
LVIS Blue as a Stand-alone “Flow Diverter”

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Abstract: Flow diversion fundamentally changes the treatment approach towards intracranial aneurysms. Most currently available devices established efficacy and safety data in the proximal anterior circulation; the distal and posterior circulations remain areas of active research. LVIS Blue is a stent with 28% metal coverage approved for use as a coil adjuvant. Some studies indicate potential “flow diverter” properties. We sought to evaluate the LVIS Blue as a stand-alone “flow diverter” for the treatment of intracranial aneurysms. We performed an observational single-center study to evaluate initial occlusion and occlusion at six months follow-up for patients with distal or posterior circulation aneurysms treated with the LVIS Blue as a “flow diverter” at our institution. Ten aneurysms were treated over the course of two years with six-month angiographic follow-up. Seven lesions were in the distal anterior circulation and were unruptured (five anterior communicating artery, one M2 middle cerebral artery, one pericallosal). Three were posterior circulation (two basilar tip aneurysms, one P2 posterior cerebral artery aneurysm). Follow up demonstrated treatment effect in nine of ten aneurysms (four complete aneurysm occlusions, five lesions with decreased size and flow). One lesion showed no treatment response. No ischemic or hemorrhagic complications were noted during placement or clinical follow-up. LVIS Blue can function safely as a “flow diverter” in the distal and posterior circulations. Further data regarding long-term efficacy is needed.

Keywords: Aneurysm, LVIS, Stent, Embolization, Flow Diverter

1. Introduction

The advent of flow diversion revolutionized the treatment of intracranial aneurysms. [1-3] Until recently, the availability in the United States of only a single “flow diverter” with limited indications did not preclude its use or effectiveness for the treatment of other lesions [4-9]. While in Europe multiple devices are available for the treatment of distal aneurysms, in the USA only Surpass (Stryker) and PED (Medtronic) are readily available neither are approved for distal circulation. As a result, a blossoming literature surrounding the use of “flow diverters” throughout the intracranial circulation has emerged. These studies demonstrate effectiveness of the device as a primary treatment, but with noted ischemic and hemorrhagic

complications. One of the posited explanations behind this increased complication rate is the degree of metal coverage. While not necessarily problematic in the proximal anterior circulation, this coverage in the posterior and distal circulations risks the occlusion of small perforator or branch vessels, or the parent vessel itself. [7, 10-12]

Previously, our group published the utility of the LVIS blue stent, (Microvention; Aliso Viejo, CA) as a coil adjuvant. Within that report we noted a high aneurysm cure rate despite low coil packing densities, indicating potential flow diverting properties of the device [13]. Herein, we report our experience over a two-year period with the LVIS stent used as a flow diversion device for the treatment of intracranial aneurysms.

2. Methods

We performed an IRB-approved observational, single-center retrospective review based on a prospectively maintained database evaluating occlusion at six-month follow up for patients treated with the LVIS Blue stent as a flow diversion device across the neck of an aneurysm in the posterior circulation and distal anterior circulation (beyond the ophthalmic segment). Use of the LVIS Blue was at the discretion of the treating physician and all patients were consented with regards to FDA off-label use of the device. The records of all patients treated with an LVIS Blue stent were evaluated, $n = 58$. The study sample was collected by reviewing the neuro-endovascular database within the study period. All historical, clinical, radiographic, and follow-up information was obtained from the electronic medical record in accordance with the Health Insurance Portability and Accountability Act (HIPAA). Presently there are multiple employed scales for grading schema to evaluate flow diversion, but there is no consensus opinion. Thus, aneurysm closure was evaluated simplistically based on angiographic follow-up demonstrating either 1) complete resolution, 2) decreased aneurysm filling, 3) persistent aneurysm opacification [14-17].

Patient demographic data, clinical presentation, prior treatments, aneurysm characteristics, medical, and treatment data were evaluated using basic descriptive statistics. Average vessel diameter was measured as the average between the proximal and distal diameters. Device diameter was then divided by this value to obtain a ratio. All analysis was performed using R (R foundation for statistical computing, Vienna Austria 2017).

All embolizations were performed under general anesthesia with the patient pre-medicated with dual anti-platelet therapy. Elective outpatients were initiated on aspirin 325 mg and clopidogrel 75 mg for a minimum of five days prior to intervention. Emergent/urgent procedures received 650 mg of aspirin and 30 mg of prasugrel one hour prior to intervention.

We do not routinely perform platelet sensitivity testing. After achieving groin access with a 6 Fr sheath, 4000 U of heparin was administered with an additional bolus of 1000 U every hour in cases of elective treatment. After achieving parent vessel access with a 6 Fr distal access catheter angiography was performed and appropriate projections were obtained. Using roadmap angiography, a Headway 021 microcatheter (Microvention; Aliso Viejo, CA) with a Synchro 2 microwire (Neurovascular, Fremont CA) was navigated past the lesion. Embolization was performed under live fluoroscopy ensuring adequate neck coverage. Deployment of the LVIS Blue stent was achieved with a variable combination of unsheathing and loading maneuvers. Routine follow-up angiography was performed at six-months post procedure.

3. Results

3.1. Patient Characteristics

Retrospective review yielded ten patients who underwent placement of an LVIS as a sole endovascular embolization device with six-month follow-up imaging. Eight patients were female with a median age of 50. The majority of patients presented with incidental aneurysms (six), with the remainder presenting in follow-up for previously treated lesions (two), and aneurysm associated symptoms (one stroke and one rupture with subarachnoid hemorrhage).

3.2. Lesion Characteristics

The majority of lesions were located in the distal anterior circulation, (five anterior communicating artery, one M2 middle cerebral artery, one pericallosal), and three in the posterior circulation (two basilar tip aneurysms, one P2 posterior cerebral artery aneurysm). One posterior communicating artery aneurysm was treated. Five patients were treated with LVIS flow diversion at aneurysm recurrence or noted residual of a previously treated aneurysm (Table 1).

Table 1. Patient aneurysm characteristics and treatment outcomes at 6 months.

	Presentation	Location	Aneurysm size (mm)	Average vessel diameter (mm)	Ratio device/vessel
1	Incidental	Pericallosal	4.0 × 2.0	2.05	1.8
2	Stroke	P2 PCA	9.5 × 2.2	2.0	2.3
3	Incidental	Anterior communicating	2.4 × 1.8	2.8	1.3
4	Incidental	Basilar tip	2.3 × 1.1	2.8	1.3
5	Prior SAH	Anterior communicating	2.0 × 1.7	2.0	1.8
6	Incidental	Posterior communicating	5.1 × 4.1	4.1	1.1
7	Incidental	M2 MCA	11 × 9.3	2.6	1.4
8	Prior SAH	Anterior communicating	4.4 × 5.5	2.3	1.5
9	SAH	Basilar tip	0.8 × 1.0	3.3	1.1
10	Incidental	Anterior communicating	3.8 × 2.0	2.2	1.6

Table 1. Continued.

	Device diameter (mm)	Configuration	Decreased filling at 6 months follow-up	Complete occlusion at 6 months follow-up
1	3.5	sidewall	Yes	Yes
2	4.5, 3.5 x 2.0	fusiform	No	No
3	3.5	bifurcation	Yes	Yes
4	3.5	bifurcation	Yes	No
5	3.5	bifurcation	Yes	No

	Device diameter (mm)	Configuration	Decreased filling at 6 months follow-up	Complete occlusion at 6 months follow-up
6	4.5 x 2.0	sidewall	Yes	No
7	3.5	bifurcation	Yes	Yes
8	3.5	bifurcation	Yes	Yes
9	3.5	bifurcation	Yes	No
10	3.5	bifurcation	Yes	No

Device to Vessel Ratio: $P = 0.66$.

Fusiform versus Saccular Configuration: $P = 0.9$.

Most were bifurcation aneurysms (six), with the remainder as sidewall (two), or fusiform (two) lesions. Vessel diameters ranged from 2 to 4 mm with device to vessel ratio ranging from 2.2-1.0. Eight patients were treated with a single device, one patient was treated with three stents and one patient treated with two devices.

3.3. Follow up

At six-months follow up, four lesions were completely obliterated with no residual aneurysm filling. Of the remainder, five patients demonstrated significantly decreased filling, with the remaining one having persistent filling. The sole residual lesion was a giant fusiform aneurysm further described in case three. Associated daughter vessel stenosis at follow-up was noted in two patients and in-stent stenosis in one patient, all of which were clinically silent. There was no statistically significant correlation between aneurysmal cure and device to vessel ratio ($p = 0.34$) or type of aneurysm (fusiform versus saccular $p = 0.9$), Table 1 No complications were observed at the time of treatment, and no clinical complications were observed at time of treatment or six-month follow up.

3.4. Case Examples

3.4.1. Case One

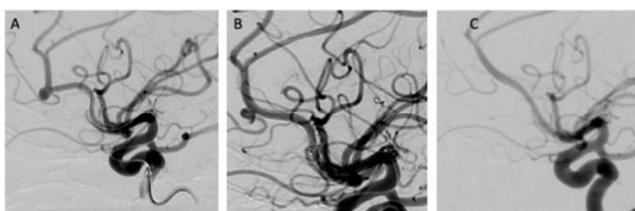


Figure 1. A) Pre-intervention lateral projection digital subtraction angiography demonstrating right pericallosal artery aneurysm with wide neck. B) Immediate post-placement angiogram demonstrating early decreased lesion filling. C) 6-month follow-up angiography demonstrating complete aneurysm resolution.

A 52-year-old female was found to have an incidental 4.0mm x 2mm irregular right pericallosal artery aneurysm with the callosal marginal artery arising from the neck of the lesion. A single 3.5 mm x 22 mm LVIS Blue was placed across the neck of the aneurysm with stasis immediately noted within the dome on repeat angiography. Follow-up angiogram at 6 months demonstrated complete occlusion of the pericallosal aneurysm, with mild to moderate stenosis of the right pericallosal artery (Figure 1).

3.4.2. Case Two

A 47-year-old female presented with an incidental bilobed aneurysm arising at the right middle cerebral artery bifurcation, measuring 11 mm x 9.3 mm and with the anterior temporal artery arising from the neck of the lesion. Surgical clipping was initially attempted; only partial clipping was achieved. Two months postoperatively the patient underwent placement of a single LVIS Blue. Follow-up angiography at six months demonstrated complete occlusion of the lesion (Figure 2) with mild diminution of the ipsilateral covered A1.



Figure 2. A) Pre-intervention magnified oblique digital subtraction angiography of right M2 middle cerebral artery aneurysm, post attempted clipping. B) Unsubtracted imaging demonstrating placement of device. C) 6-month follow-up demonstrating complete occlusion of the lesion. Mild-moderate stenosis of the associated right A1 is noted.

3.4.3. Case Three

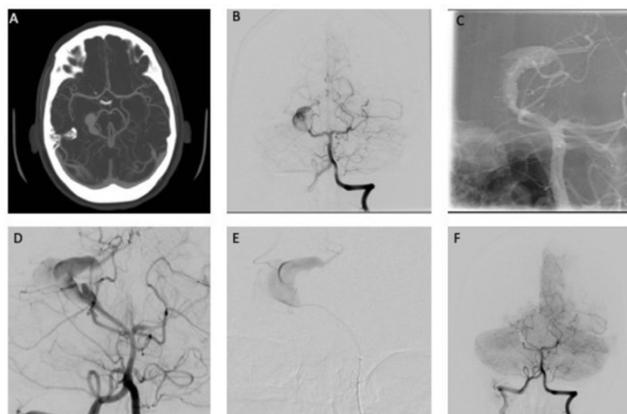


Figure 3. A) CTA with MIP reconstructions demonstrating fusiform right posterior cerebral artery P2/3 aneurysm. B) Angiography demonstrating the right PCA aneurysm. C) Post Embolization demonstrating the three telescoping LVIS devices spanning the fusiform aneurysms. D) Six-month follow-up angiography demonstrating occlusion of the stent construct. E) Aneurysm angiography demonstrating multiple perforators arising from the dome of the aneurysm. F) Post coil sacrifice of the P1.

A 19-year-old female presented with left hemi-body numbness and was found to have a left thalamic infarct with a partially thrombosed fusiform 20 mm x 14.5 mm left P2 aneurysm (Figure 3a, 3b). Three overlapping LVIS device

were placed to reconstruct the vessel lumen (Figure 3c). On follow-up angiography the construct was noted to be occluded with persistent flow into the aneurysm dome from the center of the construct (Figure 3d). Microangiography demonstrated thalamic perforators filling from the dome of the aneurysm so a proximal vessel sacrifice was performed (Figure 3e, 3f). The patient tolerated the occlusion with noted MCA collateralization and no ischemic complications.

4. Discussion

Over time, endovascular techniques and technology have expanded to make previously untreatable or difficult to treat lesions treatable. Flow diversion represents the latest advancement within the endovascular tool kit. These devices were initially brought to market to specifically treat large, wide-necked aneurysms of the proximal internal carotid artery circulation [1, 2, 18, 19]. As with all new medical devices, its release led to a variety of applications outside of the initial indications, including for variable pathology (blister aneurysms, dissecting aneurysms) and in variable locations (the posterior circulation and distal anterior circulation).

For alternate vascular locations, recent studies demonstrate the ability to treat aneurysms of the anterior circulation beyond the communicating segment of the internal carotid artery with flow diversion. Primiani *et al* in a large cohort study demonstrated good occlusion rates at of, ~95% with increased complications noted in the distal and posterior circulation. [9, 20] Although initial studies demonstrated an unfavorable risk profile for “flow diverters” in the posterior circulation, a paucity of other readily available treatments has led to continued study of these devices as a primary means of treatment. Unfortunately, despite advances in techniques and second generation devices, the complication rates remain ~ 10% in several recent retrospective cohorts and registry based studies. [4, 5, 8, 21]

Several reasons have been postulated as to the reason for the higher rates of complication in alternate locations when compared with treatment of aneurysms of the proximal anterior circulation. Technical factors revolve around the larger catheters, the support necessary to achieve distal access, and the force needed to deploy “flow diverters,” while anatomic considerations center on the eloquence of perforator vessels without readily available collateral blood supply. These considerations in tandem indicate the >30% coverage of these devices and the numerous devices often used in these earlier studies may account for a component of observed complications. Our study, while limited in power, demonstrates the feasibility and application of the LVIS device as a primary “flow diverter” within this niche.

Ex vivo studies have evaluated the flow diverting properties of the LVIS Blue device [22, 23]. Other groups have demonstrated the LVIS Blue as a primary means of treatment when used with other endo-luminal devices to achieve flow diversion effect [24]. Further, our prior investigations and other case report studies demonstrated an initial indication that

the device could be used as a “flow diverter” [24]. The high rates of aneurysm occlusion were beyond what would be expected based on prior stent coil aneurysm obliteration rates, despite a lower than normal coil packing density [13]. These initial studies combined with our current findings all suggest that the LVIS Blue stent construct has flow diverting properties. The use of the LVIS device in more distal circulations is preferred in our practice because of the lower profile of the delivery system (0.021 catheters), the visibility of the device and the ease and predictability of deployment relative to existing “flow diverters” on the market. These advantages of the LVIS Blue offer substantial benefits for trackability, need for proximal support, deployment challenges, use in ruptured aneurysm cases and case duration.

Although our cohort is limited in numbers it does demonstrate a significant challenge with the LVIS Blue device in the treatment of large fusiform lesions. Unfortunately, this corroborates the experience of most “flow diverters” in the literature. The dysplastic nature of these vessels and associated perforators as demonstrated in case three make these lesions notoriously difficult to treat. Flow diversion, though not shown to be the ideal option, is often the only endovascular option for the treatment of these lesions.

Despite robust results in approximately half of treated aneurysms, five demonstrated significantly decreased but persistent filling on follow-up. While the results are less robust as those observed with PEDs in the distal and posterior circulation several factors may explain this difference. The first being the short interval follow-up; most flow diversion studies now use the one year time point as an indicator of treatment success [25]. Longer term occlusion data is pending for our treated patients. Secondly the decreased nominal metal coverage of the device (28%), while potentially beneficial in terms of perforator coverage risk, may necessitate a longer period of time to achieve aneurysm cure. This must be reconciled with the consideration that device-vessel mismatch, as noted in our cohort, changes the metal coverage. The relationship of vessel diameter and device size remains a pertinent but otherwise poorly defined factor in the use of flow diversion. Several *in vitro* studies have demonstrated increased metal coverage as expected with a greater device to vessel diameter ratio [26-28]. Thus, a greater than nominal 28% coverage of the LVIS may explain the “flow diverter” properties observed in our cohort. Although not statistically significant in our small cohort, further focused studies on device vessel size discrepancy may explain some of the variable results observed in our cohort and other studies. [9] Additionally, woven stents are able to be “packed” to allow for additional coverage at the lesion neck, yet presently there is no way to objectively measure this. Consideration of these noted effects in the distal circulation and *in vitro* study are needed as we improve our treatment of distal and posterior circulation lesions.

Our study is subject to the typical limitations of a single-center, retrospective study with limited patient numbers. Treatment was at the sole discretion of the operating provider and thus an inherent selection bias of aneurysms suitable for

flow diversion or not suitable for alternative treatments is present. However, we preset a treatment approach to distal and posterior circulation lesions that often represent a challenge to manage. Further study of the devices' wider application as a "flow diverter" with long term follow up is warranted.

5. Conclusion

We demonstrate the novel use of the LVIS Blue device as a sole treatment through flow diversion. Our study demonstrates an acceptable and encouraging in-vivo safety profile and sufficient aneurysmal coverage to function as a flow diverting embolization device in the distal anterior and posterior circulations.

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