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ORIGINAL ARTICLE

Relief of epilepsy and headache and quality of life after microsurgical treatment of unruptured brain AVM—audit of a single-center series and comprehensive review of the literature

Benjamin Rohn[1] · **Daniel Hänggi**[1] · **Nima Etminan**[1] · **Bernd Turowski**[2] · **Hans-Jakob Steiger**[1,3]

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Abstract Although the benefit of intervention for unruptured arteriovenous malformation (AVM) with regard to stroke rates and long-term disability remains unclear, most patients present with symptoms, such as epilepsy, headache, or neurological deficits, compromising their quality of life. Detailed analysis of the long-term effects of microsurgical treatment on quality of life, epilepsy, and headache was the purpose of this audit. A series of 25 microsurgically treated patients were interviewed on average 7 ± 5 years after treatment. Detailed information was obtained regarding frequency and severity of seizures and headaches. Outcome data was compared with the initial complaints and neurological findings. The Short Form (SF)-36 was used to assess health-related quality of life. On average, the SF-36 scores did not differ significantly from the age-matched German norm values. Patients suffering from chronic headache prior to treatment scored worse in most SF-36 subscales than patients without headache at the time of treatment, and the difference was significant in the SF-36 dimensions physical role functioning and emotional role functioning ($P = 0.04$). In contrast, there was a trend for patients treated for incidental AVM to score somewhat better than the age norm. Twelve patients had been admitted with epilepsy. At the time of follow-up, all patients were seizure free (Engel class I), although 7 of them continued to take antiepileptic medication. Two of 13 patients without epilepsy at the time of treatment experienced seizures sometime during the post treatment course and were under medication at the time of long-term follow-up interview. At the time of the audit, 7 of 11 patients admitted with chronic headache necessitating regular use of pain medication indicated not to use pain medication any longer. Our data suggest that initial symptoms leading to diagnosis and treatment of unruptured AVM may influence long-term quality of life following treatment. Patients admitted with headache as the chief complaint appear to fare worse than patients with epileptogenic or incidental AVMs.

Keywords Unruptured cerebral arteriovenous malformation · Quality of life · Epilepsy · Headache

Introduction

The role of intervention for unruptured arteriovenous malformation (AVM) with regard to stroke rates and long-term disability remains unclear after the recent publication of the results of the ARUBA trial and Scottish Audit of Intracranial Vascular Malformations [1, 19]. However, most patients diagnosed with unruptured brain arteriovenous malformations present with partially disabling symptoms, such as seizures and headache, reducing their quality of life [7, 10, 18]. Besides preventing hemorrhage, improving these symptoms and therefore quality of life is the main purpose of treatment. There is presently no information available on the quality of life after treatment of unruptured AVM. Anecdotal evidence from case series regarding the effect of microsurgical and radiosurgical treatment indicates variable rates of long-term seizure control. Data on the benefits of microsurgery is scarce and conflicting. Epilepsy was reported to be improved [11, 21,

✉ Hans-Jakob Steiger
steiger@uni-duesseldorf.de

[1] Department of Neurosurgery, Heinrich-Heine-Universität, Düsseldorf, Germany

[2] Division of Neuroradiology, Heinrich-Heine-Universität, Düsseldorf, Germany

[3] Neurochirurgische Klinik, Universitätsklinikum, Moorenstr. 5, Geb. 13.71, 40225 Düsseldorf, Germany

29], or unchanged or worse [20]. Seizure risk following any type of intervention was reported unchanged by the Scottish Audit of Intracranial Vascular Malformations [14, 15]. Headache was reported to be improved after radiosurgery or multimodal treatment in a few reports [3, 16].

Here, we performed a cross-sectional long-term follow-up evaluation of a cohort of 25 microsurgically treated patients with unruptured cerebral AVM with the purpose of better defining the late outcome. Furthermore, we reviewed the literature with regard to the differential effects of microsurgery, radiosurgery, and endovascular and multimodality therapy on AVM-associated seizures and headache.

Patients and methods

A sample of 25 patients, who had undergone microsurgical resection of an unruptured AVM between November 1994 and June 2009, was available for a detailed follow-up interview on average 7 ± 5 years after microsurgical treatment.

The total number of unruptured AVMs treated microsurgically during the period was 46. In order to exclude a potential selection bias, we compared the specific pre- and postoperative characteristics between the sample and the total group. No difference existed between the groups with regard to age, gender, neurological deficits at admission and at discharge, and Spetzler-Martin grade (see Table 1).

The follow-up evaluation focused on epilepsy, neurological deficits, headaches, and quality of life.

The interdisciplinary management of AVM during the pertinent period has been described elsewhere [23, 25]. In short, options offered to the patients at that period included endovascular embolization, microsurgery, and Gamma Knife radiosurgery. Individual treatment recommendations were discussed within interdisciplinary conferences.

For the present analysis, entry characteristics of the patients were extracted from the medical records. For the follow-up evaluation, information was gathered using a structured telephone interview conducted by one of us (BR). Questions during the follow-up interview focused on control of epilepsy, headache, and possible residual disability. The Short Form (SF)-36 in its German translation was used to assess the subjective health-related quality of life of patients in terms of physical, mental, emotional, and social aspects. The German age-matched norm values as published by M. Radoschewski and B.-M. Bellach were used for comparison [22]. The SF-36 questionnaire probes physical, mental, and emotional functioning. The 36 individual items are grouped into eight higher-level scales, which measure the health-related quality of life. For overall information, the eight individual scales are summarized into two group scales, physical and psychological functions (see Table 2).

Exploratory statistics correlated the postoperative outcome data to potential influencing factors by univariate comparison. T-statistics were used to compare mean values of stratified groups and Fisher's exact test was used for proportions.

Results

Entry characteristics

The profile of the sample available for follow-up with regard to age at the time of treatment, gender, presurgical epilepsy, presurgical chronic headache, Spetzler-Martin grade, the use of preoperative endovascular embolization, and discharge morbidity is given in Table 1. Twelve of the 25 patients had epileptic seizures prior to treatment and 11 out of 25 had had chronic headache. Four of the 25 patients had some degree of hemiparesis at the time of treatment and the AVM had been an incidental finding in three patients. Early treatment morbidity at the time of discharge from the hospital had been noticed in five patients (20 %).

Outcome regarding epilepsy

Twelve patients had been admitted with epilepsy which was chronic in ten and recent in two. At the time of follow-up, all

Table 1 Baseline characteristics of initial and follow-up sample

Baseline characteristic	Present in total cohort ($n = 46$)	Initially present in follow-up sample ($n = 25$)	Significance at $P = 0.05$
Age at the time of treatment	39 years	40 years	ns
Male/female	25/21	14/11	ns
GCS at discharge <15	2 (4 %)	1 (4 %)	ns
Motor deficit at discharge	8 (17 %)	5 (20 %)	ns
Epilepsy in history	25 (54 %)	12 (48 %)	ns
Chronic headache in history	16 (35 %)	11 (44 %)	ns
Spetzler-Martin grades 1, 2, 3, 4	26 %, 33 %, 28 %, 11 %	24 %, 28 %, 32 %, 16 %	ns
Preoperative embolization	26 (57 %)	14 (56 %)	ns

ns not significant

Table 2 SF-36 scores of the total audit group and subgroups

SF-36 domain	All patients[#]	Admitted with epilepsy[*]	Admitted with headache[*]	Incidental AVM[*]	Age-matched German norm
Physical functioning (physical health)	89 ($P=0.42$)	87 ($P=0.38$)	83 ($P=0.38$)	93 ($P=0.38$)	80
Physical role functioning (physical health)	68 ($P=0.42$)	81 ($P=0.07$)	50 ($P=0.04$)	90 ($P=0.02$)	75
Bodily pain (physical health)	76 ($P=0.18$)	86 ($P=0.07$)	66 ($P=0.11$)	88 ($P=0.15$)	67
General health perceptions (physical health)	64 ($P=0.69$)	70 ($P=0.15$)	57 ($P=0.14$)	64 ($P=0.50$)	66
Vitality (physical health)	58 ($P=0.96$)	62 ($P=0.18$)	55 ($P=0.26$)	60 ($P=0.43$)	58
Social role functioning (mental health)	79 ($P=0.27$)	75 ($P=0.27$)	75 ($P=0.30$)	90 ($P=0.15$)	86
Emotional role functioning (mental health)	79 ($P=0.31$)	75 ($P=0.32$)	60 ($P=0.04$)	100 ($P=0.01$)	88
Mental health (mental health)	70 ($P=0.46$)	71 ($P=0.39$)	66 ($P=0.42$)	74 ($P=0.32$)	73
Physical sum score (physical health)	50 ($P=0.54$)	54 ($P=0.03$)	46 ($P=0.14$)	52 ($P=0.26$)	51
Mental sum score (mental health)	47 ($P=0.12$)	46 ($P=0.26$)	44 ($P=0.14$)	51 ($P=0.16$)	51

[#] *P* values refer to two-tailed comparison with German norm values

[*] *P* values refer to one-tailed comparison with patients not suffering from the respective condition

patients were seizure free (Engel class I), although seven of them continued to take antiepileptic medication.

Two of 13 patients without epilepsy at the time of treatment experienced seizures sometime during the post treatment course and were under medication at the time of long-term follow-up interview.

Outcome regarding headache

Eleven of the 25 patients available for long-term follow-up had been admitted with the complaint of chronic and progressive headache. At the time of follow-up, four reported to suffer no longer of headaches while the others reported the headaches to persist. However, only four of the 11 patients admitted with headache indicated to use aspirin occasionally for headache at the time of follow-up. All of them had used non-steroidal antirheumatics (NSAR) prior to surgery and one of them pregabalin (see Fig. 1). The reported frequency and severity of headache at the time of follow-up were not statistically different from those of the group who had been admitted primarily for epilepsy or for an incidental AVM. Within the pain category of the SF-36 form, scores of patients admitted for headache tended to be lower than those of patients admitted with epilepsy or incidental AVM ($P=0.11$). Figure citations were not in sequence so the figures were renumbered. Kindly check.The figures 1 and 2 must be switched. legends end citations in text are ok. So just switch the images!

Long-term quality of life

All but one patient with a persistent disability and a Barthel index of 50 % at the time of the audit reported a Barthel index of 100 %. On average, the SF-36 scores did not differ significantly from the age-matched German norm values (Table 2, Fig. 2). Patients admitted with chronic headache scored worse in most dimensions of the SF-36 form. The difference between patients admitted with headache and the other patients reached statistical significance for the SF-36 dimensions physical role functioning ($P=0.04$) and emotional role functioning ($P=0.04$). Physical and emotional role functioning address problems with work or other daily activities as a result of physical health and emotional problems, respectively. Conversely, patients treated for incidental AVM tended to score somewhat better in most dimensions of the SF-36 form, reaching significance for dimensions physical role functioning ($P=0.02$) and emotional role functioning ($P=0.01$).

Discussion

The current analysis provides for the first time information on quality of life following microsurgical resection of unruptured AVM. The data suggest that the presenting symptoms may be important determinants of subsequent quality of life. In a radiosurgically treated cohort, Yang and coworkers reported results after radiosurgical treatment [27, 28]. They recognized freedom of epilepsy as an important factor for quality of life.

While on average long-term quality of life in our patients operated on for unruptured AVMs did not differ substantially from the age-matched German norm values, patients admitted with headache as the main complaint faired substantially worse. The underlying reasons may originate in persistent headaches, or in the premorbid personality of patients admitted for headaches. The analysis of the effect of AVM treatment on headaches in our patient cohort revealed a discrepancy between the subjective and objective perception of pain relief. While seven of 11 patients admitted with headaches indicated during follow-up that the headaches were the same or worse as

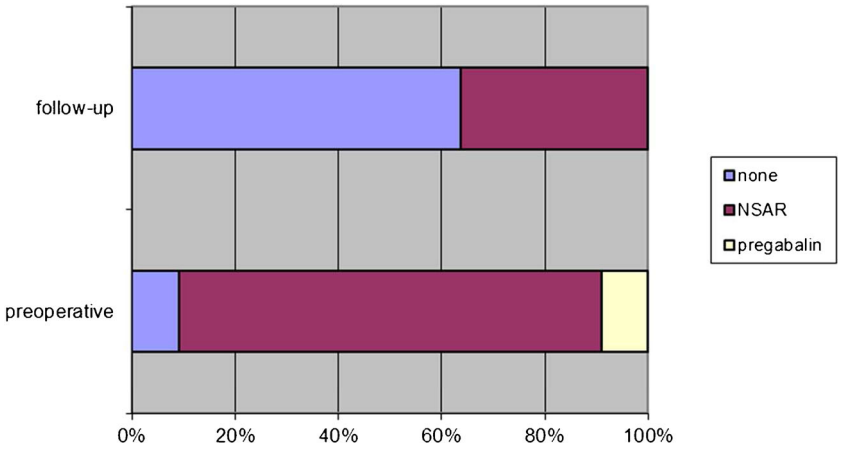

Fig. 1 Consumption of analgesics in patients admitted with headache. Comparison of the pretreatment consumption and the use at the time of follow-up

before surgery, regular consumption of pain medication at the time of follow-up was less frequent compared with the time of hospital admission.

Data on the effect of AVM treatment on headaches is scarce (see Table 3). Some reports on radiosurgical treatment of AVM suggest improvement in patients with headache as presenting symptom [3, 9, 16]. Additionally, some data with respect to multimodal therapy is available. Dehdashti and coworkers reported that 83 % of the patients with occipital AVMs and headache as presenting symptom improved after multimodal therapy, in contrast to only 30 % who improved with conservative management. In our analysis including not only occipital AVMs, the results were somewhat less positive; 39 % of patients with preoperative chronic headache reported improvement, 54 % no change, and 8 % deterioration. However, the discrepancy between the patient's perspective and the more objective comparison of the consumption of analgesics underline that pain perception and relief are difficult to measure.

The effect of AVM treatment on epilepsy is somewhat better known than the effect on headache and quality of life. The reported results of radiosurgery, microsurgery, and multimodality therapy are summarized in Table 4. On behalf of the *Scottish Audit of Intracranial Vascular Malformations*, Josephson et al. reported that there was no significant difference in the 5-year risk of seizures with AVM treatment or conservative management, irrespective of whether the AVM had presented with hemorrhage or epileptic seizures [14]. The study did not differentiate between treatment modalities, and the control group of conservatively managed epileptogenic unruptured AVM consisted only of 21 patients. Despite the limitations of this prospective analysis, the effect of treatment remains doubtful. A positive effect has been mentioned after radiosurgery in a number of reports [2, 4–6, 8, 13, 14, 17, 24, 26–28]. Regarding microsurgery, Heros and colleagues reported that of the patients who had seizures before surgery, over half were either cured or greatly improved with respect to the seizures. Of the patients who did not have seizures before surgery, 8.2 % had only one or two seizures during the immediate postoperative period, and 7.1 % had late seizures that were well controlled with medication [11]. Piepgras and coworkers reported their results with 110 patients with preoperative seizures [21]. Eighty-three percent were seizure-free,

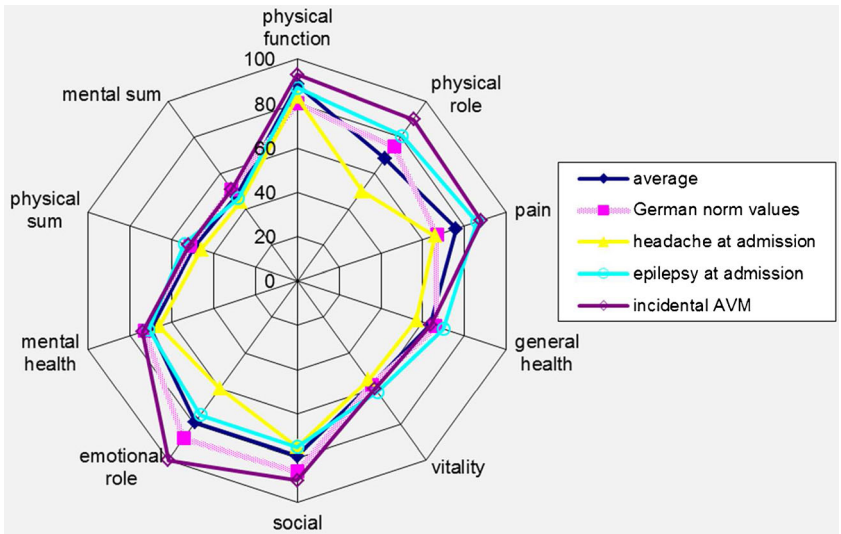

Fig. 2 SF-36 scores on average 7 years after microsurgical treatment of unruptured AVM compared with the age-matched German norm values. In addition to the average values, the subgroups of patients presenting with headache, with epilepsy and incidental AVM are shown separately. Patients with preoperative headache scored significantly worse in the SF-36 dimensions emotional role functioning and physical role functioning ($P = 0.04$)

Table 3 Summary of reports on headache after treatment of AVM

Author, year	Treatment modality	Proportion of improvement	Comment
Kurita, 2000	Radiosurgery	71 % cured or improved	Occipital AVMs only
Ghossoub, 2001	Radiosurgery	53 % cured, improved in 20 %	
Dehdashti, 2010	Multimodality	83 % improvement	30 % improvement in control group under observation
Actual series	Microsurgery	Subjective improvement indicated by 33 % after 7 years	Consumption of analgesics by 91 % preoperatively, by 37 % at follow-up

with 48 % no longer receiving anticonvulsant therapy, while 17 % still suffered intermittent seizures. Of the patients without seizures preoperatively, 6 % were having new ongoing seizures. Yeh and coworkers reported their experience with an epilepsy surgery approach to epileptogenic AVM [29]. All patients underwent preoperative electroencephalography and intraoperative electrocorticography, and total excision of the AVM. Additional cortical excision was performed in 25 cases, and they also found remote seizure foci in the ipsilateral mesial temporal or frontal structures in 20 % of their patients. Postoperative seizure control during a follow-up study of 5 years on average was excellent in 70 % (Engel class I, free of disabling seizures) and good (Engel class II, rare disabling seizures) in another 20 %. Englot and coworkers reported follow-up information of 130 patients with supratentorial epileptogenic AVMs [6]. After resection, 96 % of patients had a modified Engel class I outcome, characterized by freedom from seizures or only one postoperative seizure during the average follow-up of 21 months. Hoh and coauthors reported seizure outcome in 141 epileptogenic AVMs following multimodal treatment [12]. There were 66 % class I, 10 % class II, 0.9 % class III (worthwhile improvement), and 20 % class IV (no worthwhile improvement) outcomes. Hyun colleagues recently reported their experience with the multidisciplinary treatment of 399 patients including surgical resection, radiosurgery, and embolization, either alone or in combination [13]. After a median follow-up period of 6.0 years, 70 % of patients suffering from preoperative epilepsy were seizure-free. The authors also compared the results between the treatment modalities. Seizure-free outcomes one year after microsurgery, radiosurgery, or embolization were 78, 66, and 50 %, respectively. They concluded that microsurgery led to the highest

Table 4 Summary of reports on epilepsy after treatment of AVM

Author, year	Treatment modality	Proportion of improvement	Comment
Murphy, 1985	Microsurgery	50 % seizure free	De novo seizures in 26 %
Heros, 1990	Microsurgery	>50 % seizure free or greatly improved	New late postoperative seizures in 7 %
Piepgras, 1993	Microsurgery	83 % seizure free, 17 % intermittent seizures	New late postoperative seizures in 6 %, median follow-up 7.5 years
Yeh, 1993	Microsurgery	70 % Engel class I, 20 % class II	Epilepsy surgery approach with intraoperative corticography
Englot, 2012	Microsurgery	96 % modified Engel class I	3 % de novo seizures during follow-up of 21 months
Eisenschenk, 1998	Radiosurgery	59 % seizure free, 19 % improvement	
Kurita, 1998	Radiosurgery	80 % seizure free	Mean follow-up 2.8 years
Ghossub, 2001	Radiosurgery	58 % seizure free, 18 % improvement	De novo seizures in 2 %
Schäuble, 2004	Radiosurgery	51 % seizure free, 27 % rare non-disabling seizures	3 years follow-up
Yang, 2012	Radiosurgery	77 % seizure free	13 % de novo seizures
Chen, 2014	Radiosurgery	44 % seizure free, 25 % improved	
Ding, 2015	Radiosurgery	20 % seizure free, 57 % improved	De novo seizures in 1.7 %
Hoh, 2002	Multimodality	66 % Engel class I, 10 % class II, 1 % class III, 34 % idem or worse	Median follow-up 6 years
Hyun, 2012	Multimodality	Overall 70 % seizure free at 1 year	80 % seizure free 1 year after microsurgery, 66 % after radiosurgery and 50 % after embolization
Josephson,2012	Multimodality	52 % seizure free at 5 years	57 % seizure free with observation
Wang, 2013	Multimodality	40 % seizure free	18 % de novo seizures
Actual series	Microsurgery	All patients seizure free	de novo seizures in 15 %

percentage of seizure-free outcomes. Wang recently reported a somewhat less positive view of their results [25]. Of the 49 patients (30 %) presenting with seizures, 60.4 % experienced seizure persistence after treatment. Patients treated with radiosurgery fared worse than patients treated microsurgically. Patients presenting without seizures experienced de novo seizures after treatment in 18.4 %, and here, surgical patients fared worse than radiosurgically managed patients.

The results of our survey provided comparable data in that all patients suffering from preoperative epilepsy became free of disabling seizures, while de novo seizures became apparent in some 15 % of patients without preoperative epilepsy. The data in the literature are currently too scarce to work out clear differences between radiosurgery and microsurgery with regard to the effect on epilepsy. In summary, elimination of the AVM in patients with epileptogenic AVM leads to good seizure control in the majority of patients, while de novo seizures appear to occur in 10–20 % of patients without preoperative seizures. However, since many patients undergo resection after one or few seizures, it remains unclear whether the long-term course is due to treatment or not. The results of the mentioned Scottish audit suggest that the issue remains unsettled and further prospective controlled trials that differentiate between treatment modalities are required.

Conclusion

Our data suggest that initial symptoms leading to diagnosis and treatment of unruptured AVM may determine long-term quality of life following treatment. Patients admitted with headache as chief complaint appear to fare worse than patients with epileptogenic or incidental AVMs. Regarding the effect of microsurgery on headache and epilepsy, our results confirm previous positive reports. Clearly, in view of the small sample size, all statistics should be taken with some degree of caution, but for more definitive conclusions, larger prospective studies using standardized questionnaires would be necessary, which might be difficult in the post ARUBA era.

Compliance with ethical standards

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

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