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Learning curve and embolisation strategy in single-stage surgery combined embolisation and microsurgery for brain arteriovenous malformations: results from a nationwide multicentre prospective registry study

Tengfei Yu,[1] Heze Han ,[1] Li Ma,[1,2] Yang Zhao ,[1,3] Yukun Zhang,[1,3] Youxiang Li,[1] Shuo Wang ,[1] Yu Chen ,[1] Xiaolin Chen[1]

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[1]Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing, China
[2]Department of Neurological Surgery, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, USA
[3]Department of Neurosurgery, Peking University International Hospital, Beijing, China

Correspondence to
Yu Chen; chenyu_tiantan@126.com

Xiaolin Chen; xiaolinchen488@hotmail.com

ABSTRACT

Objective Single-stage surgery combining embolisation and microsurgery has been increasingly used as a stand-alone procedure to cure complex AVMs. This study aimed to investigate the learning curve and embolisation strategy for single-stage surgery for AVMs.

Methods This prospective cohort study used data from the nationwide Multimodality Treatment for Brain Arteriovenous Malformations (MATCH) registry in China, conducted between August 2011 and December 2023. A total of 213 complex AVMs were divided into two groups. Group 1 included the first 25 patients. The 188 cases in group 2 included patients numbered 26–213. A case-crossover design was employed to evaluate the influence of complications, unfavourable outcomes and worsening modified Rankin Scale (mRS) score. Cumulative summation analysis was performed to assess the learning curve.

Results The rate of major complications decreased from 52.00% in group 1 to 34.57% in group 2 (p=0.089), while the rate of unfavourable outcomes decreased from 44.00% in group 1 to 18.62% in group 2 (p=0.004). The distribution of the three preoperative embolisation strategies was as follows: curative: 72.00% and 19.15%, palliative: 24.00% and 67.55%, and targeted: 4.00% and 13.30%, respectively (p<0.001). Multivariable regression analysis showed that surgeon experience was associated with a lower rate of unfavourable outcomes (p=0.022, OR=0.333). The mean follow-up duration was 49.90±20.54 months. The follow-up mRS score of 5–6 decreased from 9.09% in group 1 to 0.8% in group 2 (p=0.035).

Conclusions Performing single-stage combined surgery in 25 AVM cases is necessary to achieve reproducibility. Rates of major complications and unfavourable outcomes decreased significantly after the first 50 procedures. Palliative and targeted embolisation strategies are associated with a lower rate of unfavourable outcomes.

Trial registration number NCT04572568.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Several studies have proposed that a single-stage combined embolisation and microsurgery strategy might benefit the long-term neurofunctional outcomes of complex arteriovenous malformations (AVMs). Although previous studies have shown an association between operator experience and patient outcomes, the learning curve has rarely been visually depicted.

WHAT THIS STUDY ADDS

⇒ The operator experience and major complications and unfavourable outcomes were linear. Single-stage surgery for AVMs requires a learning curve of 25 cases to achieve reproducibility. Palliative and targeted embolisation strategies are associated with a lower rate of unfavourable outcomes.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The study is of significance in that it assists neurosurgeons in the expeditious mastery of this novel procedure, thereby leading to the enhancement of patient prognosis.

INTRODUCTION

Arteriovenous malformations (AVMs) are complex and rare cerebral vascular dysplasias characterised by a dense tangle of abnormally dilated vessels. AVMs usually manifest as intracranial haemorrhage (30%–70%), seizure (10%–30%), headache or incidental findings (0%–15%).[1–3] Curative treatments include microsurgical resection, endovascular therapy and stereotactic radiosurgery, which are often performed individually or in combination. Complex AVMs may require extended periods of multiple hospitalisations, along with intensive multimodal treatments.[4 5] Several studies have proposed that a single-stage combined embolisation and microsurgery strategy might benefit the long-term neurofunctional outcomes of complex AVMs.[6–8] This procedure is becoming increasingly common due to its numerous advantages, including reduced intraoperative bleeding and shorter surgeries. Patients benefit from a reduction in the psychological stress and financial burden associated with multiple treatments. However, experience with this strategy in low-volume neurovascular centres remains somewhat preliminary. Learning and promoting these surgical techniques can enhance the safety and long-term outcomes of procedures. There is still not enough information about how many procedures are needed to become skilled at single-stage surgery for AVM treatment. It helps us understand the risks of poor results, make decisions in difficult cases and create training programmes.[9] Although previous studies have shown an association between operator experience and patient outcomes, the learning curve has rarely been visually depicted.[10–12]

Cumulative summation (CUSUM) analysis has successfully assessed the learning curve of specific interventions using historical outcome data as a baseline for comparison.[13 14] Therefore, the purpose of this study was to evaluate the learning curve for single-stage surgical treatment and identify the factors that influence procedural safety and success.

METHODS

Study design and participants

This was a prospective cohort study using nationwide multicentre registry data from the registry of multimodality treatment for brain AVMs (BAVMs) in MATCH registry (NCT 04572568). This study was conducted in accordance with the Strengthening the Reporting of Cohort Studies in Surgery criteria.[15] Previous studies have demonstrated the validity and quality of databases for research, and the inclusion criteria for MATCH have been previously reported.[16] All AVMs included in the MATCH registry between 1 August 2011 and 31 December 2023 were reviewed. The inclusion criteria were as follows: (1) diagnosis of AVM, (2) patients who underwent single-stage surgery and (3) follow-up for more than 3 months. Patients with multiple AVMs, hereditary haemorrhagic telangiectasia, or who underwent invasive procedures before admission were excluded. The patients were categorised as follows: Group 1 (first 25 procedures) and group 2 (procedures 26–213). CUSUM analysis was the basis for dividing patients into two groups (figure 1). Dividing the study population into two groups at the peak of the learning curve is a generally accepted practice for studying the learning curve of a certain medical technology with the CUSUM.[13 14]

Data collection and definition

Demographic characteristics, clinical features and imaging data were collected as the baseline data. The definition of eloquent area and deep venous drainage was consistent with the Spetzler-Martin grading system. Associated aneurysms were defined as nidal, perinidal or flow related. Major complications were defined as one or more of the four postoperative complications of haemorrhagic events, ischaemic events, intracranial infections and seizures within 1 week after the operation. Unfavourable outcomes were defined as a discharge modified Rankin Scale (mRS) score of 5–6 or worsening mRS, which meant discharge mRS elevation ≥2 over the preoperative mRS.[17] The long-term outcomes were evaluated at the last follow-up visit. Clinical follow-up was conducted within the first 3–6 months and annually after discharge.

Single-stage surgery details

The single-stage surgery team proactively planned each AVM operation at a multidisciplinary vascular conference held every weekday at our centre. AVMs with a large nidus (>3 cm), deep location, multisource blood supply, and critical eloquent areas were considered as complex AVMs. The definition of complex AVM was based on the angioarchitectural factors of DSA (Digital Subtraction Angiography) . The definitions of all variables have been published in the previous protocol.[16] The operation was performed in a hybrid angiosurgical suite. All procedures were performed after the induction of general anaesthesia. There was no standardised protocol for the embolisation strategy. It was formulated after a collective discussion of the patient's specific angioarchitectural factors before surgery. During embolisation, three strategies were used based on the preoperative plan: (1) Curative: embolise as much AVM nidus as possible. (2) Palliative: embolisation of select, high-flow feeders and margins of the nidus aimed to reduce intraoperative bleeding and determine surgical borders. (3) Targeted: embolisation of the part with a high rupture risk (flow-related aneurysms or high-flow arteriovenous fistula).

After embolisation, microsurgery was performed. After resection and before skull closure, cerebral angiography was performed to determine if the lesion was completely occluded. Anti-epilepsy and anti-brain oedema treatment were routinely performed after the operation. All patients underwent CT on the first day after surgery.

Statistical analysis

CUSUM analysis

The CUSUM analysis was performed using the following equation:

$$E_n = E_{(n-1)} + X_n \text{ with } E_0 = 0,$$

where E_n is the CUSUM after n iterations. X_n denotes the result following the nth procedure, with X_n=1–X_0 if a failure occurred and X_n=0–X_0 if it did not. X_0 can be calculated either as an overall frequency if this is known in this case or on a case-by-case basis, as with paired control trials. Seven indicators were used to evaluate the learning curve: (1) unfavourable outcomes: (a) worsen mRS; (b) discharge mRS 5–6 and (2) complications: (c) haemorrhagic events; (d) ischaemic events; (e) intracranial infections; (f) seizure and (g) intraoperative blood loss. In the present study, seven X_0 were X_{a0}=0.224, X_{b0}=0.035, X_{c0}=0.127, X_{d0}=0.067, X_{e0}=0.272, X_{f0}=0.033 and X_{g0}=0.394 based on the overall frequency in this case, and

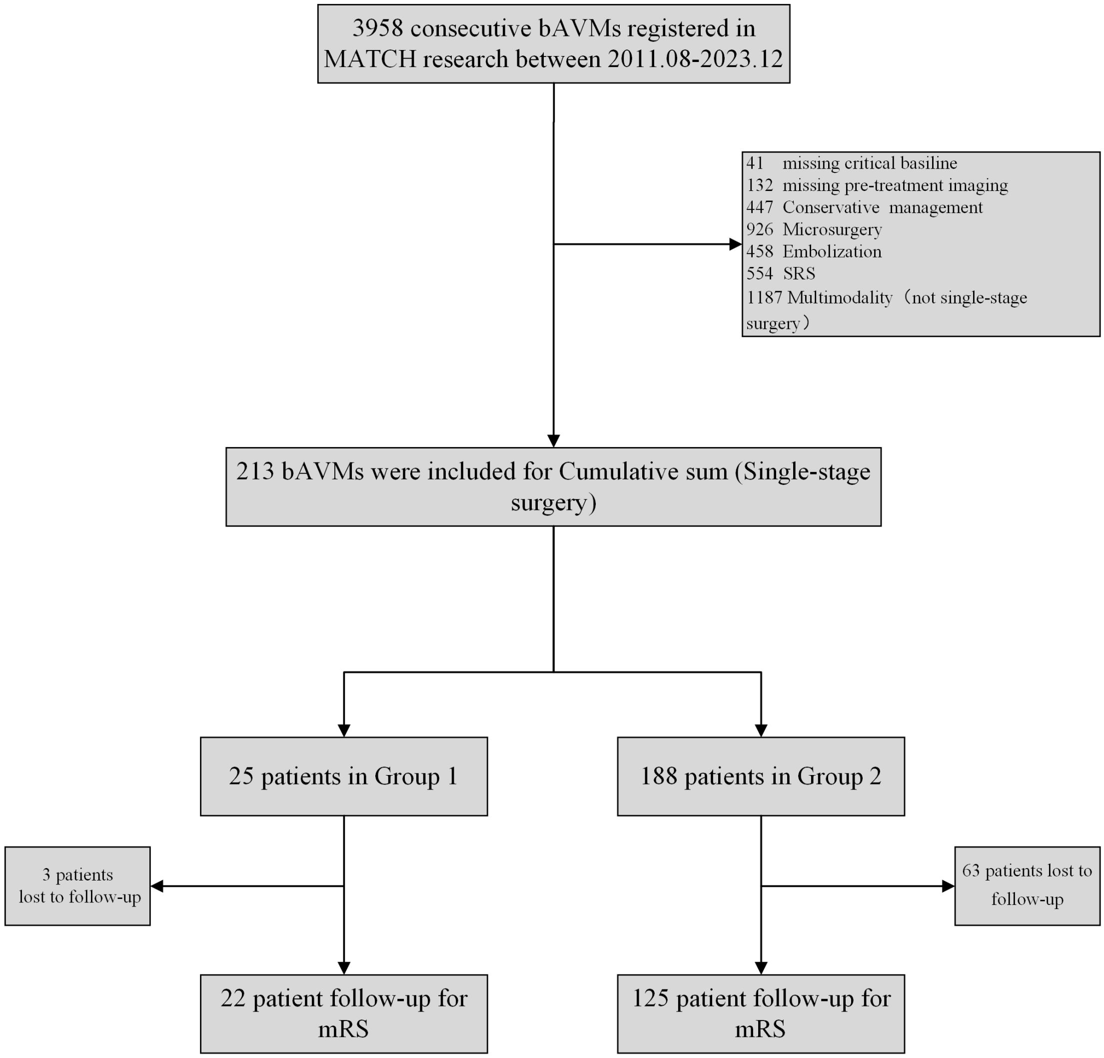

Figure 1 Flow chart of the study. bAVMs, brain arteriovenous malformations; mRS, modified Rankin Scale；SRS,stereotactic radiosurgery；MATCH,Multimodal treatment for brain ArTeriovenous malformation in mainland CHina.

the accuracy data provided by two meta-analyses included 1088 and 1352 surgeries combining embolisation and microsurgery, respectively.[18 19] Intraoperative blood loss of >549 mL was defined as failure.

Single-factor analysis

Categorical variables are presented as percentages and continuous variables as mean with SD or median with IQR. The baseline characteristics of patients were compared using the two-tailed t-test or Mann-Whitney U test for continuous variables, and the χ^2 test or Fisher's exact test was used for categorical variables, as appropriate.

Multifactor analysis and restricted cubic splines analysis

Multivariable logistic regression models were fitted to evaluate the effect of operator experience on the probability of major complications and unfavourable outcomes at discharge. ORs with 95% CIs were estimated for different surgical groups.

Statistical analyses were performed using SPSS Statistics V.27.0 (IBM) and R software V.4.3.0, and all tests were two-sided, with a significance level set at p<0.05.

RESULTS

Study population and baseline characteristics

A total of 213 patients were included in our hospital (table 1). Of these patients, 40.85% (87/213) were female, and the mean age was 29.45±14.17 years (with a range of 5–64 years). Common comorbidities in the study population included hypertension (5.63%, 12/213) and diabetes (0.94%, 2/213). In total, 49.77% (106/213) of the AVMs ruptured before surgery. The baseline characteristics were compared across cohorts (table 1). In summary, baseline demographics between the two groups appeared similar, without statistical differences.

Procedural variables

All 213 AVMs were completely resected. No statistical differences were observed in the preoperative mRS

Table 1 Comparison of baseline, procedural variables and complications among patient groups

Characteristics	Total (n=213)	Group 1 1–25 (n=25)	Group 2 26–213 (n=188)	P value	Statistic
Demographic variables					
AVM patients treated	213	25	188		
Age, years	29.45±14.17	31.96±16.12	29.11±13.90	0.346	t=0.94
Female sex, n (%)	87 (40.85)	11 (44.00)	76 (40.43)	0.733	χ^2=0.12
Alcohol abuse, n (%)	21 (9.86)	5 (20.00)	16 (8.51)	0.146	χ^2=2.11
Smoking, n (%)	38 (17.84)	5 (20.00)	33 (17.55)	0.982	χ^2=0.00
Hypertension	12 (5.63)	1 (4.00)	11 (5.85)	0.706	χ^2=0.00
Diabetes	2 (0.94)	0 (0.00)	2 (1.06)	0.604	–
Presentation, n (%)				0.218	χ^2=3.05
Incidental	10 (4.69)	0 (0.00)	10 (5.32)		
Symptomatic	97 (45.54)	9 (36.00)	88 (46.81)		
Ruptured	106 (49.77)	16 (64.00)	90 (47.87)		
Preoperative mRS				0.693	–
0–2	196 (92.02)	24 (96.00)	172 (91.49)		
3–4	14 (6.57)	1 (4.00)	13 (6.91)		
5–6	3 (1.41)	0 (0.00)	3 (1.60)		
AVM variables					
AVM size, mm	39.15±15.34	44.33±14.48	38.47±15.35	0.072	t=1.81
Spetzler-Martin grades				0.214	χ^2=3.08
I–II	94 (44.13)	7 (28.00)	87 (46.28)		
III	89 (41.78)	13 (52.00)	76 (40.43)		
IV–V	30 (14.08)	5 (20.00)	25 (13.30)		
Eloquent location	120 (56.34)	15 (60.00)	105 (55.85)	0.694	χ^2=0.15
Deep venous drainage	66 (30.99)	8 (32.00)	58 (30.85)	0.907	χ^2=0.01
Associated aneurysms	42 (19.72)	4 (16.00)	38 (20.21)	0.818	χ^2=0.05
AVM location, n (%)				0.354	–
Superficial	160 (75.12)	17 (68.00)	143 (76.06)		
Deep	34 (15.96)	4 (16.00)	30 (15.96)		
Cerebellum	16 (7.51)	4 (16.00)	12 (6.38)		
Brainstem	3 (1.41)	0 (0.00)	3 (1.60)		
Embolisation strategy, n (%)				<0.001	χ^2=32.79
Curative	54 (25.35)	18 (72.00)	36 (19.15)		
Palliative	133 (62.44)	6 (24.00)	127 (67.55)		
Targeted	26 (12.21)	1 (4.00)	25 (13.30)		
Major complications, n (%)	78 (36.62)	13 (52.00)	65 (34.57)	0.089	χ^2=2.89
Haemorrhagic events	13 (6.10)	3 (12.00)	10 (5.32)	0.386	χ^2=0.75
Ischaemic events	10 (4.69)	3 (12.00)	7 (3.72)	0.182	χ^2=1.78
Intracranial infections	57 (26.76)	8 (32.00)	49 (26.06)	0.529	χ^2=0.40
Seizure	7 (3.29)	0 (0.00)	7 (3.72)	> 0.999	–
Blood loss ≥549 mL	85 (39.91)	14 (56.00)	71 (37.77)	0.080	χ^2=3.06
Blood loss, mL, median (Q_1, Q_3)	500 (300, 1000)	750 (500, 1500)	500 (300, 1000)	0.135	Z=−1.49
Unfavourable outcomes, n (%)	46 (21.60)	11 (44.00)	35 (18.62)	0.004	χ^2=8.40
Worsen mRS	41 (19.25)	8 (32.00)	33 (17.55)	0.147	χ^2=2.11
Discharge mRS=5–6	5 (2.35)	3 (12.00)	2 (1.06)	0.012	–

Continued

Table 1 Continued

Characteristics	Total (n=213)	Group 1 1–25 (n=25)	Group 2 26–213 (n=188)	P value	Statistic
Discharge mRS score, n (%)				0.002	–
0–2	160 (75.12)	13 (52.00)	147 (78.19)		
3–4	48 (22.54)	9 (36.00)	39 (20.74)		
5–6	5 (2.35)	3 (12.00)	2 (1.06)		
Follow-up time,month	49.90±20.54	72.26±3.83	46.00±19.75		
Follow-up patients	147 (69.01)	22 (88.00)	125 (66.49)		
Follow-up mRS score, n (%)				0.035	χ^2=6.71
0–2	124 (84.35)	18 (81.82)	106 (84.80)		
3–4	20 (13.61)	2 (9.09)	18 (14.40)		
5–6	3 (2.04)	2 (9.09)	1 (0.80)		

–: Fisher's exact test.
AVM, arteriovenous malformation; mRS, modified Rankin Scale; Z, Mann-Whitney test.

score and AVM variables. A lower curative embolisation strategy of 19.15% (36/188) and a higher palliative strategy (67.55%, 127/188) and targeted strategy (13.30%, 25/188) were observed in group 2, while the corresponding values in group 1 were 72.00% (18/25), 24.00% (6/25) and 4.00% (1/25), respectively (p<0.001) (table 1).

Subgroup analyses

The learning curve has two key inflection points, namely the peak value and the 0 value. These are the two most important demarcation points in the CUSUM study of the learning curve. The significance of the peak value was that the failure rate showed a decreasing trend starting from the 25th operation. The significance of the zero value was that the failure rate of each variable has reached a stable level starting from the 50th operation. Grouping was based on the key threshold of CUSUM=0. The study population was divided into group 3 (1–50 n=50) and group 4 (51–213 n=163). The results showed that palliative embolisation and targeted embolisation still accounted for a relatively large proportion in group 4, and there were statistical differences (online supplemental material 1). There were no statistical differences in other variables. This was consistent with the results in table 1.

Groups were compared using populations of equal size. After the surgical failure rate stabilised, the 51st to the 75th operations were selected as the other group. The study population was divided into group 1 (1–25 n=25) and group 5 (26–75 n=25) (online supplemental material 2). The result was consistent with the online supplemental material 1 and table 1.

Complications and functional outcomes

A reduction in the rate of complications and poor outcomes was observed in the cohort. Specifically, the rate of major complications decreased from 52.00% (13/25) in group 1 to 34.57% (65/188) in group 2. Although there was no statistical difference, haemorrhagic events (5.32%, 10/188), ischaemic events (3.72%, 7/188), intracranial infections (26.06%, 49/188) and intraoperative blood loss ≥549 mL 37.77%, 71/188) all decreased in group 2, while the corresponding values in group 1 were 12.00% (3/25), 12.00% (3/25), 32% (8/25) and 56.00% (14/25), respectively. Intraoperative blood loss showed a non-normal distribution, and the median values were 750 (IQR, 500–1500) mL in group 1 and 500(IQR, 300–1000) mL in group 2. However, the incidence of postoperative seizures was higher in group 2 than in group 1 (3.72% (7/188) vs 0.00% (0/25)).

For unfavourable outcomes, group 2 had significantly lower and statistically different rates than group 1 (18.62% (35/188) vs 44.00% (11/25), p=0.004). Further analysis revealed that this difference appeared in the discharge mRS=5–6, which was 1.06% (2/188) lower in group 2 than in group 1 (12.00%, 3/25) (p=0.012). As for worsening mRS, although the rate was also lower by 17.55% (33/188) in group 2 than 32.00% (8/25) in group 1, the difference was not statistically significant. In comparison with group 1, group 2 had an increase in the rate of discharge mRS=0–2 (78.19% vs 52.00%) along with a decrease in the rates of discharge mRS=3–4 (20.74% vs 36.00%) and discharge mRS=5–6 (1.06% vs 12.00%).

A total of 147 (69.01%) AVMs were followed up, and the mean follow-up time was 49.90±20.54 months(3.3 to 77.4). Group 2 was significantly lower in achieving a poor outcome (mRS=5–6) (0.8% vs 9.09%, p=0.035), while the rates of group 2 at mRS=0–2 and mRS=3–4, respectively, were 84.80% (106/125) and 14.40% (18/125), respectively. Correspondingly, the rates for group 1 were 81.82% (18/22) and 9.90% (2/22), respectively. In summary, group 2 exhibited a lower incidence of unfavourable

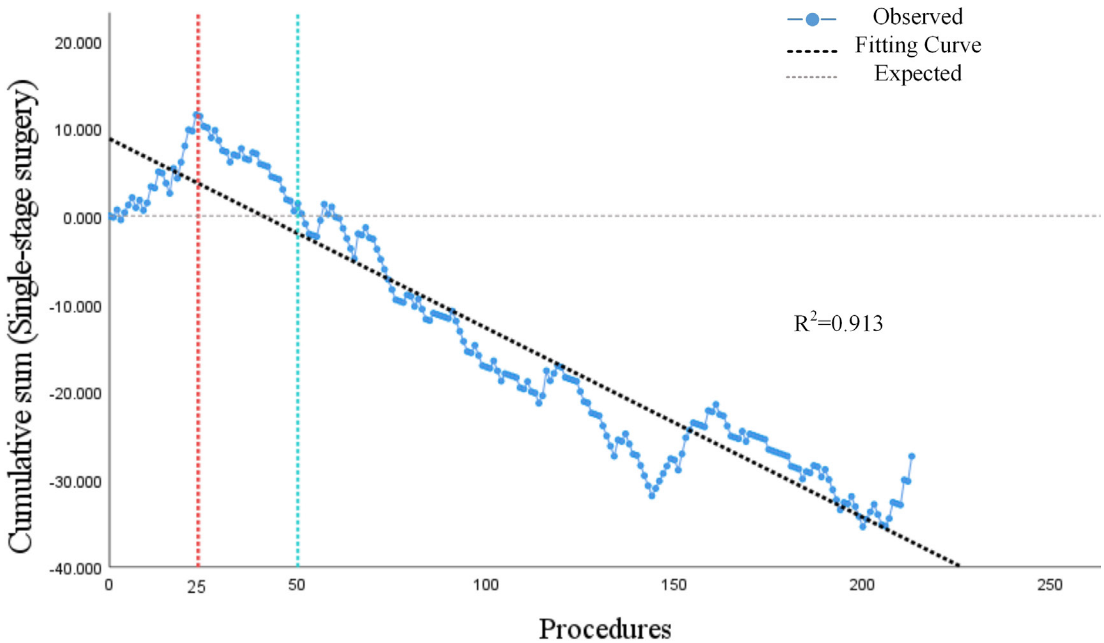

Figure 2 Cumulative summation (CUSUM) analyses for single-stage surgery. A downward gradient implies that the procedure is safe and does not increase risk compared with the control (other hybrid treatment modalities). Any change to an upward gradient should alert the investigators to an increase in the potential risk of the operation (as can be seen between procedures 1 and 25). This was also the basis for dividing patients into two groups. The end of the learning curve is regarded as the point where the failure rate remains at the expected level (CUSUM=0) or lower. The observed CUSUM scores reduced below the expected required up to 50 cases. Dots represent the actual observed CUSUM score; lines represent the fitted linear regression model. The fitting curve of the learning curve was linear and its equation was as follows: y=–0.2155624221311349 *x+8.778743751358391.

outcomes, a lower discharge mRS score and a lower follow-up mRS score compared with group 1.

CUSUM analysis and learning curve assessment

The CUSUM analyses for single-stage surgery are presented in figure 2. The plot for single-stage surgery showed a downward trend with a high correlation (R^2=0.913), indicating that the procedure became safer as the operator gained experience. The observed CUSUM value reached the highest point in 25 procedures, then gradually decreased and began to fall below the expected value (CUSUM=0) in 50 procedures. Similarly, the fitting curves for unfavourable outcomes and complications showed linear declines (R^2=0.837 and 0.905, respectively). The end of the learning curve was defined as the point at which the failure rate remained at the expected level or lower. The observed CUSUM values of unfavourable outcomes and complications were reduced below the expected required up to 50 cases and peaked at 28 and 24, respectively (figure 3).

A linear decline in the fitting curve was also found for discharge mRS=5–6 and worsening mRS (R^2=0.737 and 0.755, respectively) (figure 4). As for complications, haemorrhagic and ischaemic events showed a linear downward trend (R^2=0.982 and 0.771, respectively). Intracranial infections showed a curvilinear decline (R^2=0.746), and although it rose after a nadir in 145 procedures, it was still below the expected value. The curve for epilepsy fluctuated (R^2=0.719); however, the overall curve was below the expected line. The fitting curve for intraoperative blood loss showed large fluctuations (R^2=0.841), which increased after 150 procedures, and the last individual values exceeded the expected line, which reminded us that haemorrhage requires more long-term attention than other complications (figure 5).

Multivariable logistic regression and restricted cubic spline

The relationship between operator experience and major complications was non-linear. The overall trend of the OR values clearly decreased but with small fluctuations. However, the relationship between the procedures and unfavourable outcomes was linear (figure 6). The OR decreased progressively as the number of procedures increased. After 50 procedures, both risks were significantly lower (OR<1). This result was consistent with the results shown in figure 3 and could be verified with each other. Although the association with fewer major complications did not reach statistical significance, group 2 was still associated with a decreased risk of unfavourable outcomes at discharge (OR 0.333, 95% CI 0.130 to 0.852, p=0.022) (table 2).

DISCUSSION

This study reports the safety of single-stage surgery based on a large series of BAVMs treated at multiple institutions in China. CUSUM analyses were employed to evaluate the learning curve for single-stage surgery, which has not

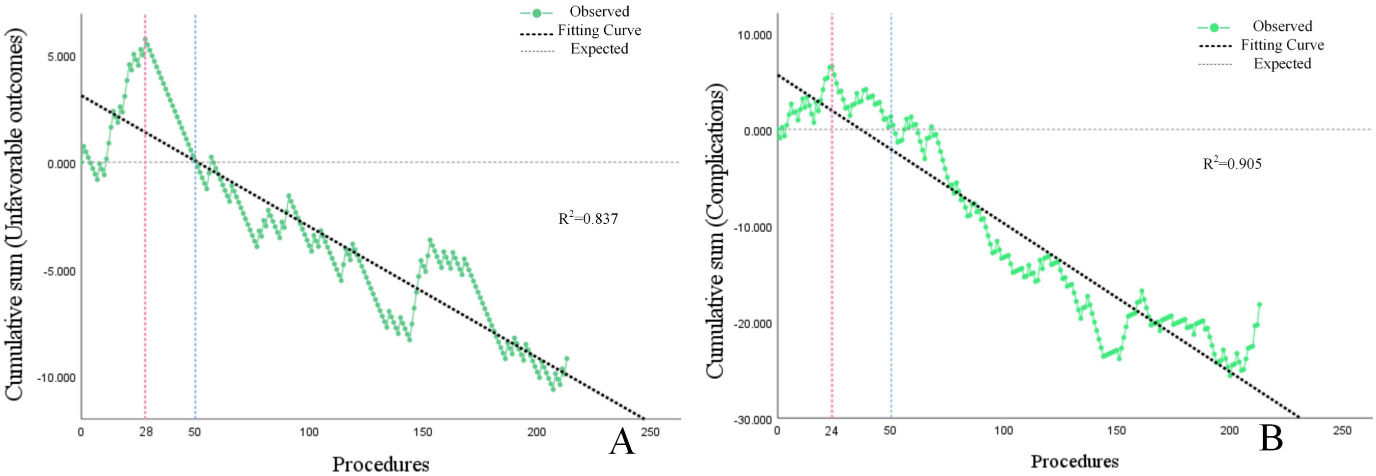

Figure 3 Cumulative summation (CUSUM) analyses for unfavourable outcomes and complications. CUSUM analysis for unfavourable outcomes (A) and complications (B). The unfavourable outcomes and complications rate reduced below the expected required up to 28 and 24 cases. The end of the learning curve is regarded as the point where the failure rate remains at the expected level (CUSUM=0) or lower, which both required up to 50 cases. The fitting curves were linear and their equations were as follows: (A) y=−0.06116976713574208*x+3.113323190610737. (B) y=−0.1543926549953929 *x+5.665420560747661.

been previously investigated. A minimum of 25 cases are required to achieve reproducibility of both complications and unfavourable outcomes.

Surgeons prefer to evaluate the disease progression and treatment efficacy whenever possible. CUSUM analysis has the potential to be used as a warning detector and an indicator for the quality assurance of operator revalidation. The present study demonstrates that single-stage surgery is associated with low complication and mortality rates for AVMs that are often deemed high-risk or unsuitable for traditional treatments. The major complication and unfavourable outcome rates (36.62% and 21.60%, respectively) in our study population were consistent with those of previously published studies. A multinational retrospective study reported a 39.18% complication rate of 22.37% neurological mortality involving 1088 patients.[19] In a pooled analysis that included 1352 patients, the complication rates of haemorrhagic and ischaemic events were 12.7% and 6.7%, respectively. In this study, the rates were 6.10% and 4.69%, respectively.[18] Haemorrhagic events were the most common complications associated with single-stage surgery for AVMs. Of the five patients who experienced poor outcomes (discharge mRS=5–6) in our study, four reported haemorrhagic complications and the other patient developed a postoperative ischaemic event.

Unlike the standard strategy, single-stage surgery requires neurosurgeons and interventional neuroradiologists to perform the procedure together. The single-stage strategy represents a fairly challenging procedure requiring better technical flexibility, sophisticated skills,

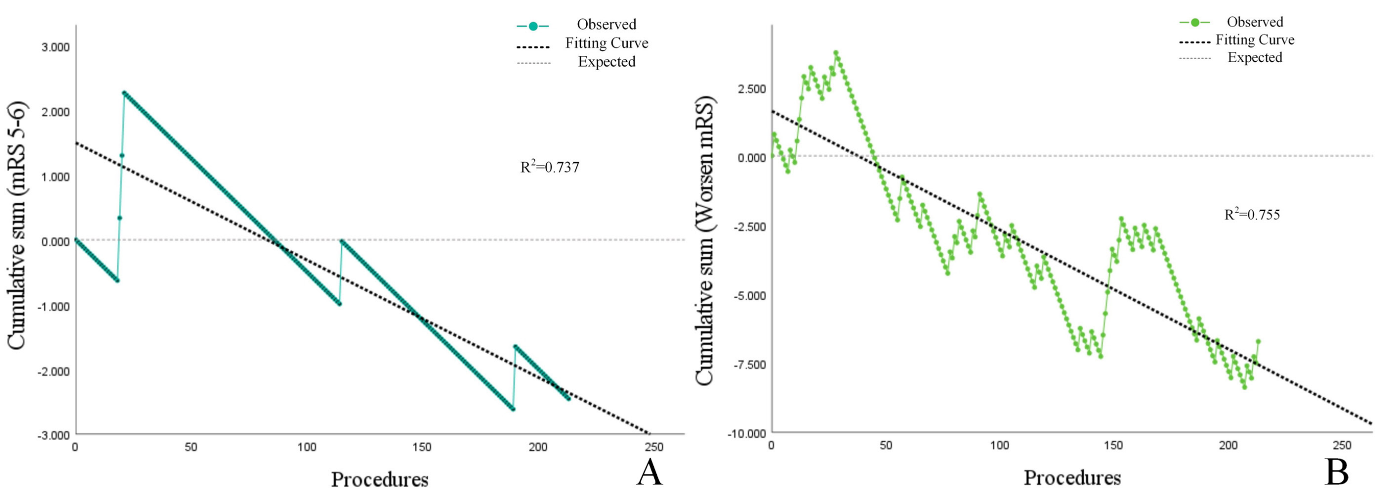

Figure 4 Cumulative summation (CUSUM) analyses for discharge modified Rankin Scale (mRS)=5–6 and worsen mRS. CUSUM analysis for discharge mRS=5–6 (A) and worsen mRS (B). Unfavourable outcomes included discharge mRS=5–6 and worsen mRS. Both fitting curves showed a linear downward trend. The fitting curve equations were as follows: (A) y=−0.018112 67299515414*x+1.495892197348401. (B)y=−0.04305709414058793*x+1.617430993262333.

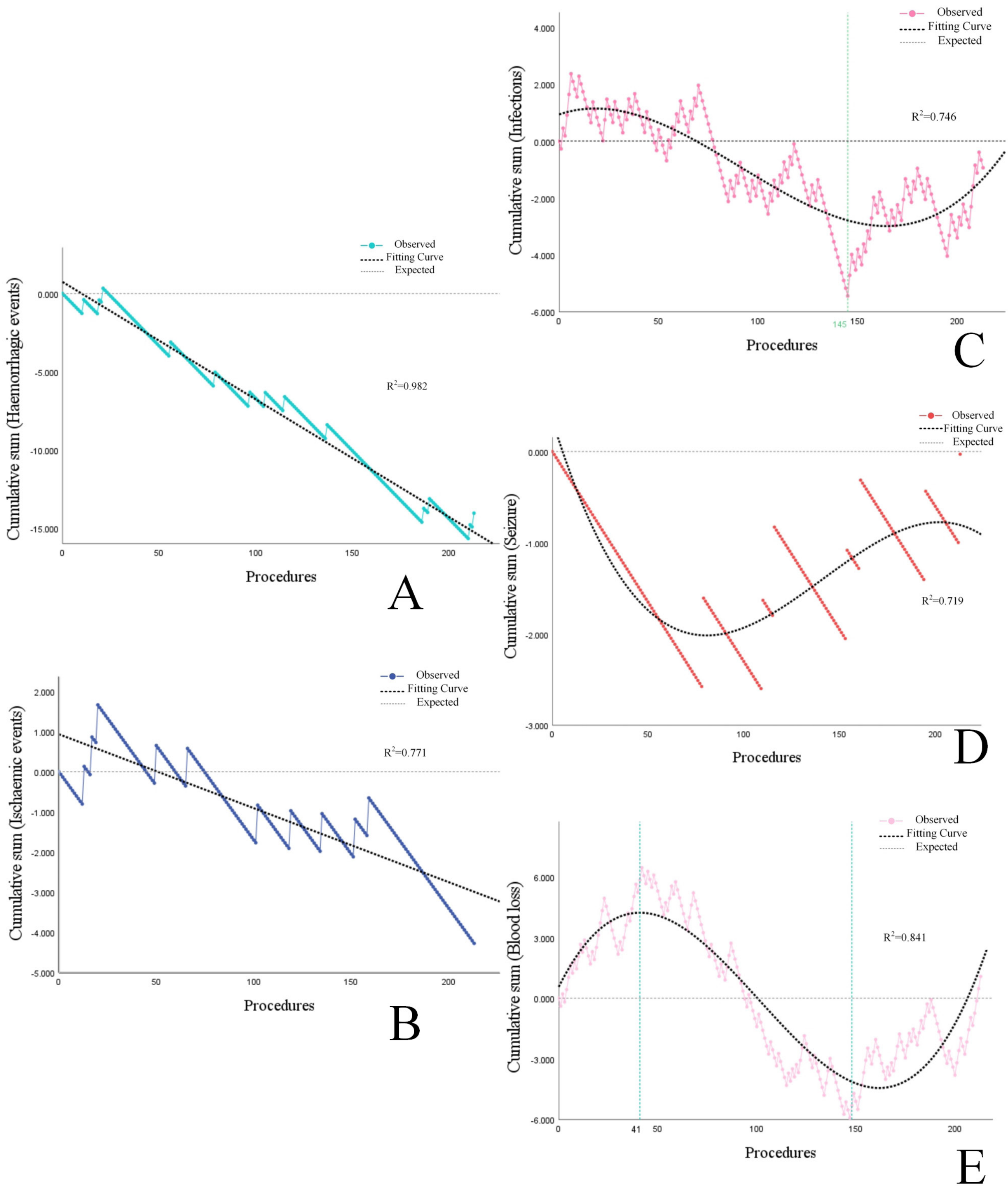

Figure 5 Cumulative summation (CUSUM) analyses for haemorrhagic events, ischaemic events, infections, seizures, blood loss. Haemorrhagic events (A) and ischaemic events (B) showed a linear downward trend. The fitting curve equations were as follows: (A) $y=-0.07515150411270054*x+0.7444903281895225$. (B) $y=-0.01840493034276076*x+0.932101717018039$. Intracranial infections (C) showed a curvilinear decline, and although it rose after a nadir at 145 procedures, it was still below the expected value. The fitting curve equation was as follows: $y=0.9370831804525919+0.02376376455737684*x-0.0007243051247589228*x^2+0.000002643860078836753*x^3$. The curve for epilepsy fluctuated (D), but the overall curve was all below the expected line. The fitting curve equation was as follows: $y=0.3457569999974757-0.06753806242850539*x+0.0005858781173788112*x^2-0.000001381084293180291*x^3$. The fitting curve for intraoperative blood loss showed large fluctuations (E); it rose after 150 procedures, and the last individual values exceeded the expected line, which reminded us that haemorrhage requires more long-term attention than other complications. The fitting curve equation was as follows: $y=0.5579249173672096+0.195632227723806*x-0.00299286579847285*x^2+0.000009845240618328809*x^3$.

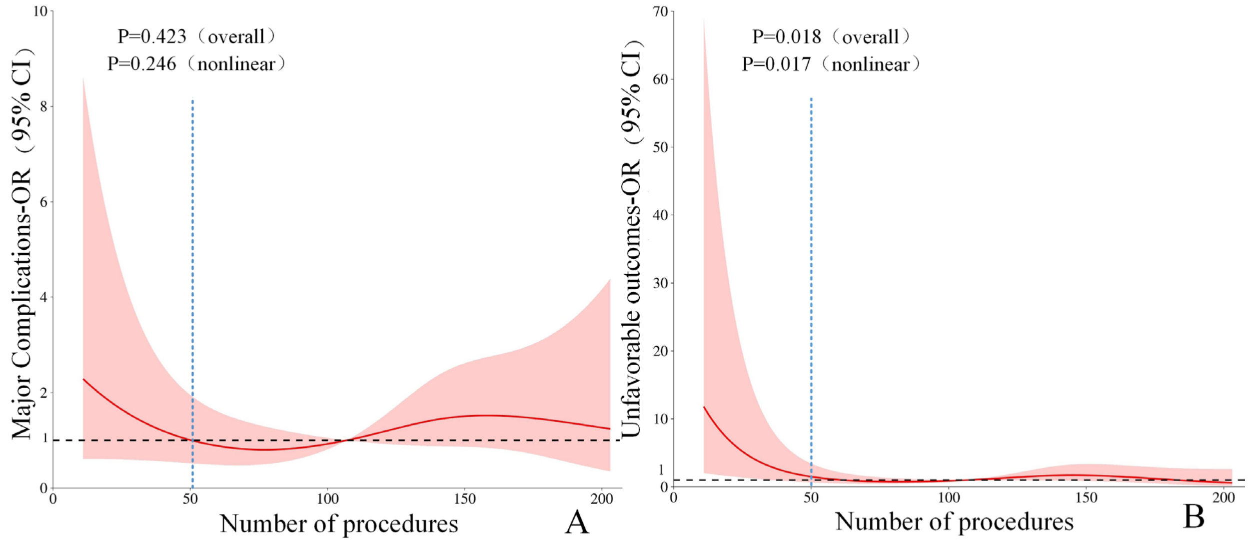

Figure 6 RCS for major complications and unfavourable outcomes. RCS for major complications (A) and unfavourable outcomes (B) showed that OR values decreased progressively as the number of these procedures increased. After 50 procedures, both risks were significantly lower (OR<1). This result was consistent with the result in figure 3. There was a non-linear relationship between surgical experience and major complications, but a linear relationship between procedures and unfavourable outcomes. RCS, restricted cubic spline.

precise teamwork and strong mutual trust. Our study also observed similar results for single-stage surgery consistent with previous reports.[20 21] This study had the largest number of single-centre single-stage surgical cases, far exceeding those of other studies, and the obtained results were more reliable. The rate of major complications declined from 52.00% in group 1 to 34.57% in group 2, and the rate of unfavourable outcomes decreased from 44.00% during the first 25 procedures to 18.62% in group 2. Alshehri *et al*[22] reported that the decreasing complication rate could be related to the evolution of the embolisation strategy. Although there was no statistical difference, compared with group 1, group 2 showed a decrease in haemorrhagic events, ischaemic events, intracranial infection and blood loss (p=0.089). This study did not incorporate specific variables regarding the severity of complications, such as the amount of bleeding, the area of infarction and the type of epileptic seizure. Instead, only the incidence of complication variables was included. Since the prognosis of patients in group 2 was better, it is reasonable to infer that the severity of postoperative complications in patients in group 2 was lower. For example, the amount of postoperative bleeding was less, the area of infarction was smaller and the condition of epileptic seizures was milder. Regarding the treatment for BAVM, both the interventional team and the surgical team in this study have many years of experience. The treatment team had reduced the incidence of postoperative complications of embolisation therapy and surgical resection to a satisfactory clinical level. It was extremely difficult to further significantly reduce the incidence of complications, but reducing the severity of complications was the direction of current research. The results of this study were in line with this actual clinical phenomenon. The postoperative seizure rate in group 2 was higher than that in group 1, but the difference was not statistically significant, which may be due to the increase in the number of operations. The rates of unfavourable outcomes, discharge mRS and follow-up mRS scores were significantly lower in group 2 than in group 1, indicating that group 2 had a better functional outcome. Only embolism strategies were significantly different; specifically, palliative and targeted strategies were used more frequently in group 2. De Leacy *et al*[23] and Shakur *et al*[24] believed that the embolisation strategy has a key influence on the difficulty of single-stage surgery and, thus,

Table 2 Adjusted ORs of outcomes according to consecutive series of procedures

Outcomes	Surgical experience	N	Events, n (%)	Adjusted OR (95% CI)*	P value
Major complications	Group 1	25	13 (52.00)	Ref	Ref
	Group 2	188	65 (34.57)	0.597 (0.251 to 1.422)	0.244
Unfavourable outcomes	Group 1	25	11 (44.00)	Ref	Ref
	Group 2	188	35 (18.62)	0.333 (0.130 to 0.852)	0.022

*Adjusted for age, sex, AVM size, location, deep venous drainage and associated aneurysms.
AVM, arteriovenous malformation; mRS, modified Rankin Scale.

the outcome of patients, which is consistent with the findings of this study. Palliative and targeted strategies result in fewer complications and better functional outcomes. The mechanism for this difference remains unclear, and possible reasons are listed below.

The goal of curative embolisation is to embolise as many AVMs as possible, which causes sclerosis of more tissues in the area to be surgically removed. This limits the surgical manoeuvring space and surgical field of view, which are two of the most important surgical requirements for neurosurgeons and indeed all surgeons. Especially in the deep surgical phase, which is the most challenging phase of AVM surgery for the surgeon, the sclerotic tissue takes up more space and is difficult to pull and shift, which increases the difficulty of the surgery, duration of the surgery and chances of postoperative complications. Curative embolisation usually requires additional, more complex operations, which can also increase operative time. Surgical teams that have experienced this difficulty naturally consider the use of palliative and targeted embolisation, which allows for a more precise definition of the surgical area boundaries and reduced blood supply. These findings suggest the presence of an initial learning curve in single-stage surgery and that increased operator experience is associated with procedural safety.

Our findings support the linear relationship between operator experience, complications and unfavourable outcomes. Although there is no clear distinction between the plateau and learning phases, the risk of major complications and unfavourable outcomes dropped rapidly over the initial 25 procedures. Notably, this study represents the first description of the learning curve for single-stage surgery for AVMs based on the CUSUM analysis. The learning curve for major complications and unfavourable outcomes fell below the expected line after 50 procedures. Therefore, up to 50 formal training procedures may be necessary to achieve a very low risk of complications and unfavourable outcomes. It is worth noting that while billions are invested in bioinformation research at all levels, little effort is dedicated to understanding how surgeons improve their performance, which could have significant benefits in achieving better patient outcomes.[25 26] It would be beneficial to investigate potential confounding factors in greater depth. For instance, the impact of evolving surgical techniques and technologies over the course of the study period should be taken into account. The exploration of these factors was challenging due to the limitations in the content of the databases used in this study. It is our hope that this study will provide a groundbreaking foundation for more relevant studies.

Institutional experience also plays a crucial role in the success of these novel procedures. Compared with other studies,[27–29] the risk of haemorrhagic events (6.10%), ischaemic events (6.69%) and seizures (3.29%) in our cohort remained relatively low due to the presence of an experienced team that managed incipient complications. Notably, the collective data from all other centres in the database amounted to only 17 cases, representing less than 10% of the total cases in this study. Moreover, the minimum number of curves required for inclusion in the study was not met by any of the other centres, and thus no data from these centres were incorporated into the final analysis. The results of this study are wholly representative of the surgical situation in high-volume centres in China.

This study has some limitations. First, this study was limited by its prospective design. The study population consisted mainly of patients with complex AVMs, and the procedures were performed by skilled neurointerventional and neurosurgical teams. Future research could be extended to low-volume centres.

CONCLUSIONS

This study showed that performing single-stage combined surgery in 25 AVM cases is necessary to achieve reproducibility. Furthermore, the rates of major complications and unfavourable outcomes decreased significantly after the first 50 procedures. Palliative and targeted embolisation strategies are associated with a lower rate of unfavourable outcomes. These findings support the use of CUSUM analysis as a valuable tool for quality control in single-stage procedures for AVMs.

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ORCID iDs
Heze Han http://orcid.org/0000-0001-9155-038X
Yang Zhao http://orcid.org/0000-0001-8774-6945
Shuo Wang http://orcid.org/0000-0003-4919-5390
Yu Chen http://orcid.org/0000-0003-2491-3974

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