injection [23, 26, 38]. In two cases the cerebral perfusion was additionally impaired due to a preexisting severe atherosclerotic ICA stenosis or occlusion, which also made selective catheterization for papaverine infusion impossible. Three patients did not respond to papaverine application and were not considered for additional endovascular treatment like angioplasty by interventional neuroradiologists. Two patients failed to qualify for a further aggressive intensive care treatment because of their age and previous medical history. In one further case, part of the ICA wall had to be included in the clip to allow total occlusion of a blistering ICA aneurysm as mentioned above, resulting in a local ICA stenosis.

One can argue that surgery in these cases leads to manipulation of already spastic vessels. But in most cases vasospasm just affects the proximal vessels which are not touched when performing an anastomosis to a M4 or A4 branch. Moreover, from the physiological standpoint it makes sense to restore peripheral circulation, which is altered by the vasospasm. In most of our cases intraoperative dopplersonography showed an improved blood flow in cortical vessels after the revascularization, although quantitative measurements were not made.

Good post-surgical results after EC-IC bypass surgery for the management of therapy refractory vasospasm have already been reported in 1985 in a patient with a posterior communicating aneurysm by Rosenstein *et al.* [39]. Others, including the largest series with 11 patients of Batjer and Samson [6], Benzel and Kesterson [7] followed along with good documentation of improvement of the CBF associated with neurological improvement by Korosue *et al.* [6, 7, 25]. At this time, most of the patients had unsecured aneurysms, so triple-H therapy was not used. Symptomatic vasospasm refractory to medical and/or endovascular therapy especially on the basis of additional cerebrovascular occlusive disease fulfills in our opinion the criteria for a revascularization procedure in these patients. From the clinical point of view it is like a stroke in evolution for which revascularization has been described to be beneficial prior to the development of newer drug therapies [11]. Although an STA-MCA bypass provides a blood flow of only approximately 25 to 50 ml/min [35] it seems to be sufficient to restore function and preserve brain tissue, as during vasospasm the affected tissue is normally not fully deprived from blood supply. As mentioned before, the timing for decision making is crucial and surgery has to be performed as fast as possible after failure of additional treatment to catch up within 3 h. Under these circumstances an improvement in outcome can be achieved, as shown by a good outcome in 60% of our small group, in this difficult to treat patients.

Conclusions

Emergency EC-IC bypasses are not very often needed in the treatment of intracranial aneurysms but worthwhile to be taken into consideration in risky conditions. The time taken in making a bypass should not be too long, so early and in-time decision making along with a fast and secure construction of the bypass are considered to be prerequisites. Emergency bypass in vasospasm re-

fractory to medical and endovascular therapy may help to improve outcome in selected patients.

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Bonnet bypass in multiple cerebrovascular occlusive disease

D. Zumofen, N. Khan, P. Roth, A. Samma, Y. Yonekawa

Department of Neurosurgery, University Hospital Zurich, Zurich, Switzerland

Summary

The rationale and technique of the bonnet bypass procedure is discussed in two cases of multiple cerebrovascular occlusive disease.

Method. Cerebral revascularization was achieved using respectively a radial artery interposition graft and a brachiocephalic vein interposition graft to connect the contralateral STA with a cortical branch of the ipsilateral MCA.

Findings. This alternate bypass technique proved to be an effective means of cerebral revascularization in selected cases where ipsilateral extracranial donor vessels were unavailable for classic STA-MCA bypass surgery.

Conclusion. Clinical and hemodynamic improvement can be achieved by a bonnet bypass in selected cases of multiple cerebrovascular occlusive disease. In addition to its previously described role in skull base tumor surgery, the procedure should therefore earn consideration in the treatment of cerebral ischemia and stroke prevention.

Keywords: Bonnet bypass; EC–IC bypass; radial artery interposition graft; saphenous vein interposition graft; multiple cerebrovascular occlusive disease; cerebral revascularization surgery.

Abbreviations

<i>CBF</i>	cerebral blood flow
<i>CCA</i>	common carotid artery
<i>DSA</i>	digital subtraction angiography
<i>ECA</i>	external carotid artery
<i>EC–IC bypass</i>	extracranial-intracranial bypass
<i>ICA</i>	internal carotid artery
<i>MCA</i>	middle cerebral artery
<i>Pcom</i>	posterior communicating artery
<i>PET</i>	positron emission tomography
<i>SA</i>	subclavian artery
<i>STA</i>	superficial temporal artery
<i>TIA</i> s	transient ischemic attacks
<i>VA</i>	vertebral artery

Introduction

The bonnet bypass is a variant of the classic EC–IC bypass pioneered by Yasargil and Donaghy in 1967 [4, 11].

Correspondence: Daniel Zumofen, M.D., Department of Neurosurgery, University Hospital Zurich, Frauenklinikstrasse 10, CH-8091 Zurich, Switzerland. e-mail: zumofen7@mac.com

It was first reported in 1980 by Spetzler *et al.* [9] in the scope of skull base tumor surgery. The word “bonnet”, meaning “hat” in French, describes the DSA image in coronal section of an interposed vascular graft running in the subcutaneous tissue from the contralateral donor-vessel (e.g. branch of the STA), over the head, to the ipsilateral recipient-vessel (e.g. cortical branch of the MCA).

To date, the indication and technique variations of the bonnet bypass have not been investigated except in three cases of skull base tumor surgery [3, 9]. In the present report we illustrate two cases of a bonnet bypass to discuss its potential role in the treatment of cerebral ischemia and stroke prevention.

Case report

Case 1

A 64-year-old male presented to our clinic in reason of forgoing minor strokes. He was already known for coronary, peripheral and renal artery disease, diabetes mellitus, arterial hypertension, nicotine abuse and hyperlipidemia. Three years before, he had undergone double combined aorto-coronary bypass surgery including a right internal mammarian artery bypass to the right coronary artery, and a left internal mammarian artery bypass to the left anterior descending artery. Ensuing follow-up examinations had indicated ongoing left ventricle hypoperfusion, as well as an increasing stenosis of the left CCA causing secondary left media territory hypoperfusion. Left CCA endarterectomy, followed by a saphenous vein interposition graft between the left CCA and the cardiac circumflex artery had been performed to improve the cardiac hemodynamic situation. Simultaneously, a left-sided STA-MCA bypass had been performed to alleviate the left media territory hypoper-

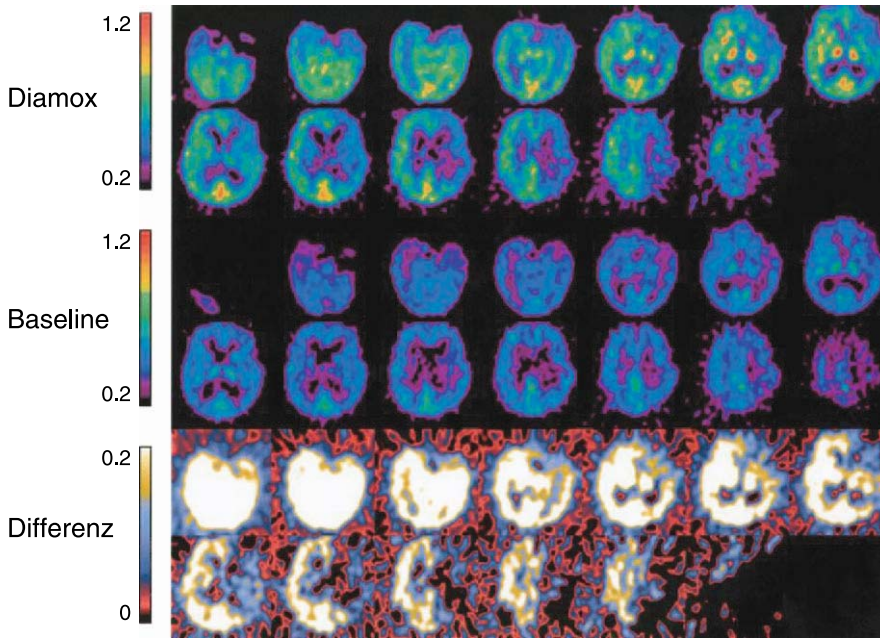


Fig. 1. Illustration concerning the first case. The pre-operative PET scan study shows a critical baseline perfusion in both cerebral hemispheres and a significantly reduced perfusion reserve after Diamox challenge in the dominant left hemisphere. Courtesy by the Department of Nuclear Medicine, University Hospital Zurich, Switzerland

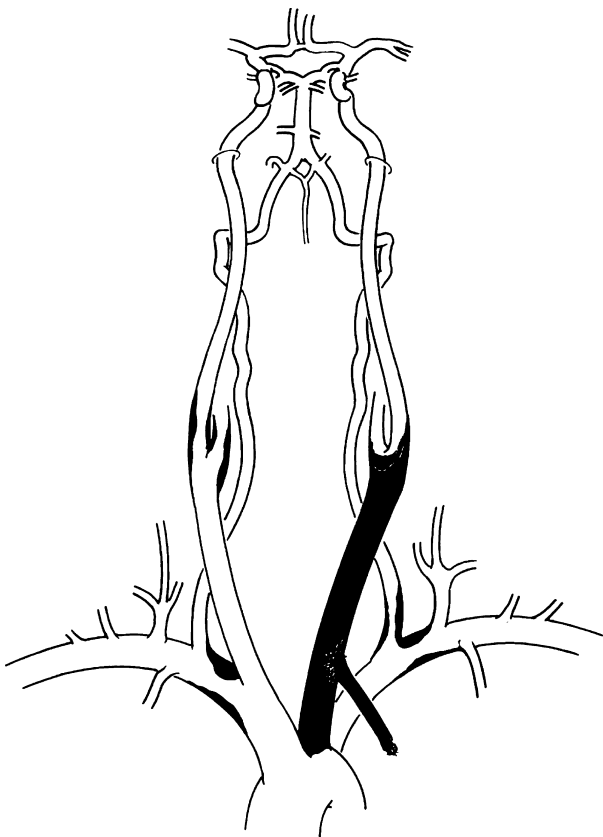


Fig. 2. Illustration concerning the first case. The supra-aortic vascular situation at the moment of the bonnet bypass surgery is marked by severe atherosclerotic occlusive processes including complete occlusion after thrombarterectomy of the left CCA, high-grade stenosis of the right SA and the left VA, as well as low-grade stenosis of the proximal right ICA, the proximal right ECA and the left SA. Illustration by P. Roth

fusion. Unfortunately, the CBF situation and the clinical symptomatology had remained unchanged due to rapid reocclusion of the CCA. When the patient represented to

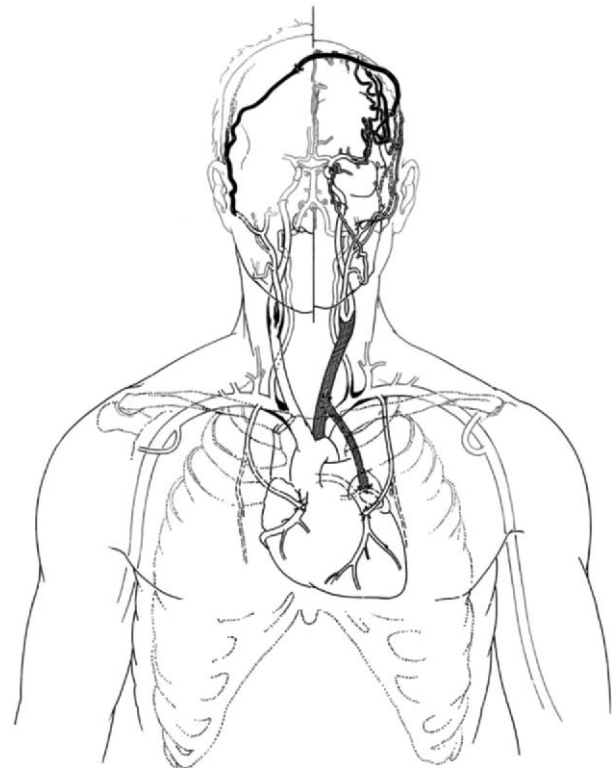


Fig. 3. Illustration concerning the first case. Adequate perfusion of the dominant left hemisphere is re-established through the bonnet bypass between the frontal branch of right STA and a cortical branch of the left MCA. Illustration by P. Roth

our department, he suffered from recurrent left-hemispheric TIAs inducing aphasia and a right sensorimotor hemisindrome despite adequate anticoagulant and antiplatelet medication. H₂O-PET scans showed critical baseline perfusion in both cerebral hemispheres and significantly reduced perfusion reserves after Diamox challenge in the dominant left hemisphere (Fig. 1). DSA revealed severe atherosclerotic occlusive processes of the supra-aortic vessels (Fig. 2). These processes included complete occlusion after thrombarterectomy of the left CCA, high-grade stenosis of the right SA and the left VA, as well as low-grade stenosis of the proximal right ICA, the proximal right ECA and the left SA. Left media territory perfusion was shown to rely critically on collateralization via the left Pcom and the still patent left STA-MCA bypass.

Facing clinical and radiological evidence that justifies cerebral revascularization surgery [1, 2, 5–8], and lacking an appropriate donor-vessel on the left side for a classic EC–IC bypass, we resolved to a bonnet bypass procedure. Consequently, the right radial artery was har-

vested and interposed between the right frontal branch of the STA and the posterior parietal artery (Fig. 3). Bypass patency was intra-operatively evaluated by micro-Doppler and confirmed three-month post-operatively by DSA (Fig. 4a–d). Perfusion improvement was evaluated by three-month post-operative H₂O-PET scan (Fig. 5). Clinically speaking, the patient showed recovery of all symptoms including cessation of the TIAs at three-month of follow-up.

Case 2

A 69 year-old male on adequate anticoagulant and antiplatelet medication presented to our department with recurrent left-hemispheric TIAs inducing a right hemiparesis, aphasia, and ipsilateral amaurosis fugax. He was already known for coronary, peripheral and renal artery disease, diabetes mellitus, arterial hypertension, nicotine abuse and hyperlipidemia. DSA and angio-MRI revealed severe stenosis of the left CCA, VA, SA, and right ICA, as well as low-grade stenosis of the right VA and ECA

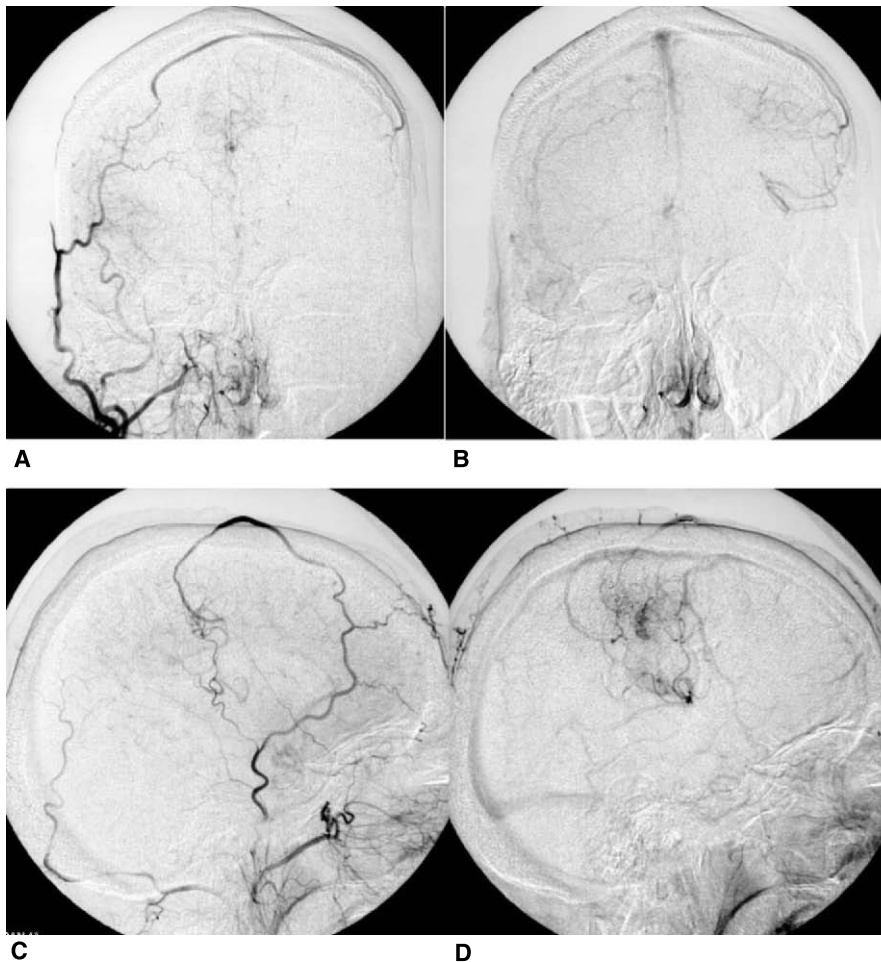


Fig. 4. Illustrations concerning the first case. The post-operative DSA shows the bonnet bypass between the frontal branch of the right STA and a cortical branch of the left MCA. The graft's patency (A and C) and an appropriate arterial blush in the left media-territory (B and D) are illustrated (A) Early phase in coronal view (B) Late phase in coronal view (C) Early phase in lateral view (D) Late phase in lateral view. Courtesy by the Department of Neuro-radiology, University Hospital Zurich, Switzerland

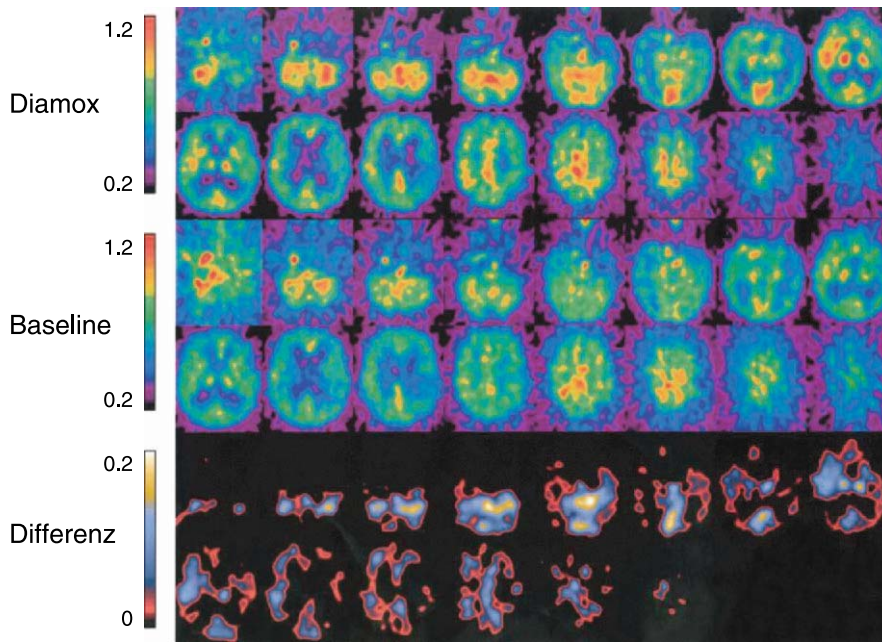


Fig. 5. Illustrations concerning the first case. The post-operative PET scan study shows adequate baseline perfusion in both hemispheres and sufficient perfusion reserve after Diamox challenge in the dominant left hemisphere. Courtesy by the Department of Nuclear Medicine, University Hospital Zurich, Switzerland



A



B

Fig. 6. Illustrations concerning the second case (A) The pre-operative angiogram shows severe stenosis of the left CCA, VA, SA, and right ICA, as well as low-grade stenosis of the right VA and ECA. Courtesy by the Department of Neuroradiology, University Hospital Zurich, Switzerland (B) Schematic illustration of the supra-aortic vascular situation at the moment of the "bonnet" bypass surgery. Illustration by P. Roth

(Fig. 6A, B). Left media territory perfusion thus greatly relied on collateralization via the left Pcom and ophthalmic artery.

Facing this clinical and radiological evidence of left media territory hypoperfusion that justifies cerebral re-

vascularization surgery [1, 2, 5–8], and lacking an appropriate donor-vessel on the left side for a classical EC-IC bypass, we choose to perform a bonnet bypass. Unfortunately, bilaterally positive Allen's tests and ischemic disease in both lower extremities excluded radial

artery or saphenous vein harvest. We therefore decided to interpose the right brachiocephalic vein between the frontal branch of the right STA and a cortical branch of the left MCA. Bypass patency was intraoperatively evaluated by micro-Doppler. Following the intervention, the patient showed a short period of clinical improvement in terms of cessation of the TIAs and some regression of the right hemi paresis. Regretfully, he expired 3 weeks after surgery due to cardio-pulmonary decompensation.

Discussion

Why did we choose a bonnet bypass procedure?

With respect to the discussion concerning the role of the EC-IC bypass surgery in the treatment of cerebral ischemia and stroke prevention [1, 2, 5–8], our aim was to improve the disturbed cerebral hemodynamic situation in patients with multiple cerebrovascular occlusive disease and well-proven media territory hypoperfusion. Due to severe stenosis, respectively complete occlusion of the ipsilateral CCA in both cases, the ipsilateral STAs could not be used as a donor-vessel for a classic STA-MCA bypass. Alternatively, a high-flow bypass using a venous interposition graft between an ipsilateral supra-aortic artery (e.g. VA, SA) and a cortical branch of the MCA had to be discarded in reason of the high risk of hemorrhage into a hypoperfusion-area after reperfusion by a high-flow bypass [10]. Moreover, surgical invasiveness and peri-operative risks would have been considerable especially in patients with pre-existing multiple-organ-disease.

Which vessels should be harvested for the interposition graft?

In the initial report by Spetzler *et al.* [9], a saphenous vein interposition graft was used to provide adequate vessel length between the contralateral STA and an ipsilateral cortical branch of the MCA. Deshmukh *et al.* [3] reported more recently two case of a bonnet bypass using a radial artery interposition graft. In the present two cases, the saphenous veins had either already been used for coronary bypass surgery, or harvesting was not possible because of severe ischemic disease of the inferior extremities. Therefore, the radial arteries were the donor vessels of choice, although, in the second case, the brachiocephalic vein had to be taken because of bilaterally intolerable Allen's tests. In summary, our ex-

perience revealed that a radial artery graft, if it is available, is more suitable than the saphenous vein graft. Firstly due to the smaller diameter difference to the stump end of the STA and the cortical MCA, and secondly because of its lesser distensibility, and hence better adaptability to low-flow qualities.

Conclusions

We have learned from our two cases that clinical and hemodynamic improvement can be achieved by a bonnet bypass procedure in well-selected cases of multiple cerebrovascular occlusive disease. As a result we state that the role of this variant of the classic EC-IC bypass surgery should be extended beyond skull base tumor surgery. However, we were also reminded that patients suffering from multiple cerebrovascular occlusive disease are at particularly high peri-operative risk and hence require highly specialized peri-operative management and care.

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Combined treatment using CEA and CAS for carotid arterial stenosis

T. Tsukahara, T. Hatano, T. Nakakuki, Y. Tsuji, T. Aoyama, H. Ogata

Kyoto Medical Center, Department of Neurosurgery and Clinical Research Center, National Hospital Organization, Kyoto, Japan

Summary

In this study we report our surgical results of CAS and CEA for carotid stenosis and suggest an appropriate treatment strategy for patients with high risks such as bilateral carotid stenosis or medical risk factors. From January 2001 to December 2005 we surgically treated 182 patients with carotid stenosis. Seventy-nine lesions were treated by CEA and 145 by CAS, respectively. Although CEA was considered the first choice for severe carotid stenosis, CAS was chosen for treatment when CEA was considered a higher risk for patients. Stenosis of carotid arteries was relieved in all cases after CEA or CAS. Surgical mortality of CEA was 1.1% (1/94). Surgical mortality of CAS was 0.7% (1/145). Carotid stenotic lesions can be treated with comparably low morbidity and mortality rates using CEA or/and CAS considering each characteristic of carotid stenosis of patients even with medically high risk or bilateral carotid stenosis.

Keywords: Carotid endarterectomy (CEA); carotid artery stenting (CAS).

Introduction

The efficacy of carotid endarterectomy (CEA) for carotid stenosis is well documented and has been generally accepted as a treatment for severe carotid stenosis [5, 8]. On the other hand, the remarkable improvement in endovascular treatment in recent years has developed carotid arterial stenting (CAS) for elective treatment of carotid stenosis, although the superiority of this endovascular procedure, in terms of safety, efficacy and durability, has not been confirmed by randomized clinical trials (RCT) [3, 6, 7, 13]. A recent consensus statement from the American Heart Association emphasized that this endovascular treatment should be restricted to limited subgroups of patients with carotid artery stenosis [1] and the Japanese guidelines for the treatment of cerebral

stroke in 2004 also recommends CEA for symptomatic severe carotid stenosis more strongly than CAS. In Japan, however, the number of CAS has markedly increased as the incidence of carotid lesions, and the number of surgical interventions for these lesions has also increased recently. This is mainly due to the development of new techniques and refined instruments for endovascular treatment [10, 11] and the specific characteristics of high cervical lesions of Japanese patients, which sometimes complicate the operative procedure of CEA [14]. Although recent studies have suggested that CAS is more beneficial than CEA for high-risk patients [4, 7, 12] some points remain to be clarified for the indication of CAS, such as the patient subgroup at high risk for CEA, and whether long the term surgical results of CAS are better than CEA.

In this study we report our surgical results of CAS and CEA for carotid stenosis and suggest an appropriate treatment strategy for patients with high risks such as bilateral carotid stenosis or medical risk factors.

Clinical materials and methods

Patient population and surgical treatments

From January 2001 to December 2005 we surgically treated 182 patients with carotid stenosis. Seventy-nine lesions were treated by CEA and 145 by CAS, respectively. The number of cases is shown in Fig. 1.

Surgical treatment (CEA or CAS) was performed for patients with 1) angiographically severe stenosis (60–99% stenosis), 2) echographically severe stenosis (75–99% stenosis) and 3) symptomatic stenosis with intra-luminal ulceration. Although CEA was considered the first choice for severe carotid stenosis, CAS was chosen for treatment when CEA was considered a higher

Correspondence: Tetsuya Tsukahara, M.D., Kyoto Medical Center, Department of Neurosurgery, National Hospital Organization, 1-1 Mukaihata-cho, Fushimi-ku, Kyoto 612-8555, Japan.
e-mail: tsukahara@kyotolan.hosp.go.jp

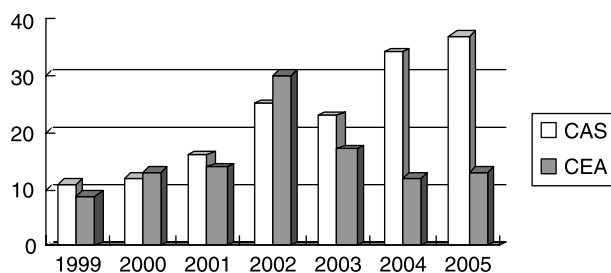


Fig. 1. CEA and CAS at Kyoto Medical Center Distal Blocking used after September 2002

risk for patients with 1) contra-lateral ICA lesion, 2) distal ICA lesion, 3) higher level lesion (higher than C2 level) and 4) medical risk factors (cardiac disease, etc.).

Thirty-two patients (18%; 28 male, mean age of 71.4, range 62–82) had bilateral carotid stenosis. Bilateral CAS was performed in seven cases for which CEA was considered high risk because of coexistent medical factors such as untreated coronary artery disease. Bilateral CEA was performed in the first case. Subsequently, in 24 patients, a carotid lesion on one side was treated by CEA and the other side by CAS. We basically treated the symptomatic side first and the more severe stenotic side by CEA except when a high hemodynamic risk was anticipated during CEA. In such cases we treated the contralateral side first by CAS, and then the symptomatic side by CEA, thus, CAS was performed before CEA in 13 cases.

The contralateral carotid artery was occluded in 13 patients (7%) with carotid stenosis. These patients received STA-MCA anastomosis on the occluded side and carotid stenosis was treated by CEA in three patients and by CAS in ten patients.

The patient population with CEA is shown in Table 1 and with CAS in Table 2. Coexistent medical risk factors are shown in Table 3.

Table 1. Patient population with CEA

Cases (79)	Age (mean range)	M:F (%)	S:A (%)	Stenosis rate 83%
Unilateral St. (54)	69.5 (42–82)	85:15	87:13	
Bilateral St. or Occ. (25)	71.4 (62–82)	84:16	88:12	

Table 3. Coexistent medical risk factors

Risk factors (%)	Hypertension	Diabetes mellitus	Hyperlipidemia	Coronary heart disease
CEA	70	24	20	17 (unstable: 0%)
CAS	40	18	21	19 (unstable: 10%)
Bilateral stenosis	67	27	47	33
Contra lateral occlusion	77	39	23	23

Table 2. Patient population with CAS

Cases (145)	Age (mean range)	M:F (%)	S:A (%)	Stenosis rate 55%
Unilateral St. (96)	71.3 (54–86)	78:22	28:7	
Bilateral St. or Occ. (49)	71.4 (62–82)	84:16	6:94	

Age and male dominance were not different between patient groups of CEA and CAS; however, more severe stenosis and more symptomatic cases were treated by CEA than by CAS.

Regarding coexistent medical factors, the incidence of hypertension was higher in the CEA-treated group. The incidence of other factors was not different between these patient groups; however, all coronary heart disease in the CEA group was stable. On the other hand, coronary heart disease in the CAS group was not surgically treated before CAS in ten patients (10/18 total patients) who received CABG (coronary artery bypass graft) or PCI (percutaneous coronary artery intervention) after CAS.

Surgical procedure

CEA was performed under general anesthesia with intra-operative monitors of INVOS (SaO₂), EEG and SEP. Intra-operative carotid arterial shunt was not used during cross-clamping. A balloon occlusion test (BOT) of ICA was performed for selective cases before the surgical intervention. When BOT was not tolerable, the carotid lesion was treated by CAS.

CAS was performed under local anesthesia. Pre-dilatation was performed after distal protection was inserted in the internal carotid artery, and then a stent (Smart[®]) was placed.

Surgical results

Vascular dilatation

Stenosis of the carotid arteries was relieved in all cases after CEA or CAS. Mean stenotic rates of carotid arteries were 83% in CEA cases and 55% in CAS cases preoperatively, and 3% after CEA and 6% after CAS, respectively.

Surgical complications

Surgical mortality with CEA was 1.1% (1/94). A 74-year-old male died five days after CEA of renal failure and subsequent multiple organ failure caused by radical scavengers.

Surgical mortality with CAS was 0.7% (1/145). A 76-year-old male died three months after CAS of blue toe syndrome and subsequent multiple organ failure.

There were no neurological deteriorations in the acute phase after CEA or CAS treatment, although diffusion-weighted brain MRI showed asymptomatic small ischemic lesions in three of nine cases after CAS and none after CEA.

Palsy of lower cranial nerves was not apparent in any of the treated cases.

Follow-up

Follow-up angiography was performed in all cases at least six months after the treatment during the follow-up period (mean 40 months). After CEA, symptomatic restenosis of ICA occurred in one case (1/94, 1.1%) and asymptomatic restenosis of ICA occurred in two cases (2/94, 2.2%), which were successfully treated by CAS. After CAS, asymptomatic occlusion of ICA occurred in one case (1/145, 0.7%).

Discussion

In our series of treatments, CEA and CAS for carotid stenosis were performed with a comparably low rate of complications even for high-risk patients. These results suggest that our treatment strategy for carotid stenosis is basically acceptable, although there are some points for discussion.

We chose CEA as the first choice for the treatment of severe carotid stenosis, since its efficacy of CEA for carotid stenosis is well confirmed by randomized clinical trials (RCT) [5, 8] however, treatment options for carotid stenosis have changed since the introduction of CAS. We also chose CAS for specific subgroups of patients such as those with a contralateral ICA lesion, distal ICA lesion, higher-level lesion and other medical risk factors, for whom the beneficial effect of CEA is not apparent because of the complication rate [9].

The number of CAS has remarkably increased recently in Japan, although the Japanese guidelines for the management of stroke 2004 favored CEA over CAS for the treatment of symptomatic severe carotid stenosis. The number of CEA and CAS registered at the Japanese Neurosurgical Society was 2395 cases of CEA and 1851

cases of CAS in 2003, and 2662 cases of CEA and 2353 cases of CAS in 2004, respectively. The main reason for this increase is increased safety by the introduction of self-expandable stents and distal embolization blocking systems [10, 11], however, specific characteristics of high cervical lesions in Japanese patients and the limited number of patients with carotid lesions in Japan may also be counted as important reasons for the remarkable increase of CAS. The mean cervical level of the lesion in Japanese patients is C3 or C4 and more than few patients have the lesion at the C2 vertebral level, which is at least one vertebral level higher than the lesions of European patients [14]. This situation sometimes complicates the operative procedure of CEA and induces more complications of lower cranial nerve palsy.

The Japanese Neurosurgical Society estimated that the number of surgical interventions for carotid stenosis performed throughout Japan, namely CEA at that time, was less than 2,000 per year 20 years ago. Although the number has increased by more than double or three times, the operative technique is not popular among Japanese neurosurgeons or vascular surgeons. The development of endovascular treatment has overlapped the period of increase of carotid stenotic lesions in Japan.

Although the safety and durability of CAS have remarkably improved, it is still not suitable for treatment of soft plaque, eccentric or tortuous lesions and narrow residual lumen. Cao *et al.* reported that when comparing CAS to CEA, the risk of any neurological events is higher, particularly during catheterism and ballooning despite the use of cerebral protection devices [2]. The risk may be reduced after an appropriate learning curve involving series of patients even larger than those usually required for qualification.

We also experienced mortality by catheterization complications such as blue toe syndrome and small ischemic lesions on diffusion-weighted brain MRI even if they were asymptomatic in our treatment series. We therefore consider that CEA is the first choice for severe carotid stenosis and tortuous lesions.

The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial was the first completed controlled, prospective randomized trial in which CEA was compared with state of the art CAS with cerebral protection [7].

The SAPPHIRE trial only enrolled patients who were considered high risk for CEA as follows: Octogenarian, carotid reoperation, cervical radiation, contralateral carotid occlusion, severe tandem lesion, high cervical lesion (at least C2), lesion below the clavicle, and con-

tralateral laryngeal palsy. The perioperative risks of stroke (CAS, 3.1%, CEA, 3.3% $P = 0.94$) and mortality (CAS, 0.6%, CEA, 2.0%, $P = 0.29$) were similar; however, more patients suffered postoperative myocardial infarction (MI) in the CEA group than in the CAS group (6.6% vs. 1.9%, $P = 0.04$).

In our series of treatments we chose CAS for patients with untreated coronary disease. After the coronary disease was treated and was stable, CEA did not induce MI in the perioperative period; however, other risks have been over-represented in SAPPHERE. Regarding octogenarians, the age of our patients was not different between patient groups of CEA and CAS. CEA can be performed safely enough for aged patients if they do not have other medical risk factors. As for patients with carotid reoperation and cervical radiation, we think that CAS is the first choice since plaque in these patients sometimes adheres tightly to the medial layer, so it is sometimes difficult to make a smooth intraluminal wall by CEA.

Although the restenosis rate of CAS compared favorably with CEA patients in SAPPHERE, a longer observation period is required for confirmation.

In conclusion, we can design an appropriate treatment strategy using CEA or/and CAS considering each characteristic of carotid stenosis of patients, even those at high risk.

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Part 4:
Moyamoya angiopathy, history

Present status of Moyamoya disease in Japan

T. Iwama, S. Yoshimura

Department of Neurosurgery, Gifu University Graduate School of Medicine, Gifu, Japan

Summary

To gain an overview of the current status of Moyamoya disease in Japan, we reviewed the 2002–2004 report of the Research Committee on Moyamoya Disease and the clinical data of Moyamoya patients treated at Gifu University Hospital during the past 2 years.

According to the report, a nationwide epidemiological survey performed in 2004 revealed that approximately 7500 Japanese were treated for Moyamoya disease; their number doubled during the last 10 years. Moyamoya associated with headache was newly added as a subtype; as many as 5% of Moyamoya patients experience headache. Three-dimensional (3D) stereotactic statistical cerebral blood flow (CBF) analysis was reported as useful for the stratification of the cerebral hemodynamics in Moyamoya disease. To develop treatment guidelines for hemorrhagic Moyamoya, a prospective randomized control trial begun in 2001 is ongoing.

During the past 2 years, 23 patients with Moyamoya disease were treated at our hospital. Of these, 17 presented with transient ischemic attacks/infarction, 4 with intracranial hemorrhage (ICH), and 2 with headache. One patient who presented with ICH died during the acute stage, the remaining 22 patients were successfully treated by direct bypass surgery.

Keywords: Moyamoya disease; present status; Japan; Research Committee on Moyamoya Disease; epidemiology; diagnosis; treatment of hemorrhagic type.

Introduction

The first Japanese Moyamoya disease patient was documented in 1957 [10], subsequently, reports of Moyamoya increased and its clinical features have been revealed gradually. Moyamoya first appeared in the English nomenclature in 1969 [9]. In Japan, the Research Committee on Moyamoya Disease was established in 1977; it was funded by grants from the Ministry of Health, Labor and Welfare. These grants promoted clinical and basic research on Moyamoya disease in Japan. At present, the committee is supported by Health and Labor Science research grants for Research on Measures against Intractable Diseases.

Although many studies addressed the mechanisms underlying Moyamoya disease, its etiology remains unknown. On the other hand, clinical investigations conducted during the last 30 years clarified the clinical features of Moyamoya disease and diagnostic criteria have been established. The efficacy of direct and/or indirect extracranial-intracranial (EC–IC) bypass surgery for the prevention of ischemic attacks in Moyamoya patients is now widely recognized [3, 4].

To gain an overview over the current status of Moyamoya disease in Japan, we reviewed the latest report submitted by the Research Committee on Moyamoya Disease and also inspected the clinical data of patients treated during the past 2 years at Gifu University Hospital, a typical Japanese medical center.

Materials and methods

The 2002–2004 report of the Research Committee on Moyamoya Disease (Chairman: Prof. T. Yoshimoto, Tohoku University) was published in March 2005 [13].

Gifu University Hospital is located in Gifu City situated in the center of the main island of Japan. The population in and around Gifu City is about one million. Among the 6 neurosurgical clinics in the area, the Department of Neurosurgery at Gifu University Hospital is the largest. During the past 2 years, 525 open-, 217 endovascular-, and 64 stereotactic radiosurgeries were performed and 23 Moyamoya patients have been treated at Gifu University Hospital. Their clinical data were analyzed retrospectively to elucidate the current status of Moyamoya management in Japan.

Results

Summary of the 2002–2004 report of the research committee

The main topics of this report were the epidemiology, diagnosis, and treatment of hemorrhagic Moyamoya disease.

Correspondence: T. Iwama, Department of Neurosurgery, Gifu University Graduate School of Medicine, 1-1 Yanagido, Gifu 501-1194, Japan. e-mail: tiwama@gifu-u.ac.jp

The nationwide epidemiological survey conducted in 2004 revealed that the total number of patients with Moyamoya disease treated in Japan was approximately 7500; their number doubled during the last 10 years [12]. Moyamoya in patients who initially present with headache was recorded as headache-type Moyamoya. As many as 5% of patients present with this new disease subtype [1].

Three-dimensional stereotactic statistical cerebral blood flow (CBF) analysis has been introduced as a general diagnostic method in Japan. It was reported to be useful for the stratification of the cerebral hemodynamics in Moyamoya disease [8].

To develop treatment guidelines for hemorrhagic Moyamoya, a randomized controlled trial (Japan Adult Moyamoya [JAM] Trial) was started in 2001; it is still ongoing [11]. It is a multicenter prospective randomized controlled trial; the participants are 23 Japanese institutions. Patients with spontaneous typical (bilateral) Moyamoya who suffered intracranial bleeding during the preceding 12 months were enrolled in this trial. Patients between 16 and 65 years of age who are able to lead an independent daily life (Modified Rankin scale [mRS]: 0–2) are eligible.

Treatment is randomized by computer to the best medical care alone (medical group) or the best medical care plus bilateral direct EC–IC bypass (surgical group). All patients are followed for 60 months. The primary endpoints are recurrent bleeding, complete stroke leading to significant morbidity (mRS: 3–5), significant morbidity or death from other causes, and additional EC–IC bypass for reasons of progressive ischemic stroke or a crescendo of transient ischemic attacks (TIA). Secondary endpoints are recurrent bleeding on the side of previous bleeding and disease-related death or severe disability (mRS: 3–5). As of January 2006, 66 patients were enrolled in this trial. There were no significant differences with respect to the primary endpoints between the medical and the surgical group.

Moyamoya patients treated at Gifu university hospital

During the past 2 years, 23 Moyamoya patients were treated at Gifu University Hospital. They were 5 pediatric/juvenile (3–16 years old) and 18 adult (22–69 years old) patients. Of these, 10 presented with TIA, 17 with infarction, 4 with intracranial hemorrhage (ICH), and 2 with headache. Of the 4 patients with ICH, one died during the acute stage, another was in a deep coma at admission and became bed-ridden (mRS: 4), and the

other 2 were referred to Gifu University Hospital at 1 and 5 years after their last ICH episode.

Our first treatment in patients with ischemic and headache-type Moyamoya is the administration of antiplatelet therapy. Subsequently, we measure the CBF at rest and under acetazolamide loading. If a decrease in cerebrovascular reserve capacity is detected, direct EC–IC bypass surgery is performed in the hemisphere with the hemodynamic insufficiency. In patients with hemorrhagic-type Moyamoya we perform direct EC–IC bypass in the bilateral hemispheres.

We performed 36 bypass surgeries on the 22 surviving patients. The procedures were superficial temporal artery (STA)-middle cerebral artery (MCA) double anastomosis ($n = 22$), STA-MCA and STA-anterior cerebral artery (ACA) anastomosis ($n = 2$), STA-MCA single anastomosis ($n = 11$), and occipital artery (OA)-MCA single anastomosis ($n = 1$).

Of the 19 patients with ischemic or headache-type Moyamoya, 3 manifested transient neurological deterioration on days 2–14 after surgery. In one of these 3 patients, postoperative single photon emission computed tomography (SPECT) detected transient hyperperfusion (Figs. 1, 2). All 3 patients recovered from the neurological deterioration. The final outcome was mRS 0–1 in 17 patients and mRS 3 (due to initial infarcts) in 2. None of the 3 patients with hemorrhagic-type Moyamoya devel-

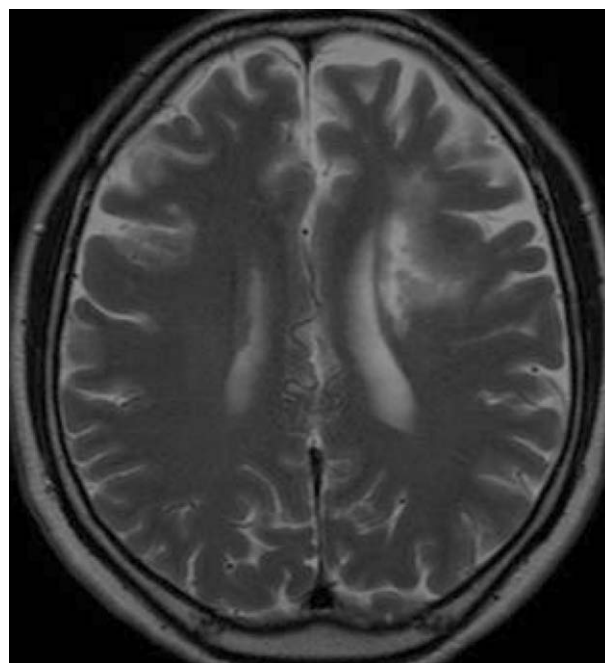


Fig. 1. A 52-year-old woman who presented with minor completed stroke. T2-weighted MRI demonstrated an infarct in the deep white matter of the left frontal lobe

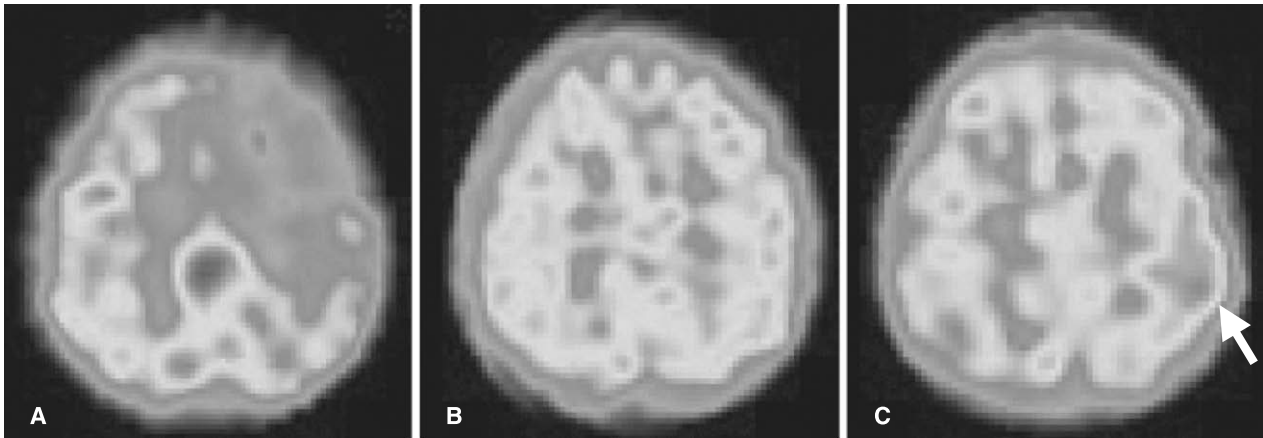


Fig. 2. The same patient as in Fig. 1. This 52-year-old woman underwent STA-MCA anastomosis on the left side. Her aphasia was transiently exacerbated during days 2 to 14 after the operation. (A) The preoperative SPECT image shows hypoperfusion in the left frontal lobe. (B) A SPECT image obtained 3 days after the operation demonstrates an increase in CBF in the left frontal lobe; there is no CBF laterality. (C) A SPECT image obtained on postoperative day 10 depicts hyperperfusion in the left fronto-parietal lobe (arrow)

oped postoperative transient neurological deterioration; the final outcome was mRS 0 in 2- and mRS 4 (due to initial hemorrhage) in 1 patient.

Discussion

The number of Moyamoya patients treated in Japan has doubled during the last 10 years. One reason for the apparent increase is the spread of less invasive diagnostic methods, i.e. MRI and magnetic resonance angiography (MRA).

Diagnostic guidelines for Moyamoya have been established and patients with the ischemic type are treated by direct- or indirect bypass surgery [3, 4]. As postoperative hyperperfusion may lead to neurological deterioration [2], the blood pressure must be carefully controlled in operated patients.

The prognosis of patients with hemorrhagic-type Moyamoya remains unsatisfactory [5–7]. Intracranial bleeding is thought to be attributable to rupture of fine, spontaneously developed collateral vessels. The newly-developed collateral flow after bypass surgery may re-

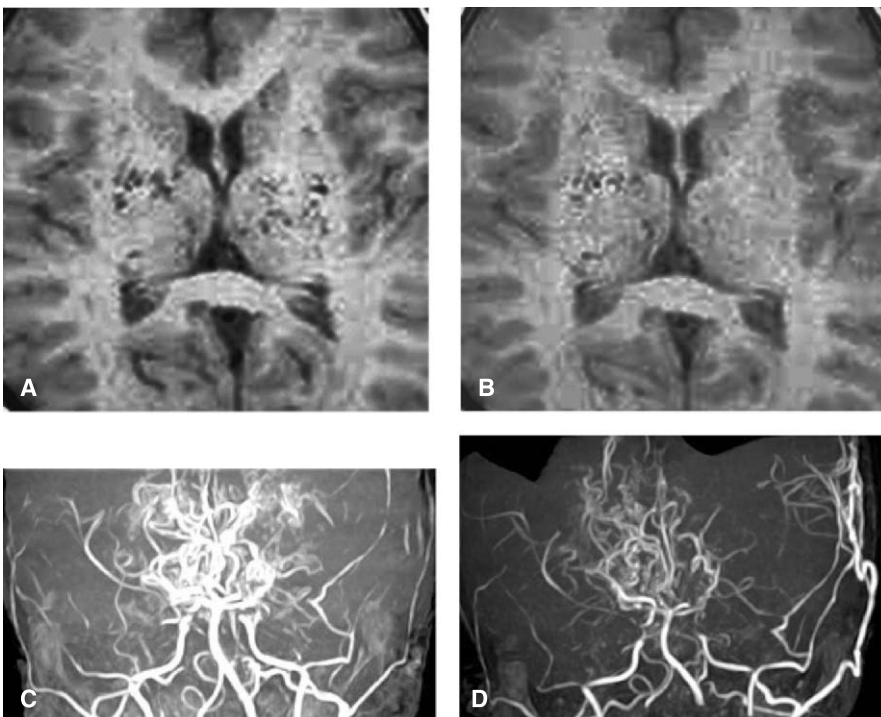


Fig. 3. A 7-year-old boy who presented with bilateral transient ischemic attacks. (A) Preoperative T1-weighted MRI scan demonstrating multiple flow-voids at the bilateral basal ganglia. (B) T1-weighted MRI performed after left-sided STA-MCA anastomosis shows disappearance of the flow-voids in the left basal ganglia. (C) Preoperative MRA demonstrating bilateral stenosis of the internal carotid arteries and well-developed collateral vessels (basal Moyamoya vessels). (D) MRA obtained after left-sided STA-MCA anastomosis shows development of collateral flow through the bypass. The basal Moyamoya vessels on the left side appear faint

duce hemodynamic stress on these vessels. In fact, Moyamoya vessels are often faint after bypass surgery (Fig. 3). However, the efficacy of bypass surgery in reducing the risk of intracranial bleeding remains unclear. The ongoing Japanese prospective randomized control trial to establish treatment guidelines for patients with hemorrhagic Moyamoya [11] is expected to shed light on this issue.

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Results of direct and indirect revascularisation for adult European patients with Moyamoya angiopathy

D. Hänggi¹, J. H. Mehrkens², R. Schmid-Elsaesser², H.-J. Steiger¹

¹ Department of Neurosurgery, Heinrich-Heine-University, Düsseldorf, Germany

² Department of Neurosurgery, Ludwig-Maximilians-University, Munich, Germany

Summary

There is little information concerning clinical data and revascularization procedures in adult European patients with Moyamoya disease. More data are available on juvenile European Moyamoya angiopathy and its microsurgical therapies. This analysis summarizes our clinical experience in European adult patients with Moyamoya angiopathy.

Nine adult European patients underwent surgical revascularization for Moyamoya angiopathy between 1997 and 2005. Direct intracranial-extracranial (EC-IC) bypass was considered the primary surgical modality. In case of unsuitable donor or recipient arteries, encephalomyo-synangiosis (EMS) was chosen as an indirect modality.

The current analysis confirms that direct EC-IC-bypass is a feasible option for most cases of adult European Moyamoya disease. Exact definition of long-term benefits would require a multicentric study. EMS appears to be of questionable value in the adult European population.

Keywords: Moyamoya angiopathy; European population; direct and indirect revascularisation; EC-IC bypass.

Introduction

The Moyamoya disease was first described in Japan and published in 1957 [15]. The main feature of Moyamoya angiopathy is the progressive occlusion of both internal carotid forks associated with a fine vascular network, the “Moyamoya” vessels [13]. Multiple clinical reports are available about the juvenile and adult form of Moyamoya disease for the Asian especially for the Japanese population [1]. For the European Caucasian adult population an increasing number of cases is registered [6]. However, there is less information regarding clinical condition and therapeutic impact. We analysed our European adult patients with Moyamoya disease of the last years to gain more information on the clinical

symptomatology in this group, awareness of the disease, pre- and postoperative management and the chosen surgical method.

Patients and methods

Nine adult patients with the diagnosis of Moyamoya angiopathy were surgically managed between 1997 and 2005. All patients were of European-Caucasian origin. Mean age at presentation was 36 years (range 24–60 years). Seven patients were female and two were male. In addition to clinical evaluation a preoperative 6 vessel cerebral angiography (DSA), a computed tomography (CT) and/or a magnetic resonance tomography (MRI) was performed in all patients. Moreover, cerebral blood flow (CBF) was documented in all patients by single proton emission tomography (HMPAO-SPECT) and/or perfusion MRI with and without acetazolamide challenge. The patients underwent direct or indirect revascularisation procedures. The follow-up was documented clinically and by CBF measurements.

Results

The clinical, diagnostic, therapeutic and outcome results of all nine patients are summarised in Table 1.

Clinical appearance

The preoperative clinical symptomatology consisted of ischaemic events in eight patients represented by transient ischemic attacks (TIAs) compared with one haemorrhagic onset in a 24-year-old pregnant woman. This haemorrhage was exclusively intraventricular involving both lateral ventricles. The onset of haemorrhage could be related to a hypertensive episode. Based on individual evaluation of each patient's history, the mean time interval from the first prodromal symptoms related to the Moyamoya angiopathy until the first neurosurgical admission was 6.4 years (range of 18 months to 14 years).

Correspondence: Dr. D. Hänggi, Neurochirurgische Klinik, Universitätsklinikum, Moorenstraße 5, D-40225 Düsseldorf, Germany.
e-mail: Daniel.Haenggi@uni-duesseldorf.de

Table 1. Summary of patient characteristics, treatment modality and outcome

Patient ID	Clinical appearance	Angiographic image preoperative	CBF preoperative	Mode of therapy	Procedure related complications	Angiographic image postoperative	CBF postoperative	Neurological condition
#1 33/m	ischaemic l	occlusion ICA l/r	haemodynamic insufficiency l/r	EC-IC bypass l	no	bypass patency l	increased l	improved
#2 39/m	ischaemic l/r	occlusion ICA l/r	haemodynamic insufficiency l/r	EC-IC bypass l/r	intracerebral haematoma	bypass patency l/r	increased l/r	improved
#3 29/f	ischaemic l	occlusion ICA l/r	haemodynamic insufficiency l/r	EC-IC bypass l/r	no	bypass patency r/l?	increased r/l?	unchanged
#4 24/f	haemorrhage intraventricular	occlusion ICA l/r	haemodynamic insufficiency l/r	EC-IC bypass l Sec. EMS r	no	bypass patency l	increased l	improved
#5 60/f	ischaemic r	occlusion ICA r	haemodynamic insufficiency r	EC-IC bypass r	no	bypass patency r	increased r	improved
#6 24/f	ischaemic l	occlusion ICA l/r	haemodynamic insufficiency l/r	Sec. EMS l/r	no	EMS	?	unchanged
#7 44/f	ischaemic l	occlusion ICA l occlusion MCA r	haemodynamic insufficiency l	EC-IC bypass l	no	EMS	?	improved
#8 27/f	ischaemic r	occlusion ICA l/r	haemodynamic insufficiency l/r	EC-IC bypass l	no	bypass patency l	increased l	improved
#9 43/f	ischaemic l/r	occlusion ICA l stenosis MCA r	haemodynamic insufficiency l/r	EC-IC bypass l	no	bypass patency l	unchanged	deteriorated

CBF Cerebral blood flow; ICA internal carotid artery; MCA middle cerebral artery; EC-IC bypass extracranial-intracranial bypass; EMS encephalomyo-synangiosis; l left-sided; r right-sided.

Radiological classification

A preoperative 6 vessel DSA was performed as mentioned in all nine patients. DSA revealed a bilateral occlusion of the internal carotid artery (ICA) in six patients, in two patients a unilateral occlusion of the ICA and a contralateral occlusion of the middle cerebral artery (MCA) and in one patient unilateral occlusion of the ICA with a normal angiogram contralaterally. In two patients the posterior circulation was additionally affected angiographically in terms of stenosis of the posterior cerebral artery (PCA). The preoperative MRI showed major infarction in four hemispheres in four patients.

Cerebral blood flow measurements

The preoperative haemodynamic study with SPECT was performed in all patients under baseline condition and acetazolamide challenge. The reserve capacity was insufficient in seven patients with a territorial distribution corresponding to the MCA on both sides whereas we

documented unilateral haemodynamic insufficiency in the MCA area in two patients. Among the latter group there was one patient with occlusion of the ICA on one side and MCA on the other side and one patient with the unilateral occlusion of the ICA. Moreover the results of SPECT showed no other perfusion deficits in the territories of the anterior cerebral artery (ACA) and the PCA.

Mode of therapy

Preoperatively the surgical goal was defined primarily in performing a single standard superficial temporal artery to middle cerebral artery (STA-MCA) bypass. The indirect revascularisation technique was only chosen if the bypass procedure was intraoperatively not possible and therefore according to our protocol not as primary alternative or as an additional procedure. The encephalomyo-synangiosis (EMS) was chosen as the method of choice for indirect revascularisation. According to this

strategy the quantitative preoperative surgical goal was to perform 13 standard STA-MCA bypasses for the nine patients. The exclusion criteria for the bypass procedure were major territorial infarction and of course the unilaterally normal perfusion to unilateral pathology.

In two patients the bypass was performed bilaterally. In six patients a unilateral bypass was carried out. Direct revascularisation on one side and EMS on the other side was applied in one patient. Bilateral EMS was performed in one patient.

Procedure related complications

One patient developed a deep thalamic haematoma on the third postoperative day due to a hypertensive episode with a consecutive hemiparesis. The haematoma was evacuated surgically and the patient recovered well without any deficit. In addition there was one injury of the frontal branch of facial nerve due to microsurgical dissection of the STA.

Follow-up

In all patients a postoperative DSA was performed within 24 h after surgery and approximately six months later. Bypass patency was documented in all ten bypass procedures immediately after surgery (within 24 h) and after approximately six months. For classification of the EMS revascularisation a grading scale suggested by Perren and colleagues was used [12]. According to this grading the angiography approximately six months after the EMS procedure demonstrated extensive neorevascularisation (more than four vessels) in one case, moderate neorevascularisation (one to four vessels) in one case and absent neoangiogenesis (no vessel) in one case.

The CBF measurements performed two to twelve months after the surgical therapy by HMPAO-SPECT revealed no impaired reserve capacity in seven hemispheres (seven STA-MCA bypasses), an unchanged condition in four hemispheres (one STA-MCA bypass and all EMS procedures) and no documentation in two hemispheres (two patients with STA-MCA bypass).

The neurological condition investigated at least three to six months after surgery demonstrated for the bypass group improvement in six patients, an unchanged clinical situation in one patient and deterioration in one patient due to progressive disease. In all patients treated with EMS, we registered an unchanged neurological condition.

Discussion

Between 1997 and 2005 nine adult patients with Moyamoya disease were admitted to the neurosurgical centres of Munich and Düsseldorf. Previously the incidence of adult patients with Moyamoya angiopathy in Europe was calculated as 0.3 patients per centre per year, which is approximately one tenth of the incidence in Japan [17]. Our adult European group represented a clearly female predominance which is well known from recent studies in Japan [8], the United States [16] as well as in Europe [6]. The clinical onset leading to neurosurgical admission was in the present group an ischaemic one in eight of nine cases. Other reports documented in the adult group more haemorrhagic complications [7]. It is important to point out that the mean time interval from the first prodromal symptoms (e.g. epileptic event) related to the Moyamoya angiopathy to the first neurosurgical admission was 6.4 years (range of 18 months to 14 years). This lack of adequate diagnosis could be interpreted as a consequence of insufficient awareness in Europe. This estimation is underlined by the fact that we had in our group four major hemispheric infarctions with multiple moderate ischemic events in the past.

Six of our patients had a classical bilateral affection with stenosis or occlusion of the ICA; in three patients the ICA alteration was unilateral. Among this group there were two patients with additional alteration of the MCA. Moreover we had two patients with additional PCA alteration. These radiological findings are similar to previous reports [6]. Nevertheless the CBF measurements performed by HMPAO-SPECT demonstrated the haemodynamic insufficiency exclusively in the territory of the MCA and not of the territories of the ACA or PCA. We used the STA-MCA bypass as our gold standard in order to address the territorial haemodynamic insufficiency centred around the MCA. For the juvenile group of Moyamoya angiopathy the direct and the indirect methods of revascularisation have been reported and compared with each other [2–5, 9, 10, 14]. For the adult population there is less information even in the Japanese population but indirect revascularisation procedures tend to be much less effective [11]. According to this observation our primary surgical goal was the STA-MCA bypass. The indirect revascularisation procedure by EMS was only chosen if the bypass was technically not possible or successful. Three of 13 intended bypasses in two patients failed intraoperatively despite careful preoperative examination of the vessel status. The reason declared by the surgeon was the fragile condition of the vessels of patients with Moyamoya disease [7]. In this

situation the EMS was performed. All successfully completed bypasses were patent on the postoperative DSA.

The postoperative CBF measurements by HMPAO-SPECT showed recovered hemispheric reserve capacity in seven of ten bypasses, an impaired reserve capacity after one bypass and unfortunately no documentation in two cases. For the EMS procedures the CBF measurements revealed in all cases an unchanged postoperative condition with impaired reserve capacity. This result underlines also for the European population the questionable treatment strategy of indirect revascularisation procedures in adults [11]. Corresponding to the demonstrated flow augmentation we registered a neurological improvement in six patients after the bypass procedure. There was an unchanged clinical situation in one patient and one neurological deterioration due to progressive disease which was recently described for the adult Japanese population [8]. In the patients treated with EMS, we registered an unchanged neurological condition.

Conclusion

Despite increasing numbers of registered patients with Moyamoya angiopathy in the adult European population there is still a lack of particular awareness and information regarding this disease. The current analysis summarised clinical features and confirms that the direct revascularisation by EC-IC bypass is a feasible option for adult European Moyamoya disease. Moreover our results demonstrated that EMS appears to be of questionable value for this population. Nevertheless, confirmation of long-term benefits would require a multicentric study. Clinical information about the disease in Europe should be compiled in a European Moyamoya registry.

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Experiences using 3-tesla magnetic resonance imaging in the treatment of Moyamoya disease

K. Kikuta

Department of Neurosurgery, Kyoto University Graduate School of Medicine, Kyoto, Japan

Summary

Purpose. To introduce our initial experiences using 3-tesla (3T) magnetic resonance (MR) imaging in the treatment of moyamoya disease (MMD).

Methods. 3T MR imaging was used to study 63 consecutive patients with MMD. Evaluation of regional cerebral blood flow (rCBF) was performed with ^{123}I IMP-SPECT or $^{15}\text{O}_2$ gas steady-state PET. T2*-weighted gradient-echo imaging was used to study the incidence of asymptomatic cerebral microbleeds (MBs) in the 63 patients. Preoperative targeting of a recipient artery in 12 recent operations for STA-MCA anastomosis on 9 patients was performed as follows. The MR angiography (MRA) and rCBF data sets were registered with the MPRAGE data set through the coregistration function of the SPM2 software in order to obtain a fusion of all images. In the fusion images of the MRA and rCBF images, we selected the cortical artery with the largest diameter as the target recipient artery from the candidates located on or near the cortex where the rCBF was markedly decreased.

Results. Asymptomatic MBs were found in 25 (40%) of the 63 patients and a successful bypass to the target was achieved in all 12 operations.

Conclusion. Use of 3T MR imaging provides new types of information for the treatment of MMD.

Keywords: Moyamoya disease; microbleeds; T2*; 3-tesla; magnetic resonance imaging; direct bypass; recipient; navigation; coregistration.

Abbreviations

3-DCT	three-dimensional computed tomography
3-D TOF MRA	three-dimensional time-of-flight magnetic resonance angiography
EMS	encephalo-myo-synangiosis
ICA	internal carotid artery
^{123}I IMP	iodine-123(123I)-labeled N-isopropyl-iodoamphetamine
MMD	moyamoya disease
MPRAGE	magnetization-prepared rapid acquisition gradient-echo
MR	magnetic resonance

PET	positron emission CT
rCBF	regional cerebral blood flow
ROI	region of interest
SPECT	single-photon emission computed tomography
STA-MCA	superficial temporal artery to middle cerebral artery
TIA _s	transient ischemic attacks

Introduction

Moyamoya disease (MMD) is a progressive steno-occlusive disease at the terminal portion of bilateral internal carotid arteries (ICAs) with the development of moyamoya vessels as collateral channels [2]. Although direct bypass surgery appears more effective than indirect bypass for improving ischemia, it is often disregarded because of its technical difficulty [2]. One reason is the difficulty of finding suitable recipient arteries during the operation. Although MMD can cause potentially fatal cerebral hemorrhage, the mechanism remains uncertain. The author previously reported that 3-tesla (3T) magnetic resonance (MR) imaging is better than 1.5T MR imaging at describing moyamoya vessels [1]. Here we review our recent experiences with 3T MR imaging and an image-guided navigation system in the treatment of MMD.

Materials and methods

Beginning October 2003, 63 patients with MMD were admitted to our institution. On admission, all patients underwent a 3T MR imaging study with an MR scanner (Magnetom Trio; Siemens, Erlangen, Germany) with T2*-weighted gradient-echo sequences, MPRAGE sequences, T2-weighted turbo spin echo sequences, and 3D TOF MRA. Detailed information on the sequences was presented in our previous paper [1, 4]. Evaluation of regional cerebral blood flow (rCBF) was performed by means of ^{123}I IMP-SPECT performed with a three-head rotating gamma camera (PRISM 3000, Shimazu Co., Ltd., Kyoto, Japan) or by means of $^{15}\text{O}_2$ gas steady-state PET performed with a PET scanner (Advance/GE Healthcare, Chalfont St Giles, U.K.).

Correspondence: Ken-ichiro Kikuta, M.D., Ph.D., Department of Neurosurgery, Kyoto University Graduate School of Medicine, 54 Kawaharacho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan.
e-mail: kikuta@kuhp.kyoto-u.ac.jp

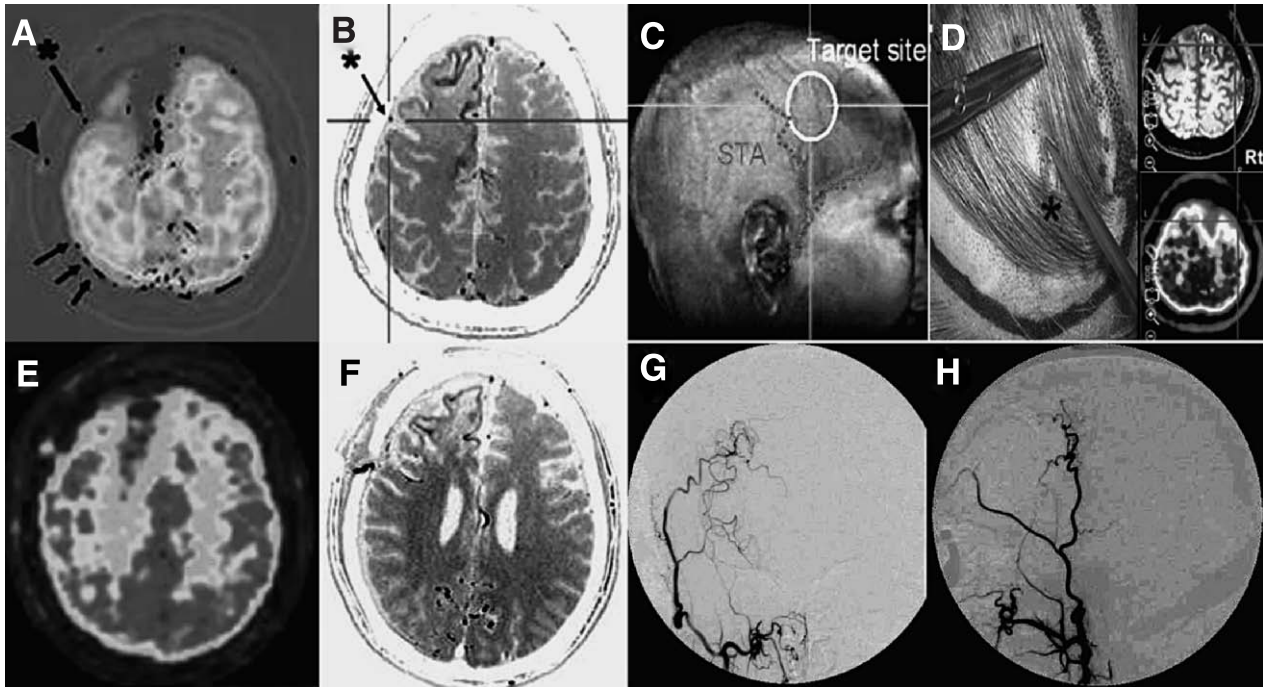


Fig. 1. In the fusion images between the MRA and rCBF images obtained with MRIcro, the cortical artery with the largest diameter could be selected as the target recipient artery from the candidates located on or near the cortex where the rCBF was markedly decreased (A, B: *asterisks*: target, *arrowheads*: STA; *arrows*: candidate recipient arteries). The location of the target in the coregistered scalp images was visible, which provided the site of the craniotomy (C). The navigation system (Stealth Station, Medtronic, Sofamor Danek, Memphis, TN, U.S.A.) enabled us to confirm the site of the target for the operation (D: *asterisk*). The postoperative PET study (E), MRA (F), and external angiograms (G: A–P view, H: lateral view) revealed an improvement in rCBF in the right hemisphere, the success of the bypass to the target, and the patency of the bypass (Modification of Figs. 2–4 in Neurosurgery (Suppl): ONS 320–327, 2006)

Microbleed study

T2*-weighted images obtained with a 3T MR imaging unit were used to study the incidence of asymptomatic cerebral microbleeds (MBs) in the 63 patients with MMD. The initial results of this MB study were previously reported. The 18 men and 45 women ranged in age from 8 to 68 years (mean age: 38.4 ± 17.1 years). Patient characteristics are shown in the table. In cases of hemorrhagic MMD, hypointense lesions representing MBs in the T2*-weighted images were defined as small hypointense areas (<10 mm in diameter) with well-defined margins located apart from the previous cerebral hemorrhage. The other sequences were used to distinguish and exclude hemorrhagic masses such as cavernous angiomas and signal voids of cerebral arteries [4]. The difference in clinical parameters was estimated by the chi-square test with JMP software (Version 6.0, SAS Institute Inc., Cary, NC, U.S.A.), and $p < 0.05$ was used as the level of significance.

Method of preoperative targeting of a recipient artery in a direct bypass (“target bypass”)

We attempted preoperative targeting of a recipient artery in 12 consecutive operations for STA-MCA anastomosis in 9 patients with MMD or moyamoya-like disease as follows. The patients were 2 men and 7 women ranging in age from 8 to 67 years (mean age: 34.0 years). The MRA data set obtained through 3T studies and the rCBF data set were registered with the MPRAGE data set through the coregistration function of SPM2 software (Wellcome Department of Imaging Neuroscience, London, U.K.; www.fil.ion.ucl.ac.uk/spm) to create a registered data set with anatomical information of MPRAGE (Fig. 1A). By adjusting the slice and the region of interest (ROI) with the free MRIcro software

(www.mricro.com) and using the coregistered data sets of MPRAGE, MRA and rCBF, it is possible to fuse the MRA and rCBF images and coregister the surface of the scalp. From the fusion of the MRA and rCBF images, we selected the cortical artery with the largest diameter as the target recipient artery from the candidates located on or near the cortex where the rCBF was markedly decreased (Fig. 1A and B; *asterisks*: target, *arrowheads*: STA; *arrows*: candidate recipient arteries). The location of the target was visible in the coregistered scalp images, thus providing the site of the craniotomy (Fig. 1C). On the day before surgery, a three-dimensional high-resolution CT (3-DCT) scan of the whole brain was obtained with a 64-detector-row CT scanner (Aquilion; Toshiba Medical, Tokyo, Japan) in order to obtain the reference images. The data sets of rCBF, MRA, and 3-DCT were applied to the neuronavigation system (Stealth Station, Medtronic, Sofamor Danek, Memphis, TN, U.S.A.). The navigation system enabled us to confirm the site of the target for the operation (Fig. 1D; *asterisk*) [3].

Results

Characteristics of MBs in MMD

Asymptomatic MBs were found in 25 (40%) of the 63 patients with MMD. The total number of MBs in the 25 patients was 72 and the number of MBs in each patient ranged from 1 to 15 (median: 2). A total of 71% of the MBs were located in the periventricular white matter. Statistical analysis revealed that the presence of MBs

Table 1. Characteristics of the 63 patients with MMD included in the MB study. Gender, age, symptoms of onset, completion of bypass surgery, and history of antiplatelet therapy or antihypertensive therapy are shown. The presence of MBs was correlated to increased age, TIA alone, or intracerebral hemorrhage as onset symptoms, and to a history of antihypertensive therapy, by means of statistical analysis with the chi-square test or Student *t*-test

		Total (<i>n</i> = 63)	MB present (<i>n</i> = 25)	MB absent (<i>n</i> = 38)	<i>p</i> value
Age	mean ± SD (years)	38.4 ± 17.1	48.3 ± 3.0	31.8 ± 2.5	<0.05
Female	<i>n</i> (%)	45 (74.0)	18 (72.0)	27 (71.1)	0.9351
Past vascular events					
TIA	<i>n</i> (%)	41 (65.1)	15 (64.0)	25 (65.8)	0.8851
Cerebral infarction	<i>n</i> (%)	22 (34.9)	10 (40.0)	12 (31.6)	0.4927
Intracerebral hemorrhage	<i>n</i> (%)	21 (33.3)	10 (40.0)	11 (29.0)	0.3626
Under antiplatelet medication	<i>n</i> (%)	44 (69.8)	16 (64.0)	28 (73.7)	0.6635
Under antihypertensive medication	<i>n</i> (%)	12 (19.0)	7 (28.0)	5 (13.2)	0.1422
Completion of bypass surgeries	<i>n</i> (%)	26 (41.3)	12 (48.0)	14 (36.8)	0.3788

* Indicates *p* < 0.05.

in MMD was correlated with increased patient age (Table 1).

Target bypass

The patency of the bypass and the postoperative improvement in rCBF were confirmed in all cases. Successful bypass to the target was also achieved in all cases. For example, in right STA-MCA anastomosis performed on a 56-year-old female with moyamoya-like disease who presented with frequent transient left hemiparesis, our method enabled preoperative targeting of a recipient

artery in the right frontal lobe (Fig. 1A and B). A postoperative PET study (Fig. 1E), MRA (Fig. 1F), and external angiograms (Fig. 1G and H) revealed improvement in rCBF in the right hemisphere, the success of the bypass to the target, and the patency of the bypass. This patient's ischemic attacks disappeared immediately after surgery. In another operation of left STA-MCA anastomosis performed on a 63-year-old female with MMD, a keyhole bypass could be performed in the same manner (Fig. 2C: MRA, Fig. 2D: rCBF imaging). A quarter-dollar-sized craniotomy (Fig. 2E) was used to expose the targeted recipient artery at the center of the craniotomy (Fig. 2F: arrowhead), and enabled a successful bypass to the target. Postoperative common carotid angiograms showed the patency of the bypass (G: A-P view, H: lateral view)

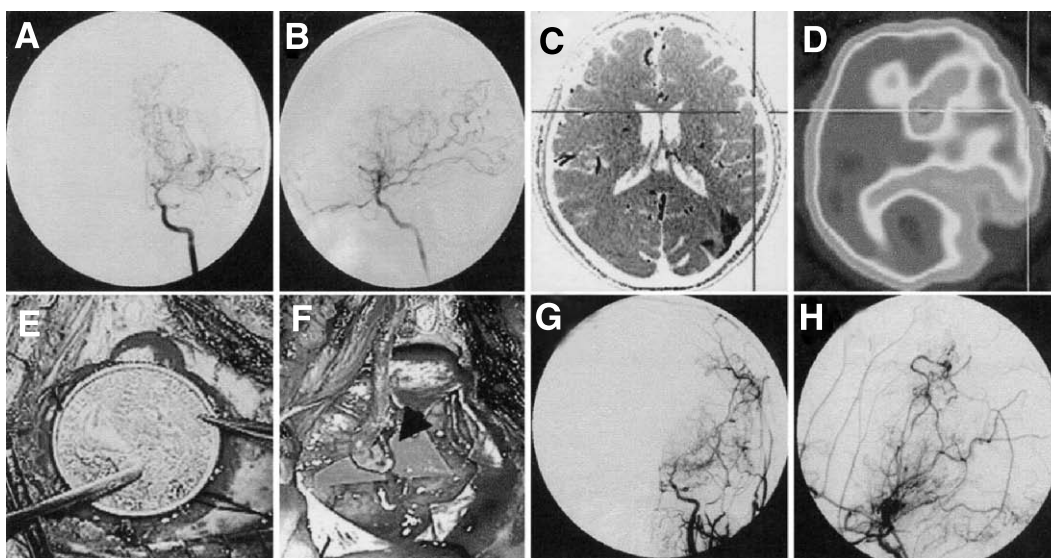


Fig. 2. Preoperative left internal carotid angiogram of a 63-year-old female with MMD showed several candidates for a recipient artery (A: A-P view, B: lateral view). Preoperative targeting of a recipient artery was performed before left STA-MCA anastomosis (C: MRA, D: rCBF imaging). A craniotomy the size of a quarter-dollar (E) was used to expose the targeted recipient artery at the center of the craniotomy (F: arrowhead), and enabled a successful bypass to the target. Postoperative common carotid angiograms showed the patency of the bypass (G: A-P view, H: lateral view) (Modification of Fig. 5 in Neurosurgery (Suppl): ONS 320–327, 2006)

otomy and enabled successful bypass to the target (Fig. 2F). Postoperative common carotid angiograms showed the patency of the bypass (Fig. 2GH).

Discussion

The mortality of cerebral hemorrhage in MMD approaches 20%; it is the largest risk factor contributing to the poor prognosis associated with this entity. However, the exact mechanism remains uncertain [2]. Cerebral MBs were detected with gradient-echo T2*-weighted MR imaging in 51–80% of patients with primary intracerebral hemorrhage (pICH); in 20–36% of patients with ischemic stroke; in 32% of patients with Alzheimer disease; and in only 6.4–9.8% of healthy individuals. Therefore, MBs can be considered a general marker of various types of bleeding-prone cerebral angiopathy [4]. We previously reported that the incidence of asymptomatic MBs in 25 patients with MMD was 44%, significantly higher than that of healthy volunteers [4]. In this study of 63 patients, we confirmed that the incidence remained about 40%. The character of MBs in MMD was somewhat different from that in patients with lacunar stroke or pICH. First, the number of MBs in patients with MMD was much smaller than that in patients with lacunar infarction or pICH. Second, MBs in MMD were frequently found in the white matter in addition to the ventricular systems, while MBs in patients with lacunar infarction and pICH were located in the basal ganglia and subcortical regions. In this study, 71% of the MBs were located in the periventricular white matter. This might be related to the fact that intracerebral hemorrhage in MMD is frequently accompanied by frequent intraventricular perforation. Some investigators have reported in prospective studies that the presence of MBs appears to be a potential predictor of subsequent cerebral hemorrhage after ischemic stroke. The author has also encountered, after detection of MBs, several cases of moyamoya disease with subsequent hemorrhage. The presence of MBs might also serve as a predicting marker in the estimation of the risks of subsequent hemorrhage in MMD.

3D TOF MRA with a 3-tesla unit is capable of well describing small arteries with a diameter of less than 1 mm, such as moyamoya vessels [1]. High-resolution imaging could also identify the target bypass [3]. This method has made it possible to identify the location of the recipient artery with sufficient accuracy before scalp incision. It would appear to be effective in cases, such as MMD, in which preoperative angiograms demonstrate only a few candidates for the recipient artery. It also enables the use of a small craniotomy for STA-MCA anastomosis. However, surgery through a small craniotomy with our method cannot be recommended for all cases of MMD, because many cases need to be treated with a combination of direct and indirect bypass such as EMS through a large craniotomy, especially in pediatric cases. Surgery through a small craniotomy might be useful in STA-MCA anastomosis for patients with systemic disease such as a heart dysfunction. Target bypass also enables selective revascularization to the region where rCBF is reduced. However, whether selective bypass to the site with decreased rCBF is the best approach for preventing recurrent stroke of MMD remains controversial. Future studies should be undertaken to determine the best way to select an appropriate recipient artery with this method.

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Moyamoya angiopathy in Europe: the beginnings in Zurich, practical lessons learned, increasing awareness and future perspectives

N. Khan, Y. Yonekawa

Department of Neurosurgery, University Hospital Zurich, Zurich, Switzerland

Summary

The number of patients, especially children, diagnosed with Moyamoya angiopathy and being referred to us for treatment from all across Europe, has increased over the last few years. An increase in awareness of the occurrence of stroke in children in the general and medical population might be the main cause of this phenomenon.

Increasing awareness does not happen “spontaneously” nor does it manifest overnight!

It requires regular platforms of communication between the general population and amongst the different medical specialists mainly neurologists, paediatric neurologists, neuropsychologists, neuroradiologists, neurorehabilitation specialists, nursing staff and neurosurgeons. Presently we were lucky to conduct the first Moyamoya Symposium ever to be conducted at a European-Japanese level with participation of specialists of this particular field from across Europe and Japan.

Ever since the first child with Moyamoya was managed at the University hospital in Zurich some 7 years ago the number of patients referred to us from all across Europe increased rapidly [6–8, 11–14]. The importance of interdisciplinary communication, trust and support amongst specialists and increasing the awareness of the disease among the patients, medical personnel was and remains to be just as important as making the correct diagnosis and treatment of choice in these patients.

We present the lessons we learned during these previous years and look into the future perspectives that require our further and urgent attention.

Keywords: Moyamoya; angiopathy; (extracranial-intracranial bypass surgery) EC-IC bypass surgery; (superficial temporal artery to branch of middle cerebral artery) STA-MCA; (superficial temporal artery to branch of anterior cerebral artery) STA-ACA; increasing awareness.

The beginnings in Zurich, lessons learned, increasing awareness and future perspectives

The beginnings in Zurich and the lessons learned

Sixty patients have been treated in Zurich. The majority (75%) of patients were children. The children

were sent from all across Europe and their ages ranged from 4 months to 16 years. This number of referral increased from just 1–2 patients per year in 1999 to 3–6/year in the later years. These numbers exclude the referrals and patient chart consultations performed from time to time for confirmation of diagnosis of Moyamoya in certain patients and the guideline/recommendation of a follow-up plan in certain asymptomatic patients.

Hence a systematic presurgical workup protocol was developed and used regularly to direct us in the planning of the optimal revascularisation procedure to be performed. This included a presurgical work up with clinical and neuropsychological assessment, 6-vessel cerebral angiography, transcranial Doppler, H₂¹⁵O-PET with a Diamox challenge. The choice of number and location of revascularisation procedures was then based mainly on the severity and extent of disease observed in the preoperative angiography and the Diamox PET studies (Fig. 1a and b).

The entire patient management could not have been possible without the close collaboration of the entire team of physicians and nurses of the children’s University hospital in Zurich, Kinderspital Zurich as well as the close collaboration of a motivated team of anaesthetists, neuroradiologists and colleagues of the Department of nuclear medicine of the university hospital in Zurich and of course all the referring physicians from across Europe.

We performed multiple direct bypass procedures of revascularisation bilaterally (STA-MCA and STA-ACA bypass) in the majority of our patients [6, 7]. Indirect revascularisation procedures (STA arteriosynangiosis, durasynangiosis) were used in combination in cases

Correspondence: PD Dr. med. Nadia Khan, Department of Neurosurgery, University Hospital Zurich, Frauenklinikstrasse 23, 8091 Zurich, Switzerland. e-mail: nadiaakhann@gmail.com, nadia.khan@tiscali.ch

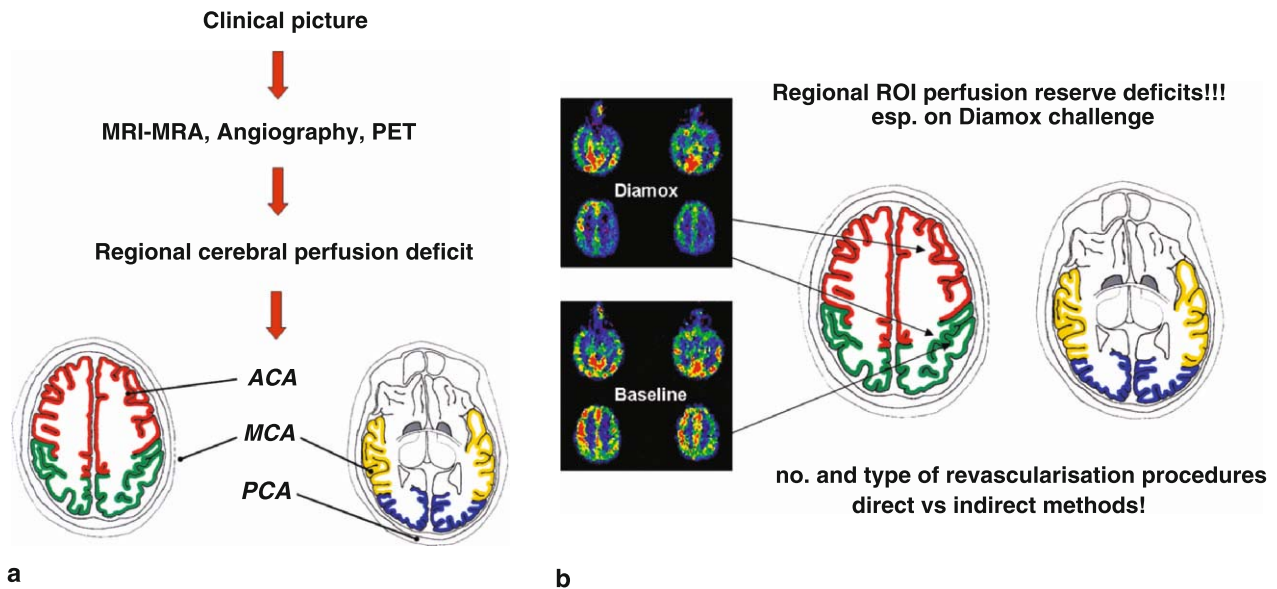


Fig. 1. (a) Scheme of preoperative evaluation: 6-vessel cerebral angiography and Diamox challenge ($H_2^{15}O$ -PET) are the most important examinations on which the number and hence the location (arterial distribution territory of MCA middle cerebral ACA anterior cerebral or PCA posterior cerebral artery) of revascularisation procedures (STA-MCA, STA-ACA or PCA bypass) depends upon. (b) Regional ROI (region of interest) perfusion reserve deficits are demonstrated

where the donor or recipient arteries were not available or were of inadequate calibre for the anastomosis. The postoperative follow-up showed no further stroke and improvement in cognitive functions in children who demonstrated a preoperative frontal lobe executive functional impairment.

Reviewing the American and Japanese literature [1, 5, 9] although STA-MCA bypass procedures are performed frequently for Moyamoya angiopathy, little importance is given to frontal brain reperfusion, therefore only few STA-ACA bypass are being performed [3, 4, 10], especially in children.

The need to reperfuse the frontal brain regions is extremely important in preventing mental retardation in children before the age of 5 years. Hence frontal brain hypoperfusion especially in the dominant side guided us to perform STA-ACA bypass procedures. Also the importance of pre- and postoperative neuropsychological assessment especially of the frontal brain regions in children should be incorporated in the surgical management.

Increasing awareness and future perspectives

Children's book project

A project of increasing awareness of Stroke prevention and Moyamoya angiopathy was undertaken end of 2005

and completed in 2006. Apart from regular lectures and presentation on the topic of Moyamoya and especially stroke in children regionally and internationally, a children's book project was initiated and completed in August 2006. Two books "Sven" and "Fatma's fantastic journey" were launched to explain the disease to the parents, children, affected patients as well as the medical personnel managing them. These books have been published in English and German and further sponsoring is required and underway to publish them in French, Italian and Dutch. Sven will be published in Japanese soon (Fig. 2).

Self-help group on Moyamoya

The first Moyamoya self-help group was also initiated in May of 2006 and parents, children and patients met with us to outline the problems faced during the period of securing a diagnosis of Moyamoya where up to 3 years of waiting had been lost, getting the diagnosis, finding a specialist and a hospital providing the infrastructure for managing and treating this illness.

Epidemiological study

The last epidemiological study on the number of patients diagnosed in Europe was performed in 1996 [2, 13]. It is time to perform a European epidemiologi-



Fig. 2. Children's book project: written and published by the first author in relation to a "Moyamoya awareness" Project carried out by the first author. Sven: a children's book for children up to 7 years of age defining the Moyamoya angiopathy, the diagnosis and preoperative investigation methodology and the bypass procedure. This book helps in eliminating the anxiety the children and parents suffer from when the term "Moyamoya" first falls on the scene. Fatma's fantastic journey, a comic for children above 7 years of age: Sven returns to Zurich for his follow-up examinations and meets Fatma and two other children suffering from Moyamoya. Together they make an adventurous journey into the human brain

cal study to find out the burden of this disease here in Europe and to outline the different management protocols (conservative vs neurosurgical) being followed. A consensus to perform such a Questionnaire was reached during the Moyamoya Symposium and will soon be underway.

Concluding remarks

Creating and managing a practical working environment for diagnosis, preoperative evaluation, surgical treatment, regular postoperative follow-up, patient and family support along with continuous awareness, education and research is what is required in the future in Europe to provide for the optimal care for the European Moyamoya patients especially children. Also the importance of basic and specialised continuous microsurgical training in the lab has to be a must in the neurosurgical training programmes across Europe motivating young neurosurgeons in the field of vascular neurosurgery.

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Historical landmarks in vascular Neurosurgery “On July 10th 2006, at the 70th Anniversary of the Department of Neurosurgery of Zürich Medical School”

J. Hernesniemi, R. Dashti, O. Mateo, P. Cancela, A. Karatas, M. Niemelä

Department of Neurosurgery, Helsinki University Central Hospital, Helsinki, Finland

Summary

Direct aneurysm surgery started more than 70 years ago. Introduction of cerebral angiography by Moniz in 20s and operating microscope by Yaşargil in 60s were the real cornerstones in vascular neurosurgery. Since then the development of neuroanesthesiology and further development of non-invasive imaging (MRA and CTA) together with the latest development of operating microscopes with intraoperative ICG angio have shifted vascular microneurosurgery to a different level to still compete with the ‘non-invasiveness’ of endovascular therapy. There is an increasing demand to perform the already forgotten bypasses mastered only by few and with the high-flow techniques (e.g. ELANA) we can treat lesions that some time ago were considered impossible. Endovascular embolization to reduce the flow in AVM before surgery is very helpful in those cases that can not be treated by embolization or radiosurgery alone.

We still need to find a way to detect aneurysms before they rupture and especially those thin-walled that are in an increased risk of rupture. Recent data on the pathobiology of the aneurysm wall may help us to better understanding of the growth mechanisms and it might be possible to develop more potent local or systemic pharmaceutical therapy to induce myo-intimal hyperplasia occluding the aneurysm and strengthening the wall to prevent rupture.

Keywords: History; cerebrovascular; vascular; microneurosurgery; neurosurgery.

“An aneurysm is the dilatation of an artery full of spirituous blood.”

Jean Fernell, 1581

“It’s a great game, neurosurgery. I’ve been lucky.”

C.G. Drake, The London Free Press, July 26, 1998

There was a lack of knowledge of human anatomy before 16th century due to religious and cultural reasons. Before that, Avicenna (980–1037) might have had more

knowledge of human body based on his wide surgical expertise [45], but many important diseases were described much later [16]. The first descriptions of cerebral aneurysms were in autopsy reports of Morgagni (1761 Padua), Biumi (1763 Milan), and Gilbert Blane (1800) (describing in autopsy a case John Hunter had reported 1792) [8, 18, 34]. Introduction of lumbar puncture just 115 years from now by Heinrich Quincke (1891) made the diagnosis of subarachnoid hemorrhage possible, later the cause was verified in autopsies to be mainly a saccular cerebral aneurysm [7]. It was notably known that an oculomotor palsy may be caused by an internal carotid aneurysm in the patients.

In 1805 Cooper performed carotid ligation for a carotid aneurysm with a fatal result. He was not discouraged and repeated the same procedure three years later, and this time with good outcome [10]. In London in 1885, Sir Victor Horsley exposed a tumor of middle cranial fossa which proved to be an aneurysm. He changed his operative strategy and performed carotid ligation [30]. One of the first aneurysms diagnosed before surgery was during the visit of Sir Charles Symond (1923) to the Cushing’s clinic. Harvey Cushing was operating on a pituitary tumor, which proved to be a giant aneurysm – a brisk bleeding resulted in puncturing the aneurysm and verified Sir Charles Symond’s excellent preoperative diagnosis. This aneurysm surgery remained exploratory, as was the case in numerous consecutive operations all over the world. Later, in 1929 Cushing wrapped an aneurysm by muscle [9].

In the late 19th and early 20th century radiological diagnosis of intracranial aneurysms was possible only in exceptional cases with calcifications in the aneurysm-

Correspondence: Juha Hernesniemi, M.D., Ph.D., Department of Neurosurgery, Helsinki University Hospital, 00260 Helsinki, Finland. e-mail: juha.hernesniemi@hus.fi

mal wall or bony erosions around them in the skullbase. The use of Hunterian ligation, i.e. occlusion of the artery proximal to the lesion, was the main possible treatment used. This technique was successfully introduced by a war surgeon Hunter (1728–1793) for peripheral arterial injuries, and later widened to include ligation of carotid artery by Cooper in 1805 and 1808 [10]. Hunterian ligation was kept popular also in the beginning of modern neurosurgery era, namely by Magnus in Copenhagen (1927), Dandy in Baltimore (1928), and later by Drake and Peerless [17]. High morbidity and mortality seen after carotid ligation necessitates differentiation of the tolerating patients i.e. by Mata's compression test (1911) [31]. Clever methods of gradual ligation like Mata's band, double fascia band, ligation over fascia, and Neff clamp were also developed meanwhile [35]. Crutchfield's or Shelden's clamps remained in regular use until late 1970s when introduction of microneurosurgery and endovascular surgery made them outdated [11].

Direct surgery for cerebral aneurysms

Dott in Edinburgh was the first one to attack directly a ruptured cerebral aneurysm. In 1931; a carotid bifurcation aneurysm was successfully wrapped with muscle after a recurrent bleeding [15]. The patient, who learned to be financial director of Dott's hospital, made a good recovery. The founder of the Scandinavian neurosurgical school, Herbert Olivecrona, was a pioneer in many fields. He was the first to treat effectively a posterior circulation aneurysm; in 1932 a large PICA aneurysm was trapped and excised after producing a lower angle syndrome in Stockholm. The patient was in good condition 17 years later [13, 16].

The birth of modern aneurysm surgery, however, had to wait until March 23, 1937. In his previous experience with trapping aneurysms, Walter Dandy in Baltimore, realized that the aneurysm neck might be ligated with a clip preserving the parent artery [12]. As the first real aneurysm surgeon he performed it on an internal carotid-posterior communicating aneurysm [13]. Interestingly, Dandy's first aneurysm operation, as well as the following ones documented in Dandy's monograph on cerebral aneurysms, were performed without pre or post-operative angiography. For modern era of aneurysm surgery full use of cerebral angiography, and introduction of spring clip were necessary.

Portuguese neurologist Antonio Caetano de Egas Moniz, with the help of his country man neurosurgeon

Almeida Lima, had described cerebral angiography already 10 years (1927) before Dandy's first direct aneurysmal operation [33]. In 1933, two years after his initial success of direct surgery on carotid aneurysm, Dott was using Moniz's method in preoperative diagnosis of aneurysms [23]. In the same year Moniz published an aneurysm case demonstrated by angiography. Swedish and Swiss school adapted soon Moniz's and Lima's method for regular use in cerebrovascular surgery. Although Moniz had opacified even the posterior circulation by open retrograde subclavian injection in 1934, it was Kraysenbühl in 1941, who first demonstrated an aneurysm on the vertebral-basilar system using the same method. Both schools were able to refine in the methods 1950's with several publications and classical monograph of Kraysenbühl and Richter (later replaced by Yaşargil). A young Swede, Seldinger, introduced technique of cerebral angiography via percutaneous transfemoral route in Stockholm in 1953 [23]. Some of the advocates of the so called four vessel study were Lysholm in 1964 in Stockholm, and af Björkesten and Halonen in Helsinki [1–3], who extensively applied this technique in their high number of aneurysm patients.

The first silver clips were introduced by Cushing in 1911. This was as revolutionary as Bovie monopolar coagulation device which was introduced to Cushing during his trip to Europe. McKenzie refined these clips, and later Olivecrona introduced a double clip with wings that would permit reopening. Dr. Mayfield and his technician Mr. Kee produced most popular spring clip during the 1950s and 1960s. With time, smaller shank, various shapes and sizes were developed. One special step was in November 1969: during weekend Mr. Kee made three ring-clips for preservation of arteries during basilar tip aneurysm surgery for Dr. Drake [17]. Later, Heifetz, and especially Yaşargil and Sugita pioneered in planning modern series of spring clips, with MRI-compatible alloys and with predictable closing pressure; 50–100 shapes and designs [13, 20].

Better diagnostics and development of clips made earlier and more aggressive surgical treatment possible. Kraysenbühl and Hamby in the 1940s were the first to compare the natural history with the operative results, which had the sad one third mortality even in selected cases. Early surgery before microneurosurgical era resulted in high mortality, as was testified in the early 1970s by a Finnish close-to-retire neuropathologist Ritama as "they died like flies after surgery". These were resulted to practice of delayed surgery in 1960s and 70s.

The same operative deaths happened in first attempts to obliterate vertebrobasilar artery aneurysms. However, in 1954, Olivecrona using a subtemporal approach, was able to clip a ruptured forward projecting aneurysm at the basilar bifurcation. The same experience was repeated successfully by his pupil Einar Bohm in the same year. Jamieson (1964), Duvoisin and Yahr (1965) published their sad series on surgery on vertebrobasilar aneurysms, and it remained for Dr. Drake to master posterior circulation aneurysm surgeries. In 1969, Drake exposed his overall experience of 43 cases, with 70% satisfactory outcome [16]. Hypothermia introduced by Rosomoff as an adjunct to protect the brain was in world wide use in the same period.

Natural outcome of subarachnoid hemorrhage was scrutinized in a careful epidemiological study in Helsinki by Pakarinen in 1967 [39]. Clinical randomized studies were performed by McCissock (1960) and Troupp [50]. Of particular fame is the first cooperative study on primary subarachnoid hemorrhage, which proved carotid ligation to be better than direct surgery [26]. In the classification of patients with intracranial aneurysms two widely used grading systems were introduced by Botterell in 1956 and by Hunt-Hess in 1967 [13].

Four great pioneers of pre-microsurgical era were the Swedish Gösta Norlen in Stockholm and Gothenburg, Swiss Hugo Krayenbühl in Zürich, Finnish Gunnar af Björkesten in Helsinki (with operative cases from 50s to 60s of more than 400 patients with cerebral aneurysms) and Japanese Jiro Suzuki in Sendai (with operative cases from 60s and 70s of more than 1000 patients with cerebral aneurysms). Japanese neurosurgery had one decade of delay derived from Second World War

as no contrast media available. Even so, Suzuki, Sugita and Sano were the names to influence the cerebrovascular surgery in the whole world. Dr. Drake began to his never to be repeated series of 4000 aneurysm patients in 1947, and ligated his first basilar aneurysm 1959, the first one of a consecutive series of 1767 patients with vertebrobasilar aneurysms to follow [17]. Dr. Drake took microscope in use in 1971 after his co worker Peerless returned from Zürich.

Era of microneurosurgery

Zeiss company with Hans Littman developed first neurosurgical microscope named "OPMI1". In 1962 a cardiac surgeon in Zürich, Professor Åke Senning, asked Professor Hugo Krayenbühl (Fig. 1) and his pupil M. Gazi Yaşargil to remove an embolus of a middle cerebral artery causing hemiplegia after cardiac surgery in a young patient. This was not possible but the idea remained, and in 1965 Professor Yaşargil left to Burlington to be trained by Donaghy [6]. This well known learning period culminated in the development of microneurosurgery, whose miracle like banner was the STA-MCA bypass operation performed in the same time by Yaşargil (Oct. 30, 1967, Zürich), and Donaghy (Oct. 31-Nov. 1, 1967, Burlington) [56]. STA-MCA bypass technique spread world wide until the results of cooperative study by Barnett and Peerless stopped it abruptly at 1985 [49]. Imhof (Zürich), Schmiedek (Mannheim), and Yonekawa (Japan and later in Zürich) were the only few neurosurgeons who sustained STA-MCA bypass. However, the STA-MCA bypass operation is becoming popular again. At the same time other sophisticated high-flow bypass techniques have been developed especially by Tulleken in Utrecht [52, 53].

Yaşargil came back to Zürich in 1967 and on February 1st the first microsurgical operation in Zürich was performed by him. This was followed with development of microscope, special microinstruments, and a tremendously well documented series. After only 10 years (1978) Donaghy the teacher of Professor Yaşargil wrote: "Little was it realized at this time (1965), even by Hugo Krayenbühl, that this young Turk was destined to do more for the development of microsurgery in the human nervous system than any man". Two-point coagulation with bipolar coagulation introduced by Leonard Malis became another cornerstone in microneurosurgery.

From the first day of his microneurosurgical work, Professor Yaşargil, was surrounded by a constant flow of visiting colleagues from all around the world (Fig. 2).



Fig. 1. Professor Krayenbuehl, sketched by Hans Peter Weber, during one of his last neurosurgical interventions dated 10.4.73, shortly prior to his emeritation



Fig. 2. Professor Yaşargil and his team during a microsurgical operation together with visiting surgeons, sketched by Hans Peter Weber 23.5.1972

More than 3000 neurosurgeons visited Zürich during his chairmanship (until 1992). Zürich was the Mecca of neurosurgeons in 1970s–1990s, and the little big city



Fig. 3. Professor Yasuhiro Yonekawa just before his emeritation (2007) at surgery of OA-PCA bypass by supracerebellar transtentorial approach in the sitting position, sketched by Peter Roth

for fruitful discussions and further developments. This was also the place for Professor Yonekawa to be trained by Professor Yaşargil for 6 years, and then to be his successor (1993–2007) (Fig. 3). Important females influencing microneurosurgery were Miss Esther Roberts in Vermont, teaching and helping Professor Yaşargil in microvessel surgeries, Mrs Dianne Yaşargil Zürich, Little Rock assisting and helping in most of the microsurgical developments, and Mrs Rosemarie Frick continuing the microsurgical animal laboratory in Zürich.

With the development of sophisticated microneurosurgical techniques, reintroduction of early surgery for cerebral aneurysms was possible in 1970s. The Swedish (Ljungren) and Japanese school (Sano) were especially active in this achievements. Temporary intracranial arterial clipping had a brief vogue after 1959 when Pool reintroduced the concept of using the early Mayfield spring clip. After occasional use in 1970s the use of temporary clipping flourished in 1980s, especially on the basilar artery, using the modern gentle temporary clips. These were in routine use during extracranial to intracranial (EC–IC) bypass procedures.

Gold standards of treatment in intracranial aneurysms were achieved by pioneering works of Yaşargil (1984–1992, 723 patients with 1.7% mortality) [55], and Drake & Peerless (1982–1992, 681 patients with non-giant vertebrobasilar aneurysms with 3.7% mortality)



Fig. 4. Professor Drake, the pioneer in surgery of posterior circulation aneurysms, took microscope in use in 1971 after his co-worker Peerless returned from Zürich

[17] motivating the future generation of microneurosurgeons (Fig. 4).

Treatment of unruptured aneurysms of all sizes became increasingly in routine in many centers since 1980's. However, the results of ISUIA study indicating "Cerebral aneurysms less than 10 mm in diameter do not rupture and should not be treated!" started a period of confusion thereafter [29]. This might be best described by Mark Twain: "The arduous work of countless researchers has already thrown much darkness on the subject, and if they continue, we shall soon know nothing at all about it". More carefully planned studies later balanced this issue.

Developments in neuroimaging and endovascular surgery

Development of CT scan by Hounsfield in 1972 revolutionized diagnostics of brain diseases, and was further improved by MRI. Angiographic studies were further developed by DSA, and later MRA and CTA making also non-invasive screening of cerebrovascular lesions possible [13, 23].

Endovascular surgery was developed and improved in parallel with the developments in microneurosurgery. In 1969 Serbinenko (Burdenko Neurological Institute, Moscow) published his experience in balloon occlusion of parent arteries or aneurysms [46, 47]. Later the French school headed by Djindjian, further developed the methods introduced by the Russian school of Serbinenko and Scheklov, treating both intra- and extracranial lesions, including aneurysms, AVMs, AVFs and tumors [14]. In 1980–90s Professor Valavanis was trained by Professor Yaşargil for endovascular work by teaching the anatomy and demonstrating the surgeries. A special era of endovascular surgery to compete with exovascular surgery began in 1990 with the Guglielmi detachable coils [25] to culminate in ISAT study with its revolutionary message "EVT is significantly more likely to result in survival free of disability 1 year after SAH than microsurgery!" [32]. Provocative articles of Ausman in 1997 [4] and 2001 [5]: "The Death of Cerebral Aneurysm Surgery" nailed those "continuing to enjoy placing the perfect clip around the base of those deadly sacs" (Peerless, Hernesniemi 1996).

Surgery of cerebral AVMs

The most skillful neurosurgeon of his time, Walter Dandy wrote in 1928: "...the radical attempt to cure

is attended by such supreme difficulties and is so exceedingly dangerous as to be contraindicated except in certain selected cases". With this advise, decompressive surgery, partial ligation of feeders, muscle injections and X-ray therapy were tried. It was again Olivecrona who was able as first (maybe not knowing of Dandy's opinion) to remove a cerebral AVM in 1932. He published his series of 24 operated cases in 1948 and later, with Ladenheim, a monograph of these lesions. Pioneering work in AVM treatment was done by Krayenbühl, followed by Yaşargil whose large and unique series are published in *Microneurosurgery III a and IIIb* [55]. Finland is one of the countries very suitable for epidemiological studies, and the long term studies of Troupp and Helsinki clinics since the second world war have contributed in natural course of these lesions [38].

Partial, or even total occlusion of cerebral AVMs by endovascular means has been a major step in treatment of these challenging lesions. Leksell's Gamma Knife developed in Stockholm (1972) was an important adjunct for treating cerebral AVMs. Nowadays, a combined treatment with all three modalities has become the so called fourth option for total elimination of cerebral AVMs. Gold standards of cerebral AVM treatment for future generations were also formed by Yaşargil (overall mortality of 2.4% in 414 patients), and Drake & Peerless (with a 2% mortality in 320 patients). In 1986 Spetzler and Martin [48] published "A proposed grading system for arteriovenous malformations" which contributed in tailoring the treatment of these most difficult lesions (assessed inoperable by Dandy).

Present state of microneurosurgery (Clean, fast surgery while preserving normal anatomy) and future

Clean surgery without bleeding means fast surgery, as in neurosurgical operations a great amount of time is spent for hemostasis [27]. Better imaging makes smaller and appropriate incisions and small bone flaps possible [26]. Effective neuroanesthesia provides slack brain enhancing the gentle handling of brain and vessels with little or no retraction [42]. Temporary clips provide proximal control, and sharp dissection has replaced any blunt dissection of the aneurysm/AVM or its surroundings. With intraoperative opening and coagulation, total occlusion of the aneurysm is verified, and objectively shown by intraoperative ICG angiography [40, 41]. Atraumatic techniques and extremely careful closure have made postoperative hematomas and infections rare. Rare patients with difficult to treat lesions are referred to

a few centers specialized in the treatment of complex cerebrovascular lesions to minimize technical and medical complications [36]. Early treatment to prevent rebleedings should be advocated.

At the moment, in the times of both exo- and endovascular surgery, we should work together not only in the clinics to tailor the treatment accordingly but also in research. We, in Helsinki, have found different wall types in cerebral aneurysms making them more or less prone to rupture [21]. The next step is to identify and treat them before rupture. Families with aneurysms should be screened, and those with the actual gene defect should be followed and treated [43, 54]. The wall of an aneurysm is undergoing continuous destruction and repair processes [22, 51]. We have found evidence of inflammatory processes expressing different growth factors behind aneurysm rupture [21]. However, the pathobiology of the aneurysm wall should be elucidated in detail before developing simple bioactive coils that are easier to set or even pharmaceutical therapy to prevent aneurysm rupture in a less complicated way than today.

“Identification and treatment of aneurysms before rupture will likely improve management results by far more than any technical or medical advance” [17].

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Author index

- Alfieri, A. 87
Andoh, T. 83
Aoyama, T. 109
- Banic, A. 87
Baumann, F. 19
Baumgartner, R. W. 47
Becker, K. 15
Bregy, A. 87
- Cancela, P. 131
Cesnulis, E. 93
Constantinescu, M. 87
- Dashti, R. 131
- El Beltagy, M. 37
- Frenz, M. 87
Fujioka, M. 29
- Hänggi, D. 119
Hashimoto, N. 11
Hatano, T. 109
Hernesniemi, J. 131
Hongo, K. 51
- Imhof, H.-G. 37, 61, 93
Inoue, T. 79
Ishihara, S. 51
Iwama, T. 115
- Jinnouchi, J. 79
- Kakizawa, Y. 51
Kaku, Y. 83
Karatras, A. 131
Khan, N. 19, 29, 61, 93, 103, 127
Kikuta, K. 11, 123
Kokuzawa, J. 83
Krayenbühl, N. 93
- Manabe, H. 5
Mateo, O. 131
Matsutani, M. 51
Mehdorn, H. M. 73
Mehrkens, J. H. 119
Mohr, J. P. 3
Muroi, C. 29, 37
- Nakakuki, T. 109
Niemelä, M. 131
Nishino, A. 57
Nozaki, K. 11
- Ogata, H. 109
Oracioglu, B. 29
Orakcioglu, B. 15
Otani, N. 29
- Reinert, M. 87
Roth, P. 29, 61, 103
- Sakowitz, O. W. 15
Sakurai, Y. 57
- Samma, A. 103
Satoh, A. 51
Schaffner, T. 87
Schellinger, P. D. 15
Schmid-Elsaesser, R. 119
Steiger, H.-J. 119
Stuker, F. 87
Sugiyama, T. 51
Suzaki, N. 9
Suzuki, I. 57
Suzuki, S. 57
- Takada, S. 9
Takagi, Y. 11
Takahashi, T. 9
Tanaka, T. 83
Tsugane, S. 9
Tsuji, Y. 109
Tsukahara, T. 109
- Uenohara, H. 57
Unterberg, A. 15
Utsunomiya, A. 57
- Watarai, H. 83
- Yamauchi, K. 9
Yonekawa, Y. 19, 29, 37, 61, 93, 103, 127
Yoshimura, S. 115
- Zumofen, D. 61, 103

Index of keywords

- Aneurysm 19, 47, 93
Aneurysm clipping 61
Angiopathy 127
Antithrombotic treatment 47
Arterial dissection 51, 57
Arteriovenous malformation 11
- Balloon catheter 9
Bonnet bypass 103
Brain arteriovenous malformations 3
Brain atrophy 79
Brain infarction 79
Bypass surgery 61
- Carotid artery stenting (CAS) 109
Carotid endarterectomy (CEA) 109
Cavernous angioma 29
Cerebral 57
Cerebral aneurysm 5
Cerebral blood flow 79
Cerebral hemodynamic insufficiency 73
Cerebral reserve capacity 73
Cerebral revascularization 93
Cerebral revascularization surgery 103
Cerebrovascular 131
Cerebrovascular disease 29
Characteristics 19
Contact 87
Coregistration 123
3D CT angiography 83
- Diagnosis 115
Diffusion tensor imaging 11
Direct and indirect revascularisation 119
Direct bypass 123
Dissecting aneurysms 61
Dissection 47
DWI 15
- EC-IC bypass 37, 83, 103, 119
EC-IC bypass surgery (extracranial-intracranial bypass surgery) 79, 127
- Entrapment 61
Epidemiology 19, 115
European population 119
Extra-intracranial arterial bypass 73
Extra-intracranial bypass 93
- Fusiform 37
- GDC embolization 5
Giant aneurysm 9
- History 131
- IC dorsal aneurysm 51
ICH 15
Increasing awareness 127
Infratentorial supracerebellar approach 29
Intracranial 19
In-stent stenosis 5
Internal carotid artery 47
Intracranial aneurysm 37
Ischemia 15, 93
- Japan 115
- Laser tissue soldering 87
Less invasive technique 83
Ligation 61
Long-term observation 5
- Magnetic resonance imaging 11, 123
Microbleeds 123
Microneurosurgery 131
Middle cerebral artery 37
Moyamoya 73, 127
Moyamoya angiopathy 119
Moyamoya disease 115, 123
MRI 15
Multiple aneurysms 19
Multiple cerebrovascular occlusive disease 103
Nationwide surveillance 51
- Natural history 3
Navigation 11, 123
Neurosurgery 131
Non-hemorrhagic 57
- Positron emission tomography 73
Present status 115
PWI 15
- Radial artery interposition graft 103
Rats 15
Recipient 123
Research Committee on Moyamoya Disease 115
Review 19
- Sandwich technique 87
Saphenous vein interposition graft 103
Side-to-side anastomosis 87
STA-ACA (superficial temporal artery to branch of anterior cerebral artery) 127
STA-MCA (superficial temporal artery to branch of middle cerebral artery) 127
Stent 5
Stroke 19, 79
Stroke outcome 79
Stroke prevention 47
Suction decompression 9
Surgical approach 29
Surgical outcome 29
- T2* 123
3-Tesla 123
Tractography 11
Transcranial Doppler sonography 73
Trapping 37
Treatment of hemorrhagic type 115
- Vascular 131
Vascular reactivity 79
Vasospasm 93