



# Multimodal treatments of brain arteriovenous malformations: a comparison of microsurgical timings after endovascular embolization

Chaofan Zeng<sup>1#</sup>, Mingze Wang<sup>1#</sup>, Xiaowen Song<sup>1</sup>, Chaoqi Zhang<sup>1</sup>, Fa Lin<sup>1</sup>, Qiheng He<sup>1</sup>, Wuyang Yang<sup>2</sup>, Yong Cao<sup>1,3,4,5</sup>, Shuo Wang<sup>1,3,4,5</sup>, Wenjun Tu<sup>1</sup>, Jizong Zhao<sup>1,3,4,5,6</sup>

<sup>1</sup>Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing, China; <sup>2</sup>Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, MD, USA; <sup>3</sup>China National Clinical Research Center for Neurological Diseases, Beijing, China; <sup>4</sup>Center of Stroke, Beijing Institute for Brain Disorders, Beijing, China; <sup>5</sup>Beijing Key Laboratory of Translational Medicine for Cerebrovascular Disease, Beijing, China; <sup>6</sup>Savaid Medical School, University of the Chinese Academy of Sciences, Beijing, China

*Contributions:* (I) Conception and design: C Zeng, M Wang; (II) Administrative support: Y Cao, S Wang, W Tu, J Zhao; (III) Provision of study materials or patients: Y Cao, S Wang, W Tu, J Zhao; (IV) Collection and assembly of data: C Zeng, M Wang, X Song, C Zhang, F Lin, Q He; (V) Data analysis and interpretation: C Zeng, M Wang, W Yang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

<sup>#</sup>These authors contributed equally to this work.

*Correspondence to:* Jizong Zhao; Wenjun Tu. Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, No. 119 South 4th Ring West Road, Fengtai District, Beijing 100070, China. Email: zhaojizong@bjtth.org; tuwenjun@irm-cams.ac.cn.

**Background:** To compare the clinical outcomes of hybrid microsurgery and embolization with multi-staged procedure for patients harboring brain arteriovenous malformations (bAVMs).

**Methods:** We retrospectively reviewed bAVM patients from a multicenter, prospectively collected database (NCT03774017) between June 2016 and June 2020. Patients were divided into single-staged hybrid operation (HO) group and multi-staged operation (MO) group according to the received treatment, in which microsurgeries were performed with embolization in a single setting or with multi-stage procedure, respectively. Cases were 1:1 matched between the two groups. Outcomes were compared between groups, which included neurological deficits (NDs), perioperative rupture, and proportion of complete resection. Variables associated with NDs were analyzed.

**Results:** In total, 198 out of 544 cases were identified, including 120 in the HO group and 78 in the MO group. Sixty-six cases were matched in each group resulting in a total of 132 patients in this case-controlled study. Mean age was 29.2 years old, with 82 (62.1%) being male. No significant difference was observed in baseline demographics and clinical characteristics between the two groups. There were 7 ruptures occurred in the interval between embolization and microsurgery for MO group while none in the HO group ( $P=0.023$ ). This yielded a rupture risk of 4.1% per year for the MO group. Duration of surgical resection was significantly reduced in HO group ( $P=0.001$ ). Compared to MO, HO was more favorable to avoid short-term NDs (3.0% vs. 15.2%,  $P=0.021$ ), but long-term outcomes were similar. The HO modality (OR, 0.110; 95% CI: 0.017–0.737;  $P=0.023$ ) was confirmed as the protective factor for short-term NDs.

**Conclusions:** HO is an effective setup to treat complex bAVMs with avoiding interval hemorrhage risk and reducing surgical risk. We also observed overall similar obliteration rate and resulting clinical outcomes between HO and MO.

**Keywords:** Arteriovenous malformation (AVMs); multimodal treatment; endovascular embolization; single-staged hybrid operation (single-staged HO); outcome

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## Introduction

Brain arteriovenous malformations (bAVMs) are anomalies of dilated arteries and veins without capillary networks, allowing high-flow arterial blood to shunt directly into the venous system (1-3). The combination of endovascular embolization followed by microsurgical resection is commonly referred in the treatment of bAVMs as a traditional multi-modal approach, in which embolization is generally considered as an adjunct procedure to microsurgical resection. Appropriate embolization by taking out pedicle feeders in anticipation of a subsequent surgical resection would significantly reduce arterial inflow to the bAVMs to facilitate safer resection (4-6), creating distinct arachnoid planes for more effective nidus dissection and maximizing the protection of surrounding eloquent structures (7,8).

Despite the established concept of multi-modality approach, the timing of the subsequent microsurgery remains undefined. During a multi-staged operation (MO), preoperative embolization is presumed to gradually change the hemodynamics of high-flow lesions and minimize the risk of hemorrhage and parenchymal hyperemia (4,9). Nevertheless, potential risks exist during the interval between embolization and definitive resection, including hemorrhage and epilepsy (10-12). Single-staged hybrid operation (HO) is an emerging multimodal setup to enable performing embolization and microsurgical resection in one treatment session, which has been proven by many to be feasible in the definitive treatment of complex bAVMs (13-16). The timing of subsequent microsurgery is the essential difference between multi-stage and single-stage approaches. To our knowledge, no existing literature has compared the two approaches in a single study. In correspondence, this study was undertaken with the aim to compare the clinical outcomes between multi-staged and single-staged HOs in the treatment of bAVMs. We present the following article in accordance with the STROBE reporting checklist (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-811/rc>).

## Methods

### *Study design and population*

Patients with bAVMs were retrospectively retrieved and reviewed from the database of a multicenter prospective cohort study (NCT03774017) from June 2016 to June 2020. Those who received treatments of both embolization

and microsurgical resection were enrolled in this study. Patients with bAVMs of Spetzler-Martin Grade (SM) V or higher were excluded, as per our institution's treatment algorithm was a relative contraindication to undergo surgical resection.

A case-control study, with MO in one group and single-staged HO in another, was conducted with a 1:1 matching ratio and matched according to morphological characteristics of bAVMs. Microsurgery and embolization were performed by a multidisciplinary team comprised of both neurosurgeons and neuro-interventionists. In MO group, patients received elective microsurgery after single or multiple embolizations, with an interval duration ranging from days to months. In the HO group, patients underwent surgical resection immediately after embolization in a hybrid operating room in a single session.

The risks of HO and MO were explained in detail to patients and families. Preference from patient was taken account into our treatment algorithm. The management strategy was dependent on objective conditions and neurosurgeons in different medical centers. The HO followed a single study protocol across the multi-centers in the aforementioned prospective study (17). The paradigms of HO and MO were objectively recorded. This study was conducted following the Declaration of Helsinki (as revised in 2013) and was approved by the Institutional Review Board of Beijing Tiantan Hospital (No. KY2016-034-02). Written consent was provided by all participants or their legal representatives.

### *Outcome evaluation*

Clinical outcomes were compared between MO and HO group. Primary outcomes included neurological deficits (NDs), defined as a score of the modified Rankin Scale (mRS) >2. NDs presented at three months after microsurgery was regarded as the short-term, and those that lasted for  $\geq 6$  months were regarded as long-termed. Our secondary outcomes included residual bAVM, post-embolization hemorrhage, immediate post-operative complications, and mortality. Residual bAVM was defined as persistent nidus in post-operative angiograms. Post-embolization hemorrhage was defined as the diagnosed intracranial hemorrhage (high-density volume >5 mL on CT scan) due to bAVMs occurring during the interval between embolization and microsurgery. Immediate post-operative complications were defined as infarction, seizure, and intracranial or pulmonary infection within seven days

after surgery, and surgery-related mortality was defined as a result of microsurgery or operation-related complications within 30 days after resection. Two experienced neurosurgeons (C Zeng, M Wang) independently evaluated the clinical outcomes.

### Data collection and follow-up

Data were extracted from the database of the cohort. General information, such as demographics, personal and treatment history, and comorbidity history were included. bAVM-specific data included presenting symptoms, past procedural history, angio-architectural, localization and morphological information of the bAVMs, and Spetzler-Martin grades. Presenting symptoms were summarized into four categories: hemorrhage, seizure, neurological dysfunction, and incidence (with headache included). Hemorrhagic events were carefully distinguished between the primary symptom and the complication of conducted endovascular embolization. Neuro-images provided information on morphology, spatial relation with eloquence, and angioarchitecture of lesions. According to the morphological data, the bAVM volume was calculated by  $(\text{width} \times \text{height} \times \text{length})/2$  (18). Operative duration and hematoma volume were used for evaluations of operative risk and difficulty. Clinical outcomes, such as postoperative complications, residual bAVMs, neurological outcomes, and procedure-specific mortality, were acquired from the evaluation of discharge and outpatient follow-ups in the 3rd, 6th, and 12th months after microsurgery.

### Statistical analyses

IBM® SPSS® Statistics (Version 26, IBM, NY, United States) was used for all statistical analyses of this study. Data were categorized into categorical and continuous variables. Descriptive analyses were reported, with categorical variables in proportion and continuous variables in mean  $\pm$  standard deviation (SD) and median  $\pm$  interquartile range (IQR). A 1:1 case-control matched analysis was adopted with regards to bAVM size, eloquent location, and deep venous drainage, to reduce the heterogeneity and bias in baseline characteristics between groups. The variables in two groups were assessed with the standardized mean difference, which was calculated as the difference in the means or proportions of a variable divided by the pooled estimate of the SD of the variable (19). A standardized mean difference  $<0.1$  indicates a negligible difference;  $0.1-0.3$

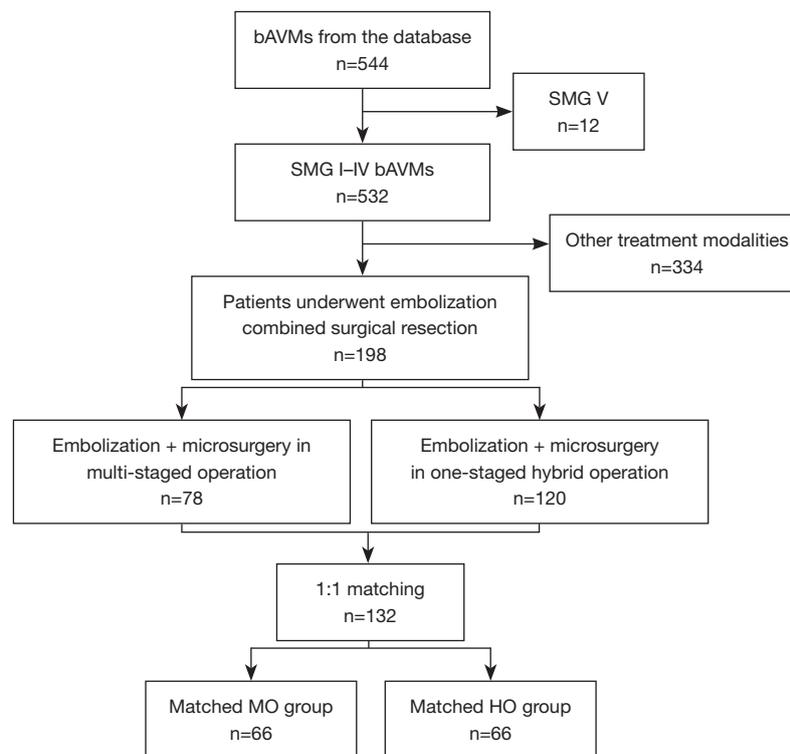
indicates a small difference;  $0.3-0.5$  indicates a moderate difference;  $>0.5$  indicates a considerable difference (19). McNemar tests were conducted to compare categorical variables between groups. Paired *t*-tests or Wilcoxon tests were used to compare continuous variables between groups. Univariate and multivariate logistic regression analyses were performed to obtain the independent predictors of NDs. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for each variable. Statistical significance was defined as  $P < 0.05$ .

### Results

Five hundred and forty-four patients were involved in the prospective multicentered registry. Twelve patients harboring bAVMs in SMG V and 334 patients being cured by a single modality with either endovascular or microsurgery were excluded from this study. A total of 198 patients met inclusion and exclusion criteria and were enrolled in the study, including 78 (39.4%) patients in MO group and 120 (60.6%) patients in HO group (*Figure 1*). Prior to 1:1 case-control matching, patients who underwent the HO were more likely to present with poor mRS (mRS  $>2$ ,  $P=0.014$ ) and larger bAVM volume ( $P=0.046$ ) as compared to the MO group. Sixty-six pairs of cases were matched in HO group (male to female is 44:22) and MO group (male to female is 38:28). The demographic and clinical characteristics of two groups were shown in *Table 1*. Intergroup comparisons of baseline were performed on demography, primary symptoms, neurological function on admission, and morphological and angio-architectural features of lesions. There was no significant difference observed in baselines between groups.

### Outcomes

Clinical outcomes were shown in detail in *Table 2*. For the MO paradigm, 23.9% of patients received  $\geq 2$  secessions of embolizations prior to microsurgery. The mean interval between different secessions of embolizations was  $11.2 \pm 5.1$  weeks. The average length between the last embolization and microsurgery was  $4.9 \pm 3.7$  weeks. A total of seven patients (10.6%) in MO group encountered post-embolization hemorrhage in a total interval of 170.7 patient years, correlating to an annual hemorrhagic risk of 4.1% per year. No hemorrhage occurred during the immediate interval between embolization and microsurgery in the HO group. During the microsurgical operation, HO group had



**Figure 1** Schematic illustration of the study protocol. bAVMs, brain arteriovenous malformations; SMG, Spetzler-Martin grade; MO, multi-staged operation; HO, single-staged hybrid operation.

less blood loss ( $734.1 \pm 620.7$  vs.  $915.9 \pm 1,049.3$  mL,  $P=0.267$ ) and significantly shorter duration of operation ( $5.5 \pm 2.5$  vs.  $7.5 \pm 4.1$  hours,  $P=0.001$ ) compared to MO group.

Postoperative complications were seen in 18 patients from the MO group and 12 patients from the HO group ( $27.3\%$  vs.  $18.2\%$ ,  $P=0.286$ , shown in *Table 2*). Postoperative infection was the most frequent complication with morbidity of  $12.9\%$  ( $n=17$ ), and there was no significant difference between the MO and HO groups ( $15.2\%$  vs.  $10.6\%$ ,  $P=0.549$ ). Intracranial hemorrhage was observed in 3 cases ( $4.6\%$ ) in the MO group and 1 case ( $1.5\%$ ) in the HO group ( $P=0.625$ ). The overall risk of postoperative complications was similar between the MO and HO groups. Length of stay inpatient was  $19.3 \pm 7.9$  days on average, including  $19.1 \pm 8.8$  days in the MO group and  $19.6 \pm 6.9$  days in the HO group ( $P=0.700$ ).

When comparing preoperative and postoperative mRS, neurological function improved or unchanged in  $75.8\%$  and  $80.3\%$  in the MO group and the HO group at discharge, respectively. During a mean follow-up of  $26.2 \pm 12.5$  months, the difference between pre- and post-operative neurological function was similar between the MO and HO groups at

3 months ( $81.8\%$  vs.  $90.9\%$  with improved or unchanged neurological function respectively,  $P=0.128$ ), and at 6 months ( $86.4\%$  vs.  $92.4\%$  with improved or unchanged neurological function respectively,  $P=0.258$ , *Figure 2*). NDs occurred in 24 patients ( $18.2\%$ ) at discharge, including 15 ( $22.7\%$ ) in the MO group and 9 ( $13.6\%$ ) in the HO group ( $P=0.176$ ). The risk of NDs was significantly higher in MO group than HO group at the 3-month follow-up ( $15.2\%$  vs.  $3.0\%$ ,  $P=0.015$ ). This difference was attenuated to non-significance at 6-months (MO vs. HO,  $7.6\%$  vs.  $3.0\%$ ,  $P=0.437$ ).

In angiographic follow-ups, complete oblations were achieved in  $95.5\%$  of cases ( $n=63$ ) in MO group and  $100\%$  of cases in HO groups at 3 months (Fisher exact test,  $P=0.243$ ). At 6 months, the incidence of residues was  $3.0\%$  ( $n=2$ ) and  $0\%$  ( $n=0$ ) in MO and HO group (Fisher exact test,  $P=0.240$ ), respectively. There was no operation-related death occurred in the groups.

### *Independent predictors of NDs*

Variables associated with short-term NDs were analyzed.

**Table 1** Baseline characteristics between groups after matching

Variables	After matching			
	MO (n=66)	HO (n=66)	P value	Standardized mean difference <sup>†</sup>
Age, mean ± SD [range], years	29.0±13.92 [7–58]	29.3±12.37 [3–66]	0.891	0.023
Sex (male), n (%)	44 (66.7)	38 (57.6)	0.345	0.189
Prior radiosurgery, n (%)	3 (4.5)	2 (3.0)	>0.999	0.079
Primary symptom, n (%)				
Hemorrhage	37 (56.1)	33 (50.0)	0.618	0.122
Seizure	18 (27.3)	22 (33.3)	0.585	0.131
Neurological dysfunction	6 (9.1)	5 (7.6)	>0.999	0.054
Incidence	8 (12.1)	9 (13.6)	>0.999	0.045
Headache	7 (10.6)	2 (3.0)	0.180	0.205
Admission mRS score				
Mean ± SD	1.2±1.29	1.2±1.02	0.833	0.000
Poor neurological status (mRS >2), n (%)	4 (6.1)	4 (6.1)	>0.999	0.000
Spetzler-Martin grade, n (%)				
I	6 (9.1)	6 (9.1)	>0.999	0.000
II	24 (36.4)	23 (34.9)	>0.999	0.033
III	26 (39.4)	26 (39.4)	>0.999	0.000
IV	10 (15.2)	11 (16.7)	>0.999	0.041
bAVM morphology and angioarchitecture				
Maximum diameter (median ± IQR), cm	3.7±1.83	3.7±1.43	0.878	0.027
Volume (median ± IQR), cm <sup>3</sup>	13.6±17.97	13.8±16.11	0.477	0.012
bAVM location, n (%)			>0.999	0.059
Supratentorial	62 (93.9)	61 (92.4)		
Infratentorial	4 (6.1)	5 (7.6)		
Eloquence, n (%)	34 (51.5)	34 (51.5)	>0.999	0.000
Deep perforator supply, n (%)	8 (12.1)	12 (18.2)	0.481	0.171
Deep venous drainage, n (%)	16 (24.2)	16 (24.2)	>0.999	0.000

<sup>†</sup>, standardized mean difference <0.1, negligible difference; 0.1–0.3, small difference; 0.3–0.5, moderate difference; >0.5, considerable difference. MO, multi-staged operation; HO, hybrid operation; SD, standard deviation; mRS, modified Rankin Scale; bAVM, brain arteriovenous malformation; IQR, interquartile range.

In the univariate analysis, poor neurological status, bAVM maximum diameter and HO modality were correlated with the occurrence of short-term NDs. After adjusting for age, sex, eloquence and deep venous drainage, poor neurological status (OR, 7.612; 95% CI: 1.633–35.486; P=0.010) and bAVM maximum diameter (OR, 2.010; 95% CI: 1.167–

3.461; P=0.012) were confirmed as risk factors for short-term NDs. HO modality (OR, 0.110; 95% CI: 0.017–0.737; P=0.023) was confirmed as the protective factor for short-term NDs (Table 3).

Analyzing variables related to long-term NDs, the univariate analysis demonstrated that poor neurological status

**Table 2** Intergroup comparison of outcomes

Variables	Total (n=132)	MO (n=66)	HO (n=66)	P value
Embolization degree <sup>†</sup> , n (%)				
<30%	55 (41.7)	27 (40.9)	28 (42.4)	>0.999
30–60%	38 (28.8)	22 (33.3)	16 (24.2)	0.417
>60%	39 (29.5)	17 (25.8)	22 (33.3)	0.522
Microsurgical characteristics				
Blood loss (mean ± SD), mL	825.0±863.61	915.9±1,049.29	734.1±620.74	0.267
Microsurgical duration (mean ± SD), h	6.5±3.53	7.5±4.09	5.5±2.53	0.001*
Post-embolization hemorrhage, n (%)	7 (5.3)	7 (10.6)	0 (0.0)	0.023*
Post-surgical complications, n (%)	30 (22.7)	18 (27.3)	12 (18.2)	0.286
Intracranial hemorrhage	4 (3.0)	3 (4.6)	1 (1.5)	0.625
Cerebral ischemia	1 (0.8)	1 (1.5)	0 (0.0)	>0.999
Seizure	5 (3.8)	3 (4.6)	2 (3.0)	>0.999
Intracranial infection	17 (12.9)	10 (15.2)	7 (10.6)	0.549
Pulmonary infection	6 (4.6)	3 (4.6)	3 (4.6)	>0.999
NDs, n (%)				
Discharge	24 (18.2)	15 (22.7)	9 (13.6)	0.263
3-month	12 (9.1)	10 (15.2)	2 (3.0)	0.021*
6-month	7 (5.3)	5 (7.6)	2 (3.0)	0.375
bAVMs residue, n (%)				
3-month	3 (2.3)	3 (4.6)	0 (0.0)	0.248
6-month	2 (1.5)	2 (3.0)	0 (0.0)	0.480

<sup>†</sup>, embolization degree was recorded according to the maximum degree among stages for MO group, and intraoperative embolization degree for HO group. \*, P<0.05, significant difference. MO, multi-staged operation; HO, hybrid operation; SD, standard deviation; NDs, neurological deficits; bAVMs, brain arteriovenous malformations.

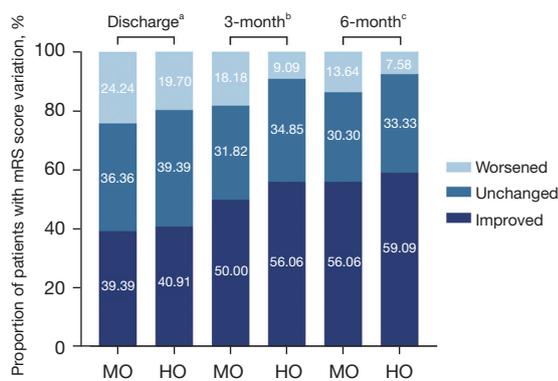
was associated with the occurrence of long-term NDs. After adjusting for age, sex, bAVM maximum diameter, eloquence and deep venous drainage, poor neurological status (OR, 28.138; 95% CI: 4.129–191.770; P=0.001) were shown as the significant predictor of long-term NDs (*Table 4*).

## Discussion

From our prospective multicenter registry, 198 out of 544 patients who have received microsurgical resection combined with pre-/intra-operative embolization were enrolled. Patients were divided into HO and MO groups according to the treatment received in one-stage or multi-stage. One-hundred and thirty-two of them were 1:1 case-

control matched into HO and MO group (n=66 cases for each group). Patients in HO group were obviously protected from the post-embolization hemorrhage due to the elimination of intervals between endovascular and microsurgical treatments. Significant advantages were achieved by HO group in microsurgical duration and neurological outcome at 3 months. Besides, single-staged HO showed its potential in decreasing the volume of intraoperative blood loss, incidences of postoperative complications and residue.

Multimodality treatment consisting of endovascular embolization and microsurgical resection has been routinely utilized in the treatment of bAVMs (20). Compared to the traditional multi-stage approach, HO with embolization



**Figure 2** Intergroup comparisons of neurological outcomes at different evaluating point-in-time. <sup>a</sup>, comparison of mRS score variation at discharge ( $P=0.815$ ), worsened status (24.24% vs. 19.70%,  $P=0.528$ ). <sup>b</sup>, comparison of mRS score variation in 3 months ( $P=0.314$ ), worsened status (18.18% vs. 9.09%,  $P=0.128$ ). <sup>c</sup>, comparison of mRS score variation in 6 months ( $P=0.524$ ), worsened status (13.64% vs. 7.58%,  $P=0.258$ ). mRS, modified Rankin Scale; MO, multi-staged operation; HO, single-staged hybrid operation.

and microsurgical resection in one single setting has unique advantages in regard to treatment workflow and patient convenience. However, quantification of this advantage has been lacking in current literature. It has been established that pre-surgical embolization may gradually reduce bAVM arterial supply and enable complete surgical resection while minimizing the risk of normal perfusion pressure breakthrough (NPPB), which was proposed as the leading cause of postoperative hemorrhage, especially in large bAVMs (5,21,22). Martin *et al.* and Young *et al.* proposed that stepwise occlusion of the arteriovenous shunting of large-size or high-flow bAVMs may also normalize cerebral hemodynamics and improve disturbed vascular reactivity (23,24).

Conversely, one might argue that committing patients to multi-stage embolization with repeated anesthesia is not without significant risk, and the prolonged interval before definitive resection of the bAVMs is also suboptimal, as hemorrhagic risk might be increased with embolization of bAVMs in short term (11,12). Corroborating the

**Table 3** Logistic regression analysis for short-term NDs

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Age	1.035	0.989–1.083	0.140	1.053	0.998–1.110	0.060
Male	1.243	0.354–4.363	0.734	1.193	0.253–5.636	0.824
Onset symptom						
Hemorrhage	1.267	0.381–4.215	0.700	–	–	–
Seizure	1.337	0.342–5.226	0.676	–	–	–
Neurological dysfunction	2.467	0.468–13.015	0.287	–	–	–
Poor neurological status	8.810	2.322–33.430	0.001	7.612	1.633–35.486	0.010*
bAVM location						
Supratentorial	Ref	Ref	Ref	–	–	–
Infratentorial	0.786	0.090–6.876	0.828	–	–	–
bAVM maximum diameter	1.773	1.128–2.788	0.013	2.010	1.167–3.461	0.012*
Eloquence	3.102	0.800–12.022	0.102	4.748	0.921–24.486	0.063
Deep venous drainage	0.600	0.124–2.894	0.525	0.525	0.081–3.394	0.499
Treatment modality						
MO	Ref	Ref	Ref	Ref	Ref	Ref
HO	0.175	0.037–0.833	0.029	0.110	0.017–0.737	0.023*

\*,  $P<0.05$ , significant difference. NDs, neurological deficits; OR, odds ratio; CI, confidence interval; bAVM, brain arteriovenous malformation; MO, multi-staged operation; HO, hybrid operation.

**Table 4** Logistic regression analysis for long-term NDs

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Age	1.051	0.991–1.115	0.098	1.061	0.986–1.143	0.114
Male	1.558	0.291–8.353	0.604	1.568	0.167–14.707	0.693
Onset symptom						
Hemorrhage	2.308	0.431–12.344	0.328	–	–	–
Seizure	2.721	0.317–23.372	0.362	–	–	–
Neurological dysfunction	2.810	0.296–16.659	0.368	–	–	–
Poor neurological status	32.222	5.464–190.031	<0.001	28.138	4.129–191.770	0.001*
bAVM location						
Supratentorial	Ref	Ref	Ref	–	–	–
Infratentorial	0.410	0.044–3.834	0.435	–	–	–
bAVM maximum diameter	1.105	0.996–1.034	0.119	1.618	0.750–3.488	0.220
Eloquence	1.271	0.273–5.913	0.760	1.141	0.163–8.009	0.894
Deep venous drainage	1.267	0.234–6.868	0.784	1.125	0.118–10.762	0.918
Treatment modality						
MO	Ref	Ref	Ref	Ref	Ref	Ref
HO	0.381	0.071–2.039	0.260	0.438	0.053–3.643	0.445

\*, P<0.05, significant difference. NDs, neurological deficits; OR, odds ratio; CI, confidence interval; bAVM, brain arteriovenous malformation; MO, multi-staged operation; HO, hybrid operation.

forementioned point, we have observed that 10.2% of all postembolization patients in MO group experienced a post-embolization hemorrhage in the interval. The morbidity of the hemorrhagic events was reported to be 5.9–20% (11,25,26), with accumulative risk following additional endovascular therapies (27,28). Several studies had proved hemorrhagic risk between the procedures of multi-staged treatments (29,30). Notably, the single-staged mode in HO eliminated this risk by minimizing of embolization-microsurgery interval. Additionally, likely attributed to the recanalization of the nidus and the recruitment of neo-collateral feeders from adjacent feeding arteries after embolization (31,32), we have observed a relatively higher volume of intraoperative blood loss in MO group as well as significantly longer microsurgery duration.

The benefit of improved neurological prognosis in multimodality treatment has been discussed in the existing literature. Kocer *et al.* reported morbidities of 6-month NDs to be 4.5% in bAVMs treated with multimodal treatments (33). In our study, NDs at 6 months occurred

in 5.3% of cases, conforming to the result of the previous study. The declining morbidity of NDs was suggested to be associated with the advantages in microsurgeries brought by the prior endovascular embolization on the following aspects: (I) decreasing the intraoperative blood loss and operating time by occluding the blood supply to the nidus, with lowering the SM grade of bAVMs, and thus reducing the risk of hemorrhage, particularly for large or high-flow bAVMs (28,34–36); (II) eliminating the bAVMs in difficult regions which gains more time for neurosurgeons to operate (34); (III) embolizing feeding arteries that are inaccessible in the subsequent resection (e.g., deep perforators) or flow-related aneurysms (6,27,37). The single-staged HO also resulted in better neurological outcomes than the multi-staged. It suggested that HO occupied more potential in the protection of neurological function.

Complete obliteration is the ultimate goal of bAVM treatments. As reported in our study, the obliteration rates were achieved in 96.7% in 3 months and 98.5% in 6 months in total, which were similar to the outcomes reported

in the literature of microsurgery without embolization (~96%) (28). There were differences in patient selection between multimodal treatments and microsurgery. The former approach provided the potential of total resection for complex bAVMs, while the microsurgical resection is appropriate for lesions with SM grade I–III (20). In this study, the average diameter of bAVMs treated with MO/HO is >3 cm. Therefore, the advantage of multimodal treatments is significant for medium-high grade bAVMs. However, the treatment planning is different between HO and MO. Although the embolization facilitates the subsequent resection in the HO modality, the outcomes before microsurgery commonly remain uncertain. Thus, the capacity requirements are increased for the operators. For MO modality, the process of embolization tends to be more aggressive, which may explain the higher rate of hemorrhage after embolization. The treatment strategy of bAVMs requires well-designed plans made by a multidisciplinary team.

There are limitations to our study. First, the sample size of our study was limited, which reduced the efficiency of case-control matching analysis. Second, variables (e.g., coexisting aneurysm or arteriovenous fistula, diffusiveness of bAVMs nidus) could not be entirely enrolled in the case-control matching, which might result in potential bias of baselines. Third, a propensity score matching (PSM) analysis would be a better solution to nonrandomized clinical trials. However, PSM had been attempted and made available cases much fewer. Fourth, patterns of minor and major hemorrhagic complications should be distinguished. Fifth, a longer-term angiographic follow-up was not available, and the recurrent and residual bAVMs could not be detected.

## Conclusions

HO for bAVMs resection utilizing pre-operative embolization and microsurgery in a single setting is an effective setup to treat complex bAVMs that need multimodal management. Compared to MO, the unique workflow advantages in HO reduced the perioperative risk by avoidance of repeat anesthesia, as well as obliteration of interval hemorrhagic risk by eliminating embolization-resection interval. With careful planning and selection of patients, HO may offer reduced surgical risk from less intraoperative blood loss and shorter operative duration compared to MO. The obliteration rate and resulting clinical outcomes are overall similar between patients

undergoing HO and MO.

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## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at <https://atm.amegroups.com/article/view/10.21037/atm-22-811/rc>

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted following the Declaration of Helsinki (as revised in 2013) and was approved by the Institutional Review

Board of Beijing Tiantan Hospital (No. KY2016-034-02). Written consent was provided by all participants or their legal representatives.

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