Int J Clin Exp Med 2015;8(7):11014-11019
www.ijcem.com /ISSN:1940-5901/IJCEM0008542

Original Article

Risk factors of intracranial hemorrhage after brain AVM interventional therapy and its effects on prognosis

Guobin Li, Kun Han, Haiying Yang, Hui Huang, Hong Yang, Dezhang Zhu

Department of Neurosurgery, The Affiliated Hospital of Qingdao University, Qingdao 266003, Shandong Province, P.R. China

Received March 28, 2015; Accepted May 31, 2015; Epub July 15, 2015; Published July 30, 2015

Abstract: Objective: This study is to investigate risk factors of intracranial hemorrhage and their effects on prognosis in patients with brain intracranial arteriovenous malformation (AVM) after interventional therapy. Methods: A total of 80 cases of brain AVM patients were admitted to our hospital and received interventional embolism treatment from December 2011 to July 2014. The patients all were confirmed by digital subtraction angiography. Risk factors of intracranial hemorrhage after interventional therapy were analyzed by multivariate analysis. The factors included age, sex, AVM diameter, vein drainage types, embolism area, etc. Meanwhile, the patients were followed up for 60 months after interventional embolism therapy, so as to assess the impact of related risk factors on prognosis. Results: By logistic regression analysis, it was found that age, AVM diameter, AVM combined with aneurysm, embolism area and venous drainage types were related risk factors those could lead to intracranial hemorrhage. Meanwhile, it was identified by receiver operating characteristic curve that embolism area, AVM diameter and AVM combined with aneurysm were risk factors had considerable influence on prognosis while the diagnosis significance of age and venous drainage types was poor ($P > 0.05$). The survival curves of embolism area and AVM diameter on prognosis had been identified by Kaplan-Meier analysis and it showed that embolism area < 50% and AVM diameter ≥ 3 cm had a better prognosis than embolism area ≥ 50% and AVM diameter < 3 cm ($P < 0.05$). Conclusions: A series of risk factors were related to intracranial hemorrhage and some of them had considerable influence on prognosis, which, could help to reduce the risk of intracranial hemorrhage and improve long-term survival rate.

Keywords: Intracranial arteriovenous malformation, intervention, embolism, intracranial hemorrhage, prognosis

Introduction

Intracranial arteriovenous malformation (AVM) is a congenital disease caused by abnormal cerebral vascular growth, which, accounts for about 50% in brain vascular malformations [1]. The reported incidence of AVM intracranial hemorrhage is up to more than 70% [2]. Short circuit between arteriovenous due to the lack of the capillary network between brain arteriovenous, can cause cerebral hemodynamic disorder, thus inducing a variety of clinical symptoms. With the development of interventional devices and improvement of operation technology, endovascular therapy has become an important part of clinical treatment for cerebral vascular malformation.

These days, micro catheter technique and embolic material have improved rapidly, and the importance of interventional embolization for cerebral AVM has increased gradually. However, the defect that could not be ignored is the high risk complication of hemorrhage that occurs at early stage after interventional embolization [3]. It is reported that the risk factors of cerebral AVM hemorrhage include combined aneurysm, deep venous drainage or individual venous drainage, the size of the AVM, ect [4, 5]. Therefore, a clear understanding of the risk factors of intracranial hemorrhage after cerebral AVM embolization can effectively help to perform preoperative evaluation and postoperative nursing, prevent intracranial hemorrhage occurring and reduce complications.

In the present study, 80 cases of cerebral AVM patients were enrolled. The general clinical characteristics of patients such as brain arteriovenous malformations, imaging and treatment were observed and the risk factors these

Table 1. Basic clinical characteristics of brain AVM patients

General information	Clinical data
Sex	
Male	47
Female	33
Age (years)	50.72 ± 11.51
AVM diameter	
< 3 cm	34
≥ 3 cm	46
AVM combined with aneurysm	26
S-M grading (cases)*	
I	11
II	39
III	19
IV	9
V	2
Embolism area	
≥ 50%	15
< 50%	65
Venous drainage types	
Superficial vein type	57
Deep vein type	16
Mixed type	7

Note: *S-M grading represents an abbreviation of Spetzler-Martin grading.

lead to intracranial hemorrhage after cerebral AVM endovascular embolization were analyzed, so as to provide theory basis and experience support for preventing cerebral AVM bleeding and reducing complications.

Materials and methods

Patients' data

A total of 80 cases of patients who were diagnosed as cerebral AVM by cerebral angiography and admitted to our hospital from December 2011 to July 2014 were enrolled in this study. They all were treated with interventional embolism treatment. Among them, 47 cases were male and 33 cases were female. They aged from 30-70 years old, with an average of 50.72 ± 11.51 years old.

Prior written and informed consent were obtained from every patient and the study was approved by the ethics review board of The Affiliated Hospital of Qingdao University.

Surgical method

Digital subtraction angiography (DSA) scan by femoral artery intubation was performed before operation in all the patients. Cerebral angiography was carried out to make sure of the illness followed by selectively catheterization of micro catheter before embolization. Corresponding embolism agent was given for embolotherapy after angiography showed no obvious blood supply to normal brain tissue. Heparin with a dosage of 100 U/Kg was given after the intraoperative catheter reached the lesion position. Postoperative neurologic examinations were carried after the recovery of the patients. And patients these were suspected with neurological damage had taken MRI inspection in time.

Analyzed factors

Related indexes such as general data of the patients, characteristics of AVM and interventional embolism process were taken as suspected risk factors of hemorrhage after embolism therapy. The specific factors included gender, age, S-M grade, AVM diameter, embolism area (≥ 50% or < 50%), draining vein types and complicated aneurysms.

Prognosis evaluation

According to the results of imaging examination and the follow-up status, classification and statistics of related clinical data were performed. Meanwhile, the risk factors influencing prognosis and leading to intracranial hemorrhage after embolization were analyzed so as to make sure of the postoperative survival time.

Statistical analysis

All the statistical analyses were performed using SPSS version 18.0 (SPSS Inc, Chicago, IL, USA) for Windows. Independent samples t test was used and the measurement data were expressed as mean standard deviation ($\overline{X} \pm S$). The chi-square test was used for categorical data and multivariate analysis was carried while there was statistical difference firstly analyzed with one-way ANOVA. Non conditional logistic regression analysis was performed to identify the effects of multi factors on prognosis. Receiver operating characteristic (ROC) curve was used to analyze the area under the curve so as to identify which factor had the greatest impact on intracranial hemorrhage.

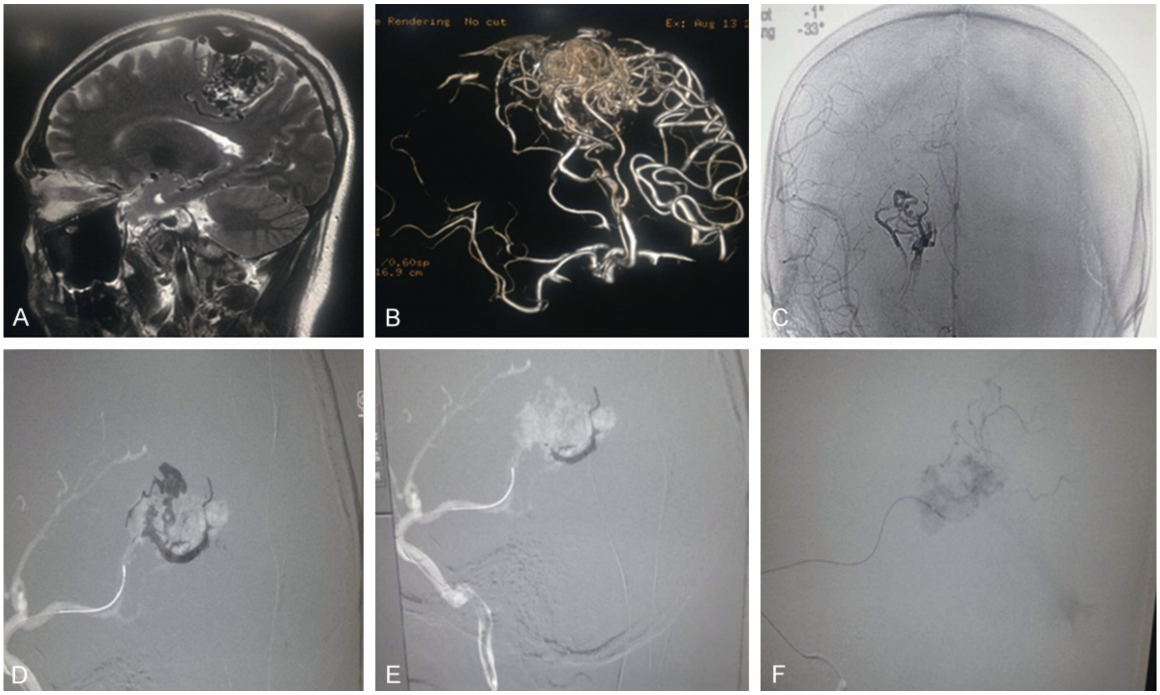

Figure 1. MRI and DSA images of brain AVM patients before and after AVM embolization. A. Brain AVM lesion showed by MRI. B. AVM malformation in MRI image. C. Performance of AVM in DSA image preoperative. D. Intraoperative performance of brain AVM in DSA image in patient termed case 1. E. Intraoperative performance of brain AVM in DSA image in patient termed case 2. F. AVM malformation could not be found in DSA image after AVM embolization.

Table 2. Multivariate logistic regression analysis of brain AVM hemorrhage risk factors

Variables	Exp (B)	95% Exp (B)		*P* value
		Lower limit	Upper limit	
Age	0.91	0.75	0.98	0.08
Sex	0.97	0.92	0.98	0.97
AVM diameter	0.09	0.07	1.25	0.05
AVM combined with aneurysm	12.7	8.4	21.9	0.01
Embolism area (≥ 26.4%)	0.26	0.07	6.98	0.04
Venous drainage types	1.36	3.65	32.5	0.26
S-M grading	6.34	3.65	34.8	0.63

Then Kaplan-Meier analysis was performed to analyze the effect of risk factors on survival curve after embolization. A *P* value less than 0.05 was considered as statistically significant.

Results

Clinical characteristics of the patients

To carry symptomatic treatment, the general clinical characteristics of the patients were analyzed. The detailed information was shown in **Table 1**. Among the patients, 47 cases were male and 33 cases were female. The clinical manifestations were sudden intracranial hemorrhage, epilepsy, headache and so on. According to the S-M classification [6], 11 cases were I grade, 39 cases were II grade, 19 cases were III grade, 9 cases were IV grade and 2 cases were V grade. These results indicated that embolization therapy was suitable to the patients enrolled here.

Evaluation of curative effect

In order to evaluate the efficacy of surgery, preoperative, intra-operative and postoperative imaging examination results were analyzed. As shown in **Figure 1**, changes in brain AVM of preoperative, intraoperative and postoperative were obvious. After interventional embolization, the malformation disappeared and there was no obvious drainage vein around. The result showed that curative effect of interventional embolization was very good.

Influence of related risk factors on hemorrhage after AVM embolization

In order to identify the influence of related risk factors on bleeding after AVM embolization, logistic regression analysis was performed.

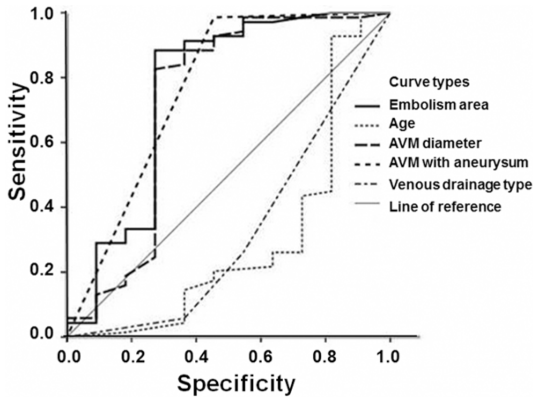

Figure 2. ROC curve of related risk factors of hemorrhage after AVM embolization. The AUCs of embolism area, age, AVM diameter, AVM associated with aneurysms and draining vein types were 75.8%, 29.8%, 72.8%, 76.5% and 32.6%. Embolism area, AVM diameter and AVM associated with aneurysms had better diagnostic value for intracranial hemorrhage after embolization, while age and venous drainage type had no diagnostic significance (P > 0.05).

Detailed information of the analyzing results was shown in **Table 2**. It was found that age, AVM diameter size, AVM combined with aneurysm, embolism area and venous drainage types all had striking effect on intracranial hemorrhage after operation with statistical significant difference (P < 0.05). However, sex and S-M classification had no explicit effect on intracranial hemorrhage (P > 0.05). We could argue that age, AVM diameter size, AVM with aneurysm, embolism area and venous drainage types were risk factors on bleeding after AVM embolization while sex and S-M classification were not.

ROC curve of related risk factors of hemorrhage after AVM embolization

To analyze risk factors of intracranial hemorrhage caused by embolization, ROC curve was drawn using SPSS18.0 software and area under ROC curve (AUC) of related factors were calculated. The AUCs of embolism area, age, AVM diameter, AVM associated with aneurysms and draining vein types were 75.8%, 29.8%, 72.8%, 76.5% and 32.6%. As shown in **Figure 2**, according to the ratio of the measured area under the curve to AUC was 0.5. In conclusion, the result indicated the related risk factors of embolism area, AVM diameter and AVM associated with aneurysms had better diagnostic value for intracranial hemorrhage after embolization (P < 0.05), while age and venous drainage types had no diagnostic significance (P > 0.05).

Effects of the risk factors of embolism area and AVM diameter on the prognosis

To identify which risk factor could affect prognosis, the patients were followed up for a total time of 60 months. It showed that, among the intracranial hemorrhage related risk factors, embolism area and AVM diameter had considerable influence. Related data was analyzed by Kaplan-Meier grade and survival curves of embolism area coupled with AVM diameter on prognosis were tested. Based on the results, we argued that embolism area < 50% and AVM diameter ≥ 3 cm had a better prognosis (P < 0.05, **Figure 3**) than embolism area ≥ 50% and AVM diameter < 3 cm.

Discussion

It is reported that AVM classification and intracranial hemorrhage associated risk factors have no significant relationship with thromboembolic complications [7]. However, Debrun et al. [8] reported that the risk of post embolization increased with the increase of AVM level in AVM patients after treatment. It is also found by multivariate analysis that intracranial hemorrhage after embolization is related with lesion size, complicated aneurysms and combined venous drainage. In this study, in cerebral AVM patients those underwent embolization, we found that age, AVM diameter, AVM combined with aneurysm, embolism area and venous drainage types were related risk factors those could leading to intracranial hemorrhage while sex and S-M classification had no clear effect. We consider that the reasons for this result might be as follows. Intracranial hemorrhage is apt to occur in old patients after embolization because vascular sclerosis is more serious in them, which, often resulting in luminal stenosis and increased perfusion pressure. Brain AVM diameter usually is small and without much venous drainage, however, the relative perfusion pressure is rather high, which, is prone to induce haemorrhage. Different drainage location, pattern and amount have different drainage resistance and perfusion pressure, which, have different bleeding risk probability. AVM combined with aneurysm as one of the risk factors that leading to intracranial hemorrhage

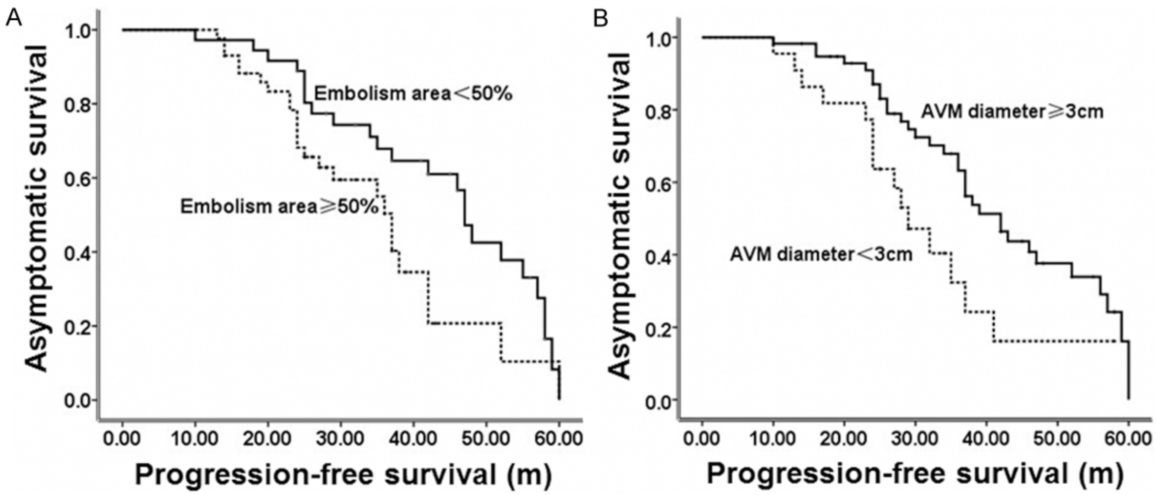

Figure 3. Effects of the risk factors of embolism area and AVM diameter on the prognosis. A. AVM patients with embolism area < 50% had better good prognosis than patients with embolism area ≥ 50%. B. AVM patients with AVM diameter ≥ 3 cm had better prognosis than patients with AVM diameter < 3 cm.

has already been reported [9]. Embolism area change can lead to blood flow redistribution, residual malformation and normal vessels around it would accept a large amount of blood filling, which, might lead to increased perfusion pressure after surgery [10].

It has been documented that AVM diameter, AVM combined with aneurysm and embolism area are not risk factors of intracranial hemorrhage after embolization [11-14]. However, in the present study, by drawing the ROC curves of age, AVM diameter, AVM combined with aneurysm, embolism area and venous drainage types and further detailed analysis, it was found that AVM diameter, AVM combined with aneurysm and embolism area had better diagnostic significance. Among the intracranial hemorrhage related risk factors, after a 60 months' follow-up, it was found that embolism area and AVM diameter had considerable influence. After analyzing related data by Kaplan-Meier and observing the survival curves of embolism area and AVM diameter on prognosis, it was shown that embolism area < 50% and AVM diameter ≥ 3 cm had a better prognosis than embolism area ≥ 50% and AVM diameter < 3 cm. This indicated that an explicit understanding of the lesion size preoperative and accurate intraoperative embolization could effectively reduce operation complications and improve long-term survival rate.

To sum up, in this study, we found that age, AVM diameter, AVM combined with aneurysm, embolism area and venous drainage types were related risk factors those could lead to intracranial hemorrhage. Meanwhile, we found that AVM diameter and embolism area were risk factors those had considerable influence on prognosis. Therefore, an explicit understanding of the high risk group who are easy to occur intracranial hemorrhage after embolization, and timely treatment to patients those with the aforementioned risk factors could greatly reduce morbidity and mortality rate. There were some shortcomings in this study. Firstly, the sample size was not big enough. Secondly, the reasons those could induce bleeding were too much and the relationships among them were too complicated, as a result, we did not analyze whether there was mutual correlation.

Acknowledgements

We greatly appreciate Professor Feng Ling from Department of Neurosurgery, Xuanwu Hospital, Capital Medical University, for his helpful suggestions on experiment designing and detailed criticism of the manuscript.

Disclosure of conflict of interest

None.

Address correspondence to: Guobin Li, Department of Neurosurgery, The Affiliated Hospital of Qingdao University, No.16 Jiangsu Road, Qingdao 266003, Shandong Province, P.R. China. Tel: +86-532-829-

12324; Fax: +86-532-82912324; E-mail: Lgb333@126.com

References

[1] Lawton MT and Du R. Effect of the neurosurgeon's surgical experience on outcomes from intraoperative aneurysmal rupture. Neurosurgery 2005; 57: 9-15; discussion 19-15.

[2] Choi JH, Mast H, Hartmann A, Marshall RS, Pile-Spellman J, Mohr JP and Stapf C. Clinical and morphological determinants of focal neurological deficits in patients with unruptured brain arteriovenous malformation. J Neurol Sci 2009; 287: 126-130.

[3] Zhang L. Analysis of brain AVM baseline and risk factors of hemorrhage. Hangzhou: Zhejiang University; 2013.

[4] Hartmann A, Pile-Spellman J, Stapf C, Sciacca RR, Faulstich A, Mohr JP, Schumacher HC and Mast H. Risk of endovascular treatment of brain arteriovenous malformations. Stroke 2002; 33: 1816-1820.

[5] Stapf C, Mast H, Sciacca RR, Choi JH, Khaw AV, Connolly ES, Pile-Spellman J and Mohr JP. Predictors of hemorrhage in patients with untreated brain arteriovenous malformation. Neurology 2006; 66: 1350-1355.

[6] Spetzler RF and Martin NA. A proposed grading system for arteriovenous malformations. J Neurosurg 1986; 65: 476-483.

[7] Gobin YP, Laurent A, Merienne L, Schlienger M, Aymard A, Houdart E, Casasco A, Lefkopoulos D, George B and Merland JJ. Treatment of brain arteriovenous malformations by embolization and radiosurgery. J Neurosurg 1996; 85: 19-28.

[8] Debrun GM, Aletich VA, Shownkeen H and Ausman J. Glued Catheters during Embolisation of Brain AVMs with Acrylic Glue. Interv Neuroradiol 1997; 3: 13-19.

[9] Liu L. Endovascular embolization treatment in patients with cerebral AVM characterized by primary intraventricular hemorrhage. Changchun: Jilin University; 2013.

[10] Weber W, Kis B, Siekmann R and Kuehne D. Endovascular treatment of intracranial arteriovenous malformations with onyx: technical aspects. AJNR Am J Neuroradiol 2007; 28: 371-377.

[11] Ovalle F, Shay SD and Mericle RA. Delayed intracerebral hemorrhage after uneventful embolization of brain arteriovenous malformations is related to volume of embolic agent administered: multivariate analysis of 13 predictive factors. Neurosurgery 2012; 70: 313-320.

[12] Sun Y, Li A, Li Y, Chen J, Shi H, Liu L, Jiang Y, Jiang P and Lv X. Diagnosis and treatment of onyx cerebral AVM embolization combined with hemorrhage. Chinese Journal of Neurosurgery 2011; 27: 619-621.

[13] Purdy PD, Batjer HH and Samson D. Management of hemorrhagic complications from preoperative embolization of arteriovenous malformations. J Neurosurg 1991; 74: 205-211.

[14] Stefani MA, Porter PJ, terBrugge KG, Montanera W, Willinsky RA and Wallace MC. Angioarchitectural factors present in brain arteriovenous malformations associated with hemorrhagic presentation. Stroke 2002; 33: 920-924.