Evaluation of Hemodynamic Alterations after Flow Diverter Placement using the AneurysmFlow™ tool

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Abstract

Background. AneurysmFlow (Phillips Healthcare) is the flow measurement tool, utilizing an optical flow-based algorithm from DSA, lacks sufficient published studies. This study aimed to assess the significance of flow velocity changes and the Mean Aneurysm Flow Amplitude (MAFA) ratio in evaluating outcomes following flow-diverting treatments.

Methods. Between June 2021 and October 2022, 41 patients with 42 aneurysms underwent FDS treatment with AneurysmFlow measurement at the Bach Mai Radiology Center.

Results. The tool achieved a 90.5% success rate in 38 out of 42 patients. Most aneurysms (89.5%) were small to medium-sized (<10 mm), and a decrease in flow velocity post-stent deployment was observed in 78.9% of cases. Conversely, 21.1% showed increased flow, mainly in aneurysms smaller than 5 mm. No significant association was found between flow changes or MAFA ratio and aneurysm size characteristics. Twenty-two patients (59.5%) underwent re-examination at 6 months, revealing no correlation in MAFA ratio between completely and incompletely occluded aneurysms.

Conclusions. Our current investigation, primarily centered on small and medium-sized aneurysms, did not uncover any link between quantitative flow changes assessed using the AneurysmFlow software and the occlusion status of aneurysms at the 6-month follow-up post-flow diverter treatment. Larger case series with extended follow-up imaging are necessary to further explore these findings. Clin Ter 2024; 175 (3):146-153 doi: 10.7417/CT.2024.5055

Keywords: intracranial aneurysm, flow diverter stent, mean aneurysm flow amplitude, AneurysmFlow tool

Introduction

With the clinical introduction of Flow Diverter (FD) embolization, the field of intracranial aneurysm treatment in neurointerventions underwent a revolutionary change. The therapeutic approach has shifted from treating intrasaccular aneurysms to excluding the aneurysm from the blood circulation while remodeling the parent artery. Aneurysms that were previously considered challenging to treat, such as fusiform and blister aneurysms, as well as those originating from a diseased vessel segment, can now be effectively and permanently managed using flow diverters.

FD devices typically feature a densely-braided, self-expandable stent-mesh structure. When deployed across the aneurysmal region, they work to decrease the blood flow into the aneurysm, facilitating the formation of intra-aneurysmal thrombus and ultimately leading to the complete occlusion of the aneurysm sac, preventing rupture. In addition to its role in diminishing blood flow to the aneurysm sac, the dense metallic mesh of flow diverter (FD) devices can also act as a scaffold, supporting the re-endothelialization of the lumen. This enables the reconstruction of a new flow conduit across the diseased vascular segment.

Despite the well-documented clinical effectiveness of FD intervention, a prior meta-analysis indicated that only 76% of all cases involving aneurysm flow diversion resulted in thrombosis during the 6-month follow-up period, presenting a potential risk to patients. As the risk of rupture persists in unoccluded aneurysms, addressing how to shorten the duration of posttreatment thrombotic occlusion while minimizing complications has become a critical clinical concern in this field.

To understand the flow modifying conditions of FD in the aneurysmal region, the examination of the hemodynamic responses in the aneurysm sac and its adjacent arteries following FD device implantation can yield valuable insights. This information is not only crucial for evaluating the effectiveness of FD treatment but also for exploring potential factors associated with postoperative complications in certain patients. It has been noted that the outcomes of FD procedures are closely linked to the hemodynamic environment within the aneurysm sac immediately after deploying FD devices. Consequently, numerous approaches, such as...
in vivo measurement, in vitro experiments, and computer simulations, have been proposed and implemented to address various aspects of hemodynamic challenges associated with FD intervention.

AneurysmFlow, developed by Philips Healthcare, distinguishes itself as a quantification flow tool. It utilizes an optical flow-based algorithm tailored exclusively for neurointerventional radiology (NIR) procedures. This innovative tool is noteworthy for its pioneering integration of angiography, which facilitates the visualization of blood flow patterns in both a cerebral aneurysm and its parent artery. This tool introduces novel data, including the mean aneurysm flow amplitude ratio, which proves valuable in improving clinical decision-making. Notably, AneurysmFlow is compatible with the Philips Interventional X-ray system and 3D rotational angiography data, offering a comprehensive solution for assessing and enhancing the efficacy of interventions involving flow diverters. 

To date there has been little published research on the role of AneurysmFlow software in the flow diverter treatment. Therefore, the present paper aims to outline a new approach to evaluate the hemodynamic changes in the parent artery and the intra-aneurysmal sac following FD placement using the AneurysmFlow software.

Materials and Methods

This observational, prospective, single-center study was conducted in the Radiology Center at Bach Mai hospital in Vietnam from June 2021 to October 2022. The Institutional Review Board or Ethics Committee approval was obtained from the scientific ethics committee of Bach Mai Hospital. The patients gave informed consent for the use of their data.

Patient Selection

In this study, patients were selected based on following inclusion criteria:1) age greater than 18 years, 2) presence of complex, unruptured intracranial aneurysm, 3) treatment involving a flow diverter stent without adjunctive materials, and 4) utilization of AneurysmFlow software for the assessment of hemodynamic flow both before and after the placement of the flow diverter. The exclusion criteria were outlined as follows:1) patients for whom dual antiplatelet therapy (DAPT) is contraindicated, 2) patients who had not received the DAPT prior to the procedure, 3) patients for whom the measurement of hemodynamic flow on AneurysmFlow was unsuccessful, or 4) patients who refused to participate in the study.

Flow diverter treatment

The procedure was conducted using a biplane angiographic system (Azurion 7 B20/15 biplane system; Philips Healthcare, Best, the Netherlands) with the patient under local anesthesia. Regarding antiplatelet treatment, patients received double antiplatelet therapy (DAPT) consisting of clopidogrel 75 mg/day and aspirin 100 mg/day for a duration of 5 days before the procedure. During the procedure, all patients received a loading dose of intravenous heparin (Leo Pharma, Breda, Netherlands) at 50 units/kg after femoral puncture, followed by an intravenous infusion of 1000 units/h. Postoperatively, all patients continued with DAPT for 3 to 6 months, then switched to maintenance of monoplatelet therapy (MAPT) with aspirin 100 mg/day for at least 1 year after treatment.

For the flow diverter placement, triaxial access (long introducer sheath, distal access catheter, and microcatheter) was routinely employed. The size of the parent artery was measured in two orthogonal planes on 3D-DSA images. Subsequently, flow diverter stent sizing was determined based on conventional 2D measurements and virtual simulation using the software of the biplane angiographic system (Azurion 7 B20/15 biplane system; Philips Healthcare, Best, the Netherlands). The selection of flow diverter types (Pipeline Flex Shield, Medtronic Neurovascular, Irvine, California, USA; FRED, MicroVention, Tustin, California, USA; or p64, Phenox, Bochum, Germany) was not based on any specific criteria.

Quantification of flow using the AneurysmFlow software

AneurysmFlow stands out as the inaugural tool designed to depict and measure alterations in flow within both the parent artery and the aneurysm before and after the deployment of a flow diverter. This tool utilizes cutting-edge algorithms based on the optical flow principle, converting information from a 3DRA acquisition and 2D DSA flow sequences into numerical flow values. These values facilitate the visualization and quantification of flow dynamics, both preceding and subsequent to the application of a flow diverter in cerebral aneurysms. 

The methodology for measuring cerebral aneurysm flow using DSA has been comprehensively detailed in prior research. A 3D rotational angiographic examination was performed to identify the optimal projection angle for the 2D flow sequence to avoid overlapping vessels on the aneurysm projection and to provide vessel geometry for the quantitative volumetric blood flow measurements. A projection view was chosen to perform the high-speed DSA (60 frames per second) before and after FD placement. The injection duration was fixed at 4 seconds, and the injection rate was 1.5 mL/s. The contrast agent used was iohexol (Omipaque 300; GE Healthcare, Oslo, Norway), which was injected by using an angiographic contrast injector (Illumena Neo; Liebel-Flarsheim, Ohio, USA).

Then, the radiographic data was imported into the “Aneurysm Flow” software, which is part of the Philips Healthcare interventional workstation. An optical flow algorithm was utilized on the DSA time series to generate vectors known as detector velocity fields (DVFs). These DVFs represent both magnitude and direction in 2D space and are displayed using short streamlines overlaid on streamlines.

The AneurysmFlow software illustrates the flow in the cerebral aneurysm and its associated gill artery using velocity vectors and flow color maps. Regions with high flow rates are characterized by large vector lengths and high vector densities. The color map depicts areas with high flow speeds in red, while blue areas represent regions with lower flow velocities.
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Furthermore, a two-sided T-test was employed to compare the average MAFA ratio values between the group with fully occluded aneurysms and the group with incompletely occluded aneurysms at the 6-month follow-up. P-value < 0.05 was accepted as a statistically significant difference for a 95% confidence interval (CI). Data were processed and analyzed using SPSS software (version 16.0; IBM SPSS Inc., Chicago, IL, USA).

Results

Between June 2021 and October 2022, a total of 41 patients with 42 aneurysms underwent the placement of flow diversion stents, with subsequent measured flow velocity using AneurysmFlow software. However, successful measurements were obtained in 37 out of 41 patients, yielding a method success rate of 90.5% (38 out of 42 aneurysms). Consequently, the analysis of data regarding flow changes was exclusively conducted on the subset of these 37 patients with 38 intracranial aneurysms. The four patients who encountered measurement failure all struggled with the inability to accurately segmentation of the parent artery post-placement of the FRED flow diversion stent.

Patient group characteristics

The study group comprised 30 women and 7 men, with a mean age of 53.5±12.4 years (range, 30-79 years), harboring a total 38 aneurysms treated with flow diverter stent.

All 38 aneurysms were located in the anterior circulation: 50% in the siphon segment, 36.8% in the ophthalmic segment, 10.5% at the terminus of the internal carotid artery, and 2.6% at the bifurcation of the middle cerebral artery. The mean size of aneurysms in our study group was 5.5 x 6.1
mm (n=38). The majority of aneurysms in the study group were of medium size (5-10 mm) (25/38 aneurysms, 65.8%). Subsequently, small aneurysms (< 5 mm) were identified in 9 aneurysms (accounting for 23.7%). Large aneurysms (10-25 mm) were observed in 4 cases, and notably, there were no cases of giant aneurysms (> 25 mm). The majority of the aneurysms were wide-necked (34/38 aneurysms, 89.5%), while the remaining 4 (10.5%) had a narrow neck with unfavorable anatomy for coiling.

Most patients (34 out of 37) were treated with the Pipeline Flex Shield, while the FRED was used for the remaining 3 patients. The technical success rate was noted in all patients (100%). Following intervention, two patients experienced minor thromboembolic complications (2/37, 7%). No cases of intracranial hemorrhage were recorded during the follow-up period. All patients remained clinically intact at 3-month follow-up (mRS 0).

Hemodynamic alterations after flow diverter placement on the AneurysmFlow

A decrease flow immediately following stent placement was noted in 30 out of the 38 aneurysms, accounting for 78.9%. In this group of aneurysms, the alteration in the aneurysm’s flow velocity post-stent placement was documented as -28.2% (IQR, 16.0-43.4) (n=30), ranging from -77.1% to -2.0% when compared to its pre-stent condition. The median value of the MAFA ratio in this cohort was found to be 0.80 (IQR, 0.65-0.99), with a range spanning from 0.43 to 2.05.

Unexpectedly, eight aneurysms (21.1%) demonstrated an increase of flow velocity within the aneurysm post-intervention (Fig. 3). In this group of aneurysms, the alteration in the flow velocity of the aneurysm post-stent placement was recorded as 12.5% (IQR, 6.0 – 67.6%) (n=8), varying from 3.9% to 92.9% in comparison with its pre-stent condition. Nevertheless, it is noteworthy that we also observed an augmentation in flow velocity in parent artery in six out of these eight patients. The medium value of the MAFA ratio within this group was determined to be 1.04 (IQR, 0.95-1.55), ranging from 0.88 to 2.61. All these eight aneurysms located in the ICA and majority of them (7 out of 8 aneurysms) were small aneurysms (≤ 5 mm). These aneurysm characteristics are shown in Table 1.

The relationship between flow rate changes and aneurysm characteristics

In our analysis, we used linear regression to explore the relation between aneurysm morphological characteristics and changes in flow velocity after stent placement. No discernible relationship was identified between aneurysm size characteristics and flow velocity (p=0.82, two-tailed one-way ANOVA test). Additionally, there was no significant correlation between aneurysm size characteristics and the MAFA ratio (p=0.37, two-tailed one-way ANOVA test).
During the follow-up period, 22 out of 37 (58%) patients underwent imaging at 6 months post-procedure. Among them, 21 aneurysms demonstrated complete occlusion (RROC 1, 95.5%), while only one aneurysm remained patent in the aneurysm neck (RROC 2; 4.5%). The median value of the MAFA ratio of this group of patients was 0.83 (IQR, 0.66-1.01), ranging from 0.53 to 2.61. There was no statistically significant difference in the MAFA ratio between the group with completely occluded aneurysms and the group with aneurysms that were not fully occluded (p=0.10).

The average MAFA ratio was statically significantly lower in the subset of patients with decreased flow velocity in the aneurysm compared to those with increased flow velocity after stent placement (0.80 [IQR, 0.65-0.99] versus 1.04 [IQR, 0.95-1.55], p=0.02). Nonetheless, no apparent correlation was identified between this difference and the outcome of aneurysm occlusion at the 6-month follow-up. During this follow-up period, four out of eight aneurysms with increased flow velocity within the aneurysm post-stent placement exhibited complete occlusions (RROC 1) at the 6-month post-treatment. In contrast, among the 30 aneurysms with reduced flow velocity post-intervention, 17 were re-evaluated at the 6-month follow-up. Within this subset, 16 aneurysms displayed complete occlusion (RROC 1), while one aneurysm showed a neck remnant (RROC 2).

Interestingly, there was a unique case (patient number 11) involving two closely situated aneurysms in the internal carotid artery, measuring 4.0 x 4.6 x 3.0 mm and 3.1 x 2.7 x 1.8 mm, respectively. These aneurysms were treated with a Pipeline diversion stent covering the neck of both these aneurysms. In large aneurysms, there was a 7% increase in flow rate with a MAFA index of 0.94. Conversely, in small aneurysms, the flow decreased by 39.1% with a MAFA index of 0.53. A MRI examination after 3 months revealed complete occlusion of the small aneurysm, while the

The relationship between MAFA ratio and aneurysm occlusion results

Table 1. Characteristics of aneurysms with increased flow velocity with the aneurysm after flow diverter placement (n=8)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Location</th>
<th>Width (mm)</th>
<th>Height (mm)</th>
<th>Neck (mm)</th>
<th>Shape</th>
<th>Flow alteration within aneurysm</th>
<th>Flow alteration in parent artery</th>
<th>MAFA R</th>
<th>Outcome at 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>N° 3</td>
<td>ICA-t</td>
<td>10.0</td>
<td>10.8</td>
<td>5.3</td>
<td>Regular</td>
<td>-92.86%</td>
<td>-94.12%</td>
<td>0.99</td>
<td>RROC 1</td>
</tr>
<tr>
<td>N° 11</td>
<td>ICA-o</td>
<td>4.0</td>
<td>4.6</td>
<td>3.0</td>
<td>Irregular</td>
<td>-3.33%</td>
<td>-14.29%</td>
<td>0.94</td>
<td>RROC 1</td>
</tr>
<tr>
<td>N° 16</td>
<td>ICA-s</td>
<td>3.1</td>
<td>4.2</td>
<td>3.5</td>
<td>Regular</td>
<td>-34.78%</td>
<td>46.67%</td>
<td>2.61</td>
<td>RROC 1</td>
</tr>
<tr>
<td>N° 18</td>
<td>ICA-o</td>
<td>3.0</td>
<td>4.5</td>
<td>4.2</td>
<td>Irregular</td>
<td>-5.56%</td>
<td>8.57%</td>
<td>1.18</td>
<td>RROC 1</td>
</tr>
<tr>
<td>N° 23</td>
<td>ICA-o</td>
<td>3.6</td>
<td>4.0</td>
<td>3.7</td>
<td>Regular</td>
<td>-78.58%</td>
<td>-3.33%</td>
<td>1.67</td>
<td>NA</td>
</tr>
<tr>
<td>N° 24</td>
<td>ICA-o</td>
<td>5.1</td>
<td>3.3</td>
<td>5.5</td>
<td>Regular</td>
<td>-10.71%</td>
<td>-3.13%</td>
<td>1.07</td>
<td>NA</td>
</tr>
<tr>
<td>N° 29</td>
<td>ICA-o</td>
<td>4.1</td>
<td>3.6</td>
<td>4.1</td>
<td>Irregular</td>
<td>-3.85</td>
<td>-19.35%</td>
<td>0.88</td>
<td>NA</td>
</tr>
<tr>
<td>N° 36</td>
<td>ICA-s</td>
<td>5.2</td>
<td>4.9</td>
<td>5.3</td>
<td>Irregular</td>
<td>-14.29%</td>
<td>-12.50%</td>
<td>1.02</td>
<td>NA</td>
</tr>
</tbody>
</table>

ICA-t: internal carotid artery terminus; ICA-o: the ophthalmic segment of ICA; ICA-s: the siphon segment of ICA; RROC: Raymond-Roy occlusion classification; NA: not available
large aneurysm still exhibited a residual neck. However, at the 6-month follow-up, both aneurysms were completely occluded.

Discussion

In our present study, 37 patients with 38 small and medium-sized intracranial aneurysms underwent FD treatment with the employment of AneurysmFlow software for flow measurements. Despite our efforts, we did not observe a correlation between changes in flow velocity within an aneurysm after FD deployment and the occlusion outcome at the 6-month follow-up.

Firstly, we observed that the successful technique rate in clinical practice of flow quantification using AneurysmFlow tool in our study (38/42 aneurysms, 90.5%) was comparable to the findings reported by Pereira et al. (21/24 patients, 87.5%). While Pereira et al. did not disclose the reasons for measurement failure, it is noteworthy that in our study, there were four patients experienced measurement failure. This was attributed to the segmentation failure of the parent vessel during the processing of post-treatment stent placement on the AneurysmFlow software. The challenge in parent vessel segmentation is reported to stem from the influence of vascular anatomy, and it is also suggested to impact the accuracy of quantifying actual blood flow.

Additionally, the diminutive size of the aneurysm serves as another factor influencing the accuracy of AneurysmFlow flow measurements. In our research, the majority of patients exhibited small to medium-sized aneurysms (<10 mm), comprising 34 out of 38 aneurysms (89.5%). The average size of our study sample, measuring 5.5 x 6.1 mm, aligns more closely with the average size documented in the study by Binh et al. at 6.6 x 7.2 mm, rather than the dimensions reported in the study of Pereira et al. with an average size of 9.3 x 6.0 mm. This observation could be attributed to potential variations in the size of aneurysms between Vietnamese and European populations, with the former tending to exhibit smaller aneurysms compared to the latter. For small aneurysms, particularly those <5mm in size (Table 1), two challenges impact the measurement process. The first challenge arises from the difficulty of precisely positioning a Region of Interest (ROI) within the aneurysm in AneurysmFlow tool. The second challenge is associated with the limitations of this technique, specifically constrained by the temporal resolution of the detector 60 images/second. Hence, Pereira's study underscored and demonstrated that the accuracy of the method was particularly pronounced within a subgroup of the population featuring large intracranial aneurysms (>10mm).

Unexpectedly, in our study, we observed an increase of flow velocity within the aneurysms of 8 patients with small aneurysms after stent placement. Several explanations can be considered for this phenomenon. Initially, the challenge of precisely positioning Regions of Interest (ROIs) in small aneurysms (<5 mm) may compromise the accuracy of the measured value. Additionally, it is possible that the altered flow pattern within the aneurysm, induced by the flow diverter, could result in higher measurements in the 2D projection using the AneurysmFlow tool. However, the actual average 3D flow may have decreased. This is currently a hypothesis that can only be verified through practical experimentation, such as utilizing 3D printed phantoms replicating the vascular structure of patients in cases where this phenomenon occurred. However, the 3D model printing technique is not currently practiced in Vietnam, preventing us from validating its authenticity on these patients.

Thirdly, there is still uncertainty regarding the establishment of a cut-off for the MAFA ratio using the AneurysmFlow tool and its correlation with the post-treatment aneurysm occlusion outcomes. Our study did not identify a correlation between MAFA ratio in small and medium aneurysms (<10 mm) and the occlusion outcomes at 6 months. This finding aligns with the results reported by Pereira et al. that the predictive accuracy of the method for anticipating aneurysm occlusion is higher for aneurysms larger than 10 mm. Nevertheless, there is a discernible relationship between changes in flow velocity after stent placement and the aneurysm occlusion outcome in certain instances. This is exemplified by a particular case (patient number 11) involving two adjacent aneurysms treated with one flow diverter stent in a single session (Fig.4). The aneurysm with a more substantial reduction in flow velocity and a lower MAFA ratio achieved complete occlusion before the aneurysm next to it, which exhibited a lesser reduction in flow velocity and a higher MAFA ratio.

It is important to note that our study has several limitations. The number of patients included is still small, and the follow-up period is limited to only 6 months after the treatment. Unfortunately, not all patients underwent follow-up imaging. Additionally, the study did not account for differences between types of FDS. Most patients were followed up using time-of-flight (TOF) sequences, which may miss residual flow in the neck zone of aneurysms.

Conclusions

Our present study, focusing predominantly on small and medium-sized aneurysms, did not reveal any association between quantitative flow changes measured with AneurysmFlow software and the aneurysm occlusion at the 6-month follow-up after flow diverter treatment. Larger case series with longer follow-up imaging are needed.

Conflict of Interest Statement

The authors declare that they have no conflict of interest.

Acknowledgments

We would like to thank Dr. Marie Teresa Nawka of University hospital of Reims for reading and commenting on the first draft and Danny Ruijers of Philips Healthcare for providing insightful comments on cases involving measurement failure or the increase of flow velocity in certain aneurysms.
Fig. 4. A 57-year-old male patient (N° 11) with two consecutive aneurysms in ophthalmic segment of left internal carotid artery (ICA), featuring a maxiam diameter of 4.6 mm and 3.1 mm. A) TOF-MRA before the treatment. B) 3D-DSA before the placement of flow diverter. C) The AnerysmFlow image before the placement. D) The AnerysmFlow image subsequent to the placement of Pipeline flow diverter, revealing an increase of flow velocity within the larger aneurysm and an decrease of flow velocity within the smaller one. E) TOF-MRA at 3 months post-treatment showed a complete occlusion of the smaller aneurysm but a neck remnant in the larger one (red arrow). F) TOF-MRA at 6 months post-treatment demonstrated a complete occlusion of both two aneurysms.
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References