Article

When flow diverters fail: short review and a case illustration of a device failure

Marco Zenteno[1], Angel Lee[1], Jennifer Lorena Herrera Bejarano[2], Guru Dutta Satyarthee[3], Hernando Raphael Alvis-Miranda[2],Luis Rafael Moscote-Salazar[2]

[1]MEXICO, [2]COLOMBIA, [3]INDIA

DE GRUYTER OPEN

DOI: 10.1515/romneu-2016-0075

DOI: 10.1515/romneu-2016-0075

When flow diverters fail: short review and a case illustration of a device failure

Marco Zenteno[1], Angel Lee[2], Jennifer Lorena Herrera Bejarano[3], Guru Dutta Satyarthee[4], Hernando Raphael Alvis-Miranda[5], Luis Rafael Moscote-Salazar[6]

[1]"Manuel Velasco Suarez" National Institute of Neurology and Neurosurgery, Ciudad de Mexico, MEXICO
[2]Hospital Angeles Inn Universidad, Ciudad de Mexico, MEXICO
[3]Physician, Universidad del Rosario, COLOMBIA
[4]Associate Professor of Neurosurgery, All India Institute of Medical Sciences, New Delhi, INDIA
[5]Resident of Neurosurgery, Universidad de Cartagena, Cartagena de Indias, COLOMBIA
[6]Red Latino, Latin American Trauma & Intensive Neuro-Care Organization, Bogota, COLOMBIA

Abstract: The ultimate aims of treatment of the intracranial aneurysms are reconstruction the vessel wall and correcting the hemodynamic disturbance. A flow diverter (FD) is a stent placed inside lumen of the parent artery with aim to blood flow reduction into the aneurysms sac to the extent of almost stagnation leading to gradual onset of progressive thrombosis and neointimal lining of arterial wall remodeling to maintain blood outflow into perforators the side and branches. Flow diverter is considered as an effective treatment for fusiform, wide-necked, large and giant intracranial unruptured aneurysms. However, FD implantation may also be associated with growth and rupture of residual aneurysms. The most frequent complication of endovascular aneurysms management is thromboembolic events and less common are intra and postoperative hemorrhagic aneurysmal rupture. Authors report a case where a lack of operation of the device as illustration is presented to demonstrate the shortcomings of this new type of devices.

Key words: Flow diverter device, aneurysms, neuro-intervention

Introduction

The treatment of intracranial aneurysms (IA) is based on principle of isolating aneurysm from parent vessels, occluding blood flow into the aneurysm and to restore the physiological flow. The aneurysm treatment can be accomplished by surgical clipping of aneurysm at neck allowing definitive and complete aneurysm isolation

but carries a high risk of complications such as cerebral edema, arterial vasospasm, and infarction. A large variety of new devices for the treatment of IA are popping up in recent years with the aim to improve the prognosis of patients , however, the understanding of local hemodynamics is not still incomplete. Flow diverter devices (FD) are device, which is similar to the stent, designed with aim to achieve normal vessel reconstruction, and causing blood flow diversion along the anatomical course and sparing out of the flow vector of the neck and dome of the aneurysm. Recent publication show successful use of flow in the management of intracranial aneurysm, but these may fail also. [1–4] Hemodynamic factors are considered to play the biggest factor in the progression and rupture of IA. Recently several cases of FD failure are reported. [1, 2] authors reports an additional case of FD device and hence these devices should be considered for experimental use.

According to the proposed goal in the treatment of intracranial aneurysms, FD is designed in a way to ensure complete management of IA and preventing possible associated post-treatment complication [5] i.e. bleeding, reconstruction of the vessel wall and correction of the hemodynamic flow abnormality [1]. Flow Diverters represents a new generation of stents as a superior new alternative treatment for IA. [4, 10, 11, 12- 16].

Flow diverters are a stent, placed inside the lumen of the main artery to reduce blood flow to the aneurysm causing stasis and gradually progressive thrombosis and subsequent remodeling of the inner layers of the blood vessel wall [4, 11, 13, 15]; keeping and maintaining normal blood flow [1] into the branches of the main artery.

The ability of a stent to accomplish these goals is dependent on the amount of metal on its surface, the rigidity of FD, and bioactivity of the stent material [15].

Additionally, the placement of the Flow diverters could change vessel anatomy, aneurysm and finally flow to brain regions [1, 10].

Hemodynamic studies suggest stent with a porosity above 50-70 % , can cause significant reduction of the flow rate to the aneurysm sac [1, 9, 10, 12, 13, 14], leading to progressive formation of thrombus and this finally causing total occlusion [3, 4, 10, 13, 14, 16]. However, clinical results of Flow diverters can be varied [4] and also dependent on morphology of aneurysm, size of neck and presence of branching vessel originating from fundus. In addition to the Flow diverters, other treatment options of IA include coil embolization and surgical clipping [3]. The middle cerebral artery aneurysms were evaluated in the study of International cohort subarachnoid aneurysms (ISAT) observed required two complementary procedures including surgical approaches and endovascular for the complete occlusion of the aneurysm [6, 15]. The surgical aneurysm clipping of has been considered for the treatment of middle cerebral artery aneurysms after endovascular therapy as presence of branches growing from where the aneurysm arises or the same within are always considered as risk factors [6].

Bracard et al. analyzed 140 patients with middle cerebral artery aneurysms, 73 had unruptured aneurysms. All cases received as

embolization coil treatment without any other adjuvant technique [12]. Thromboembolic complications were noted in 8.5%, a high incidence of these complications was evident in ruptured cases 13.7% versus 3.8% unruptured aneurysms [6, 9]. However, most frequent criticisms associated with coil Embolization therapy are high rate of aneurysm recurrence after treatment, incomplete occlusion and the presence of remnants of the aneurysm [6].

Description of Flow Diverters:

The pipeline embolization device (PED) is a mesh made tube like, composed of platinum (25%) and rest 75% of the alloy of cobalt and nickels (Fig. 1) [1, 11]. It can provides a coverage of 30-35% of the vessel in question and the common diameter of pore is 0.02 to 0.5 mm2 [1, 14]. The coverage area provided by the PED is about three times of intracranial stent [1, 11]. Once the device is positioned through the segment of the aneurysm is released, beginning to expand and rotate for clockwise [1].

Flow Diverters with a low degree of porosity but a high pore density can achieving a further reduction of flow within the aneurysm sac [3, 4, 5, 10, 11]. The blood flow into the aneurysm is influenced by the geometry, the surrounding vasculature, the size and position of the aneurysm [4, 9, and 13]. The aneurysm diameter also plays a very important role in predicting a possible rupture of intracranial aneurysm [4, 9, and 13]. The theoretical advantage of this technique is based on reconstruction of the main vessel, thrombosis of aneurysm sac of any morphology regardless of the aneurysm neck diameter [6]. These are important considerations which play a role in making a proper decision during treatment and influencing its possible outcomes [4].

Bleeding complications of Flow Diverters:

Bleeding complications with the use of PED device are estimated to be 1.75%, with of 0.75% morbidity and approximately 1%mortality [1, 8]. Among the most frequent complications include ipsilateral parenchymal hemorrhage and subarachnoid hemorrhage [1]. Complications usually occur between 2-135 days after implantation of the device [1].

The inflow of blood in the residual aneurysm during post-implantation is considered a risk factor [1]. Furthermore, leukocytes contained in the process of thrombus formation, activity of lytic enzymes such as elastase with increased activity and presence in the thrombi of red blood cells in white cell; which leave an organized formation of these thrombi [15] which could explain the subsequent breaking of intracranial aneurysms [1]. Wan et al. reported three patients treated with Flow Diverters which showed massive stroke after device implantation and bleeding during the procedure [2].

Thromboembolic complications:

Among the most frequent risks of endovascular treatment the hemorrhagic aneurysm rupture is among them, intraoperative and postoperative level [7]. Thromboembolic complications are much more common [7]. The frequency of thromboembolic complications may vary, it was 7% in unruptured aneurysms cases in the

ATHENA study by and in 12.5% of cases showed thromboembolic complications e CLARITY study [7]. Morbidity and mortality occurred in 3.8% of cases [7]. The stents use leads to increase in the perioperative stroke risk and usually occurs within the first 48 postoperative hours in 10% of cases [7]. The risk factors for thromboembolic events are size and length of aneurysms [7]. The increased frequency of thromboembolic events may also be associated with the development of subarachnoid hemorrhage [7]. The use intra and post-operative anticoagulants and antiplatelet have been proposed to reduce the frequency and severity of thromboembolic events [7, 9].

Use of heparin:

Heparin is recommended during interventions due to intravascular use of multiple tools and prolonged duration of procedure lasting up to many hours [7] prolonging the rest period the patient during surgery. Heparin should be initiated with a bolus of 3000-5000 IU followed by a dose of 20-40 IU / kg / h continuously monitored blood thinners to keep clotting times between 200 and 300 seconds [7]. This is used to manage irrigation thromboembolic and hemorrhagic of Flow diverters. World and Interventional Neuroradiology Federation and Therapeutics (WFITN) bolus administration recommends use of 500-1000 IU / h continuously, with monitoring of clotting times around the 200s [7]. It is not possible to determine the concentrations of heparin in the blood during surgery. Usually it carried out prior monitoring of clotting times in order to see the effectiveness of this drug before shifting the patient to surgery [7]. Doses of 70-80 U / kg have been proposed in protocols using heparin in cardiac care obtaining an effective anticoagulation [7]. After administration of boluses of 70 U / kg continues with an adjustment in the dose of 18U / kg / h and the levels of clotting times [7].

The WFITN do not recommend the use of postoperative anticoagulation [7]. No clutch, published clinical results have not been convincing, finally from a biological perspective seems more relevant the use of antiplatelet agents [7]. Furthermore it should be noted patients usually remain long period for resting on the bed during recovery time favoring venous stasis and possible thrombotic event; Ray et al. Justified the use of low molecular weight heparins in the post-operative prophylactic doses in [7].

Antiplatelets:

Treating an aneurysm with the use of a foreign body within a vascular lumen, having of high velocity blood flow and the possibility of being associated with injuries in the vessel wall. [7] These leads to platelet aggregation thus justifying the use of antiplatelet agents to prevent and treat intra and postoperatively thromboembolic complications [7, 8].

A study in which, protocol based use of antiplatelet are reviewed in three stages: treatment is not only in the post-operative and post-operative Yamada et al. [7] reported thromboembolic complications rates of 16%, 2.3% and 1.9% respectively [7]. They also report a reduction in the rate of angiographically visible blood clots in patients who received antiplatelet pre-procedure compared with those who did not receive [7].

The commonly used antiplatelets are acetylsalicylic acid, clopidogrel, prasugrel, among others [7].

Schemes:

Unruptured aneurysms: Treatment should be simply coil embolization or remodeling ball when needed [7]. The use of anticoagulants and antiplatelet agents increases the risk of bleeding during the procedure [7]. The use of intraoperative heparin is recommended after surgery infusions of heparin should be stopped [7]. Simple antiplatelet therapy: 75 mg of aspirin only for long-necked aneurysms in accordance with the recommendations of the WFITN [7]. Should be given a loading dose of Clopidogrel 600 mg two hours before surgery and inject 250 mg of aspirin immediately after the other possibility is to inject antagonists of the glycoprotein IIb / IIIa after the aneurysm has assured [7] .

Coil embolization and stent placement: The patient should be prepared with 75 mg / day of aspirin and 75 mg / day Clopidogrel for 4-7 days prior to surgery [7], a loading dose of 600 mg of Clopidogrel could be administered two hours before stent placement [7].

Management of thromboembolic complications:

Intraoperative management of thromboembolic events demand a constant verification of clinical and biological parameters of each patient e.g. blood pressure and the degree of anticoagulation requirement [7]. Clotting times should be kept greater than 250 seconds, if below, additional bolus administration of 2000 IU [7] is recommended. To reduce the risk of embolisms one flow diverter telescoping functioning as a bypass this provides an "incarceration "clot is used. [13] The device expands distal to proximal opening a new road and catching the clot that is occluding against the vessel wall; thus can prevent distal embolization [13]. When clots are accessible in the proximal artery thrombectomy could be considered as part of the approach [7].

Case Illustration

A 56-years-old Female patient reported to the endovascular therapy service at the "Manuel Velasco Suarez" Neurology and Neurosurgery National Institute, for presenting headache with red flag symptoms. As precedents, various months earlier she was treated of giant carotid aneurysm with a FD (Pipeline®) in a hospital from USA. (Figure 1) During initial evaluation she had power 4/5 in left upper extremity, while the rest of the motor balance was within normal range. She underwent imaging study including MRI brain, Dynamic cranial CT angiography, showed which evidenced of residual aneurysmal flow and the presence of recent thrombus, associated with significant perilesional edema with mass effect. The patient is advised to undergo repeat MRI and cerebral magnetic resonance angiography after two weeks showing the findings (Figure 2). The management was conservative.

Review

Subarachnoid hemorrhage is a devastating disease, whose treatment depends at time interval following ictus, needs advice of

various specialties i.e. neurosurgery, neurology, intensive care, and neuroradiology and to various forms of treatment for complication are medical or endovascular vasospasm treatment, surgical clipping / embolization). The concept of Flow Diverters for aneurysm occlusion is not new and almost since past ten years, it was studied in dogs to assess the effects of flow dynamics in experimental aneurysms of the carotid arteries. (15, 16, 17, 18).

Filling the aneurysm and blocking or deflecting the inflow may promote thrombosis, preserving the parent vessel. Turowski et al [5] reported a – 69- year- old patient, who required the placement of a FD SILK-Stent, for a large par ophthalmic aneurysm, she developed fatal subarachnoid hemorrhage. Author proposes that a reduction in the strength of the aneurysm walls can act in conjunction with the residual flow as a weak point for mechanical rupture. This case demonstrates that FD is a technology to be tested in future, for its effectiveness, despite series showing good results, although such complications are also reported in the literature with unfavorable outcomes.

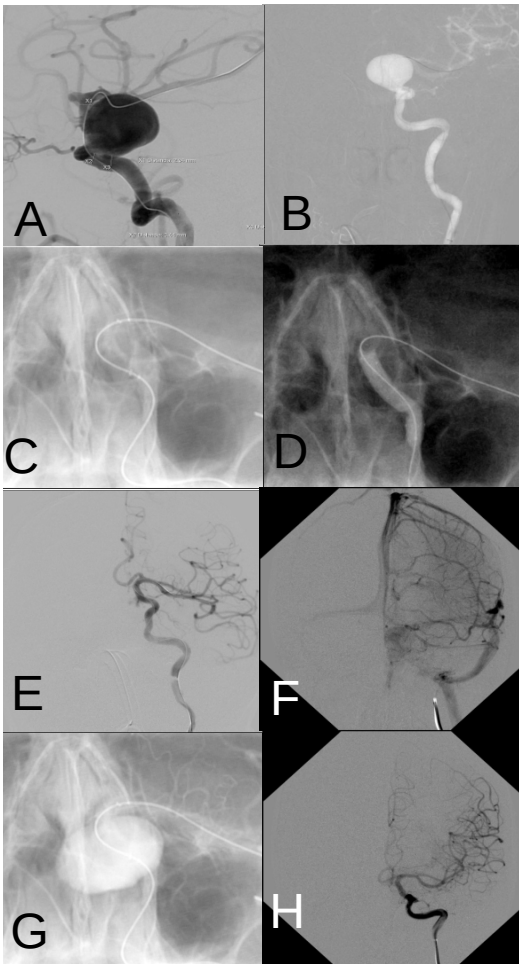

Figure 1 - Digital subtraction angiography showing the micro-guide navigability through the internal carotid artery (ICA); also showing the stent measurements (A and B). Stent unfolding, through the eluting balloon insufflations (C and D). Total exclusion of the aneurysm (E). No alteration on the venous phase (F). Intracranial vasculature is intact (H)

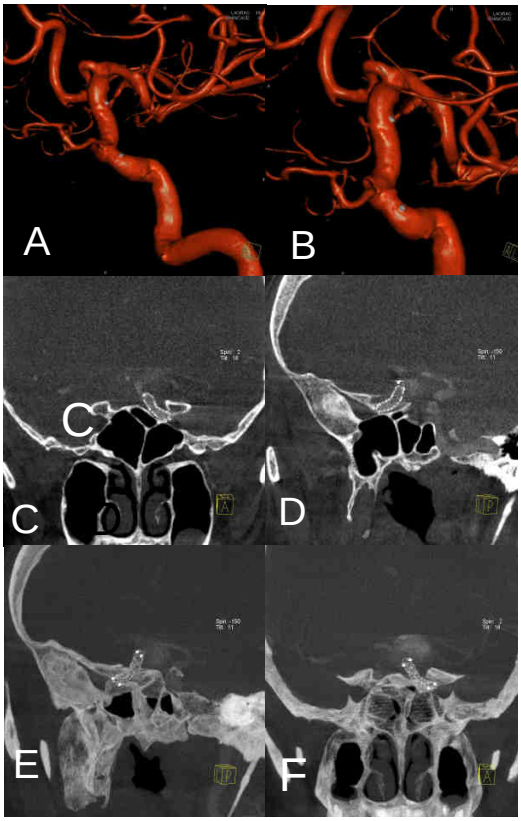

Figure 2 - Three-dimensional reconstruction, in which is appreciated complete absence of the aneurysm, with appropriate visualization of the proximal and distal stent markers (A and B). – Dynamic CT angiography coronal and sagittal sections, where appropriate stent patency and showing minimal filling of the aneurysm (C, D, E and F)

Conclusions

Endovascular reconstruction using Flow Diverters although represent an effective treatment option for fusiform, long, giant, wide-necked aneurysms, but associated with 5-10% of morbidity and mortality [1]. Flow Diverters stents assisted therapy of aneurysm proposes a new method of endovascular reconstruction of complex aneurysms, using a fine mesh placed outside the aneurysm sac reducing the flow within it subsequently cause thrombosis [16]. The results of the next studies could answer the question of how to prevent complications, if Flow Diverters could replace coil embolization or when it would certainly indicated the use of Flow Diverters [1]. Flow Dividers could reduce the risk of embolization associated with recanalization following endovascular treatment of aneurysms [20, 21, 22]. Treatment with a single stent can alter hemodynamic of aneurysm creating the right conditions making more favorable flow thrombus formation [14, 15]. The most important goal should be complete elimination of the risk of post-procedural aneurysmal rupture, can be achieved with use of a single technique that does not produce alteration of the hemodynamic flow [20, 21, 22]. Recent reports of multiple stent implantations through aneurysm neck could improve the effectiveness of Flow Diverters against reduction of blood flow to the aneurysm sac [20, 21, 22].

Correspondence
Dr. Luis Rafael Moscote-Salazar
E-mail: mineurocirujano@aol.com

References

1. Darsaut TE, Rayner-Hartley E, Makoyeva A, Salazkin I, Berthelet F, Raymond J. Aneurysm rupture after endovascular flow diversion: the possible role of persistent flows through the transition zone associated with device deformation. Interv Neuroradiol. 2013; 19(2):180-5.

2. Cebral JR, Mut F, Raschi M, Scrivano E, Ceratto R, Lylyk P, et al. Aneurysm rupture following treatment with flow-diverting stents: computational hemodynamics

analysis of treatment. AJNR Am J Neuroradiol 2011; 32:27–33.
3. Clarençon F, Di Maria F, Biondi A, Chiras J, Sourour N-A. Distant and delayed (>7 days) hemorrhage after treatment by flow-diverter stents in intracranial aneurysms: a rare but potentially serious complication. AJNR Am J Neuroradiol 2013; 34:E81–2.
4. Raymond J, Salazkin I, Georganos S, Guilbert F, Desfaits A-C, Gevry G, et al. Endovascular treatment of experimental wide neck aneurysms: comparison of results using coils or cyanoacrylate with the assistance of an aneurysm neck bridge device. AJNR Am J Neuroradiol 2002; 23:1710–6.
5. Turowski B, Macht S, Kulcsár Z, Hänggi D, Stummer W. Early fatal hemorrhage after endovascular cerebral aneurysm treatment with a flow diverter (SILK-Stent): do we need to rethink our concepts? Neuroradiology 2011; 53:37–41.
6. Wong G, Kwan M, Ng R, Yu S, et al. Flow diverters for treatment of intracranial aneurysms: Current status and ongoing clinical trials. Journal of Clinical Neuroscience 2011; 18: 737-740.
7. Wong G. Why current evidence is against flow diverters for treatment of carotid blowout syndrome. European Journal of Radiology 2013; 82: 191.
8. Karacozoff A, Shellock F, Wakhloo A. A next generation, flow diverting implant used to treat brain aneurysms: in vitro evaluation of magnetic field interactions, heating and artifacts at 3-T. Magnetic Resonance Imaging. 2013; 31: 145-149.
9. Wu Yo, Yang Pe, Shen J, Huang Q et. al. A comparison of the hemodynamic effects of flow diverters on wide-necked and narrow-necked cerebral aneurysms. Journal of Clinical Neuroscience. 2012; 19: 1520-124.
10. Wong G, Ponn W.S. Current status of computational fluid dynamics for cerebral aneurysms: The clinician's perspective. Journal of Clinical Neuroscience 2011; 18: 1285-1288.
11. Machi P, Lobotesis K, Vendrell JF, Riquelme C, Eker O, Costalat V, Bonafe A Endovascular therapeutic strategies in ruptured intracranial aneurysms. Eur J Radiol. 2013 Oct; 82(10):1646-52.
12. Bracard S, Barbier C, Derelle AL, Anxionnat R. Endovascular treatment of aneurysms: Pre, intra and post-operative management. Eur J Radiol Eur J Radiol. 2013; 82(10):1633-7.
13. Bendok B, Aoun S. Flow Diversion for Intracranial Aneurysms: Optimally Defining and Envolving a New Tool and Approach. World Neurosurgery 2011; 76 (5): 401-404.
14. Sfyroeras et al. Flow diverting stents for the treatment of arterial aneurysms. Journal of vascular surgery (2012) 840-845.
15. Anzai H et al. Optimization of flow diverters for cerebral aneurysms. Journal of Computational Science 2012; 3:1-7.
16. Duffis Ej, et al. Recent advances in neuroendovascular therapy. Clin Neurol Neurosurg (2013) 1-6.
17. J.E. Cohen et al. The use of flow diverter stents in the management of traumatic vertebral artery dissections. Journal of Clinical Neuroscience 2013; 20: 731-734.
18. J.E. Cohen et al. The use of telescoped flow diverters as an endovascular bypass in the management of symptomatic chronic carotid occlussion. Journal of Clinical Neuroscience 2012; 19: 1026-1028.
19. Chalouhi N, Jabbour P, Tjoumakaris S, Strake RM, Dumont AS, Liu H, Rosenwasser R, El Moursi S, Fernando Gonzalez L. Treatment of large and Giant Intracranial Aneurysms: Cost Comparison of Flow Diversion and Traditional Embolization Strategies, World Neurosurgery (2013) 1-25.
20. Tremmel M et al. Alteration of Intraaneurysmal Hemodinamics for Flow Diversion Using Enterprise and Vision Stents. World Neurosurgery (2010) 1-10.
21. Zhang Y, Chong W, Qian Y. Investigation of intracranial aneurysms hemodynamics following flow diverter stent treatment. Medical Engineering & Physics 35 (2013) 608-615.
22. Mangiafico S, et al. Endovascular strategy for unruptured cerebral aneurysms. Eur J Radiol (2012) 1-8.