

Single-center Retrospective Analysis of One-stop Hybrid Surgery for Brain Arteriovenous Malformations

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Abstract

Objectives To evaluate the safety and effectiveness of one-stop hybrid surgery of microsurgical resection combined with preoperative embolization or intraoperative angiography for brain arteriovenous malformations (bAVMs) and compare the efficacy of one-stop hybrid surgery with nonhybrid surgery (endovascular embolization alone) in the treatment of bAVMs.

Methods A single-center retrospective study was performed to recruit 70 patients with bAVMs at our hospital between July 2017 and April 2020. Patients were divided into 2 groups depending on the mode of surgery: hybrid group (i.e., microsurgical resection combined with preoperative endovascular embolization or intraoperative angiography in the hybrid operating room), and nonhybrid group (i.e., endovascular embolization, stereotactic radiosurgery, or microsurgical resection alone). The hybrid group was divided into two subgroups: the microsurgical resection combined with preoperative embolization, and the microsurgical resection combined with intraoperative angiography subgroups. All patients' demographic variables, clinical manifestations, and imaging features, postoperative complications, and long-term clinical prognosis were recorded and analyzed.

Results Among 70 patients, 48 (68.6%) of whom presented cerebral hemorrhage due to bAVMs rupture. 36 (51.4%) patients in the hybrid group were treated with the combination of pre-operative embolization or intraoperative angiography combined with microsurgical resection, whereas 34 (48.6%) in the nonhybrid group underwent embolization alone. There was no statistical difference in gender, age, ruptured bAVM rate, Spetzler-Martin grades between the 2 groups. Regular clinical and radiological follow-up examinations cure rates were 94.4% in the hybrid group compared to 38.3% in the nonhybrid group ($P < 0.01$). The percentage of patients with favorable outcomes was 94.1% in the hybrid group and 90.6% in the nonhybrid group, although this difference was not statistically significant.

Conclusions One-stop hybrid surgery could be a safe and effective intervention to treat bAVMs clinically, whereas further follow-up is needed to determine the long-term effects after operation.

Introduction

Brain arteriovenous malformations (bAVMs) refer to the congenital malformation with direct arteriovenous communications characterized by an abnormal connection between feeding arteries and draining veins lack of the brain capillary network [17]. However, the accurate etiology and pathogenesis of bAVMs remain inconsistent. The potential mechanism may be attributed to congenital aberrancies of vascular development in the embryo. bAVMs usually occur in young adults between the age of 20 and 40 years old, with an average age of 34 years [11]. The most commonly observed neurological presentation is intracranial hemorrhage (3%), followed by focal or generalized seizure (1%), chronic headache, progressive neurological deficit, or no symptoms [3, 4, 6, 7]. To achieve the goal of preventing cerebral hemorrhage and decreasing the frequency of seizures, various treatments have emerged in an endless stream in recent years.

The major treatment modalities for bAVMs including endovascular embolization, microsurgical resection, stereotactic radiosurgery, either alone or in combination to improve the rate of complete nidal obliteration [37]. Generally, microsurgical resection is recommended as a treatment modality for patients with low-grade bAVMs (grade I-II) [24]. Moreover, endovascular embolization is now recognized as an effective treatment performed alone or combined with microsurgical resection [14, 35]. However, three traditional treatments for bAVMs have the limitations that approximately 30% of patients remain untreatable despite successfully eliminating the lesion.

In the past ten years, further studies on the treatment of bAVMs tend to be multimodality treatment [10, 22, 23]. A recent expert consensus on the treatment of bAVMs suggested that hybrid intervention of microsurgery, intraoperative angiography, and endovascular embolization in a hybrid operating room may be an advanced and effective approach for the management of bAVMs [13]. Although a few studies have confirmed its effectiveness and benefits such as a high rate of immediate, complete, and permanent AVM obliteration, its exact efficacy has yet to be completely revealed [9, 21, 33]. Here, we report a series of bAVMs treated with a hybrid intervention or endovascular treatment alone. Furthermore, we compared the clinical outcome and prognosis between hybrid operation and nonhybrid operation (i.e. endovascular embolization). and introduced the therapeutic concepts of hybrid surgery for bAVMs.

Methods

Patients

In the present study, we conducted a retrospective analysis of the continuous clinical data of 70 patients with cerebral AVMs who underwent surgical treatment in the Department of Neurosurgery, Zhongnan Hospital of Wuhan University from July 2017 to April 2020. To reduce selection bias, we excluded patients who did not receive any history of AVM treatment during the study period. All Patients were classified into two main groups: hybrid surgery group (pre-operative embolization/intraoperative digital subtraction angiography (DSA) with subsequent microsurgical resection) and nonhybrid surgery group (endovascular embolization alone). Thus, we compared the baseline clinical data and clinical outcomes between the hybrid operation group and the endovascular embolization alone group.

Clinical data and Radiological features

The general data analyzed mainly included gender, age, rupture status, clinical symptoms (i.e. headache, seizure, neurological deficits, incidental findings), and all patients underwent DSA and MRI for initial diagnosis. The characteristics of bAVM including Spetzler-Martin (SM) score, location of the bAVM, functional area, the pattern of venous drainage for each patient were assessed using MRI and DSA. The AVM lesions were evaluated based on morphologic characteristics, according to the SM grading system [30].

Treatment

bAVM resection and preoperative embolization were completed at a single stage in all. Both endovascular embolization and intravascular embolization was performed by using a biplane flat-panel angiographic suite (UNIQ FD2020 Hybrid-OR, Philips, Eindhoven, The Netherlands) with 3D reconstruction under general anesthesia. Intraoperative DSA is generally performed during the operation and before craniotomy closure to confirm whether the bAVM lesion is completely removed. Presurgical embolization was performed by using either n-butyl cyanoacrylate (Trufill, Cordis Neurovascular, Inc., Miami Lakes, FL, USA) or ethylene-vinyl copolymer (Onyx 18 or 34, Medtronic, Inc., Minneapolis, Minnesota, USA), detachable coils. The whole operation was carried out in a sterile environment with the use of sterile techniques, without changing the position of the patient during hybrid surgery or endovascular embolization alone.

Outcome assessment

Prognostic factors of functional outcome were assessed based on the modified Rankin Scale (mRS). The mRS score was estimated immediately before and one week after the treatment of intravascular embolization or hybrid operation. The neurological functional outcome was dichotomized into 2 groups: mRS score ≤ 2 was regarded as a good prognosis, whereas mRS score > 2 was defined as a poor prognosis. The change value of mRS was evaluated in postoperative vs. preoperative and follow-up vs. preoperative. Clinical follow-up for all patients averaged 6 months. Long-term follow-up was through regular clinical follow-up postoperative clinical visits, hospitalization, or a combination of telephone interviews obtained.

Statistical analysis

All normally distributed continuous variables were reported as mean \pm standard deviation (SD), and categorical data as percentages or frequencies for descriptive characteristics. We assessed the differences between the two groups by t-tests or Mann-Whitney U for continuous variables and χ^2 or Fisher exact tests for continuous and categorical variables, respectively. The statistical significance level was set at $P \leq 0.05$, and all data were analyzed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, New York, USA) for statistical analysis.

Ethics approval

All procedures performed in studies involving human participants were in accordance with the 2013 Helsinki declaration. This retrospective study was approved by the Ethics Committee of Zhongnan Hospital of Wuhan University. At the same time, we have already obtained informed consent from all included patients. This article does not contain any studies with human participants or animals performed by any of the authors.

Results

Patient demographics & Clinical manifestations

In this series, a total of 70 cases with bAVMs were included in the final analysis. Of 70 patients who underwent bAVM treatment, 36 underwent hybrid surgeries and 34 patients underwent nonhybrid surgeries (Figure 1). In the subgroup, there were 20 subjects in the Embolization + Microsurgery subgroup, 16 subjects in the Radiography + Microsurgery subgroup. The mean age of all bAVMs patients including 46 males was 36.49 ± 17.38 years old, ranging from 4 to 71 years. Among them, 36 patients (24 males, mean age 34.11 ± 17.75 years) received the hybrid operation, whereas 34 patients (22 males, mean age 39.76 ± 17.25 years) underwent the nonhybrid operation (Gender: $P = 0.863$; Age: $P = 0.478$). In total, 48 patients (68.6%) presented with ruptured AVMs. Among all patients, the most initial presenting clinical symptom was headache (45.7%), followed by neurological deficits (32.9%), incidental findings (11.4%), and seizure (10%). 78.6% of patients showed a maximum mRS score of ≤ 2 (nonhybrid group: 76.47% mRS score ≤ 2 , 23.53% mRS score > 2 ; hybrid group: 80.56% mRS score ≤ 2 , 19.44% mRS score > 2) ($P = 0.677$). The patient demographics and clinical manifestations are summarized in Table 1.

By subgroup comparisons in hybrid group, there were no significant differences in terms of age ($P = 0.438$), gender ($P = 0.635$), and preoperative mRS ($P = 0.109$), except for ruptured AVMs ($P = 0.013$). The detailed information is presented in Table 2.

AVM Characteristics

There were 7 cases in SM grade I, 25 grade II, 26 grade III, 11 grade IV, and 1 grade V AVMs, according to Spetzler-Martin score (Figure 2). Nidus sites were localized on supratentorial brain areas in 34 patients (94.44%) from the hybrid group and in 29 cases (85.29%) from the nonhybrid group. The functional areas of the brain were involved in 14 cases (38.89%) from the hybrid group and in 18 cases (52.94%) from the nonhybrid group. However, there was no statistically significant difference in these results (Table 1). In the hybrid subgroup, there were no differences between the two groups regarding SM score, nidus site, functional area, and venous drainage (Table 2).

Treatment and clinical outcomes

Immediate post-procedural angiography indicated angiographic cure rate in 94.44% of patients from the hybrid group, whereas 35.29% were from the nonhybrid group ($P < 0.001$, Table 3). Intraoperative DSA shows that residual AVM nidus was completely excised during this same period in the hybrid group. The majority (66/70) patients (94.3%) had short term follow-up (> 90 days) in these series (Tables 3 and 4). The rates of a good outcome were 94.1% in the hybrid group and 90.6% in the nonhybrid group, although there was no statistically significant difference between patients with good or unfavorable outcomes (Table 3).

Operation-related general complications occurred in 13 patients (36.1%) in the hybrid group and 5 patients (14.7%) in the nonhybrid group ($P = 0.041$, Table 3). Among the hybrid group, the rate of procedure-related complications in the presurgical embolization (Embolization + Surgery) subgroup is significantly higher compared with the radiography and surgery (Radiography + Surgery) subgroup ($P = 0.008$, Table 4). Preoperative embolization worsened the clinical condition of 7 patients (19.4%) through a

delayed postoperative intracerebral hemorrhage, while 4 patients were received emergency hematoma evacuation. Among the patients with embolization alone, embolization worsened the clinical condition in 3 patients (8.8%) through a delayed post-embolization intracerebral hemorrhage (Table 2). One 39-year-old patient in the embolization alone group died from rehemorrhage after one-year of treatment. No patients died in the hybrid operation group. Among the patients in hybrid group, presurgical embolization was performed in 55.6% of patients and achieved a good clinical outcome (Figure 3, 4).

Discussion

Cerebral AVMs are important causes of intracerebral hemorrhage in young adults. For previously unruptured brain AVMs, the rate of developing hemorrhage was approximately 1% per year, but increases by five folds once ruptured [15, 19, 20]. Our single-center retrospective study showed 48 patients (68.6%) presenting ruptured AVMs. The treatment for AVMs aimed to minimize the risk of blood vessel rupture and resect lesions. Currently, treatment approaches mainly include microsurgical resection, endovascular embolization, and stereotactic radiosurgery [1, 2, 26].

Microsurgical resection

Microsurgical resection is still a primary or “gold-standard” method for the authoritative management of low-grade AVMs [25]. Its main advantages lie in the high rate of complete elimination, the immediate elimination of bleeding risk, and its long-term stability, thus reducing morbidity and mortality [34]. Johannes et al reported that a consecutive series of 288 cases underwent microsurgical resection. And microsurgical resection of a cerebral AVM has a high cure rate [29]. Although microsurgery is currently the mainstream surgical method for the treatment of AVMs, it also has its shortcomings, such as large trauma, long recovery time, and the risk of related neurological defects. Endovascular embolization is often used to improve the safety of microsurgery. The main objectives of preoperative embolization include occlusion of the supplying arteries, reduction of blood flow or malformation of vascular mass volume to allow safer surgical excision, and management of those high-risk angiography features, including aneurysm located on supplying arteries and malformation [28]. Intraoperative angiography has also been used to guide AVM surgical treatment. The main purpose of DSA during the operation was to verify whether the deformed vascular mass was completely removed, while the main purpose of fluorescein or indocyanine green angiography during the operation was to show AVM vascular architecture. Therefore, the use of these surgical auxiliary means may improve patients’ selection, reduce surgical complications, and promote patients’ recovery, although these advantages are difficult to be definitively determined in clinical studies.

Endovascular embolization

Endovascular embolization has been generally recognized as a safe and effective means for the AVMs [18]. It is generally accepted that endovascular embolization is also an effective adjunctive treatment in a variety of clinical situations to facilitate complete surgical excision and reduce the risk of intra-operative bleeding [8, 33]. In some cases, the healing effect of AVMs is achieved by embolization

alone, which is helpful in the application of the healing embolization strategy [12]. This is corroborated in the study by Adam et al [27]. They drew the conclusion that only 15% of patients achieved safely complete angiographic obliteration of the bAVM with embolization alone. However, our outcomes of complete bAVM obliteration are far superior to their study. They speculate that proximal occlusion of feeding arteries may be associated with recurrence. Another indication for endovascular therapy is as a substitute for microsurgery or stereotactic radiosurgery [36]. In this study, endovascular embolization helps to reduce AVMs volume or occlusion of high-risk characteristics, such as ruptured aneurysms in or around the deformed vascular cluster, and final treatment of remaining AVMs. Finally, embolization has been used as palliative care to reduce vascular irregular blood flow to malformed vascular masses, thereby improving the underlying symptoms associated with blood theft.

Hybrid operation

Recently, multimodality treatment, especially hybrid surgery, has been paid more and more attention as an effective treatment of intracranial AVM [8, 9]. Preoperative partial embolization of the malformation can assist surgical positioning, reduce blood flow to the malformation, and reduce intraoperative bleeding risk and surgical difficulty [5]. Intraoperative angiography can detect the residual malformation immediately for one-stop resection, greatly reducing the residual rate of postoperative malformation and the risk of postoperative rebleeding [16, 17, 21, 31]. Despite the lack of large sample evidence, multiple single-center randomized controlled studies have reported that the application of a hybrid operating room provides more satisfactory therapeutic effects compared with traditional surgery. However, for grade III or above, especially for complex bAVM lesions located in functional areas, simultaneous intraoperative angiography or embolization combined microsurgical resection under a hybrid operating room can achieve a better therapeutic effect and long-term prognosis, as well as a good functional protective effect.

Few reports were addressing the surgical efficacy between several above treatments. Procedure-related complications were higher in the hybrid group in comparison with the embolization alone group in our study, but the results showed no significant difference between the hybrid operation and embolization alone groups in any of the favorable clinical outcomes. These results are consistent with our results. Wang et al. found that better long-term outcomes in 92.5% of unruptured AVM patients compared with ruptured AVMs in long-term follow-up [32]. These results support our finding that the immediate neurological deficits are usually transient and that many patients recover over time. Immediate post-operative radiological findings demonstrated complete obliteration in 99.4% of patients in the hybrid surgery group, whereas 38.3% in the embolization alone group. Wen et al. also found that the hybrid operation presented distinct advantages in cure rates, especially for complex AVMs [33]. In our series, the cured rate of the embolization alone group was lower than that in other studies on the safety of embolization with large case series. Among the embolization alone group, disorders were located in functional areas in a large percentage of patients. This selection bias for embolization might be the cause of a lower cure rate in the embolization alone group. In our study, the removal of AVM in several patients was supposed to be completed safely through the hybrid operation in our cases, though with

high-grade AVM lesions, which was similar to Wen's results [33]. Furthermore, the mortality rate in the hybrid group was much lower than that in the embolization alone group, although this difference was not found to be statistically significant. Wang et al. reported lower operation-related morbidity in their series of low-grade AVMs. They attributed the low morbidity to several reasons [32]. The most important target is embolizing the feeding arteries to reduce intraoperative bleeding rather than the AVM nidus. We also believed that it was important to follow this strategy, particularly for high SM grade and complex AVMs.

Limitations

Admittedly, our research also has some defects. First, the main limitation of our study is a retrospective analysis, single-center, non-randomized study design, and sample size of patients with cerebral arteriovenous malformation small, which may result in patient selection and registration of bias. Secondly, the clinical results are carefully evaluated through medical record review, but they are prone to deviation without blind evaluation and document errors. Finally, some patients were lost to follow-up, although the low rate did not influence final results.

Conclusion

One-stop hybrid operation combined embolization and microsurgical resection could be a safe and effective method of intervention for the AVMs. It can be used for effective and complete occlusion of low-grade or high-grade and complex arteriovenous malformations. Certainly, further follow-up is needed to determine the long-term effects after operation.

Declarations

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Conflict of interest: The authors declare no conflict of interest.

Availability of data and material: Restrictions apply to the availability of these data due to privacy restrictions.

Code availability: Not applicable.

Ethics approval: This study was obtained from the Zhongnan Hospital of Wuhan University Ethics Committee (Kelun-2017005).

Consent for publication: All authors agreed to the publication of the manuscript.

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Tables

Table 1 Baseline characteristics of patients

Variable	Nonhybrid Group	Hybrid Group	P	Total
Total	34	36		70
Sex (%)			0.863	
Male	22(64.71)	24(66.67)		46
Female	12(35.29)	12(33.33)		24
Age (years), mean ± SD	39.76±17.25	34.11±17.75	0.478	
Ruptured AVM (%)			0.058	
Yes	27(79.41)	21(58.33)		48
No	7(20.59)	15(41.67)		22
Symptoms at Presentation (%)				
Headache	17(50.00)	15(41.67)		32
Seizure	1(2.94)	6(16.67)		7
Neurological deficits	11(32.35)	12(33.33)		23
Incidental findings	5(14.71)	3(8.33)		8
Spetzler-Martin Score (%)			0.826	
Ⅰ-Ⅱ	16(47.06)	16(44.44)		32
Ⅲ-Ⅳ	18(52.94)	20(55.56)		38
Nidus site (%)			0.202	
Supratentorial	29(85.29)	34(94.44)		63
Infratentorial	5(14.71)	2(5.56)		7
Functional area (%)			0.238	
Yes	18(52.94)	14(38.89)		32
No	16(47.06)	22(61.11)		38
Preoperative mRS (%)			0.677	
0-2	26(76.47)	29(80.56)		55
>2	8(23.53)	7(19.44)		15
Venous drainage (%)			0.009	
Deep	20(58.82)	10(27.78)		30
Superficial	14(41.18)	26(72.22)		40

Table 2 Baseline characteristics of Patients in the Subgroup of Hybrid operation

Variable	Embolization + Microsurgery	Radiography + Microsurgery	<i>P</i>
Total	20	16	
Sex (%)			0.635
Male	14(70.00)	10(62.50)	
Female	6(30.00)	6(37.50)	
Age (years), mean ± SD	33.00±16.53	35.50±19.64	0.438
Ruptured AVM (%)			0.013
Yes	8(40.00)	13(81.25)	
No	12(60.00)	3(18.75)	
Symptoms at Presentation (%)			
Headache	11(55.00)	4(25.00)	
Seizure	4(20.00)	2(12.50)	
Neurological deficits	3(15.00)	9(56.25)	
Incidental findings	2(10.00)	1(6.25)	
Spetzler-Martin Score (%)			0.051
Ⅱ-Ⅲ	6(30.00)	10(62.50)	
>Ⅲ	14(70.00)	6(37.50)	
Nidus Site (%)			0.193
Supratentorial	18(90.00)	16(100)	
Infratentorial	2(10.00)	0(0)	
Functional area (%)			0.593
Yes	7(35.00)	7(43.75)	
No	13(65.00)	9(56.25)	
Preoperative mRS (%)			0.109
0-2	18(90.00)	11(68.75)	
>2	2(10.00)	5(31.25)	
Venous drainage (%)			0.067
Deep	2(10.00)	0(0)	

Superficial

12(60.00)

14(87.50)

Table 3 Neurological Outcome of Patients between Nonhybrid Group and Hybrid Group

Variable	Nonhybrid Group	Hybrid Group	<i>P</i>
Postoperative mRS of one week (%)			0.917
0-2	24(70.59)	25(69.44)	
>2	10(29.41)	11(30.56)	
Number of patients lost to clinical follow-up	2	2	
mRS at follow-up			0.592
0-2	29(90.63)	32(94.12)	
>2	3(9.37)	2(5.88)	
Change (mRSΔ, postoperative vs. preoperative)			0.051
Improved or unchanged	32(94.12)	28(77.78)	
Deterioration	2(5.88)	8(22.22)	
Change (mRSΔ, follow-up vs. preoperative)			0.519
Improved or unchanged	30(93.75)	33(97.06)	
Deterioration	2(6.25)	1(2.94)	
Post-resection angiographic outcome			<0.001
Complete	12(35.29)	34(94.44)	
Residual	22(64.71)	2(5.56)	
Rehemorrhage			0.204
Yes	3(8.82)	7(19.44)	
No	31(91.18)	29(80.56)	
Complications			0.041
Yes	5(14.71)	13(36.11)	
No	29(85.29)	23(63.89)	

Table 4 Neurological Outcome of Patients in the Subgroup of Hybrid operation

Variable	Embolization + Surgery	Radiography + Surgery	<i>P</i>
Postoperative mRS of one week (%)			0.517
0-2	13(65)	12(75)	
>2	7(35)	4(25)	
Number of patients lost to clinical follow-up	1	1	
mRS at follow-up			0.863
0-2	18(94.74)	14(93.33)	
>2	1(5.26)	1(6.67)	
Change (mRSΔ, postoperative vs. preoperative)			0.004
Improved or unchanged	12(60)	16(100)	
Deterioration	8(40)	0(0)	
Change (mRSΔ, follow-up vs. preoperative)			0.367
Improved or unchanged	18(94.74)	15(100)	
Deterioration	1(5.26)	0(0)	
Post-resection angiographic outcome			0.193
Complete	18(90.00)	16(100)	
Residual	2 (10.00)	0(0)	
Rehemorrhage			0.008
Yes	7(35.00)	0(0)	
No	13(65.00)	16(100)	
Complications			0.008
Yes	11(55.00)	2(12.50)	
No	9(45.00)	14(87.50)	

Figures

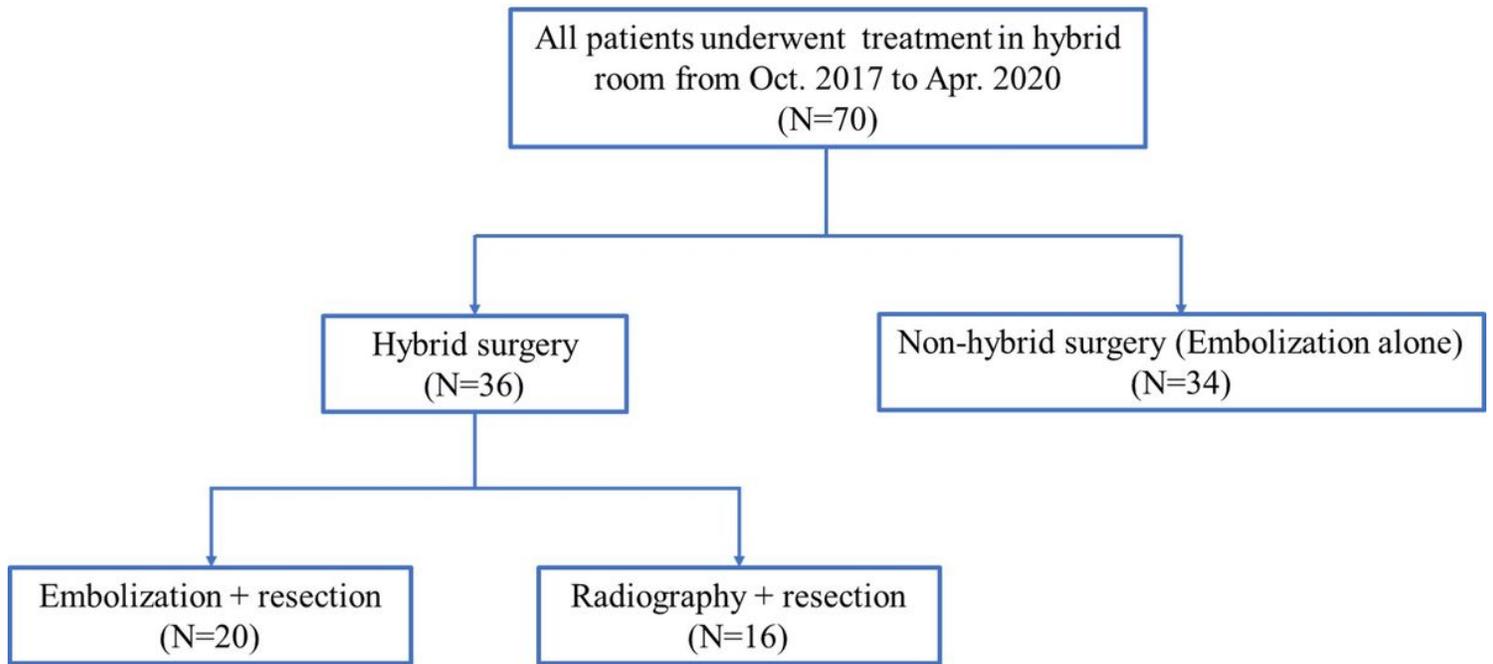


Figure 1

Flow diagram for the process of study screening and assignment of the study patients.

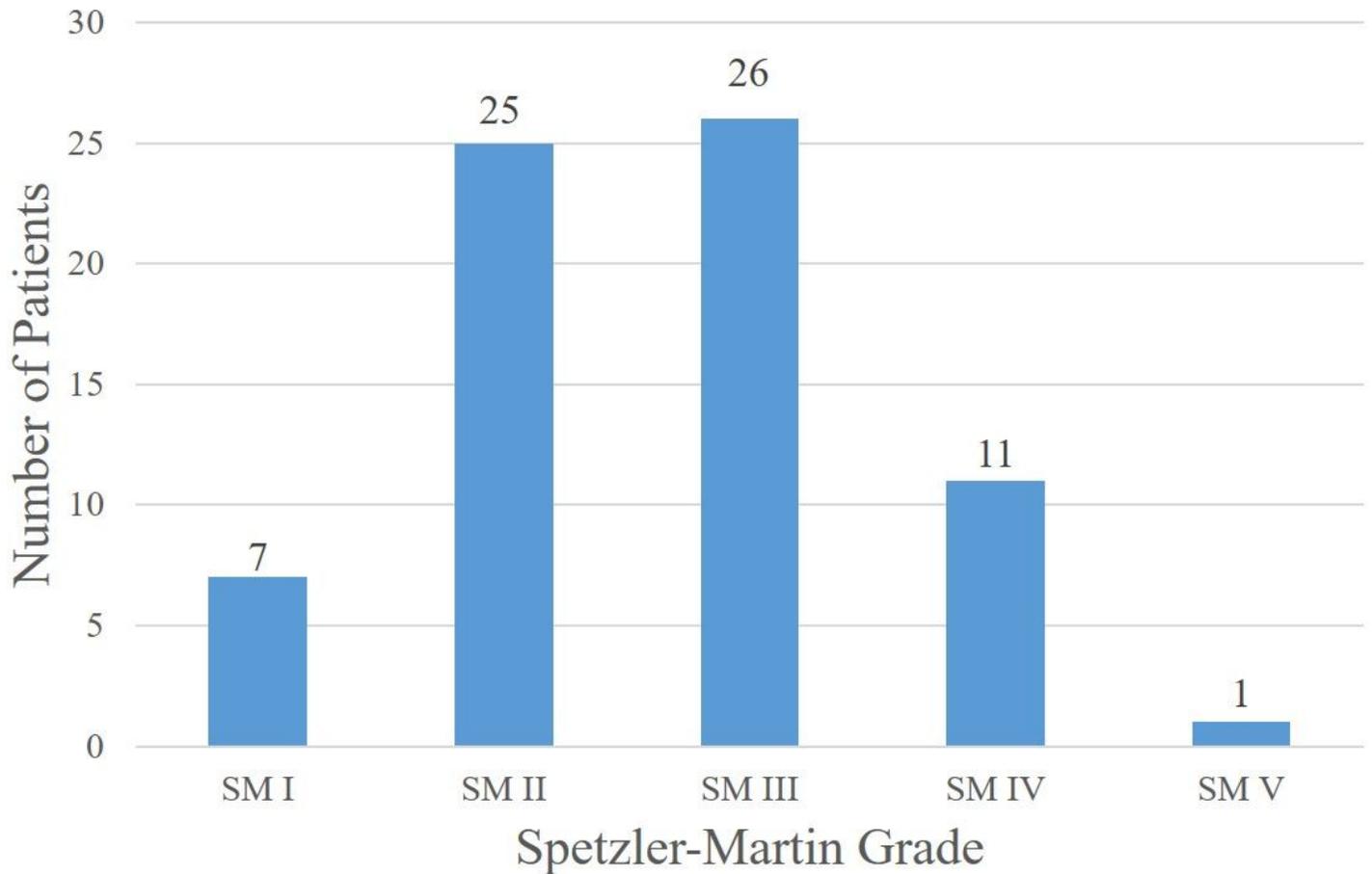


Figure 2

Distribution of SM Grade in bAVM patients.

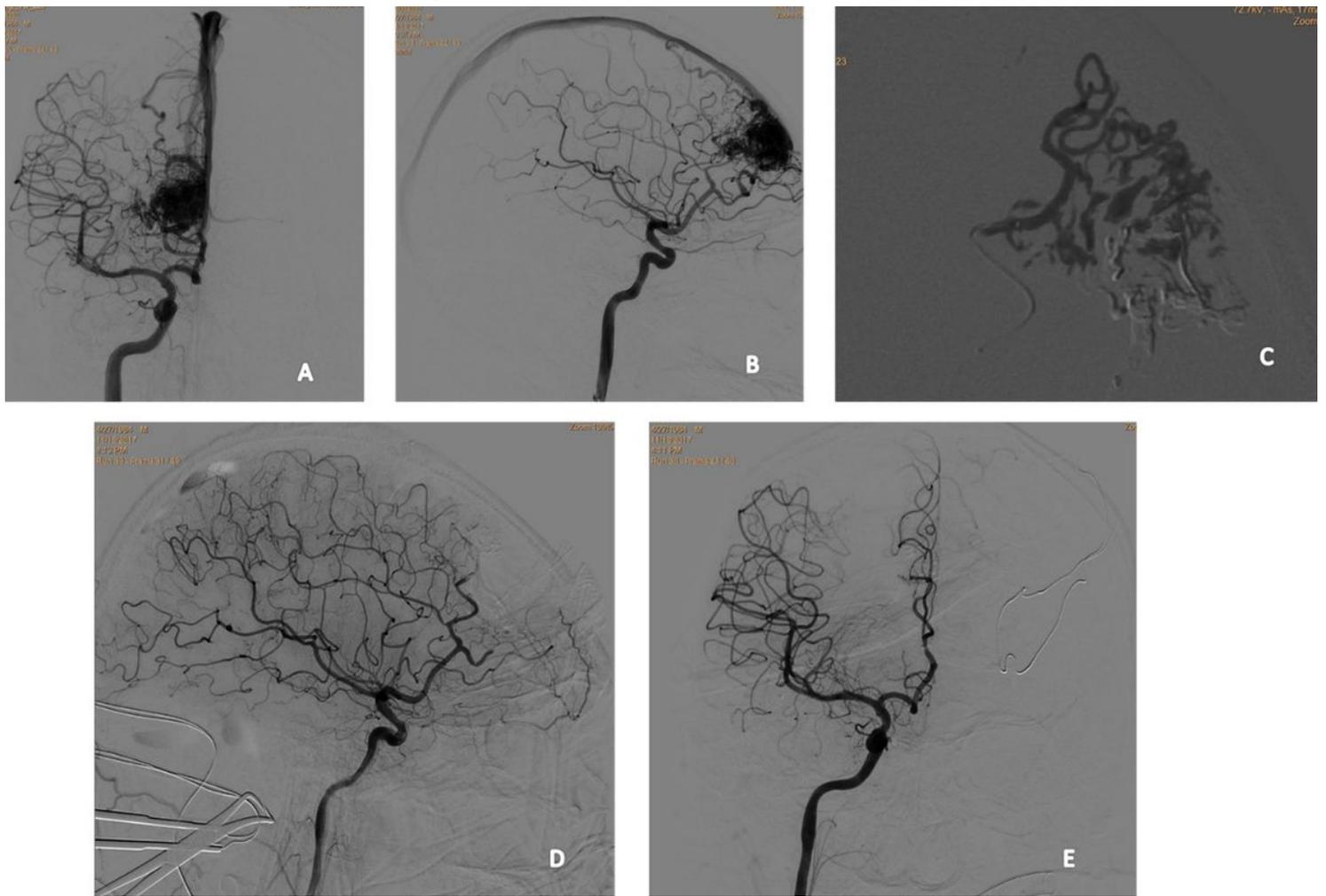


Figure 3

Radiological profiles of a male patient with a seizure. (A, B) Anteroposterior and lateral projection angiograms show a midline frontal arteriovenous malformation supplied by the right anterior cerebral artery (ACA) drainage into the superior sagittal sinus. (C) Intraoperative angiography demonstrates subsequent injection of Onyx18 with obliteration of the AVM. (D, E) Intraoperative anteroposterior and lateral projection angiograms following resection demonstrate the obliteration of the AVM.

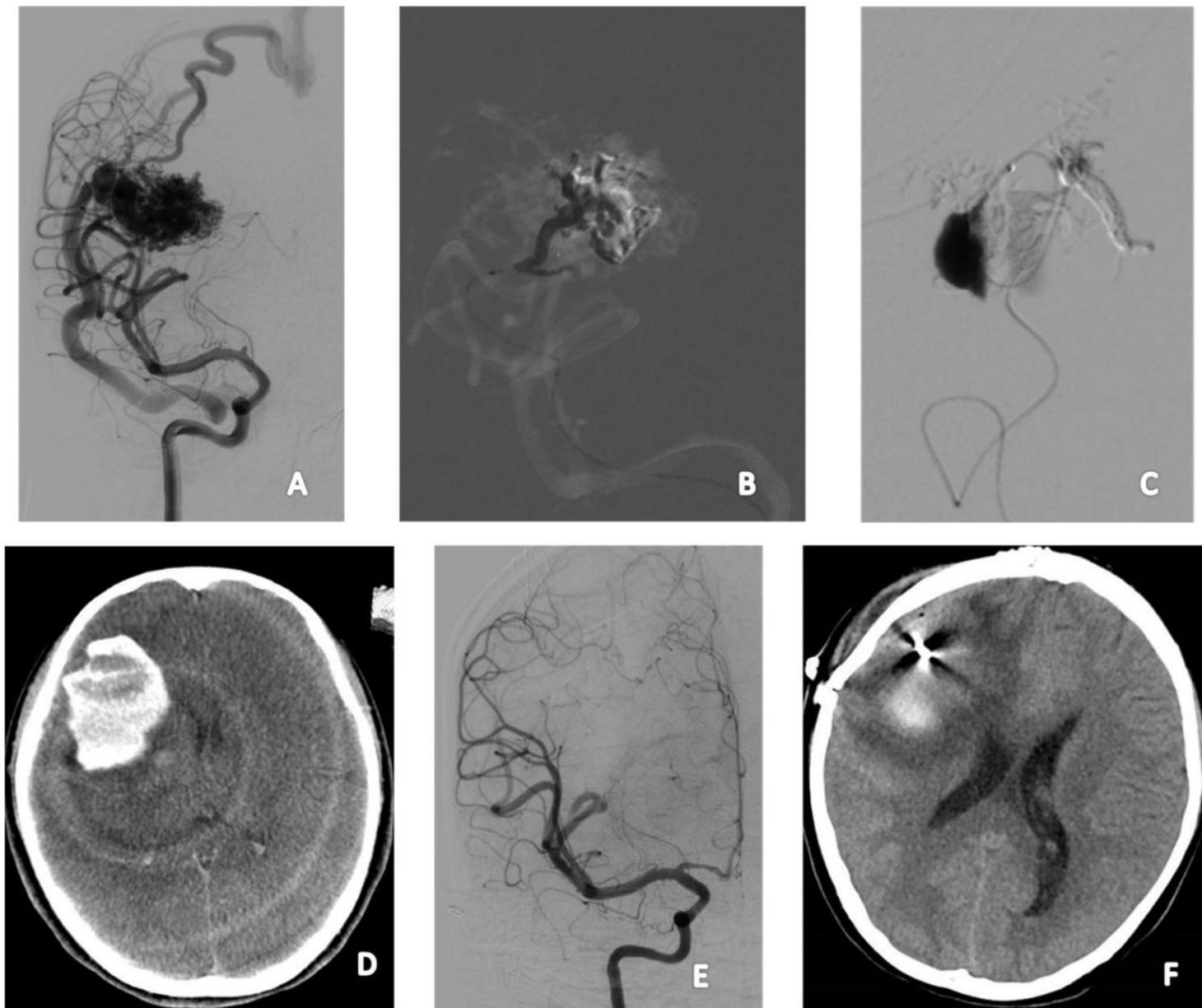


Figure 4

Radiological profiles of another male patient with seizure. (A) Anteroposterior projection angiogram shows a frontal arteriovenous malformation supplied by the right middle cerebral artery (MCA) drainage into the superior sagittal sinus. (B) Intraoperative angiography demonstrates subsequent injection of Onyx18 with obliteration of the AVM. (C) Intraoperative angiography demonstrates contrast medium overflow. (D) Intraoperative X per CT demonstrates cerebral hemorrhage. (E) Intraoperative anteroposterior projection angiogram following resection demonstrates the obliteration of the AVM. (F) Postoperative non-contrast head CT demonstrates the evacuation of hematoma and obliteration of the AVM.