



# Effectiveness of Preradiosurgical Embolization with NBCA for Arteriovenous Malformations - Retrospective Outcome Analysis in a Japanese Registry of 73 Patients (J-REAL study)

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**Purpose:** Recent reports have posed doubts about the effect of preradiosurgical embolization in brain arteriovenous malformation (AVM) because it makes the planning of stereotactic radiosurgery (SRS) difficult and has the risk of recanalization out of the target. We investigated whether the performance and quality of embolization may influence the success of SRS based on a retrospective case cohort study.

**Materials and Methods:** Seventy-three patients who underwent embolization followed by SRS between 2003 and 2012 in eight institutes with neurointerventionists were considered. They were divided into the following two groups at 3 years of follow up after the final SRS: "successful occlusion group" (S group), with radiologically complete occlusion of AVM; and "non-successful occlusion group" (N group) with persistent remnant nidus or abnormal vascular networks. Patient background, AVM profile, embolization performance grade and complications were compared in each group. The quality of embolization was evaluated with the new grading system: embolization performance grade (E grade), specializing the achievement of nidus embolization. E grade A was defined as sufficient nidus embolization with more than half of the total number of feeders achieving nidus penetration. E grade B was defined as less than half achievement of nidus embolization,

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and E grade C was defined as failure to perform nidus embolization.

**Results:** Forty-three patients were included in the S group, and 29 patients were included in the N group. The size and Spetzler-Martin grade of AVM and the rate of diffuse type was higher in the N group without statistical significance. The embolization performance level according to E grade indicated a significantly higher rate of successful embolization with more than 50% of nidus penetration in the S group ( $P < 0.001$ ). This difference was also confirmed in the subanalysis for limited cases, excluding smaller AVMs with complete occlusion with SRS alone ( $P = 0.001$ ).

**Conclusion:** The cause of the unsuccessful result of post-embolization SRS might be the large, diffuse angioarchitecture, but proper embolization with a high rate of nidus penetration to avoid recanalization is more important. Effective embolization is essential to contribute to and promote the effect of radiosurgery.

**Key Words :** Arteriovenous malformation; Nidus; Embolization; Radiosurgery; Quality

Preradiosurgical embolization of cerebral arteriovenous malformations (AVMs) has been warranted as a significant treatment to eliminate the risk of hemorrhage during the latency period after radiosurgical treatment, and to achieve AVM volume reduction to a size amenable to radiosurgical treatment, resulting in earlier obstruction [1, 2]. The treatment of inappropriate factors, such as flow-related aneurysms, is warranted because proximal and pedicular aneurysms and intranidal aneurysms have a 7% to 10% annual risk of hemorrhage [3, 4].

However, embolization has recently been criticized as a useless option for radiosurgery because embolization decreases the obliteration rates after stereotactic radiosurgery (SRS) compared with radiosurgical treatment alone [5]. Recanalization of embolized feeder after RS is seen in 5–7% of patients, and some reports question the efficacy of embolization [6–14]. The recanalization or vascular remodeling of remaining feeders tends to occur in cases with incomplete nidus embolization and far proximal feeder occlusion [15,16]. For this reason, radiosurgeons may struggle to plan the interested area because the part with pretended obstruction after embolization with a risk of late recanalization is outside the target. By contrast, proper nidus embolization will prevent recanalization [2, 7] and can contribute to achieving a preferable result from SRS.

In Japan, where there are a large number of Gamma Knife centers, the treatment option with SRS following embolization has a comparatively higher rate among the combined therapeutic modalities [17], and this difference affects the rate of favorable results. This multicenter study, J-REAL (Japanese registry of

Radiosurgery following Embolization for Arteriovenous malformations), is a retrospective analysis of the selected AVM cases treated with SRS following embolization that was planned to clarify the efficacy of embolization and address the discrepancy in the results between Japan and western countries.

## MATERIALS AND METHODS

### Outline of the study

A retrospective review of AVMs treated between 2003 and 2012 with embolization followed by SRS was performed. The data were harvested from institutes, enrolling experienced neurointerventionists who had proper and secure strategies for the endovascular treatment of AVM. The clinical materials were AVMs with a maximum diameter of more than 1 cm in patients older than 6 years of age. Patients who underwent SRS or direct surgery before embolization, except for emergency ventricular drainage, were excluded. All AVMs were embolized with NBCA mixture in one or staged sessions, and no cases with Onyx embolization were included. The SRS tool was a Gamma Knife in all cases. Patients treated with other methods, such as LINAC and X knife, were excluded. The timing of SRS was specified as within 6 months after the final embolization, and the decision of the marginal dose and targeting area was based on the guidelines of each Gamma Knife center. The operators of endovascular treatment were senior board experts trained by the Japanese society of neuroendovascular therapy with experience in more than 20 cases of AVM embolization. Similarly, the operators of the Gamma Knife were required to have experience with more than

50 radiosurgery cases for AVM.

The performance of endovascular treatment was impartially judged by multiple neurointerventionists, and the final image judgment was performed by the experienced multiple radiosurgeons 3 years after the final radiosurgery. This study was approved of the local institutional review board.

### Clinical data

We investigated patient profile including gender, age, clinical manifestation, undergone initial treatment and general complications, and AVM profile including location, Spetzler-Martin grade[18], maximum diameter; volume, modified radiosurgery-based arteriovenous malformation score (mRBAS)[19] and angioarchitecture including nidus type, daughter nidus, draining pattern, varix, associated aneurysm, and meningeal feeders. AVM volumes were calculated from a 3-dimensional angiogram after determination of the radius ( $r$ ) on three orthogonal planes using the formula for an ellipsoid ( $4\pi r_1 \times r_2 \times r_3/3$ ). mRBAS were determined by the following equation: AVM score =  $(0.1 \times \text{volume in cm}^3) + (0.02 \times \text{age in years}) + (0.5 \times \text{location})$ . The location values are as follows: frontal/temporal/parietal/occipital/intraventricular/corpus callosum/cerebellar = 0, and basal ganglia/thalamus/brainstem = 1. Nidus type was categorized into compact type and diffuse type. Compact type was defined as AVM with clearly demarcated nidus without daughter ones. While, diffuse type was defined as AVM with abnormal vessel dilatation or a non-shunting abnormal vascular network surrounding the nidus, particularly expressed at the watershed area between different perfusion territories.

### Performance of the treatment

#### A. Performance of embolization

Data were collected for the total number of accessible / inaccessible feeders, successful / incomplete occlusion of fistulous feeders, and successful / unsuccessful nidus penetration as proximal feeder occlusion alone. The achievement level of embolization was defined in the newly provided categorization, embolization performance grade (E-grade), to exclude the operator's subjective preference (Table 1). E grade A was defined as sufficient nidus embolization with more than 50% of total number of feeders achieving nidus penetration. E grade B was defined as less than 50% achievement of nidus embolization, and E grade C was defined as failure to perform nidus embolization due to a lack of access, technical error or fistulous AVM with no nidus components. Grades A and B were subdivided according to the components and treatment of fistulous feeders. The final embolization rate was calculated as the result of the three-dimensional volume reduction of the nidus. The size of the remaining nidus after embolization was expressed as the maximum diameter of the residual nidus. Procedure-related or perioperative complications associated with embolization and the neurological deterioration due to the complications were registered.

#### B. Performance of radiosurgery

The effect of SRS was evaluated at 2 years after the first operation. The post-SRS radiological evaluation was performed using the original grading system (SRS-grade). Patients with complete occlusion of AVM in the final angiogram were classified as SRS grade A. Patients who had a fine abnormal vascular network without AV shunt remaining in the site of the nidus were classified as SRS grade B, and those with a remaining nidus with obvious AV shunt were classified

**Table 1.** Classification of the Grade of Embolization Performance (E Grade)

E Grade A1: $\geq 50\%$ of successful nidus embolization for compact (plexiform) type AVM
E Grade A2: $\geq 50\%$ of successful nidus embolization and proximal occlusion of fistulous feeders for mixed (plexiform + fistulous) type AVM
E Grade B1: $< 50\%$ of successful nidus embolization for compact (plexiform) type AVM
E Grade B2: $< 50\%$ of successful nidus embolization and proximal occlusion of fistulous feeders for mixed (plexiform + fistulous) type AVM or remaining daughter nidus on diffuse type*
E Grade C: No successful embolization (all proximal occlusion) for all feeders in any types of AVM or failed obvious size reduction (only change of vascular density)

\*: Including remnant daughter nidus on diffuse type

as SRS grade C. Other information concerning the radiosurgery, including the duration between embolization and SRS; major adverse events after the radiosurgery, such as rupture or delayed complications; and the final clinical outcome were registered.

### Statistical analysis

Patients with SRS grade A were categorized as the “successful occlusion group” (S group), and the patients in SRS grades B and C were categorized as the “non-successful occlusion group” (N group). These two groups were compared in terms of patient background, AVM profile and embolization performance. As a sub-analysis, SRS grade-B patients were independently studied to determine differences from SRS grade-C patients. The statistical analysis of categorical variables was performed using the  $\chi^2$  and Fisher exact tests. The comparison of means was performed using Student’s t-test, and an analysis of variance (ANOVA) followed by Bonferroni post hoc testing was performed, as appropriate. Predictive factors in the univariate analysis concerning size and embolization specification were entered into a multivariate logistic regression analysis using a stepwise method. The percentage of incidence and 95% confidence intervals (CI) were calculated for all considered variables and results. P-values <0.05 were considered to indicate significance.

## RESULTS

### Patient profile

A total of 73 patients met the inclusion criteria and underwent embolization followed by SRS during the study period (Table 2). There were 40 males and 33 females ranging from 6–78 years old with a mean age of 35.8 years. Of the 30 unruptured AVMs, the clinical manifestations were asymptomatic in 10, convulsion in 10, headache in five, and focal neurological deficits including cognitive and psychological function deficits in five. Of 43 patients with ruptured AVMs, 20 patients had intracerebral hemorrhage, 16 had intraventricular hemorrhage, and seven had subarachnoid hemorrhage. The initial treatments before embolization were medication for seizure, intracranial pressure control, and vital stabilization in 23 patients, as well as ventricular drainage in four patients. Precedent general complications were recognized in 4 patients and neurological deficits before treatment were observed in 18 patients, including mild deficits (mRS 1) in 9 patients, middle (mRS 2) in 3 patients and severe (mRS

4) in 6 patients.

### AVM profile

The AVM profile is summarized in Table 3. Of the AVMs, the location was frontal in 20, temporal in 8, parietal in 10, occipital in 11, cerebellum in 16, thalamo-ostriate in three and brain stem in four. Large AVMs extending over multiple areas were sorted according to the area containing of the largest part. For the Spetzler-Martin grade, there were nine AVMs in grade 1, 17 in grade 2, 32 in grade 4 and one in grade 5. The preoperative mean maximum diameter was 31.6 mm (range 11–72 mm) and the mean volume was 13.8 ml (range 1–46 ml). The distribution of the volume was less than 5 ml in 24 AVMs, 6–10 ml in 15 AVMs, 11–20 ml in 13 AVMs, 21–30 ml in 10 AVMs, 31–40 ml in 9 AVMs and more than 40 ml in 2 AVMs. The median mRBAS before embolization was 2.13, and the distribution of AVMs in mRBASs was as follows:  $\leq 1.00$  in 14, 1.01–1.50 in 11, 1.51–2.00 in 16 and  $>2.00$  in 31.

Regarding the angioarchitecture of the AVMs, 52 were classified as compacted types and 21 were classified as diffuse types; a daughter nidus was observed in five AVMs. The draining pattern of the AVMs was as follows: single superficial drainage in 18, single deep drainage in 11, multiple superficial drainage in 32 and multiple deep drainage in 12. The cases with both superficial and deep drainers were classified to the category of the main drainage side. Varices on the drainers were observed in six AVMs. Associated aneurysms were found in 22 AVMs, including 13 proximal feeder aneurysms, 3 flow-related aneurysms and 6 intranidal aneurysms. Of these, 12 aneurysms were treated with embolization in addition to the embolization for AVM. Seventeen AVMs were also supplied by meningeal feeders, and 9 of these were embolized in a manner similar to that use for AVMs supplied by pial feeders.

### Performance of embolization

According to our embolization grading system, the AVMs were distributed in grades as follows: 12 in E-Grade A1, 20 in E-Grade A2, 19 in E-Grade B1, 18 in E-Grade B2 and two in E-Grade C (Table 4). The mean final volume reduction rate was 61.2%. The maximum diameter of the remaining nidus was almost zero in 7 AVMs,  $<1$  cm in 22 AVMs, 1–2 cm in 24 AVMs, 2–3 cm in 13 AVMs, and  $\geq 3$  cm in 7 AVMs. Perioperative complications occurred in 14 patients, including perioperative or delayed hemorrhage in eight patients, postoperative convulsion in two patients, and other

minor complications in four patients. Of these, two patients had neurological deterioration with score changes of  $\geq 2$  on the modified Rankin Scale.

### Performance of radiosurgery

The AVMs classified by SRS grade as follows: 44 in SRS-grade A, 18 in SRS-Grade B and 11 in SRS-Grade C (Table 4). The median duration between final embolization and SRS was 1.9 months. Delayed adverse events occurred in 4 patients, including hemorrhage in three patients and cyst formation in one patient. Of these, two patients presented with neurological deterioration and a score change of  $\geq 2$  on the modified Rankin Scale.

### Comparison of profiles by SRS grade

The data of patients and AVM profiles were

compared between the S and N groups (Tables 2 and 3). For patient profiles, there was no difference between the two groups in terms of age distribution, clinical manifestation, and initial treatment methods. While the dominance of gender is different between S group (female: 16/44 (36%)) and N group (17/29 (59%)) with female dominance, in particular significantly different between S group and SRS grade C (9/11(82%)) with female dominance ( $P=0.015$ ).

For the clinical manifestation, initial treatments and preceding neurological deficits, there were no significant differences between the two groups. The AVM location and Spetzler-Martin Grade showed no deviation and had a similar distribution in both groups. The sizes of the AVMs also had a similar distribution. However, the mean maximum diameter (SRS-grade A: 28.7 mm, B: 32.9 mm, C: 40.7 mm) showed no signifi-

**Table 2.** Patient Profile

Grade of radiosurgical effect (SRS grade)		Total	A	B	C	B + C		
category of group			S group			N group		
total number		73	44	18	11	29	S vs N group	
<b>Patient profile</b>								
Gender (M:F)		40 vs. 33	28 vs. 16	10 vs. 8	2 vs. 9	12 vs. 17	NS	
Mean age (range)		38.3 (6~78)	38.5 (6~78)	30.9 (10~58)	33.2 (13~62)	31.8 (10~62)	NS	
Clinical		Unruptured					NS	
Manifestation	No symptom	10	6	2	2	4		
	Convulsion	10	4	4	2	6		
	Headache	5	4	1	0	1		
	Focal neurological symptoms	5	2	1	2	3		
Clinical		Ruptured					NS	
		Intracerebral hemorrhage	20	14	4	2	6	
		Intraventricular hemorrhage	16	9	4	3	7	
		Subarachnoid hemorrhage	7	5	2	0	2	
Initial treatment							NS	
		No treatment	42	25	9	8	17	
		Medical treatment	23	15	7	1	8	
		Ventricular drainage	4	2	2	0	2	
		Others	4	2	0	2	2	
Precedent neurological deficits							NS	
		None (mRS 0)	55	32	13	10	23	
		Mild (mRS 1)	9	5	3	1	4	
		Medium (mRS 2, 3)	3	2	1	0	1	
		Severe (mRS $\geq 4$ )	6	5	1	0	1	

## Effectiveness of Preradiosurgical Embolization of Brain AVM

**Table 3.** AVM Profile

Grade of radiosurgical effect (SRS grade)		Total	A	B	C	B + C		
category of group			S group			N group		
total number		73	44	18	11	29	S vs N group	SRS grade A vs C
<b>AVM profile</b>								
location							NS	NS
	Frontal	20	15	4	1	5		
	Temporal	8	4	2	2	4		
	Parietal	10	4	3	3	6		
	Occipital	11	6	2	3	5		
	Cerebellum	16	11	5	0	5		
	Thalamostriate	3	2	1	0	1		
	Brainstem	4	1	2	1	3		
Spetzler-Martin grade							NS	NS
	Grade 1	9	8	1	0	1		
	Grade 2	17	12	3	2	5		
	Grade 3	32	18	10	4	14		
	Grade 4	14	6	3	5	8		
	Grade 5	1	0	1	0	1		
size	maximum diameter (mm)	31.6 (11-72)	28.7 (12-55)	32.9 (11-45)	40.7 (20-72)	35.9 (11-72)	NS	0.013
	initial volume (ml)	13.8 (1-46)	12.0 (1-45)	12.4 (1-35)	23.5 (2-46)	16.6 (1-46)	NS	0.004
	≤ 5 ml	24	18	6	0	6		
	6-10 ml	15	11	3	1	4		
	11-20 ml	13	6	3	4	7		
	21-30 ml	10	4	4	2	6		
	31-40 ml	9	4	2	3	5		
	>40 ml	2	1	0	1	1		
mBRAS	mean value	2.13	2.01	1.94	2.97	2.33	NS	<0.001
	≤ 1.00	15	11	3	0	4		
	1.01-1.50	11	6	4	1	5		
	1.51-2.00	16	11	4	1	5		
	≥ 2.01	31	16	7	9	15		
<b>Angioarchitecture</b>								
Nidus type	compact	52	37	12	3	15	0.004	<0.001
	diffuse	21	7	6	8	14		
Daughter nidus	5	2	1	2	3	NS	NS	
Draining pattern	single (superficial)	18	14	3	1	4	0.031	0.0013
	single (deep)	11	8	3	0	3		
	multiple (superficial main)	32	17	8	7	15		
	multiple (deep main)	12	5	4	3	7		
Associated varix		6	5	1	0	1	NS	NS
Associated aneurysm	no aneurysms	52	33	13	6	19	NS	NS
	proximal (treated)	13(5)	6(2)	3(0)	4(3)	7(3)		
	flow-related (treated)	3(3)	2(2)	1(1)	0	1(1)		
	intranidal (treated)	6(4)	3(3)	2(1)	1(0)	3(1)		
Meningeal feeders	no	56	38	16	4	18	0.023	0.002
	yes (treated)	17(9)	6(4)	4(1)	7(4)	11(5)		

mBRAS: modified radiosurgery-based arteriovenous malformation (AVM) score

cant difference between the SRS-grade A and B groups, but they were significantly larger in the SRS-grade C group than group A ( $P=0.013$ ). The mean initial volume (SRS-grade A: 12.0 ml, B:12.4 ml, C: 23.5 ml) showed similar tendency and significant difference between Grade A and C groups ( $P=0.004$ ). The mean mRBAS (SRS-grade A: 2.01, B: 1.94, C: 2.97) was also significantly higher in SRS-Grade C AVMs ( $P<0.001$ )

Regarding angioarchitecture, a diffuse type of nidus was significantly more frequent in the N group (14/29 (48%),  $P=0.004$ ), particularly in Grade C AVMs (8/11 (73%),  $P<0.001$ ), than the S group (7/44 (16%)). Multiple drainers were significantly more frequent in the N group (22/29 (76%)) than the S group (22/44 (50%)) ( $P=0.031$ ). The presence of a daughter nidus, associated aneurysm and varix were not different among the groups. The supply from the meningeal feeder (S group: 6/44 (14%), N group:11/29 (38%))

was significantly frequent in the N group ( $P=0.023$ ).

### Comparison of embolization performance by SRS grade

Table 4 shows the comparison of embolization performance by SRS grade. The E grade groups were divided into two groups by the rate of successful nidus embolization; one was the successful embolization group, including E grades A1 and A2 ( $n=32$ ); and the other was the unsuccessful group, including E grades B1, B2 and C ( $n=41$ ). In the former group, SRS grade A was achieved in 30 patients (94%), while in the latter, SRS grade A was achieved in only 14 patients (34%). There was a significant difference between the two groups ( $P<0.001$ ). Because a small AVM has more potential for complete occlusion after SRS without the aid of embolization, subanalysis was performed to target the relatively larger AVMs ( $n=43$ ; S group: 21 (49%), N group: 22 (51%)), excluding AVMs less than

**Table 4.** Performance of Embolization

Grade of radiosurgical effect (SRS grade) category of group total number		Total	A S group	B	C	B + C N group	S vs N group
Performance of embolization		73	44	18	11	29	
Embolization grade	E grade A1	12	12	0	0	0	<0.001
	E grade A2	20	18	2	0	2	
	E grade B1	19	8	7	4	13	
	E grade B2	18	6	5	7	12	
	E grade C	2	0	2	0	2	
Final embolization rate		61.2%	63.6%	60.0%	53.6%	57.6%	NS
Final results of embolization	complete occlusion	7	6	1	0	1	NS
Size of remained nidus (diameter)	<1 cm	22	16	5	1	6	
	1-2 cm	24	8	2	10		
	2-3 cm	13	3	4	6	10	
	$\geq 3$ cm	7	0	2	2		
Procedure-related complications	total	14	7	5	2	7	NS
	hemorrhage (inta- & perioperative)	8	6	2	0	2	
	convulsion	2	0	1	1	2	
	others	4	1	2	1	3	
Influence of complication on outcome	none	11	7	2	2	4	NS
	mRS 1 rank down	1	0	1	0	1	
	mRS 2 rank down	1	0	1	0	1	
	mRS 3 rank down	1	0	0	1	1	

## Effectiveness of Preradiosurgical Embolization of Brain AVM

**Table 5.** Performance of Radiosurgery

grade of radiosurgical effect (SRS grade)		Total	A	B	C	B + C	
category of group			S group			N group	
total number		73	44	18	11	29	S vs N group
<b>Performance of radiosurgery</b>							
Post-radiosurgery complications	total	4	0	1	3	4	0.022
	hemorrhage, rebleeding	3	0	1	2	3	
	delayed cystic formation	1	0	0	1	1	
Influence of complication on outcome	none	0	0	0	0	0	0.022
	mRS 1 rank down	2	0	0	2	2	
	mRS 2 rank down	1	0	1	0	1	
	mRS 3 rank down	1	0	0	1	1	

3 cm in diameter. These results also showed a significant difference between small and larger AVMs ( $P < 0.001$ ). The size of the remaining nidus, one of the main factors defining the marginal dose of radiosurgery, was compared between the S and N groups. Remaining nidus was observed following embolization in 67 AVMs (S group: 38/44 (86%), N group: 28/29 (97%)). The comparison was performed between two groups that had a maximum remaining nidus diameter of more and less than 2 cm. A smaller remaining nidus (less than 2 cm in maximum residual nidus diameter) was seen in 22 cases (50%) in the S group but was seen in only 7 cases (24%) in the N group. There were significant differences in this analysis ( $P = 0.03$ ), and the subanalysis in the 43 cases of larger AVMs excluding AVMs less than 3 cm in maximum diameter also demonstrated a difference ( $P = 0.05$ ).

When we performed another subanalysis with another categorization, SRS-group A + B vs. group C, there was a significant difference in the rate of successful embolization ( $P < 0.002$ ). There was no significant difference in the rate of procedure related complications (S group: 7/44 (16%), N group 7/29 (24%)) and the rate of morbidity between the two groups. Post-radiosurgery complications were not encountered in the S group and significantly higher in the N group (4/29(14%) ( $P = 0.022$ )).

### Multivariate analysis between the size and embolization specification

We performed a selective multivariate study focusing on AVM size and embolization specification. As important factors corresponding to either the S or N group, the mRBAS, nidus type, embolization grade and

residual nidus size were selected and analyzed. Of these four factors, a significant difference was obtained in the nidus type (odds ratio 0.261, 95% CI: 0.073–0.938,  $P = 0.04$ ) and embolization grade (odds ratio = 4.397, 95% CI 2.113–9.149,  $P < 0.001$ ).

## DISCUSSION

There have been many reports supporting the usefulness of embolization preceding surgical removal and SRS, which can make the subsequent treatment easier, safer and more successful [1–5, 16]. By contrast, recent reports addressed the negative effect of preradiosurgical embolization. Embolization prior to SRS was associated with a lower rate of total obliteration than radiosurgery alone [12, 14] and had no sufficient role in reducing the recurrence correlated with deep regions [10]. The main reasons for such a result might include the followings: 1) the embolization blurs the nidus margin and causes a targeting error, 2) a part of the nidus that disappears just after the proximal feeder occlusion due to the temporary flow regression is outside of the radiosurgery target and may later recanalize due to hemodynamic remodeling [11–14, 20, 21].

For the adverse events secondary to the radiosurgery, the rate of post-radiosurgery hemorrhage is not affected by preceding embolization [21, 22]. There are conflicting reports on radiation-induced change; one shows no correlation and larger complications with preceding embolization [4, 14, 23]. Additionally, it is obvious that the larger AVM may result in a lower obliteration rate for SRS. A higher tendency of the larger nidus of the virgin state was observed in the N group in our study. Therefore, we performed a multivariate study to clarify



the significance of specification or quality of the embolization independent of the original AVM size. The result suggested that a successful SRS is expected to increase by more than four times for each increase in embolization grade. Therefore, the embolization grade was a strongly independent factor that influenced the success of SRS, which may suggest that a proper and meticulous embolization strategy, highly skillful microcatheterization, and best performance of injecting liquid embolic materials are essential for achieving good results. The diffuse type of AVM makes it a challenge to perform the ideal embolization. Therefore, we should preoperatively evaluate the type of nidus, and cases without the possibility of sufficient embolization should be omitted from the plan of preradiosurgical embolization. By contrast, cases with high odds of embolization that affect the positive use of embolization will contribute to and complement the desirable result of SRS.

Although we did not compare the results between two groups with and without embolization, we showed that a high quality embolization is essential to achieve ideal radiosurgery results. The embolization of nidus is particularly important for avoiding recanalization and regional vascular remodeling, as mentioned in many previous reports from the past century [2,3,17]. However, when treating cases with a diffuse, large AVM in which effective embolization is difficult, we should consider novel combined treatment options. Yashar et al. [24] recommends that the compartments of an embolized AVM should be contained within the radiosurgery plan. According to this concept, volume-staged radiosurgery [25–27] and preembolization radiosurgery [11] may be useful.

This study is a retrospective case cohort study of the limited institutes employing operators with a reliable and proper technique and strategy for AVM embolization. Therefore, larger prospective studies will be needed to confirm the findings.

## CONCLUSION

Embolization before radiosurgery remains a controversial neoadjuvant therapy. It is clear that reducing the size and shunt flow of AVMs improves the effect of SRS. Although sufficient volume reduction should be the most important goal of embolization, false occlusion due to the temporary depression of hemodynamics may disappoint radiosurgeons. This study showed that proper embolization with a high rate of nidus penetration to avoid recanalization is important

for complete, cooperative combined treatments. A proper strategy and technique is essential for promoting occlusion following SRS.

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