

The efficacy and deficiency of contemporary treatment for spinal cord arteriovenous shunts

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Contemporary treatments for spinal cord arteriovenous shunts are only based on clinicians' treatment experiences and expertise due to its rarity. We reviewed the clinical course of the largest multicentred cohort to evaluate the efficacy and deficiency of contemporary interventional treatments for spinal cord arteriovenous shunts.

The clinical features, treatment results and clinical outcomes of 463 patients with spinal cord arteriovenous shunts were retrospectively assessed. The main outcome was the neurological deterioration that was evaluated based on the modified Aminoff and Logue scale. According to post-treatment digital subtraction angiography, complete obliteration was defined as disappearance of the intradural lesion, whereas partial obliteration was defined as any residual intradural lesion remaining visible and was further categorized as shunt-reduction obliteration (the nidus or shunt points were reduced) or palliative obliteration (only obliterated aneurysms or feeders).

Cure rate was 40.6% for the whole cohort, 58.5% after microsurgery, and 26.4% after embolization. The curative resection was associated with non-metameric lesions, lesions with a maximum diameter <3 cm and lesions without anterior sulcal artery supply. The curative embolization was associated with fistula-type lesions, non-metameric lesions, and main drainage diameter <1.5 mm. The permanent treatment-related neurological deficits rate was 11.2% for the whole cohort, 16.1% after microsurgery, and 5.6% after embolization. The pretreatment clinical deterioration rate was 32.5%/year, which decreased to 9.3%/year after clinical interventions. Following partial treatment, the long-term acute and gradual deterioration rates were 5.3%/year and 3.6%/year, respectively. The acute deteriorations were associated with metameric lesions, craniocervical lesions, lesions with a maximum diameter ≥2 cm and residual aneurysm. Residual aneurysm was the only predictor of acute deterioration for non-metameric spinal cord arteriovenous shunts. The gradual deteriorations were associated with palliative obliteration, absence of pretreatment acute deterioration and intact main drainage.

Although clinical risks of spinal cord arteriovenous shunts were reduced following clinical interventions, contemporary treatments for spinal cord arteriovenous shunt remains associated with considerable risks and incomplete efficacy. Individualized treatment plans should be adopted according to the angio-architectural features and major clinical risks of specific lesions. There is a higher opportunity for complete obliteration for lesions with simple angio-architecture. However, for most of spinal cord arteriovenous shunts with complex vascular anatomy, partial treatment is the only choice. For these patients, palliative obliteration targeting the aneurysms is recommended for reducing haemorrhagic risk, whereas shunt-reduction obliteration is necessary for non-haemorrhagic myelopathy. Contemporary treatment is ineffective in reducing haemorrhagic risk of incurable metameric spinal cord arteriovenous shunts.

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Abbreviations: AVS = arteriovenous shunt; DSA = digital subtraction angiography; SCAVS = spinal cord arteriovenous shunt; SMAVS = spinal metameric arteriovenous shunt

Introduction

Spinal cord arteriovenous shunt (SCAVS) leads to severe neurological deficits in young patients.¹ After initial presentation, the annual rate of neurological deterioration is > 30%.¹ Due to the poor natural history, early clinical intervention is recommended for patients with SCAVS.¹ Current therapeutic modalities, including microsurgical resection and endovascular embolization, can be used alone or in combination to obliterate the arteriovenous shunt (AVS).^{2,3}

However, therapeutic procedures for SCAVSs are challenging because of the highly heterogeneous angio-architecture and their close relationship with the spinal cord.^{1–3} The incidence of permanent treatment-related neurological deterioration was reported to be between 5% and 25%.^{3,4} To avoid iatrogenic neurological deficits, most SCAVSs were partially obliterated only, based on the treatment experiences and expertise of clinicians.^{1–5} Meanwhile, the rarity of SCAVS has restricted the understanding of clinical outcomes of contemporary interventional treatments.^{1,5} Thus, the therapeutic efficacy has not been well assessed, and the treatment strategy for SCAVS is ambiguous.^{2,3,6}

In this study, we investigated the clinical course of the largest multicentred SCAVS cohort to reveal the efficacy and deficiency of contemporary clinical interventions for SCAVSs.

Materials and methods

Patients

We included consecutive patients with SCAVS who were admitted to Xuanwu Hospital, Beijing Haidian Hospital and Beijing United Family Hospital between January 2007 and December 2018. Patients were eligible if they had been surgically or endovascularly treated in our institutes and the intradural AVS location ranged from the atlas to the tip of the conus medullaris. Patients who received their first treatment in other institutes were not included. Patients with concurrent tethered cords, spinal tumours or any other kind of disease that impairs spinal cord function were excluded, as were patients without complete digital subtraction angiography (DSA) data. The study was reviewed and approved by the local ethics committee with waiver of informed consent from patients given its retrospective nature.

Treatment and follow-up

Treatment options included embolization and microsurgery alone or in combination based on the angio-architecture. The endovascular embolization was the prioritized treatment if the neuroradiologist predicted that the arterial route and therapeutic safety were favourable. Except for patients who could not co-operate, endovascular procedures were performed with the patients under local anaesthesia so that the propofol test could be performed when necessary. Glue [n-butylcyanoacrylate (NBCA) or Glubran® 2] was the main embolic agent but was used only when the microcatheter could reach the AVS distal enough to avoid obliteration of the normal spinal supply. Particulate embolization was performed when the microcatheter could not reach the shunts. Coils were used for aneurysmal structures and venous pouches. Ethylene-vinyl alcohol copolymer (Onyx®; ev3™) was used exclusively for extradural AVSs of spinal metameric arteriovenous shunts (SMAVSs).

If endovascular treatment could not completely obliterate the AVSs and the neurosurgeon predicted that the lesion was surgically accessible, microsurgery was performed with the goal of complete resection (Fig. 1). Motor-evoked potential and somatosensory-evoked potential monitoring were performed for all surgical patients.⁷ Since 2013, intraoperative DSA and methylene blue angiography have been used to facilitate the recognition of the angioarchitecture as well as residual AVSs during operation⁸ (Supplementary Video 1).

Digital subtraction angiography evaluation

The angio-architecture parameters of lesions were derived from DSA images by senior interventional neuroradiologists. AVSs were classified as nidus type or fistula type, according to the existence of the intervening nidus; SMAVSs featured multiple AVSs, and the non-spinal cord AVSs were located at the same metameric region as spinal cord lesions. Lesion depth was classified as embedded or superficial based on whether the medial side of lesion reached the midline of the vertebral canal or not on both anteroposterior and lateral view angiograms; the relationship between the lesion and spinal cord (lesion location) was categorized as ventral, lateral, dorsal and central; and the segment of the lesion was classified into five groups, including the cranio-cervical cord (C1–C2), the mid-cervical cord (C3–C5), the cervico-thoracic cord (C6–T2), the mid-thoracic cord (T3–T9) and the thoraco-lumbar cord (T10 to the conus medullaris).

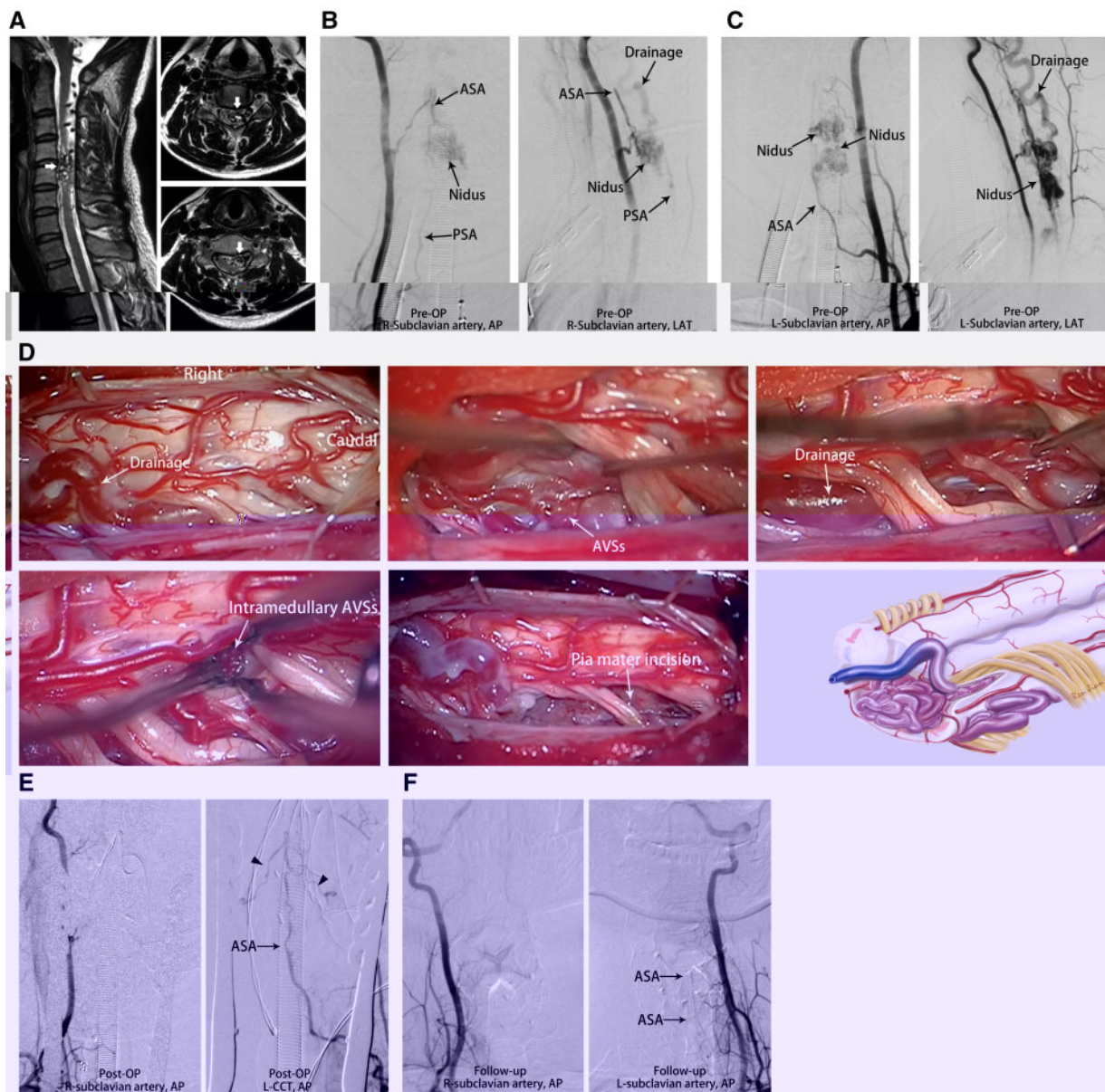


Figure 1 Complete resection of a SCAVS in a 30-year-old female patient who suffered from acute back pain and hemiplegia. (A) Dilated perimedullary vessels and intramedullary (C4–C5) flow void signal (arrow) were noted on T₂-weighted image. (B and C) Preoperation DSA showed the AVSs were supplied by both anterior spinal artery (ASA) and posterior spinal artery (PSA). Main drainage vein of the lesion was on the dorsal side of the spinal cord. (D) The patient received microsurgery in a hybrid operating room. *Top left:* The dura and arachnoid were opened. *Top middle and right:* Perimedullary AVSs were anterior to the dorsal nerve roots. *Bottom left and middle:* Through anterior to dorsal root entry zone myelotomy,³³ intramedullary AVSs were resected. *Bottom right:* Illustration of the lesion and the surgical approach. (E and F) Postoperation DSA (E) and follow-up DSA at 6 months after the operation (F) showed the AVSs were completely resected and the ASA was intact (arrowhead: radiculomedullary artery). No surgery-related neurological deficit was observed. Follow-up at 6 months after surgery revealed the patient fully recovered. AP = anterior-posterior view; CCT = costocervical trunk; L = left; LAT = lateral view; OP = operation; R = right.

Patients in our institutes would receive a DSA immediately after the treatment procedures. Complete obliteration was defined as disappearance of the intradural AVS, whereas partial obliteration was defined as any residual intradural AVS remaining visible and was further categorized as shunt-reduction obliteration (the size of the nidus or the number of shunt points was reduced) and palliative obliteration (only the aneurysmal structure or feeder was obliterated).

DSA performed more than 3 months after the treatment was considered as a follow-up DSA. In the follow-up DSA, aneurysms that were invisible in pretreatment DSA were defined as newly

formed; AVSs that were invisible in pretreatment DSA were defined as lesion proliferation, whereas a recurrence of obliterated AVS was defined as recanalization. A negative follow-up DSA following partial treatment was defined as spontaneous obliteration of residual lesion.

Clinical evaluation

Follow-up was planned at discharge, 1 month after discharge, 6 months after discharge and then at yearly intervals, through direct clinical interviews or telephone contact. The follow-up period

was defined as the interval between initial treatment and last follow-up. A follow-up period of >6 months or with death related to SCAVS was defined as long-term follow-up.

Spinal cord function was evaluated according to the modified Aminoff and Logue scale (mALS).⁹ An increase in mALS of ≥ 1 point was defined as clinical deterioration. Clinical deterioration that occurred within 2 weeks after treatment and was sustained for more than 6 months or until death was defined as permanent treatment-related deterioration. Clinical deterioration that occurred after >2 weeks after treatment was defined as long-term deterioration and was dichotomized into acute and gradual: acute deterioration was defined as an increase in mALS of >1 point within 24 h or severe sudden spinal pain of ≥ 5 on the numerical rating scale (0–10). In the clinical deterioration risk analysis, the end point was defined as the clinical deterioration or the last follow-up (i.e. no deterioration occurred), and the inception was the latest treatment of that end point.

To evaluate the efficacy of the clinical interventions, we also assessed the pretreatment clinical course from the first presentation to the initiation of interventional treatment. The end point of this period was the clinical deterioration or initiation of treatment (i.e. no deterioration occurred). The detailed analysis procedures for pretreatment clinical course were described in our previous study.¹

Statistical analysis

Differences between groups were tested using Pearson's chi-square test. Categorical variables were tested by Student's t-test or Mann-Whitney U-test. Multivariate models included variables that were significant at $P \leq 0.05$ in the univariate analysis for the outcome of interest. The annual risk of clinical deterioration was calculated as the number of patients with deterioration during follow-up divided by person-years of follow-up. The Kaplan-Meier curves were compared using the log-rank test. The Cox proportional hazards model was used to estimate the significance of several variables in predicting the relative risk (hazard ratio) of clinical deterioration. Statistical analysis was performed using SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA). All statistical tests were two-sided, and P -values ≤ 0.05 were considered statistically significant.

Data availability

Data collected for the study will be made available upon reasonable request to the corresponding authors.

Results

Baseline characteristics

A total of 548 SCAVS patients were included, 463 (84.5%) of whom, with long-term follow-up data, were eligible for further analysis. The median follow-up period was 45.1 months [interquartile range (IQR) 25.0–70.3 months]. Four hundred and sixty patients were symptomatic and had a median onset age of 23 years (IQR 16–32 years). Among the included patients, 144 (31.1%) were confirmed as SMAVS. Compared with non-metameric AVSs, SMAVSs demonstrated a younger onset age, a larger intradural lesion (diameter of lesion, main feeder and main drainage) that was prone to be located at the centre of the spinal cord. Nidus-type shunts, embedded lesions, anterior sulcal artery supply and multiple drainage veins were significantly more common in SMAVSs (Table 1).

Treatment

Two hundred and fifty-eight patients (55.7%) underwent embolization, 122 (26.3%) underwent microsurgery, and 83 (17.9%) underwent combined treatment modalities. Four hundred and sixty-three patients received a total of 735 treatments (median = 1, IQR 1–2), including 525 embolization and 210 microsurgies. Multivariate analysis indicated that lesions located on the dorsal or lateral side of the spinal cord were more prone to receive microsurgery. Patients younger than 15 years, lesions with aneurysms and lesions located at the C3–T2 segments were more likely to receive embolization (Supplementary Table 1).

Overall, complete obliteration was achieved in 188 patients (40.6%). Twenty-six (18.1%) of 144 patients with SMAVSs were cured, which was a significantly lower percentage than that for non-metameric lesions (50.8%) ($P < 0.001$). The complete obliteration rate of nidus-type lesions was significantly lower than that of fistula-type lesions (29.3% versus 74.8%, $P < 0.001$).

Among 258 patients who only received embolization, 68 (26.4%) were cured. Multivariate logistic analysis indicated that fistula-type lesions, non-metameric lesions and diameter of main drainage <1.5 mm were independent predictors for complete embolization (Table 2).

One hundred and twenty (58.5%) of 205 patients, who underwent microsurgery, were cured. Multivariate logistic analysis indicated non-metameric lesions, lesions with maximum diameter <3 cm and lesions without anterior sulcal artery supply were independent predictors for complete resection (Table 3).

Clinical deterioration

Following treatment, 52 patients (11.2%) experienced permanent treatment-related deterioration, 54 (11.6%) experienced long-term acute deterioration, and 45 (9.7%) experienced long-term gradual deterioration. Overall, if the above three kinds of clinical deterioration were defined as one end point, 133 patients experienced clinical deterioration during the total follow-up of 1431.03 patient-years, yielding an annual rate of 9.3%. Compared to the overall clinical deterioration rate before treatment (32.5%/year, 276 patients experienced clinical deterioration over 850.1 patient-years), the post-treatment deterioration risk was significantly decreased ($P < 0.001$).

Permanent treatment-related deterioration

Of 341 patients who received embolization, 19 (5.6%) experienced permanent embolization-related deterioration. Statistical analysis failed to find any angio-architectural or therapeutic procedure-related risk factor (Supplementary Table 2). Notably, for patients receiving palliative obliteration only, no permanent treatment-related deterioration was observed.

Of 205 patients who received microsurgery, 33 (16.1%) experienced surgery-related deterioration and mid-thoracic segment location was the only risk factor. Complete resection did not increase the risk (16.1% versus 16.1%, $P = 0.999$) (Supplementary Table 3). For patients who received complete resection, the mid-thoracic segment location was also the only risk factor for the permanent treatment-related deterioration (Supplementary Table 4).

Long-term acute deterioration

Forty of 54 (74.1%) patients who experienced long-term acute deterioration had radiological or surgical evidence of spinal haemorrhage. In 53 cases, the deterioration occurred following partial obliteration. One patient exhibited acute deterioration 23.7 months after complete embolization, but a subsequent DSA indicated

Table 1 Baseline characteristics

Parameter	All n = 463	Metameric n = 144	Non-metameric n = 319	P
Onset age ^a	23 (16–32)	21 (15–28)	25 (16–34)	0.005
Sex				0.985
Male	273 (59.0%)	85 (59.0%)	188 (58.9%)	
Female	190 (41.0%)	59 (41.0%)	131 (41.1%)	
Presentation pattern before treatment				0.503
Acute	318 (68.7%)	103 (71.0%)	216 (67.7%)	
Gradual	145 (31.3%)	42 (29.0%)	103 (32.3%)	
Shunt types				< 0.001
Nidus-type	348 (75.2%)	124 (86.1%)	224 (70.2%)	
Fistula-type	115 (24.8%)	20 (13.9%)	95 (29.8%)	
Segment				0.086
C1–C2	32 (6.9%)	5 (3.5%)	27 (8.5%)	
C3–C5	76 (16.4%)	20 (13.9%)	56 (17.6%)	
C6–T2	65 (14.0%)	26 (18.1%)	39 (12.2%)	
T3–T9	96 (20.7%)	35 (24.3%)	61 (19.1%)	
Lower than T9	194 (41.9%)	58 (40.3%)	136 (42.6%)	
Maximum diameter of lesions, cm	1.7 (1.0,2.6)	2.6 (1.7,3.5)	1.5 (0.8,2.0)	< 0.001
Aneurysmal structure				0.233
Yes	310 (67.0%)	102 (70.8%)	208 (65.2%)	
No	153 (33.0%)	42 (29.2%)	111 (34.8%)	
Anterior sulcal artery supply				< 0.001
Yes	234 (50.5%)	98 (68.1%)	136 (42.6%)	
No	229 (49.5%)	46 (31.9%)	183 (57.4%)	
Diameter of main feeder, mm	1.1 (0.9,1.4)	1.2 (1.0,1.5)	1.1 (0.8,1.4)	0.001
Diameter of main drainage, mm	1.7 (1.2,2.5)	2.0 (1.4,2.8)	1.6 (1.0,2.3)	< 0.001
Number of drainage veins				0.008
1	92 (19.9%)	18 (12.5%)	74 (23.2%)	
> 1	371 (80.1%)	126 (87.5%)	245 (76.8%)	
Lesion depth				< 0.001
Embedded	198 (42.8%)	84 (58.3%)	114 (35.7%)	
Superficial	265 (57.2%)	60 (41.7%)	205 (64.3%)	
Lesion location				< 0.001
Dorsal	152 (32.8%)	35 (24.3%)	117 (36.7%)	
Lateral	126 (27.2%)	40 (27.8%)	86 (27.0%)	
Ventral	93 (20.1%)	22 (15.3%)	71 (22.3%)	
Central	92 (19.9%)	47 (32.6%)	45 (14.1%)	
mALS before treatment	3 (1–6)	3 (2–6)	3 (1–6)	0.622

Data are presented as n (%) or median (IQR). mALS = modified Aminoff and Logue scale.

^aThree of 463 patients in this cohort were asymptomatic.

recanalization. The total observational period following partial obliteration was 993.5 patient-years, yielding an annual long-term acute deterioration rate of 5.3%. Compared to the acute deterioration rate before treatment (9.3%/year, 74 patients experienced clinical deterioration over 796.1 patient-years), the risk following partial treatment was significantly decreased ($P = 0.001$).

Cox multivariate analysis indicated that the long-term acute deteriorations following partial obliteration were associated with SMAVSSs, cranio-cervical lesions, lesions with maximum diameter ≥ 2 cm, and residual aneurysms (Fig. 2 and Supplementary Table 5). For patients with any of the above parameters, statistical analysis revealed that the acute deterioration rate following partial obliteration was not significantly different from the pretreatment rate (Supplementary Table 6). For non-metameric SCAVSSs, residual aneurysm was the only predictor for the event (Supplementary Table 7).

Ten of 42 patients (23.8%) experienced acute deterioration following palliative obliteration. Five of them harboured a residual aneurysm following the latest treatment and the other five were patients with SMAVSSs. Cox multivariate analysis showed no significant difference in the long-term acute deterioration risks for

the palliative and shunt-reduction treatment strategies (Supplementary Table 5).

Long-term gradual deterioration

Thirty-six of 45 (80.0%) patients experienced long-term gradual deterioration following partial obliteration. The total observational period after partial obliteration was 988.28 patient-years, yielding an annual long-term gradual deterioration rate of 3.6%. Compared to the gradual deterioration rate before treatment (17.1%/year, 126 patients experienced clinical deterioration over 735.78 patient-years), the risk following partial treatment was significantly decreased ($P < 0.001$).

Cox multivariate analysis indicated that the long-term gradual deteriorations following partial obliteration were associated with absence of pretreatment acute deterioration, palliative obliteration and intact main drainage (Fig. 3 and Supplementary Table 8). For patients with the above parameters, the long-term gradual deterioration rate following partial obliteration was still significantly decreased compared to their pretreatment gradual deterioration rate (Supplementary Table 9).

Table 2 Predictors for complete endovascular embolization

Parameter	Complete embolization n = 68	Partial embolization n = 190	P	Multivariate logistic analysis	
				Odds ratio (95% CI)	P
Shunt types			< 0.001		
Nidus-type	24 (35.3%)	167 (87.9%)		Reference ^a	
Fistula-type	44 (64.7%)	23 (12.1%)		10.259 (3.373–31.205)	< 0.001
Metameric lesions			< 0.001		
Yes	10 (14.7%)	82 (43.2%)		Reference ^a	
No	58 (85.3%)	108 (56.8%)		2.476 (1.062–5.771)	0.036
Segment			0.004		
C3–C5	5 (7.4%)	47 (24.7%)		Reference ^a	
C1–C2	6 (8.8%)	12 (6.3%)		2.495 (0.780–7.983)	0.123
C6–T2	12 (17.6%)	37 (19.5%)			
T3–T9	11 (16.2%)	40 (21.1%)			
Lower than T9	34 (50.0%)	54 (28.4%)			
Maximum diameter of lesion			< 0.001		
0.1–0.9 cm	30 (44.1%)	18 (9.5%)		1.546 (0.622–3.844)	0.348
1–1.9 cm	21 (30.9%)	64 (33.7%)		Reference ^a	
2–2.9 cm	12 (17.6%)	51 (26.8%)			
≥ 3 cm	5 (7.4%)	57 (30.0%)			
Anterior sulcal artery supply			< 0.001		
Yes	15 (22.1%)	136 (71.6%)		Reference ^a	
No	53 (77.9%)	54 (28.4%)		1.182 (0.334–4.190)	0.795
Aneurysms			0.085		
Yes	40 (73.5%)	158 (83.2%)			
No	18 (26.5%)	32 (16.8%)			
Diameter of main feeder			0.092		
< 1 mm	23 (33.8%)	42 (22.1%)			
1–1.5 mm	29 (42.6%)	108 (56.8%)			
> 1.5 mm	16 (23.5%)	40 (21.1%)			
Diameter of main drainage			0.001		
< 1.5 mm	35 (51.5%)	50 (26.3%)		3.751 (1.520–9.255)	0.004
1.5–2.5 mm	16 (23.5%)	77 (40.5%)		Reference ^a	
> 2.5 mm	17 (25.0%)	63 (33.2%)			
Number of drainages			0.005		
1	22 (32.4%)	31 (16.3%)		1.207 (0.501–2.909)	0.675
> 1	46 (67.6%)	159 (83.7%)		Reference ^a	
Lesion depth			< 0.001		
Embedded	11 (16.2%)	120 (63.2%)		Reference ^a	
Superficial	57 (83.8%)	70 (36.8%)		1.113 (0.296–4.189)	0.875
Lesion location			< 0.001		
Dorsal	18 (26.5%)	35 (18.4%)		1.322 (0.349–5.002)	0.681
Ventral	13 (19.1%)	44 (23.2%)			
Lateral	33 (48.5%)	49 (25.8%)			
Central	4 (6.1%)	62 (32.6%)		Reference ^a	

^aCompared as reference.

Digital subtraction angiography follow-up Digital subtraction angiography follow-up after microsurgery

Seventy-nine patients received follow-up DSA after microsurgery (38.5%, 79/205), including 37 cases after complete resection and 43 cases after partial resection (one patient had received two micro-surgical operations, the lesion was partially resected at the first operation but the residual shunts were completely resected at the second operation; follow-up DSA was available following both operations). The median DSA follow-up period was 8.0 months (IQR, 6.2–17.0 months).

The follow-up DSA was negative for all completely resected lesions. For partially resected cases, proliferation and spontaneous obliteration of residual lesion was found in 10 (23.3%) and five cases (11.6%), respectively. Statistical analysis indicated that

proliferation of residual lesions following microsurgery was only associated with longer DSA follow-up period ([Supplementary Table 10](#)).

Digital subtraction angiography follow-up after endovascular embolization

Two hundred and nineteen patients received the follow-up DSA after endovascular embolization (64.2%, 219/341), including 30 cases following complete embolization and 191 cases following partial embolization (two patients had received multiple endovascular operations, the lesion was partially embolized at the first treatment but the residual shunts were completely obliterated at the last embolization; follow-up DSA was available for all of the embolization). The median DSA follow-up period was 8.4 months (IQR, 4.5–20.9 months).

Table 3 Predictors for complete resection

Parameters	Complete resection n = 120	Partial resection n = 85	P	Multivariate logistic analysis	
				Odds ratio (95% CI)	P
Shunt types			< 0.001		
Nidus-type	78 (65.0%)	79 (92.9%)		0.443 (0.141–1.392)	0.163
Fistula-type	42 (35.0%)	6 (7.1%)		Reference ^a	
Metameric lesions			< 0.001		
Yes	16 (13.3%)	36 (42.4%)		Reference ^a	
No	104 (86.7%)	49 (57.6%)		4.219 (1.723–10.333)	0.002
Segment			0.138		
C3–C5	17 (14.2%)	7 (8.2%)			
C1–C2	5 (4.2%)	9 (10.6%)			
C6–T2	8 (6.7%)	8 (9.4%)			
T3–T9	23 (19.2%)	22 (25.9%)			
Lower than T9	67 (55.8%)	39 (45.9%)			
Maximum diameter of lesion			< 0.001		
0.1–0.9 cm	48 (40.0%)	10 (11.8%)		9.327 (2.053–42.372)	0.004
1–1.9 cm	55 (45.8%)	31 (36.5%)			
2–2.9 cm	14 (11.7%)	17 (20.0%)			
≥ 3 cm	3 (2.5%)	27 (31.8%)		Reference ^a	
Anterior sulcal artery supply			< 0.001		
Yes	21 (17.5%)	62 (72.9%)		Reference ^a	
No	99 (82.5%)	23 (27.1%)		8.352 (3.174–21.981)	< 0.001
Diameter of main feeder			< 0.001		
< 1 mm	58 (48.3%)	24 (28.2%)		1.336 (0.540–3.304)	0.531
1–1.5 mm	55 (45.8%)	45 (52.9%)		Reference ^a	
> 1.5 mm	7 (5.8%)	16 (18.8%)			
Diameter of main drainage			< 0.006		
< 1.5 mm	71 (59.2%)	31 (36.5%)		Reference ^a	
1.5–2.5 mm	30 (25.0%)	32 (37.6%)		0.667 (0.279–1.592)	0.361
> 2.5 mm	19 (15.8%)	22 (25.9%)			
Aneurysm					
Yes	60 (50.0%)	42 (49.4%)			
No	60 (50.0%)	43 (50.6%)			
Number of drainage			0.026		
1	29 (24, 2%)	10 (11.8%)		Reference ^a	
> 1	91 (75, 8%)	75 (88.2%)		0.712 (0.240–2.114)	0.540
Lesion depth			< 0.001		
Superficial	18 (15.9%)	49 (57.6%)		Reference ^a	
Embedded	102 (85.0%)	36 (42.4%)		0.782 (0.289–2.119)	0.629
Lesion location			0.006		
Dorsal	68 (56.7%)	31 (36.5%)		Reference ^a	
Lateral	9 (7.5%)	4 (4.7%)			
Central	9 (7.5%)	17 (20.0%)		1.347 (0.567–3.198)	0.500
Ventral	34 (28.3)	33 (38.8)			

^aCompared as reference.

Recanalization was observed in 73 of 219 patients (33.3%). Multivariate analysis indicated that particulate embolization, lesions with multiple drainage veins and lesions with intact main drainage following embolization tended to be associated with recanalization (Supplementary Table 11). For completely embolized lesions, recanalization was found in 15 cases (50.0%, 15/30).

For partially embolized cases, follow-up DSA found newly formed aneurysms in 22 patients (11.5%), lesion proliferation in 22 patients (11.5%), and spontaneous obliteration of residual lesions in three patients (1.6%). Statistical analysis indicated that lesion proliferation following embolization was only associated with the longer DSA follow-up period (Supplementary Table 12), whereas

newly formed aneurysm was associated with SMAVs and the longer DSA follow-up period (Supplementary Table 13).

Discussion

This is the most extensive clinical outcome analysis for SCAVS to date. We found that the clinical deterioration risk significantly decreased after interventional treatments, suggesting that patients may benefit from contemporary clinical intervention. However, the treatment risk was considerable and the cure rate was hardly satisfying. Meanwhile, the results indicated that contemporary treatments were insufficient for patients with

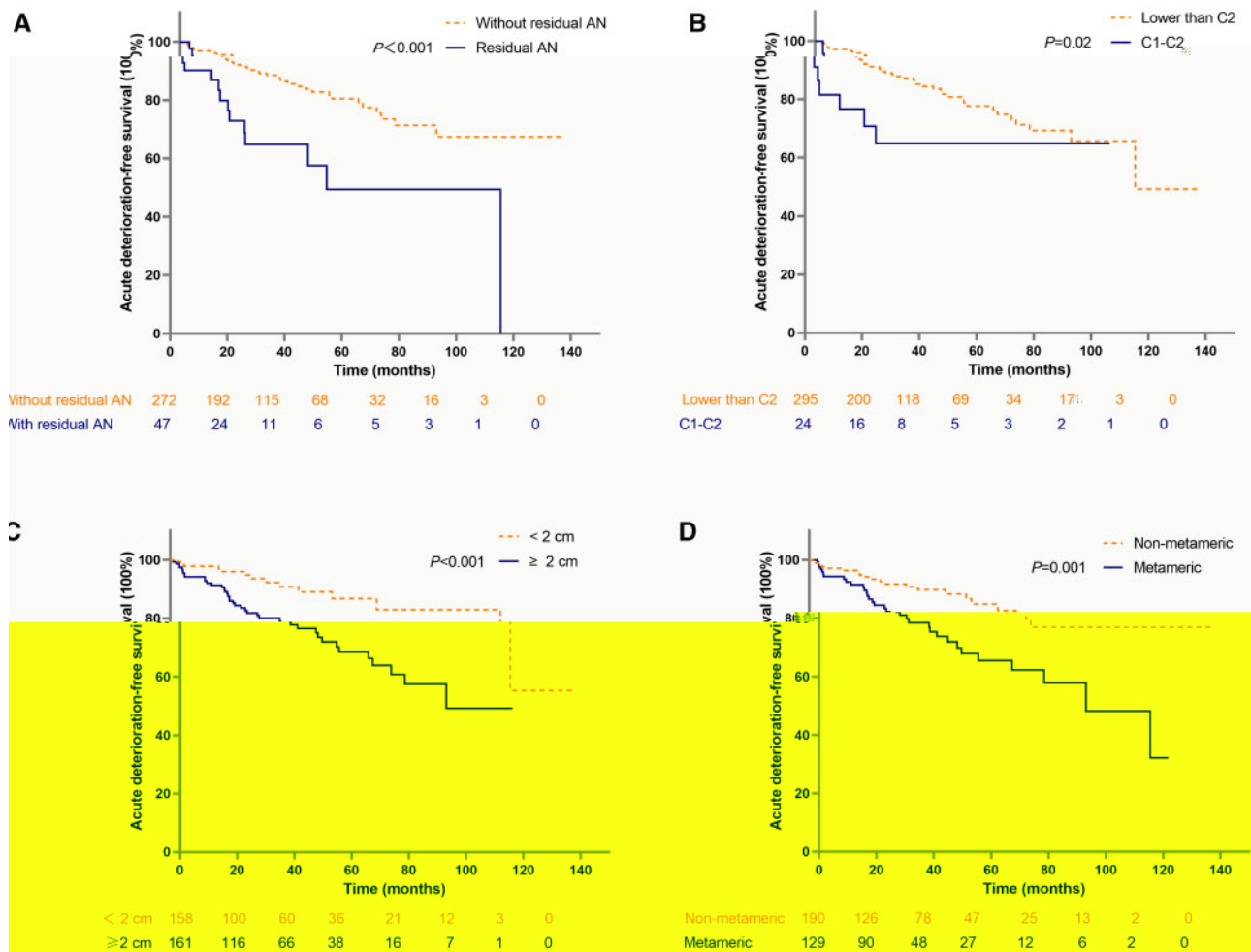


Figure 2 Kaplan-Meier curves demonstrating cumulative rates of long-term acute deterioration for partial obliterated SCAVs as the function of follow-up time in months. (A) Stratified by residual aneurysm, (B) stratified by segment, (C) stratified by lesion diameter, and (D) stratified by metamerism involvement. AN = aneurysm.

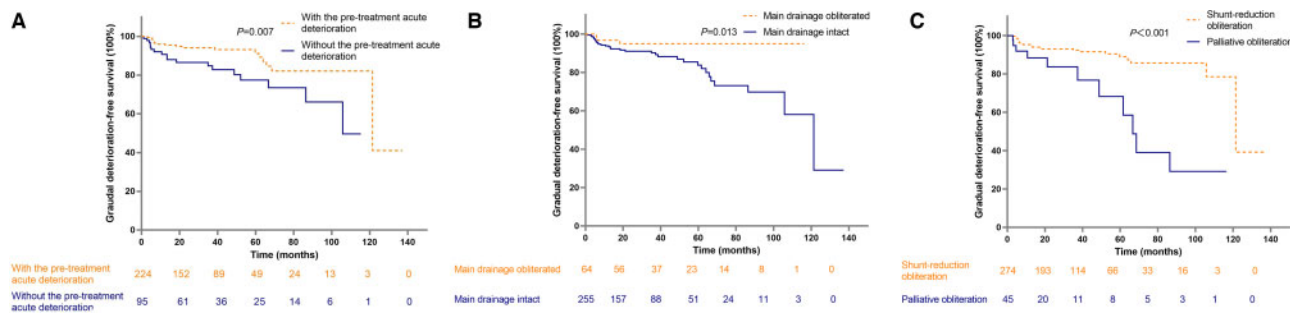


Figure 3 Kaplan-Meier curves demonstrating cumulative rates of long-term gradual deterioration for partial obliterated SCAVs as the function of follow-up time in months. (A) Stratified by the pretreatment clinical presentation pattern, (B) stratified by status of main drainage after treatment, and (C) stratified by partial obliteration strategy. AN = aneurysm.

SMAVs. Since the management for this rare disease is still a challenge, centralization of patients to the expert referral centres and individualized treatment strategy are encouraged.

The indication of complete obliteration

Our previous study revealed that a complete obliteration can almost eliminate the risk of long-term deterioration for SCAVs.¹ Unfortunately, curative treatment for SCAVs is difficult.

According to different therapeutic indications and plans, previously reported cure rate widely varies between 0% and 90%.^{1–6,10} Because of the invasive nature of current treatment modalities and the lesion’s complex anatomical features, it was believed that a higher complete obliteration rate may be accompanied by a higher treatment risk in an unselected cohort.^{2,3} Therefore, clarifying the indication for safely curative treatment is meaningful.

In our institutes, endovascular embolization is the prioritized treatment modality because it can be performed simultaneously

with diagnostic DSA. In this cohort, complete embolization was associated with fistula-type lesions, non-metameric lesions and lesions with a main drainage diameter <1.5 mm. The embolization-related clinical deterioration risk was acceptable. Meanwhile, statistical analysis failed to reveal any angio-architectural or therapeutic procedure-related risk factor for embolization-related clinical deterioration. These findings demonstrated that the benefit/risk balance for our endovascular procedures could be acceptable. Therefore, complete embolization should be given full consideration for patients with the above parameters.

We confirmed several predictors for complete resection, which could provide valuable information for surgery plans. Of note, the data indicated that mid-thoracic lesions harboured a significantly higher surgical risk. Our previous natural history study found that the spontaneous recovery rate after spinal haemorrhage was also significantly decreased for mid-thoracic lesions.¹ The phenomena might result from the poor vascularization of the mid-thoracic cord.^{11,12} Therefore, surgery in this area should be performed with caution.

Target of partial obliteration

It is accepted that partial obliteration is the only choice for most SCAVSs with complex angio-architecture.³ However, such a treatment strategy covers a wide spectrum.¹³ Some clinicians may choose to obliterate the nidus and the shunt points directly; while others may adopt a relatively conservative strategy by only eradicating structures conferring significant risk, such as aneurysms. Until now, few reports have evaluated the relationship between treatment target of partial obliteration and the clinical outcome of patients with SCAVS. In this study, we revealed the applicability of the two partial treatment strategies for the control of acute and gradual deterioration risks, respectively.

Acute deterioration is of greatest concern because such events usually indicate the rupture of residual AVSs.^{5,13–15} In this cohort, we confirmed that a subset of patients still harboured a notable acute deterioration risk if the lesion were not cured. Among these patients, SMAVS is a baffling phenotype; they usually harboured larger and more complex intradural AVSs. Some clinicians defined them as a subtype parallel to the spinal arteriovenous malformation.^{16–18}

If SMAVSs were excluded, residual aneurysm was the only independent risk factor for acute deterioration. Aneurysmal structure was regarded as the main cause for the rupture of intracranial AVSs.^{19,20} Our results revealed that the long-term acute deterioration rate of SCAVS patients with residual aneurysms was similar to their pretreatment rate. Therefore, aneurysms should be the primary target for the control of the acute deterioration risk of SCAVSs. It is worth noting that the data showed equal effectiveness of both palliative and shunt-reduction obliteration for the acute deterioration risk. Considering that the therapeutic safety of palliative obliteration may be superior to shunt-reduction treatment (in this cohort, no patient suffered from treatment-related deterioration after palliative obliteration), the palliative obliteration targeting only aneurysms could be an ideal option to reduce haemorrhagic risk for incurable SCAVSs.

On the other hand, however, we found that palliative obliteration is insufficient for managing the risk of the long-term gradual deterioration, conferring a 2.9-fold increased risk compared with shunt-reduction obliteration. Previous studies suggested that gradual deterioration was mainly a result of spinal venous congestion or local spinal cord ischaemia related to blood steal.^{3,5,6,21,22} Our finding suggested that only with sufficient flow reduction can the above pathophysiological processes be reduced or reversed. The result that main drainage obstruction after treatment was an

independent protective factor for the risk also supports this hypothesis. In our institutes, to avoid iatrogenic spinal cord oedema or the residual AVS rupture, the main drainage would be maintained unless most of the lesion was obliterated.

The dilemma of SMAVS management

The treatment outcome of SMAVSs is unsatisfactory regarding the low complete obliteration rate and high risk of long-term acute deterioration after partial obliteration. Furthermore, the acute deterioration rate after partial treatment was not reduced compared to the pretreatment rate, which indicated that the contemporary interventional treatments are invalid for the control of haemorrhagic risk in patients with incurable SMAVS. It seems that SMAVSs were more prone to forming new aneurysms, which may be the underlying cause of the higher risk of post-treatment acute deterioration. With insights from cerebral aneurysm pathogenesis,^{23–25} we speculate that lesions of SMAVSs may feature a more fragile structure of vessel wall. We suggest increasing the follow-up DSA or magnetic resonance angiography (MRA) frequency appropriately aiming at early detection and timely elimination of newly formed aneurysms.

On the other hand, the unsatisfactory results underscored an urgent need for the development of new therapeutic modalities for SMAVSs. Stereotactic radiosurgery is a reliable treatment method for brain AVSs.²⁶ Although there was little experience in radiosurgical treating SCAVSs in the literature, the clinical outcome of reported cases was encouraging. The latest systematic review, including 64 patients, found no post-treatment haemorrhage event had been reported during a mean follow-up period of 47 months.²⁷ Therefore, stereotactic radiosurgery might be a promising option for SMAVSs and other refractory SCAVS lesions.

Limitations

We did not use haemorrhage as the end point in this study. The diagnosis of spinal haemorrhage is difficult because of its small size, and the signal of flow voids and oedema could obscure the signs of small bleeds. Meanwhile, all long-term acute deteriorations occurred after discharge, nine patients in this cohort did not receive timely radiological examination after the events happened.

In our institute, non-adhesive liquid embolic agents have not been used to embolize intradural spinal AVSs because we believe the necessity of embolic agent reflux and the neurotoxicity of dimethyl sulfoxide (DMSO) may increase the treatment risks.^{28,29} However, a few institutes obtained satisfactory treatment results by using Onyx[®].^{30,31} The superior penetration property of this material could facilitate the AVSs embolization from arterial to venous side in sequence, which may increase the curative embolization rate.³⁰ Therefore, for selected cases with a favourable security margin, such as fistula-type lesions, non-adhesive liquid embolic agents may be a proper choice.

Proliferation and newly formed aneurysm could be detected by follow-up DSA, which suggested SCAVSs are dynamic lesions. However, spinal cord AVSs are more stable compared with their peripheral counterparts, whose recurrence or proliferation rate has been reported to be >90%.³² Of note, these data should be interpreted cautiously because the DSA follow-up of the study is not comprehensive. Although DSA could be the most sensitive and accurate tool to reveal the angio-architecture changes of SCAVSs, the invasive nature and nationwide distribution of the patients limit its application. We will develop an MRA-based radiological follow-up strategy in future clinical practice.

In summary, although clinical risks of SCAVSs were reduced after interventional treatments, contemporary management of SCAVS remains associated with considerable risks and incomplete efficacy. Therefore, treatment strategy should be individualized according to the angio-architectural features and major clinical risks of specific lesions. Fistula-type lesions, non-metameric lesions and lesions with main drainage diameter <1.5 mm have a higher chance of complete embolization. For lesions that are surgically accessible, non-metameric lesions, lesions with a maximum diameter <3 cm and lesions without an anterior sulcal artery supply are the indications for complete resection. However, the surgical resection for SCAVSs located at mid-thoracic segments should be performed with caution. Regarding SCAVSs with a complicated angio-architecture, palliative obliteration targeting the aneurysms is recommended for reducing the risk of acute deterioration, whereas shunt-reduction obliteration is necessary for non-haemorrhagic myelopathy. Contemporary interventional treatment is invalid in reducing haemorrhagic risk of incurable SMAVSs, which requires a more intense angiography follow-up.

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Competing interests

The authors report no competing interests.

Supplementary material

Supplementary material is available at *Brain* online.

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