Natural history of spinal cord arteriovenous shunts: an observational study

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The natural history of intradural spinal cord arteriovenous shunts is unknown. We performed an observational study in a consecutive patient cohort with symptomatic intradural spinal cord arteriovenous shunts who were admitted to three institutes to investigate the clinical course of this complex disease, which would provide valuable evidence to inform clinical decision-making. The clinical course of patients with symptomatic intradural spinal cord arteriovenous shunts from initial presentation to occurrence of clinical deterioration, initiation of treatment, or last follow-up was analysed. Patients with at least 1 month of observation were included in this study. Clinical onset and deterioration patterns were divided into acute and gradual. Annual and cumulative rates of clinical deterioration as well as their risk factors were analysed using Kaplan-Meier life table analysis and Cox proportional hazards model. To assess risks and benefits of treatment, post-treatment clinical courses were further assessed. Four hundred and sixty-six patients with a mean observational period of 36.9 ± 58.8 months were included; 56.7% of patients presented with acute onset, of whom 77.3% experienced spontaneous recovery. Age of onset older than 28 years, initial modified Aminoff and Logue scale of ≥3, mid-thoracic lesions and non-ventral lesions were independent predictors of failure for spontaneous recovery. The annual risk of general, acute and gradual clinical deterioration after onset was 30.7%, 9.9% and 17.7%, respectively. Risk of deterioration was highest in the early period after initial onset. Acute onset was the only independent risk factor [hazard ratio 1.957 (95% confidence interval, CI 1.324–2.894); P = 0.0008] of acute deterioration and gradual onset was the strongest predictor [hazard ratio 2.350 (95% CI 1.711–3.229); P < 0.0001] of the gradual deterioration among all the stratifying factors. After invasive treatment, complete obliteration was achieved in 37.9% of patients (138 of 364) and improved or stable clinical status was noted in 80.8% of patients. Forty-two patients (11.5%) experienced permanent complications. Overall post-treatment deterioration rate was 8.4%/year, and 5.3%/year if permanent complications were excluded. The natural history of symptomatic spinal cord arteriovenous shunts is poor, especially in the early period after onset, and early intervention is thus recommended. Initial onset pattern significantly affects the natural history of the lesion, which prompts a differentiated treatment strategy.
Keywords: natural history; spinal arteriovenous malformation; perimedullary arteriovenous fistula; spinal metameric arteriovenous malformation; arteriovenous shunt

Abbreviations: mALS = modified Aminoff and Logue scale; PMAVF = peri-medullary arteriovenous fistula; SAVM = spinal arteriovenous malformation; SCAVS = spinal cord arteriovenous shunt; SMAVMs = spinal metameric arteriovenous malformation

Introduction

Spinal cord arteriovenous shunts (SCAVSs) are pathological connections between spinal cord arteries and veins without a normal intervening capillary network. They can be subclassified into intramedullary spinal arteriovenous malformations (SAVMs), perimedullary arteriovenous fistulas (PMAVFs) and spinal metameric arteriovenous malformations (SMAVMs) (Bao and Ling, 1997; Rodesch et al., 2002; Kim and Spetzler, 2006; Krings, 2010). These lesions may lead to severe neurological deficits resulting from haemorrhage, spinal venous congestion or cord compression (Rosenblum et al., 1987; Rodesch et al., 2004; Flores et al., 2017; Ho et al., 2018).

Treatment strategy of these lesions is controversially discussed as these are rare diseases with challenging treatment that may in itself result in potentially disabling complications (Boström et al., 2007, 2009; Krings, 2010, Krings et al., 2010; Flores et al., 2017; Ho et al., 2018). Complication rates reported in the literature vary between 5% and 25% irrespective of treatment modality (Flores et al., 2017). Only with comprehensive understanding of the natural history can treatment-associated hazards be weighed against the prognosis, leading to an appropriate decision-making in the individual case. Unfortunately, SCAVSs are very rare diseases: based on an estimation of data from major German referral centre, an analysis of a US hospital database and our own referral pattern, the incidence of SCAVSs is believed to be between 1 and 2.5 per million per year (Thron, 2001; Lad et al., 2009). Given the rarity of SCAVSs, few studies have thus far investigated their natural history (Aminoff and Logue, 1974; Gross and Du, 2013a, b, 2014; Lee et al., 2014).

The present observational study in an unselected, consecutive patient cohort with SCAVSs admitted to three institutes was undertaken to reveal the natural history of this complex disease, which would provide valuable evidence to inform clinical decision-making.

Materials and methods

The China-INI spinal vascular malformations database is an ongoing prospectively maintained database capturing clinical data on consecutive patients with spinal vascular malformations admitted to three referral centres (Xuanwu Hospital, Beijing Haidian Hospital, and Beijing United Family Hospital). As tertiary centres specializing in spinal vascular diseases, our institutions draw patients from across China. This study was reviewed and approved by the ethics committee of our institutions with waiver of informed consent from patients given its retrospective nature.

The study included patients with symptomatic SCAVSs who were initially admitted to Xuanwu Hospital between January 2007 and December 2017, and to Haidian and Beijing United Family Hospitals between February 2014 and December 2017. Patients were eligible if: (i) their SCAVSs was not detected incidentally; (ii) their symptoms were attributed to the SCAVSs; (iii) they had been initially treated in our centres with an interval of at least 1 month between onset and treatment, or they were not treated; (iv) the location of the shunt was intradural; and (v) the level of lesion was from C1 to the tip of conus medullaries.

Patients with spinal epidural vascular malformations, spinal dural arteriovenous fistulas, spinal radicular arteriovenous fistulas, filum terminale arteriovenous fistulas, spinal cavernous malformations or paravertebral spinal shunts were not included in this study. Patients with concurrent tethered cord, herniated disc, spinal tumour or any other kind of disease that could impair the spinal cord function were excluded, as well as patients without complete spinal digital subtraction angiography (DSA) data. Patients younger than 1 year old were not eligible because their spinal cord function could not be evaluated objectively.

Baseline clinical characteristics, including age of onset and sex, were derived from the database. Angio-architecture features were determined from DICOM DSA. Lesion subtypes included SAVM, PMAVF and SMAVM. Lesion location was classified into the cranio-cervical cord (C1–C2), the mid-cervical cord (C3–C5), the cervicothoracic cord (C6–T2), the mid-thoracic cord (T3–T9) and the thoracolumbar cord (from T10 to the tip of conus medullaries). The relationship between the major part of each lesion and the spinal cord was defined as ventral, lateral, central, and dorsal.

The observational period was defined as the interval between onset and invasive treatment or last follow-up (for patients who did not receive an invasive treatment). The clinical course during the observational period was evaluated using the modified Aminoff and Logue scale (mALS) (Aminoff and Logue, 1974). The onset pattern was dichotomized into acute and gradual: an acute onset was defined as an increase in mALS of >1 point within 1 day or severe sudden spinal pain of >4 on the numerical rating scale.

We defined the endpoint of the natural history analysis as either further clinical deterioration during the observational period, or invasive treatment (if no deterioration occurred) or last follow-up (if neither deterioration nor invasive treatment occurred). The follow-up period was the interval between initial presenting symptom onset and the endpoint as defined...
above. SCAVs differ from brain arteriovenous malformations in that gradual deterioration unrelated to haemorrhage is more common than acute deterioration (Flores et al., 2017; Ho et al., 2018). Thus, in our analysis, clinical deterioration was further divided into acute and gradual, using the same definition for acute versus gradual as used in onset description. Patients with multiple time points of deterioration were censored at their first event. Although observation was continued after an endpoint was reached, further data were not included in the natural history analysis.

To assess the risk of clinical deterioration after treatment, data of treatment and post-treatment follow-up in this series were analysed. Follow-up plan was at discharge, 1 month, 6 months and at yearly intervals through direct interview or telephone contact. Patients with more than 6 months follow-up or death were enrolled in this part of the analysis. Permanent complications were defined as clinical deterioration that occurred within 2 weeks after treatment and sustained for more than 6 months or death.

Statistical analysis

Differences between groups were tested using Pearson’s χ² test for categorical variables and the Wilcoxon rank sum test for continuous variables. Multivariate models included variables that were significant at P < 0.1 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. Cumulative rates of deterioration were estimated using the Kaplan-Meier product-limit method, and the resulting 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 the 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

The authors are willing to provide the raw data related to this work upon request.

Results

Baseline characteristics

A total of 607 consecutive patients with SCAVs were identified, 466 of whom were eligible for further analysis (Fig. 1).

Baseline characteristics are shown in Table 1. The mean observational period was 36.9 ± 58.8 months (range, 1 month–33 years; median, 12 months). The distribution of the observational period for all patients is shown in Supplementary Fig. 1. Of patients studied, 60.7% were male. Average age of onset was 25.3 ± 13.3 years old. The whole cohort included 269 cases with SAVMs, 118 cases with SMAVMs and 79 cases with PMAVFs.

Age of onset, lesion location and onset pattern were statistically different between SAVMs, SMAVMs and PMAVFs (Table 1). The average age of onset of SAVMs, SMAVMs and PMAVFs was 26.4 ± 11.8, 21.9 ± 10.0 and 27.0 ± 19.9 years, respectively. Compared to the other subtypes, PMAVFs had a bimodal age distribution with peaks in both the paediatric age group and the older adult age group. In addition, they were more prone to affect the thoracolumbar cord and present with gradual onset.

Onset

Acute versus gradual onset was observed in 264 (56.7%) versus 202 patients (43.3%) respectively (Supplementary Table 1). There was no statistically significant difference in the observational period between patients with acute and gradual onsets. For those with gradual onset, multivariate analysis revealed that increasing age of onset, PMAVFs and dorsal lesions were independent positive predictors while mid-cervical (C3–C5) lesions was a negative predictor. Pairwise comparison indicated that the rate of gradual onset for PMAVFs was significantly higher as compared to that of SAVMs and SMAVMs, while there was no significant difference between SAVMs and SMAVMs in onset pattern (Supplementary Table 1).

Only 4.5% of patients with gradual onset experienced a suspicious trigger incident, while in 21.2% of acute onset patients a trigger incident was identified. The most common trigger incidents (67.9%) found in acute onset were incidents that increased the thoracic and abdominal pressure, such as strenuous exercise, defecation, pregnancy and childbirth.

Spontaneous recovery

Spontaneous recovery after onset was observed in 210 patients. The spontaneous recovery rate of patients with acute onset (77.3%) was significantly higher compared to those with gradual onset (3.0%), P < 0.001.

The outcome of spontaneous recovery after acute onset was favourable. Until one of the endpoints of natural history analysis was reached, the degree of relief as estimated by mALS was 100% in 141 patients (69.1%), 99–71% in 26 patients (12.7%), 70–51% in 16 patients (7.8%), and <50% in 21 patients (10.3%).

The intervals between acute onset and spontaneous recovery were generally short. The intervals were <1 week in 93 patients (45.6%), from 1 week to half a month in 54 patients (26.5%), from half a month to 1 month in 44 patients (21.6%), from 1 month to 2 months in nine patients (4.4%) and >2 months in four patients (2.0%).

For acute onset patients with a follow-up period of >2 months, no spontaneous recovery was confirmed in 29 patients. Compared to the 204 patients who presented with spontaneous recovery after acute onset, multivariate analysis showed an age of onset older than 28 years, an initial mALS of >3, mid-thoracic lesions and non-ventral lesions were independent predictors of failure of spontaneous recovery (Table 2).
Deterioration of spinal cord function

Acute versus gradual deteriorations were observed in 122 (26.2%) versus 212 patients (45.5%) respectively. Twenty-two patients (4.7%) presented with both acute and gradual deterioration during their observational period. The analysis of risk factors of clinical deterioration included three parts.

First, to explore the total risk of clinical deterioration (coined ‘general’ deterioration), the endpoints of acute and gradual deterioration were combined. For patients who had experienced both patterns, the endpoint was

Table 1 Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n = 466)</th>
<th>SAVM (n = 269)</th>
<th>SMAVM (n = 118)</th>
<th>PMAVF (n = 79)</th>
<th>P-value</th>
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<td>Male</td>
<td>283 (60.7)</td>
<td>161 (59.9)</td>
<td>70 (59.3)</td>
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<td>15–28</td>
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<td>70 (59.3)</td>
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<tr>
<td>&gt; 28</td>
<td>153 (32.8)</td>
<td>94 (34.9)</td>
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<td>12.0 (2.3, 48.0)</td>
<td>12.0 (3.0, 48.0)</td>
<td>8.3 (2.0, 32.0)</td>
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<td>25 (9.3)</td>
<td>4 (3.4)</td>
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<td>C3–C5</td>
<td>78 (16.7)</td>
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<tr>
<td>C6–T2</td>
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<td>31 (11.5)</td>
<td>22 (18.6)</td>
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<td>97 (36.1)</td>
<td>43 (36.4)</td>
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<td>Ventral</td>
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<td>64 (23.8)</td>
<td>26 (22.0)</td>
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<td>Lateral</td>
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<td>78 (29.0)</td>
<td>44 (37.3)</td>
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<td>Dorsal</td>
<td>146 (31.3)</td>
<td>76 (28.3)</td>
<td>32 (27.1)</td>
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<td>Acute</td>
<td>264 (56.7)</td>
<td>164 (61.0)</td>
<td>71 (60.2)</td>
<td>29 (36.7)</td>
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<tr>
<td>Gradual</td>
<td>202 (43.3)</td>
<td>105 (39.0)</td>
<td>47 (39.8)</td>
<td>50 (63.3)</td>
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</table>

aThe relationship between PMAVF lesions and the spinal cord did not include the ‘Central’ group, so the difference between three subtypes was not analysed.
defined as the earlier event. During the total follow-up period of 1016.24 person-years, 312 patients experienced either acute or gradual clinical deterioration, yielding an annual general deterioration rate of 30.7%. The cumulative clinical deterioration rate was 72.1% in 4 years after initial onset. The risk of general clinical deterioration was higher during the first few months after onset, decreasing thereafter (Fig. 2). The annual general deterioration rate was almost 2.5 times higher during the first 6 months (76.4%) compared to the entire follow-up period.

The second endpoint we evaluated was acute deterioration. During the total follow-up period of 1237.7 person-years, 122 patients experienced acute clinical deterioration, yielding an overall annual rate of 9.9%. The cumulative rate was 32.5% in 4 years after initial onset. The risk of acute deterioration was highest during the first few months after onset. The annual acute deterioration rate was more than two times higher during the first 6 months (21.2%) compared to the entire follow-up period (Fig. 2 and Table 3). Log-rank test and Cox multivariate analysis indicated that an acute onset was the only risk factor for subsequent acute deterioration [hazard ratio (HR) 1.957 (95% CI: 1.324–2.894); \( P = 0.0008 \)] (Fig. 3, Table 3 and Supplementary Fig. 2). The annual acute deterioration rates of SAVMs, PMAVFs and SMAVMs were similar. Pairwise comparison log-rank test and multivariate analysis failed to show any significant difference between them (Supplementary Tables 2 and 3).

The third endpoint we evaluated was gradual deterioration. During the total follow-up period of 1197.1 person-years, 212 patients experienced gradual deterioration, yielding an annual gradual deterioration rate of 17.7%. The cumulative gradual deterioration rate was 56.2% in 4 years after initial onset. The risk of gradual deterioration was highest during the first few months after onset, regardless of stratifying factors. The annual gradual deterioration rate was nearly 3 times higher during the first 6 months (52.1%) as compared to the whole follow-up period (Fig. 2 and Table 3). Log-rank test indicated that all stratifying factors significantly affect gradual deterioration rates (Fig. 3, Table 3 and Supplementary Fig. 3). While Cox multivariate analysis showed gradual onset, male gender, PMAVF, and age of onset older than 14 years were independent risk factors for gradual deterioration. Among all the stratifying factors, gradual onset was the strongest predictor of gradual deterioration [HR 2.350 (95% CI 1.711–3.229); \( P < 0.0001 \)] (Table 4). The annual gradual deterioration rates of SAVMs, SMAVMs and PMAVFs increased in sequence. Pairwise comparison log-rank test and Cox multivariate analysis showed the gradual deterioration rate of PMAVF was significantly higher than that of SAVM, while the differences between PMAVFs and SMAVMs and between SAVMs and SMAVMs were not significant (Supplementary Tables 2 and 3).

### Treatment and outcomes

Of the 466 patients enrolled, 442 patients underwent invasive treatment and 364 patients (82.4%) had qualified...
follow-up data (range, 3.0–146.3 months; mean, 54.6 ± 30.8 months; median, 50.3 months) (Fig. 1). Patients were treated with microsurgery in 105 cases (28.8%), embolization in 193 cases (53.0%), and combined embolization–surgery in 66 cases (18.1%). Complete obliteration was achieved in 138 patients (37.9%). At the last follow-up, improved or stable clinical status was noted in 294 cases (80.8%). Forty-two patients (11.5%) experienced permanent complications, the complication rates in patients with completely and partially obliterated lesion were similar (13.0% versus 10.6%, $P = 0.482$). Overall, during the total follow-up period of 1291.3 person-years after treatment, 109 patients experienced clinical deterioration events, yielding an overall annual post-treatment clinical deterioration rate of 8.4%. The risk of clinical deterioration for patients who achieved complete obliteration was significantly lower than those with partial obliteration (19 versus 90 events; 3.7 versus 11.5 per 100 person-years; HR 2.868 (95% CI 1.747–4.708); $P = 0.0001$) (Fig. 4). If the permanent complications were excluded, during the total follow-up period of 1427.8 person-years, 76 patients experienced clinical deterioration, yielding an annual post-treatment clinical deterioration rate of 5.3%. This risk for patients who achieved completely obliteration was also significantly lower than those with partial obliteration (6 versus 70 events; 1.1 versus 8.1 per 100 person-years; HR 7.424 (95% CI 3.224–17.095); $P < 0.0001$) (Fig. 4).

**Discussion**

Our study is the most extensive natural history study of SCAVSs in the largest patient cohort to date, which was based on Kaplan-Meier life table analysis and Cox multivariate modelling. In this cohort, the pretreatment annual general deterioration rate was 30.7% during the entire follow-up period. The cumulative general deterioration rate in 4 years after onset was 72.1%. Of note, the risk was highest in the early period after symptom onset. These data indicate that the natural history of symptomatic SCAVSs is poor and therefore early treatment is suggested in our opinion.

Previously, the most cited natural history research of spinal vascular malformations was based on a series of 60 patients and half of patients were confined to a wheelchair or bed within 3 years of onset of gait impairment (Aminoff and Logue, 1974). However, because of the limited radiological techniques, the classification of these 60 patients was unclear. According to their clinical characteristics (acute onset rate was only 10%, age of onset older than 40 years in 81.7% of patients), we speculate the majority of those patients actually harboured spinal dural arteriovenous fistulas, and as such, the results of this study may not accurately represent the natural history of SCAVSs. Gross and Du published a series of pooled analysis of SAVMs, SMAVMs and PMAVFs; the annual haemorrhage rate of the three subtypes was 4%, 2.1% and 2.5%, respectively (Gross and Du, 2013a, b, 2014). However, because of the low incidence of these lesions, these studies are limited by the heterogeneity of included reports.

Similar to brain arteriovenous malformations (Mast et al., 1997; Hernesniemi et al., 2008; da Costa et al., 2009), the initial onset pattern affects the clinical course of SCAVSs. Acute onset was associated with higher rates of spontaneous recovery but was also the only independent
<table>
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<td>Dorsal</td>
<td>146</td>
<td>20.6</td>
<td>82.4</td>
<td>14.5</td>
</tr>
</tbody>
</table>

FU = follow-up.
risk factor of subsequent acute deterioration. In contrast, the majority of patients with gradual onset of symptoms did not spontaneously recover and they were at the highest risk for gradual deterioration. Moreover, Cox multivariate analysis indicated that gradual onset was the strongest predictor for further gradual deterioration. The difference between acute and gradual onset prompt, therefore, a differentiated treatment strategy at our institutions.

The majority of patients who present with acute onset of symptoms harbour a spinal haemorrhage (Rodesch et al., 2004; Ho et al., 2018). For these patients, determining the necessity of emergency decompression surgery is the first challenge for clinicians. Our data indicated that 77% of acute onset patients presented with a favourable spontaneous recovery in the early period after onset. This observation is comparable with the results reported by Rodesch.
et al. They found a spontaneous recovery rate after haemorrhagic presentation of >70%. Because the limited operative field of emergency surgery resulting from haematoma and swollen cord may lead to higher surgical complication rates and lower obliteration rates of the underlying arteriovenous shunts, these authors argued that emergency open surgery was not indicated (Rodesch et al., 2004). However, given our data in a large cohort of patient, we believe this conclusion may benefit from a more differentiated approach. More than 15% of acute onset patients did not spontaneously recover in the observational period of 2 months. Predictive factors for failure to recover were an initial mALS of >3, age of onset older than 28 years, mid-thoracic and non-ventral lesions. We presume that the above-mentioned factors reflect relatively limited compensatory capability of spinal cord function or a severe primary injury of the spinal cord. For example, the vascularization of mid-thoracic segment is the weakest of the cord (Lasjaunias et al., 2001) and the size of mid-thoracic spinal canal is relatively small among the whole spinal segments (Kang et al., 2012), which means that these segments of the spinal cord are more vulnerable when a haemorrhage occurs. Thus, we believe that, while for the majority of patients emergent open surgery is not necessary, a specific subset of patients does benefit from this strategy. The risk of acute deterioration is significantly increased during the first few months after acute onset, which is similar to brain arteriovenous malformation (Mast et al., 1997; Hernesniemi et al., 2008; da Costa et al., 2009). Therefore, although an emergent open surgery is not necessary for the majority of patients with acute onset, we suggest an early endovascular embolization of weak points such as intranidal aneurysms to prevent subsequent haemorrhage.

For patients presenting with gradual deterioration, the subsequent risk of further deterioration was very high especially during the early period after onset and spontaneous recovery was rather rare. The mechanism of this phenomenon is likely multifactorial and includes venous congestion, progressive venous thrombosis or mass effect (Flores et al., 2017; Ho et al., 2018). However, this finding has important implications for early invasive treatment of these patients particularly if they harbour additional risk factors for further deterioration. Given the pathological mechanism, surgical complications caused by a haematoma are of no concern for these patients; thus, early surgical or endovascular management are advised according to angio- and anatomical characteristics of the lesions.

The differences in angio-architecture of SAVMs, SMAVMs and PMAVFs affect the complexity of treatment. Therefore, differences in natural history between these entities are of interest. SMAVMs were previously considered as more unstable lesions given their complex nidus anatomy. Niimi et al. (2013) investigated the clinical course of 28 SMAVMs patients and found that their haemorrhagic rate was higher compared to non-metameric lesions. This is comparable with our results. In addition, these lesions were more prone to present with multiple hemorrhages, although this result did not reach statistical significance (Niimi et al., 2013). Our data did not show significant differences between the three subtypes of SCAVSs regarding their risk for acute deterioration. However, gradual deterioration was seen significantly more often in PMAVFs compared to SAVMs and SMAVMs. We believe that this is related to PMAVFs presenting more often with venous congestion rather than haemorrhage (Flores et al., 2017; Ho et al., 2018). Compared to the other two subtypes, the angio-architecture of most PMAVFs is relatively simple which relates to a relatively easier therapeutic intervention with higher obliteration rates and lower risk of complication (Lee et al., 2014). We therefore propose that PMAVFs should be completely treated in the early
period after symptom onset. Multivariate analysis showed that male gender and increasing age of onset were independent risk factors for gradual deterioration after initial onset. These phenomena have not been reported before and their mechanism remains unclear; however, this finding may have to be factored into management decisions. We found that a large proportion of patients who presented with acute onset or acute deterioration experienced a trigger event with raised thoracic or abdominal pressure. Although we do not have sufficient statistical evidence, we believe it is wise to avoid such events for patients harbouring SCAVSs.

Outcomes of intervention were reported in various previous articles and obviously vary widely between different groups and are different in nidus-type arteriovenous malformations as compared to perimedullary fistulous type arteriovenous malformations. In the Korean cohort, clinical deterioration rate immediately after treatment was 25% and, for SAVMs patients, no recovery was documented at last follow-up (Cho et al., 2013). In the experience of the Toronto group, complication rates of ~4% were reported for both surgery and endovascular management (Lee et al., 2014). In the Barrow series, the permanent complication rate of 13.6% was found for SAVMs (Rangel-Castilla et al., 2014). Our experience is consistent with previous reports, as in this series we found that permanent complication rate related to treatment was 11.5% and the total post-treatment annual deterioration rate was 8.4%. Comparing favourably to the natural history, the treatment results support our approach of early invasive treatment for SCAVSs.

Our data indicate that residual lesions may still harbour the risk of post-treatment clinical deterioration. Therefore, complete obliteration is the goal of SCAVS treatment, which may be difficult in some cases (Lee et al., 2014). The major challenge of the operation is to accurately recognize the angioarchitecture under the microscope and to determine the residual lesion during the procedure. Based on our experience, intraoperative DSA combined with methylene blue angiography is a key technique to achieve complete obliteration with neurological function preservation (Tani et al., 2001; Osanai et al., 2017). The intraoperative DSA can localize the AVM nidus precisely, confirm complete obliteration right after resection and identify residual shunting. Methylene blue angiography can reveal the angioarchitecture of the SCAVSs and identify residual shunting in the operative field of view. In addition, intraoperative neurophysiological monitoring is a reliable tool to preserve spinal function (Li et al., 2018).

There are limitations to our study. We cannot eliminate the possibility that the pattern of referral to our institutes might have affected the results. However, as the only referral centres specialized in spinal vascular diseases within the whole country since 2000, most diagnosed or suspected SCAVSs in China are transferred to our departments. Thus, we believe that our SCAVSs cohort is representative of the general SCAVSs population.

Since most of our patients eventually received surgical or endovascular treatments, patients were inevitably followed for a limited period of time, and 50% of patients in our study were observed within 12 months. Thus, our natural history findings should be interpreted cautiously, especially for patients with a longer history of presentation. Because patients with a long history of mild symptom or transient manifestation may not seek medical counselling unless symptoms deteriorate, one may presume that the risk of deterioration for these patients may be overestimated. However, because of the poor natural history, especially during the early period after onset, and the available modern treatment options, it may not be possible to obtain prospective data of the long-term, untreated clinical course of SCAVSs.

Another limitation of the study is that the endpoints lack objective criteria such as haemorrhage, which is widely used in the natural history study of brain arteriovenous malformations (Mast et al., 1997; Hernesniemi et al., 2008; da Costa et al., 2009). However, the diagnosis of spinal haemorrhage is more difficult than brain haemorrhage. First, compared to the brain, the size of the spinal cord is small, and the signal of flow voids and oedema may obscure small bleeds. Second, spinal subarachnoid hemorrhage with a small volume might be difficult to detect on MRI or CT. In addition, haemorrhage is only one potential cause of SCAVSs to become symptomatic and thus relying only on haemorrhage to determine the natural history is not sufficient for SCAVSs. The mALS was initially designed to assess spinal cord function for patients with spinal vascular diseases and was widely used in clinical practice. It could be obtained by some simple inquiries rather than physical examination, which makes it the best tool to assess the spinal function for observational studies of SCAVSs.

Conclusions

The natural history of symptomatic spinal cord arteriovenous malformations is poor, especially in the early period after onset, and an early intervention is therefore recommended. Our data on stratifying factors which affect the natural history may prove valuable for the decision-making process in individual patients with these complex lesions. We propose emergency open surgery for acute onset patients harbouring non-spontaneous recovery risk factors. For acute onset patients with spontaneous recovery, emergency open surgery is avoided; however, early endovascular embolization may be considered to reduce the risk of subsequent haemorrhage during the early period after the onset. For gradual onset patients, especially for patients harbouring risk factors for subsequent deterioration, early surgical or endovascular managements should be performed according to the angiographic and anatomical characteristics of the lesions. The acute deterioration risks of SAVMs, PMAVFs and SMAVMs are similar, while PMAVFs harbour a
significantly higher risk of gradual deterioration, which necessitates an early invasive treatment.

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**Competing interests**

The authors declare no competing financial interests.

**Supplementary material**

Supplementary material is available at Brain online.

**References**


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