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RESEARCH

Comparison of Long-Term Outcomes in Ruptured Diffuse Brain Arteriovenous Malformations Between Interventional Therapy and Conservative Management

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Abstract

Brain arteriovenous malformations (AVMs) with a diffuse nidus structure present a therapeutic challenge due to their complexity and elevated risk of hemorrhagic events. This study examines the long-term effectiveness of interventional therapy versus conservative management in reducing hemorrhagic stroke or death in patients with ruptured diffuse AVMs. The analysis was conducted based on a multi-institutional database in China. Patients were divided into two groups: conservative management and interventional therapy. Using propensity score matching, patients were compared for the primary outcome of hemorrhagic stroke or death and the secondary outcomes of disability and neurofunctional decline. Out of 4286 consecutive AVMs in the registry, 901 patients were eligible. After matching, 70 pairs of patients remained with a median follow-up of 4.0 years. The conservative management group showed a trend toward higher rates of the primary outcome compared to the interventional group (4.15 vs. 1.87 per 100 patient-years, $P = 0.090$). While not statistically significant, intervention reduced the risk of hemorrhagic stroke or death by 55% (HR, 0.45 [95% CI 0.18–1.14], $P = 0.094$). No significant differences were observed in secondary outcomes of disability (OR, 0.89 [95% CI 0.35–2.26], $P = 0.813$) and neurofunctional decline (OR, 0.65 [95% CI 0.26 –1.63], $P = 0.355$). Subgroup analysis revealed particular benefits in interventional therapy for AVMs with a supplemented S-M grade of II-VI (HR, 0.10 [95% CI 0.01–0.79], $P = 0.029$). This study suggests a trend toward lower long-term hemorrhagic risks with intervention when compared to conservative management in ruptured diffuse AVMs, especially within supplemented S-M grade II–VI subgroups. No evidence indicated that interventional approaches worsen neurofunctional outcomes.

Keywords Arteriovenous malformations · Diffuseness · Conservative management · Interventional therapy · Hemorrhagic stroke

Introduction

Brain arteriovenous malformations (AVMs) are congenital vascular anomalies due to defective capillary network formation, with direct connections between arteries and veins [1]. Diffuse AVMs represent a notably challenging subclass, characterized by indistinct borders that pervasively intermingle with surrounding normal cerebral tissue [2]. Various scoring systems for assessing AVMs universally recognize diffuseness as a risk factor, indicating increased surgical complexity and poorer therapeutic prognosis [3–5]. As a result, conservative treatment is often the preferred approach for patients diagnosed with diffuse AVMs.

For those opting for conservative management, hemorrhage remains the most frequent and life-threatening complication [6]. AVMs with a prior incidence of hemorrhage are considerably more susceptible to future hemorrhagic episodes [7–10]. Typically, clinicians advocate for

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Extended author information available on the last page of the article interventional therapy in cases of ruptured AVMs to lessen the likelihood of future rupture. However, the intricate pathology of diffuse AVMs, marked by the mixture of normal brain tissue, complicates the development of effective treatment strategies. Additionally, the diffuse structure of the AVM itself poses an independent risk factor for rupture [11]. As a result, determining whether to initiate interventional therapy for ruptured diffuse AVMs and how to balance the risk of intervention-induced functional deficits against future hemorrhagic risks constitutes a considerable challenge for neurovascular specialists.

Despite the critical nature of the issue, there exists a notable scarcity of research addressing the complex decision-making process surrounding the treatment of patients with ruptured diffuse AVMs. Accordingly, the aim of this study is to evaluate the effectiveness of interventional therapy in reducing the long-term risk of hemorrhagic stroke or death and neurological deficits among patients with ruptured diffuse AVMs, as compared to conservative management.

Methods

Data Sources, Study Design, and Cohort Definition

We performed a retrospective analysis of data from the MATCH study (the registry of multimodality treatment for brain AVMs in mainland China, NCT 04572568), a prospectively sustained, nationwide, multi-institutional database from August 2011 to December 2021 [12]. The primary goal of the MATCH study was to explore the natural history of AVMs within an Asian population and to identify the most effective, personalized treatment strategies for AVM patients. The reliability of the MATCH registry has been validated through established protocols and peer-reviewed publications [13–15].

In this study, we focused on patients suffering from AVM rupture with a diffuse nidus structure. These individuals were eligible for inclusion. We excluded patients missing essential clinical baseline data, pre-treatment imaging, or post-treatment radiological and clinical outcomes. Diffuse AVMs were identified by the presence of lesions with irregular edges, poorly defined niduses, and intervening normal brain tissue between the abnormal vessels [2]. Data consistency among collectors was ensured during the data recording phase, following a specific protocol for quality assurance (Supplementary Method 1). Ethical approval for this study was granted by the institutional ethics committee (IRB approval number: KY 2020–003-01) in adherence to the 1964 Helsinki Declaration. Additionally, all patients in the MATCH study provided their written informed consent upon their admission. This study was conducted in accordance with the STROBE guideline observational cohort studies.

In this study, the cohort was divided into two groups to compare the treatment effect between conservative management and interventional therapy. Conservative management was described as receiving medical treatment alone, without direct intervention on the nidus structure. Those who underwent emergency procedures, like external ventricular drainage (EVD) or decompressive craniectomy, without addressing the AVMs, were also considered to be under conservative management. Interventional therapy included all treatments aiming to obliterate the nidus, such as microsurgery, stereotactic radiosurgery (SRS), endovascular embolization, and the combination of these strategies.

Baseline Characteristics

The study assessed baseline characteristics encompassing demographic variables (age at rupture, sex), clinical presentations (hemorrhage, seizure, neurological deficit, modified Rankin scale [mRS] at admission, Glasgow Coma Scale [GCS] at admission), and specific morphological and angioarchitectural features of AVMs. The morphological characteristics included nidus location, ventricular system involvement, size, eloquent region, and Spetzler-Martin (S-M) grade. Angioarchitectural parameters were aligned with the reporting terminology guidelines [16]. The angioarchitectural parameters were examined using digital subtraction angiography (DSA) and magnetic resonance imaging and were verified by neurosurgery residents who received training from qualified senior neuroradiologists using pre-interventional imaging.

Outcomes and Follow-up

The primary outcome consisted of the composite event of hemorrhagic stroke or death during the follow-up period. Hemorrhagic stroke was clinically characterized by any new focal neurological symptoms, seizures, or acute severe headaches, substantiated by imaging (e.g., intracranial hematoma or subarachnoid hemorrhage visualized through computed tomography or MRI, in association with AVM). We excluded hemorrhages that occurred within 2 weeks post-surgery from our primary outcome to emphasize long-term therapeutic results. The death outcome was limited to cases directly related to AVMs. Secondary outcomes involved evaluating neurofunctional outcomes at follow-up via the mRS system. Disabilities were defined as an mRS score above 2 at the final follow-up, and the neurofunctional decline indicated a deteriorating mRS at follow-up compared to admission.

Clinical outcomes were evaluated through phone interviews or record review, conducted by experienced clinical research coordinators at intervals of 3 months, annually (1, 2, and 3 years), and every 5 years subsequent to treatment. To mitigate follow-up bias, strategies were employed to ensure participant retention and optimize follow-up completion, encompassing flexible methods and statistical analyses for non-responders (as detailed in Supplementary Method 2). The inception point of follow-up was designated as the date of rupture for conservative management and the first treatment date for interventional therapy. The endpoint for the primary outcomes was determined as the date of hemorrhagic stroke or death, or the last follow-up date, whichever occurred first. For the secondary outcome, the endpoint was the final follow-up.

Controlling for Confounding

To address potential confounding bias, we employed propensity scores to balance pre-treatment differences in baseline characteristics—specifically targeting the issue known as "confounding by indication" [17]. Propensity score matching (PSM) methodologies were employed to counter this issue within the context of clinical research [18]. The matched factors included all available baseline attributes, such as demographic variables, clinical presentation at admission, morphological attributes, angioarchitectural parameters, and emergency treatment, between the conservative management and interventional therapy groups. Propensity scores were computed through logistic regression, followed by 1:1 patient matching with a caliper radius of 0.1 via the nearest-neighbor method without replacement. Covariate balance was subsequently assessed through standardized mean differences, with the values less than 0.1 indicating satisfactory matching.

Statistical Analyses

The data were analyzed using R software (version 4.2.2), with statistical significance established at a two-sided $P < 0.05$. Baseline characteristics were compared between the conservative management and interventional therapy groups before and after PSM. Continuous variables were expressed as mean ± standard deviation or median (interquartile ranges [IQR]) according to the distribution of data, and categorical variables were recorded as counts with percentages (n%). Statistical tests such as the student t-test or Mann–Whitney U-test for continuous data and Pearson's χ^2 test for categorical data were employed. To investigate the natural history of diffuse rupture AVMs, annual re-rupture rates were calculated using pre-PSM population. The rate was derived by dividing the total re-rupture events by the total person-years, represented as a rate per 100 person-years.

All subsequent analyses were conducted using post-PSM cohorts, except for the last sensitivity analysis with stabilized inverse probability of treatment weighting (sIPTW). Kaplan–Meier curves were used to visualize the cumulative incidence of hemorrhagic stroke or death between the two groups. Both the log-rank test and Breslow-Wilcoxon test were employed to distinguish differences between conservative management and interventional therapy. The Breslow-Wilcoxon test is particularly sensitive to early differences in survival curves, thereby allowing a more focused examination of outcomes in the early post-rupture or post-treatment period. We calculated the attributable risks (ARs) for all outcomes in the post-PSM cohort. For the primary outcomes, we tabulated the number of events, incidence rates, and ARs—expressed as rate differences per 100 person-years. Hazard ratios (HRs) with 95% confidence intervals (CIs) were estimated using Cox proportional hazard models for primary outcomes, with the proportional hazard assumption assessed through Schoenfeld's global test and visual inspection for potential biases. For secondary outcomes, ARs were interpreted as risk differences, and odds ratios (ORs) were computed via logistic regression analysis.

Prespecified Subgroup and Sensitivity Analyses

For the investigation of whether certain AVMs could benefit from conservative management or interventional therapy after accounting for the hemorrhage risk and neurofunctional outcomes, we performed prespecified subgroup analyses. The analyses were structured according to key factors including age at rupture (either < 18 years or ≥ 18 years), S-M grade (I–II, III, or IV–V), eloquent regions (yes or no), nidus size (< 3 cm, 3–6 cm, or > 6 cm), and supplemented S-M grade (II–VI or VII–X).

To investigate the stability of the main findings, we performed a series of sensitivity analyses on the primary outcomes. First, the interventional cohort was segregated into single modality (microsurgery, SRS, and embolization) and multimodality treatment groups. Patients within these intervention categories were individually matched with those in the conservative management group. Second, the effect of the intervening time from rupture to treatment (categorized as < 1 month, 1–3 months, and > 3 months) on primary outcomes was inspected independently. Third, in order to mitigate the bias introduced by procedures, patients who received life-saving care during emergency admission were excluded from this specific analysis. Fourth, to verify the robustness of the propensity score approaches, the sIPTW method, an alternative approach advised for confounder control, was applied in comparing the two groups. PSM methods were utilized in the initial three analyses. Post-match or post-weighted groups, along with their corresponding sample sizes, events, and incidence rates, were also tabulated.

Results

Study Population and Baseline Characteristics

A total of 4286 patients diagnosed with AVMs were registered in the MATCH database from August 2011 to December 2021. After careful screening, 1070 patients were identified as ruptured AVMs with a diffuse structure. Of these, 169 patients (15.8%) were lost to follow-up, leaving 901 patients for the final analysis (78 receiving conservative management and 823 undergoing interventional therapy). Detailed baseline comparisons between the analyzed cohort and those lost to follow-up showed no significant differences and are presented in Supplementary Table 1. Figure 1 provides an in-depth depiction of the patient selection process. The incidence rate of re-rupture for diffuse AVMs in this population was observed to be 9.30 per 100 patient-years during the observation period before intervention (patients underwent intervention) or at the last clinical follow-up (patients maintained conservation).

After PSM, 70 pairs of patients remained for further analysis. In the pre-PSM cohort, AVMs with higher S-M grade, deep-seated location, and perforating artery supply were more likely to opt for conservative management, while in the post-PSM cohort, all recorded baseline characteristics were statistically similar between conservative management and interventional therapy (Table 1). Supplementary Fig. 1 also plots the balance achieved between the two treatment options. The majority of the AVMs were of S-M grade I–II (47.1% in the conservative management group and 51.4% in the interventional therapy group) and mild GCS at rupture (70.0% in the conservative management group, and 68.6% in the interventional therapy group).

Outcome Assessment

After PSM, the median follow-up duration was 4.0 years (IQR, 2.0 to 7.0) for assessing the primary outcome (conservative management 3.4 years [IQR, 1.0 to 5.7]; interventional therapy 4.4 years [IQR, 2.9 to 7.5]). A total of 13 adverse events were recorded in the conservative

Fig. 1 Flowchart of patient selection. AVM, arteriovenous malformation; MATCH, registry of multimodality treatment for brain AVMs in mainland China

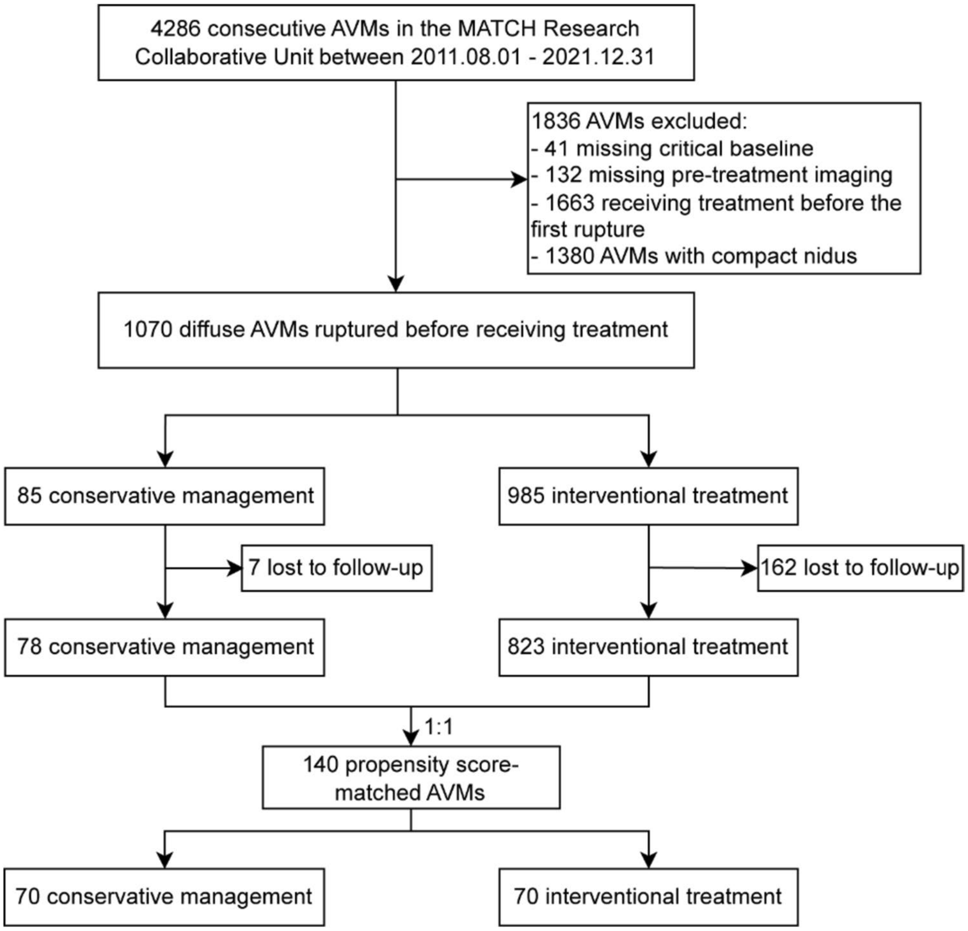


Table 1 Baseline characteristics before and after propensity score matching

Characteristics	Before PSM			After PSM		
	Conservative management	Interventional therapy	*P*	Conservative management	Interventional therapy	*P*
No. of patients	78	823		70	70	
Sex (female)	31 (39.7)	363 (44.1)	0.533	29 (41.4)	25 (35.7)	0.602
Age at rupture, mean (SD)	26.56 (16.91)	23.86 (14.96)	0.133	27.36 (17.18)	26.11 (15.75)	0.654
Admission mRS, median (IQR)	1.0 [1.0, 2.0]	1.0 [1.0, 2.0]	0.442	1.0 [1.0, 2.0]	1.0 [1.0, 2.0]	0.787
Seizure	11 (14.1)	88 (10.7)	0.465	10 (14.3)	13 (18.6)	0.648
Neurological deficiency	14 (17.9)	206 (25.0)	0.210	13 (18.6)	7 (10.0)	0.227
GCS at rupture			0.335			0.966
Mild (13–15)	54 (69.2)	556 (67.6)		49 (70.0)	48 (68.6)	
Moderate (9–12)	13 (16.7)	184 (22.4)		13 (18.6)	13 (18.6)	
Severe (3–8)	11 (14.1)	83 (10.1)		8 (11.4)	9 (12.9)	
S-M grade			0.001			0.595
I–II	33 (42.3)	447 (54.3)		33 (47.1)	36 (51.4)	
III	22 (28.2)	266 (32.3)		19 (27.1)	21 (30.0)	
IV–V	23 (29.5)	110 (13.4)		18 (25.7)	13 (18.6)	
Size, cm			< 0.001			0.775
< 3	45 (57.7)	546 (66.3)		43 (61.4)	47 (67.1)	
3–6	20 (25.6)	245 (29.8)		18 (25.7)	15 (21.4)	
> 6	13 (16.7)	32 (3.9)		9 (12.9)	8 (11.4)	
Location						
Frontal lobe	19 (24.4)	148 (18.0)	0.218	16 (22.9)	17 (24.3)	> 0.999
Temporal lobe	19 (24.4)	217 (26.4)	0.802	16 (22.9)	20 (28.6)	0.562
Parietal lobe	10 (12.8)	195 (23.7)	0.041	10 (14.3)	7 (10.0)	0.605
Occipital lobe	8 (10.3)	161 (19.6)	0.063	6 (8.6)	6 (8.6)	> 0.999
Basal ganglia	19 (24.4)	137 (16.6)	0.118	18 (25.7)	16 (22.9)	0.844
Cerebellum	14 (17.9)	119 (14.5)	0.507	13 (18.6)	12 (17.1)	> 0.999
Brain stem	8 (10.3)	21 (2.6)	0.001	5 (7.1)	5 (7.1)	> 0.999
Ventricular system involvement	58 (74.4)	570 (69.3)	0.419	51 (72.9)	54 (77.1)	0.696
Eloquent region	51 (65.4)	504 (61.2)	0.550	46 (65.7)	41 (58.6)	0.486
Feeding artery						
Single feeder	30 (38.5)	370 (45.0)	0.325	27 (38.6)	30 (42.9)	0.731
Multiple sources	22 (28.2)	134 (16.3)	0.012	17 (24.3)	9 (12.9)	0.128
Perforating artery	50 (64.1)	370 (45.0)	0.002	44 (62.9)	43 (61.4)	> 0.999
Flow-related aneurysm	14 (17.9)	129 (15.7)	0.716	14 (20.0)	11 (15.7)	0.659
Venous draining						
Stenosis	18 (23.1)	141 (17.1)	0.246	16 (22.9)	15 (21.4)	> 0.999
Any deep drainage	41 (52.6)	383 (46.5)	0.368	35 (50.0)	38 (54.3)	0.735
Exclusively deep drainage	29 (37.2)	296 (36.0)	0.928	26 (37.1)	29 (41.4)	0.729
Venous aneurysm	4 (5.1)	41 (5.0)	> 0.999	4 (5.7)	5 (7.1)	> 0.999
Emergency treatment						
External ventricular drain	6 (7.7)	82 (10.0)	0.655	5 (7.1)	12 (17.1)	0.121
Hematoma evacuation	11 (14.1)	106 (12.9)	0.896	9 (12.9)	8 (11.4)	> 0.999
Decompressive craniectomy	4 (5.1)	32 (3.9)	0.817	4 (5.7)	1 (1.4)	0.362
Others	0 (0.0)	11 (1.3)	0.626	0 (0.0)	0 (0.0)	–

GCS Glasgow Coma Scale, *IQR* interquartile range, *mRS* modified Rankin scale, *PSM* propensity score matching, *SD* standard deviation management group, compared to 7 in the interventional group. Among these, two events were classified as AVM-related deaths without accompanying hemorrhagic events (in the conservative management group, one patient died 51 days post-rupture due to complications; in the interventional group, one patient died from post-operative complications, occurring 43 days after surgical resection). A trend toward a higher incidence rate was noted in the conservative management group compared to the interventional group (4.15 vs. 1.87, AR, −2.29 [95% CI −4.93–0.36] per 100 patient-years, $P = 0.090$), with interventional therapy linked to a 55% reduced risk of hemorrhagic stroke or death (HR, 0.45 [95% CI 0.18–1.14], $P = 0.094$) (Table 2). The Kaplan–Meier curves further supported these findings, revealing a higher cumulative incidence of hemorrhagic stroke or death in the conservative management group (Fig. 2). However, the differences were not statistically significant as per both the log-rank ($P = 0.086$) and Breslow-Wilcoxon tests ($P = 0.064$).

Secondary outcomes including disability and neurofunctional decline were evaluated. Disability was observed in 11 patients (15.71%) in the conservative management group,

Table 2 Outcomes of conservative management and interventional therapy after propensity score matching

	Conservative management (%)	Interventional therapy (%)	Attributable risk* (95% CI)	*P*	HR (95% CI)/OR (95% CI)*	*P*
Primary outcomes						
Hemorrhage stroke or death	13 (4.15)	7 (1.87)	−2.29 (−4.93–0.36)	0.090	0.45 (0.18–1.14)	0.094
Symptomatic hemorrhagic stroke	12 (3.83)	6 (1.60)	−2.23 (−4.75–0.28)	0.082	0.42 (0.16–1.12)	0.084
AVM-related death	2 (0.64)	2 (0.53)	−0.11 (−1.26–1.05)	0.858	0.83 (0.12–5.93)	0.856
Secondary outcomes						
Disability	11 (15.71)	10 (14.29)	−1.43 (−13.26–10.40)	0.813	0.89 (0.35–2.26)	0.813
Neurofunctional decline	13 (18.57)	9 (12.86)	−5.71 (−17.73–6.31)	0.351	0.65 (0.26–1.63)	0.355

*The results were calculated with the conservative management group as the reference. The metrics of the primary outcomes were expressed as rate per 100 patient-years and hazard ratios, and the secondary outcomes were expressed as proportion and odds ratios

Abbreviation: *AVM* arteriovenous malformation, *CI* confidence interval, *HR* hazard ratio, *OR* odds ratios

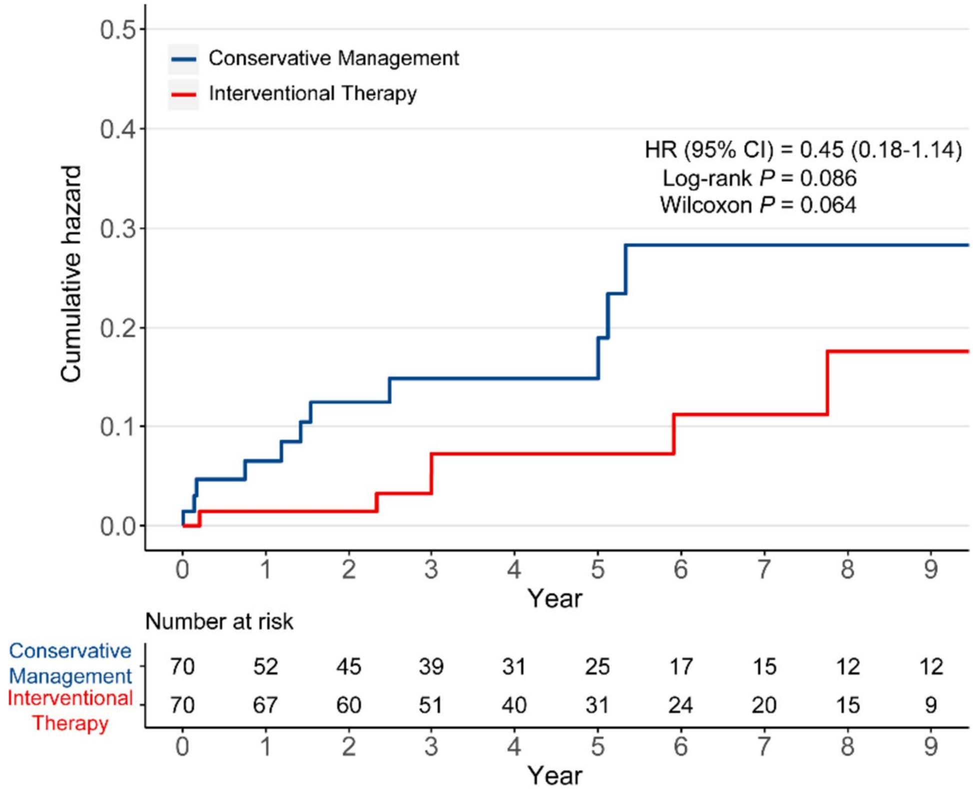


Fig. 2 Cumulative incidence for hemorrhagic stroke or death by therapeutic strategies

compared to 10 (14.29%) in the interventional therapy group, with an AR of − 1.43 (95% CI − 13.26–10.40, $P = 0.813$) and an OR of 0.89 (95% CI 0.35–2.26, $P = 0.813$). Neurofunctional decline was less frequent in the interventional group (AR, − 5.71 [95% CI − 17.73 to 6.31], $P = 0.351$; OR, 0.65 [95% CI 0.26 to 1.63], $P = 0.355$). No evidence was found to suggest that interventional therapy for ruptured diffuse AVMs were associated with a higher likelihood of severe neurofunctional deficits.

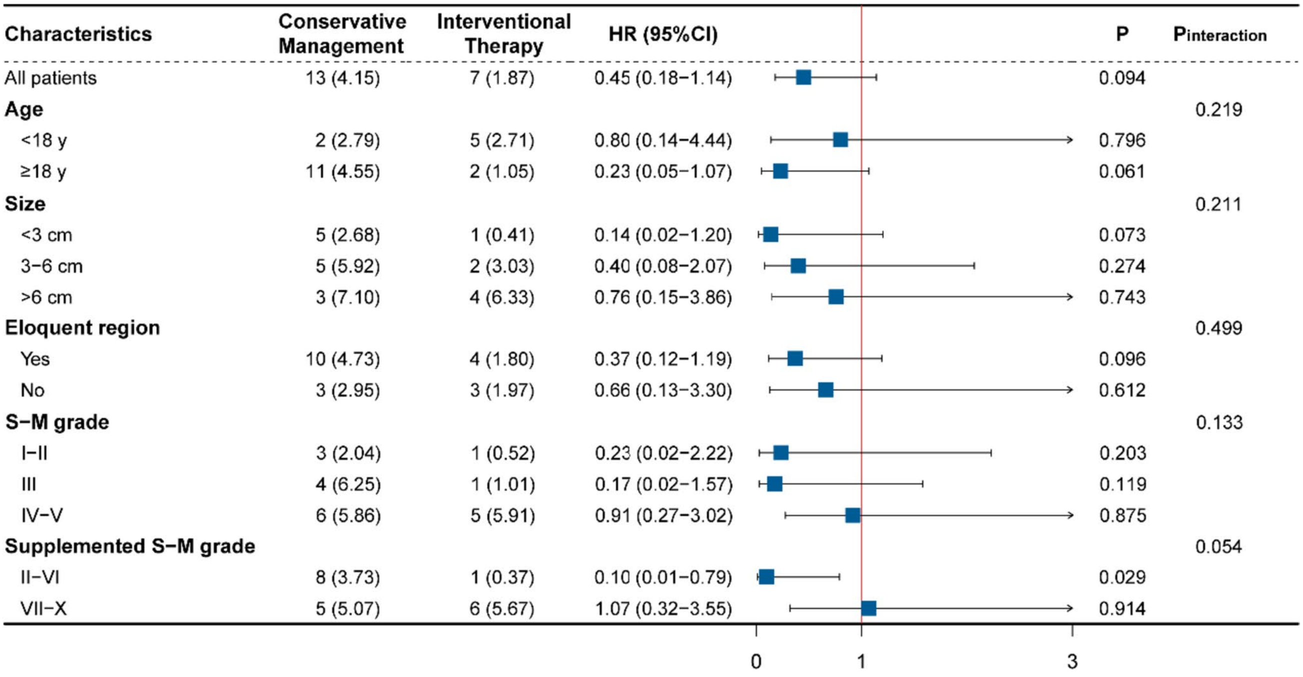
Subgroup Analyses

The subgroup analyses on the risk of the primary outcome revealed no significant interaction between treatment modalities and age, size, eloquent location, S-M grade, or supplemented S-M grade. Figure 3 illustrates a consistent but statistically non-significant decrease in the long-term risk of hemorrhagic stroke or death across all examined subgroups: age, lesion size, eloquent location, and S-M grade. Notably, in the supplemented S-M grade II-VI stratum, interventional therapy demonstrated a statistically significant protective effect against future hemorrhagic events or death when compared with conservative management (HR, 0.10 [95% CI 0.01–0.79], $P = 0.029$).

Subgroup analyses focusing on disability and neurofunctional decline did not show substantial differences across the age, lesion size, eloquent location, and S-M grade subgroups. Nonetheless, there was a tendency toward a higher proportion of adverse neurofunctional outcomes in cases with larger lesions, eloquent locations, and higher S-M grades, as illustrated in Supplementary Fig. 2. Importantly, the evaluation of neurofunctional decline revealed that AVMs with supplemented S-M grade II–VI could derive significant benefit from interventional therapy compared to conservative management (OR, 0.24 [95% CI 0.06–0.93], $P = 0.039$).

Sensitivity Analyses

The sensitivity analyses (Supplementary Fig. 3) consistently suggested that patients undergoing interventional therapy had lower risks of hemorrhagic stroke or death compared to those receiving conservative management. Specifically, when examining different interventional strategies separately, both microsurgery resection (HR, 0.18 [95% CI 0.04–0.86], $P = 0.031$) and SRS (HR, 0.12 [95% CI 0.03–0.59], $P = 0.009$) identified as significantly beneficial treatment options. Additionally, analyses focusing on the timing of intervention post-rupture indicated that delayed intervention (> 3 months) was linked to a significantly lower risk of adverse outcomes (HR, 0.23 [95% CI 0.06–0.86], $P = 0.029$). When patients receiving immediate life-saving treatments at emergency admission were excluded from the study, interventional therapy was associated with a 33% reduction in the risk of long-term hemorrhagic events, although this was not statistically significant (HR, 0.67 [95% CI 0.25–1.76], $P = 0.414$). The methodological sensitivity analysis using sIPTW also validated the robustness of our propensity score methods (HR, 0.52 [95% CI 0.21–1.30], $P = 0.161$).



Characteristics	Conservative Management	Interventional Therapy	HR (95%CI)	P	$P_{\text{interaction}}$
All patients	13 (4.15)	7 (1.87)	0.45 (0.18−1.14)	0.094	
Age					0.219
<18 y	2 (2.79)	5 (2.71)	0.80 (0.14−4.44)	0.796	
≥18 y	11 (4.55)	2 (1.05)	0.23 (0.05−1.07)	0.061	
Size					0.211
<3 cm	5 (2.68)	1 (0.41)	0.14 (0.02−1.20)	0.073	
3−6 cm	5 (5.92)	2 (3.03)	0.40 (0.08−2.07)	0.274	
>6 cm	3 (7.10)	4 (6.33)	0.76 (0.15−3.86)	0.743	
Eloquent region					0.499
Yes	10 (4.73)	4 (1.80)	0.37 (0.12−1.19)	0.096	
No	3 (2.95)	3 (1.97)	0.66 (0.13−3.30)	0.612	
S−M grade					0.133
I−II	3 (2.04)	1 (0.52)	0.23 (0.02−2.22)	0.203	
III	4 (6.25)	1 (1.01)	0.17 (0.02−1.57)	0.119	
IV−V	6 (5.86)	5 (5.91)	0.91 (0.27−3.02)	0.875	
Supplemented S−M grade					0.054
II−VI	8 (3.73)	1 (0.37)	0.10 (0.01−0.79)	0.029	
VII−X	5 (5.07)	6 (5.67)	1.07 (0.32−3.55)	0.914	

Fig. 3 Subgroup analysis for primary outcomes. CI, confidence interval; HR, hazard ratio; S-M grade, Spetzler-Martin grade

Discussion

In this propensity score-matched study, we aimed to assess the efficacy of interventional therapy in comparison to conservative management for patients with ruptured AVMs complicated by a diffuse nidus structure. The results demonstrate that interventional therapy for these AVMs might decrease the risk of long-term hemorrhagic stroke or death by 55% compared with conservative management. And no evidence was found to suggest that interventional treatment for ruptured diffuse AVMs was associated with an increased likelihood of neurofunctional deficits. The benefits of intervention appear most pronounced among AVMs with supplemented S-M grade II–VI in reducing the risk of subsequence hemorrhagic stroke or death and neurological decline. The beneficial trend toward interventional treatment was consistent in all our sensitivity analyses.

Diffuseness has been identified as a critical feature in grading systems designed for evaluating the surgical operability and outcomes of AVMs [3–5]. Regardless of the strategy employed, interventional treatment for eradicating diffuse AVMs presents unique challenges. When microsurgical approaches are considered, the ambiguous planes pose significant challenges for neurosurgeons in separating the nidus from intermixed brain tissue, increasing the risk of hemorrhagic events due to incomplete lesion removal, or neurological impairment due to radical resection [3, 4, 19–21]. SRS is similarly compromised by the irregular borders of AVMs, complicating the task of radiosurgical planning [11, 22, 23]. Furthermore, the frailty of the deep perforating arterial supply and perinidal dilated capillary network also renders embolization a precarious procedure [19, 24]. As such, conservative management remains a viable option for these patients. However, it is essential to note that patients with a history of AVM rupture face a significantly heightened risk of re-bleeding [7–10]. Coupled with the fact that a diffuse structure is also a risk factor for rupture, conservative treatment may not necessarily be safer than interventional approaches [11]. Consequently, choosing between conservative and interventional management is a considerable challenge for patients and clinicians alike, especially in the absence of clear clinical guidelines.

For diffuse AVMs, the ultimate objective is not necessarily complete obliteration. Instead, the primary focus is to mitigate the long-term risks associated with hemorrhage and mortality. Overemphasizing the goal of obliteration may inadvertently result in unfavorable neurological outcomes. And since obliteration is not a consideration in conservative treatment, it was not included in our outcome comparisons. Our study found a 55% reduction in the risk of hemorrhagic stroke or death in the group that underwent interventional therapy, compared to those managed conservatively. However, this difference did not reach statistical significance, which may be attributed to the limited sample size after matching. The Kaplan–Meier curves consistently demonstrated an elevated cumulative risk of hemorrhage in the conservative management group compared to the interventional cohort without crossover. Our findings are consistent with those of Kim et al., where our subgroup analyses also indicated that interventional therapy had a significantly lower risk of hemorrhagic events and reduced likelihood of neurological decline, particularly in supplemented S-M graded II–VI AVMs [25]. Additionally, the subgroup analyses also substantiated that higher AVM grades (S-M grade IV–V, supplemented S-M grade VII–X) correspond to higher risks of post-interventional neurological dysfunction, aligning with their clinical applications [4, 26].

In our exploratory sensitivity analyses, both microsurgical resection and SRS showed significant reductions in the long-term risks of hemorrhage or death compared to conservative treatment. Microsurgical resection demonstrated marked risk mitigation, largely due to its potential for complete lesion eradication, while caution must be exercised to avoid neurofunctional impairment from overly aggressive resection. Previous studies have noticed that diffuse AVMs frequently localize to deep regions and are associated with obscure perforating feeders, features recognized as potential risk factors for rupture [4, 8, 19, 27, 28]. Therefore, SRS manifested greater efficacy than conservative treatment in the mitigation of long-term hemorrhage risk. In terms of intervention timing, our study found that delayed treatment was associated with lower risks of hemorrhagic stroke or death. This finding might be due to improved hemodynamic stability and reduced hematoma-related mass effect at later stages, thereby promoting better therapeutic outcomes [15]. However, this result should be interpreted cautiously as it could be influenced by selection bias; patients at greater risk of rebleeding might seek earlier treatment.

Our study primarily investigates whether to intervene in the case of ruptured AVMs with a diffuse structure, but the ambiguity in defining "diffuse" warrants attention. Since the introduction of the concept by Chin et al. [2], later studies have displayed considerable variation in defining diffuseness and the imaging techniques used to identify it, resulting in interobserver reliability scores ranging from fair to substantial [3, 29–32]. To mitigate this subjectivity, Du et al. proposed a quantitative method based on transition intensity calculations using DSA [19]. However, this method has not gained widespread acceptance due to its computational complexity. In contrast, Jiao et al. suggested using artificial intelligence for automatic diffuseness assessment, which could be more clinically feasible but requires specific imaging sequences [33]. To ensure optimal data utilization, the current study adopted the definition consistent with supplemented S-M grade [4], relied on manual interpretation, and used preliminary training to achieve a more consistent evaluation standard. Additionally, previous research indicates that diffuseness can present in various forms with distinct nidus structures and arterial supplies [25]. Future research aiming to classify these diverse types of diffuseness are encouraged, as they may correspond to unique pathophysiological mechanisms in AVM development and progression [34].

Our study had several limitations. First, the scope of the research was limited to comparing conservative and interventional treatments for diffuse, ruptured AVMs. We did not compare different types of interventional modalities; rather, we only explored their efficacy in sensitivity analyses. Future research is needed to provide more targeted treatment recommendations, particularly for large, diffuse AVMs where a combination of treatment approaches may offer advantages. Second, the median follow-up period of 4 years may not provide a long-term perspective on the natural history of AVMs. However, it is important to recognize that the 4-year duration remains relevant for understanding trends, given the heightened risk of recurrent bleeding in patients with ruptured, diffuse AVMs. Third, although a standardized treatment protocol was followed in the registry, variations in intervention could still occur across different interventionalists, due to empirical judgment and ambiguous guidelines from existing literature. Our research has the potential to serve as an important clinical reference and reduce this variability in future studies.

Conclusions

Our study indicates a trend suggesting that interventional therapy may be more favorable than conservative management in reducing the long-term risks of hemorrhagic stroke or death in cases of ruptured diffuse AVMs, although these findings were not statistically significant. In particular, AVMs with a supplemented S-M grade of II–VI show significant benefits from interventional approaches. Our results did not support the association between interventional therapy and severe or worsened neurofunctional outcomes. Future research employing comparative effectiveness methods is urgently needed to tailor treatment recommendations to individual patients.

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Data Availability All original data are available upon reasonable request to the corresponding authors.

Declarations

Ethics Approval This study was approved by Institutional Research Ethics Committee of Beijing Tiantan Hospital (IRB approval number: KY 2020-003-01) and conducted under the guidance of the Declaration of Helsinki.

Consent for Publication Not applicable.

Competing Interests None declared.

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