Surgical Outcome of Very Small Intracranial Aneurysms Utilizing the Double Clip Technique

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■ OBJECTIVES: **To report the outcome of patients with very small intracranial aneurysm (VSIA) undergoing surgical clipping using a double-clip technique.**

■ METHODS: **This cross-sectional study was conducted in Namazi Hospital, the main referral neurovascular center in Southern Iran during a 6-year period from September 2010 to March 2016. All patients with VSIAs (≤3 mm) undergoing surgery with double-clip technique were included. This technique reduces the clip slippage. The short- and long-term outcomes determined by Glasgow outcome score (GOS), modified Rankin Scale (MRS), and complications.**

■ RESULTS: **Operations were performed on 32 VSIAs in 26 patients with a mean ± SD age of 55.7 ± 10.1 years. Middle cerebral artery was the most common location for VSIA (50.0%). There was no neck remnant, and the complete occlusion rate was 100%. The rate of intraoperative aneurysm rupture was 30.8%, and none of the patients experienced rebleeding. The 6-month mortality rate was 0% in ruptured VSIAs and 6.25% in unruptured VSIAs. Most of the patients had favorable outcomes (88.5%), and the overall mortality rate was 11.5%. The rate of permanent neurologic deficit was 10.0% in ruptured and 12.5% in unruptured VSIAs. Multivariate logistic regression analysis revealed no association between baseline and clinical characteristics and outcome in this series.**

■ CONCLUSION: **VSIAs are difficult to treat because of their small sizes; therefore, with a double-clip technique, one can reduce complications related to the treatment of small aneurysms.**

INTRODUCTION

Very small intracranial aneurysms (VSIAs), defined as intracranial aneurysms measuring 3 mm or less,[1,2] are rare, and their management remains a dilemma for neurosurgeons.[3] As the natural course and life-time risk of bleeding in unruptured VSIAs is not fully understood, there is controversy regarding their management.[4,5] Most of the authors believe that microsurgery is an acceptable option for treatment of ruptured VSIAs, because coiling of these aneurysms is technically demanding and is associated with higher complication rates compared with larger aneurysms.[6] The surgical outcomes for VSIAs (both ruptured and unruptured) have been excellent with low mortality and morbidity rates.[1,7-9]

Surgical management of VSIAs requires special considerations to minimize the complications and morbidity rates. These aneurysms should be clipped with mini-clips, which have a smaller closing force than the standard aneurysm clips.[7,10] Surgeon and operating room experience are among the most important factors determining the outcome in surgical management of patients with VSIAs.[1,2,7,8] Recently, a Helsinki team[7] presented a novel technique in which two mini-clips are applied parallel to each other for obliterating the VSIAs (double-clip technique), and now there is a desire to check study this methodology in different environment. The aim of the current study was to report the feasibility and safety of the

Key words
- Double-clip technique
- Outcome
- Surgical clipping
- Very small intracranial aneurysms
- VSIA

Abbreviations and Acronyms
CT: Computed tomography
GOS: Glasgow outcome score
MRS: Modified Rankin Scale
VSIA: Very small intracranial aneurysm

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double-clip technique for microsurgical management of VSIAs in a large referral center in southern Iran.

MATERIALS AND METHODS

Study Population

This cross-sectional study was conducted during a 6-year period from September 2010 to March 2016 in Namazi Hospital, a tertiary healthcare center affiliated with Shiraz University of Medical Sciences. This center is the main referral center for neurovascular diseases in southern Iran with a high volume of patients and operations (both open and endovascular); it is well equipped and has good resources.[11,12] We included all the patients with VSIAs ($\leq$3 mm) who underwent operations in our center during the study period using a double-clip technique. We included ruptured (those presenting with subarachnoid hemorrhage) and unruptured (those being detected in neurovascular imagines) VSIAs. The study protocol was approved by the institutional review board and medical ethics committee of Shiraz University of Medical Sciences. As this was a retrospective review of the medical charts, no informed written consents were required.

Study Protocol

All the medical charts of the eligible patients were retrieved and reviewed for demographic, clinical, radiologic, and outcome data.

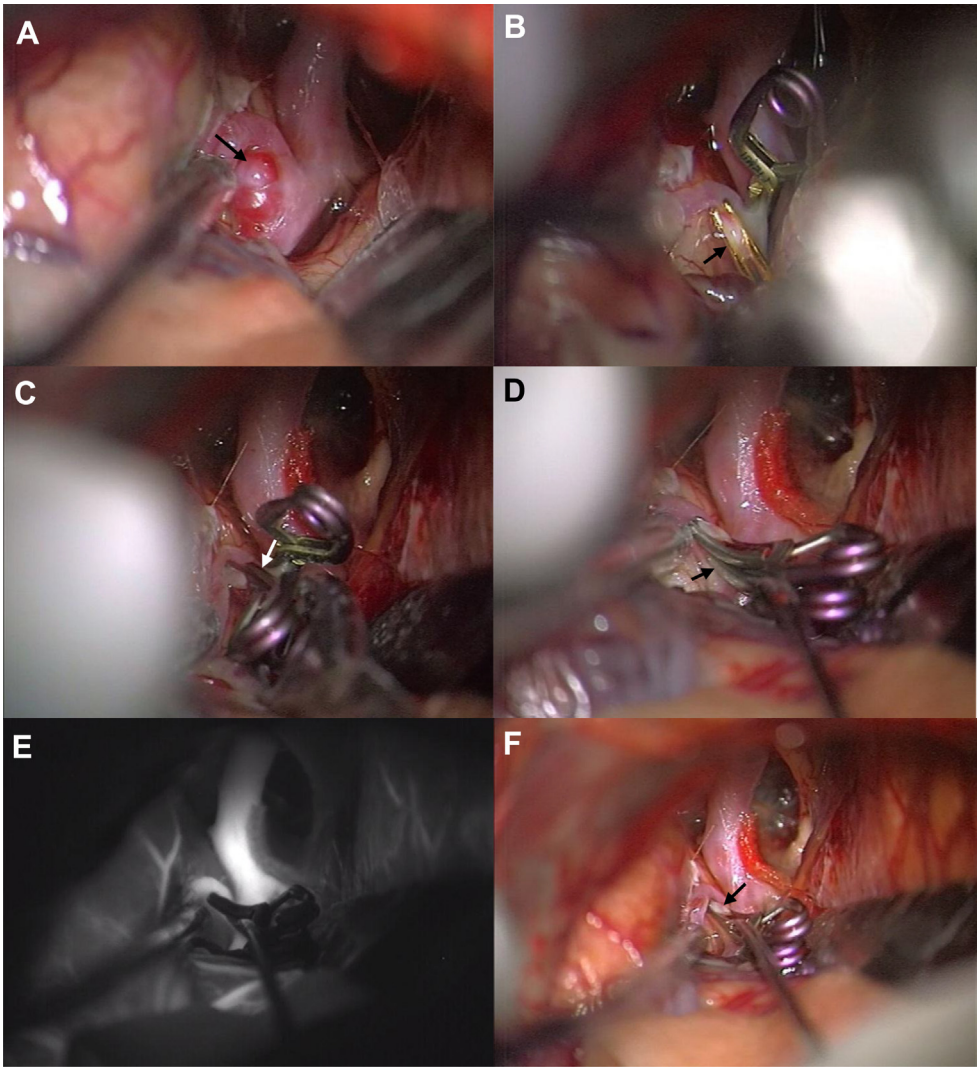

Figure 1. (**A**) A very small intracranial aneurysm (*arrow*) at right middle cerebral artery bifurcation. (**B**) Applying the first mini-clip (No. 4) on the aneurysm dome as helper clip (*arrow*) after applying a temporary clip on the M1 segment. (**C**) Applying the second mini-clip (No. 4) (*arrow*) on the aneurysm neck. (**D**) Advancing the second mini-clip (*arrow*) to occlude the aneurysm neck. (**E**) Intraoperative indocyanine green angiography demonstrating complete occlusion of the aneurysm with intact both M2 segments. (**F**) Final view of the clipped aneurysm (*arrow*) with the double-clip technique.

We recorded age, sex, presentation, number of total aneurysms, number of VSIAs, location of aneurysms, and patients' clinical information (Glasgow Coma Scale score on admission, comorbidities). We reviewed the initial computed tomography (CT) scans and CT angiography of the patients and determined the total number and location of the intracranial aneurysms. We also determined the Fisher and Hunt and Hess grades in all the patients.[13,14] All the data were recorded with a data gathering form. We also reviewed the outpatient documents to record the information regarding the outcome scales. All the patients underwent open surgical occlusion of the VSIAs by the first author (A.R.) in our center. Postoperative CT angiography was performed in all patients to determine the residual aneurysm. All the patients were followed for at least 6 months, and the functional recovery was evaluated using Glasgow outcome scale (GOS) and modified Rankin Scale (mRS).[15] We also recorded the intraoperative variables (duration, bleeding, and number of applied clips).

Surgical Technique

We used lateral supraorbital or interhemispheric approaches for operation based on the aneurysm location and direction. After dissection of the arachnoid, we exposed the optic nerve and internal carotid artery and exposed the VSIA (**Figure 1A**). Next, an appropriate temporary clip was applied (**Figure 1B**). All patients underwent operations with the double-clip technique as described previously.[7] In this technique, we apply the first mini-clip on the aneurysm dome, leaving a small neck that is appropriate for applying the next clip (**Figure 1B**). The second mini-clip is then applied parallel to the first clip, obliterating the aneurysm neck completely (**Figures 1C** and **D**). This method decreases the risk of clip slippage, because the aneurysm neck is too small for the mini-clip to be stabilized. The patency of the main artery was checked intraoperatively with intraoperative indocyanine green angiography and Doppler sonography (**Figure 1**E). Next, the first clip can be removed or left in place based on the surgeon's preference (**Figure 1**F). The procedure is demonstrated in **Video 1**.

Video available at WORLDNEUROSURGERY.org

Statistical Analysis

Statistical analysis was completed using SPSS version 18.0 (SPSS, Chicago, Illinois, USA). Data are presented as mean ± SD and proportions as appropriate. To investigate the determinants of outcome in our series, we compared the baseline and clinical characteristics between those with favorable and unfavorable outcomes. The favorable outcome was defined as GOS of 4 and 5, and unfavorable outcome was defined as GOS of 1–3. The proportions were compared using Fisher exact test, and the parametric variables were compared using the independent t test. A two-sided P value less than 0.05 was considered statistically significant.

RESULTS

We included 26 patients with 32 VSIAs who underwent operations in our center with the double-clip technique. The mean age of the patients was 55.7 ± 10.1 years (range, 28–74 years), and there were 17 (65.4%) women and 9 (34.6%) men among the patients. Total number of 32 VSIAs were diagnosed in these 26 patients. Sixteen (61.5%) patients had ruptured aneurysms, and 10 patients (38.5%) had unruptured ones. Hypertension was the most common comorbidity (50.0%), followed by ischemic heart disease (23.1%). The baseline characteristics of the patients are summarized in **Table 1**.

The middle cerebral artery was the most common location of VSIAs (50.0%), followed by the anterior communicating artery (34.3%; **Table 2**). Preoperative hydrocephalus was detected in 14 patients (53.8%), of whom 1 patient (3.8%) required ventriculoperitoneal shunt insertion before surgery. There was no remnant, and the complete occlusion rate was 100%. None of the patients experienced rebleeding in follow-up. The intraoperative rupture of the VSIA occurred in 8 patients (30.8%). The intraoperative characteristics of the patients are summarized in **Table 2**. Most of the patients had favorable outcomes (88.5%) determined by good recovery in 80.7% according to 6-month GOS and no significant disability in 61.5% according to 6-month mRS score; 81.25 of those with unruptured VSIAs had favorable outcomes, and 18.75% of them unfavorable outcomes. Ninety percent of those with ruptured VSIAs had favorable outcomes, and 10% of them had unfavorable outcomes. **Table 3** summarizes the outcome measures of the patients. We also compared the baseline and clinical characteristics between those with favorable and unfavorable outcome to determine the prognostic factors. However, we found that none of the factors were associated with the outcomes (**Table 4**). Even after adjusting for the confounders through a multivariate logistic regression model, we found no predictor of the outcome.

DISCUSSION

VSIAs are a dilemma for neurovascular surgeons because their management remains controversial.[1,4,16] Some trials have found that neurosurgical clipping is superior to endovascular coiling in patients with ruptured VSIAs[2,7,17,18]; however, recent evidence suggests that these two are equal and in some parameters, endovascular coiling is superior to surgical clipping.[19-22] In the current study, we reported the outcomes for 26 patients with 32 VSIAs in our referral center in southern Iran undergoing surgery with the double-clip technique. We found that most of the patients had excellent outcomes after 6 months. The mortality rate was 0% among unruptured and ruptured VSIAs, and it was 3.8% among those with ruptured aneurysms other than a VSIA. To our knowledge, this is the first study reporting surgical outcomes of patients from Iran with VSIAs treated using a double-clip technique.

In the current study, we demonstrated that the total occlusion rate was 100%; none of the patients had remnant aneurysms, and none experienced rebleeding. The mortality rate was 0% in unruptured and ruptured VSIA groups, and was it 3.8 in ruptured aneurysms other than VSIA. The rate of permanent neurologic deficit was 0% in unruptured and 3.8% in ruptured VSIA groups. The technique has been described previously by Kiran et al.[7] for patients with VSIA. In this technique, the first clip helps the second one to be applied properly, occluding the aneurysm. The second clip then can be removed according to the surgeons' preference. Kiran et al.[7] reported a surgery associated mortality and morbidity of 0% in 39 patients with 40 VSIAs undergoing surgical clipping using a double-clip technique.

Table 1. Baseline Characteristics of 26 Patients With 32 Very Small Intracranial Aneurysms Undergoing Microsurgery Using a Double-Clip Technique

Variable	Value
Age (years), mean ± SD	55.7 ± 10.1
Sex, n (%)	
Men	9 (34.6)
Women	17 (65.4)
Presentation	
Ruptured VSIA, n (%)	16 (61.5%)
Unruptured VSIA, n (%)	10 (38.5%)
GCS score on admission, mean ± SD	14.1 ± 1.76
Hunt and Hess grade, n (%)	
1	8 (30.8)
2	8 (30.8)
4	1 (3.8)
5	2 (7.7)
Fisher grade, n (%)	
1	2 (7.7)
2	4 (15.4)
3	12 (46.2)
4	1 (3.8)
Comorbidities, n (%)	
Hypertension	13 (50.0)
Ischemic heart disease	6 (23.1)
Smoking	7 (26.9)
Diabetes mellitus	2 (7.7)
Opium addiction	3 (11.5)
Total number of intracranial aneurysms, n (%)	
1	12 (46.2)
2	6 (23.1)
3	6 (23.1)
5	2 (7.7)
Total number of VSIAs, n (%)	
1	22 (84.6)
2	2 (7.7)
3	2 (7.7)

VSIA, very small intracranial aneurysm; GCS, Glasgow Coma Scale.

Table 2. Preoperative and Intraoperative Characteristics of 32 Very Small Intracranial Aneurysms in 26 Patients Undergoing Microsurgery With a Double-Clip Technique

Characteristics	Frequency
Location of VSIAs	
MCA (%)	16 (50.0%)
A-Com (%)	11 (34.3%)
P-Com (%)	3 (9.3%)
ACA (%)	1 (3.2%)
Internal Carotid (%)	1 (3.2%)
Intraoperative variables	
Intraoperative rupture (%)	8 (30.8%)
First clip slippage	23 (71.8%)
Preoperative VP-Shunt insertion (%)	2 (7.7%)
Intraoperative bleeding (mL)	180.1 ± 137.4
Operation duration (min)	68.9 ± 47.1
Surgery Approach	
Lateral supraorbital (%)	25 (96.2%)
Interhemispheric (%)	1 (3.8%)
Prognosis*	
Favorable (%)	23 (88.5%)
Unfavorable (%)	3 (11.5%)

VSIA, very small intracranial aneurysm; MCA, middle cerebral artery; A-Com, anterior communicating artery; P-Com, posterior communicating artery; ACA, anterior cerebral artery; VP, ventriculoperitoneal.
*Favorable prognosis: Glasgow outcome score (GOS) of 4 or 5. Unfavorable prognosis: GOS of 1, 2, or 3.

One of the interesting findings of our study was the rate of clip slippage (71.8%) and intraoperative rupture of VSIA (30.8%). The high rate of clip slippage in patients with VSIA has been reported previously with different frequencies in different series.[1,2,7,8] This is probably because of elastic consistency of the aneurysm wall in addition to its low dome/neck ratio, which makes it difficult for the first mini-clip to stand on the aneurysm neck. The double-clip technique provides a decreased rate of clip slippage by providing a substructure for the second clip to occlude the neck completely. In our series, there was no second clip slippage and no remnant. The intraoperative rupture of the VSIA has also been reported previously in different series with various frequencies.[23-25] Several factors such as timing of surgery, male sex, epileptic seizures, presence of SAH, aneurysm location, and surgical experience affect the incidence of intraoperative aneurysm rupture.[23-25] The management of the intraoperative rupture is also devastating. In the case of intraoperative rupture of a VSIA, proximal and distal control with applying temporary clips should be performed, and the mini-clips should be readjusted to occlude the aneurysm. Other options include the complete occlusion of the parent vessel (if there is contralateral circulation), proximal-to-distal anastomosis, and removal of the aneurysmal segment.[24,25] In our series, all the situations were managed by proximal and distal control along with clip readjusting using the double-clip technique.

Another factor worthy of discussion is the rate of the multiple intracranial aneurysms including VSIAs, which might affect the

Table 3. The Outcome of 26 Patients With Very Small Intracranial Aneurysms Undergoing Surgery With a Double-Clip Technique Determined With 6-Month Glasgow Outcome Score and Modified Rankin Scale Score

Outcome Scales	Unruptured VSIA (n = 16)	Ruptured VSIA (n = 10)
6-month GOS		
Good recovery (%)	12 (75.0%)	9 (90.0%)
Moderate disability (%)	1 (6.25%)	0 (0.0%)
Severe disability (%)	1 (6.25%)	0 (0.0%)
Persistent vegetative state (%)	1 (6.25%)	1 (10.0%)
Death (%)	1 (6.25%)	0 (0.0%)
6-month mRS score		
No symptoms (%)	3 (0.0%)	2 (20.0%)
No significant disability (%)	9 (55.6%)	7 (70.0%)
Slight disability (%)	1 (11.1%)	0 (0.0%)
Moderate disability (%)	0 (0.0%)	0 (0.0%)
Moderately severe disability (%)	0 (0.0%)	0 (0.0%)
Severe disability (%)	2 (22.2%)	1 (10.0%)
Dead (%)	1 (11.1%)	0 (0.0%)

GOS, Glasgow outcome score; mRS, modified Rankin Scale.

outcome and the risk of aneurysm rupture. In our series, 14 (53.8%) had multiple intracranial aneurysms including VSIA, whereas the rate was 17%–25.8% in other series.[26,27] Multiple intracranial aneurysms have been reported to be associated with polycystic kidney disease (PKD); however, none of our patients had PKD. We did not find any association between the outcome and the multiple intracranial aneurysms, whereas previous studies have demonstrated that those with multiple intracranial aneurysms are at higher risk for developing aneurysm rupture and SAH.[28] Large cohort studies have also demonstrated that the multiplicity of intracranial aneurysms affects the natural course and risk of rupture in VSIAs.[4,29] Further study is required to shed light on the issue.

In the report by Bruneau et al.,[1] the mortality rate was 0% and the rate of total occlusion was 98.2%, and only 2.7% of patients experienced persistent neurologic complications, which is comparable to our study. In another recent study, Grasso and Perra[2] reported the outcomes for 53 patients with ruptured VSIAs undergoing surgical clipping. Ischemia related to surgery was observed in 15% of patients, and hemorrhage occurred in 13.2% if patients. No mortality related to clipping was observed. Overall, major and minor neurologic deficits related to clipping were 5.2% and 2.2%, respectively. At the time of discharge, 84.9% of patients attained a favorable outcome (moderate, mild, or no disability). Only 8 patients (15.1%) had poor clinical outcomes, which is comparable with our study.[2] Krisht et al.[8] reported the surgical outcomes for 25 patients with unruptured VSIAs. Surgery-related mortality was 0.82%. Surgery-related permanent morbidity was

Table 4. The Determinants of Favorable Outcome Measured by Glasgow Outcome Score in 26 Patients With Very Small Intracranial Aneurysms and Undergoing Microsurgical Clipping Using a Double-Clip Technique

Variables	Favorable Outcome (n = 23)	Unfavorable Outcome (n = 3)	*P* Value
Age (years), mean ± SD	55.26 ± 10.5	59.33 ± 6.02	0.522
Sex, n (%)			
Male	9 (39.1)	0 (0.0)	0.529
Female	14 (60.9)	3 (100.0)	
Presentation, n (%)			—
Ruptured VSIA	16 (61.5)	—	
Unruptured VSIA	10 (38.5)	—	
GCS score on admission, mean ± SD	14.21 ± 1.73	12.33 ± 1.15	0.082
Hunt and Hess grade, n (%)			
1	8 (50.0)	0 (0.0)	0.266
2	6 (37.5)	2 (66.7)	
4	1 (6.3)	0 (0.0)	
5	1 (6.3)	1 (33.3)	
Fisher grade, n (%)			
1	2 (12.5)	0 (0.0)	0.091
2	4 (25.0)	0 (0.0)	
3	10 (62.5)	2 (66.7)	
4	0 (0.0)	1 (33.3)	
Comorbidities, n (%)			
Hypertension	11 (48.8)	2 (66.7)	0.500
Ischemic heart disease	4 (17.4)	2 (66.7)	0.123
Smoking	7 (30.4)	0 (0.0)	0.540
Diabetes mellitus	2 (8.7)	0 (0.0)	0.778
Opium addiction	3 (13.0)	0 (0.0)	0.681
Number of VSIAs, n (%)			
1	19 (82.6)	3 (100.0)	0.735
2	2 (8.7)	0 (0.0)	
3	2 (8.7)	0 (0.0)	
Location of VSIAs, n (%)			
MCA	14 (43.7)	2 (6.4)	0.722
A-Com	7 (21.8)	0 0 (0.0)	
P-Com	3 (9.4)	0 0 (0.0)	

VSIA, very small intracranial aneurysm; GCS, Glasgow Coma Scale; MCA, middle cerebral artery; A-Com, anterior communicating artery; ACA, anterior cerebral artery; VP, ventriculoperitoneal.

Continues

Table 4. Continued

Variables	Favorable Outcome (n = 23)	Unfavorable Outcome (n = 3)	*P* Value
ACA	4 (12.5)	1 (3.1)	
Internal carotid artery	1 (3.1)	0 (0.0)	
Intraoperative variables			
Intraoperative rupture, n (%)	6 (26.1)	2 (66.7)	0.215
Preoperative VP-shunt insertion, n (%)	2 (8.7)	0 (0.0)	
Intraoperative bleeding (mL), mean ± SD	166.52 ± 113.7	283.33 ± 275.3	0.171
Operation duration (minutes), mean ± SD	62.7 ± 42.2	116.6 ± 65.1	0.060

VSIA, very small intracranial aneurysm; GCS, Glasgow Coma Scale; MCA, middle cerebral artery; A-Com, anterior communicating artery; ACA, anterior cerebral artery; VP, ventriculoperitoneal.

3.44%, and transient surgery-related mild morbidities were 7.7%. Immediate and 3-month postsurgical good outcome (Glasgow outcome score of 4–5) was recorded in 87.93% and 95.68%, respectively. Residual aneurysms were seen in none of the postoperative angiograms.[8] These statistics are comparable to those reported in the current study. The different statistics presented in the current study could be a result of these studies including patients with unruptured VSIAs in which the surgery was performed in an elective setting. Most of our patients had ruptured VSIAs or other ruptured intracranial aneurysms with high Hunt and Hess grades, which affected the outcomes negatively. The definition of *small intracranial aneurysm* also differs between these studies; Krisht et al.[8] define it as having a diameter less than 7 mm. Kiran et al.[7] and Bruneau et al.[1] define VSIAs as having a diameter less than 3 mm, whereas Wiebers et al.[4] define them as having a diameter less than 2 mm. In our study, we assumed the maximum diameter to be 3 mm.

There are some limitations to our study. First, we included both unruptured and ruptured VSIAs or other intracranial aneurysms and reported the outcomes in this mixed population. The aim of the current study was to report the outcome in patients with VSIAs undergoing surgery with a double-clip technique. Thus, we included all the patients to increase the sample size population and to determine the outcome measures. In addition, this limited number of included patients might be the explanation for not finding a predictor of the outcome in this series. Larger study populations are required to investigate the predictors. Second, this retrospective study used data from our registry. As a result, we could not retrieve some important information, such as long-term outcomes for all patients. Currently, we are creating and devising our online neurovascular registry to solve these problems. The other important limitation of the current study was that we used 16-slice spiral CT angiography with three-dimensional reconstruction for the evaluation of postoperative outcomes and complete occlusion. Remnants of a 3-mm aneurysm can be easily missed with this method. Thus, follow-up imaging with 4-vessel digital subtraction angiography is recommended.

CONCLUSION

The double-clip technique is a safe and effective technique for clipping of VSIAs (both ruptured and unruptured), and it is associated with low mortality and morbidity. The technique requires dexterity and can be learned and applied through practice and repetition.

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