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Flow Diversion for Intracranial Aneurysms

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Abstract

Background: An intracranial aneurysm (cerebral aneurysm) is a cerebrovascular disorder characterized by a localized dilation or ballooning of a blood vessel in the brain due to a weakness in the vessel wall. Treatment options include surgical clipping and endovascular coiling; both aimed at preventing further bleeding. The purpose of this research was to assess the results, risks, and effectiveness of endovascular treatment of cerebral aneurysms using flow diverters (FDs).

Methods: The study includes 10 patients suffering from cerebral aneurysms, presented with headaches and had non-ruptured aneurysms. All patients received endovascular treatment (EVT) as the primary modality of treatment of their cerebral aneurysms, in the form of endoluminal flow diversions devices, with or without the adjuvant use of detachable coils. Patients followed by angiography at 3 and 6-month after the procedure.

Results: Early (Short-Term) Angiographic Findings Showed: Successfully sealed off the sac surrounding two patients' aneurysms. Two individuals experienced incomplete occlusion in which the aneurysms were filled. three patients whose treatment only included flow diversion experienced aneurysm filling with contrast stagnation in the aneurysm sac right after the procedure, while three patients whose treatment just included diversion did not have this problem. None of the cases showed neck filling or classified as Class 5 (stable remodeling with flow modification. On follow up only one case complicated with ataxia and incomplete filing.

Conclusions: FD is suitable alternative management modality for cerebral aneurism. It showed a high rate of aneurysmal occlusion, with a low rate of mortality and disabling morbidity. So, FD is a reasonable option in the non-ruptured setting and in the anterior circulation location.

Keywords: Cerebral Aneurism, Flow Diversion, Invasive and Microvascular Surgery

Introduction

In terms of disability-adjusted life-years (DALYs) lost, stroke ranks third globally and is the second greatest cause of mortality, behind only ischemic heart disease. There is a serious variant of hemorrhagic stroke known as spontaneous subarachnoid hemorrhage (SAH). On average, those who are impacted are 55 years old ^[1].

The main lines of medical management of subarachnoid hemorrhage are advanced neurological intensive care support, multidisciplinary clinical expertise and nimodipine, the calcium channel blocker used for the prevention of vasospasm. Hence, it is recommended that such cases are managed in high-volume centers with well-established multidisciplinary teams specialized in the management of such vascular malformations ^[2].

The general population has a 2.3% cerebral aneurysm prevalence, those with one affected first-degree relative have a 4% prevalence, and those with two affected first-degree relatives have an 8% prevalence. Approximately 3% of middle-aged adults have saccular, unruptured intracranial aneurysms (UIAs) ^[2].

The ISUIA study found that there is a 38% case fatality rate in the 30 days following SAH and a 0.7% annual chance of aneurysm rupture ^[3].

According to the underlying pathology, different types of cerebral aneurysms have been described in the literature, each with preferred therapeutic approaches. These types include the classic saccular (berry) aneurysms, segmental ectasia, dissection, intramural hemorrhage, mycotic (microbial or infectious) and others ^[4].

Both microsurgical and endovascular approaches to securing intracranial aneurysms have versatile techniques. Brain aneurysms can be managed endovascularly with a variety of techniques, including stent-assisted coiling, balloon remodeling, Onyx HD 500, and flow diversion. Over time, these techniques have evolved from simple to more complex techniques, of course, with increased technical difficulties, learning curve and possible complications [3].

Multiple studies have shown superiority of endovascular interventions over microsurgical clipping of ruptured aneurysms. Coiling reduced the absolute risk of death by 7.4 percent compared to clipping in the International Subarachnoid Trial (ISAT). Researchers at the Barrow Institute found that 33.7 percent of patients with clips and 21.3 percent of patients with coils had mRS scores greater than 2. Full occlusion of the aneurysm was achieved in 93.3% of patients using the Pipeline Embolization Device in the Intracranial Treatment of Aneurysms (PITA) evaluation [3].

The microcatheter, micro-guidewire, or coil could perforate aneurysms, and thromboembolic events are among the common side effects of endovascular coiling. Blood pressure control, intracranial pressure control, heparin reversal, ongoing and immediate aneurysm occlusion, diversion of cerebrospinal fluid (CSF), typically by installation of an external ventricular drain, and rapid leak recognition are all necessary procedures for perforations. Immediate thrombus clearance is essential to prevent the thrombus from enlarging after detection; prevention is the best approach to avoid thromboembolic complications [5].

The aim of this work was to evaluate the efficacy, safety and outcome of endovascular management of intracranial aneurysms with flow diverters (FDs).

Patients and Methods

This prospective study was carried out on 10 patients aged > 18 years old, both sexes, with any type of cerebral aneurysm: saccular, large and giant, bifurcation, saccular aneurysms with large necks and low dome-to-neck ratio, large and giant aneurysms, bifurcation aneurysms, fusiform or dissecting aneurysms. After receiving approval from the Ethical Committee Tanta University Hospitals, Tanta, Egypt, the study was conducted from June 2022 to May 2023. Patients were asked to sign an informed consent form. Exclusion criteria were patients with impaired renal and hepatic functions, coagulation disorders and pregnancy.

Every patient underwent a thorough medical history review, physical examination, and laboratory testing, including a full blood count (CBC), tests for liver and kidney function, prothrombin time and activity, viral markers for hepatitis B, hepatitis C, and HIV/AIDS, and a pregnancy test for adult females who are in the reproductive age. together with radiological studies, such as CT angiography (CTA), conventional angiography (DSA), and multi-slice head computed tomography (CT) scans with thin slices or brain magnetic resonance imaging (MRI).

DSA was done for all patients, either as a part of radiological investigations or at the beginning of endovascular intervention. It was sensitive in the visualization of the aneurysm, its geometry, neck localization and different measurements required for choosing suitable flow diverter and coils sizes.

For the intervention, all patients were given dual antiplatelet medication. One medicine, ticagrelor 80 mg twice daily, was started two days before the surgery, and the other, aspirin 100 mg once daily, was started five days before the procedure. Both drugs were continued post-operatively for 6 months, with only one drug continued for life.

Endovascular Techniques

A detailed explanation of the technique expected results and complications was relayed to the patient. Once the patient agreed, the patient signed an informed consent. All patients were operated upon in the neuroangiography suite. General anesthesia was administered to all. In order to flush the guiding catheter and microcatheter, a mixture of 2500 IU heparin and 5 ml of nimotop (2 mg) in 500 ml of 0.9% normal saline was prepared. The medication is known as Nimotop®. Two to three times the normal value was maintained for activated clotting time. All patients were treated using the conventional transfemoral technique. The optimum projection for defining the aneurysm, its neck, and the parent artery was defined through the use of high-resolution monoplane fluoroscopy, road-mapping, and initial cerebral angiography, which included 3D rotational angiography. In conventional angiography, the anteroposterior (AP) views correspond to the coronal sections of the MRI while the lateral views correspond to the sagittal sections. The materials used in the diagnostic angiography included the introducer needle, 5-F introducer sheath (Radifocus® introducer, Terumo or Prelude introducer, Merit Medical), 5-F multipurpose diagnostic catheter (Bern, Stryker) and the Hydrophilic Guide Wire (ZIPwire™, Stryker). The 5-F sheath was replaced with an 8-F sheath and an 8-F guiding catheter (Guider Softip™ XF, Stryker) during therapeutic angiography. Specifically, the guiding catheter is positioned at the level of the C2 cervical vertebra (axis) within the cervical section of the internal carotid artery. We used the Sofia intermediate catheter from MicroVention in every case. In order to insert the pipeline embolization device (PED), a microcatheter manufactured by Marksman and distributed by Medtronic was utilized. It was guided along a Synchro microwire (Stryker) that was only 0.014 diameter. Along with flow diversion, coils were utilized in four patients, accounting for 40% of the total. A smaller microcatheter (the Excelsior SL-10, manufactured by Stryker) was used to deliver them along the same microwire. Jailing technique was used in one case with A1 aneurysm. In this technique, the coiling microcatheter is placed in the aneurysm sac, followed by flow diverter deployment, and finally coiling is done afterwards. In all other cases with adjuvant coiling, coiling was done as a first step with the smaller microcatheter, which was then withdrawn, and diversion is accomplished with its microcatheter.

Statistical analysis

The SPSS v26 software, developed by IBM and located in Chicago, IL, USA, was used for the statistical analysis. Both the mean and the standard deviation (SD) were used to display the quantitative values. The percentage and frequency counts of the qualitative factors were given.

Results

Among the studied patients 4 were males and 6 were females with their age ranged from 36 – 51 (mean and SD = 43.5 ± 4.33).

All (100%) patients in this study had saccular aneurysms located in the anterior cerebral circulation. Only one patient had bilateral (mirror) supra-clinoid aneurysms, with only one of them included in the current study as the other aneurysm was treated after the end of the study.

Out of the total number of patients, six had aneurysms in the supra-clinoid internal carotid artery (ICA), two had carotid bifurcation aneurysms, one had a recurrent aneurysm in the first segment (M1) of the right middle cerebral artery (MCA), and one (10%) had an aneurysm in the first segment (A1) of the left anterior cerebral artery (ACA).

Regarding laboratory investigations, all were within normal for all patients, including specifically kidney function tests and prothrombin time and activity. No female patient in our study was pregnant.

Of the 10 patients who underwent endovascular intervention for securing cerebral aneurysms, angiographic outcome at

final control angiogram was evaluated as: Class 1: Complete occlusion of aneurysm sac in 2 (20%) patients. In both patients, compact coiling was intended with flow diversion. These were the two individuals that had aneurysms type M1 and A1. No patients in Class 2 exhibited neck filling. Two patients (20%) in Class 3 had incomplete occlusion when the aneurysm was filled. In both patients, coiling was used as an adjunct to flow diverter. Carotid bifurcation aneurysms were found in these two patients. Class 4A: in three patients (30%) receiving flow diversion alone, aneurysm filling with contrast stagnation in the aneurysm sac immediately following diversion. Class 4B: in three patients (30%) treated with flow diversion alone, aneurysm filling without contrast stagnation in the aneurysm sac immediately following diversion came to light. Stable remodeling with flow modification is the fifth category, and none of the instances fell into that. The area around the neck, which remains the same or shrinks; with two separate control angiographies spaced at least six months apart, and continuing for at least a year at an expanded size. Table 1

Table 1: Immediate angiographic outcome

	Males	Females
Class 1	2(20.0%)	0(0.0%)
Class 2	0(0.0%)	0(0.0%)
Class 3	2(20.0%)	0(0.0%)
Class 4A	0(0.0%)	3(30.0%)
Class 4B	0(0.0%)	3(30.0%)
Class 5	0(0.0%)	0(0.0%)

Data are presented as frequency (%).

Nine (90%) patients had a Glasgow Outcome Scale (GOS) of five, they all had good recovery without neurological deficits. Only one (10%) patient, with non-ruptured supra-clinoid aneurysm, had a GOS of 4 as she had headache and ataxia. Due to the aneurysm's location in the anterior

circulation (ICA) and the absence of a fetal posterior communicating artery (PCommA), a diffusion weighted imaging (DWI) and apparent diffusion coefficient (ADC) map of the brain revealed a distant ischemic stroke in the territory of the right superior cerebellar artery (SCA) and the right posterior cerebral artery (PCA). Figure 1

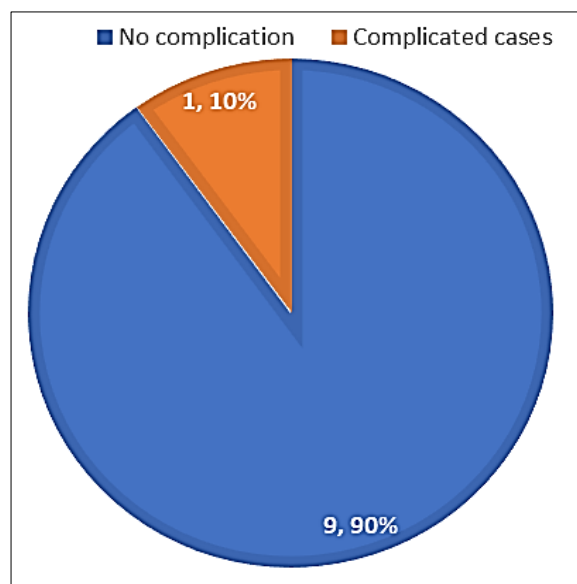


Figure 1: Immediate post operatives' complications of the studied groups

All patients were discharged on the third post-operative day, except for the patient who experienced an ischemic stroke after the procedure. Patients was kept in the hospital for 5

days to ensure that there was no progression of her manifestations. Figure 2

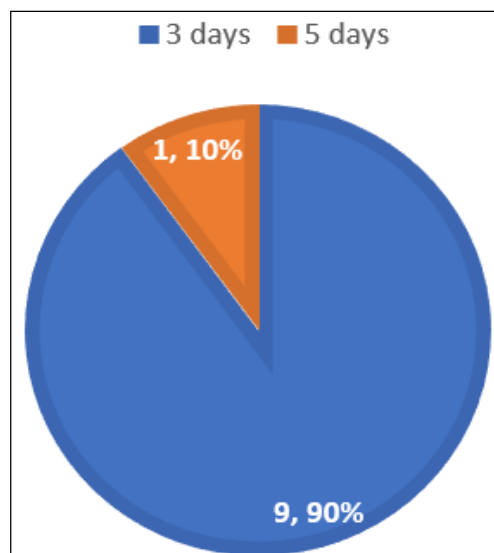


Figure 2: Length of hospital stay of the studied groups

Out of 10 aneurysms treated in 10 patients, 2 showed complete occlusion of the aneurysmal sac immediately after the procedure and did not show for later follow up. These are the aneurysms located in the A1 and M1 segments. Three (30%) patients were followed by digital subtraction angiography (DSA) at 6-month post-procedure and two of them showed angiographic cure with non-opacification of the aneurysm, while only one (10%) showed residual aneurysmal filling of 7 mm in diameter.

Three (30%) patients were followed by DSA at 12-month post-procedure and showed angiographic cure, including the patient with bilateral (mirror) supra-clinoid aneurysms, regarding the aneurysm which was included in the study. Twenty percent of patients with incomplete aneurysmal occlusion were observed using MRI and MRA alone; these patients did not experience ischemic complications, and the remaining two individuals demonstrated non-opacification of the aneurysm in addition to patency of the parent arterial. Figure 3

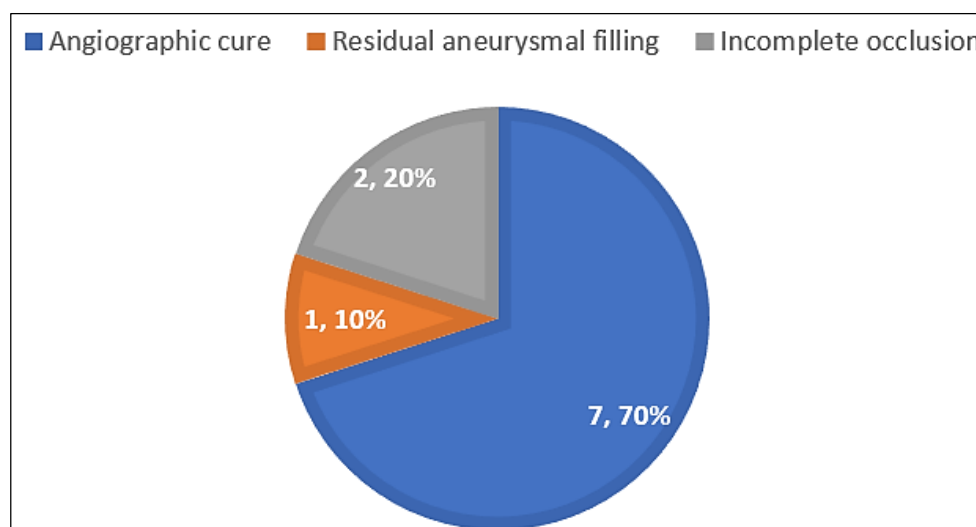


Figure 3: Angiographic follow up of the studied groups

The patient who had post-operative headache and ataxia showed total resolution of her symptoms, but she experienced also visual impairment in the form of reduced visual acuity and restriction of the visual fields. Her follow up DSA showed residual aneurysm filling, but she refused any additional form of treatment. One patient (10%) with carotid bifurcation aneurysm had an ischemic stroke in the area of the ipsilateral middle cerebral artery (MCA) approximately four months after the intervention during the clinical follow-up period, which lasted from three to eighteen months. The patient's left sided hemiparesis came on suddenly. Normal motor power was restored to him after approximately one month.

Case 1

A female patient aged 38 years, presented by severe persistent headaches. MRI of the brain and conventional angiography showed bilateral supra-clinoid ICA aneurysms with their necks distal to the origin of the ophthalmic arteries (Ophism). Maximum diameter of the right sided aneurysm was 12 mm. Flow diversion was done for the right sided aneurysm using 4 mm X 20 mm pipeline embolization device (PED) without coiling. Control digital subtraction angiography (DSA) did not show stasis in the aneurysmal sac. Follow up MRA at 6 months showed no complications with patency of the parent artery (ICA). The other aneurysm was treated after the end of the study. Figure 1

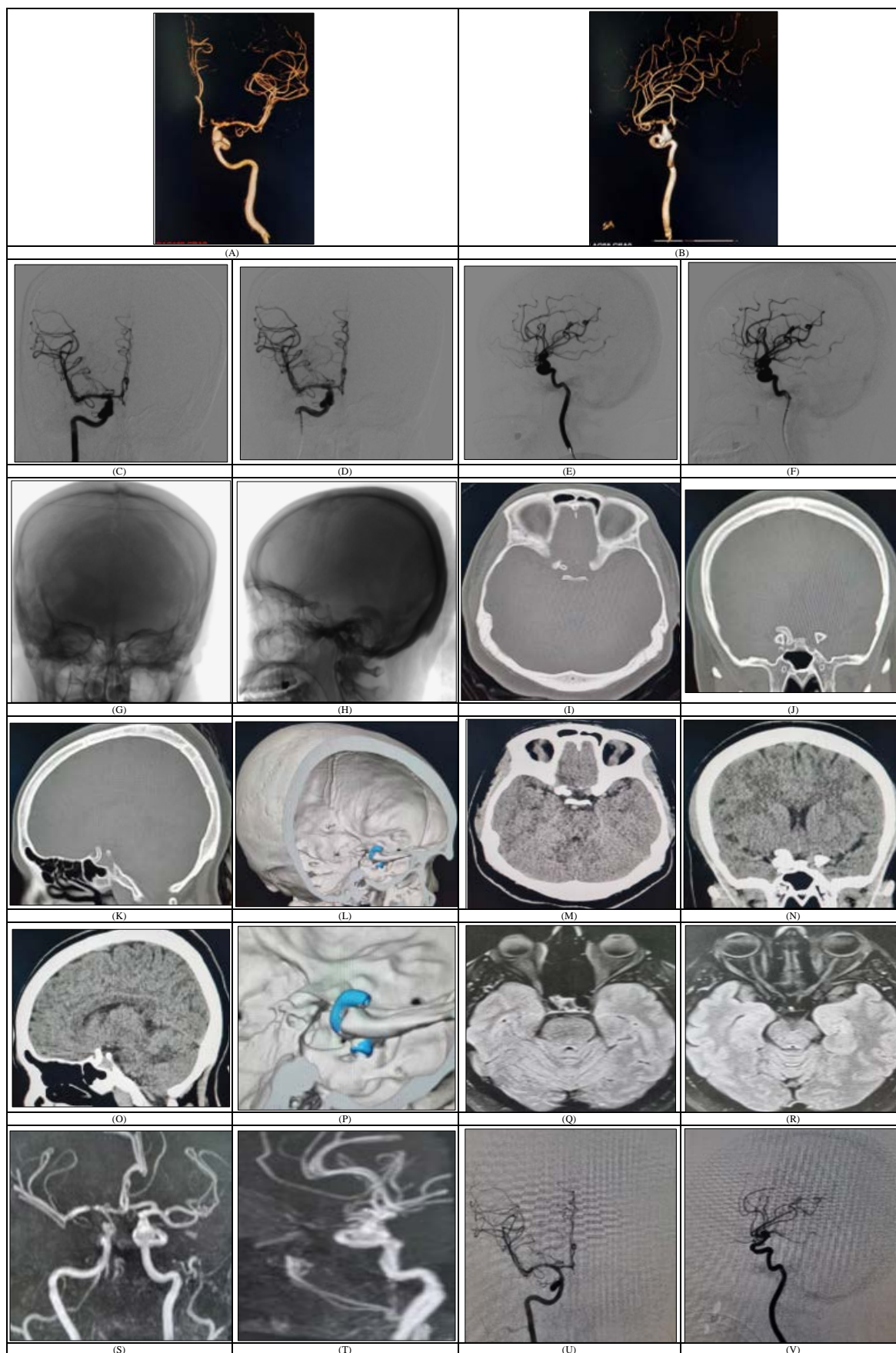


Figure 1: (A, B) 3D reconstruction of the right internal carotid artery (ICA) angiogram in different angles showing the aneurysmal neck and its relation to the ICA, pre-diversion (C) and post-diversion (D) Right ICA angiogram in the AP view. Pre-diversion (E) and post-diversion (F) Right ICA angiogram in the lateral view. Fluoroscopic images (AP (G) and lateral (H) views) showing the flow diverter, which is more evident in the lateral view. Post-operative head CT, bone window (axial (I), coronal (J), sagittal (K) and 3D reconstruction (L)) showing flow diverter in the para-clinoid region. Post-operative head CT, brain window (axial (M), coronal (N) and sagittal (O)) and a close-up view of the 3D reconstruction (P) showing flow diverter in the para-clinoid region and no intracranial hemorrhage. MRI of the brain (axial FLAIR (Q and R)) and cerebral MRA (S and T) at 6 months. Follow up DSA at 12 months, right ICA angiogram (AP (U) and lateral (V) views) showing complete aneurysm occlusion

Discussion

Endovascular techniques for the management of brain aneurysms have taken a large step forward in the last few decades. Progression from simple coiling to assisted techniques and finally to flow diversion has represented an alternative to microsurgical clipping in many centers. Silva et al. [6] observed that lengthy sheaths, guiding and intermediate catheters, and flow diversion with clipping and coiling are more convenient than previous methods for treating paraclinoid aneurysms.

Management of a large subset of aneurysms, including giant and large aneurysms, nonruptured aneurysms, and recurrent aneurysms after simple coiling, is now possible thanks to advances in biplane imaging with rapid subtraction fluoroscopy, new flow diversion devices, and increasing experience [7].

This study included 10 patients harboring 11 cerebral aneurysms. Endovascular treatment was offered as a single session of flow diversion with or without adjuvant coiling. The procedure resulted in complete aneurysm occlusion in 2(20%) patients, incomplete occlusion in another 2(20%) patients and persistent aneurysm filling immediately after the procedure in the remaining 6 (60%) patients, half of these showed stagnation and half did not.

Eight patients, or 80% of the total, had access to longer angiographic follow-up that lasted anywhere from three to twelve months. Of these, two patients, or 20% of the total, demonstrated complete aneurysm occlusion by three months' MRA, two patients, or 20% by six months' DSA, and three patients, or 30%, by twelve months' DSA.

In total, 9 (90%) patients showed total aneurysm occlusion including 2 patients immediately after the procedure and 7 patients followed up. One patient showed an aneurysm filling of 7 mm in diameter by DSA at 12 months of follow up. One aneurysm in the patient with mirror aneurysms was not followed.

Also, other researchers found complete occlusion after follow up in a considerable percentage of their patient where Bender et al. [8] administered catheter angiography to patients six and twelve months after the embolization procedure. Within 5 years, 445 out of 491 (41% of the total) pipeline embolization device (PED) treatments done to treat anterior circulation aneurysms had this follow-up accessible. Most of their patients were women, and the most common type of aneurysm they saw was a saccular one, located in the internal carotid artery (ICA). Complete occlusion was reached in 82% of instances at 14 months of follow-up, suggesting that the rate of occlusion increased over time. At 6, 12, and 24 months, the corresponding rates were 72%, 78%, and 87%. Occlusion was predicted by adjunctive coiling, while aneurysm persistence was indicated by integrated branch vessels, male sex, and increasing aneurysm size. In addition, the number of devices employed, fusiform shape, the origin vessel, and previous treatments were not predictive of blockage.

A lower occlusion rate was reported by Madaelil et al. [9] reported 62.4% (148/237) complete occlusion (class D, O'Kelly-Marotta grading scale). They reported higher occlusion rates with adjunctive coiling and multiple device use.

The small sample size and the relatively small diameter of aneurysms in our series could explain the high occlusion rate. The maximum aneurysm diameter in our series was 22 mm (none of the aneurysms exceeded 25 mm in maximum dimension).

Alternatives to flow diversion exist for the treatment of massive and enormous aneurysms. The effectiveness of parent vessel occlusion (PVO) versus flow diversion in treating these aneurysms was recently tested in a randomized, non-blinded experiment. Although the concept of each procedure is totally different, the results showed comparable angiographic results and complication rates. Most aneurysms in this study were carotid aneurysms [10].

As PVO requires adequate collateral circulation with balloon test occlusion (BTO). So, PVO is considered contraindicated if collateral circulation is inadequate. This assessment requires simultaneous arterial and venous phases on the angiographic runs. On the other hand, flow diversion may not be feasible with increased vascular tortuosity [10].

No patients in our study were treated with PVO or BTO. The use of temporary balloon occlusion has been documented prior to the management of direct carotid cavernous fistula (CCF) by flow diversion, as the deployment of FDs requires sufficient imaging of the parent channel. With the fistula location temporarily closed, the parent vessel can be imaged using a road map [11].

All our cases were managed by the PED flow diverter with or without adjuvant coiling. Adjuvant coiling was used in the cases with M1, A1 and carotid bifurcation aneurysms.

Other more complex techniques have been described in the literature. One of these techniques is the use of multiple "telescoping" diverters, a technique which was described initially with stents and later with FDs [12].

The use of multiple devices has the potential advantage of increasing metal coverage and reducing flow into the aneurysm. On the other hand, the use of multiple devices has the potential risk of perforator occlusion, but this has not been proven [12].

The treatment of aneurysms with PED with or without coils (PEDC) has been compared in a recent systematic review and meta-analysis including 3001 subjects from 9 observational studies, with no randomized trials included. Patients in whom dense coiling was done were excluded from the study.

Clinical Outcome of Pipeline Embolization Device with and without Coil to Treat Intracranial Aneurysm found that PEDC has a better rate of complete occlusion at 6 months, a lower rate of retreatment, and a higher rate of post-operative stroke of both hemorrhagic and ischemic nature. Also, the study found fewer cases of retreatment. Intraprocedural complications were not significantly different [13].

In our study, we did not encounter intra-procedural complications, but we faced 2 post-operative ischemic complications (20%). One occurred in the immediate post-operative period in the territory of the right SCA and the right PCA and the other occurred in the 4th post-operative month in the territory of the ipsilateral MCA.

TE events occurring after FD have been attributed to multiple factors including resistance to antiplatelet therapy especially aspirin. Other factors discussed in the literature include age, aneurysm characteristics and location and procedural events. Middle cerebral artery and vertebrobasilar system occlusions were associated with the highest morbidity. [14].

Lauzier et al. [15] reported 8% rate of ischemic strokes in patient harboring proximal MCA aneurysms treated with flow diversion (2 out of 24 patients). All of these ischemic events occurred with M1 segment aneurysms, while none occurred in the MCA bifurcation aneurysms. The smaller

sample size may explain why our study found a higher incidence of ischemia problems.

Among aneurysms treated with flow diversion, a recent meta-analysis and comprehensive review found that symptomatic infarct occurred at a rate of 13% in the posterior circulation and 5% in the anterior circulation. Additionally, the posterior circulation had a greater incidence of aneurysmal rupture^[16].

No mortality occurred in our study. Also, Lauzier et al.^[15] reported no mortality in proximal MCA aneurysms managed with flow diversion. In a multicenter study of 131 posterior circulation aneurysms, Griessenauer et al.^[17] reported 14 (11.2%) deaths after PED implementation. The mortality rate was highest among patients with dissecting aneurysms. Limitations of our study include the low number of cases which could be attributed to the limited indications of the approach being used mainly in nonruptured aneurysms, the limited resources and the patient selection. Other limitations include that the study is a single center series and that it did not include double arms or randomization.

Recommendations of our study include flow diversion is a reasonable option in the non-ruptured setting and in the anterior circulation location. Its use in the posterior circulation and in the ruptured setting requires further validation. Multicenter studies and large number of cases are required to ensure its validity as a reasonable technique for the occlusion of cerebral aneurysm.

Conclusions

flow diversion showed an alternative management modality to surgery and simple endovascular techniques especially in large and complex aneurysms. It showed a high rate of aneurysmal occlusion, with low rate of mortality and disabling morbidity.

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