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# Combined Microsurgery and Endovascular Intervention in One-Stop for Treatment of Cerebral Arteriovenous Malformation: The Efficacy of a Hybrid Operation

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**Abstract**

To investigate the efficacy of a hybrid operation combining microsurgical resection and endovascular interventions in a one-stop treatment of cerebral arteriovenous malformation (AVM). Patients were divided into two groups: patients who received a hybrid operation, and patients receiving a non-hybrid operation. The hybrid operation group consisted of microsurgical resection with intraoperative angiography, or endovascular embolization. The non-hybrid operation group consisted of microsurgical resection or endovascular embolization, or microsurgery combined with embolization in multiple steps. Comprehensive clinical data was collected for all patients, including preoperative Glasgow Coma Scale score, Spetzler-Martin grade, rehemorrhagia, image follow-up, and 6-month outcomes of the modified Rankin Scale (mRS) score. This study included 22 cases in the hybrid operation group. The remnants were noted on intraoperative angiography in the four patients that were resected within the same session. The non-hybrid group consisted of 52 patients. There were no statistical differences between the two groups with GCS and Spetzler-Martin grade score. The mortality rate in the hybrid operation group was 4.5%, which was lower than the 7.6% obtained in the control group. No patients experienced post-operation rehemorrhagia in the hybrid operation group, but five cases occurred in the control group. The follow-up radiological cure rates were 100% in the hybrid group and 65.9% in the control group. The rate of good outcome was 81.8% in the hybrid operation group and 69.2% in the control group, although there was no significant difference. The hybrid operation is a safe and efficacious strategy for treating cerebral AVMs.

**Keywords**

cerebral arteriovenous malformation, hybrid operation, one-stop

## Introduction

Cerebral arteriovenous malformation (AVM) is a common cause of spontaneous cerebral hemorrhage. Treatment of AVMs is aimed at reducing hemorrhage risks and eliminating lesions. Current mainstream treatments include microsurgical resection, stereotactic radiosurgery, and endovascular embolization. A guideline proposed by the American Stroke Association recommends surgical resection as the first-line treatment for Spetzler-Martine AVM lesions, grades I and II. Surgical resection and preoperative endovascular embolization is recommended for grade III lesions. Stereotactic radiosurgery should be considered for AVMs involving the functional cortex. Expectant management may be most appropriate for grade IV and V lesions[1].

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Because a higher Spetzler-Martine grade (grade III–V) is associated with greater severity of treatment risks[1,2], developing an optimal treatment strategy for high-grade AVM is essential. In addition, although surgical resection is recommended as the first-line treatment for low-grade AVM (grade I–II), intraoperative residue remains a problem, because you cannot be sure that the nidus has been completely removed in the absence of intraoperative angiography. Although progress in endovascular intervention and stereotactic radiosurgery has been made, but the outcomes are still not ideal. Endovascular intervention is considered as a method for improving treatment efficacy, with a reported cure rate of 20%[3,4]. The hemodynamic changes resulting from the partial embolization of an AVM may increase the hemorrhagic risk. Stereotactic radiosurgery has poor efficacy in medium or large AVMs[5,6], with a low long-term AVM control rate and a risk of bleeding in the interim[7–10].

Previous studies have indicated that a combination of microsurgery, intraoperative angiography, and endovascular intervention in a hybrid operating room could be an advanced, safe, and effective approach for the treatment of AVMs, particularly for high grade AVMs[11–13]. As of yet, its definitive efficacy is not fully understood. Here, we present a series of cases of intracranial AVMs cases treated with a hybrid or non-hybrid operation. We compared the efficacy of a hybrid operation with a non-hybrid operation for the treatment of AVMs, and introduce the treatment concept of a hybrid operation for treating complex AVMs.

## Methods and Materials

### Patients

We reviewed the clinical profiles of 74 patients with AVM who were treated in our institution between October 2013 and March 2017. From October 2013 to June 2015, 52 AVM patients were treated with a non-hybrid operation. The non-hybrid operation consisted of microsurgical resection or endovascular embolization, or a combined treatment throughout different sessions. The hybrid operation was introduced to treat AVMs in our institution in July 2015, and 22 AVM patients were treated by March 2017. To reduce selection bias, we excluded patients who had not received the hybrid operation treatment during the same period. The hybrid operation consisted of microsurgical resection with intraoperative angiography or endovascular embolization performed at the same time. The AVM lesions were evaluated with the Spetzler-Martin grading system[2]. The clinical data collected from patients included their age and gender, preoperative Glasgow Coma Scale (GCS) score, postoperative neurological functions, AVM locations, and 6-month outcomes. The neurological functions were assessed in accordance with the modified Rankin Scale (mRS). A mRS score of $\leq 2$ was considered a good outcome. The experimental protocol was established in accordance with the ethical guidelines of the Helsinki Declaration, and was approved by the Human Ethics Committee of the First Affiliated Hospital of Jinan University. Written informed consent was obtained from each participant.

### Treatment

Both intraoperative angiography and endovascular embolization were performed with an X-ray angiography machine (Artiszeego, Siemens, Erlangen, Germany). Angiographies of the internal carotid, the external carotid, and the vertebral arteries were performed bilaterally, in order to identify the feeding artery and the draining vein, to guide the operative approach, and to evaluate the remnant of AVM lesions via 2-dimensional (2D), 3-dimensional (3D), and double-volume image reconstructions. The entire procedure was conducted in a sterile environment without adjusting the patient's position for the hybrid operation. The propofol injection test was performed on the feeding artery before the embolization was performed when the AVMs involved the brain functional area, which guaranteed the safety of the brain functional area. DynaCT was performed preoperatively, as a routine imaging procedure for outcome evaluation. Some patients in the non-hybrid operation group underwent gamma knife treatment when residual AVMs were found.

### Data Analysis

Statistical analysis was performed using SPSS. A $\chi^2$ test was used for the compare of rate. Rank sum test of ordered variables was used for the compare Spetzler–Martine grade among the two groups. Differences were considered as statistically significant when $p < 0.05$.

## Results

### Demographic Data and Clinico-Radiological Evaluation

In total, 22 patients (14 male, mean age 31.0 years) underwent the hybrid operation, and 52 patients (28 male, mean age 32.2 years) underwent the non-hybrid operation. The AVMs were of grades I ($n = 5$), II ($n = 7$), III ($n = 6$), IV ($n = 3$), and V ($n = 1$) in the hybrid operation group, and grades I ($n = 13$), II ($n = 17$), III ($n = 14$), IV ($n = 6$), and V ($n = 2$) in the non-hybrid operation group, as per the Spetzler-Martin grading system. There was no statistical difference between the two groups using rank sum test of ordered variables ($p = 0.7592$). Nineteen AVMs (86.3%) were located at supratentorial brain tissue in the hybrid operation group and 44 (84.6%) in the non-hybrid operation group, 6 AVMs (27.2%) were involved functional areas of the brain in the hybrid operation group, and 11 (21.1%) in the non-hybrid operation group, both with no significant difference between them. Eighteen AVMs (81.8%) were ruptured in the hybrid operation group and 41 (78.8%) in the non-hybrid operation group, with no statistical difference between them (Table 1).

**Table 1.** Characteristics of Patients Within the Two Groups with AVMs.

| Characteristics | Hybrid | Non-hybrid | *p* value |
|---|---|---|---|
| Number of patients | 22 | 52 | |
| Mean age | 31.0 | 32.3 | |
| Number of females | 8 | 16 | 0.417 |
| Number of supratentorial AVMs | 19 (86.3%) | 44 (84.6%) | 0.578 |
| Number of ruptured AVMs | 18 (81.8%) | 41 (78.8%) | 0.521 |
| Number of functional area AVMs | 6 (27.2%) | 11 (21.2%) | 0.787 |

### *Treatment*

In the hybrid operation group with intraoperative angiography, 10 patients (4 grade II, 3 grade III, 2 grade IV and 1 grade V) underwent endovascular embolization followed by microsurgical resection. Twelve patients (5 grade I, 3 grade II, 3 grade III, and 1 grade IV) underwent microsurgical resection, which included 1 patient (grade II) who underwent *in situ* occlusion to devascularize the feeding artery. Remnants of the AVM lesion were noted in the intraoperative angiography of four patients. The residual AVM lesion was resected during the same session. There were 22 procedures in total.

In the non-hybrid operation group, 26 patients underwent single microsurgical resection, 20 underwent single endovascular embolization, and the remaining 6 patients underwent combined treatment. There were 84 procedures in total, notably more than the hybrid operation group.

Fifteen patients from the non-hybrid operation group underwent gamma knife treatment.

### *Postoperative Course and Follow-up*

There were no occurrences of rehemorrhagia during follow up for the hybrid operation group. There were five occurrences of AVMs in the non-hybrid operation group. The mortality rate was 4.5% in the hybrid operation group and 7.6% in the non-hybrid operation group, with no statistical significance. The digital subtraction angiographic follow-up data was available for 17 patients in the hybrid operation group and 41 in the non-hybrid operation group (mean 13.5 months). The radiological cure rates were 100% and 65.9%. The rate of good outcome (mRS $\leq$ 2) was 81.8% in the hybrid operation group and 69.2% in the non-hybrid operation group, with no significant difference between them (Table 2).

### *Typical Cases Analysis*

*Case 1.* Male, 29 years old, sudden severe headache accompanied by vomiting. Diagnosed as a ruptured aneurysm of the posterior cerebral artery and AVM in the right temporooccipital lobe, Spetzler-Martine grade III. The aneurysm was coiled and we decided to embolize the large feeding arteries, as well as the deep feeding arteries originating from the posterior cerebral artery. The superficial feeding arteries from the middle cerebral artery were ligated during open microsurgery and the AVM nidus was excised. He scored 0 on the mRS at follow-up (Fig. 1).

*Case 2.* Male, 25 years old, repeated left occipital headache for half a year. Diagnosed as an AVM in the left parietooccipital lobe. Spetzler-Martine grade IV. We used endovascular intervention to embolize the nidus, which was adjacent to the visual cortex and the peripheral AVM nidus. This shrunk the AVM nidus and facilitated surgical resection. The postoperative visual field was not damaged. He scored 0 on the mRS at follow up (Fig. 2).

## Discussion

An optimal treatment strategy for treating AVM has not yet been established. Surgical resection is often a safe and effective therapy with very few complications for Spetzler-Martine grades I and II AVM lesions located in the non-functional cortex[1,14].The complete resection of AVM lesions is challenging, and it appears that intraoperative angiography would be beneficial. Chalouhi et al.[15] used intraoperative angiography to identify the AVM remnants in 9 of 101 patients who had undergone surgical resection. A further resection was performed to facilitate the complete removal. Intraoperative angiography in a hybrid operating room could provide 2D or 3D images that show the AVM lesion remnants and guide the surgical procedure, thereby guaranteeing the accuracy and the safety of the surgical resection[16]. The current case series found AVM remnants in four patients via intraoperative angiography, thus avoiding retreatment or the possibly of postoperative rehemorrhagia . Two of these

**Table 2.** Treatment and Outcomes of Patients Within the Two Groups with AVMs.

| Treatment and outcome | Hybrid | Non-hybrid | *p* value |
|---|---|---|---|
| Therapeutic method | Resection+embolization:10<br>Intraoperative angiograph+resection: 12 | Resection:26 Embolization:20<br>Resection+embolization: 6 | |
| Number of procedures | 22 | 84 | |
| Number of rehemorrhages | 0 | 5 | |
| Radiological cure rate | 100%(17/17) | 65.9% (27/41) | |
| mRS $\leq$ 2 | 81.8%(18) | 69.2% (36) | 0.206 |
| Mortality rate | 4.5% | 7.6% | 0.658 |

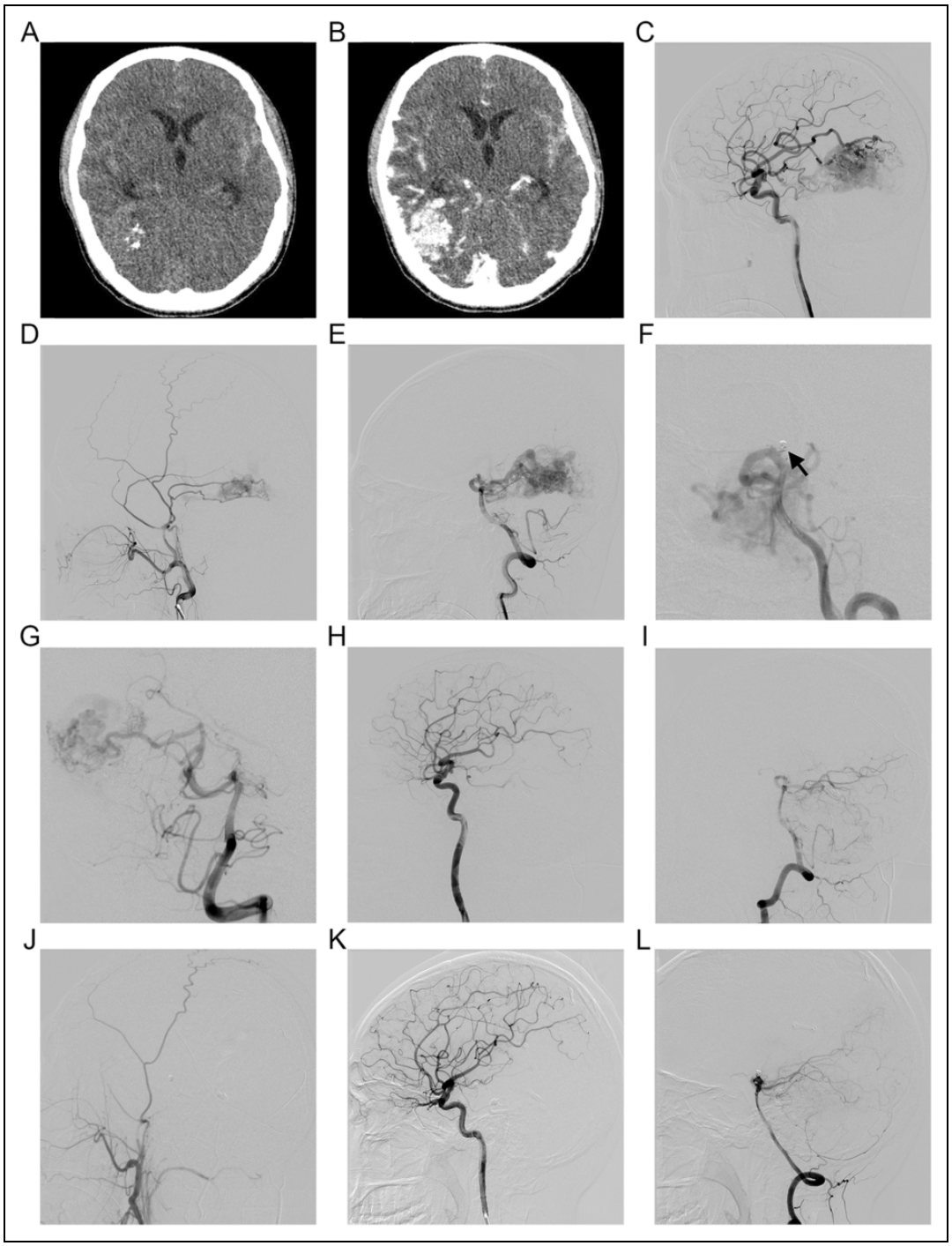


**Fig. 1.** Radiological profiles of a 29-year-old male diagnosed with a Spetzler-Martine grade III AVM in the right temporooccipital lobe. (A and B) Preoperative computed tomography illustrates the subarachnoid hemorrhage and an AVM lesion in the right temporooccipital lobe. (C–E) Preoperative angiography shows the AVM lesion. (F) Intraoperative angiography shows a ruptured aneurysm in the P2 segment that was embolized. (G) Intraoperative angiography shows a deep feeding artery from the right vertebral artery that was embolized. (H–J) Intraoperative angiography after resection demonstrated the obliteration of the AVM. (K and L) Angiography 15 months postoperatively shows there was no recurrence.

patients were Spetzler-Martine grade II lesions. This could be the main reason why there was no post-operation rehemorrhagia in the hybrid operation group, which was superior to the control group that had five rehemorrhagia patients. However, during the relatively short follow-up time, there were no significant differences between the two groups in terms of clinical good outcome rates and mortality rates. The digital subtraction angiographic follow-up found that the

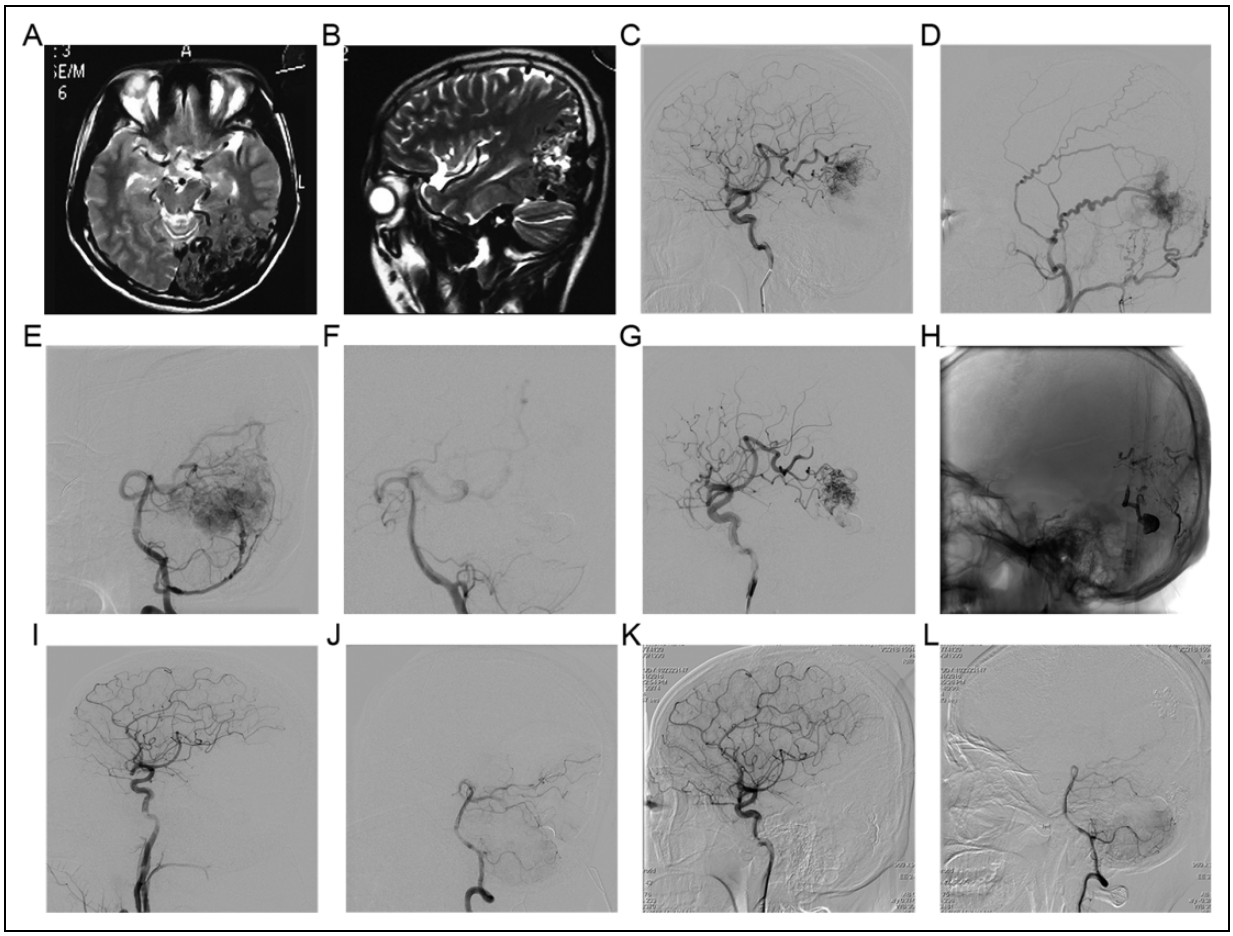


**Fig. 2.** Radiological profiles of a 25-year-old male diagnosed with a Spetzler-Martine grade IV AVM in the left parietooccipital lobe. (A and B) Preoperative magnetic resonance imaging depicts a large AVM lesion in the left parietooccipital lobe. (C–E) Preoperative angiography depicted the AVM lesion. (F–H) Intraoperative angiography shows the left internal carotid and the left vertebral arteries. (I and J) Intraoperative angiography following resection demonstrates the obliteration of the AVM. (K and L) Angiography 5 months following the operation shows there was no recurrence.

cure rate was 100%, which was significantly better than the non-hybrid operation group that had a cure rate of 65.9%. All patients in the hybrid operation group were treated with one procedure, which was less than the average 1.6 procedures in the non-hybrid operation group. Therefore the hybrid operation showed obvious advantages, particularly for complex AVMs.

Previous literature has reported treating AVMs with hybrid operation: Fandino et al reported five cases of ruptured AVMs, Murayama et al reported eight cases of AVMs, and Tian et al reported eight high-grade AVMs[11–13]. No previous report has provided guidance for managing AVMs with combined surgical and endovascular procedures during the same session. We believe that it is important to make a deliberate plan, particularly for complex AVMs.

When the AVMs are medium sized and deep, the feeding artery is typically deep and the lesion is usually adjacent to important brain tissue. If a single microsurgery or endovascular embolization is used, or a combination of these the two methods in multiple steps is used, it would have a considerable treatment risk of damaging important brain tissue, losing excessive blood, or rehemorrhagia occurrences due to residual AVMs. The one-stop hybrid operation could solve these problems. Endovascular intervention could be used to embolize the deep feeding artery and the ruptured perilesional aneurysms[17], but the preoperative endovascular intervention should target embolization of the feeding arteries rather than of the AVM nidus. Subsequent surgical resection could undertake ligation of the superficial feeding arteries and remove the entire AVM lesion. The risks of endovascular intervention and surgical resection are reduced in this way. Weber et al.[18] suggested that preoperative endovascular embolization of large feeding arteries could reduce the intranidal pressure, thereby lowering the risk of intraoperative bleeding. As a result, we followed this strategy in the treatment of a patient with temporooccipital Spetzler–Martine grade III AVM (Case 1). For Spetzler-Martine grade IV or V AVMs, previous studies have shown that surgical

resections are associated with high disability rates[1,8]. These AVMs are frequently monitored or treated conservatively via stereotactic radiosurgery. In our study, several patients with high-grade AVM lesions were treated successfully through the hybrid operation. One of these AVM lesions was large (>6 cm) and involved the visual cortex (Case 2). The goal of endovascular treatment for AVMs should be to shrink and degrade the AVM nidus, which could increase the safety of subsequent surgical resections. Furthermore, according to the normal perfusion pressure breakthrough (NPPB) theory[19], endovascular embolization could assist the hypoperfused brain tissue in adapting to hyperperfusion, thus reducing the occurrence of hemorrhage and edema. The recommended interval between embolization and surgical resection is 1–3 weeks. Our preliminary experience suggests that this is an unproven theory, and that the hybrid operation could cure large AVMs in a one-stop. This approach could also reduce the risk of hemorrhage from the residual AVM, which could also be the underlying reason for the NPPB. We recommend that the invasive arterial blood pressure should be monitored perioperatively.

However, our study has some limitations, This present study was retrospective and non-random, and the sample size relatively small. In addition, follow-up duration in the study was limited, with some cases, with gamma knife treatment especially, requiring a longer follow up. The rates of rehemorrhagia or mortality may have been higher in the nonhybrid operation group if the follow-up time had been extended.

## Conclusion

A one-stop hybrid operation combined with microsurgical resection and endovascular interventions is likely to be a safe and efficacious strategy for the treatment of AVMs. It could improve the radiological cure rate and reduce rehemorrhagia, especially in complex AVMs.

### Ethical approval

This study was approved by the Human Ethics Committee of the First Affiliated Hospital of Jinan University.

### Statement of Human and Animal Rights

The experimental protocol was conducted in accordance with the ethical guidelines of the Helsinki Declaration and was approved by the Human Ethics Committee of the First Affiliated Hospital of Jinan University.

### Statement of Informed Consent

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

### Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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