Risk factors for worsened muscle strength after the surgical treatment of arteriovenous malformations of the eloquent motor area

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OBJECTIVE Case selection for the surgical treatment of arteriovenous malformations (AVMs) of the eloquent motor area remains challenging. The aim of this study was to determine the risk factors for worsened muscle strength after surgery in patients with this disorder.

METHODS At their hospital the authors retrospectively studied 48 consecutive patients with AVMs involving motor cortex and/or the descending pathway. All patients had undergone preoperative functional MRI (fMRI) and diffusion tensor imaging (DTI), followed by resection. Both functional and angioarchitectural factors were analyzed with respect to the change in muscle strength. Functional factors included lesion-to-corticospinal tract distance (LCD) on DTI and lesion-to-activation area distance (LAD) and cortical reorganization on fMRI. Based on preoperative muscle strength, the changes in muscle strength at 1 week and 6 months after surgery were defined as short-term and long-term surgical outcomes, respectively. Statistical analysis was performed using the statistical package SPSS (version 20.0.0, IBM Corp.).

RESULTS Twenty-one patients (43.8%) had worsened muscle strength 1 week after surgery. However, only 10 patients (20.8%) suffered from muscle strength worsening 6 months after surgery. The LCD was significantly correlated with short-term ($p < 0.001$) and long-term ($p < 0.001$) surgical outcomes. For long-term outcomes, patients in the $5 \text{ mm} \geq \text{LCD} > 0 \text{ mm}$ ($p = 0.009$) and $\text{LCD} > 5 \text{ mm}$ ($p < 0.001$) categories were significantly associated with a lower risk of permanent motor worsening in comparison with patients in the $\text{LCD} = 0 \text{ mm}$ group. No significant difference was found between patients in the $5 \text{ mm} \geq \text{LCD} > 0 \text{ mm}$ group and $\text{LCD} > 5 \text{ mm}$ group ($p = 0.116$). Nidus size was the other significant predictor of short-term ($p = 0.021$) and long-term ($p = 0.016$) outcomes. For long-term outcomes, the area under the ROC curve (AUC) was 0.728, and the cutoff point was 3.6 cm. Spetzler-Martin grade was not associated with short-term surgical outcomes (0.143), although it was correlated with long-term outcomes (0.038).

CONCLUSIONS An AVM with a nidus in contact with tracked eloquent fibers ($\text{LCD} = 0$) and having a large size is more likely to be associated with worsened muscle strength after surgery in patients with eloquent motor area AVMs. Surgical treatment in these patients should be carefully considered. In patients with an $\text{LCD} > 5 \text{ mm}$, radical resection may be considered to eliminate the risk of hemorrhage.

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KEY WORDS functional magnetic resonance imaging; diffusion tensor imaging; cerebral arteriovenous malformations; surgery; motor function; risk factor

ABBREVIATIONS AUC = area under the ROC curve; AVM = arteriovenous malformation; BOLD = blood oxygen level–dependent; CST = corticospinal tract; DSA = digital subtraction angiography; DTI = diffusion tensor imaging; DW = diffusion weighted; EPI = echo-planar imaging; FA = fractional anisotropy; FAPA = feeding artery from perforating artery; fMRI = functional MRI; LAD = lesion-to-activation area distance; LCD = lesion-to-CST distance; MS = preoperative muscle strength; MS₁ = muscle strength 1 week postoperatively; MS₂ = muscle strength 6 months postoperatively; NPPB = normal perfusion pressure breakthrough; ROC = receiver operating characteristic; ROI = region of interest; SM = Spetzler-Martin; TOF = time-of-flight.

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SURGICAL treatment of arteriovenous malformations (AVMs) close to motor cortex or motor projection systems is challenging. In patients with Spetzler-Martin (SM) Grade III to V AVMs in eloquent cortex, the risk of surgery is greater than 16% and can be as high as 41%.⁹ Therefore, identifying AVMs in eloquent motor areas that can be safely resected becomes a priority. Although Spetzler and Martin²⁸ and Lawton et al.²³ have proposed grading systems to estimate the risk of surgery based on architectural features, case selection for the surgical treatment of eloquent motor area AVMs remains difficult. Case selection for surgery depends on a sophisticated understating of the angioarchitecture and relationships to surrounding eloquent brain structures.⁶ Advances in imaging techniques, for example functional MRI (fMRI) and diffusion tensor imaging (DTI), may present new opportunities to select individual patients more safely. Functional MRI enables functional mapping of at-risk cortex in the vicinity of an AVM,^{1,8} and DTI allows assessment of important white matter tracts.^{5,27} However, the literature regarding the prognostic utility of factors derived from these functional images is limited to a few case reports and small series (Table 1). Therefore, evidence of a positive impact from these functional factors on patient selection is pending. The aim of this study was to determine risk factors for worsened muscle strength after surgery in patients with this challenging entity. Both functional and angioarchitectural factors were analyzed with respect to surgical outcomes in patients with eloquent motor area AVM.

Methods

Clinical Material

Between September 2012 and September 2014, 48 patients with AVMs involving primary and secondary motor cortex, corona radiata, and posterior limb of the internal capsule were enrolled and surgically treated in a prospective clinical trial assessing the effect and safety of fMRI navigation in brain AVM surgery.³³ Radical resections were documented with postoperative digital subtraction angiography (DSA). All procedures in the present study

were performed in accordance with the sixth revision (2008) of the Declaration of Helsinki and the principles of our institutional review board. Written informed consent was obtained from all the patients involved. Two experienced neurosurgeons (F.L., J.W.) collected the clinical information from the prospectively collected database and electronic medical records system. During the above-mentioned study period, 22 patients were conservatively observed in our hospital.

Neuroimaging

Computed tomography, MRI, and DSA studies were obtained for all the patients. Functional MRI and DTI were performed on a 3.0-T MR system (SIEMENS Trio) within 1 week before surgery. The sagittal T1 anatomical image acquired was a gradient-echo sequence: TR 2300 msec, TE 2.98 msec, slice thickness 1 mm, slices 176, FOV 256 mm, flip angle 9°, matrix 64 × 64, voxel size 1 × 1 × 1 mm³, bandwidth 240. The blood oxygen level-dependent (BOLD) fMRI sequences were collected with standard spin-echo echo-planar imaging (EPI): TR 3000 msec, TE 30 msec, matrix 64 × 64, axial slices 30 including all cerebral areas, isotropic resolution 3 mm. The repetitive finger-to-thumb opposition movements or flexion-extension movements of the foot were used as the motor stimulation paradigms, with 64 repetitions and a 24-second task and 24-second control state alternately. The DTI was performed using the diffusion-weighted (DW)-EPI technique: TR 6100 msec, TE 93 msec, slice thickness 3 mm, slices 45, FOV 230 × 230 mm², matrix 128 × 128 with a motion-probing gradient in 30 orientations. Axial time-of-flight (TOF)-MRA was performed using a 3D TOF gradient-echo acquisition sequence: TR 22 msec, TE 3.86 msec, slice thickness 1 mm, slices 36 × 4, FOV 220 × 220 mm², flip angle 120°, matrix 512 × 512.

Generated image sets were processed on the iPlan 3.0 workstation (BrainLab). All image sets were automatically coregistered with each other and fused to the anatomical images by an automatic rigid registration. A significance threshold of $p < 0.001$ ($T = 6.5$) was considered for identification of activated clusters. Two neurosurgery

TABLE 1. Prognostic utility of functional factors derived from fMRI and DTI in the literature

Authors & Year	Factor(s)	Sample Size*	Statistical Method	Conclusion
Lee et al., 2013	Cortical Reorganization	3	Fisher exact test	Cortical reorganization on fMRI is correlated w/ good surgical outcomes
Gallagher et al., 2013	LAD	<24†	Chi-square test, multivariate regression test	No significant relationship is found btwn LAD & postop motor deficits
Lepski et al., 2012	LAD+LCD	12	Chi-square test	Detailed functional assessment makes resection of AVM in eloquent motor area feasible
Ellis et al., 2012	LCD	2	—	Functionally guided DTI is useful in preop planning
Tunttiatorm et al., 2011	LAD	3	—	Short LAD is correlated w/ iatrogenic deficits
Baciu et al., 2003	Cortical reorganization	1	—	Cortical reorganization is an important factor for surgical decision

Cortical reorganization = cortical reorganization on preoperative fMRI.

* The number of patients who had undergone surgery in the cited article.

† Exact number not reported.

residents (B.Z., L.W.), on consensus, documented the anatomical locations of the activation and peak motor activity point for each paradigm. They were blinded to the patient outcomes. We used the inferior portion of the pons and precentral gyrus as the regions of interest (ROIs) to track the corticospinal tract (CST). A default fractional anisotropy (FA) threshold of 0.20 and a minimum fiber length of 70 mm were used. The 2 neurosurgery residents also documented on consensus the locations of the ROIs and the information about the tracked fiber tracts. All the processed data sets were incorporated into the neuronavigation platform for intraoperative neuronavigation.

Data Collection and Definition

Patient demographics including age and sex were collected. Angioarchitectural variables for each AVM such as size, diffuseness, feeding artery from perforating arteries (FAPAs), deep draining veins, and Spetzler-Martin (SM) grade were determined from preoperative angiograms and MRI scans.²³ Functional variables were measured depending on the location of the vascular lesion. The function with its activated areas closer to the lesion was selected (contralateral hand or foot). If the lesion involving only the descending pathway or both the precentral knob and the paracentral lobule were involved, the function of the contralateral hand was selected as representative. Lesion-to-activation area distance (LAD)¹⁴ and lesion-to-CST distance (LCD)²⁶ were measured. Sections for measurement were manually selected where the activated area or the tracked fiber appeared to be nearest to the margin of the nidus on the TOF images (Fig. 1). Subjects were assigned to 1 of the following groups according to the mea-

sured distances: Group 1, distance > 5 mm; Group 2, 5 mm $\geq$ distance > 0 mm; Group 3, distance = 0 mm. The BOLD activation patterns were dichotomized into with- or without-reorganization groups. Cerebral reorganization occurred when the extent (number of activated pixels) of motor activation at other areas was at least equal to or greater than motor activation in the anatomically expected functional area. Normal perfusion pressure breakthrough (NPPB) was also recorded for its dramatic influence on surgical outcomes.

The muscle strength of the hand or foot that had been chosen to measure functional variables was used to grade surgical outcomes. Muscle strength assessments (Medical Research Council Scores 0–5) were performed preoperatively (MS), 1 week postoperatively (MS₁), and up to 6 months postoperatively (MS₂; Table 2). Surgical outcomes were analyzed in terms of the change between preoperative and postoperative muscle strength (MS₁ – MS [short-term outcome] or MS₂ – MS [long-term outcome]). Good outcome was defined as a change of greater than or equal to 0 (improved or stable) in the muscle strength score, and bad outcome was defined as a change of less than 0 (worsened or dead) in the muscle strength score.

Surgery

The selection of surgical or conservative treatment for eloquent motor area AVM was based on clinical presentation, patient condition, patient requirements, and prospective surgical risks. If a patient had no hemorrhagic history and symptoms were controlled by medications or the SM grade was VI,²⁸ conservative treatment was often recommended. Surgery was only recommended for pa-

FIG. 1. Preoperative and postoperative functional images from a representative patient. Sections for measurements were manually selected where the tracked fiber (**A and B**) or activated area (**D and E**) appeared to be nearest to the margin of the nidus on the TOF images. Postoperative images showed that both the descending fiber (**C**) and the motor cortex (**F**) were well preserved.

TABLE 2. Preoperative and postoperative muscle strength of patients with eloquent motor area AVMs

Muscle Strength Score*	No. (%)		
	Preop MS	Postop MS ₁	Postop MS ₂
0	0 (0.0)	0 (0.0)	1 (2.1)
1	0 (0.0)	4 (8.3)	0 (0.0)
2	0 (0.0)	3 (6.3)	2 (4.2)
3	1 (2.1)	5 (10.4)	1 (2.1)
4	4 (8.3)	13 (27.1)	8 (16.7)
5	43 (89.6)	23 (47.9)	36 (75.0)

MS = preoperative muscle strength; MS₁ = muscle strength 1 week postoperatively; MS₂ = muscle strength 6 months postoperatively.
* According to the Medical Research Council scale of 0–5.

tients with serious headache, intractable seizure, progressive neurological deficit, and previous hemorrhage. Operations were performed or supervised by an experienced vascular neurosurgeon (S.W.). All patients underwent a craniotomy under general anesthesia without the use of muscle relaxants. Each AVM resection was completed while taking special care to preserve functional cortex

and white matter tracts with the help of cortical/subcortical electrical stimulation and the neuronavigation system (Figs. 2 and 3). After operation, patients were maintained in a hypotensive state and treated with mannitol, barbiturates, and dexamethasone therapy. Postoperative CT scanning was performed immediately to rule out intracranial hemorrhage if any neurological symptoms were found. Five days later, DSA was performed to confirm the radical obliteration.

Statistical Analysis

Statistical analysis was performed using the statistical package SPSS (version 20.0.0, IBM Corp.). An independent-samples t-test was used for continuous variables. For the significant continuous variables, receiver operating characteristic (ROC) analysis was applied to determine the predictive value and cutoff point based on long-term outcomes. A chi-square test or Fisher exact test was used for categorical variables. A Spearman test was used for ordered multiple categorical variables. For the statistically significant ordered multiple categorical variables, differences between the subgroups were analyzed using the Fisher exact test or chi-square test. A p value < 0.05 was considered statistically significant.

FIG. 2. Intraoperative identification of the motor cortex in the same patient whose images are featured in Fig. 1. The navigation system guided to the possible position of the motor cortex (A and B), which was then confirmed by direct cortical electrical stimulation (C). Cortex with positive sites on stimulation was marked (D). Tracings (E) from direct cortical electrical stimulation of eloquent motor cortex.

Results

Clinical Characteristics and Surgical Outcomes

Of the 48 surgically treated patients, 28 were male and 20 were female, and their mean age was 26.9 ± 11.1 years. Preoperative motor function was intact in most of the patients (89.6%). In 1 patient, no activation was found in either hemisphere during movements of the left hand, so the functional factors derived from fMRI were available in 47 patients (97.9%). Two patients (4.2%) suffered from NPPB postoperatively; 1 patient died and the other had permanent paralysis. No residual lesion was found according to postoperative DSA. Twenty-one patients (43.8%) had worsened muscle strength at 1 week after surgery. However, only 10 patients (20.8%) suffered from permanent muscle strength deterioration 6 months after surgery (Table 3).

Risk Factors

Significant differences in LCD ($p < 0.001$) and nidus size ($p = 0.021$) were found between the patient cohorts

with and without postoperative muscle strength worsening in short-term outcomes. Age ($p = 0.053$), LAD ($p = 0.071$), and cortical reorganization on fMRI ($p = 0.063$), only showed a trend toward significance. However, no significant difference was found in the other factors (Table 4). In the subgroup analysis of LCD, the chi-square and Fisher exact tests showed that patients in the $5 \text{ mm} \geq \text{LCD} > 0 \text{ mm}$ ($p = 0.006$) and $\text{LCD} = 0 \text{ mm}$ ($p = 0.001$) categories were more likely to have worsened motor function in comparison with $\text{LCD} > 5 \text{ mm}$ group at 1 week after surgery. However, no significant difference was found between patients in $5 \text{ mm} \geq \text{LCD} > 0$ group and $\text{LCD} = 0$ mm group ($p = 0.457$; Table 5).

For long-term surgical outcomes, among the architectural factors, a large nidus size ($p = 0.016$), higher SM score (0.038), and diffuse nidus ($p = 0.016$) were significantly associated with an increased risk of worsened muscle strength. An ROC analysis was performed to test the predictive value of the nidus size. The area under the ROC curve (AUC) was 0.728, and the cutoff point was 3.6 cm (Fig. 4). Among the functional factors, significant differ-

FIG. 3. Intraoperative monitoring of CSTs in the same patient whose images are featured in Fig. 1. The AVM resection was completed while taking special care to preserve the white matter tracts with the help of the navigation system (A–C) and subcortical electrical stimulation (D). Tracings (E) from subcortical electrical stimulation of the area close to the CST.

TABLE 3. Demographic and clinical characteristics of patients with eloquent motor area AVM

Variable	No. (%)
No. of patients	48
Age (yr)	26.9 ± 11.1
Sex	
Male	28 (58.3)
Female	20 (41.7)
Nidus size (cm)	4.2 ± 1.4
Preop muscle strength score	
5	43 (89.6)
0–4	5 (10.4)
AVM nidus	
Compact	42 (87.5)
Diffuse	6 (12.5)
FAPA	
No	34 (70.8)
Yes	14 (29.2)
Deep draining vein	
No	44 (91.7)
Yes	4 (8.3)
Mean SM grade	3.04 ± 0.6
LAD (mm)	
>5	32 (66.7)
5 ≥ LAD > 0	9 (18.8)
0	7 (14.6)
LCD (mm)	
>5	33 (68.8)
5 ≥ LCD > 0	10 (20.8)
0	4 (8.3)
Cortical reorganization	
No	37 (77.1)
Yes	11 (22.9)
NPPB	
No	46 (95.8)
Yes	2 (4.2)
Residual lesion	
No	48 (100.0)
Yes	0 (0.0)
Worsened muscle strength 1 wk after surgery	
No	27 (56.3)
Yes	21 (43.8)
Worsened muscle strength 6 mos after surgery	
No	38 (79.2)
Yes	10 (20.8)

Cortical reorganization = cortical reorganization on preoperative fMRI.

ences in LCD ($p < 0.001$) and LAD ($p = 0.001$) were found between the patient cohorts with and without long-term muscle strength worsening. When grouped by LAD, most of the patients with LAD > 5 mm had excellent outcomes (90.9%). However, muscle strength worsening appeared frequent and permanent in patients with LAD = 0 (75%; Table 3). In the subgroup analysis, a significant difference was found between patients in LAD = 0 mm group and in

LAD > 5 mm group ($p = 0.01$). However, there was no difference between the 5 mm ≥ LAD > 0 group and the other 2 groups (Table 5). When grouped by LCD, all the patients with LCD > 5 mm were free from worsened muscle strength except 1 patient, who had a large and diffuse nidus and suffered from NPPB. Conversely, all patients with LCD = 0 had permanent muscle strength worsening (Table 3). In the subgroup analysis, the 5 mm ≥ LCD > 0 mm ($p = 0.009$) and LCD > 5 mm ($p < 0.001$) categories were significantly associated with a lower risk of permanent muscle strength worsening in comparison with the LCD = 0 mm group. No significant difference was found between 5 mm ≥ LCD > 0 and LCD > 5 mm groups ($p = 0.116$; Table 5). Cortical reorganization had a trend but was not significantly correlated with worsened muscle strength in long-term outcomes ($p = 0.062$). The NPPB was associated with a significant higher risk of a bad outcome compared with patients with an uneventful outcome ($p = 0.04$).

Discussion

At present, there is no standard guideline for selecting for surgery those patients with AVMs in eloquent motor areas. Conservative follow-up or radiosurgery are often recommended for patients with AVMs close to eloquent motor areas.³² For conservatively treated patients, although the overall annual hemorrhage rate is 3.0% (95% CI 2.7%–3.4%), AVM hemorrhage has been associated with long-term neurological morbidity and mortality as high as 35% and 29%, respectively.¹⁶ The results of published series describing stereotactic radiosurgery in larger AVMs are no more promising than those from surgical series, with a low obliteration rate, bleeding during the latent period, and an increasing risk of radiation-induced complications.⁹ Recently, advanced functional imaging techniques have significantly contributed to reducing perioperative morbidity.²⁵ Therefore, when performed in conjunction with proper patient selection criteria, including functional factors, resection of AVMs in eloquent motor areas may be considered a safe option. Krishnan et al.²² investigated the correlation between the lesion-to-fMRI voxel activation distance and the occurrence of new postoperative motor deficits in 54 patients with peri-rolandic tumors. These authors concluded that an LAD < 5 mm may be associated with a higher risk of postsurgical neurological deterioration. On the other hand, in most cases, radical resection is often needed in patients with AVMs to eliminate the risk of bleeding after surgery. Thus, the nidus in contact with eloquent tissue (distance = 0 mm) may be a significant risk factor for a bad surgical outcome. Therefore, we chose 5 and 0 mm as the cutoff points to investigate the correlation between functional measurements and surgical outcomes.

In this study, LCD was significantly associated with the occurrence of postoperative muscle strength worsening in both the short-term and the long-term. Patients with an LCD ≤ 5 mm had a significantly higher risk of worsened muscle strength in the short-term compared with patients having an LCD > 5 mm. However, 6 months after surgery, only patients with an AVM nidus in contact with the tracked fiber (LCD = 0) showed a significantly higher risk of permanent motor deterioration. During the

TABLE 4. Difference in demographic, angioarchitectural, and functional features between patients with and without postoperative worsened motor function

Variable	No. (%)					
	Postop MS ₁			Postop MS ₂		
	Improved/Stable	Worsened	p Value*	Improved/Stable	Worsened	p Value*
No. of patients	27 (56.3)	21 (43.8)	—	38 (79.2)	10 (20.8)	—
Mean age (yrs)	29.5 ± 12.5	23.5 ± 8.2	0.053	27.6 ± 11.6	24.3 ± 9.2	0.416
Sex			0.461			0.810
Male	17 (60.7)	11 (39.3)		23 (82.1)	5 (17.9)	
Female	10 (50.0)	10 (50.0)		15 (75.0)	5 (25.0)	
Nidus size (cm)	3.8 ± 1.2	4.7 ± 1.6	0.021	3.9 ± 1.6	5.2 ± 1.4	0.016
Preop muscle strength score			0.513			1.000
5	23 (53.5)	20 (46.5)		34 (79.1)	9 (20.9)	
0–4	4 (80.0)	1 (20.0)		4 (80.0)	1 (20.0)	
AVM nidus			0.099			0.016
Compact	26 (61.9)	16 (38.1)		36 (85.7)	6 (14.3)	
Diffuse	1 (16.7)	5 (83.3)		2 (33.3)	4 (66.7)	
FAPA			0.936			1.000
No	19 (55.9)	15 (44.1)		27 (79.4)	7 (20.6)	
Yes	8 (57.1)	6 (42.9)		11 (78.6)	3 (21.4)	
Deep draining vein			0.792			0.566
No	24 (54.5)	20 (45.5)		34 (77.3)	10 (22.7)	
Yes	3 (75.0)	1 (25.0)		4 (100.0)	0 (0.0)	
Mean SM grade	2.93 ± 0.6	3.19 ± 0.6	0.143	2.95 ± 0.6	3.40 ± 0.5	0.038
LAD (mm)			0.071			0.001
>5	21 (63.6)	12 (36.4)		30 (90.9)	3 (9.1)	
5 ≥ LAD > 0	4 (40.0)	6 (60.0)		6 (60.0)	4 (40.0)	
0	1 (25.0)	3 (75.0)		1 (25.0)	3 (75.0)	
LCD (mm)			<0.001			<0.001
>5	25 (78.1)	7 (21.9)		31 (96.9)	1 (3.1)	
5 ≥ LCD > 0	2 (22.2)	7 (77.8)		7 (77.8)	2 (22.2)	
0	0 (0.0)	7 (100.0)		0 (0.0)	7 (100.0)	
Cortical reorganization			0.063			0.062
No	24 (64.9)	13 (35.1)		32 (86.5)	5 (13.5)	
Yes	3 (27.3)	8 (72.7)		6 (54.5)	5 (45.5)	
NBBP			0.186			0.040
No	27 (58.7)	19 (41.3)		38 (82.6)	8 (17.4)	
Yes	0 (0.0)	2 (100.0)		0 (0.0)	2 (100.0)	

* Bolded values signify statistical significance.

6-month follow-up period, 5 (71.4%) of 7 patients with 5 mm ≥ LCD > 0 recovered from transient muscle strength worsening. This finding may be attributable to the elimination of the surrounding edema or minor iatrogenic damage to the CST, which could be completely compensated for. Diffusion tensor imaging has a unique advantage in identifying and estimating neural tracts at the subcortical level.²⁷ In the literature, DTI reconstructions of the CST are reasonably accurate and reliable and therefore can be used in the preoperative period for trajectory and resection strategy planning in brain tumor patients.^{1,34} In stroke studies, authors have proposed that preservation or recovery of the CST on DTI is mandatory for good recovery of impaired motor function.^{15,20} However, the impact of LCD on surgical outcomes in patients with AVMs in eloquent areas has not been determined.⁶ In recent years the

feasibility of DTI in tracking fibers in AVM patients has been proven, although it has some methodological limitations.^{11–13,19,26} Thus, it is reasonable to assume that LCD can be used in predicting the surgical outcomes in patients with eloquent motor area AVMs, and our results confirmed this hypothesis.

The predictive value of LAD was not as significant as we had expected in this patient series. A significant difference in long-term outcomes was found only between patients with an LAD = 0 and an LAD > 5 mm. The validity of BOLD activation has been shown to be sensitive (83%) and specific (83%) for mapping language and motor functions in the context of brain tumor.⁷ However, there is no study to validate the accuracy of BOLD activation in brain AVM patients by intraoperative electrocortical mapping. Therefore, the predictive value of LAD is still contro-

TABLE 5. Comparison between LAD and LCD subgroups based on short-term and long-term surgical outcomes

Subgroups Based on Measured Distances*	p Value†	
	LAD	LCD
Short-term outcomes		
Group 1 vs 2	0.336	0.006
Group 1 vs 3	0.344	0.001
Group 2 vs 3	1.000	0.457
Long-term outcomes		
Group 1 vs 2	0.067	0.116
Group 1 vs 3	0.010	<0.001
Group 2 vs 3	0.554	0.009

* Group 1, distance > 5 mm; Group 2, 5 mm ≥ distance > 0 mm; Group 3, distance = 0 mm.

† Bolded values signify statistical significance.

versal in AVM patients, especially as concerns different functions according to the various authors (Table 1). The probable explanations for the weak correlation between LAD and surgical outcomes are as follows. 1) Pathophysiological factors, including gliosis, hemosiderosis, neovascularity, and AVM-induced hemodynamic effects, may cause neurovascular uncoupling and reduce fMRI signal in perilesional eloquent cortex.³¹ 2) Observational methods such as fMRI do not prove necessity or sufficiency of a particular area for function; instead, fMRI is only able to demonstrate a particular area's involvement in motor function.¹ 3) White matter involvement could be contributing to and confounding the relationship.¹⁴

As AVMs are formed early in fetal development, we usually postulate that when they develop in the usual anatomical site of eloquent cortex, neuroplasticity will result in cortical reorganization of the functional areas.^{3,24} Many authors have concluded that cortical reorganization on fMRI is correlated with good surgical outcomes and is an important factor for surgical decision making (Table 1). However, in this study cortical reorganization had a trend but was not significantly correlated with worsened muscle strength in the long-term (45.5% vs 54.5% $p = 0.062$). Until now, the reliability of cortical reorganization on fMRI has been controversial in the context of AVM. Ulmer et al. proposed that lesion-induced neurovascular uncoupling causing reduced fMRI signal in perilesional eloquent cortex may simulate lesion-induced cortical reorganization.³¹ On the other hand, in a more recent study, functional brain mapping using navigated transcranial magnetic stimulation showed that no plastic relocation of the primary motor cortex was observed in the 6 patients with AVMs near the rolandic region, even if the anatomy was severely obscured by the rolandic AVM.²¹ Therefore, it seems that cortical reorganization on fMRI is not a significant predictor of surgical outcomes.

Nidus size was another significant predictor of long-term surgical outcome ($p = 0.016$; AUC = 0.728), and the cutoff point was 3.6 cm. This result is consistent with the widely accepted SM grading system ($p = 0.038$), in which nidus size is the most weighted part.²⁸ The larger an AVM

FIG. 4. Receiver operating characteristic (ROC) analysis curve for the nidus size. The AUC was 0.728, and the cutoff point was 3.6 cm. Figure is available in color online only.

the greater the amount of normal adjacent neural tissue exposed to injury, the longer the operating time, the greater the number of feeding arteries, the larger the amount of flow, and the higher the degree of steal. The larger amount of flow and the higher degree of steal are associated with a higher risk of postoperative NPPB.²⁹ Furthermore, a larger AVM nidus size means a deeper location and a larger number of feeding arteries including the FAPA. Feeding arteries from perforating arteries are thin, fragile, and difficult to occlude with cautery. Bleeding during surgery can escape into deep white matter tracts and cause significant deficits.¹⁰ However, in this study the FAPA was not an independent risk factor for short- or long-term outcomes. As most of the lesions in this study were superficial AVMs involving motor cortex, only 14 (29.2%) of the lesions possessed an FAPA. The small sample size may have tempered the significance of FAPA. A diffuse nidus was another significant predictor of worsened muscle strength in the long-term in this study. Diffuse AVMs with ragged borders and intermixed brain force the neurosurgeon to establish dissection planes that may extend into eloquent brain tissues.^{10,18}

Suggestions for Patient Selection

Based on our results and the literature, we put forward some suggestions for patient selection in surgically treating this challenging entity. 1) In patients with an LCD > 5 mm, radical resection may be considered to eliminate the risk of hemorrhage. 2) In patients with an LCD = 0, surgical obliteration is more likely to cause permanent muscle strength worsening; therefore, alternative therapeutic strategies might be applied, such as stereotactic radiosurgery,² endovascular embolization,¹⁷ or conservative treatment. 3)

In patients with $5 \text{ mm} \geq \text{LCD} > 0$, surgical treatment seems to have a high risk of transient muscle strength worsening, and a meticulous technique should be performed to protect the CST during surgery.

Study Limitations

This study has some limitations. First, it was a retrospective study with a relatively small number of patients, so it is difficult to avoid selection bias, information bias, and confounding factors. Second, we have no data on patients treated with radiosurgery and embolization and thus we could not compare the outcomes of different treatment modalities. Nonetheless, we determined the risk factors for motor outcomes following radical resection. These results may help to select patients for surgical treatment of eloquent motor area AVMs.

Conclusions

An AVM nidus in contact with tracked eloquent fibers ($\text{LCD} = 0$) and with a large size is more likely to be associated with worsened muscle strength following surgery in patients with eloquent motor area AVMs. Surgical treatment in these patients should be carefully considered. However, in patients with an $\text{LCD} > 5 \text{ mm}$, radical resection may be recommended to eliminate the risk of hemorrhage.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: S Wang, Lin, Cao. Acquisition of data: Lin, Wu, L Wang, Jin. Analysis and interpretation of data: Lin, Zhao, Wu, L Wang, Cao. Drafting the article: Lin, Zhao. Critically revising the article: S Wang, Lin, Cao. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: S Wang. Statistical analysis: Lin, Zhao, Wu. Administrative/technical/material support: S Wang, Lin, Wu, Jin, Cao. Study supervision: S Wang, Jin, Cao.

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