

Single coil endovascular embolization of very tiny (≤ 2 mm) intracranial aneurysms: one center's experience

Yao Li¹, Peng Bai¹, Jinghui Li¹, Shouwei Xiang¹, Xin Geng¹, Yanghong Zou¹, Wenqiang Huang¹, Hualin Yu^{1,*}

¹Department of Neurosurgery, The First Affiliated Hospital of Kunming Medical University, 650032 Kunming, Yunnan, China

*Correspondence: xuhl@ydy.cn (Hualin Yu)

DOI:10.31083/j.jin2101027

This is an open access article under the CC BY 4.0 license (<https://creativecommons.org/licenses/by/4.0/>).

Submitted: 14 April 2021 Revised: 25 April 2021 Accepted: 22 August 2021 Published: 28 January 2022

Background: To investigate the safety and efficacy of endovascular embolization of very tiny (≤ 2 mm) intracranial aneurysms with single coil and summarize experience. **Methods:** A retrospective analysis was performed for 15 consecutive patients with very tiny aneurysms treated by coil embolization alone or stent-assisted coil embolization between January 2017 and January 2020. 15 patients with six unruptured aneurysms and nine ruptured aneurysms were included in this study. There were eight males and seven females with a mean age of 50.0 ± 5.2 years (range 41 to 57 years old). Intraoperative complications, imaging outcomes, clinical outcomes and follow-up data were analyzed. **Results:** All aneurysms were embolized with a single coil. Lvs stents were used in all coil assisted embolizations. The embolization success rate was 100%. The average volume embolization ratio (VER) of aneurysm embolization was $53.7 \pm 25.5\%$. An intraoperative aneurysm re-rupture complication occurred in one patient (6.7%). 11 patients (73.3%) had immediate complete occlusion after embolization. After a mean follow-up period of 6.7 ± 1.4 months, 13 patients (86.7%) had complete occlusion. No patients had aneurysm re-rupture, an ischemic event or recurrence during follow-up. All patients achieved favorable clinical outcomes with a modified rankin scale (MRS) of 0–2. **Conclusions:** This study demonstrates that endovascular embolization of very tiny intracranial aneurysms with a single coil is safe and effective. However, the follow-up period was not long enough and studies with larger numbers of patients are required. The summary of experience reported here is expected to provide significant patient benefits.

Keywords

Endovascular embolization; Intracranial aneurysms; Very tiny aneurysms; Single coil

1. Introduction

The phrase “intracranial aneurysm” refers to the abnormal bulge formed by gradual expansion of the vascular wall under the continuous action of hemodynamics [1]. The incidence of aneurysms in the population is about 1–3.2% [2, 3]. They are most commonly observed in people of age 40–60 years and more commonly in women than men [2, 4]. Patients with aneurysms often have a history of hypertension and smoking [2]. Once an aneurysm ruptures, a subarachnoid hemorrhage (SAH) occurs, and the high disability rate and mortality associated with this severely affects patient prognosis. Tiny

aneurysms are a special type of intracranial aneurysm. With a maximum diameter < 3 mm, the term “tiny aneurysm” has been widely recognized [5–7].

Patients with such a rupture are usually confirmed during a hospital visit by the clinical symptoms caused by a SAH. Patients with an unruptured tiny aneurysm are generally identified by a screening brain checkup, incidental examination, or other unspecified symptoms [8]. With the development of medical imaging technologies such as digital subtraction angiography (DSA) and three dimensional digital subtraction angiography (3D-DSA) reconstruction now widely used in clinical practice, increased numbers of tiny aneurysms are being identified [9, 10]. Nowadays, treatment methods include conservative medication and surgical or endovascular treatment [11, 12]. Surgical clipping and endovascular embolization are the accepted treatment methods.

Currently, the international subarachnoid aneurysm trial (ISAT) has been the largest, multi-center and prospective randomized controlled treatment study for comparison of surgical clipping with endovascular embolization of aneurysms. It includes 2143 patients with ruptured aneurysms in the United Kingdom and many European countries. The results of 10–18 years of long-term follow-up suggest that patients undergoing embolization exhibit a lower disability rate and mortality compared with these who undergo clipping. The probability of aneurysm re-rupture is very low. Endovascular embolization has become the main treatment for intracranial aneurysms in Europe, and 85% of patients in the United Kingdom have received endovascular embolization for ruptured aneurysms [13, 14]. However, tiny aneurysms were not included in that study. No authoritative demonstration has been made to clarify the most advantageous way to treat tiny aneurysms.

In the case of a tiny aneurysm both surgical clipping and endovascular embolization are highly difficult due to their size and thin walls with most presenting with a wide neck [5, 15, 16] and are also associated with morbidity [17–19]. In the case of surgical clipping, the tiny size of the aneurysm makes it difficult to clip firmly. Complete occlusion of tiny aneurysms requires part of the parent artery to be clipped, otherwise the clip may be unstable and even fall off. Ad-

ditionally, during aneurysm clipping, the clip may tear the neck of an aneurysm, which may result in aneurysm rupture during surgery. In the case of endovascular embolization, a tinier aneurysm body increases the difficulty of placing a micro-catheter into the aneurysm. Thus a micro-catheter may not remain in a stable position and result in instability of detached coils in an aneurysm. Further, aneurysms are more likely to rupture during endovascular embolization and it may also be difficult to fill an aneurysm with coils resulting in treatment failure. Such intraoperative aneurysm rupture is a severe complication and is associated with high rates of disability and mortality [20, 21].

Recently, for endovascular treatment of tiny aneurysms there has been great progress with the development of intervention-related equipment and materials, assisted by accumulated operative experience and improved operative techniques. Many studies have verified that the endovascular treatment of tiny aneurysms achieves a low incidence of complications and a higher rate of cure [5–7]. Very tiny intracranial aneurysms (maximum diameter <2 mm) are not rare in clinical practice. It is necessary for the treatment of these aneurysms to prevent re-rupture and improve the clinical prognosis of patients but it has higher operative difficulty and risk. In this study, the clinical, imaging and follow-up data of 15 patients with very tiny intracranial aneurysms treated by coil embolization were analyzed. The safety and efficacy of endovascular embolization for these very tiny aneurysms were evaluated and the relevant treatment experiences summarized.

2. Materials and methods

A retrospective analysis of patients treated for very tiny aneurysms between January 2017 and January 2020 by coil embolization alone or stent-assisted coil embolization was performed. This study was approved by the Ethics Committee of The First Affiliated Hospital of Kunming Medical University. The patients were informed and they signed a fully-informed consent form. 15 consecutive eligible patients including six unruptured aneurysms and nine ruptured aneurysms were included in this study. There were eight males and seven females (mean age 50.0 ± 5.2 years, range 41–57 years old). Patients with ruptured aneurysms presented with headache as the first symptom and were diagnosed with subarachnoid hemorrhage by computerized tomography scan. Patients with unruptured aneurysms were found by computed tomography angiography or magnetic resonance angiography due to unrelated symptoms such as headache and dizziness. The Hunt-Hess grade was used to assess the patients' medical condition. This resulted in four grade one and grade two patients and one grade three patient. The Modified Fisher Scale was applied to evaluate the risk of cerebral vasospasm. Six patients were classified as grade one, two patients as grade two and one patient as grade three. All patients were diagnosed with a very tiny aneurysm by DSA. The maximum diameter of an aneurysm ranged from 1.1 to

2.0 mm (average diameter 1.83 ± 0.27 mm). Six aneurysms were on the left side and nine were on the right side. Twelve aneurysms were located in the anterior circulation and three were located in the posterior circulation (Tables 1,2).

2.1 Inclusion criteria

Patients with a maximum aneurysm diameter ≤ 2 mm based on DSA; those who were treated by endovascular embolization and those with a completed follow-up were included.

2.2 Exclusion criteria

Patients with treatment by conservative observation or surgical clipping; those complicated by vascular malformation and other cerebrovascular diseases; and those who failed to complete the follow-up were excluded.

2.3 Treatment of very tiny aneurysm

All patients underwent aneurysm embolization under general anesthesia. Femoral artery puncture was performed using the modified Seldinger puncture technique in the patient's right inguinal region. According to the patient's vascular conditions, a 6F short sheath or a 6F long sheath was placed in the right femoral artery. After systemic heparinization, a 6F guiding catheter was placed by guide wire and a 5F angiographic catheter by using the coaxial technique. The guiding catheter was placed in the lacerum segment of the internal carotid artery (C3) or the transversary segment of the vertebral artery (V2). Under the procedure, the micro-wire guided the micro-catheter to reach the aneurysm neck. If necessary, steam molding of the micro-catheter tip was performed according to the angle between the aneurysm and parent artery and the bending morphology of the parent artery. According to the shape and size of the aneurysm, after adjusting the micro-catheter tip to be stabilized at the aneurysm neck, a coil of appropriate size was placed into the aneurysm body. Subsequently, cerebral angiography was performed to confirm that neither the parent nor distal arteries were affected and the coil was detached to complete the embolization. For some wide-necked aneurysms it was difficult to perform embolization by coiling alone. In these cases, stent-assisted coil embolization was performed. After selecting the appropriate Lvis stent according to the width of the aneurysm neck and the diameter of the parent artery measured by angiography, the procedure employed a micro-wire to guide the stent catheter to the distal parent artery. The stent was introduced into the stent catheter and then released across the aneurysm neck based on the condition of aneurysm embolization. All operations included in this study were completed by three neurosurgeons, each of whom independently completed more than 100 cases of interventional operations annually.

2.4 Perioperative drug use methods

Preoperative: (1) Dual antiplatelet therapy: Patients requiring stent-assisted coil embolization received an oral loading dose of aspirin 300 mg combined with clopidogrel 225 mg to prevent intraoperative thrombosis. For patients receiving

Table 1. Patients' basic data and characteristics of very tiny intracranial aneurysms.

Patient number	Sex	Age (y)	Ruptured or not	H-H grade	MFS	Side	Location	Length × Width (mm)	Neck (mm)
1	M	48	Unruptured	—	—	R	ACOA	2.0 × 1.6	1.7
2	M	40	Unruptured	—	—	L	ICA	2.0 × 1.9	1.9
3	F	57	Unruptured	—	—	R	ICA	1.4 × 1.4	1.8
4	F	53	Unruptured	—	—	R	MCA	1.6 × 1.6	1.7
5	F	48	Unruptured	—	—	R	ICA	2.0 × 1.9	1.8
6	M	46	Unruptured	—	—	R	ICA	2.0 × 1.8	2.0
7	M	52	Ruptured	2	2	L	ACA	0.8 × 1.1	1.3
8	F	48	Ruptured	1	1	R	PCOA	1.8 × 1.9	1.9
9	F	41	Ruptured	1	1	R	ICA	1.9 × 2.0	2.0
10	F	55	Ruptured	2	1	L	ACOA	1.9 × 1.8	1.9
11	M	51	Ruptured	2	1	R	ACA	1.8 × 1.4	1.2
12	F	48	Ruptured	2	1	R	PCOA	1.9 × 1.8	2.0
13	M	52	Ruptured	1	2	L	ACOA	1.8 × 1.7	1.8
14	F	55	Ruptured	1	1	L	PCOA	2.0 × 1.8	2.0
15	M	57	Ruptured	3	3	L	ACOA	1.9 × 2.0	2.0

M, male; F, female; H-H grade, Hunt-Hess grade; MFS, Modified Fisher Scale grade; R, right; L, left; ACOA, anterior communicating artery; ICA, internal carotid artery; MCA, middle cerebral artery; ACA, anterior cerebral artery; PCOA, posterior communicating artery.

embolization by coiling alone, dual antiplatelet therapy was not given. (2) Anti-vasospasm: Intravenous pumping of nimodipine was routinely given to the patient to alleviate vasospasm.

Intraoperative: (1) Systemic heparinization: The first heparin dose (IU) was $2/3 \times$ the patient's body weight (kg) \times 125 IU. Then, half of the previous dose was given every hour, with a minimum of 1250 IU and this dose was maintained. (2) Intraoperative thrombosis: The released stent or coil protrusion into the parent artery induced acute thrombosis. Intraoperative thrombolysis was performed by intravenous pumping of tirofiban (glycoprotein IIb/IIIa receptor antagonist). (3) Intraoperative unexpected stent placement: For patients who were not expected to receive a stent and were not given dual antiplatelet therapy, intravenous pumping of tirofiban prevented acute thrombosis if stent-assisted coiling embolization had to be performed. (4) Contrast agent use: Preoperative hematological tests were performed; Ioversol was used in patients with good renal function or under 70 years of age; alternatively, iodixanol was used in patients with renal insufficiency or 70 years old and above.

Postoperative: (1) Anti-vasospasm: following endovascular embolization of the aneurysm, a patient was continuously perfused with nimodipine by intravenous pump for one week. This was then changed to nimodipine tablets by oral administration for a further two weeks to prevent postoperative cerebral vasospasm. (2) Dual antiplatelet therapy: For patients with stent-assisted coil embolization, aspirin 100 mg/day combined with clopidogrel 75 mg/day was given postoperatively for three months, followed by aspirin alone for six months; the drug dose was adjusted according to DSA reexamination.

2.5 Postoperative evaluation and follow-up

The imaging and clinical outcomes of patients and follow-up data were recorded. The degree of aneurysm occlusion was roughly calculated by using VER proposed by Yamazaki [22]. It was also evaluated by DSA based on the Raymond-Roy Occlusion Classification. Grade 1, complete occlusion, defined as the aneurysm neck and aneurysm body are not filled with contrast medium; Grade 2, near-complete occlusion, defined as the contrast agent fills up the aneurysm neck but not the aneurysm body; Grade 3, incomplete occlusion, defined as the aneurysm body is clearly filled with contrast medium. The patients' clinical outcome was evaluated by the MRS. MRS included 0: No symptoms; 1: No significant disability; 2: Slight disability; 3: Moderate disability; 4: Moderately severe disability; 5: Severe disability; 6: Dead. Follow-up was performed through return visits and phone calls.

3. Results

The very tiny aneurysms of all 15 patients underwent endovascular embolization successfully by coiling alone and stent-assisted coiling. The minimum coil used was 1 mm \times 1 cm and the maximum coil was 1.5 mm \times 3 cm. The average VER of aneurysm embolization was $53.7 \pm 25.5\%$. All aneurysms were embolized with single coil and to assist coil embolization Lvis stents were used in all patients. The success rate of embolization was 100%. The aneurysms of six patients were embolized by coiling alone and nine patients received stent-assisted coiling embolization. A complication that involved an intraoperative aneurysm re-rupture occurred for one patient (6.7%) (Fig. 1). Complete occlusion after embolization was noted in 11 patients (73.3%) (Fig. 2) and near-complete occlusion was noted in three patients (20%), while one patient (6.7%) had an incomplete occlusion. The follow-up period ranged from four to ten months and DSA was performed in each patient. After a mean follow-up pe-

Table 2. Clinical data of of endovascular coil embolization and patients' follow-up.

Patient number	Coil size (mm/cm)	VER (%)	Stent	Operation-related complication	RROC after embolization	MRS at discharge	F-U periods (m)	RROC at F-U	MRS at F-U
1	1.5 × 2	43.4	Lvis	None	1	0	6	1	0
2	1.5 × 3	46.9	Lvis	None	3	0	7	3	0
3	1 × 1	41.1	Lvis	None	2	0	6	2	0
4	1.5 × 2	55.1	—	None	1	0	6	1	0
5	1.5 × 3	49.4	Lvis	None	1	0	8	1	0
6	1.5 × 2	34.7	Lvis	None	1	0	8	1	0
7	1 × 1	139.4	Lvis	None	1	0	6	1	0
8	1.5 × 3	52.1	Lvis	None	2	1	10	1	0
9	1.5 × 3	44.5	—	None	1	1	6	1	0
10	1.5 × 2	36.6	—	None	1	0	8	1	0
11	1.5 × 2	62.6	—	None	1	2	7	1	0
12	1.5 × 3	55	Lvis	None	1	0	6	1	0
13	1.5 × 3	65	—	Intraoperative re-rupture	2	1	4	1	0
14	1.5 × 2	34.7	Lvis	None	1	1	6	1	0
15	1.5 × 3	44.5	—	None	1	3	7	1	0

VER, volume embolization ratio; RROC, Raymond-Roy Occlusion Classification; MRS, Modified Rankin Scale; F-U, Follow-Up.

riod of 6.7 ± 1.4 months, 13 patients (86.7%) had complete occlusion (Fig. 3). Two patients (13.3%) had near-complete occlusion and one patient (6.7%) had incomplete occlusion. No patients had re-rupture, an ischemic event or recurrence during follow-up. All patients achieved favorable clinical outcomes with a modified Rankin scale score of 0–2 (Tables 1,2).

4. Discussion

In recent years with the development of 3D-DSA technology the detection rate of tiny intracranial aneurysms is increasing, but their natural history remains unclear [23, 24]. Sonobe's study reported the annual rupture rate of single and multiple unruptured small aneurysms were 0.34% and 0.95% [25]. The results of their incidence in various studies are different. Iskandar's study [26] of 956 cases of intracranial aneurysms showed that tiny aneurysms accounted for 11.6% of all aneurysms, unruptured tiny aneurysms accounted for 16.1% of unruptured aneurysms and ruptured tiny aneurysms accounted for 10.8% of ruptured aneurysms. Weir [27] analyzed 507 cases of intracranial aneurysms and found the incidence of tiny aneurysms was 13.2%, including 9.1% unruptured tiny aneurysms and 4.1% ruptured ones. Rooji [28] studied 1295 cases of intracranial aneurysms and found that tiny aneurysms accounted for 15.1%, unruptured and ruptured tiny aneurysms accounted for 3.6% and 11.5% respectively. Very tiny aneurysms are different, characteristically exhibiting a smaller aneurysm body, wide neck and thin wall, so their treatment is correspondingly more challenging than that of tiny aneurysms. The uncertain natural history of tiny unruptured cerebral aneurysms make their management remains controversial [5, 29]. PHASES risk scores and UIATS scores are used to assess the aneurysm rupture risk [30, 31]. Both of the scores indicated that a smaller aneurysm had a lower rupture rate. But other risk factors including patient

population, hypertension, age, earlier SAH and aneurysm location should be taken into account during the development of individualized treatment strategies.

4.1 Endovascular treatment

Although it is unclear whether unruptured tiny intracranial aneurysms need treatment or not [32], the necessary treatment of ruptured tiny aneurysm is beyond doubt. Endovascular treatment of very tiny aneurysms is almost identical to that for tiny aneurysms and there are many treatment methods. Currently, treatment methods primarily include coil embolization alone, stent-assisted coil embolization, multi-stent placement, covered stent placement and liquid embolic agent embolization [26, 33, 34]. However, each of these treatment methods have both advantages and disadvantages. Under the premise of stable embolization of aneurysm, it is the opinion of the authors that coil embolization alone would be the best choice. Coil embolization significantly reduces the risk of aneurysm rupture and is also the most widely used endovascular treatment for aneurysms. The placement of stents may lead to intraoperative vasospasm, inducing acute and chronic stent thrombosis and long-term stent intimal hyperplasia [35, 36]. Stent malposition and incomplete stent expansion also bring greatly increased technical challenges [37]. Further, patients require antiplatelet drugs for extended periods, increasing the risk of hemorrhagic events [38]. The placement of multi-stents across the aneurysm neck can significantly reduce the blood flow into an aneurysm, playing a role in blood flow diversion and promoting thrombosis in the aneurysm [39]. The overlap of multi-stents greatly reduces the possibility of a small coil protruding into the parent artery and can stabilize any coil in the aneurysm, while the risk of using a stent use cannot be ignored. Liquid embolic agents can be used for embolization of tiny aneurysms [34, 40], where the biggest risk

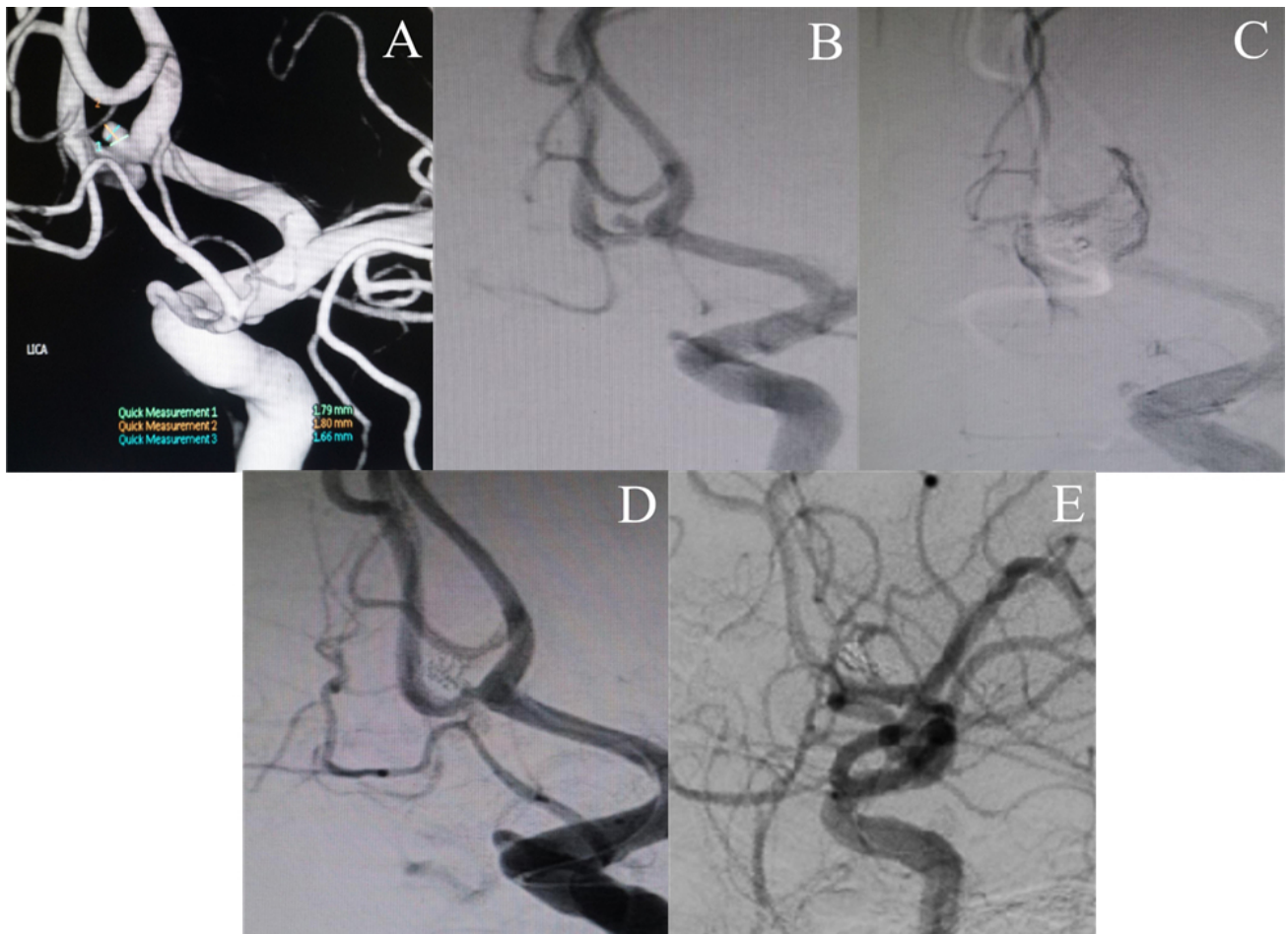


Fig. 1. Patient 13. (A) 3D reconstruction showing a very tiny aneurysm in the left anterior communicating artery. (B) DSA showing the aneurysm. (C) DSA showing the intraoperative aneurysm re-rupture. (D) DSA showing the aneurysm embolized. (E) DSA showing the aneurysm after 4 months.

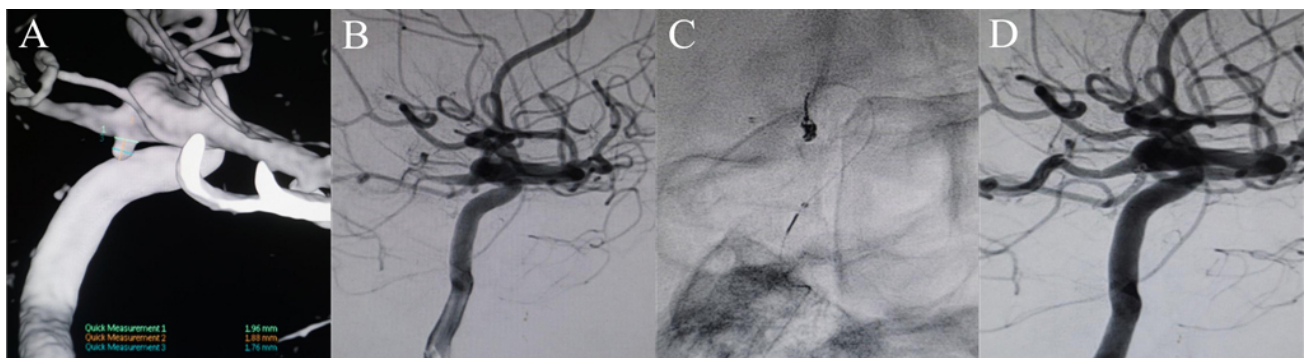


Fig. 2. Patient 12. (A) 3D reconstruction showing a very tiny aneurysm in the right posterior communicating artery. (B) DSA showing the aneurysm. (C) DSA showing the process of embolizing the aneurysm. (D) DSA showing the aneurysm embolized.

is the difficulty of controlling the flow direction of the embolic agent where it may flow into the parent artery and block the distal branch vessels to cause cerebral infarction. Generally, the application of a covered stent is the last choice [33]. The covered stent is the non-self-expandable stent, which is pre-installed on a balloon. Since the covered stent is harder than the conventional stents, the balloon filling and releasing the covered stent is easy to damage the blood vessels, and it is

easy to block the branches of the parent artery. In this study, the first two treatment methods were used. Considering the side effects of stent placement, coil embolization alone should be implemented whenever possible. Stent-assisted embolization is an option where a coil cannot be stably placed in the aneurysm body and there is a risk of protrusion into the parent artery.



Fig. 3. Patient 7. (A) DSA showing a very tiny aneurysm on the ACA. (B) DSA showing the process of embolizing the aneurysm. (C) DSA showing the aneurysm embolized. (D) DSA showing the aneurysm after 6 months.

4.2 Intraoperative complications

Endovascular treatment of very tiny aneurysms is not only difficult but also has a known failure rate [26, 41]. Although all aneurysms in this study were successfully embolized, the occurrence of intraoperative complications is an extremely awkward problem with an intraoperative aneurysm rupture one of the most severe complications of embolization. Nguyen's study [42] revealed that the rate of intraoperative tiny aneurysm rupture was significantly higher than that of a non-tiny aneurysm. Brinjikji [5] analyzed 71 patients with a tiny aneurysm and discovered that the intraoperative aneurysm rupture rate was 8.3%. Rooij [28] investigated 196 cases of tiny aneurysms, and the intraoperative aneurysm rupture rate was 7.7%. A meta-analysis by Yamaki [43] included 22 studies and suggested the intraoperative rupture rate was 7%. The very tiny aneurysms are not only smaller, but also further increase the difficulty and risk of coil embolization. The narrow operative space in a very tiny aneurysm makes it easier for micro-catheters, micro-wires and coil to pierce the aneurysm wall [5]. Additionally, it is difficult for the micro-wire to guide the micro-catheter into an aneurysm and the micro-catheter to reach a steady state in an aneurysm. Very tiny aneurysms can often be embolized by one or two coils. There is a dilemma if one coil does not provide complete occlusion, whereas, two coils do not completely fill the aneurysm. Blind filling of two coils may lead to either intraoperative aneurysm rupture or coil displacement [44]. The space for simultaneous placement of the micro-catheter tip and coil in an aneurysm is extremely limited, making it difficult for a micro-catheter to be stably placed into an aneurysm. In the acute phase of SAH, the occurrence of cerebral vasospasm boosts the incidence of intraoperative aneurysm rupture. In the present study, only one patient exhibited an intraoperative rupture, a much lower incidence than reported by the other cited studies. This single case was caused by the failure of a timely and effective withdrawal of the micro-catheter tip while the coil filled the aneurysm, with the result that the coil pierced the aneurysm wall. The VER of patient aneurysm embolization was 65%, which may have been the result not of wrong coil choice but misoperation. It

should be noted that improvement of interventional equipment and endovascular embolization technology also contribute to reduced intraoperative rupture. In this regard, the author's experience can be summarized as follows: (1) Only one appropriate size of coil is used for aneurysm embolization; the diameter of the coil should be slightly larger than that of the aneurysm and a longer coil is selected to form the basket and cover the aneurysm neck. An inappropriately sized coil and particularly more than one coil will increase the risk of intraoperative rupture. (2) The tip of the micro-wire should not be placed into the aneurysm body while the micro-wire guides the micro-catheter to the aneurysm. The guides should first be withdrawn into the micro-catheter at the aneurysm neck. Then, the micro-catheter tip should be placed at the aneurysm neck. When filling the aneurysm, the micro-catheter should be slowly withdrawn while releasing the coil so as to avoid the coil piercing the aneurysm. (3) The micro-catheter tip should be shaped appropriately according to the angle between aneurysm and parent artery and the shape of parent artery as to effectively place the tip of the micro-catheter at the aneurysm neck. (4) The use of a small, short and flexible coil can effectively reduce intraoperative rupture of these aneurysms. Intraoperative thrombosis is also a complication of tiny aneurysm embolization [43, 45]. There was no case of intraoperative thrombosis in this study. Intraoperative thrombosis is mainly related to stent application, coil protruding into parent artery, insufficient antiplatelet therapy [35, 46, 47], atherosclerotic plaques, insufficient anticoagulation, longer operative time, or cerebral vasospasm. Once intraoperative thrombosis occurs, intravascular super-selective thrombolysis should be performed in time [48, 49], and mechanical thrombectomy should be performed if necessary [50].

4.3 Complete occlusion

Complete occlusion is essential for ruptured tiny intracranial aneurysms. Residual aneurysm body or neck will lead to re-rupture or long-term recurrence after embolization. In this study, the average VER of aneurysm embolization was $53.7 \pm 25.5\%$. But the actual VER was probably lower due

to error in the calculation method and the placement of part of the coil into the aneurysm neck. 13 patients achieved complete occlusion after an average 6.7 ± 1.4 month follow-up. The stents used in this study were self-expanding Lvis stents. These are widely used in the coil embolization of tiny aneurysms because of their smaller mesh diameter (1 mm) and higher metal coverage. Studies have demonstrated that the use of Lvis stents in the treatment of ruptured intracranial aneurysms also has good reliability [51–54]. Lvis stents improve the complete occlusion rate of tiny aneurysms by covering the aneurysm neck and effectively avoid the coil protruding into the parent artery. The blood flow velocity in the aneurysm neck and the pressure of blood flow in blood vessels are crucial factors affecting the long-term recurrence of aneurysms [55]. The high metal coverage of Lvis stents plays a positive role in blood flow diversion and can change the hemodynamics of the aneurysm neck [56, 57]. Although most of the very tiny aneurysms are wide-necked, coil embolization was not stent-assisted when the aneurysms could be coil-embolized alone and the coil didn't escape from the aneurysm. Considering that the use of stent can boost the risk of intraoperative thrombosis and long-term ischemic events, patients need to take antiplatelet drugs for a very long time. As a result, single coils were selected to embolize these tiny aneurysms as frequently as possible. The coil selected should completely fill the aneurysm body and neck. In the process of embolization, the semi-stent jailing technique of the Lvis stent is used to suppress the prominent coil outside the stent if there is a part of the coil protruding into the parent artery. Consequently, intraoperative thrombosis induced by a prominent coil can be avoided and the aneurysm neck can be further repaired.

5. Limitations

This study had several limitations. It was a retrospective institutional study that may lead to patient selection bias. Prospective and multi-center studies are needed. The study only included 15 patients and the sample size was too small. Studies of large sample size are also required. The study follow-up period was 6.7 ± 1.4 months, which was both short and insufficient and a longer-term follow-up should be undertaken to record the future condition of patients and aneurysms. Furthermore, this study only analyzed patients with very tiny aneurysms treated by endovascular embolization. Patients with treatment by surgical clipping or conservative observation should also be included to quantify any treatment differences.

6. Conclusions

This study demonstrates that endovascular embolization of very tiny intracranial aneurysms with single coil is safe and effective. But the follow-up period is not long enough and studies with larger numbers of patients are needed. Summing up operative experience, improving operative skills and application of advanced instruments will effectively bring great

benefits to patients. Endovascular embolization for very tiny intracranial aneurysms with single coil could achieve very satisfactory results.

Abbreviations

VER, volume embolization ratio; SAH, Subarachnoid hemorrhage; DSA, Digital subtraction angiography; ISAT, International Subarachnoid Aneurysm Trial; 3D-DSA, three dimensional digital subtraction angiography; HHG, Hunt-Hess grade; MFS, Modified Fisher Scale; RROC, Raymond-Roy Occlusion Classification; MRS, Modified Rankin Scale.

Author contributions

YL, HY conceived and designed the study; YL, PB, JL performed the study; YL, SX, XG analyzed the data; YL, YZ, WH contributed reagents and materials; YL wrote the paper.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of The First Affiliated Hospital of Kunming Medical University (JSSKBMCT003). The patients were informed and they signed a fully-informed consent form.

Acknowledgment

Not applicable.

Funding

The present study was supported by the Yunnan health training project of high level talents (No. H-2018054), Yunnan Provincial Science and Technology Department-Applied Basic Research Joint Special Project of Kunming Medical University (No. 2017FE467), Subproject of Applied Basic Research Fund of Yunnan Neurological Disease Diagnosis and Treatment Center (No. ZX2019-03-05). The doctoral research fund of the First Affiliated Hospital of Kunming Medical University (No. 2020BS019).

Conflict of interest

The authors declare no conflict of interest.

References

- [1] Soldozy S, Norat P, Elsarrag M, Chatrath A, Costello JS, Sokolowski JD, *et al.* The biophysical role of hemodynamics in the pathogenesis of cerebral aneurysm formation and rupture. *Neurosurgical Focus*. 2019; 47: E11.
- [2] Vlak MH, Algra A, Brandenburg R, Rinkel GJ. Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and time period: a systematic review and meta-analysis. *The Lancet Neurology*. 2011; 10: 626–636.
- [3] Brown RD, Broderick JP. Unruptured intracranial aneurysms: epidemiology, natural history, management options, and familial screening. *The Lancet Neurology*. 2014; 13: 393–404.
- [4] Ertan N, Rinkel GJ. Unruptured intracranial aneurysms: development, rupture and preventive management. *Nature Reviews Neurology*. 2016; 12: 699–713.
- [5] Brinjikji W, Lanzino G, Cloft HJ, Rabinstein A, Kallmes DF. Endovascular treatment of very small (3 mm or smaller) intracra-

- nial aneurysms: report of a consecutive series and a meta-analysis. *Stroke*. 2010; 41: 116–121.
- [6] Kim JH, Choi CH, Lee JI, Lee TH, Ko JK. Endovascular treatment of ruptured tiny aneurysms. *Journal of Cerebrovascular and Endovascular Neurosurgery*. 2019; 21: 67.
 - [7] Anokwute MC, Braca JA, Bohnstedt B, DeNardo A, Scott J, Cohen-Gadol A, *et al.* Endovascular treatment of ruptured tiny (≤ 3 mm) intracranial aneurysms in the setting of subarachnoid hemorrhage: A case series of 20 patients and literature review. *Journal of Clinical Neuroscience*. 2017; 40: 52–56.
 - [8] Ikawa F, Morita A, Tominari S, Nakayama T, Shiokawa Y, Date I, *et al.* Rupture risk of small unruptured cerebral aneurysms. *Journal of Neurosurgery*. 2019. (in press)
 - [9] Van Rooij WJ, Sprengers ME, de Gast AN, Peluso JPP, Sluzewski M. 3D Rotational Angiography: the New Gold Standard in the Detection of Additional Intracranial Aneurysms. *American Journal of Neuroradiology*. 2008; 29: 976–979.
 - [10] Li M, Cheng Y, Li Y, Fang C, Chen S, Wang W, *et al.* Large-Cohort Comparison between Three-Dimensional Time-of-Flight Magnetic Resonance and Rotational Digital Subtraction Angiographies in Intracranial Aneurysm Detection. *Stroke*. 2009; 40: 3127–3129.
 - [11] Liu J, Gao G, Zhang S, Huang Y, Wu J, Hu X, *et al.* Cotton-Assisted Surgical Clipping of very Small Aneurysms: a Two-Center Study. *World Neurosurgery*. 2019; 127: e242–e250.
 - [12] Burkhardt J, Benet A, Lawton MT. Management of Small Incidental Intracranial Aneurysms. *Neurosurgery Clinics of North America*. 2017; 28: 389–396.
 - [13] Molyneux A, Kerr R, Stratton I, Sandercock P, Clarke M, Shrimpton J, *et al.* International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. *Lancet*. 2002; 360: 1267–1274.
 - [14] Molyneux AJ, Birks J, Clarke A, Sneade M, Kerr RSC. The durability of endovascular coiling versus neurosurgical clipping of ruptured cerebral aneurysms: 18 year follow-up of the UK cohort of the International Subarachnoid Aneurysm Trial (ISAT). *Lancet*. 2015; 385: 691–697.
 - [15] Mansour O, Megahed M, Schumacher M, Weber J, Khalil M. Coiling of Ruptured Tiny Cerebral Aneurysms, Feasibility, Safety, and Durability at Midterm Follow-up, and Individual Experience. *Clinical Neuroradiology*. 2013; 23: 103–111.
 - [16] Zheng J, Xu R, Guo X, Sun X. Small ruptured intracranial aneurysms: the risk of massive bleeding and rebleeding. *Neurological Research*. 2019; 41: 312–318.
 - [17] Perrini P, Montemurro N, Caniglia M, Lazzarotti G, Benedetto N. Wrapping of intracranial aneurysms: Single-center series and systematic review of the literature. *British Journal of Neurosurgery*. 2015; 29: 785–791.
 - [18] International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms—risk of rupture and risks of surgical intervention. *The New England Journal of Medicine*. 1998; 339: 1725–1733.
 - [19] Tsutsumi M, Aikawa H, Onizuka M, Kodama T, Nii K, Matsubara S, *et al.* Endovascular treatment of tiny ruptured anterior communicating artery aneurysms. *Neuroradiology*. 2008; 50: 509–515.
 - [20] Mitchell PJ, Muthusamy S, Dowling R, Yan B. Does small aneurysm size predict intraoperative rupture during coiling in ruptured and unruptured aneurysms? *Journal of Stroke and Cerebrovascular Diseases*. 2013; 22: 1298–1303.
 - [21] Lakićević N, Vujotić L, Radulović D, Cvrkota I, Samardžić M. Factors Influencing Intraoperative Rupture of Intracranial Aneurysms. *Turkish Neurosurgery*. 2015; 25: 858–885.
 - [22] Yamazaki T, Sonobe M, Nakai Y, Sugita K, Matsumaru Y, Yanaka K, *et al.* Predictors of angiographic changes in neck remnants of ruptured cerebral aneurysms treated with Guglielmi detachable coils. *Neurologia Medico-Chirurgica*. 2006; 46: 1–10.
 - [23] Kim DJ, Kim BM, Park KY, Ihm EH, Baek JH, Kim DI. Coil embolization of overwide and undertall small intracranial aneurysms with double microcatheter technique. *Acta Neurochirurgica*. 2014; 156: 839–846.
 - [24] Foreman PM, Hendrix P, Harrigan MR, Fisher WS, Vyas NA, Lipsky RH, *et al.* PHASES score applied to a prospective cohort of aneurysmal subarachnoid hemorrhage patients. *Journal of Clinical Neuroscience*. 2018; 53: 69–73.
 - [25] Sonobe M, Yamazaki T, Yonekura M, Kikuchi H. Small unruptured intracranial aneurysm verification study: SUAVE study, Japan. *Stroke*. 2010; 41: 1969–1977.
 - [26] Iskandar A, Nepper-Rasmussen J. Endovascular treatment of very small intracranial aneurysms. *Interventional Neuroradiology*. 2011; 17: 299–305.
 - [27] Weir B, Disney L, Karrison T. Sizes of ruptured and unruptured aneurysms in relation to their sites and the ages of patients. *Journal of Neurosurgery*. 2002; 96: 64–70.
 - [28] Van Rooij WJ, Keeren GJ, Peluso JP, Sluzewski M. Clinical and angiographic results of coiling of 196 very small ($< \text{or} = 3$ mm) intracranial aneurysms. *American Journal of Neuroradiology*. 2009; 30: 835–839.
 - [29] Rutledge C, Jonzson S, Winkler EA, Raper D, Lawton MT, Abila AA. Small Aneurysms with Low PHASES Scores Account for most Subarachnoid Hemorrhage Cases. *World Neurosurgery*. 2020; 139: e580–e584.
 - [30] Greving JP, Wermer MJH, Brown RD, Morita A, Juvela S, Yonekura M, *et al.* Development of the PHASES score for prediction of risk of rupture of intracranial aneurysms: a pooled analysis of six prospective cohort studies. *The Lancet Neurology*. 2014; 13: 59–66.
 - [31] Etminan N, Brown RD Jr, Beseoglu K, Juvela S, Raymond J, Morita A, *et al.* The unruptured intracranial aneurysm treatment score: a multidisciplinary consensus. *Neurology*. 2015; 85: 881–889.
 - [32] Johnston SC. Leaving Tiny, Unruptured Intracranial Aneurysms Untreated: why is it so Hard? *JAMA Neurology*. 2018; 75: 13–14.
 - [33] Henkes H, Reinartz J, Preiss H, Miloslavski E, Kirsch M, Kühne D. Endovascular treatment of small intracranial aneurysms: three alternatives to coil occlusion. *Minimally Invasive Neurosurgery*. 2006; 49: 65–69.
 - [34] Fang Y, Li Q, Yang P, Zhang Q, Wu Y, Feng Z, *et al.* Application of endovascular coiling and subsequent Onyx 34 embolization in anterior communicating artery aneurysms with adjacent hematoma. *Clinical Neurology and Neurosurgery*. 2014; 123: 40–44.
 - [35] Nii K, Inoue R, Morinaga Y, Mitsutake T, Hanada H. Evaluation of Acute in-stent Thrombosis during Stent-assisted Coil Embolization of Unruptured Intracranial Aneurysms. *Neurologia Medico-Chirurgica*. 2018; 58: 435–441.
 - [36] Kim YS, Lee SW, Yeom JA, Yoon CH, Baik SK. Angiographic findings of in-stent intimal hyperplasia after stent-assisted coil embolization: are they permanent findings? *Journal of Neurosurgery*. 2016; 124: 328–333.
 - [37] Kato N, Yuki I, Ishibashi T, Ikemura A, Kan I, Nishimura K, *et al.* Visualization of stent apposition after stent-assisted coiling of intracranial aneurysms using high resolution 3D fusion images acquired by C-arm CT. *Journal of NeuroInterventional Surgery*. 2020; 12: 192–196.
 - [38] Narata AP, Amelot A, Bibi R, Herbreteau D, Angoulvant D, Gruel Y, *et al.* Dual Antiplatelet Therapy Combining Aspirin and Ticagrelor for Intracranial Stenting Procedures: a Retrospective Single Center Study of 154 Consecutive Patients with Unruptured Aneurysms. *Neurosurgery*. 2019; 84: 77–83.
 - [39] Mutlu O, Olcay AB, Bilgin C, Hakyemez B. Evaluating the Effectiveness of 2 Different Flow Diverter Stents Based on the Stagnation Region Formation in an Aneurysm Sac Using Lagrangian Coherent Structure. *World Neurosurgery*. 2019; 127: e727–e737.
 - [40] Yuan Z, Woha Z, Weiming X. Intraventricular aneurysms: case reports and review of the literature. *Clinical Neurology and Neurosurgery*. 2013; 115: 57–64.
 - [41] Lu J, Liu J, Wang L, Qi P, Wang D. Tiny intracranial aneurysms: endovascular treatment by coil embolisation or sole stent deploy-

- ment. *European Journal of Radiology*. 2012; 81: 1276–1281.
- [42] Nguyen TN, Raymond J, Guilbert F, Roy D, Bérubé MD, Mahmoud M, *et al.* Association of endovascular therapy of very small ruptured aneurysms with higher rates of procedure-related rupture. *Journal of Neurosurgery*. 2008; 108: 1088–1092.
- [43] Yamaki VN, Brinjikji W, Murad MH, Lanzino G. Endovascular Treatment of very Small Intracranial Aneurysms: Meta-Analysis. *American Journal of Neuroradiology*. 2016; 37: 862–867.
- [44] Gao B, Li M, Wang Y, Fang C. Delayed coil migration from a small wide-necked aneurysm after stent-assisted embolization: case report and literature review. *Neuroradiology*. 2006; 48: 333–337.
- [45] Yang P, Zhao K, Zhou Y, Zhao R, Zhang L, Zhao W, *et al.* Stent-assisted Coil Placement for the Treatment of 211 Acutely Ruptured Wide-necked Intracranial Aneurysms: a Single-Center 11-Year Experience. *Radiology*. 2015; 276: 545–552.
- [46] Yonaha H, Hyodo A, Inaji T, Ito K, Kushi S, Tsuchida K, *et al.* Thromboembolic Events Associated with Coil Protrusion into Parent Arteries after GDC Treatment. *Interventional Neuroradiology*. 2006; 12: 105–111.
- [47] Hwang G, Jung C, Park SQ, Kang HS, Lee SH, Oh CW, *et al.* Thromboembolic Complications of Elective Coil Embolization of Unruptured Aneurysms. *Neurosurgery*. 2010; 67: 743–748.
- [48] Cho YD, Lee JY, Seo JH, Kang H, Kim JE, Jung KH, *et al.* Intra-arterial tirofiban infusion for thromboembolic complication during coil embolization of ruptured intracranial aneurysms. *European Journal of Radiology*. 2013; 81: 2833–2838.
- [49] Gentric J, Brisson J, Batista AL, Ghostine J, Raymond J, Roy D, *et al.* Safety of Abciximab injection during endovascular treatment of ruptured aneurysms. *Interventional Neuroradiology*. 2015; 21: 332–336.
- [50] Kadziolka K, Soize S, Pierot L. Mechanical thrombectomy “as a rescue treatment” of thromboembolic complications during endovascular treatment of intracranial aneurysms. *Journal of Neuroradiology*. 2013; 40: 360–363.
- [51] Wu P, Ocak PE, Wang D, Ocak U, Xu S, Li Y, *et al.* Endovascular Treatment of Ruptured Tiny Intracranial Aneurysms with Low-Profile Visualized Intraluminal Support Device. *Journal of Stroke and Cerebrovascular Diseases*. 2019; 28: 330–337.
- [52] Alghamdi F, Mine B, Morais R, Scillia P, Lubicz B. Stent-assisted coiling of intracranial aneurysms located on small vessels: midterm results with the LVIS Junior stent in 40 patients with 43 aneurysms. *Neuroradiology*. 2016; 58: 665–671.
- [53] Santillan A, Boddu S, Schwarz J, Lin N, Gobin YP, Knopman J, *et al.* LVIS Jr. stent for treatment of intracranial aneurysms with parent vessel diameter of 2.5 mm or less. *Interventional Neuroradiology*. 2018; 24: 246–253.
- [54] Gao B, Li T, Li L, Xu G, Yang B. Tiny Cerebral Aneurysms can be Treated Safely and Effectively with Low-Profile Visualized Intraluminal Support Stent-Assisted Coiling or Coiling alone. *World Neurosurgery*. 2018; 113: e426–e430.
- [55] Damiano RJ, Tutino VM, Paliwal N, Patel TR, Waqas M, Levy EI, *et al.* Aneurysm characteristics, coil packing, and post-coiling hemodynamics affect long-term treatment outcome. *Journal of NeuroInterventional Surgery*. 2020; 12: 706–713.
- [56] Turner RD, Turk A, Chaudry I. Low-profile visible intraluminal support device: immediate outcome of the first three us cases. *Journal of Neurointerventional Surgery*. 2013; 5: 157–160.
- [57] Conrad MD, Brasiliense LBC, Richie AN, Hanel RA. Y stenting assisted coiling using a new low profile visible intraluminal support device for wide necked basilar tip aneurysms: a technical report. *Journal of NeuroInterventional Surgery*. 2014; 6: 296–300.