Original Article | Neurointervention

eISSN 2005-8330
https://doi.org/10.3348/kjr.2024.1212
Korean J Radiol 2025;26(7):716-726

Korean Journal of Radiology
KJR

FloWise Flow Diverter for Treatment of Unruptured Wide-Neck Intracranial Aneurysms: A Prospective, Multicenter, Single-Arm, Open-Label, Pivotal Study

Hyun Jin Han[1]*, Keun Young Park[1]*, Byung Moon Kim[2], Yong Bae Kim[1], Hong-Jun Jeon[3], Sang Hyun Suh[4], Sangil Suh[5], Jung-Jae Kim[1], Jun-Hwee Kim[6], Chang Ki Jang[7], Dong Joon Kim[2], Jung Keun Lee[8], Sunghan Kim[9], Kyu Seon Chung[1,2], Solbi Kim[1,2], Sun Yoon[10], Min Jeoung Kim[11]

[1]Department of Neurosurgery, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea
[2]Department of Radiology, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea
[3]Department of Neurosurgery, Kangdong Sacred Heart Hospital, Hallym University College of Medicine, Seoul, Republic of Korea
[4]Department of Radiology, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea
[5]Department of Radiology, Korea University Guro Hospital, Korea University College of Medicine, Seoul, Republic of Korea
[6]Department of Radiology, Yongin Severance Hospital, Yonsei University College of Medicine, Yongin, Republic of Korea
[7]Department of Neurosurgery, Yongin Severance Hospital, Yonsei University College of Medicine, Yongin, Republic of Korea
[8]Department of Neurosurgery, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea
[9]Department of Neurosurgery, Bucheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Bucheon, Republic of Korea
[10]Department of Neurosurgery, Hallym University Dongtan Sacred Heart Hospital, Hwaseong, Republic of Korea
[11]Department of Neurosurgery, Uijeongbu St. Mary's Hospital, The Catholic University of Korea College of Medicine, Uijeongbu, Republic of Korea

Objective: We evaluated the safety and efficacy of a new flow diverter in the treatment of unruptured wide-neck aneurysms.
Materials and Methods: Patients who had unruptured intracranial aneurysms with a neck diameter ≥4 mm or dome-to-neck ratio <2 and who met other eligibility criteria were enrolled from seven institutions. The patients were treated with a new flow diverter (FloWise; Taewoong Medical, Seoul, Korea) and followed at 1, 3, 6, and 12 months after treatment. The primary efficacy endpoint was the complete occlusion of the target aneurysm at 12 months. Safety endpoints included ipsilateral stroke (National Institutes of Health Stroke Scale score ≥5), newly developed neurological deficit (modified Rankin Scale score ≥3), death at 30 days, and ≥50% parent artery stenosis or occlusion at the 12-month follow-up. The superiority of FloWise over the predefined reference value (56.7%) was investigated using a one-sided binomial test with a statistical significance of $P < 0.025$.
Results: Seventy patients (59.0 ± 9.9 years; male:female = 16:54) with 93 aneurysms (median diameter, 5.2 mm [range, 1.6–26.1 mm]; median neck diameter, 4.1 mm [range, 1.2–22.4 mm]) were included. Of these, 69 patients who completed the follow-up as planned constituted the efficacy analysis set. Complete aneurysm occlusion was achieved in 56 target aneurysms (81.2%; 95% confidence interval [CI], 69.9–89.6; $P < 0.001$). Procedural success and ≥50% aneurysm volume reduction were observed in 69 (100%) and 66 (95.7%; 95% CI, 87.8–99.1) target aneurysms, respectively. No ipsilateral strokes occurred in any of the 70 patients. Serious adverse events occurred in 6 patients; these events were causally related to the treatment in 4 (5.7%) cases and possibly related to the device in 2 (2.9%) cases.
Conclusion: FloWise flow diverter is safe and effective for the treatment of unruptured wide-neck aneurysms.
Keywords: Intracranial aneurysm; Flow diversion; New device

Received: November 26, 2024 **Revised:** April 16, 2025 **Accepted:** April 19, 2025
*These authors contributed equally to this work.
Corresponding author: Byung Moon Kim, MD, PhD, Department of Radiology, Severance Hospital, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03772, Republic of Korea
• E-mail: bmoon21@hanmail.net

Korean Journal of Radiology
KJR

INTRODUCTION

Endovascular coiling is the standard treatment for intracranial aneurysms; however, it has limitations, such as a relatively high rate of recurrence and retreatment, particularly in wide-neck, large-giant, or fusiform aneurysms, which also have high rates of treatment-related morbidity and mortality [1-4]. The introduction of flow diverters has resulted in a paradigm shift in aneurysm treatment, and recent evidence has demonstrated their good clinical and radiological efficacy and safety [5]. Flow diverters are being increasingly used for almost all types of intracranial aneurysms globally, regardless of their size and shape. Various types of flow diverters have been introduced, and advancements in previous generations have resulted in improved technical success and fewer thromboembolic complications.

In Korea, there are several hindrances to the liberal use of flow diverters for aneurysm treatment because the Korean National Health Insurance permits reimbursement of their usage only for large-sized aneurysms (equal to or greater than 10 mm in size), mainly because of their high price. As a result, no large-scale post-market flow-diverter study of small-sized aneurysms has been performed in the Korean population, even though small-sized aneurysms that are less than 10 mm in size comprise the majority of the cerebral aneurysms that have been treated. Thus, we developed a new flow diverter (FloWise; Taewoong Medical, Seoul, Korea) for domestic use with low production costs and favorable physical properties including high metal coverage (39%), acceptable foreshortening (38%), and high radial force (3.5 gf). This may lower the price of flow diverters and thus make it possible to widen the indications for the reimbursement of flow diverter-based treatments.

In an animal model study, we showed that it had a technical success rate of 96.9%, and the rate of occlusion of the stent at the 3-month follow-up was 6.2% [6]. A pilot clinical study including ten patients with 14 internal carotid artery (ICA) aneurysms also showed a 100% technical success rate for FloWise and a 66.7% complete aneurysm occlusion rate at the 6-month follow-up, without any neurologic morbidity [7].

In this prospective, multicenter, single-arm, open-label, pivotal study, we aimed to evaluate the safety and efficacy of FloWise for the treatment of intracranial aneurysms.

MATERIALS AND METHODS

This was a prospective, multicenter, single-arm, open-label, pivotal clinical study that evaluated the safety and efficacy of FloWise in a predefined population. Seven hospitals participated in this study.

This study was approved by the Institutional Review Boards of all participating institutions, and written informed consent was obtained from all the participants before enrollment (IRB numbers of the centers: 1-2020-0006, 9-2020-0058, 2019-12-010-023, 3-2020-0068, 2020GR0250, 1922-011-400, and IS19SSMV0079). Verbal explanations were provided twice to the participants as well as at least one first-degree relative, and written informed consent was obtained by the primary investigator in the presence of an observer.

Inclusion and Exclusion Criteria

Inclusion criteria were as follows: 1) age ≥19 years, 2) modified Rankin Scale (mRS) score ≤2, 3) unruptured aneurysm with a neck diameter ≥4 mm or dome-to-neck ratio <2, 4) 2.5 mm ≤ parent artery diameter ≤ 5.0 mm, and 5) written informed consent.

Exclusion criteria were as follows: 1) currently pregnant, 2) intracranial hemorrhage of less than 30 days, 3) an untreated aneurysm that had ruptured within the last 30 days, 4) any contraindication to antiplatelet medication, 5) major surgery within 30 days of treatment, 6) platelet count of less than 100000, 7) untreated cancer or immunocompromising disease, 8) serum creatinine levels >2.5 mg/dL, 9) previously inserted stent in the parent artery with the target aneurysm, 10) nitinol allergy, 11) uncontrolled hypersensitivity to iodine contrast material, 12) active infection, and 13) life expectancy <5 years. The

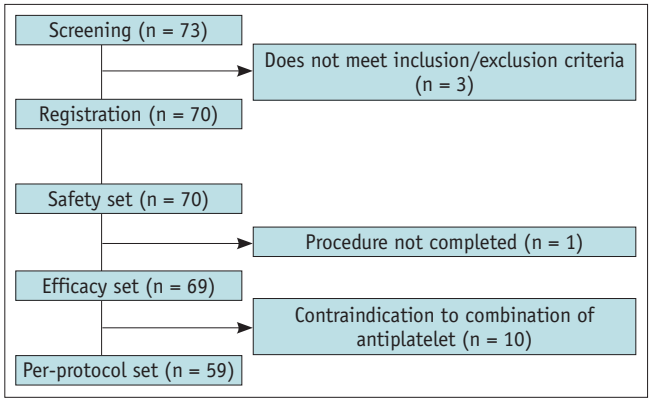

Fig. 1. Flowchart of patient registration and analysis.

https://doi.org/10.3348/kjr.2024.1212

flow of the study is summarized in Figure 1.

FloWise Flow Diverter

The specifications of the FloWise stent, in vivo experimental results in a rabbit aneurysm model, and the results of a pilot clinical study have been previously reported [6]. Briefly, the FloWise flow diverter stent is composed of 48 strands of 0.0012-inch nitinol and platinum wires that are braided and heat-treated in the expanded configuration. After deployment, FloWise expands to cover the neck of the aneurysm, forming a high-coverage mesh of approximately 33%–41% by area, with a radiopacity similar to that of the pipeline embolization device. The distal tip of the delivery wire is preshaped to a J-shape. The stent-contact portion of the delivery wire is coated with silicon such that it can grip FloWise, which allows for re-sheathing at any point prior to 70% deployment. This packaged device can be loaded into standard microcatheters with inner diameter of at least 0.021 inch. It is pushed through the microcatheter and deployed by using a combination of microcatheter withdrawal and forward pressure on the delivery wire. FloWise undergoes approximately 38% shortening when deployed completely and is available in diameters of 3.5, 3.75, 4.0, 4.25, 4.5, 4.75, and 5.0 mm, and in lengths of 10, 15, 20, 25, and 30 mm.

Implantation of the FloWise Flow Diverter

All the patients were treated under general anesthesia. After the placement of a 6F guide sheath (Shuttle, Cook Medical, Bloomington, IN, USA) in the relevant parent artery, a 5 or 6F intermediate catheter (Sofia, Microvention, CA, USA; Navien, Medtronic, CA, USA) was advanced through the guide sheath in the parent artery as far as possible. A 0.021-inch microcatheter was navigated to the parent artery across the aneurysm neck. Subsequently, a FloWise stent corresponding to the largest diameter of the parent artery was introduced into the microcatheter and deployed, completely spanning the neck of the aneurysm. After deployment of FloWise, flat-panel CT with dilute contrast material (1:4 dilution) was performed. If needed, balloon angioplasty was performed to ensure adequate wall apposition of FloWise. Follow-up angiograms were obtained at least 2 times for 10 minutes each. Based on the operator's experience, if sufficient flow diversion (shift of the inflow zone from the distal neck to the proximal neck of the aneurysm and disruption of the inflow jet) was not observed after the first FloWise was successfully implanted, another FloWise was inserted in an overlapping manner. If an acute in-stent thrombosis was detected, a glycoprotein IIb/IIIa inhibitor (tirofiban, 0.5–1.0 mg) was administered intra-arterially and maintained for 12 hours after completion of the procedure.

Antiplatelet Medication

All enrolled patients received dual antiplatelet medication (100 mg aspirin with 75 mg clopidogrel) for at least 5 days before treatment. An antiplatelet drug resistance test was performed one day before treatment. If the test results were positive, an additional antiplatelet drug with a different mechanism of action was administered. After treatment completion, the dual antiplatelet medication was maintained for 6 months and then changed to aspirin monotherapy.

Clinical and Imaging Follow-Up

Outpatient clinical follow-ups were scheduled at 1, 3, and 6 months. A CT angiogram was obtained at the 6-month follow-up. The patients were scheduled for readmission for a follow-up catheter angiography at 12 months ± 4 weeks. A data safety monitoring board (DSMB) was established to ensure patient safety. The DSMB comprised two independent physicians who did not work at the study hospital. During the clinical follow-up, telephone and e-mail contact with a clinical research assistant was possible at any time. If the patient complained of any symptoms potentially related to the treatment, they were reported to the primary investigator. These complaints were recorded and evaluated by the DSMB to determine whether they were related to the treatment.

Endpoints

The efficacy and safety endpoints were assessed in the efficacy and safety sets, respectively (Fig. 1).

The primary efficacy endpoint was the rate of complete occlusion (Raymond class 1) on 12-month follow-up angiography. Secondary efficacy endpoints were the rates of technical success and ≥50% decrease in aneurysm sac volume at 12-month follow-up angiography. Technical success was defined as complete coverage of the neck of the target aneurysm using FloWise.

The safety endpoints were ipsilateral stroke (National Institutes of Health Stroke Scale score ≥5), newly developed neurological deficit (mRS score ≥3), death at 30 days, and ≥50% parent artery stenosis or occlusion at 12-month follow-up angiography.

https://doi.org/10.3348/kjr.2024.1212

Korean Journal of Radiology
KJR

Sample Size Calculation

The number of participants required for the study was calculated based on the results of previously published reports on Food and Drug Administration (FDA)-approved flow diverters for intracranial aneurysms. The required number of participants was calculated to be 57 based on the reference value (p_0) = 56.7%, success rate = 75.61%, P = 2.5% in a one-sided test, and power = 85% (see the Supplement for further details). Assuming a 20% loss to follow-up, the final number of participants required was 70.

Statistical Analysis

The statistical analyses were performed using SAS (version 9.4, SAS Institute Inc., Cary, NC, USA). The primary efficacy endpoint is presented as incidence (%; 95% confidence interval [CI]). To investigate the superiority of the FloWise over the reference values (56.7%), a one-sided binomial test was conducted. Statistical significance was defined as $P < 0.025$.

RESULTS

Patient and Aneurysm Characteristics

Seventy patients from 7 hospitals were enrolled in the current prospective study between August 2020 and March 2022 (Table 1), of whom 69 completed the planned clinical and angiographic follow-ups. Of the 70 patients, 52 were enrolled in the principal investigator's hospital, and the other six hospitals enrolled 6, 4, 3, 3, 1, and 1 patients, respectively.

Table 1. Summary of the patient characteristics (n = 70)

Characteristic	Data
Age, yrs	59.0 ± 9.9
Sex, male	16 (22.9)
Symptomatic aneurysm	13 (18.6)
Multiple aneurysms	16 (22.9)
Number of aneurysm per patient	1.3 (1; 1–5)
Vascular risk factors	
Smoking	12 (17.1)
Alcohol	26 (37.1)
Previous ischemic stroke	2 (2.9)
Previous hemorrhagic stroke	4 (7.1)
Hypertension	15 (21.4)
Coronary artery disease	5 (7.1)
Dyslipidemia	6 (8.6)
Antiplatelet resistance	19 (27.1)
Resistance to aspirin	12 (17.1)
Resistance to clopidogrel	13 (18.6)

Data are presented as number of patients with percentages in parentheses, mean ± standard deviation, or mean (median; range), unless specified otherwise.

The average age of the participants was 59.0 years (standard deviation, 9.9). Of the 70 participants, 16 (22.9%) were male. Thirteen patients had symptomatic aneurysms that caused cranial nerve palsy and compressive neurological deficits, while 22.9% (16/70) had multiple aneurysms. In the preprocedural antiplatelet resistance test, 17.1% (12/70) of the patients exhibited aspirin resistance, while 18.6% (13/70) showed clopidogrel resistance.

The characteristics of the aneurysms and treatment groups are summarized in Table 2. In summary, 54 of the 93 aneurysms (58.1%) were located in the paraclinoid region of the ICA. The mean size of all 93 aneurysms was 5.7 ± 3.1 mm (median, 5.2 mm; range, 1.6–26.1 mm). The mean size of the target aneurysms was 6.3 ± 3.5 mm (median, 6.1 mm; range, 3.5–26.1 mm). Of the 69 patients who completed the follow-up, 53 received 1 (76.8%), 15 received 2 (21.7%), and 1 patient received 3 (1.4%) FloWise flow diverters. Multiple FloWise flow diverters were used to cover the entire vessel segment harboring multiple aneurysms (n = 14) and to bridge the proximal and distal ends of the fusiform aneurysms (n = 2). Balloon angioplasty was performed in 20 procedures to achieve adequate wall apposition (28.6%), depending on the flat-panel CT findings. During the procedures, in-stent thrombosis was detected in 7.1% of the patients; this was completely resolved by administration of a glycoprotein IIb/IIIa inhibitor (tirofiban, 0.5–1.0 mg).

Efficacy Outcomes

Sixty-nine patients were included in the efficacy analysis because the procedure was not completed in 1 patient (Fig. 1). Of the 69 patients, 10 patients had contraindications to a combination of antiplatelet agents; therefore, the per-protocol set comprised 59 patients (Fig. 1). The primary and secondary endpoints are summarized in Table 3. Assessment of the complete occlusion rate, which was the primary endpoint, was conducted in both the intent-to-treat and per-protocol sets. In the intent-to-treat set, successful occlusion (Raymond I) was achieved in 56 target aneurysms (81.2%, 95% CI: 69.9–89.6; Figs. 2-4). In the per-protocol set, complete occlusion was confirmed in 83.1% of the target aneurysms (95% CI: 71.0–91.6). In both the analysis sets, the lower limit of the 95% CI was higher than that of the reference point (56.7%, $P < 0.001$).

https://doi.org/10.3348/kjr.2024.1212

Table 2. Summary of characteristics of all treated aneurysms and procedures (n = 93)

Characteristic	Data
Side, right:left	33 (35.5):60 (64.5)
Location	
ICA cavernous	5 (5.4)
ICA ophthalmic	18 (19.4)
ICA paraclinoid	54 (58.1)
ICA PcomA	6 (6.5)
ICA AChoA	5 (5.4)
Vertebral artery V4 segment	2 (2.2)
Posterior cerebral artery P1 segment	3 (3.2)
Recurred aneurysm	4 (4.3)
s/p clipping	2 (2.2)
s/p coiling	2 (2.2)
Mean size ± SD (median; range) of all aneurysms, mm	5.7 ± 3.1 (5.2; 1.6–26.1)
Mean size ± SD (median; range) of the target aneurysms, mm	6.3 ± 3.5 (6.1; 3.5–26.1)
Neck diameter, mm	4.4 ± 2.0 (4.1; 1.2–22.4)
Dome to neck ratio <2	92 (98.9)
Volume, mm^3	1018.9 ± 4452.6 (316.5; 9.9–42989.4)
Parent artery, mm	
Proximal diameter	4.2 ± 0.6 (4.3; 2.8–5.2)
Distal diameter	3.7 ± 0.5 (3.6; 2.7–4.8)
Number of deployed stents*	
1	54 (77.1)
2	15 (21.4)
3	1 (1.4)
Balloon angioplasty*	20 (28.6)
Glycoprotein IIb/IIIa infusion*	5 (7.1)

Data are presented as number of aneurysms with percentages in parentheses, or as mean ± SD, unless otherwise specified.
*The percentage values in parentheses are calculated using 70 patients as the denominator.
SD = standard deviation, ICA = internal carotid artery, PcomA = posterior communicating artery, AChoA = anterior choroidal artery

Table 3. Summary of primary and secondary efficacy endpoints

Endpoint	Intent-to-treat set (n = 69)	Per-protocol set (n = 59)	*P*
Primary endpoint (target aneurysm occlusion)			
Success (Raymond I)	56 (81.2) [69.9–89.6]	49 (83.1) [71.0–91.6]	<0.001 for both
Failure (Raymond II or III)	13 (18.8)	10 (16.9)	
Secondary endpoint			
Procedural success	69 (100)	59 (100)	
Aneurysm volume reduction ≥50%	66 (95.7) [87.8–99.1]	57 (96.6) [88.3–99.6]	

Data are number of patients with the corresponding percentage value in parentheses and its 95% confidence interval in brackets

The technical success rate was 100%. In the 12-month follow-up angiographic evaluation, 66 target aneurysms (95.7%, 95% CI: 87.8–99.1) in the intent-to-treat analysis set and 57 target aneurysms (96.6%, 95% CI: 88.3–99.6) in the per-protocol set experienced ≥50% reduction in aneurysm volume.

Safety Outcomes

One patient experienced parent artery rupture during balloon angioplasty after FloWise deployment; this was treated with ICA sacrifice followed by bypass surgery. The patient had an mRS score of 5 at 3 months. No major ischemic stroke was observed in the ipsilateral hemisphere. No deaths occurred within 30 days. At the 12-month radiological follow-up, ≥50% parent artery stenosis was noted in 4.3% of the patients, all of whom were asymptomatic. The adverse events were classified as mild, moderate, and severe degree. Mild degree was defined as

https://doi.org/10.3348/kjr.2024.1212

Korean Journal of Radiology
KJR

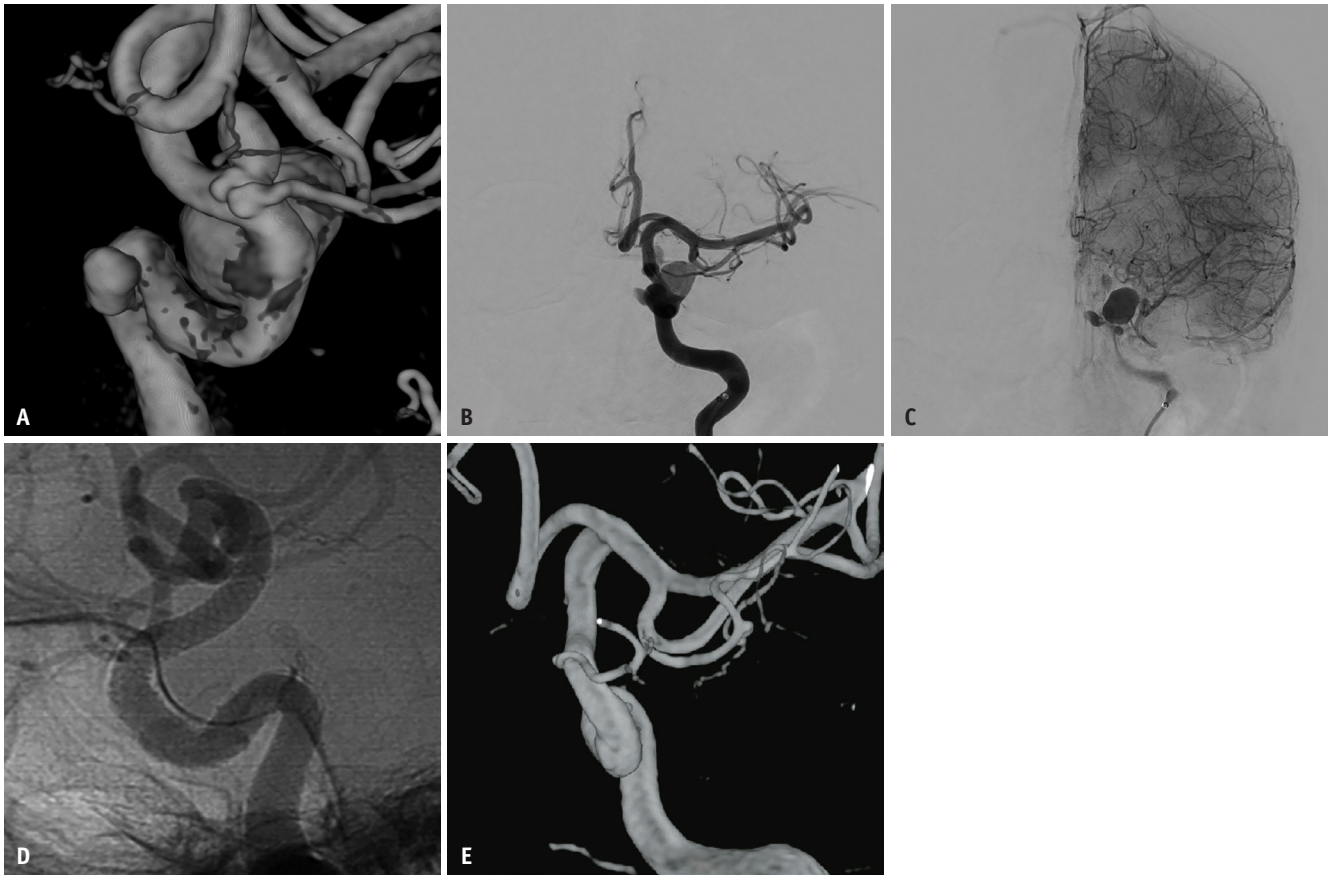

Fig. 2. A 67-year-old female with 5 aneurysms at the supraclinoid, ophthalmic, and cavernous segments of the left internal carotid artery. **A:** A 3D reconstruction image shows multiple aneurysms at the left internal carotid artery. **B:** The arterial phase image of the left carotid angiogram immediately after FloWise deployment shows markedly decreased contrast material filling in the aneurysms. **C:** The early venous phase of the left carotid angiogram reveals marked stagnation of the contrast material in the aneurysms. **D, E:** The 12-month follow-up angiogram **(D)** and 3D reconstruction **(E)** image show complete occlusion of the aneurysms with preservation of the incorporated ophthalmic artery.

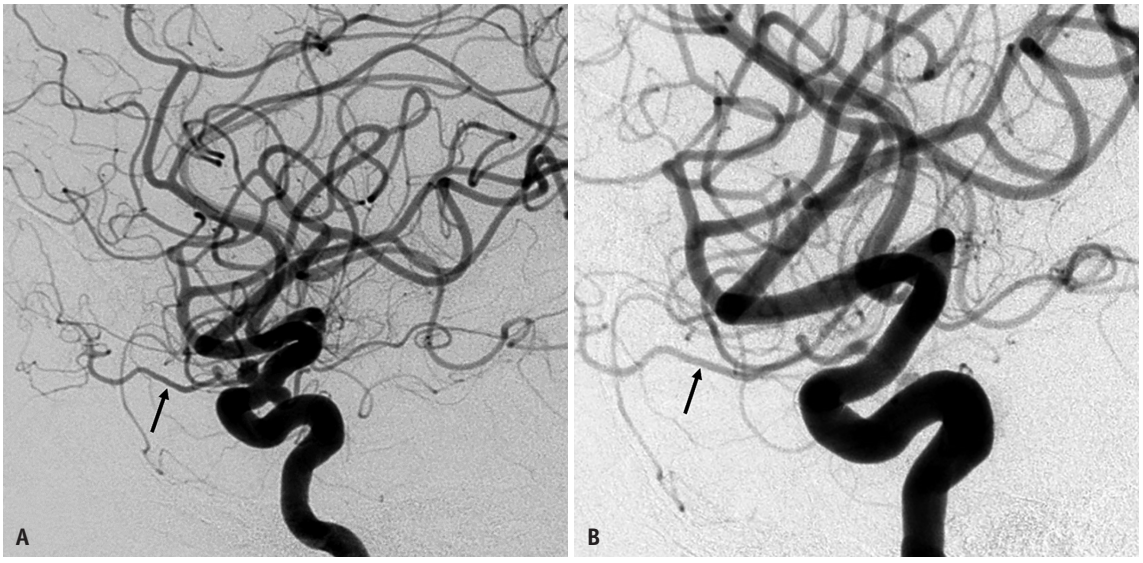

Fig. 3. A 57-year-old female with two aneurysms at the left distal internal carotid artery. **A:** Left carotid angiography shows two aneurysms, one of which incorporated the ophthalmic artery (arrow). **B:** The 12-month follow-up angiogram reveals complete occlusion of both aneurysms and a well-preserved ophthalmic artery (arrow).

https://doi.org/10.3348/kjr.2024.1212

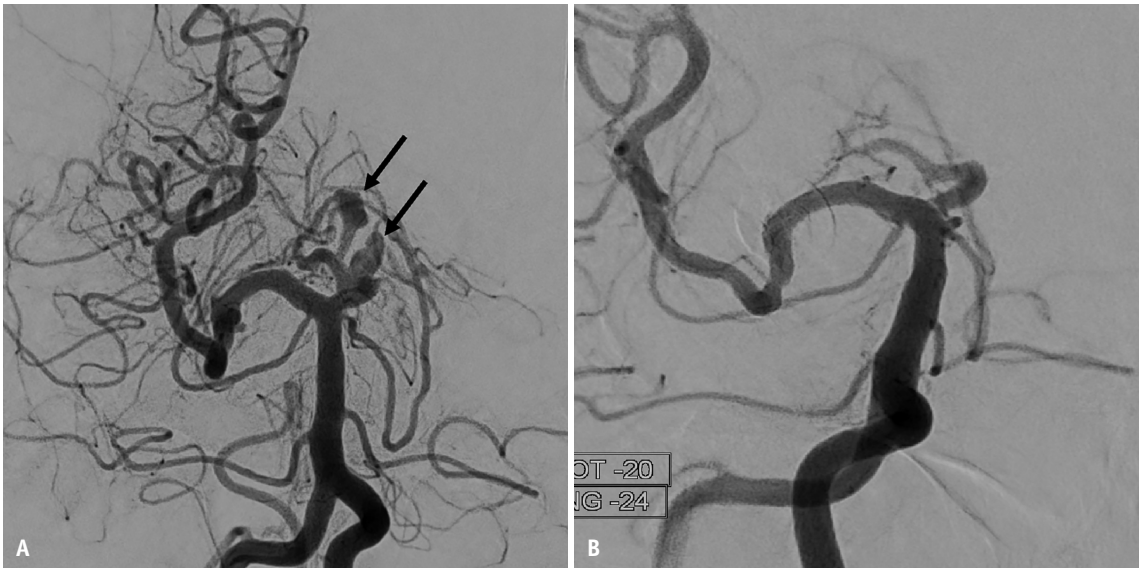

Fig. 4. A 65-year-old female with two partially thrombosed aneurysms in the left posterior cerebral artery. **A:** Vertebral artery angiogram shows two partially thrombosed aneurysms at the left posterior cerebral artery. Arrows indicate ophthalmic artery. **B:** A 12-year follow-up angiogram reveals complete occlusion of both aneurysms in the left posterior cerebral artery.

Table 4. Safety analysis (n = 70)

Adverse event	No. of patients	No. of events
Ipsilateral ischemic stroke (NIHSS score ≥5)	0	0
New neurologic deficit (mRS score ≥3)	1 (1.4)	1
30-day death	0	0
Parent artery stenosis or occlusion		
≥50% stenosis	3 (4.3)	
Occlusion	0	
Any adverse event	40 (57.1)	82
Severity		
Mild	38 (54.3)	73
Moderate	4 (5.7)	7
Severe	2 (2.9)	2
Device-related		
Not related	33 (47.1)	70
Possible	9 (12.9)	12*
Causal	0	0

Data are presented as number (%).
*Two was classified as severe degree and the remaining 10 events as mild to moderate.
NIHSS = National Institutes of Health Stroke Scale, mRS = modified Rankin Scale

events that did not disrupt the patient's daily life functions and were easily tolerable. Moderate degree was defined as events that caused the patient's daily life function to be uncomfortable. Severe degree was defined as events that rendered the patient's daily life function impossible. During the follow-up period, 82 adverse events were reported. Of these, 6 events in 6 patients were classified as serious adverse events (8.6%). Additionally, 73 events were classified as mild and 7 as moderate according to the severity definition. Seventy adverse events in 33 patients (47.1%) were adjudicated to be unrelated to the device, while 12 events in 9 patients (12.9%) were possibly related to the device (Table 4). Of the 12 possibly device-related events, 2 were classified as severe (Table 5). The most common adverse events were headache (n = 8), followed by nausea (n = 3), and skin rash (n = 1). Mild-to-moderate adverse events were completely resolved over several days with or without appropriate medication.

The 6 cases of serious adverse events are listed in Table 5. Of these, 4 events were procedure-related, and 2 were related to the device. Procedure-related events included ICA rupture during balloon angioplasty, visual impairment, visual field defects, and puncture site hematoma. Among these events, the patient with an ICA rupture did not recover (mRS score, 5), whereas another patient who complained of a visual field defect partially recovered (mRS score, 1). All the other adverse events resolved completely.

DISCUSSION

In this prospective, multicenter, single-arm, open-label, pivotal study, FloWise showed 1) complete occlusion in 81.2% of the target aneurysms and ≥50% aneurysm volume reduction at 12-month follow-up angiography in 95.7% of

https://doi.org/10.3348/kjr.2024.1212

Korean Journal of Radiology
KJR

Table 5. Summary of serious adverse events (n = 70)

Event	All	Procedure-related	Device-related	Event outcome
Any event	6 (8.6)	4 (5.7)	2 (2.9)	
ICA rupture*	1 (1.4)	Causal	Not	NR
Visual impairment	1 (1.4)	Causal	Possible	CR
Visual field defect	1 (1.4)	Causal	Possible	PR
Pancreatic cystadenoma	1 (1.4)	Not	Not	CR
Cholecystitis	1 (1.4)	Not	Not	CR
Puncture site hemorrhage	1 (1.4)	Causal	Not	CR

Data are presented as number (%).
*ICA rupture during balloon angioplasty after FloWise deployment.
ICA = internal carotid artery, NR = not recovered, CR = completely recovered, PR = partially recovered with sequelae

the target aneurysms, 2) 100% technical success rate, and 3) only one case of severe neurological deficits (1.4%), which was related to the treatment procedure (balloon angioplasty) and not to the device. These findings suggest that the FloWise flow diverter is at par with commercially available flow diverters in terms of effectiveness and safety [8-15].

Flow diverters have been developed to treat large or giant aneurysms with a wide neck or fusiform shapes [5]. Increasing evidence supports the efficacy and safety of flow diverters [11,16]. According to a recent meta-analysis including 11 long-term follow-up studies (>1 year), the complete occlusion rates were 83.5% and 85.2% in the first and third years of follow-up, respectively [17]. The retreatment rate was 5%, the in-stent stenosis rate was 4.8%, and no delayed aneurysmal rupture was identified. Another report supported procedural safety, demonstrating procedure-related morbidity and mortality rates of 5% (95% CI, 4%–7%) and 4% (95% CI, 3%–6%), respectively [18]. These results confirm that the implantation of a flow diverter yields positive results in challenging types of aneurysms compared with that via conventional coiling. Currently, flow diverters are increasingly chosen as the primary modality for almost all types of intracranial aneurysms.

In Korea, several flow diverters have been introduced, and the indications for national insurance have gradually widened. However, there are still limitations in the use of flow diverters because the Korean National Health Insurance permits reimbursement of their usage only for large-sized aneurysms (equal to or greater than 10 mm in size), mainly because of their high price, in addition to the lack of domestic data supporting their efficacy and safety. As a result, no large-scale post-market flow diverter studies involving small-sized aneurysms have been performed in the Korean population, even though small-sized aneurysms less than 10 mm in size constitute the majority of the cerebral aneurysms that have been treated. Therefore, there is a strong need for deregulation and enhanced health insurance coverage by lowering the price of flow diverters. For this purpose, we developed a new flow diverter, FloWise, and reported its promising results in an animal study and in a pilot clinical study [6,7]. The FloWise used in this study was refined in its performance and thus had low deployment and trackability forces compared with that via the commercially available flow diverters used in in-vitro studies [19]. In addition, the compatibility of FloWise was improved, and the inner diameter of the delivery microcatheter was reduced from 0.027 to 0.021 inch. These improvements may make it more convenient to perform FloWise delivery and deployment than with the use of other commercially available flow diverters.

The primary outcome was effectively achieved at the 12-month follow-up angiography, at which point the per-protocol set achieved 83.1% (49/59) and the intent-to-treat analysis set achieved 81.2% (56/69) complete occlusion rates. These results are similar to those of a previous pilot study (83.3% target occlusion rate at 12 months) [7]. These results are superior to the predefined reference values (56.7%, $P < 0.001$) and comparable to those of commercially available flow diverters [9-15]. The results of the present study are comparable to those of 2 prospective studies, which reported 1-year radiological outcomes of currently available flow diverters. The SHIELD study, a prospective, single-arm, multicenter, post-market, observational study evaluating the pipeline-shield device, showed that the primary efficacy endpoint of complete occlusion without in-stent stenosis was met in 71.7% (143/200) of the patients [20]. The SAFE study, which included 103 patients using a Flow Direction Endoluminal

 https://doi.org/10.3348/kjr.2024.1212

Device (FRED), showed that complete occlusion was observed in 66/90 aneurysms (73.3%), neck remnants were detected in 7/90 aneurysms (7.8%), and aneurysm remnants were identified in 17/90 aneurysms (18.9%) [14].

Several factors may have contributed to the favorable results of this study. First, FloWise deployment was easy and resulted in technical success in all the patients. In FloWise, the stent contact portion of the delivery wire is coated with silicon, which allows re-sheathing at any point prior to 70% deployment. Considering the parent vessel geometry and its relationship with the target aneurysm, the operators are considerably more comfortable and can easily reposition the FloWise with the distal and proximal end openings. Furthermore, FloWise can be introduced via any microcatheter with an inner diameter of 0.021 inch, which offers enhanced maneuverability and improved trackability compared with microcatheters with a larger bore. Secondly, as previously described, FloWise demonstrates a relatively high radial force, high metal coverage rate, and acceptable foreshortening [6]. These characteristics also contribute to a greater flow diversion effect. Third, flat-panel CT was performed immediately after FloWise placement in all cases. Balloon angioplasty was performed in all cases in which a gap between the FloWise and the vessel wall around the aneurysm neck was detected, and complete wall apposition was achieved around the aneurysm neck in all the cases (28.6%, 20/70). There was no significant difference in the target aneurysm occlusion rates of cases with and without balloon angioplasty. This may be because patients who did not undergo balloon angioplasty already had good wall apposition. Good wall apposition around the aneurysm neck prevented endoleaks and was eventually an important predictor of aneurysm occlusion after flow diverter treatment [21]. Finally, the mean aneurysm size in this study was smaller than that reported in previous studies, which may have improved the aneurysm occlusion rate.

In terms of safety outcomes, 6 (8.6%) serious adverse events occurred. However, only 2 (2.9%) of these events were possibly device related, and no mortality occurred. The 12-month follow-up angiography revealed ≥50% stenosis of parent artery in only 3 patients (4.3%), without any symptoms. In real-world, multicenter, North American data using the FRED, the rates of morbidity and moderate or severe in-stent stenoses were considerably higher than those reported in previous intentional studies (8.6% and 8.1%, respectively) [22]. Diversion-p64 that included the largest number of participants among flow diverter follow-up studies reported a composite morbidity and mortality rate of 2.4% (10/413), and ≥50% in-stent stenosis was observed in 3.2% (11/343) of the patients at the one-year follow-up angiography [9]. Although these results should be interpreted cautiously because of a large discrepancy in the demographics and aneurysm characteristics of included patients, these comparisons showed that the safety results of FloWise were comparable to those of other commercially available flow diverters.

This study has several limitations. An inherent limitation of the study design is that FloWise and other commercially available flow diverters were not directly compared. Therefore, we set a reference point to assess the efficacy of FloWise. However, we could only analyze its efficacy and safety in comparison with published results. The mean aneurysm size was smaller than that reported in previous studies, which may have affected the outcomes. In addition, although not intentional, multiple FloWises were used in 16 patients, and there was no difference in the target aneurysm occlusion rate between the single and multiple FloWise-usage groups. Therefore, the relatively good results of this study may have been overestimated, or could not be directly applied to the occlusion rates in larger aneurysms.

In conclusion, the FloWise flow diverter showed acceptable safety and efficacy in the treatment of unruptured intracranial aneurysms. Its performance was superior compared with the predefined reference value and comparable to that of commercially available flow diverters.

Supplement

The Supplement is available with this article at https://doi.org/10.3348/kjr.2024.1212.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: Byung Moon Kim. Data curation: Hyun Jin Han, Byung Moon Kim. Formal analysis: Hyun Jin Han, Byung Moon Kim. Funding acquisition: Byung Moon Kim.

Korean Journal of Radiology
KJR

Investigation: Hyun Jin Han, Kyu Seon Chung, Solbi Kim, Sun Yoon, Min Jeoung Kim. Methodology: Byung Moon Kim. Project administration: Byung Moon Kim. Resources: Keun Young Park, Yong Bae Kim, Hong-Jun Jeon, Sang Hyun Suh, Sangil Suh, Jung-Jae Kim, Jun-Hwee Kim, Chang Ki Jang, Dong Joon Kim, Sunghan Kim. Software: Hyun Jin Han, Byung Moon Kim. Supervision: Byung Moon Kim. Validation: Keun Young Park, Byung Moon Kim. Visualization: Byung Moon Kim. Writing—original draft: Hyun Jin Han. Writing—review & editing: all authors.

ORCID IDs
Hyun Jin Han
https://orcid.org/0000-0002-4111-4819
Keun Young Park
https://orcid.org/0000-0002-3254-4577
Byung Moon Kim
https://orcid.org/0000-0001-8593-6841
Yong Bae Kim
https://orcid.org/0000-0003-2262-7157
Hong-Jun Jeon
https://orcid.org/0000-0001-7370-1324
Sang Hyun Suh
https://orcid.org/0000-0002-7098-4901
Sangil Suh
https://orcid.org/0000-0001-8933-0492
Jung-Jae Kim
https://orcid.org/0000-0002-4669-8577
Jun-Hwee Kim
https://orcid.org/0000-0002-0259-5795
Chang Ki Jang
https://orcid.org/0000-0001-8715-8844
Dong Joon Kim
https://orcid.org/0000-0002-7035-087X
Jung Keun Lee
https://orcid.org/0000-0003-1711-0698
Sunghan Kim
https://orcid.org/0000-0001-9384-7427
Kyu Seon Chung
https://orcid.org/0009-0008-0538-6025
Solbi Kim
https://orcid.org/0000-0003-2252-4262
Sun Yoon
https://orcid.org/0000-0001-7652-7835
Min Jeoung Kim
https://orcid.org/0000-0003-0195-4431

Funding Statement
This work was supported by the Korea Medical Device Development Fund grant funded by the Korea government (the Ministry of Science and ICT, the Ministry of Trade, Industry and Energy, the Ministry of Health & Welfare, the Ministry of Food and Drug Safety) (Project number: RS-2020-KD000220, KMDF_PR_20200901_0220-2021-01) (NTIS, KMDF-RnD 1711174479).

REFERENCES

1. Gruber A, Killer M, Bavinzski G, Richling B. Clinical and angiographic results of endosaccular coiling treatment of giant and very large intracranial aneurysms: a 7-year, single-center experience. *Neurosurgery* 1999;45:793-803; discussion 803-804
2. Lim YC, Kim BM, Suh SH, Jeon P, Kim SH, Ihn YK, et al. Reconstructive treatment of ruptured blood blister-like aneurysms with stent and coil. *Neurosurgery* 2013;73:480-488
3. Sluzewski M, Menovsky T, van Rooij WJ, Wijnalda D. Coiling of very large or giant cerebral aneurysms: long-term clinical and serial angiographic results. *AJNR Am J Neuroradiol* 2003;24:257-262
4. Wakhloo AK, Mandell J, Gounis MJ, Brooks C, Linfante I, Winer J, et al. Stent-assisted reconstructive endovascular repair of cranial fusiform atherosclerotic and dissecting aneurysms: long-term clinical and angiographic follow-up. *Stroke* 2008;39:3288-3296
5. Becske T, Kallmes DF, Saatci I, McDougall CG, Szikora I, Lanzino G, et al. Pipeline for uncoilable or failed aneurysms: results from a multicenter clinical trial. *Radiology* 2013;267:858-868
6. Kim BM, Kim DJ, Kim DI. A new flow-diverter (the FloWise): in-vivo evaluation in an elastase-induced rabbit aneurysm model. *Korean J Radiol* 2016;17:151-158
7. Kim BM, Park KY, Lee JW, Chung J, Kim DJ, Kim DI. A newly-developed flow diverter (FloWise) for internal carotid artery aneurysm: results of a pilot clinical study. *Korean J Radiol* 2019;20:505-512
8. Bonafe A, Perez MA, Henkes H, Lylyk P, Bleise C, Gascou G, et al. Diversion-p64: results from an international, prospective, multicenter, single-arm post-market study to assess the safety and effectiveness of the p64 flow modulation device. *J Neurointerv Surg* 2022;14:898-903
9. Booth TC, Bassiouny A, Lynch J, Sonwalkar H, Bleakley A, Iqbal A, et al. Outcome study of the Pipeline Vantage Embolization Device (second version) in unruptured (and ruptured) aneurysms (PEDVU(R) study). *J Neurointerv Surg* 2024;16:1136-1144
10. Issa R, Al-Homedi Z, Syed DH, Aziz W, Al-Omari B. Surpass evolve flow diverter for the treatment of intracranial aneurysm: a systematic review. *Brain Sci* 2022;12:810
11. Kallmes DF, Brinjikji W, Cekirge S, Fiorella D, Hanel RA, Jabbour P, et al. Safety and efficacy of the pipeline embolization device

for treatment of intracranial aneurysms: a pooled analysis of 3 large studies. *J Neurosurg* 2017;127:775-780
12. Kallmes DF, Hanel R, Lopes D, Boccardi E, Bonafé A, Cekirge S, et al. International retrospective study of the pipeline embolization device: a multicenter aneurysm treatment study. *AJNR Am J Neuroradiol* 2015;36:108-115
13. Pierot L, Spelle L, Berge J, Januel AC, Herbreteau D, Aggour M, et al. SAFE study (safety and efficacy analysis of FRED embolic device in aneurysm treatment): 1-year clinical and anatomical results. *J Neurointerv Surg* 2019;11:184-189
14. Vollherbst DF, Lücking H, DuPlessis J, Sonnberger M, Maurer C, Kocer N, et al. The FRESH study: treatment of intracranial aneurysms with the new FRED X flow diverter with antithrombotic surface treatment technology—first multicenter experience in 161 patients. *AJNR Am J Neuroradiol* 2023;44:474-480
15. Zhang Y, Huang QH, Fang Y, Yang P, Xu Y, Hong B, et al. A novel flow diverter (Tubridge) for the treatment of recurrent aneurysms: a single-center experience. *Korean J Radiol* 2017;18:852-859
16. Zhou G, Su M, Zhu YQ, Li MH. Efficacy of flow-diverting devices for cerebral aneurysms: a systematic review and meta-analysis. *World Neurosurg* 2016;85:252-262
17. Shehata MA, Ibrahim MK, Ghozy S, Bilgin C, Jabal MS, Kadirvel R, et al. Long-term outcomes of flow diversion for unruptured intracranial aneurysms: a systematic review and meta-analysis. *J Neurointerv Surg* 2023;15:898-902
18. Brinjikji W, Murad MH, Lanzino G, Cloft HJ, Kallmes DF. Endovascular treatment of intracranial aneurysms with flow diverters: a meta-analysis. *Stroke* 2013;44:442-447
19. Jun YJ, Hwang DK, Lee HS, Kim BM, Park KD. Flow diverter performance comparison of different wire materials for effective intracranial aneurysm treatment. *Bioengineering (Basel)* 2024;11:76
20. Rice H, Martínez Galdámez M, Holtmannspötter M, Spelle L, Lagios K, Ruggiero M, et al. Periprocedural to 1-year safety and efficacy outcomes with the pipeline embolization device with Shield technology for intracranial aneurysms: a prospective, post-market, multi-center study. *J Neurointerv Surg* 2020;12:1107-1112
21. Shapiro M, Becske T, Nelson PK. Learning from failure: persistence of aneurysms following pipeline embolization. *J Neurosurg* 2017;126:578-585
22. Khorasanizadeh M, Shutran M, Schirmer CM, Salem MM, Ringer AJ, Grandhi R, et al. North American multicenter experience with the flow redirection endoluminal device in the treatment of intracranial aneurysms. *J Neurosurg* 2022;138:933-943

https://doi.org/10.3348/kjr.2024.1212