

Endovascular Treatment of Ruptured Tiny Intracranial Aneurysms with Low-Profile Visualized Intraluminal Support Device

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Background: Ruptured tiny intracranial aneurysms (TIAs) have been challenging both for endovascular and neurosurgical interventions. Thus, we aimed to evaluate the safety and efficacy of low-profile visualized intraluminal support (LVIS) device in the treatment of ruptured TIAs (rTIAs). *Material and Methods:* Among 761 intracranial aneurysms which were treated either surgically or endovascularly, 32 rTIAs underwent stent-assisted coiling with LVIS device between 2014 and 2017. Patient data were reviewed retrospectively. Clinical and radiological outcomes were recorded at discharge and mid-term follow-up. *Results:* Mean patient ages were 53 ± 14.5 years. Mean aneurysm size was $2.28 \pm .53$ mm (range, 1-2.9 mm) with a mean dome:neck ratio of 1.08 (range, .75-2.14). The LVIS stents were successfully implanted in all patients. Mean follow-up period was 9.3 ± 1.9 months (range, 6-15 months). Immediate angiographic evaluation demonstrated complete occlusion in 13 (40.6%) patients, while neck remnant and residual sac were observed in 12 (37.5%) and 7 (21.9%), respectively. All patients had moderate disability (mRS 2-3) at discharge. Number of aneurysms with complete occlusion significantly increased and 82.1% of the patients (23 of 28) demonstrated complete occlusion at follow-up ($P = .0015$). Among these, 27 had good outcome (mRS 0-1; 96.9%) with significant improvement compared to discharge ($P = .0001$). There was no recurrence or enlargement of the residual aneurysms. Additionally, there were no procedure-related complications except the one (3.6%) showing asymptomatic stenosis of the posterior cerebral artery in follow-up imagings. *Conclusions:* Stent-assisted coiling of rTIAs with LVIS device provides high rates of technical success and complete occlusion at mid-term follow-up with an excellent safety profile.

Key Words: Aneurysm—angiography—coil—LVIS stent

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Introduction

Tiny intracranial aneurysms (TIAs) are defined as aneurysms measuring less than or equal to 3 mm in diameter. Although previous large, prospective studies have

reported a low probability of rupture for intracranial aneurysms (IAs) with a diameter smaller than 7 mm, number of studies reporting higher than expected rates of rupture of TIAs, up to 15%, are increasing.^{1,2} With recent

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advances in both devices and techniques, endovascular treatment has become an alternative strategy in the management of TIAs. However, intraprocedural ruptures remain to be the major contributor to patient prognosis in about 7% of endovascular procedures.³ Thus, management strategies for ruptured TIAs (rTIAs) remain controversial as the safety of endovascular coiling is still in question and surgical treatment is also technically challenging.

The low-profile visualized intraluminal support (LVIS) stent (MicroVention Terumo, Tustin, CA) is a new, flexible, braided microstent designed for stent-assisted coiling of wide-necked IAs.⁴⁻⁶ Although several reports have confirmed its efficacy and safety,^{4,5,7,8} evidence regarding the use of the LVIS device in the treatment of rTIAs is limited. Therefore, we describe our experience with the LVIS stent by focusing on its advantages in the endovascular management of wide-necked rTIAs.

Materials and Methods

Patient and Aneurysm Characteristics

Seven hundred and sixty-one patients with IAs were treated either surgically (n = 370, 48.6%) or endovascularly (n = 391, 51.4%) at the Department of Neurosurgery, the first affiliated hospital of Harbin Medical University-Harbin, between April 2014 and February 2017. Among these, 161 patients (21.2%) underwent stent-assisted coiling with the LVIS device. After obtaining approval from the local institutional ethical review board, patient data were retrospectively reviewed. Aneurysms were defined as *tiny* based on the measurements via preprocedural digital subtraction angiography (DSA) and three-dimensional (3D) rotational angiography studies. Cases with IAs greater than 3 mm in diameter and with unruptured aneurysms were excluded from the study. Thirty-two rTIAs meeting the inclusion criteria were identified eventually and included in the study. Aneurysms were further divided into 3 categories as very wide-necked aneurysms (dome:neck ratio <1.2), wide-necked aneurysms ($1.2 \leq$ dome:neck ratio <2), and narrow-necked aneurysms (dome:neck ratio >2). Medical records including preprocedural and postprocedural notes, radiologic images, neuroradiology reports, and operative notes were reviewed. Baseline clinical data of the patients and aneurysm characteristics were recorded. Procedure-related complications and clinical and angiographic outcomes at discharge and mid-term follow-up were noted.

Endovascular Procedure

Patients were premedicated with dual antiplatelet therapy (300 mg aspirin and 300 mg clopidogrel) 2 hours prior to the intervention. All procedures were performed under general anesthesia. Patients were also systemically

heparinized after the induction of anesthesia. A 6F guiding catheter was introduced through a femoral sheath into the internal carotid artery or basilar artery, depending on the aneurysm location. Rotational angiography followed by 3D reconstruction was performed to visualize the morphology of the aneurysm and parent artery, and to determine the proper projection for stent placement and coiling. The Echelon 10 (EV3, Plymouth, MN) microcatheter tip was steam-shaped according to the actual size of the vessel and geometry of aneurysm observed in the 3D rotational angiography on the monitor before insertion. As the location of each aneurysm in relation to the parent artery varies, the shape of the microcatheter was determined for each individual case. Standard stent semi-jailing or jailing techniques were used in all patients as previously described.^{1,9,10} First, Echelon 10 (EV3) microcatheter was navigated into the aneurysmal sac or neck, and Headway 21 microcatheter (MicroVention, Tustin, CA) was then positioned across the aneurysmal neck via .014-inch Synchro (Stryker, West Valley City, UT) or Traxcess microwire (MicroVention, Tustin, CA). LVIS stent was then advanced through the Headway 21 microcatheter and it was placed at the cephalic end of the microcatheter without releasing. Aneurysm coiling was performed using 3D coils with proper diameter and length. After one or more coils were released to fill the aneurysmal cavity, stent was partially released to prevent coil protrusion into the parent artery. Aneurysmal cavity was then continuously filled with more coils until complete occlusion was achieved or until no more coils could be safely deployed within the aneurysm sac (Fig 1, A-F, Fig 2, A-D). After stabilizing the position of the last coil, stent was completely released, and the coil was isolated. Twenty-four hours after the endovascular procedure, all patients underwent noncontrast CT scan of the head to rule out postprocedural hemorrhage. A daily regimen of aspirin (100 mg/d) and clopidogrel (75 mg/d) was recommended for 6 weeks, followed by a regimen of only aspirin (100 mg/d) for at least 6 months.

Clinical and Radiologic Follow-Up

Clinical follow-up was performed in all patients. Modified Rankin Scale (mRS) was used to assess patient outcomes at discharge and at mid-term follow-up. Clinical outcomes were defined as good (mRS 0-1), moderate (mRS 2-3), or poor (mRS 4-5).

Occlusion status of the aneurysm was evaluated by DSA immediately after the procedure in all patients, and at 6-month follow-up in 28 of the patients (87.5%). A simplified 3-point Raymond Scale was used to assess the degree of occlusion. The degree of occlusion was defined as *complete* when there was no contrast filling within the aneurysm (Raymond Grade I). *Neck remnant* and *residual sac* were defined as Raymond Grade II and Raymond

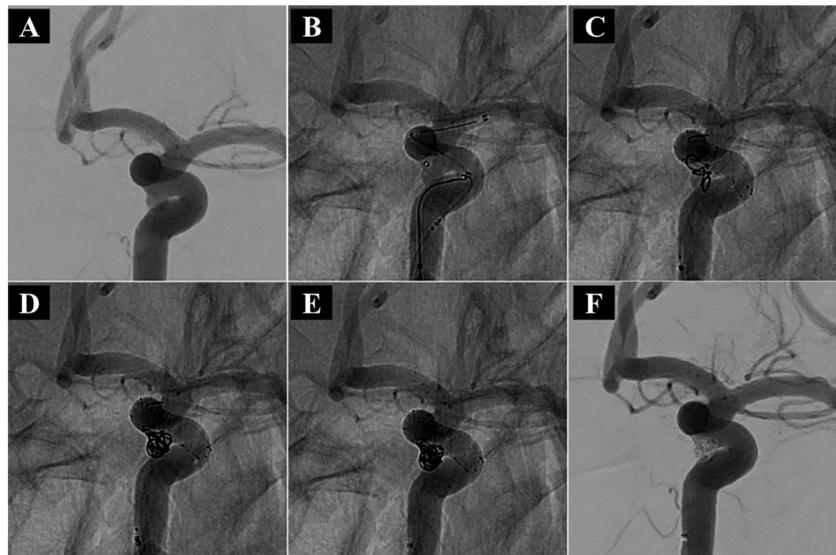


Figure 1. Demonstrative angiographic images of a ruptured right internal carotid artery aneurysm. (A) The aneurysm in the working projection before treatment. (B) The Echelon 10 microcatheter was navigated and positioned near the aneurysm neck for LVIS stent delivery. (C) The LVIS stent was advanced into the aneurysm and completely expanded. (D-F) Complete occlusion of the aneurysm with patency of the parent vessels immediately after the procedure.

Grade III occlusion when there was contrast filling in the aneurysmal neck and contrast filling in the aneurysmal cavity, respectively. Clinical and radiologic follow-ups were conducted by 2 experienced neurosurgeons, independently (Y.L. and T.Z.).

Descriptive statistics are given as number of units (n), percentage (%), median (range), and mean \pm standard deviation. Analysis was carried out with an independent-samples *t* test or Fisher exact test. Statistical differences were considered significant if the *P* value was less than .05.

Results

Patient and Aneurysm Characteristics

A total of 32 patients with rTIAs were included in the study. Mean patient ages were 53 ± 14.5 years (range, 20-81 years). Twenty-one (65.6%) of the patients were female while 11 (34.4%) were male. Twenty-seven patients (84.4%) demonstrated Hunt-Hess grade II subarachnoid hemorrhage, while 4 (12.5%) demonstrated Hunt-Hess grade III and 1 (3.1%) demonstrated Hunt-Hess grade IV subarachnoid hemorrhage.

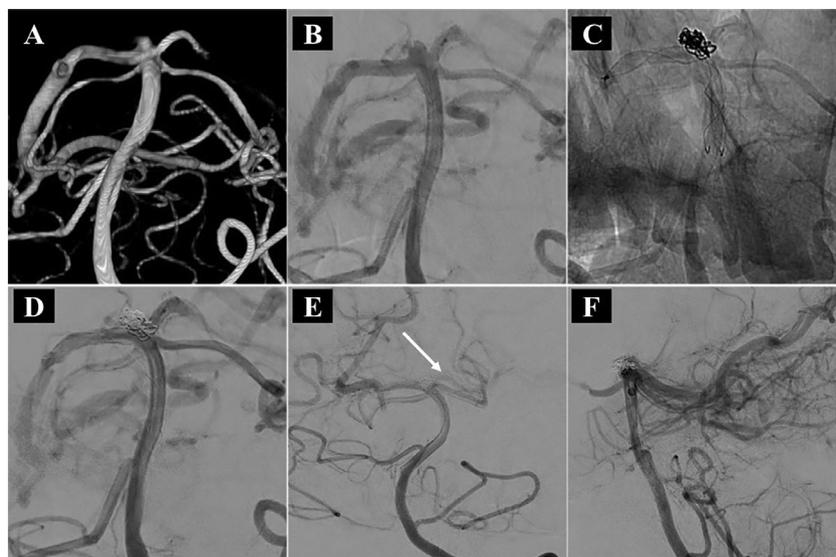


Figure 2. Demonstrative angiographic images of a ruptured basilar artery aneurysm. (A) Three-dimensional reconstruction of the aneurysm. (B) Aneurysm in the working projection before treatment. (C) Deployment of LVIS stent across the aneurysm neck for coil delivery. (D) Successful occlusion of the aneurysm immediately after the procedure. (E, F) Mid-term follow-up images demonstrating complete occlusion of the aneurysm and asymptomatic stenosis of the posterior cerebral artery (white arrow).

In decreasing order of frequency, aneurysms were located along the anterior cerebral artery (n = 11, 34.4%), internal carotid artery (n = 11, 34.4%), basilar artery (n = 4, 12.5%), middle cerebral artery (n = 4, 12.5%), and posterior inferior cerebral artery (n = 2, 6.2%). Thirty-one of the aneurysms were solitary, while 1 was associated with an accompanying unruptured aneurysm unrelated to the subarachnoid hemorrhage. Mean size of the aneurysms was $2.28 \pm .53$ mm (range, 1-2.9 mm), mean height of the domes was $2.5 \pm .4$ mm (range, 1.5-2.9 mm), and mean diameter of the necks was $2.4 \pm .5$ mm (range, .7-2.9 mm). Dome:neck ratio was less than 1.2 (very wide-necked aneurysms) in 27 of the patients (84.4%). This ratio was greater than or equal to 1.2 and less than 2 (wide-necked aneurysms) in 4 (12.5%), and greater than 2 (narrow-necked aneurysm) in 1 (3.1%) of the patients. Mean dome:neck ratio was 1.08 (range, .75-2.14). Baseline characteristics of the patients and rTIAs are summarized in Table 1.

Endovascular Procedure

A total of 33 LVIS stents were used for the treatment of 32 rTIAs since overlapping stenting technique was performed in one of the rTIA which was suspected to be a blood-blister-like aneurysm. Median number of coils used was 2.2 (range, 1-4; total, 70). Technical success rate of the procedures was 100% (32 of 32; Table 1).

Clinical and Radiologic Follow-Up

Mean postprocedural follow-up period was 9.3 ± 1.9 months (range, 6-15 months). All patients who underwent LVIS stent-assisted coiling demonstrated moderate disability (mRS 2-3 in 32; 100%) at discharge. Among these, all patients except the one (3.1%) who developed symptomatic hydrocephalus and required ventriculoperitoneal shunt insertion had good outcome (mRS 0-1; 96.9%) at mid-term follow-up. There was significant improvement in clinical outcome scores at mid-term follow-up compared to discharge ($P = .0001$).

At discharge, complete occlusion (Raymond grade I) was achieved in 13 (40.6%) of the patients, while 12 (37.5%) and 7 (21.9%) exhibited neck remnants (Raymond grade II) and residual sacs (Raymond grade III), respectively. Number of patients with Raymond grade I occlusion significantly increased during the follow-up period compared to discharge and 82.1% of the patients (23 of 28) demonstrated complete occlusion at 6-month follow-up ($P = .0015$). There was no significance between the occlusion grades of very wide-necked aneurysms compared to wide and narrow-necked aneurysms at discharge ($P = .37$) and at 6-month follow-up ($P = 1$). However, number of very wide-necked aneurysms with complete occlusion significantly increased during the follow-up period (10 of 27, 37% versus 19 of 23, 82.6%; $P = .0016$). The increase in number of completely occluded aneurysms did not show a significance in the wide-necked rTIAs

Table 1. Baseline characteristics of the patients and the aneurysms

Variable	rTIAs (n = 32)
Mean age (range), years	53 (20-81)
Gender (%)	
Female	21 (65.6)
Male	11 (34.4)
Hunt-Hess grade (%)	
I	-
II	27 (84.4)
III	4 (12.5)
IV	1 (3.1)
Fisher grade (%)	
I	-
II	20 (62.5)
III	11 (34.4)
IV	1 (3.1)
Aneurysm location (%)	
ICA	11 (34.4)
ACA	11 (34.4)
MCA	4 (12.5)
BA	4 (12.5)
PICA	2 (6.3)
Aneurysm size (range), mm	2.28 (1-2.29)
Dome:neck ratio (range)	1.08 (.75-2.14)
<1.2 (%)	27 (84.4)
≥1.2-2 (%)	4 (12.5)
>2 (%)	1 (3.1)
Number of LVIS stents used	33
Median number of coils used (range)	2.2 (1-4)
Complications (%)	
Intraprocedural rupture	0
Thromboembolic events	0
Asymptomatic stenosis	1 (3.6)

ACA, anterior cerebral artery; BA, basilar artery; ICA, internal carotid artery; LVIS, low-profile visualized intraluminal support; MCA, middle cerebral artery; PICA, posterior inferior cerebellar artery.

subgroup, most probably due to the low number of subjects in this group (2 of 4, 50% versus 3 of 4, 75%; $P = .46$). Although 21.9% of the overall patients (7 of 32) had residual sacs (Raymond grade III) immediately after the procedure, grade III occlusion significantly improved to lower grades and no patients (0 of 28) demonstrated residual sacs on 6-month follow-up imagings ($P = .01$; Fig 3). There was no recurrence or enlargement of the residual aneurysms. There were no procedure-related permanent neurological deficits or mortalities within 30 days of the intervention (Table 1). Additionally, there was no hemorrhagic or thromboembolic complications in our series except the 1 (1 of 28, 3.6%) showing asymptomatic stenosis of the posterior cerebral artery in the follow-up DSA (Fig 2, E). Distribution of the patients on the basis of postprocedural mRS scores and Raymond grades according to dome:neck ratios are presented in Table 2.

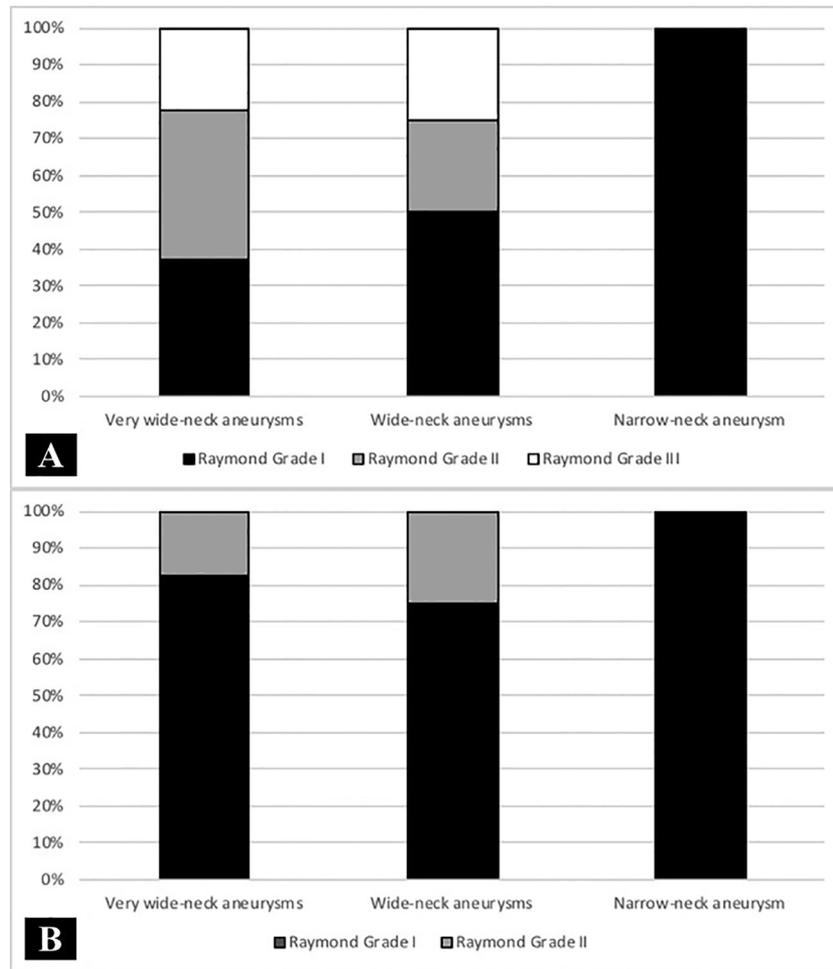


Figure 3. Bar graph showing degree of aneurysm occlusion (Raymond I: black, Raymond II: grey, Raymond III: white) based on dome:neck ratio immediately after the procedure (A) and 6-month follow-up (B).

Discussion

Endovascular coiling of TIAs are challenging because of their small sacs, and thin and fragile walls which may lead to increased risk of narrowing or tearing of the parent

vessel, intraprocedural rupture, and thromboembolic complications.¹¹

Brinjikji et al reported the first meta-analysis regarding endovascular treatment of TIAs (271 ruptured versus

Table 2. Clinical outcomes of the patients and degree of aneurysm occlusion at the time of discharge and at mid-term follow-up

Variable	Number of patients (%)					
	Discharge			Mid-term follow-up		
Dome:neck ratio	<1.2	≥1.2-2	>2	<1.2	≥1.2-2	>2
mRS scores						
0	-	-	-	24 (88.9)	4 (100)	1 (100)
1	-	-	-	2 (7.4)	-	-
2	23 (85.2)	4 (100)	1 (100)	-	-	-
3	4 (14.8)	-	-	-	-	-
4	-	-	-	1 (3.7)	-	-
Raymond scale (Grade)						
Complete occlusion (I)	10 (37)	2 (50)	1 (100)	19 (82.6)	3 (75)	1 (100)
Residual neck remnant (II)	11 (40.8)	1 (25)	-	4 (17.4)	1 (25)	-
Residual sac remnant (III)	6 (22.2)	1 (25)	-	-	-	-
Total	27	4	1	23	4	1

171 unruptured).¹² According to this meta-analysis, intraprocedural rupture rate was 10.7% in rTIAs and 5.0% in unruptured TIAs during coiling with a mortality rate of 3.1% and 1.2%, respectively. Morbidity due to thromboembolic complications was observed in 1.3% of the unruptured TIAs and 2.2% of the rTIAs. Thankfully, recent technologic advances including the development of smaller coils, better microcatheters, steerable soft microguidewires, newer distal access catheters, and balloons which are easier to navigate as well as increased operator experience have enhanced the safety and efficacy of coiling of TIAs.³ Resultantly, promising results of improved coiling techniques in the management of rTIAs have increased.¹³⁻¹⁶ According to a more recent meta-analysis regarding endovascular management of TIAs (844 ruptured versus 261 unruptured), intraprocedural ruptures and thromboembolic complications occurred in 7% and 4% of the rTIAs, respectively.³ Better results in favor of more recent studies supported the authors' hypothesis suggesting that recently published series would show lower complication rates with higher aneurysm occlusion rates and also confirmed the increased safety and efficacy of coiling in the management of TIAs. However, the same study reported higher rates of periprocedural complications as well as higher rates of recanalization with less immediate angiographic occlusion following stent-assisted coiling of TIAs compared to coiling alone.³ Lower rates of occlusion were concluded to be a result of less attenuated tamponade which is required for a satisfying stent-assisted coiling, while mandatory antiplatelet therapy and wider neck of TIAs were accused of being the cause of higher recanalization rates.

Since the introduction of Neuroform (Stryker), various types of stents have been used in clinical practice, including Enterprise (Codman), Solitaire (Ev3), Leo (Balt), and LVIS stents. LVIS is a third-generation microstent designed for coil-assisted embolization, which is produced by braiding individual strands of Nitinol onto a mandrel.⁶ Although it is difficult to define which is superior, several studies have supported the safety and efficacy of LVIS stent in the treatment of both ruptured and unruptured IAs^{4,5,8,17} with better occlusion rates compared to its counterparts.¹⁸ Turner et al reported the first case series showing that stent-assisted coiling with the LVIS device was safe and effective in the treatment of IAs.⁶ Since then, several studies have reported promising results of LVIS device with high technical success, excellent safety profile, and ongoing occlusion during the follow-up period leading to higher complete occlusion rates at follow-ups in both ruptured and unruptured IAs.^{4,5} Recently, Zhang et al published a systematic review of the literature on stent-assisted coiling of wide-necked IAs using the LVIS device and reported high rates of occlusion with procedure-related morbidity and mortality in only 1.4% and 0% of the patients, respectively.¹⁷

Currently, reconstruction of the parent vessels instead of embolizing the aneurysm sac is widely accepted as a key strategy in endovascular treatment of IAs.⁴ Reductions in velocity and wall shear stress in proportion to the stent's metal coverage have been shown to be important in preventing aneurysm recurrence and future recanalization. Thus, the amount of metal coverage of stents has gained importance since low coverage is associated with weak flow diverter effect, while too much coverage is associated with branch vessel occlusion.^{19,20} LVIS device has a mean metal coverage rate of 23% which is higher than its counterparts and lower than flow diverters. Resultantly, LVIS stent provides better flow diversion effect and promote endothelialization which facilitates delayed aneurysm thrombosis while improving long-term outcomes.^{6,18} Wang et al demonstrated that single LVIS stent causes more flow reductions compared to that of double Enterprise stent, but less than Pipeline device, while double LVIS stent results in better flow diverting effect compared to Pipeline device.²⁰ According to the same study, LVIS device is also associated with obvious reductions in velocity and wall shear stress. Recently, Fiorella et al reported the degree of complete occlusion in unruptured, wide-necked IAs with LVIS device as 17% immediately after treatment and as 75% at 6-month follow-up⁵ which is similar to that of reported by Feng et al (28.9% versus 84.2%, respectively).⁴ In the present study, consistent with previous reports, total occlusion rates at 6-month follow-up were significantly higher compared to that of immediately after the procedure (13 of 32, 40.6% versus 23 of 28, 82.1%; $P = .0015$). Number of completely occluded aneurysms significantly increased at follow-up in very wide-necked rTIAs subgroup as well (10 of 27, 37% versus 19 of 23, 82.6%; $P = .0016$). Moreover, even aneurysms with Raymond III occlusion immediately after treatment significantly improved to lower grades and no patients demonstrated residual sacs on 6-month follow-up imagings (7 of 32, 21.9% versus 0 of 28, 0%; $P = .01$).

Smaller and ruptured aneurysms are associated with increased risk of intraprocedural rupture.¹¹ Previously mentioned properties of TIAs such as their small sacs, jeopardize catheter positioning, and coil deployment which may result in rerupture of the aneurysm. To avoid this disastrous complication, the operator should keep the catheter tip out of the aneurysm sac or near the neck instead of keeping it at the center of the sac or deep in it. When used in TIAs, the braided morphology of the LVIS device allows for greater conformability with better parent vessel wall apposition and better stability via increased level of radially directed force. Additionally, the catheter tip can be pushed from outside the aneurysm into the sac by LVIS device, thus it can also reduce the difficulty of catheter positioning and coil deployment. Consistent with previous series of stent-assisted coiling of wide-necked rTIAs with LVIS device,²¹ we did not observe any intraprocedural rupture in our series.

Thromboembolic events are among the major complications of stent-assisted coiling of IAs with a reported incidence between 1.4% and 12% with different types of stents.²²⁻²⁴ Antiplatelet therapy has been shown to reduce the periprocedural thromboembolic complication rates²⁵ since the main cause is insufficient platelet inhibition.^{26,27} Although increased risk of hemorrhagic complications is the primary concern, recent studies demonstrated that antiplatelet therapy did not cause a significant increase in major systemic or intracranial hemorrhages even in cases requiring ventricular drain placement.^{25,28,29} To be noted, we elected to alleviate the symptoms of high intracranial pressure and to facilitate the clearance of blood from cerebral spinal fluid via lumbar puncture rather than ventricular drain placement as most of our patients demonstrated relatively low grades of subarachnoid hemorrhage. We believe, along with the safety of dual antiplatelet therapy, this may be another reason for not having cases of rebleeding or other hemorrhagic complications in the present series.

Using coils with proper size is crucial for successful embolization of TIAs as ultrasmall diameter coils (1 mm or 1.5 mm) can enhance the packing density while reducing the risk of intraoperative rupture.³⁰ However, coil protrusion into the parent artery is a major problem when using ultrasmall diameter coils, which can be avoided by deploying the stent to prevent thromboembolic complications.⁴ Moreover, small cell size (<.9 mm) of the LVIS device provides good protection against coil prolapse. Branch vessel occlusion, another devastating complication of stent-assisted coiling, occurs particularly when the branch originates from the neck of the aneurysm. Partial compression of LVIS stent during the release process can protect the branch vessel, thereby preventing the coil from protruding into the origin of the branch.

Incomplete expansion or kinking of the stent may also result in thromboembolic events. However, it can be ruled out by observing the helical strands under fluoroscopy when using LVIS stent as radiopaque markers which are placed at the body and either ends of the device provide good visibility and allow for full-length visualization. Intraprocedural complications including in-stent thrombosis were reported as 9.1% in a recent series of LVIS stent-assisted coiling of rTIAs, which were the results of absence of good apposition and incomplete expansion of the stent.²¹ In most cases of incomplete expansion, retrieving the stent and unsheathing it once again are useful for achieving complete expansion.⁴ In our series, all stents completely expanded, and the degree of expansion was clearly visualized under fluoroscopy (Fig 1, C). Although for the small vessels like anterior cerebral artery, LVIS Junior stent may be a more good choice, unfortunately, we did not have this stent when we did operation. However, none of the cases developed acute in-stent thrombosis which can be successfully managed by intravenous/arterial administration of glycoprotein IIb/III a inhibitors when occurred.^{17,21}

In sum up, good clinical outcomes along with the absence of hemorrhagic and ischemic complications in our series support the LVIS device as a safe method in the management of rTIAs. Moreover, progressive occlusion which resulted in increased rates of complete occlusion at mid-term follow-up favors the efficacy of LVIS device. Thus, we advocate stent-assisted coiling with LVIS device as a safe and effective treatment option in the management of rTIAs even with very wide necks. In addition, we believe that stent-assisted coiling provide better embolization in narrow-necked aneurysms as well since they allow more coils to be deployed into the aneurysm sac.

Being a retrospective analysis of the patient data from a single institution is the major limitation of our study which might have introduced selection bias. Furthermore, the results may also be influenced by the selected method of the treatment and follow-up which at least partly depend on the patients' preferences. Although the sample size is small and long-term efficacy remains unknown, our mid-term follow-up results support the use of LVIS stent in ruptured and wide-necked TIAs. However, long-term comparative clinical and radiologic outcome studies with larger sample sizes are warranted.

Conclusion

Ruptured TIAs can be safely and effectively secured endovascularly by stent-assisted coiling with LVIS device.

Authors' Contribution

Pei Wu, Pinar Eser Ocak, and Dianhong Wang have contributed equally to this paper.

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