Endovascular treatment of cerebral arteriovenous malformations with emphasis on the curative role of embolisation

A. Valavanis, A. Pangalu, M. Tanaka

Institute of Neuroradiology, University Hospital of Zurich

Summary

Valavanis A, Pangalu A, Tanaka M. Endovascular treatment of cerebral arteriovenous malformations with emphasis on the curative role of embolisation. Schweiz Arch Neurol Psychiatr 2004;155:341–7.

Cerebral arteriovenous malformations are complex and only partially understood vascular lesions of the central nervous system with a natural history characterised by significant morbidity and mortality mainly due to an increased haemorrhagic risk. Microneurosurgical removal, radiosurgical obliteration and neuroendovascular embolisation are the principal therapeutic modalities applied individually or in various combinations according to varying selection criteria for the treatment of cerebral arteriovenous malformations. In this context embolisation plays a central role either as a complementary or as the sole treatment technique. This report summarises the evolutive 18 years of continuous experience of the senior author with the neuroradiological evaluation and endovascular treatment of 644 patients with a cerebral arteriovenous malformation. Special emphasis is given to the underlying concepts and specific endovascular techniques developed for the complete, i.e. curative embolisation of cerebral arteriovenous malformations.

Precise angiographic analysis of the vascular composition and intrinsic angioarchitecture of the nidus of the arteriovenous malformation by superselective microcatheterisation is required to identify the types of feeding arteries and patterns of their supply, the number and vascular connections of nidal compartments, the types of arteriovenous shunts, the morphology of the vascular spaces composing the nidus and the number and exit patterns of draining veins. Complete angiographic investigation for recognition of secondarily induced phenomena of the cerebral vasculature, such as arterial and venous high-flow angiopathy and so-called perinidal angiogenesis is essential for a comprehensive evaluation and assessment of the associated haemorrhagic risk.

Based on a precise topographic classification, detailed angioarchitectural analysis, application of superselective multimicrocatheterisation techniques along with a controlled intranidal injection of non-absorbable liquid embolic materials, nearly 40% of cerebral arteriovenous malformations can be completely and stably obliterated and therefore curatively treated by single session or multistaged embolisation with a morbidity of 1.3% and a mortality of 1.3%, which are lower than the known natural history of this disease.

Keywords: cerebral arteriovenous malformations; embolisation; angioarchitecture; endovascular treatment; treatment outcome

Correspondence:
Prof. Dr. med. A. Valavanis
Institut für Neuroradiologie
Universitätsspital
Frauenklinikstrasse 10
CH-8091 Zürich

Introduction

Cerebral arteriovenous malformations represent one of the types within the spectrum of cerebrovascular malformation phenotypes, which also includes cerebral cavernous malformations, capillary teleangiectasias, developmental venous anomalies, mixed lesions such as developmental venous anomaly and cerebral cavernous malformation, and transitional forms [1–3]. The prevalence of cerebral arteriovenous malformations is not precisely known, but their incidence in general autopsy series is 0.15% and it has been estimated that between 0.14 and 0.8% of the population may present with a cerebral arteriovenous malformation in a given year [2, 4]. The incidence of symptomatic cerebral arteriovenous malformations in the adult population is approximately one-tenth the frequency of intracranial aneurysms [2].

The main angioarchitectural characteristic of cerebral arteriovenous malformations distinguishing them from the other types of cerebral vascular malformations is the presence of arteriovenous

shunting between arteries or arterioles and veins or venules, which exhibit mature vessel wall elements constituting the so-called nidus of the arteriovenous malformation. The nidus is responsible for a haemodynamically high-flow profile, which predisposes them to vascular recruitment, arterialisation of draining veins, gliosis of intervening and adjacent brain parenchyma as well as to secondarily induced angiopathic changes occurring over time up- and downstream to the nidus of the arteriovenous malformation, i.e. high-flow angiopathy.

The main modes of clinical presentation of patients with cerebral arteriovenous malformations include intracranial haemorrhage in approximately 45–50% of cases, seizures in 30%, headaches not-associated with haemorrhage in 10–15%, focal neurological deficits or other symptoms such as tinnitus in approximately 7–10%. In approximately 5–8% of cases cerebral arteriovenous malformations are asymptomatic and detected incidentally on neuroimaging investigation performed for other reasons [5, 6]. There is a clear correlation between most of the clinical manifestations and specific angioarchitectural characteristics of the underlying arteriovenous malformation, so that the presenting symptoms and the visualised angioarchitecture play a significant role in the indication and selection of the treatment modality or modalities in the individual patient [2, 7].

Cerebral arteriovenous malformations are pathobiologically, angioarchitecturally and haemodynamically complex systems of arteriovenous shunts with specific neurovascular relationships, a variable and mostly unpredictable clinical presentation and a dynamic, for certain features age-dependent but only partially understood natural history, associated with an annual bleeding rate of 4% and annual rates of mortality of 1% and of severe morbidity of 1.7% [7–10].

For the treatment of cerbral arteriovenous malformations microneurosurgical, radiosurgical and endovascular techniques are applied either as single or combined techniques according to various selection criteria and grading systems. Combined treatment techniques, such as preoperative embolisation in one or several sessions followed by microneurosurgical removal or radiosurgical obliteration may facilitate radical elimination of a cerebral arteriovenous malformation that might not have been curable by a single treatment modality but at an increased risk to the patient due to the cumulative effect of the risk of the individual treatment modalities applied. As a guiding principle regarding the indication for active, invasive versus conservative treatment, a patient diagnosed to have an incidental or symptomatic cerebral arteriovenous malformation should be actively treated if an improvement over the expected individual natural history, evaluated according to the clinical presentation, age, location and angioarchitecture of the patient's lesion, shall result [2, 11].

This report summarises the 18 years experience of the Institute of Neuroradiology of the University Hospital of Zurich with the role, concepts and techniques of the endovascular treatment of cerebral arteriovenous malformations as it evolved since 1986, when the first microcatheter-guided superselective exploration and embolisation of a cerebral arteriovenous malformation was performed.

Role of embolisation in the treatment of cerebral arteriovenous malformations

Since the first report on embolisation of a cerebral arteriovenous malformation by Luessenhop et Spence in 1960 [12], significant progress and innovations have taken place in the field of interventional neuroradiology including the introduction of digital subtraction technique in cerebral angiography in the early 1980s; the full implementation of structural, functional, vascular-luminal, perfusion and diffusion MR throughout the 1980s and 1990s for the pretherapeutic evaluation, precise topographic localisation and post-treatment follow-up of cerebral arteriovenous malformations; the development and subsequent refinement of flow-guided and combined flow- and guide-wire-directed microcatheters since the mid-1980s for safe precise superselective access to arteriovenous malformations of any location in the brain; the introduction of bi-plane neuroangiographic equipment in the mid-1990s with simultaneous bi-plane fluoroscopic and road-map capabilities and the use of polymerising liquid embolic materials for stable arteriovenous malformation obliteration [1, 2, 13].

Parallel to this technological and methodological progress our understanding of the multifaceted phenotypic manifestations, angioarchitecture, intrinsic vascular composition, underlying functional vascular anatomy, high-flow haemodynamics and natural history of these still enigmatic vascular lesions improved dramatically, ultimately leading to the formulation and application of solid concepts for the efficient endovascular treatment of cerebral arteriovenous malformations. In this regard, embolisation advanced from a simple endovascular technique initially con-

ceived to block feeding arteries of arteriovenous malformations to a sophisticated one with the aim to use appropriately and carefully selected feeding arteries as vascular access roots to superselectively reach and obliterate the core, i.e. the nidus of the arteriovenous malformation containing the arteriovenous shunting area [13].

Due to this progress, embolisation plays today an important and central role in the overall management of patients with brain arteriovenous malformations. Its specific applications include (1) preoperative or preradiosurgical embolisation aimed at size reduction and/or haemodynamic improvement, (2) partial-targeted or palliative embolisation aimed at elimination of identified weak areas of angioarchitecture linked to an increased haemorrhagic risk or at elimination of vascular elements responsible for epilepsy, focal neurological deficits or headaches due to rerouting of venous drainage and venous hypertension, perinidal brain-tissue hypoperfusion or excessive additional dural supply respectively and finally (3) curative embolisation aimed at complete endovascular elimination of the arteriovenous malformation and applied either as the sole treatment or more rarely following partial microneurosurgical removal or failed radiosurgical treatment [2, 13].

Topographic and angioarchitectural classification of cerebral arteriovenous malformations

The arterial and venous vascularisation of cerebral arteriovenous malformations as well as the specific types of arteries and veins participating into their supply and drainage but also the vascular and functional territories involved in a given case of arteriovenous malformation are directly related to the location and topography of the arteriovenous malformation and inherently linked to the local cyto-, myelo- and angioarchitectonics. Therefore, correct and precise localisation and topographic classification of an arteriovenous malformation is the first, basic step in the evaluation of cerebral arteriovenous malformations leading to the indication for treatment, formulation of an individual therapeutic concept and selection of the appropriate techniques and tools. Topographic classification and localisation of cerebral arteriovenous malformations is performed by high-field, high-resolution, multiplanar MRI as well as diffusion-tensor MR and 3D-tractography, which allows for identification of white matter fibre tracts around the arteriovenous malformation. The identification of specific functional cortical areas around the nidus of the arteriovenous malformation and a possible shift of such areas induced by it are now routinely performed with functional MR. MR angiography additionally provides useful information regarding the vascular composition of the arteriovenous malformation [2, 13–15].

Topographically cerebral arteriovenous malformations are categorised according to the following classification system [16, 17]:

A. Supratentorial arteriovenous malformations (86%)

1. Neopallial arteriovenous malformations (47%) (frontal, temporal, parietal, occipital and central lobes)
   a) sulcal (pure sulcal, with subgyral, with paraventricular extension)
   b) gyral (pure gyral, with subgyral, with paraventricular extension)
   c) mixed sulcal-gyral (with subgyral, with paraventricular extension)
2. Archi- and paleopallial arteriovenous malformations (9%) (i.e. limbic and paralimbic system arteriovenous malformations: cingulum, amygdalo-hippo-parahippocampal, septal, insular arteriovenous malformations).
   a) sulcal, fissural
   b) gyral, parenchymal
   c) mixed
   d) ventricular (temporal horn)
3. Deep central arteriovenous malformations, (27%) (strio-capsulo-thalamic, diencephalic, mesencephalic and intraventricular-plexal)
   a) fissural, cisternal
   b) parenchymal
   c) mixed
   d) plexal-intraventricular (lateral and/or IIIrd ventricle)
4. Vein of Galen aneurysmal malformations (3%)

B. Infratentorial arteriovenous malformations (14%)

1. Neocerebellar arteriovenous malformations (11%)
   a) sulcal, fissural
   b) folial
   c) mixed
2. Paleo-Archicerebellar arteriovenous malformations (1%)
   a) sulcal, fissural
   b) folial
   c) mixed

3. Deep-central arteriovenous malformations (2%)
   (cerebellar-nuclear, brain-stem, intraventricular arteriovenous malformations)
   a) fissural, cisternal
   b) parenchymal
   c) intraventricular (IVth ventricle and/or aqueduct)

With regard to location and topography of brain arteriovenous malformations, terms such as eloquent and noneloquent, functional, critical and silent have to do more with the fear of the neuroradiologist or neurosurgeon that iatrogenically induced neurologic deficits will be readily recognisable, than with the real function of the brain, and are, therefore, best forgotten [13, 18]. Obviously all areas of the brain should be regarded as functionally highly eloquent and this implies that the same care should be applied when embolising brain arteriovenous malformations in any location and that occlusion of vessels should be confined only and strictly to the lesion itself [11].

The angioarchitectural analysis of brain arteriovenous malformations should include: (1) the vascular composition of the nidus ([a] compact vs diffuse, [b] with or without perinidal angiogenesis, [c] mono- vs multicompartmental, [d] presence or absence of intercompartmental communications, [e] pure plexiform vs mixed plexiform and fistulous vs pure fistulous); (2) types of feeding arteries (dural, leptomeningeal, choroidal, perforating); (3) modes of supply (monoterminal, multiterminal, pseudoterminal, indirect-anterograde, indirect-retrograde, dominant vs supplementary); and (4) types and patterns of venous drainage (compartmental veins exiting isolated or joining nidal veins) and their relation to the drainage of the normal brain [2, 13].

Perinidal angiogenesis is defined as an angiogenetically induced vascular network within the perinidal brain parenchyma interposed between the terminal segments of feeding arteries and the nidus without angiographic evidence of AV shunts. It is observed in 20–25% of cases of cerebral arteriovenous malformations and can be minimal, moderate or extensive. It is mostly seen with arteriovenous malformations containing intranidal high-flow AV shunts, which may cause mild, subclinical perinidal hypoxia due to local steal effect. This hypoxia is thought to induce abnormal overexpression of vascular endothelial growth factor (VEGF) which leads to perinidal angiogenesis to compensatorily supply the hypoxic perinidal brain parenchyma. It is a vascular response of the brain to the arteriovenous malformation and should not be misinterpreted as belonging to the nidus of it. Inclusion of the perinidal angiogenesis in the therapeutic targets of the arteriovenous malformation (surgical, radiosurgical or endovascular) is a significant source of morbidity. In the authors' experience perinidal angiogenesis is reversible following elimination of the nidus of the arteriovenous malformation [13].

In addition, various types of weak angioarchitectural elements, such as flow-related aneurysms, intranidal vascular cavities, and varix formation proximal to high-grade stenosis of draining veins should be identified as factors predisposing for arteriovenous malformation rupture. A wide spectrum of secondary angiomorphological changes induced by the arteriovenous shunt of the nidus and occurring up- and downstream of the nidus should be identified as manifestations of high-flow angiopathy. These data help to better predict the natural history, understand the variable clinical presentation and define therapeutic targets of brain arteriovenous malformations [1, 2, 13, 17].

The most widely used grading system for cerebral arteriovenous malformations is the Spetzler-Martin-System which is based on the size of the arteriovenous malformation, its location in an eloquent or non-eloquent area of the brain and on the presence or absence of deep venous drainage [19, 20]. This system categorises cerebral arteriovenous malformations into five grades and assists in predicting difficulty and morbidity related to surgical removal and is not useful in the grading of arteriovenous malformations being treated endovascularly [13].

Technical aspects and strategies of endovascular treatment

The technical goal of embolisation of brain arteriovenous malformations is the strict intranidal deposition of the appropriate embolic material following usually repeated atraumatic, superselective mono- or simultaneous multimicrocatheterisations of the nidus with obliteration of the AV shunts and their associated abnormal intranidal vascular channels under preservation of the extranidal vasculature, i.e. the normal arterial supply to the adjacent and remote brain parenchyma and without compromise of the venous drainage of the brain [2, 13, 21]. The simultaneous atraumatic superselective microcatheterisation of several feeding arteries of the arteriovenous malformation belonging to one or more arterial territories through a mono- or bitransfemoral approach represents a technical and conceptual innovation that helps to better elucidate the complex angioarchitecture of a

given arteriovenous malformation and improves the intranidal delivery of the embolic material. This multimicrocatheterisation approach provides essential information particularly on (1) the types of AV shunts constituting the individual compartments of the nidus of the arteriovenous malformation, i.e. pure plexiform, fistulous or mixed types; (2) the shape and size of the vascular channels constituting the individual compartments of the nidus of the arteriovenous malformation, i.e. tubular-type vessels, coiled vessels, intranidal aneurysms, pseudoaneurysms as markers of haemorrhage, venous varix; (3) the types of draining veins and their drainage patterns, i.e. single versus multiple nidal draining veins, individual compartmental draining veins converging towards and joining the nidal draining vein or exiting isolated the nidus; (4) the presence or absence of intercompartmental communications.

Liquid polymerising materials (cyanoacrylates) are the embolic material of choice to achieve permanent obliteration of intranidal AV shunts and associated abnormal vascular channels. Among them, n-butyl-2-cyanoacrylate (NBCA), used in various concentrations of a lipiodol or ethiodol mixture, is the most widely used cyanoacrylate in brain arteriovenous malformation embolisation [2, 13, 21] and its effectiveness and safety have recently been confirmed in a prospective, randomised multicentre trial [22]. The embolisation itself is carried out after positioning the microcatheter tip at the junction of the feeding artery with the compartment supplied by that artery and therefore distal to any normal branch supplying adjacent brain parenchyma. The injection of the appropriately diluted NBCA is performed in a slow and continuous manner under permanent fluoroscopic control in order to achieve progressive obliteration of the previously identified compartmental vascular channels and penetration into adjacent compartments through intercompartmental communications. The injection of NBCA is stopped and the microcatheter rapidly withdrawn when the NBCA is seen to enter a compartmental draining vein and prior to any reflux of the NBCA occurs in the feeding artery. This procedure of intracompartmental obliteration is repeated for all compartments of the nidus of the arteriovenous malformation and usually necessitates several sequential microcatheterisations and embolisations [13, 17].

In arteriovenous malformations with significant fistulous components Guglielmi detachable coils (GDC) for larger fistulas or Berenstein liquid coils (BLC) for smaller fistulas may be used to decrease the flow through the fistula and improve the subsequent precise deposition of NBCA in the fistula itself without distal migration [2, 13, 17]. Toward the end of the endovascular procedure and provided that more than 80–90% of the nidus have already been obliterated with NBCA, one may use microparticles of polyvinylalcohol foam (PVA) as a supplementary embolic material through the remaining small indirect feeding arteries to promote progressive thrombosis of the remaining nidus [13].

Recently, a nonadhesive liquid embolic material, Onyx, consisting of ethylene-vinylalcohol copolymer (EVOH), dimethyl sulfoxide (DMSO) and tantalum has been developed and used in embolisation of brain arteriovenous malformations [23]. Its longer polymerisation time and lack of adherence theoretically permits slower filling and better occlusion of the nidus with less risk of gluing the catheter. It requires, however, as a solvent dimethyl sulfoxide which is toxic to the wall of cerebral vessels and may cause devastating consequences if injected too quickly. Onyx seems to be quite stable because recanalisation was not observed in the preliminary experimental and clinical studies reported so far [24]. However, recanalisation may appear later as has been reported recently [25].

Results of endovascular treatment

The Zurich series of endovascular treatment of brain arteriovenous malformations includes 644 patients embolised between 1986 and 2002, in 1172 sessions. Since 1990 all endovascular procedures have been performed under general anaesthesia which dramatically improved the working conditions, microcatheterisation precision, image and road-map quality, the handling of perprocedural complications and the complete obliteration rate achieved in one session. In no patient of the entire series was a selective or superselective Amytal test for prediction of neurologic dysfunction performed. Instead, precise correlation of structural MR imaging with superselective angiography and later with functional MR imaging data proved highly reliable in appropriately targeting the acrylic injections and in avoiding morbidity. In this series applying the above described technical principles 40% of all patients with a cerebral arteriovenous malformation were cured by complete embolisation of their arteriovenous malformation in one or more sessions, with an associated permanent neurological morbidity of 1.5% and a mortality of 0.4%. Of the patients 23% were cured by targeted preoperative embolisation followed by radical microneurosurgical removal of the arteriovenous

malformation, with a combined morbidity of 2.9% but no mortality, and another 8% of patients were cured by embolisation followed by radiosurgical obliteration of the remaining arteriovenous malformation, with a combined (including late) morbidity of 5.7%. Therefore, in this series a total of 71% of patients with a cerebral arteriovenous malformation were cured by either embolisation alone (40%) or by a combination of embolisation and other techniques (31%) with an overall associated permanent neurological morbidity of 2.8% and a mortality of 0.2% [13]. The combined morbidity-mortality rate of this curative treatment of cerebral arteriovenous malformations applied over the past 18 years is lower than the known natural history of this disease. Another 14% of patients underwent palliative embolisation in one or several sessions, because due to size, location and complexity of their arteriovenous malformation a curative treatment, either alone or in combination, could not be achieved. Finally, in 15% of patients the treatment is not yet completed.

Main causes for morbidity and mortality were per- or early postprocedural haemorrhage and in a few cases ischaemia. The implementation of immediate surgical removal of the haematoma and optimal neurointensive care of these patients significantly helped to eliminate the mortality and significantly improve the clinical outcome of patients with embolisation-induced haemorrhage in the last 5 years [26–28].

It is also interesting to note that following strict intranidal obliteration of the arteriovenous malformation a smooth transition and readaptation of previously dilated feeding arteries and draining veins to normal angiomorphology and haemodynamics was observed in most cases, including the diminution in size or complete shrinkage of nonembolised flow-related proximal-extranidal aneurysms, a phenomenon observed to occur in 35% of these cases on either mid- or long-term follow-up [2, 13]. Furthermore, the so-called normal perfusion pressure breakthrough phenomenon was never observed in this consecutive series of 1172 embolisation sessions in 644 patients with a brain arteriovenous malformation. All postembolisation bleedings (3.2% of cases) and oedema development (4.8% of cases) could be attributed unequivocally to a faulty endovascular action or decision, such as occlusion of a dominant draining vein in subtotally obliterated arteriovenous malformations leading to rupture of the remaining nidus or occlusion of a normal artery resulting in ischaemic oedema formation.

Angiographic and MRI/MRA-follow-up examinations performed at 6, 12, 24 and 36 months following complete obliteration of arteriovenous malformations by embolisation disclosed a recurrence rate of 3.9%. This was caused (1) by partial recanalisation of previously embolised compartments of the nidus in 2% of cases – probably through resorption of highly diluted NBCA, (2) by revascularisation of some portions of the nidus through newly recruited nearby arteries in 1.4% of cases – probably due to more proximal occlusion of the original feeding artery, and (3) by the appearance of a previously invisible and therefore not-embolised portion of the nidus in 0.5% of cases, in which the embolisation was performed as an emergency procedure during the acute phase of an associated, compressive parenchymal haematoma.

References

1 Valavanis A. The role of angiography in the evaluation of cerebral vascular malformations. Neuroimag Clin N Am 1996;6:679–704.

2 Berenstein A, Lasjaunias P, terBrugge KG. Goals and objectives in the management of brain arteriovenous malformations. In: Surgical neuroangiography. Vol. 2.2. Berlin/Heidelberg: Springer-Verlag; 2004. p. 695–736.

3 Gault J, Sarin H, Awadallah NA, Shenkar R, Awad IA. Pathobiology of human cerebrovascular malformations: basic mechanisms and clinical relevance. Neurosurgery 2004;55:1–17.

4 Jellinger K. Vascular malformations of the central nervous system: a morphological overview. Neurosurg Rev 1986;9:177–216.

5 Hofmeister C, Stapf C, Hartmann A, Sciacca RR, Mansmann U, terBrugge KG, et al. Demographic, morphological, and clinical characteristics of 1289 patients with brain arteriovenous malformation. Stroke 2000;31:1307–10.

6 Stapf C, Labovitz DL, Sciacca RR, Mast H, Mohr JP, Sacco RL. Incidence of adult brain arteriovenous malformation hemorrhage in a prospective population-based stroke survey. Cerebrovasc Dis 2002;13:43–6.

7 Mansmann U, Meisel J, Brock M, Rodesch G, Alvarez H, Lasjaunias P. Factors associated with intracranial hemorrhage in cases of cerebral arteriovenous malformations. Neurosurgery 2000;46:272–81.

8 Mast H, Young WL, Koennecke HC, Sciacca RR, Osipov A, Pile-Spellman J, et al. Risk of spontaneous hemorrhage after diagnosis of cerebral arteriovenous malformations. Lancet 1997;350:1065–8.

9 Meisel HJ, Mansmann U, Alvarez H, Rodesch G, Brock M, Lasjaunias P. Cerebral arteriovenous malformations and associated aneurysms: analysis of 305 cases from a series of 662 patients. Neurosurgery 2000;46:793–802.

10 Stefani MA, Porter PJ, terBrugge KG, Montanara W, Willinsky RA, Fallace MC. Angioarchitectural factors present in brain arteriovenous malformations associated with hemorrhagic presentation. Stroke 2002;33:920–4.

11 Stapf C, Khaw AV, Sciacca RR, Hofmeister C, Schumacher HC, Pile-Spellman J, et al. Effect of age on clinical and morphological characteristics in patients with brain arteriovenous malformation. Stroke 2003;34:2664–70.

12 Luessenhop AJ, Spence WT. Artificial embolization of cerebral arteries. Report of use in a case of arteriovenous malformation. JAMA 1960;172;1153–5.

13 Valavanis A, Yasargil MG. The endovascular treatment of brain arteriovenous malformations. Adv Tech Stand Neurosurg 1998;24:131–214.

14 Alkadhi H, Kollias SS, Crelier G, Golay X, Hepp-Raymond M-C, Valavanis A. Plasticity in the human motor cortex in patients with arteriovenous malformations: a fMRI study. Am J Neuroradiol 2000;21:1423–33.

15 Yasargil MG. Microneurosurgery. Vol. IIIA: AVM of the Brain, History, Embryology, Pathological Considerations, Hemodynamics, Diagnostic Studies, Microsurgical Anatomy. New York: Thieme Medical Publishers, Inc.; 1987.

16 Yasargil MG. A legacy of microneurosurgery: memoirs, lessons, and axioms. Neurosurgery 1999;45:1025–91.

17 Valavanis A. New techniques and results in treatment of vascular malformations. In: The Neuroradiology Education and Research Foundation Symposium 2003: Vascular Disease – Diagnosis, Therapy and Controversies. Syllabus ASNR 2003; p. 97–9.

18 Yasargil MG. Microneurosurgery. Vol. IIIB: AVM of the Brain, Clinical Considerations, General and Special Operative Techniques, Surgical Results, Nonoperated Cases, Cavernous and Venous Angiomas, Neuroanesthesia. New York: Thieme Medical Publishers, Inc.; 1988.

19 Spetzler RF, Martin NA. A proposed grading system for arteriovenous malformations. Neurosurgery 1986;65:476–83.

20 Hamilton MG, Spetzler RF. The prospective application of a grading system for arteriovenous malformations. Neurosurgery 1994;34:2–7.

21 Debrun GM, Aletich V, Ausman JL, Charbel F, Dujovny M. Embolization of the nidus of brain arteriovenous malformations with n-butyl cyanoacrylate. Neurosurgery 1997;40:112–21.

22 The n-BCA Trial Investigators. N-butyl cyanoacrylate embolization of cerebral arteriovenous malformations: results of a prospective, randomized, multicenter trial. Am J Neuroradiol 2002;23:748–55.

23 Jahan R, Murayama Y, Gobin YP, Duckwiler GR, Vinters HV, Vinuela F. Embolization of arteriovenous malformations with Onyx: clinicopathological experience in 23 patients. Neurosurgery 2001;48:984–95.

24 Duffner F, Ritz R, Bornemann A, Freudenstein D, Wiendl H, Siekmann R. Combined therapy of cerebral arteriovenous malformations: histological differences between a non-adhesive liquid embolic agent and n-butyl-2-cyanoacrylate (NBCA). Clin Neuropathol 2002;21:13–7.

25 Higashida RT. Embolization of arteriovenous malformations with Onyx: clinicopathological experience in 23 patients [comment]. Neurosurgery 2001;48:995.

26 Keller E, Yonekawa Y, Imhof HG, Tanaka M, Valavanis A. Intensive care management of patients with severe intracerebral hemorrhage after endovascular treatment of brain arteriovenous malformations. Neuroradiology 2002;44:513–21.

27 Deruty R, Pelissou-Guyotat I, Amat D, Mottolese C, Bascoulergue Y, Turjman F, et al. Complications after multidisciplinary treatment of cerebral arteriovenous malformations. Acta Neurochir (Wien) 1996;138:119–31.

28 Hartmann A, Pile-Spellmann J, Stapf C, Sciacca RR, Faulstich A, Mohr JP, et al. Risk of endovascular treatment of brain arteriovenous malformations. Stroke 2002;33:1816–20.