

Retrospective 5-Year Clinical Outcome of Interdisciplinary Treatment for Ruptured Cerebral Arteriovenous Malformation: The Lesson Learned

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Abstract

Introduction: To retrospectively evaluate 5-year clinical outcome; pre- versus post-interdisciplinary treatment for ruptured cerebral arteriovenous malformation (AVM) during 2004-2006.

Methods: The authors retrospectively reviewed the medical records of Thai ruptured AVM patient who admitted at Ramathibodi Hospital, Mahidol University during 2004-2006. Five-year follow-up pre- versus post-interdisciplinary treatment were determined using marginal homogeneity test (Stuart-Maxwell).

Results: There were 133 cases with ruptured AVM diagnosis during 2004-2006. Regarding to 5-year interval retrospective review, AVM volume, Spetzler-Martin Grading, Pollock-Flickinger Score, and the pre- versus post-interdisciplinary treatment Eastern Cooperative Oncology Group (ECOG) Score were determined.

Conclusion: There was the statistical significant difference of ECOG between before and after interdisciplinary treatment in ruptured AVM patient ($p < 0.001$). There was favorable outcome rather than unfavorable outcome under interdisciplinary treatment for cerebral AVM patient.

Keywords: AVM, Cerebral arteriovenous malformation, Eastern Cooperative Oncology Group (ECOG) Score, Retrospective 5-year clinical outcome

Introduction

The cerebral arteriovenous malformation (AVM) is a cerebral vascular anomaly comprising of arteries and arterialized veins fistulous connections without normal capillary intervening [1-4]. Because of the advent of advanced medical imaging, the majority of patient harboring AVM lesions are typically asymptomatic when they are detected or investigated [5-7]. When the rupture occurs, it is documented as a significant cause of neurological deficit for the reason that it is the origin of intracranial hemorrhage or seizure. AVM generally presents about 1 per 100,000 of all population [3,8]. Between 20-40 years of age of the patient is commonly reported [1,3,8-11]. Unfortunately, there was no cerebral AVM incidence explicitly reported in Thailand. The signs and symptoms of ruptured cerebral AVM were respectively described as about 50% of cases for intracranial hemorrhage, 10% of cases for focal seizure, 30% of cases for generalized seizure, 14% of cases for headache, 7% of cases for

persistent neurological deficit and 5% of cases for progressive neurological deficit [11,12]. About 3% of cases per year were the risk of hemorrhage for patients with only AVM. About 7% of cases per year with the risk of hemorrhage in patients with aneurysms associated AVM was reported [9]. Millar et al stated that there are potential causes of brain damage resulting from the charisma of AVM as followings "Steal" phenomenon, cerebral perfusion failure causing cerebral ischemia, hemorrhagic infarction from thrombosis of the aneurysm of the great vein of Galen, cerebral atrophy and alterations of cerebral blood flow caused by surgery [13]. Interdisciplinary treatment of cerebral AVM is accepted worldwide [1,3,4,8,10-23]. In Neurosurgery Unit, Surgery Department, Faculty of Medicine Ramathibodi Hospital, Mahidol University, there are the interdisciplinary treatments especially for cerebral AVM patient. Neurointerventionalists, neuroradiologists, radiation therapists and neurosurgeons, as a team approach conference, was held once every week to determine the appropriate treatment for cerebral AVM patient.

Only microsurgical resection, only endovascular embolization, combination of preoperative endovascular embolization subsequently with microsurgical resection and radiosurgery, only stereotactic radiosurgery, endovascular embolization followed by radiosurgical treatment, or observation alone is the clinical strategic treatment. This present study represents the authors' experiences with 133 Thai cerebral AVM patients with interdisciplinary treatment to retrospectively evaluate 5-year of the Eastern Cooperative Oncology Group (ECOG) score during 2004-2006.

Methods

Study design

After an institutional review board (IRB) approval, AVM medical records were reviewed during 2004-2006. Regarding neurosurgical aspects, they were treated by the authors in Neurosurgery Unit, Surgery Department, Faculty of Medicine Ramathibodi Hospital, Mahidol University during 2004-2006 and also with interdisciplinary treatment including endovascular embolization and radiosurgery.

Patients and grouping

To define AVM, cerebral angiography was required for clear inclusion criteria by McCormick's classification system for vascular malformations [24]. Venous malformations, cavernous malformations, telangiectases and dural AVM were excluded.

Data collection

Retrospectively analyzed information was reviewed from the medical records during 2004-2006. General identification data, cerebral AVM volume, Spetzler-Martin Grading, Pollock-Flickinger Score, and the Eastern Cooperative Oncology Group (ECOG) Score were determined. There were 133 Thai AVM patients consecutively collected and analyzed.

Statistical analysis

Data were analyzed using the marginal homogeneity test (Stuart-Maxwell) to evaluate the clinical outcome; the statistical significance difference of ECOG between before and after interdisciplinary treatment groups.

The level of statistical significance difference was set at $p < 0.05$.

Results

One hundred and thirty three cases of ruptured cerebral AVM patient were consecutively collected and analyzed (**Table 1**). There were 58.6% (N=78) of all cases accounted for men and 41.4% (N=55) of all cases was women. Average age was 33.7 ± 13.5 years. Regarding to this, AVM volume was categorized into three subgroups as less than 15 cc., 15-25 cc. and more than 25 cc. respectively. And also postprocedural MRA and DSA (digital subtraction angiography) which were found 99.2% (N=132) of all cases, AVM volume was categorized into three subgroups as less than 15 cc., 15-25 cc. and more than 25 cc. AVM was

located in eloquent area and accounted for 90.6% (N=116) of all cases, however, 9.4% (N=12) of all cases, AVM was located in non-eloquent area. Deep draining vein was found in 77.7% (N=101) while superficial draining vein was found 22.3% (N=29). Most common arterial feeder on the right side of the brain was the combination of ACA, MCA and PCA. On the left side of the brain, the most common arterial feeder was MCA. 68.9% (N=80) of all cases were reported 3-6 cm. diameter of AVM nidus. Less than 3 cm. AVM nidus diameter was found 18.9% (N=22) of all cases while 12% (N=14) of all cases were reported more than 6 cm. AVM nidus diameter. Spetzler-Martin Grading was reported and 42.1% (N=56) of all cases was found in third grade most commonly. There were 80.5% (N=107) of all cases was indicated for emergency craniotomy with clot removal because of intracranial bleeding. Fifteen percents (N=20) of all cases was undergone craniotomy with clot removal because of intracranial bleeding with progressive neurological deficit. Recurrent intracranial bleeding was found 3% (N=4) of all cases was undergone craniotomy with clot removal. According to cerebral AVM treatment, 49.6% (N=66) of all cases was undergone embolization, surgery and radiosurgery. There were 27.8% (N=37) of all cases was undergone embolization, and radiosurgery while only radiosurgery therapy was done for 22.6% (N=30) of all cases.

After five years, ECOG between before and after interdisciplinary treatment in this present study was determined as primary outcome. About 132 cases were recruited and analyzed. One case was lost to follow up. Good recovery with AVM obliterated was reported for 85.6% (N=113) subsequent postprocedural follow-up whereas 13.6% (N=18) of all cases was found in moderate disable stage and 0.76% (N=1) of all cases was vegetative stage. Average Pollock-Flickinger Score was 1.41 ± 0.35 . Retrospectively 5-year follow-up, the data was classified into two groups including unfavorable and favorable group (**Table 2**). Both two groups were defined (**Table 3**). The unfavorable group was defined as the patient had deteriorated condition after treatment. In zero grade group before interdisciplinary treatment became 3.8% (N=5) of cases in first grade and 2.3% (N=3) of cases in second grade. In first grade group before interdisciplinary treatment became improved, as the same and worst for 41.6% (N=55) of cases, 40.2% (N=53) of cases and 8.3% (N=11) of cases respectively. In second grade group before interdisciplinary treatment became improved and as the same for 2.3% (N=3) and 0.8% (N=1) respectively. In fourth grade group before interdisciplinary treatment became improved for 0.8% (N=1). So far, the unfavorable group accounted for 14.4% (N=19) of all cases after 5-year follow-up. The favorable group was defined as the patient group who had the same or improved condition after interdisciplinary treatment with AVM obliterated. In the patient group who had the same conditions after treatment, there were 40.2% (N=53) of cases in first grade and 0.8% (N=1) of cases in second grade. Additionally, the patient group who had the improved conditions after treatment including 41.6% (N=55) of cases in zero grade, 2.3% (N=3) of cases in first grade and 0.8% (N=1) of cases in second grade. Finally, the favorable group accounted for 85.6% (N=113) of all cases. There was the statistical significant difference of ECOG between before and after interdisciplinary treatment in AVM patient ($p < 0.001$).

Table 1. Data characteristics.

Characteristics	Number	%
Sex		
Male	78	58.65
Female	55	41.35
Age, mean(SD) years	133	33.68(13.51)
Location		
Non eloquent	12	9.38
Eloquent	116	90.63
Draining vein		
Deep draining vein	101	77.69
Superficial draining vein	29	22.31
Feeding artery on Rt. side		
ACA	7	13.46
MCA	4	7.69
PCA	4	7.69
ECA&MCA	1	1.92
ACA&MCA	14	26.92
ACA&PCA	1	1.92
MCA&PCA	1	1.92
ECA+ACA+MCA	4	7.69
ECA+MCA+PCA	1	1.92
ACA+MCA+PCA	15	28.85
ACA	14	19.44
MCA	16	22.22
PCA	2	2.78
BA	6	8.33
ECA&MCA	2	2.78
ECA&PCA	2	2.78
ACA&MCA	8	11.11
ACA&PCA	2	2.78
MCA&PCA	2	2.78
ECA+ACA+MCA	2	2.78
ACA+MCA+PCA	13	18.06
ECA+ACA+MCA+PCA	2	2.78
ECA+MCA+PCA+VA	1	1.39
Nidus size		
<3 cm.	22	18.97
3-6 cm.	80	68.97
>6 cm.	14	12.07
Spetzler& Martin Score		
1	2	1.50
2	30	22.56
3	56	42.11
4	41	30.83
5	4	3.01
Clinical Presentation		
Single hemorrhage	107	80.45
Recurrent hemorrhage	4	3.01
Isolated neurological deficit	1	0.75
Progressive neurological deficit	1	0.75
Single hemorrhage+ Progressive neurological deficit	20	15.04

Glasgow Outcome Score after immediate treatment		
Recovery	103	78.03
Moderate disable	28	21.21
Vegetative stage	1	0.76
Treatment modality		
Embolization+radiosurgery	37	27.82
Radiosurgery	30	22.56
Surgery+ Embolization+radiosurgery	66	49.62
Pollock Flickinger Score after treatment, mean(SD)	132	1.41(0.35)

Table 2. Comparing ECOG before and after interdisciplinary treatment.

ECOG Before Interdisciplinary treatment	ECOG After interdisciplinary treatment					
	0	1	2	3	4	total
0	0	5(3.8%)	3(2.3%)	0	0	8
1	55(41.6%)	53(40.2%)	11(8.3%)	0	0	119
2				0	0	4
	0	3(2.3%)	1(0.8%)			
3	0	0	0	0	0	0
4	0	0	1(0.8%)	0	0	1

Table 3. ECOG performance status score.

ECOG	Karnofsky	Definitions
0	100	Asymptomatic
1	80-90	Symptomatic, fully ambulatory
2	60-70	Symptomatic, in bed less than 50% of the day
3	40-50	Symptomatic, in bed more than 50% of the day, but not bedridden
4	20-30	Bedridden

Discussion

The clinical grading of AVM; Spetzler - Martin Grade, proposed the morbidity associated with surgical treatment. It is accepted that there is a low morbidity for grade I and II but will be distended increasingly for grade III, IV and V lesions. On the other hand, this morbidity will be reduced by the explicit agreement with interdisciplinary treatment. According to clinical grading of AVM, mostly of cases in this present study were found as third or fourth Spetzler - Martin Grade. Most of AVM were located in eloquent area. The combination of preoperative endovascular embolization subsequently with microsurgical resection and/ or radiosurgery is the frequently already planned modality of treatment. However, there is no specific recommendation or guideline could indicate any benefit from interdisciplinary treatment [3,25]. In this present study, about fifty percent of cases were planned and finally followed by all three procedures including preoperative embolization, surgery and radiosurgery after a team approach conference. Then the patient and their

families were also prior informed about risk and benefit of this interdisciplinary treatment. It is difficult to formulate a common decision particularly the definite use of interdisciplinary treatment as a protocol but this treatment does obviously play a great role in this present study. Individual case would be considered and the customized interdisciplinary treatment also would be established. By using radiosurgery treatment, Pollock and Flickinger proposed the grading system which indicated the patient outcome after being treated with stereotactic radiosurgery (SRS) [26-28]. Because the Spetzler -Martin Grade did not associate with patient outcome so Pollock and Flickinger stated the some predictive factors for clinical outcome of AVM patients after being treated with SRS and proposed this as a clinical outcome grading system. The predicting factors are these followings including with AVM volume, age, and AVM location. There are 4 subdivided modified radiosurgery based AVM score such as <1.00; 1.00-1.50; 1.51-2.00; and >2.00 [28]. This score are correlated with the percentage of patients with AVM obliteration with or without new deficits. In this present study, the Pollock-Flickinger Score was 1.41+0.35 which could be defined as around 70% of cases after interdisciplinary treatment have AVM obliteration without new deficits. Regarding this present study result, comparing with the calculated Pollock-Flickinger Score, the clinical result was estimated. The ECOG score also called Zubrod or the WHO score ranges from 0 to 4 (**Table 4**) [29]. This score is simply to define the post treatment clinical outcome and well accepted to evaluate general well-being, activities of daily life and to measure patient's quality of life. In this present study, five-year ECOG score comparing between pre and post treatment were indicated. So far, when comparing the unfavorable (14.4%) and favorable group (85.6%), the outcome of treatment was expected. However, there was favorable outcome rather than unfavorable outcome under interdisciplinary treatment and also concordant to several reports[3,4,11,16,17,19,22,26,30-33]. Some characteristics were considered (**Table 5**). Furthermore, there is no statistical significant difference. Our lessons learned are including first, the role of interdisciplinary treatment for cerebral AVM is necessary particularly to customize design the appropriated treatment paradigm for the patient after inform consent. Patient safety is paramount. Definite consensus treatment procedures have to postulate for each role of the disciplinary. The most common and successful treatment modality exercising for ruptured cerebral AVM patient is the combination management of cerebral angiography with embolization, surgery and following by radiosurgery. Second, the Spetzler -Martin Grade and the Pollock-Flickinger Score are very crucial for the interdisciplinary treatment team and to correlate both scores is very supportive. Third, the final decision making is customized and based on the patient safety. Simulation the best cooperation and communication among the disciplinary members even by the meeting or individual facilitated the proper and safe treatment simultaneously. Fourth, even there were 85.6% of cases had AVM obliteration with improve clinical outcome they were also followed up with neurosurgeons perpetually. The guideline treatment for the ruptured cerebral AVM is spontaneously designed and synchronized by the members of the interdisciplinary approach. Fifth, there is a significant clinical challenge in the management of inoperable

Table 4. Comparing unfavorable and favorable outcome group.

Unfavorable outcome group		5+3+11	19(14.4%)
Favorable outcome group	condition is as the same	53+1	54(40.9%)
	condition is improved	55+3+1	59(44.7%)

Table 5. Factors influenced unfavorable and favorable outcome.

Characteristics	N(%)		P-value
	Favorable outcome	Unfavorable outcome	
Sex			
male	69(57.98)	1(25.00)	0.314
female	50(42.02)	3(75.00)	
Age			
<60 years	116(97.48)	4(100.00)	1.000
≥60 years	3(2.52)	0(0)	
Location			
Non-eloquent	8(6.96)	0(0)	1.000
Eloquent	107(93.04)	4(100.00)	
Draining vein			
Deep draining vein	92(78.63)	3(75.00)	1.000
Superficial draining vein	25(21.37)	1(25.00)	
Feeding artery RT			
single	11(25.58)	0(0)	1.000
multiple	32(74.42)	2(100.00)	
Feeding artery LT			
single	36(55.38)	1(33.33)	0.588
multiple	29(44.62)	2(66.67)	
Spetzler martin grading			
mild	28(23.53)	1(25.00)	1.000
severe	91(76.47)	3(75.00)	

AVM. Palliative treatments with close follow-up for inoperable AVM cases are practical particularly in selected patients.

Conclusion

In this present study, to achieve successful clinical outcome of the AVM obliterated, the interdisciplinary treatment is designed for individual patient. The customized interdisciplinary treatment consensus with completely inform consent for patients and their families is very necessary. There was the statistical significant difference of ECOG between before and after interdisciplinary treatment in AVM patient ($p < 0.001$). Comparing the unfavorable (14.4%) and favorable group (85.6%), the outcome of interdisciplinary treatment was determined and clinically concordant with the other reports.

Limitation

This present study has a number of limitations and need to be noted including all of these followings. 1) This present study is the observational single-center, retrospective design so the selection and clinical management are the confounding

variables. 2) Being a retrospective study, this may confine our clinical findings generalizability. Consequently, our lessons learned are not the clinical guideline or consensus for overall management of ruptured AVM patients. 3) The other modeling of angioarchitectural complexity did not mention in this present study, even though their occurrence could be seen. Some angioarchitectural complexity such as dolichocarotids (DCs) which are the geometric abnormalities of the internal carotid artery (ICA) are acknowledged but there is no evidence relating to ruptured AVMs and the cerebrovascular events [34,35]. It is still controversy. 4) Some missing data most likely to occur in this present study and also the confounders which could be a major statistical determinant which might affect the difference of the factors as shown in **Table 5**. 5) Lastly, cerebral angiographic evidence of AVM obliteration was unavailable in all patients. However, the accuracy of MRI to evaluate the AVM obliteration is clinically accepted and comparable to the cerebral angiography. [36,37].

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