Long-term outcomes of Spetzler-Martin grade IV and V arteriovenous malformations: a single-center experience

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OBJECTIVE This study aimed to explore whether intervention can benefit Spetzler-Martin (SM) grade IV–V arteriovenous malformations (AVMs).

METHODS Eighty-two patients with SM grade IV–V AVMs were retrospectively reviewed from 2015 to 2018. Patients were divided into two groups: those who received conservative management (22 cases [26.8%]) and intervention (60 cases [73.2%], including 21 cases of microsurgery, 19 embolization, and 20 hybrid surgery). Neurofunctional outcomes were assessed with the modified Rankin Scale (mRS). The primary outcome was long-term neurofunctional status, and the secondary outcomes were short-term neurofunctional status, long-term obliteration rate, seizure control, and risk of subsequent hemorrhage.

RESULTS Regarding the primary outcome, after an average of 4.7 years of clinical follow-up, long-term neurofunctional outcomes were similar after conservative management or intervention (absolute difference −0.4 [95% CI −1.5 to 0.7], OR 0.709 [95% CI 0.461–1.090], p = 0.106), whereas intervention had an advantage over conservative management for avoidance of severe disability (defined as mRS score > 3) (1.7% vs 18.2%, absolute difference 16.5% [95% CI −23.6% to 56.6%], OR 0.076 [95% CI 0.008–0.727], p = 0.025). Regarding the secondary outcomes, intervention was conducive to better seizure control (Engel class I–II) (70.0% vs 0.0%, absolute difference 70.0% [95% CI 8.6%–131.4%], p = 0.010) and avoidance of subsequent hemorrhage (1.4% vs 6.0%, absolute difference 4.6% [95% CI −0.4% to 9.6%], p = 0.030). In the subgroup analysis based on different intervention modalities, microsurgery and hybrid surgery achieved higher complete obliteration rates than embolization (p < 0.001), and hybrid surgery resulted in significantly less intraoperative blood loss than microsurgery (p = 0.041).

CONCLUSIONS Intervention is reasonable for properly indicated SM grade IV–V AVMs because it provides satisfactory seizure control with decreased risks of severe disability and subsequent hemorrhage than conservative management.

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KEYWORDS arteriovenous malformation; conservative management; intervention; functional outcome; subsequent hemorrhage
servation is generally recommended for high-grade AVMs unless they rupture or lead to progressive neurological deficits.5

However, AVMs with an annual rupture risk of 1%–3% per year have been reported, and the lifetime cumulative rupture risk will reach an inevitable level if patients remain on conservative treatment.6 In addition, high-grade AVMs are more likely to incorporate high-flow and low-resistance hemodynamic features, and they are more likely to involve critical eloquent areas that may lead to severe and fatal neurological impairment if intracranial hemorrhage occurs.

Some studies proposed that the mortality rate after intervention for specified high-grade unruptured AVMs is acceptable.7,8 The purpose of our study was to clarify the long-term neurofunctional outcomes, obliteration rate, seizure control, and rupture risk of high-grade AVMs after different treatment modalities.

Methods
Study Design and Participants
The participants included in this study were prospectively registered in a multicenter research database of AVMs (MATCH study) from November 2015 to February 2018. This study was registered with the ClinicalTrials.gov database (http://clinicaltrials.gov), and its registration no. is NCT04572568. The study was carried out according to the guidelines of the Declaration of Helsinki and was approved by the institutional ethics committee. The inclusion criteria were as follows: 1) patients were diagnosed with AVM by digital subtraction angiography (DSA) or magnetic resonance imaging (MRI); 2) SM grade was IV or V; and 3) patients received follow-up for more than 3 years. The exclusion criteria were as follows: 1) concomitant diagnosis of hereditary hemorrhagic telangiectasia, arteriovenous fistula, and cavernous malformation; 2) emergency hospitalization (to exclude temporary neurological deterioration caused by acute hemorrhage); and 3) missing critical baseline information. After rigorous review, a total of 82 AVMs were included in the study cohort.

Data Collection and Definition
Demographic, clinical, and imaging data were recorded. Two distinct groups of management strategies were predefined: the conservative management group and the intervention group. Hemorrhagic presentation was attributed to AVM rupture. Morphological characteristics, including AVM size, eloquent area, deep venous drainage, flow-related aneurysm, and diffuse nidus, were based on the terminology for cerebral brain AVMs provided by a joint committee led by the American Society of Interventional and Therapeutic Neuroradiology.9–11

The primary outcome was long-term neurofunctional status, and the secondary outcomes were short-term neurofunctional status, long-term obliteration, long-term seizure control, and subsequent rupture risk. The long-term neurofunctional outcomes were evaluated at the last clinical follow-up, and the short-term neurofunctional outcomes were evaluated 1 week after the operation for the intervention group or 1 week after the treatment decision for the conservative management group. Confirmatory DSA was recommended to patients with complete obliteration on follow-up MRI. Complete obliteration was defined as a lack of abnormal flow voids on MRI or absence of anomalous arteriovenous shunting on DSA. The risk of subsequent hemorrhage was quantified on the basis of the annualized rupture rates. Neurofunctional status was assessed with the modified Rankin Scale (mRS) (favorable outcome defined as mRS score ≤ 2, neurofunctional disability mRS > 2, and severe disability mRS > 3). Seizure prognosis was evaluated with the Engel seizure outcome classification scale system (favorable control defined as Engel class I–II).

Follow-up with clinical visit and telephone interview was performed at the first 3–6 months and annually after discharge. Imaging follow-up consisted of MRI that was routinely performed semiannually for the first 2 years after discharge and annually thereafter. The researchers who assessed neurological status were blinded to the treatment strategies.

Selection of Treatment Strategies
The treatment strategy was developed on the basis of clinical symptoms, postoperative neurological dysfunc- tional risks, and patient requirements. Intervention was recommended for patients with moderate surgical risk (except those with involvement of an essential eloquent area, such as the brainstem and anterior/posterior central gyrus, or a hemispherically large diffuse nidus, etc.), intractable progressive seizure, previous rupture history, or combined rupture risk factors (aneurysm, arteriovenous fistula, etc.).

Neurosurgeons and interventional neuroradiologists prospectively planned the surgical procedure (microsurgery, embolization, and hybrid surgery) for each AVM at the multidisciplinary vascular conference held every weekday. Those patients with a large nidus (> 3 cm), deep location, multisource blood supply, and involvement of critical eloquent areas were considered to have complex AVMs. After comprehensive analysis of the angioarchitectural and hemodynamic characteristics, some complex cases were recommended for hybrid strategy. Hybrid surgery is a new interventional strategy defined as single-stage combined embolization and microsurgical resection, in which embolization is performed first on the deep feeding artery, aneurysm, arteriovenous fistula, and meningeal arteries feeding the nidus and then immediately followed by single-stage resection.12 All microsurgical procedures were performed with intraoperative neuronavigation, ultrasonography, indocyanine fluorescence angiography, and continuous monitoring of electroencephalography and somatosensory evoked potential. For patients with simple angioarchitecture and patients who received only palliative treatment, embolization was recommended as a priority.

Statistical Analysis
The mean (interquartile range) was reported for continuous data with normal and nonnormal distributions. The proportions of patients with each categorical variable were...
also recorded. The 2-tailed t-test was used to compare continuous variables with a normal distribution, whereas the Mann-Whitney U-test (Wilcoxon rank-sum test) was applied to compare nonnormally distributed continuous variables. The Pearson chi-square test and the Fisher exact test were utilized to compare categorical variables as appropriate. The Poisson rate test was employed to compare the annualized subsequent rupture rates between any two treatment strategies. The threshold for statistical significance was set at \( p < 0.05 \). Statistical analysis was performed using SPSS version 25.0 (IBM Corp.).

**Results**

**Baseline Characteristics**

We included a total of 82 patients with SM grade IV–V AVMs from our specific prospective AVM database who were treated from November 2015 to February 2018; of these, 60 (73.2%) underwent intervention (Table 1). Sixty-seven patients (81.7%) were classified with SM grade IV AVM. There were no significant differences in clinical manifestation and admission mRS score between the conservative management and intervention groups. Other angioarchitecture features were similar between these two groups, such as AVM size, eloquent area, flow-related aneurysm, deep venous drainage, and diffuse nidus. The mean ± SD duration of clinical follow-up was 4.7 ± 0.8 years.

| Characteristic                  | All Patients (n = 82) | Conservative Management (n = 22) | Intervention (n = 60) | p Value |
|--------------------------------|----------------------|---------------------------------|-----------------------|---------|
| Age, yrs                       | 30.1 ± 15.9          | 25.4 ± 17.8                     | 31.8 ± 15.0           | 0.104   |
| Male sex                       | 49 (59.8)            | 15 (68.2)                       | 34 (56.7)             | 0.262   |
| Clinical manifestation          |                      |                                 |                       |         |
| Hemorrhage                     | 54 (65.9)            | 13 (59.1)                       | 41 (68.3)             | 0.434   |
| Seizure                        | 14 (17.1)            | 4 (18.2)                        | 10 (16.7)             | >0.999  |
| Other                          | 14 (17.1)            | 5 (22.7)                        | 9 (15.0)              | 0.622   |
| Hypertension                   | 5 (6.1)              | 1 (4.5)                         | 4 (6.7)               | >0.999  |
| Admission mRS score            | 1.5 ± 0.8            | 1.6 ± 0.7                       | 1.5 ± 0.9             | 0.670   |
| Left-sided AVM                 | 45 (54.9)            | 10 (45.5)                       | 35 (58.3)             | 0.299   |
| AVM size, cm                   | 5.5 ± 1.6            | 5.9 ± 1.5                       | 5.4 ± 1.7             | 0.169   |
| Eloquent                       | 77 (93.9)            | 22 (100)                        | 55 (91.7)             | 0.381   |
| Deep venous drainage           | 57 (69.5)            | 15 (68.2)                       | 42 (70.0)             | 0.874   |
| SM grade IV                    | 67 (81.7)            | 15 (68.2)                       | 52 (86.7)             | 0.110   |
| V                              | 15 (18.3)            | 7 (31.8)                        | 8 (13.3)              |         |
| Flow-related aneurysm          | 26 (31.7)            | 7 (31.8)                        | 19 (31.7)             | 0.990   |
| Diffuse nidus                  | 18 (22.0)            | 5 (22.7)                        | 13 (21.7)             | >0.999  |
| Treatment modality             |                      |                                 |                       |         |
| Resection                      | 21 (25.6)            |                                 | 21 (35.0)             |         |
| Embolization only              | 19 (23.2)            |                                 | 19 (31.7)             |         |
| Hybrid surgery                 | 20 (24.4)            |                                 | 20 (33.3)             |         |
| Follow-up time, yrs            | 4.7 ± 0.8            | 4.6 ± 0.6                       | 4.7 ± 0.8             | 0.441   |

Values are shown as number (%) or mean ± SD unless otherwise indicated.

**Primary Outcomes**

There were no statistical differences between the conservative management and intervention groups in terms of follow-up mRS score (absolute difference -0.4 [95% CI -1.5 to 0.7], OR 0.709 [95% CI 0.461–1.090], \( p = 0.106 \)), favorable outcome (mRS score ≤ 2) (\( p = 0.730 \)), and neurofunctional disability (mRS > 2) (\( p = 0.730 \)) (Table 2). However, the intervention group had a lower incidence of long-term severe disability (mRS > 3) than the conservative management group (absolute difference 16.5% [95% CI -23.6% to 56.6%], OR 0.076 [95% CI 0.008–0.727], \( p = 0.025 \)). In patients with ruptured AVMs, intervention was associated with reduced incidence of long-term severe disability (mRS > 3) when compared with conservative management (absolute difference 20.7% [95% CI 4.4%–37.0%], OR 0.083 [95% CI 0.008–0.889], \( p = 0.040 \)). However, there were no significant differences in terms of the neurofunctional prognostic parameters among the patients with unruptured AVMs.

Long-term neurofunctional outcomes (mRS scores) between pretreatment and follow-up were similar among all patients with high-grade AVM (\( p = 0.112 \)), as well as among those with unruptured high-grade AVM (\( p = 0.156 \)) and those with ruptured high-grade AVMs (\( p = 0.303 \)) (Fig. 1). In addition, the proportions with worsened, unchanged, and improved mRS scores between pretreatment and follow-up were similar among all patients with high-grade AVMs (\( p = 0.095 \)), as well as among those
with unruptured high-grade AVMs (p > 0.999) and those with ruptured high-grade AVMs (p = 0.118) (Fig. 2).

**Secondary Outcomes**

Short-term neurofunctional outcomes (short-term mRS scores) were similar between the conservative management and intervention groups (absolute difference 0.5 [95% CI –0.6 to 1.5], OR 1.591 [95% CI 0.932–2.716], p = 0.208). However, the intervention group had decreased incidence of short-term favorable outcomes (mRS ≤2) (p = 0.042) and increased incidence of short-term disability (mRS >2) than the conservative management group (p = 0.042) (Table 3). In addition, intervention was associated with increased satisfactory obliteration rate (absolute difference 68.3%, 95% CI 43.9%–92.7%, p < 0.001) and seizure control rate (Engel class I–II) (absolute difference 70.0%, 95% CI 8.6%–131.4%, p = 0.010) in comparison with conservative management. In terms of subsequent rupture risk, the Poisson rate test suggested that the conservative group had a significant higher annualized rupture risk (6.0% vs 1.4%; absolute difference 4.6% [95% CI –0.4% to 9.6%], p = 0.030).

**Subgroup Analysis of the Intervention Group**

Of the 60 AVM patients who opted for intervention, 21 (35.0%) received microsurgical resection, 19 (31.7%) had embolization, and 20 (33.3%) had single-stage combined embolization and resection (Table 4). In the comparison of the primary and secondary outcomes, no significant differences were found between the types of interventions in terms of long-term neurofunctional outcome (p = 0.695), short-term neurofunctional outcome (p = 0.069), subsequent hemorrhage (p = 0.092), and long-term seizure control (p = 0.142). However, the long-term obliteration rate of the microsurgical resection group (95.2%) was significantly different (p < 0.001) from those of the embolization group (53.3%) and hybrid group (100%). Additionally, intraoperative blood loss of the hybrid group was lower than that of the microsurgery group (557.5 ± 313.4 ml vs 804.8 ± 414.8 ml, p = 0.041).

**Discussion**

In this study, long-term neurofunctional outcomes were similar after conservative management or intervention, whereas intervention had an advantage over conservative management for avoidance of severe disability. Additionally, intervention is conducive to better seizure control and avoidance of subsequent hemorrhage. In the subgroup analysis based on different intervention modalities, microsurgery and hybrid surgery achieved higher complete obliteration rates than embolization, and hybrid surgery had significantly reduced intraoperative blood loss than microsurgery.
FIG. 1. Comparison of mRS scores at pretreatment and follow-up.

FIG. 2. Proportions of patients with worsened, unchanged, and improved mRS scores.
Conservative Management Versus Intervention

At present, there is no unified consensus regarding the management of high-grade AVMs. Previous studies advocated conservative observation because their data showed that current intervention strategies offer a high probability of complications.\(^5\) The American Heart Association/American Stroke Association proposed a scientific statement that conservative management is the first-line therapeutic option for SM grade IV–V AVMs if the patient has no progressive neurological deficits or high risk of complications.\(^13\) The American Heart Association/American Stroke Association proposed a scientific statement that conservative management is the first-line therapeutic option for SM grade IV–V AVMs if the patient has no progressive neurological deficits or high risk of complications.\(^13\) In addition, two prospective studies—ARUBA (A Randomized Trial of Unruptured Brain AVMs) and SIVMS (the Scottish Audit of Intracranial Vascular Malformation Prospective AVM Cohort Study)—found that conservative management could achieve better clinical outcomes than intervention for patients with an unruptured AVM, regardless of SM grade.\(^14,15\)

However, intracranial hemorrhage due to AVM rupture can be catastrophic and fatal.\(^3\) Patients with AVMs reportedly have an average 15% rate of persistent disability and 15% risk of death after rupture.\(^6\) The annualized rupture risk was 6%–13.9% for ruptured SM grade IV–V AVMs, and the recurrent rupture rate varied from 6% to 16% at the 1st year after rupture.\(^7,19\) The result of hemorrhage was catastrophic and fatal.\(^5\) Patients with AVMs reportedly have an average 15% rate of persistent disability and 15% risk of death after rupture.\(^6\) The annualized rupture risk was 6%–13.9% for ruptured SM grade IV–V AVMs, and the recurrent rupture rate varied from 6% to 16% at the 1st year after rupture.\(^7,19\) The result of hemorrhage was

In this study, although short-term neurofunctional outcomes were worse after intervention than conservative management, the long-term neurofunctional outcomes were similar between these two groups. In addition, intervention was superior to conservative management in terms of better seizure control and avoidance of severe disability and subsequent hemorrhage, which means that intervention may have a better benefit-risk ratio than conservative management. However, we also found that the long-term mRS scores, proportions of patients with favorable outcomes and worsened mRS scores, and rates of death were similar between the conservative and intervention groups, which means that intervention was more likely to have had a marginal benefit than conservative management.

Different Intervention Strategies

Microsurgical resection may have the highest complete obliteration rate among embolization and stereotactic radiosurgery (SRS), especially for SM grade I–II AVMs.\(^19\) The risks of long-term disability for patients with SM grade I–II, III, and IV–V AVMs were < 5%, 17%, and 45%, respectively.\(^7,10\) In this study, 95.2% achieved complete obliteration and 28.6% experienced long-term disability after resection, and the prognosis for neurofunction was slightly better than reported in previous studies.

Embolization is commonly used as a palliative treatment strategy or as an adjunct therapy to reduce AVM volume and flow before resection or SRS for high-grade AVMs.\(^20\) However, it has been reported that > 25% volume embolization in a single session for high-grade AVMs may be associated with an increased risk of perioperative complications,\(^21,22\) and incomplete embolization may further

| TABLE 3. Secondary outcomes |
|-----------------------------|
| **Outcome** | **All Patients (n = 82)** | **Conservative Management (n = 22)** | **Intervention (n = 60)** | **Absolute Difference (95% CI)*** | **OR (95% CI)** | **p Value** |
| **Short-term neurofunctional outcome** | | | | | | |
| Short-term mRS score | 1 (1 to 3) | 1 (1 to 2) | 1.5 (1 to 3) | 0.5 (−0.6 to 1.5) | 1.591 (0.932 to 2.716) | 0.208 |
| Favorable outcomes (mRS ≤2) | 60 (73.2) | 20 (90.9) | 40 (66.7) | −24.2% (−45.8% to 2.6%) | 5.000 (1.062 to 23.545) | 0.042† |
| Neurofunctional disability (mRS >2) | 22 (26.8) | 2 (9.1) | 20 (33.3) | −24.2% (−45.8% to 2.6%) | 5.000 (1.062 to 23.545) | 0.042† |
| Death | 0 (0.0) | 0 (0.0) | 0 (0.0) | | >0.999 |
| Long-term complete obliteration | 41 (50.0) | 0 (0.0) | 41 (88.3) | 68.3% (43.9% to 92.7%) | <0.001† |
| **Long-term seizure control** | | | | | | |
| Favorable control (Engel class I–II) | 7 (50.0) (n = 14) | 0 (0.0) (n = 4) | 7 (70.0) (n = 10) | 70.0% (8.6% to 131.4%) | | 0.010† |
| De novo seizure | 3 (3.7) | 2 (9.1) | 1 (1.7) | 7.4% (−1.8% to 16.6%) | 0.169 (0.023 to 1.273) | 0.356 |
| Subsequent hemorrhage | 9 (11.0) | 5 (22.7) | 4 (6.7) | 16.0% (0.7% to 31.3%) | 0.243 (0.059 to 1.007) | 0.051 |
| Hemorrhage frequency | 10 | 6 | 4 | | | |
| Observational duration, patient-years | 383.1 | 100.4 | 282.7 | | | |
| Annualized rupture risk | 2.6 | 6.0 | 1.4 | 4.6% (−0.4% to 9.6%) | | 0.030†‡ |

* Values are shown as number, number (%), or mean (interquartile range) unless indicated otherwise.
† Positive differences indicate that the intervention group scored better than the conservative group.
‡ Statistically significant (p < 0.05).
§ The Poisson rate test was used to compare annual rupture rates between groups.
destabilize AVMs and increase intracranial hemorrhage risk by inducing HIF-1α, VEGF, and MMP-9 overexpression.\textsuperscript{23,24} In the present study, 5.3% of patients achieved complete embolization and 15.8% experienced subsequent hemorrhage after embolization. The high incidence of perioperative complication and low obliteration rate may indicate that palliative embolization cannot achieve satisfactory outcomes for high-grade AVMs.

Most previous studies suggested a multimodality strategy for high-grade AVMs.\textsuperscript{12,21,25} Hybrid surgery is a multimodality strategy that combines endovascular and microsurgical techniques in a single session. Reduction of nidus volume and flow, occlusion of deep perforating feeders, and detection of residual lesions in less time were considered unique advantages of hybrid surgery.\textsuperscript{26} Chen et al. indicated that the hybrid strategy is effective for the treatment of SM grade III/IV/V AVMs, and they recommended moderate embolization to facilitate subsequent microsurgical resection.\textsuperscript{12} Excessive embolization may harden the nidus and make the deep boundary of the nidus difficult to separate.\textsuperscript{12,27} In this study, hybrid surgery achieved the highest obliteration rate (100%) and lowest amount of intraoperative blood loss.

Single-session SRS appears to have limited efficacy for obliterating high-grade AVMs, and the outcomes of volume-stage and dose-staged SRS appear to be comparable to those of single-session SRS.\textsuperscript{28} Some studies suggested that pre-SRS embolization could effectively decrease AVM target volume, ultimately enhancing treatment efficacy.\textsuperscript{29,30} However, pre-SRS embolization may cause division of the nidus into distinct compartments, finally inducing a negative impact on obliteration.\textsuperscript{31}

### Limitations

Several potential limitations of this study should be noted. First, this was a single-center retrospective study,

### TABLE 4. Subgroup analysis of the intervention group

| Parameter                      | Microsurgery (n = 21) | Embolization (n = 19) | Hybrid Surgery (n = 20) | p Value |
|--------------------------------|-----------------------|-----------------------|-------------------------|---------|
| Age, yrs                       | 28.1 ± 17.8           | 34.0 ± 13.8           | 33.8 ± 12.6             | 0.269   |
| Male sex                       | 9 (42.9)              | 11 (57.9)             | 14 (70)                 | 0.213   |
| Hemorrhage                     | 14 (66.7)             | 14 (73.7)             | 13 (65)                 | 0.827   |
| Seizure                        | 4 (19)                | 3 (15.8)              | 3 (15)                  | 0.935   |
| Other                          | 3 (14.3)              | 2 (10.5)              | 4 (20)                  | 0.706   |
| Admission mRS score            | 1.7 ± 1.1             | 1.6 ± 1.0             | 1.2 ± 0.5               | 0.198   |
| AVM size, cm                   | 5.1 ± 2.0             | 5.4 ± 1.6             | 5.4 ± 1.4               | 0.416   |
| Eloquent                       | 19 (90.5)             | 19 (100)              | 17 (85)                 | 0.116   |
| Deep venous drainage           | 17 (81)               | 12 (63.2)             | 13 (65)                 | 0.394   |
| SM grade IV                    | 19 (90.5)             | 16 (84.2)             | 17 (85.0)               | 0.807   |
| Flow-related aneurysm          | 3 (14.3)              | 7 (36.8)              | 9 (45.0)                | 0.090   |
| Diffuse nidus                  | 6 (28.6)              | 4 (21.1)              | 3 (15.0)                | 0.569   |
| Deep perforating arteries      | 9 (42.9)              | 9 (47.4)              | 10 (50)                 | 0.898   |
| Intraoperative blood loss, ml  | 804.8 ± 424.8         | 557.5 ± 313.4         | 0.041*                  |
| Follow-up time, yrs            | 4.9 ± 1.0             | 4.6 ± 0.7             | 4.6 ± 0.7               | 0.448   |
| Follow-up mRS score            | 1.7 ± 0.9             | 1.7 ± 1.2             | 1.5 ± 0.8               | 0.695   |
| Favorable outcomes (mRS ≤2)    | 15 (71.4)             | 16 (84.2)             | 16 (80)                 | 0.606   |
| Long-term disability (mRS >2)  | 6 (28.6)              | 3 (15.8)              | 4 (20)                  | 0.606   |
| Severe disability (mRS >3)     | 0 (0.0)               | 1 (5.3)               | 0 (0.0)                 | 0.311   |
| Worsened mRS score             | 3 (14.3)              | 4 (21.1)              | 5 (25)                  | 0.679   |
| Death                          | 0 (0.0)               | 1 (5.3)               | 0 (0.0)                 | 0.311   |
| Short-term mRS score           | 2.4 ± 1.2             | 1.6 ± 1.0             | 2.0 ± 1.2               | 0.069   |
| Favorable outcomes (mRS ≤2)    | 11 (52.4)             | 15 (78.9)             | 14 (70.0)               | 0.190   |
| Disability (mRS >2)            | 10 (47.6)             | 4 (21.1)              | 6 (30.0)                | 0.190   |
| Long-term complete obliteration| 20 (95.2)             | 1 (5.3)               | 20 (100)                | <0.001* |
| Favorable seizure control (Engel class I–II) (n = 10) | 3 (75.0) (n = 4) | 1 (33.3) (n = 3) | 3 (100.0) (n = 3) | 0.142   |
| Subsequent hemorrhage          | 1 (4.8)               | 3 (15.8)              | 0 (0.0)                 | 0.092   |

Values are shown as number, number (%), or mean ± SD unless indicated otherwise.
* Statistically significant (p < 0.05).
and selection bias existed. The operative indications and treatment strategy selections may vary according to institutional philosophy and experience, which weakens the validity of this study’s conclusions. Second, many patients in this cohort presented with hemorrhage and hemorrhagic predictors, which caused a higher incidence of subsequent hemorrhage in the conservative management group than reported in the previous study. Additionally, due to the small sample size, we did not further analyze different types of the high-grade AVMs. Future studies with more cases are warranted to confirm our findings.

Conclusions

Long-term neurofunctional outcomes were similar after conservative management or intervention, whereas intervention was superior to conservative management in terms of achieving better seizure control and avoiding severe disability and subsequent hemorrhage in patients with properly indicated SM grade IV–V AVMs. When used as an intervention, hybrid surgery may be the most worthwhile strategy due to its high obliteration rate and low amount of intraoperative blood loss.

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Disclosures
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Conception and design: N Li, Yan, Z Li, R Li, Han, Meng, Jin, Yang Zhao. Acquisition of data: R Li, Han, Meng, Jin, Yang Zhao. Analysis and interpretation of data: N Li, Yan, Z Li, Y Chen, Ma. Drafting the article: N Li, Yan, Z Li. Critically revising the article: Yuanli Zhao, N Li, Yan, Z Li, X Chen, Wang. Reviewed submitted version of manuscript: Yuanli Zhao, N Li, Yan, Z Li, X Chen, Wang. Approved the final version of the manuscript on behalf of all authors: Yuanli Zhao. Statistical analysis: Y Chen, Ma. Administrative/technical/material support: Yuanli Zhao, X Chen, Wang. Study supervision: Yuanli Zhao, X Chen, Wang.

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