Correlation of Flow Diverter Malapposition at the Aneurysm Neck with Incomplete Aneurysm Occlusion in Patients with Small Intracranial Aneurysms: A Single-Center Experience

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ABSTRACT

BACKGROUND AND PURPOSE: Flow diversion treatment repairs aneurysms by altering the hemodynamics of the aneurysmal sac and providing a scaffold for endothelial cell adhesion. The purpose of this study was to investigate the correlation of flow diverter (FD) malapposition at the aneurysm neck with incomplete occlusion of small intracranial aneurysms (IAs) and investigate other factors that are possibly related to incomplete occlusion.

MATERIALS AND METHODS: From January 2019 to June 2022, the clinical and imaging data for 153 patients (175 aneurysms) with unruptured small IAs treated with flow diversion were retrospectively analyzed. FD apposition at the aneurysm neck was evaluated by high-resolution conebeam CT (HR-CBCT), and the complete occlusion rate for aneurysms was judged according to the latest follow-up conventional angiography findings (≥6 months). Multivariate logistic regression analysis was used to determine factors associated with incomplete aneurysm occlusion.

RESULTS: In total, 159 FDs were implanted in 153 patients. HR-CBCT performed after the deployment revealed FD malapposition at the aneurysm neck in 18 cases. According to the latest follow-up angiograms (average: 9.47 ± 3.35 months), the complete aneurysm occlusion rate was 66.9%. The complete occlusion rates for incomplete and complete stent apposition at the neck were 38.9% (7/18) and 70.1% (110/157), respectively. The results of regression analysis showed that an aneurysm sac with branch vessels (OR, 2.937; $P = .018$), incomplete stent apposition at the aneurysm neck (OR, 3.561; $P = .023$), and a large aneurysm diameter (OR, 1.533; $P = .028$) were positive predictors of incomplete aneurysm occlusion.

CONCLUSIONS: An aneurysm sac with branch vessels, a large aneurysm diameter, and malapposition at the aneurysm neck significantly affect aneurysm repair after FD stent-only treatment for small IAs.

ABBREVIATIONS: FD = flow diverter; HR-CBCT = high-resolution cone-beam CT; IAs = intracranial aneurysms; ISA = incomplete stent apposition; OKM = O'Kelly-Marotta

Flow diverter (FD) implantation is one of the most commonly used methods for endovascular treatment of unruptured intracranial aneurysms (IAs), with adequate safety and definite efficacy.[1-4] However, 5% of aneurysms may show incomplete occlusion even after 5 years of follow-up.[1] Therefore, it is necessary to investigate the factors affecting incomplete aneurysm occlusion.[5] Incomplete stent apposition (ISA) is associated with delayed stent endothelization, the occurrence of ischemic events, and in-stent stenosis.[6-8] In addition, animal experiments have confirmed that ISA at the aneurysm neck, also known as communicating malapposition, is closely related to incomplete aneurysm occlusion.[9,10] However, there are a few reports of clinical or animal experiments, this correlation needs to be confirmed by further systematic clinical research and exploration.[5,8,10] The use of high-resolution conebeam CT (HR-CBCT) and postprocessing software can facilitate accurate observation of stent alignment with the vessel wall after placement.[11,12] Accordingly, the aim of the present study was to investigate the correlation of FD malapposition at the aneurysm neck with incomplete occlusion of small IAs by using HR-CBCT. In addition, multivariate logistic regression analysis was used to explore other factors that are possibly related to incomplete occlusion.

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MATERIALS AND METHODS

Population

Patients with small IAs treated with flow diversion at our center from January 2019 to June 2022 were identified from the hospital's picture archiving and communication system. The exclusion criteria were as follows: aneurysms with a maximum diameter of >10 mm; aneurysms without angiographic follow-up or aneurysms with angiographic follow-up data obtained at <6 months; aneurysms that could not be observed because of parent artery occlusion; aneurysms treated with coiling or aneurysms classified as traumatic aneurysms, fusiform aneurysms, or dissecting aneurysms; aneurysms without intraoperative HR-CBCT or reconstructed images that were not clear enough to determine stent apposition; and aneurysms with previous or new subarachnoid hemorrhage. Each patient provided written informed consent for the publication of this article and any related photos. The First Affiliated Hospital of Zhengzhou University Ethics Committee approved this study, which complied with the requirements of the 2013 revision of the Declaration of Helsinki (www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/).

Clinical and Imaging Data

The specific method of FD implantation was similar to that described in related literature.[3,13] All patients were subjected to pharmacogenetic testing for aspirin and clopidogrel, and those who were sensitive to both drugs took aspirin (100 mg/day) and clopidogrel (75 mg/day) at least 5 days before surgery. Patients who were insensitive to one or both drugs were required to increase their doses or switch to ticagrelor (60 mg/day). Tirofiban (0.15 μg/kg/min) was administered for 12–24 h if no contrast agent leakage was observed on postoperative brain CBCT. The patients received continuous oral administration of dual antiplatelet drugs according to the preoperative regimen after stent placement. After continuous angiographic follow-up, dual antiplatelet therapy was continued if the aneurysm was not completely occluded; single antiplatelet therapy was adjusted if the aneurysm was completely occluded but <1 year had passed since stent placement, whereas platelet therapy was discontinued if the aneurysm had completely occluded and >1 year had passed after stent placement.

Baseline data, such as age, sex, and underlying diseases, were recorded. The shape, location (anterior or posterior circulation), and diameter of the aneurysm; neck width; diameter of the parent artery; flow incidence angle for the aneurysm sac (defined as the angle between the extension line between the midpoint of the aneurysm neck and the aneurysm apex and the midline of the proximal segment of parent artery after stent placement); and the presence of sac with branch vessels were also recorded. The degree of filling in the aneurysm sac and the residual time of the contrast medium in the lumen after the immediate implantation of FD were assessed by using the O'Kelly-Marotta (OKM) grading scale.[2,14]

Observation of FD Apposition

The detailed procedure for observation of FD apposition was as follows. If the patient underwent HR-CBCT with diluted contrast media during the surgery, the scanning information was directly used to reconstruct and observe stent apposition at the postprocessing workstation. The scanning methods and parameters used for HR-CBCT with diluted contrast media are described in the literature.[15] For patients who did not undergo HR-CBCT with diluted contrast media, HR-CBCT and 3D scan data for the parent artery were loaded into the workstation, and images of the stent and parent artery were fused and reconstructed by the dual-volume fusion reconstruction method for the observation of stent apposition. The scanning methods and parameters for the stent and vascular dual-volume fusion reconstruction technology are described in the literature.[11] The FD diameter and FD apposition at the aneurysm neck were recorded. Malapposition at the neck was defined as ISA in the parent artery proximal to the aneurysm that extended into the neck of the aneurysm, effectively creating a much larger neck area.[9] When ISA at the neck was observed intraoperatively, massage with a "J"-shaped microwire was attempted multiple times for correction of the malapposition; this was followed by another HR-CBCT scan to confirm stent apposition at the neck. If the malapposition persisted, no further treatment was attempted, and the case was considered ISA at the aneurysm neck.

Angiographic Follow-up and Analysis

The time of the latest angiography was recorded to determine the occlusion status of the aneurysm and the degree of in-stent stenosis. Complete occlusion was considered when the primary aneurysm showed an OKM filling grade of D.[16]

Aneurysms were divided into the occlusion and incomplete occlusion groups, and general clinical data for the 2 groups were analyzed and compared. Patient characteristics (eg, age, sex, smoking history, etc), aneurysm characteristics (eg, diameter, neck width, presence of sac with branch vessels, etc), characteristics of the parent artery (eg, diameter of the proximal and distal ends of the artery), stent characteristics (eg, diameter, stent apposition, etc), the OKM grade immediately after FD deployment, and other general factors that could affect aneurysm occlusion were analyzed.[5,13,17-25] Following univariate analysis of the above factors, those with a P value of <.10 were included in the multivariate logistic regression model, and independent influencing factors for incomplete aneurysm occlusion after FD deployment were identified.

Data Analysis

All data were independently judged or measured by 2 experienced neurointerventionalists. Quantitative variables were averaged, and the results were determined after consultation regarding any differences in categoric variables. All statistical analyses were performed by using SPSS 26.0 (IBM) software. Quantitative variables are expressed as mean ± SD and were compared between groups by using 1-way ANOVA. Categoric variables are presented as number with percentage and were compared between groups by using the χ^2 test or Fisher exact test. The predictors of incomplete aneurysm occlusion were determined by 1-way ANOVA, and factors with $P < .10$ were included in the logistic multivariate regression model for further analysis. A P value of <.05 was considered statistically significant.

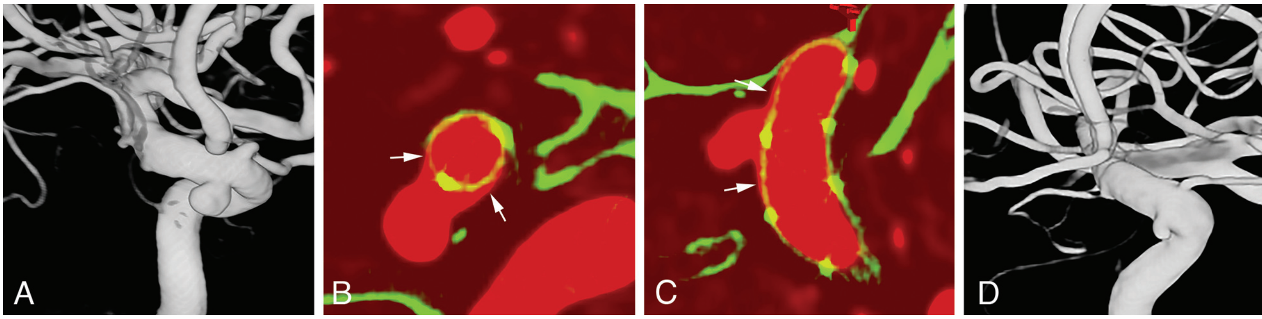

FIG 1. Representative case of FD malapposition resulting in incomplete occlusion. *A*, Image represents a hypophyseal aneurysm in the left internal carotid artery. *B* and *C*, These images were obtained by the dual-volume fusion reconstruction method. ISA on both sides of the aneurysm neck can be observed in the transverse (*B*) and sagittal planes (*C*) (*white arrows*). *D*, At 9 months after stent placement, the aneurysm has reduced in size, though the angiographic filling grade is B per the OKM grading scale.

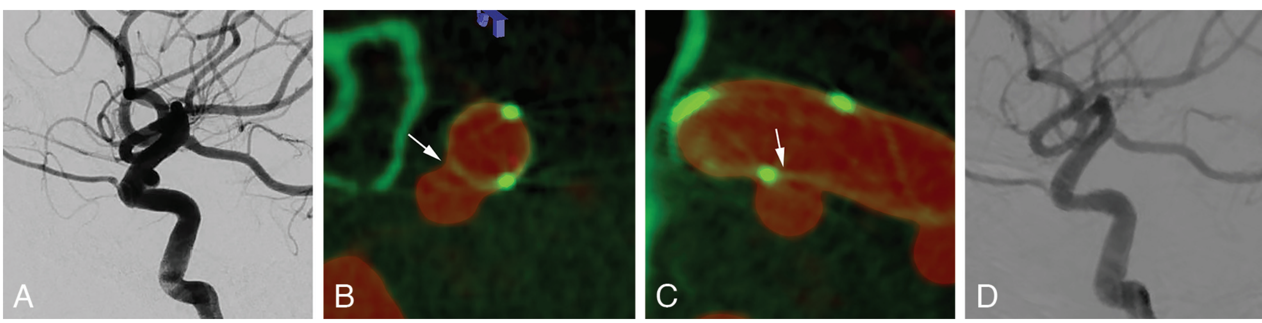

FIG 2. Representative case of complete stent apposition resulting in complete occlusion. *A*, Image represents a hypophyseal aneurysm in the left internal carotid artery. *B* and *C*, These images were obtained by the dual-volume fusion reconstruction method. Complete stent apposition at the aneurysm neck can be observed in the transverse (*B*) and sagittal planes (*C*) (*white arrows*). *D*, At 12 months after stent placement, the aneurysm is completely occluded with grade D angiographic filling per the OKM grading scale.

RESULTS

Study Cohort Characteristics

From January 2019 to June 2022, a total of 272 patients with 317 small IAs were treated with flow diversion at our center. From these, 47 IAs without angiographic follow-up or with angiographic follow-up data obtained at $<$6 months and 2 IAs that could not be observed because of parent artery occlusion were excluded. Moreover, 61 IAs that were treated with coiling or classified as traumatic aneurysms, fusiform aneurysms, or dissection aneurysms were excluded, along with 22 IAs without intraoperative HR-CBCT or with reconstruction images that were not clear enough for observation of stent apposition. Finally, 10 IAs with previous or new subarachnoid hemorrhage were excluded. Therefore, a total of 175 aneurysms in 153 patients were included in the study cohort. FDs were implanted for the treatment of a single aneurysm in 132 patients and the treatment of 2 or more aneurysms in 21 patients. A total of 137 Tubridge (MicroPort) and 22 Pipeline embolization devices (Covidien) were implanted. One FD was implanted in 147 patients, and 2 FDs were implanted in 6 patients because of the presence of aneurysms in the bilateral internal carotid artery. All stents were successfully placed.

Observation of FD Apposition

Immediately after stent placement, 23 cases of ISA at the aneurysm neck, termed immediate ISA at the neck (Fig 1), were observed, and the remaining aneurysms showed satisfactory stent apposition (Fig 2). For 13 of these cases, a microguidewire was used to form a "J" shape for correction of ISA. From these 13 cases, 5 showed improvement after this intervention and were considered to have complete stent apposition (Fig 2). The remaining 8 cases and another 10 cases of malapposition identified by retrospective analysis of imaging data were analyzed as cases of ISA at the neck (Online Supplemental Data), with the segments of the internal carotid artery classified per the nomenclature proposed by Bouthillier et al.[26] For different types of FD, the incidence of ISA at the neck immediately after release of the Tubridge and Pipeline devices was 12.5% (19/152) and 17.4% (4/23), respectively, with no significant difference ($P = .512$).

Imaging Follow-up and Analysis

The mean follow-up time for all aneurysms was 9.47 $\pm$ 3.35 months, and 58 (33.1%) aneurysms showed incomplete occlusion. The cohort was divided into the occlusion and incomplete occlusion groups and statistically analyzed. In univariate analysis, a younger age, a large aneurysm diameter, a large neck width, an aneurysm sac with branch vessels, and ISA at the neck were significantly associated with incomplete occlusion, as shown in the Online Supplemental Data ($P < .10$ for all). These factors were included in multivariate logistic regression analysis to identify predictors of incomplete aneurysm occlusion, and the predictors were identified as a sac with branch vessels, a large aneurysm diameter, and ISA at the neck, as shown in Table 1. It is worth

Table 1: Multivariable analysis of factors associated with incomplete occlusion of small IAs treated with flow diversion

	P Value	OR (95% CI)
Age	.100	1.026 (0.995–1.058)
Aneurysm diameter	.028	1.533 (1.048–2.244)
Neck width	.701	0.884 (0.471–1.659)
Sac with branch vessels	.018	2.937 (1.199–7.190)
ISA at the neck	.023	3.561 (1.187–10.679)

Table 2: Outcomes of immediate ISA at the aneurysm neck after flow diversion treatment for small IAs

	Complete Occlusion	Incomplete Occlusion	*P* Value
Complete stent apposition after intervention for ISA	2	3	1.000[a]
ISA even after intervention	3	5	

[a]Fisher exact test.

mentioning that the incomplete occlusion rates were 46.2% (12/26) and 70.5% (105/149) for sacs with branch vessels and those without branch vessels, respectively, and 38.9% (7/18) and 70.1% (110/157) for ISA at the neck and complete stent apposition at the neck, respectively. Moreover, the mean sizes of the unoccluded and occluded aneurysms were 5.8 and 4.9 mm, respectively. For cases of immediate ISA at the neck, there was no significant difference in the occlusion rate between the complete stent apposition and incomplete stent apposition after intervention with the "J"-shaped microguidewire, as shown in Table 2. With regard to the FD types, the overall occlusion rates for the Tubridge and Pipeline devices were similar ($P = .767$) at 66.4% (101/152) and 69.6% (16/23), respectively. In cases involving postoperative ISA at the neck, the occlusion rates for the Tubridge and Pipeline devices were 37.5% (6/16) and 50% (1/2), respectively, with no significant difference ($P = .512$).

DISCUSSION

FD malapposition after treatment of IAs is associated with adverse events, such as delayed endothelization, ischemic events, and in-stent stenosis.[6-8] In animal studies, ISA at the neck was associated with a higher incidence of incomplete aneurysm occlusion.[8-10] However, previous clinical studies by using FDs for the treatment of IAs have not adequately judged and classified ISA; and, to our knowledge, none has systematically investigated the effect of ISA at the neck on aneurysm occlusion in clinical practice.[2,13] The use of HR-CBCT and postprocessing software can facilitate accurate observation of stent alignment with the vessel wall after placement.[11,27] In the present study, HR-CBCT was used to scan the stent area and reconstruct the image so that stent apposition at the neck immediately after FD deployment could be observed. The incidence of immediate ISA at the neck was 13.1% (23/175), which reduced to 10.3% (18/175) after intraoperative intervention for partial patients.

The occlusion rates for IAs treated with flow diversion varies from 56% to 95% among different centers and follow-up times, with the rate even reaching 95% at 5 years.[1-3,16,20] In the present study, at the last follow-up (9.47 ± 3.35 months), the aneurysm occlusion rate was 66.9%, with complete occlusion rates of 38.9% (7/18) and 70.1% (110/157) for ISA at the neck and complete stent apposition at the neck ($P = .008$). Further multivariate analysis showed that ISA at the neck was an independent predictor of incomplete aneurysm occlusion (OR, 3.561; $P = .023$). There may be various reasons for this finding. First, ISA at the neck may have caused persistent endoleakage at the aneurysm neck and affected the hemodynamic effect of FD. Thus, the aneurysm neck and dome would continue to show a high blood flow vector and high wall shear stress. Second, Kadirvel et al[28] showed that the endothelization process of the stent at the neck gradually developed from the periphery to the center of the neck. Therefore, FD malapposition to the vascular wall at the neck may have resulted in delayed endothelization of the stent, with the continuous impact of blood flow on the dome resulting in incomplete occlusion. Third, the large neck width could be a factor affecting occlusion of the aneurysm;[20] furthermore, ISA at the neck may have enlarged the area of the neck.

Although HR-CBCT can detect ISA in a timely manner during the surgery, whether or how to deal with ISA remains controversial.[9,29] Zhang et al[29] reduced the postoperative incidence of ISA from 18.7% to 2.5% by active intervention. However, this led to problems, such as stent migration, vessel puncture caused by stent microfilaments, and thrombosis. In an animal study by King et al,[9] ISA at the aneurysm neck that was successfully corrected by balloon angioplasty showed a higher occlusion rate, which was statistically significant. In the present study, aneurysms with complete stent apposition after intervention by a "J"-shaped microguidewire showed a higher occlusion rate than did those with ISA despite the intervention (40% versus 37.5%), but the difference was not statistically significant, possibly because of the small sample size. In addition, considering the risk of balloon dilation at the neck, ISA at the neck was only managed by multiple attempts at massage with the "J"-shaped microwire, followed by another HR-CBCT scan to evaluate stent apposition at the neck. If the malapposition persisted, no further treatment was attempted for various reasons, including the limited effect of the treatment, possibility of stent displacement and intimal damage, increased patient exposure to radiation because of the multiple HR-CBCT scans, and, most importantly, the lack of clinical evidence showing the benefits of active treatment for malapposition at the aneurysm neck. Therefore, the conditions for active treatment of FD malapposition at the neck may need to be explored in further studies.

We observed complete occlusion rates of 46.2% (12/26) and 70.5% (105/149) for sacs with branch vessels and those without branch vessels, respectively ($P = .015$). Further multivariate analysis showed that a sac with branch vessels was an independent predictor of incomplete occlusion of aneurysms (OR, 2.937; $P = .018$), consistent with the findings of previous studies.[2,5,16,19,25] Branch vessels, such as the ophthalmic artery and anterior choroidal artery, are mostly patent at the long-term follow-up after FD implantation; this is related to the high blood flow through the branch vessels without distal collateral branches and the high-pressure gradient at the opening of the parent vessels.[19] Similarly, we speculate that the vessels branching from the sac have a pressure difference that allows continuous blood flow into the aneurysm dome and influences intraluminal thrombus formation. In a study by Zetchi et al,[25] further analysis of the subgroup with sacs with branch vessels showed that a larger angle between the parent artery and branch vessel could result in greater intra-aneurysmal vorticity and a lower occlusion rate; this confirmed our suspicion. Furthermore, the mean sizes of unoccluded and occluded aneurysms in this study were 5.8 and 4.9 mm, respectively, and multivariate analysis in the present study found that the aneurysm diameter was one of the independent factors affecting aneurysm occlusion (OR, 1.533; $P = .028$), similar to the findings of previous studies.[17,30] Therefore, use of multiple devices or combination with coiling in cases involving branching aneurysms or larger aneurysms may be effective in increasing the rate of obliteration.[31,32]

This study had several limitations. First, some patients failed to undergo angiographic follow-up within the prescribed time for various reasons, so there were some time differences in the observation of aneurysm occlusion, which may have affected the accuracy of our results. Second, endovascular imaging techniques, such as intravascular sonography and optical coherence tomography, have not been used to determine stent apposition. Third, the follow-up period was short, so the relationship between aneurysm occlusion and time could not be further analyzed. Fourth, this study primarily focused on results for the Tubridge device; therefore, the findings should be applied with caution to other devices. Finally, this was a single-center, retrospective analysis with a small sample size, and its conclusions need to be verified in further multicenter, prospective, randomized controlled studies.

CONCLUSIONS

An aneurysm sac with branch vessels, a large aneurysm diameter, and ISA at the aneurysm neck significantly affect aneurysm repair after FD stent-only treatment for small IAs. A younger age and a larger neck width may also be related to aneurysm persistence. Detection of FD malapposition at the aneurysm neck by using HR-CBCT followed by appropriate intervention can facilitate appropriate occlusion and repair of the aneurysm.

Disclosure forms provided by the authors are available with the full text and PDF of this article at www.ajnr.org.

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