Treatment of Unruptured Small and Medium-Sized Wide Necked Aneurysms Using the 64-Wire Surpass Evolve: A Subanalysis From the SEASE International Registry

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ORIGINAL RESEARCH

Treatment of Unruptured Small and Medium-Sized Wide Necked Aneurysms Using the 64-Wire Surpass Evolve: A Subanalysis From the SEASE International Registry

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BACKGROUND: Flow diversion has revolutionized the management of wide-necked intracranial aneurysms (IAs). We aimed to assess the effectiveness and safety of the new generation 64-wire Surpass Evolve for the treatment of unruptured small/medium-sized IAs.

METHODS AND RESULTS: This is a subanalysis from the SEASE (Safety and Effectiveness Assessment of the Surpass Evolve) registry, an observational cohort study including 15 academic institutions in North America and Europe between July 2020 and October 2022. Patients with wide-necked saccular IAs, measuring <12 mm along the internal carotid artery and vertebrobasilar system, and treated with the Surpass Evolve were included. Primary effectiveness was complete occlusion (Raymond-Roy class 1) at follow-up (core laboratory adjudicated), and primary safety was major stroke (ischemic/hemorrhagic) in the territory supplied by the target artery or death. A total of 129 cases with 135 IAs were included (median age 59 years, 85.3% women). Median maximum IAs size and neck size were 5.1 and 3.9 mm, respectively. Most IAs were in the internal carotid artery C6 (65.9%, 89/135) and C7 (14.1%, 19/135) segments. At a median follow-up time of 10.2 months (interquartile range, 6.4–12.8), complete occlusion was 77.1% (101/131), ≥50% in-stent stenosis was 8.8% (11/125), and retreatment was 0.8% (1/125). Major stroke and mortality were reported in 2 (1.6%) patients and 1 (0.8%) patient, respectively. Size was the only factor associated with higher odds of incomplete occlusion (adjusted odds ratio, 1.2 [95% CI, 1.02–1.5]; *P*=0.03).

CONCLUSIONS: Patients with small/medium-sized IAs can be effectively treated using the Surpass Evolve, a new generation, 64-wire, cobalt-chromium flow diverter.

Key Words: flow diversion ■ intracranial aneurysm ■ medium ■ small ■ Surpass Evolve

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CLINICAL PERSPECTIVE

What Is New?

- This is the first multicenter study to investigate the outcomes of the 64-wire Surpass Evolve for the treatment of small/medium-sized intracranial aneurysms.
- Complete occlusion was achieved in 77.1% (101/131) of small/medium-sized intracranial aneurysms at a median follow-up time of 10.2 months.
- Major stroke and mortality were reported in 2 (1.6%) patients and 1 (0.8%) patient, respectively, whereas retreatment was needed in 1 patient only.

What Are the Clinical Implications?

- A 64-wire Surpass Evolve can be effectively and safely used to treat small/medium-sized IAs.

Nonstandard Abbreviations and Acronyms

DSA	digital subtraction angiography
FD	flow diverter
IA	intracranial aneurysm
ICA	internal carotid artery
mRS	modified Rankin Scale
OKM	O'Kelly-Marotta
PED	pipeline embolization device
PREMIER	Prospective Study on Embolization of Intracranial Aneurysms With Pipeline Device
SE	Surpass Evolve
SEASE	Safety and Effectiveness Assessment of the Surpass Evolve

The management of wide-necked intracranial aneurysms (IAs) is technically challenging and has led to the development of several novel endovascular devices to manage these lesions.[1,2] Specifically, the emergence and approval of flow diverters (FDs) by the Food and Drug Administration in 2011 marked a fundamental change in the conceptual understanding of how wide-necked IAs can be treated.[3] Several high-quality studies initially demonstrated their safe and effective profile for the treatment of large/giant IAs. Because most IAs in clinical practice are small/medium-sized,[4,5] several studies evaluated the performance of FDs in small/medium-sized IAs, showing promising results.

The PREMIER (Prospective Study on Embolization of Intracranial Aneurysms With the Pipeline Device) study was the first to demonstrate high rates of complete obliteration of small/medium-sized IAs after implantation of the 48-wire cobalt-chromium pipeline embolization device (Medtronic).[6] This was followed by a progressive evolution and development of various nitinol-based FDs to further target this population.[7–10] In 2019, the cobalt-chromium Surpass Evolve (SE; Stryker) was introduced as an upgraded low-profile iteration of the Surpass Streamline, offering a cobalt-chromium 64-wire to provide a consistent mesh density that ensures a more even effect on flow reduction. The initial experience with the SE for the treatment of 26 wide-necked IAs, 17 of which were small/medium-sized, showed promising results with an overall occlusion of 57% at a short median follow-up of 4 months.[11] There are limited long-term data evaluating the outcome of SE for the treatment of these IAs. This study aimed to evaluate the safety and effectiveness of the SE in the treatment of wide-necked small/medium-sized IAs, located along the internal carotid artery (ICA) and the vertebrobasilar system, using data from an international, multicenter real-world registry.

METHODS

Data generated or analyzed during the study are available from the corresponding author upon reasonable request.

Study Selection

This is a subanalysis from the SEASE (Safety and Effectiveness Assessment of the Surpass Evolve) registry, a single-arm, retrospective, observational, multicentric international cohort study involving 15 academic institutions in North America and Europe between July 2020 and October 2022. This study focused on all consecutive adult patients (≥18 years of age) who underwent SE implantation for wide-necked (neck ≥4 mm or dome/neck <2 mm) saccular IAs, measuring ≤12 mm in size along the ICA segments and vertebrobasilar system up to the junction. IAs that were ruptured or previously treated were excluded from the analysis (Figure 1). Institutional review board approval was obtained at all the participating centers, and informed consent was waived because the study was purely observational. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[12]

Data Collection and Core Laboratory Adjudication

The following data were collected by the enrolled centers: demographics and patient characteristics (age,

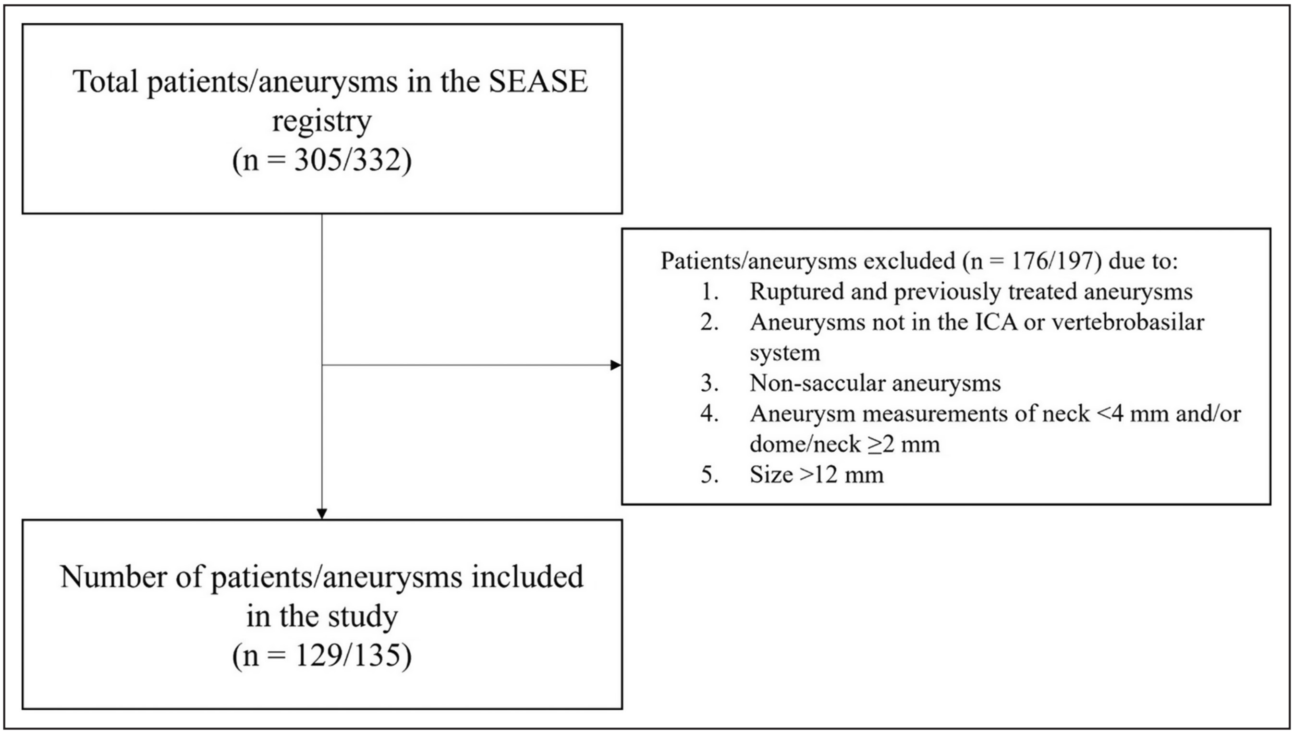

Figure 1. Flowchart for the patients and aneurysms included in this study.
ICA indicates internal carotid artery; and SEASE, Safety and Effectiveness Assessment of the Surpass Evolve.

sex, smoking, comorbidities, and baseline modified Rankin Scale [mRS] score), peri- and postprocedural treatment details (access site, number/size of FDs implanted, and posttreatment antiplatelet and anticoagulation regimen), intrahospital complications, and follow-up assessments (ischemic/hemorrhagic events, mRS, retreatment, and mortality).

Central imaging laboratory assessment with 2 independent imaging reviewers blinded to the outcome adjudicated the procedural and follow-up radiographic outcomes: IA characteristics (number, location, morphology, maximum size, neck size, and the presence of a vessel branch arising from dome/neck), vessel dimensions (proximal and distal landing zones), intraprocedural use of balloon-assisted angioplasty or adjunctive coils or stents, IA occlusion status at last follow-up, and the parent artery status at follow-up. Any disagreements were solved by discussion until consensus was achieved.

Study Device and Procedural Strategy

The SE is a braided cobalt-chromium alloy that is made of 48 and 64 wires based on its diameter (2.5 and 3.25–5 mm, respectively). It also has a high braid angle that preserves its consistent diamond cell shape and high mesh density (15–32 pores/mm^2). In this study, the 64-wire SE was used for all patients. Briefly, the 64-wire SE is deployed through a 0.027-inch microcatheter due to its low profile and expands immediately upon emerging from the microcatheter. The distal portion is identifiable through the presence of 2 markers and is safeguarded by a Teflon petal. It features a radiopaque distal tip wire measuring 15 mm in length. A third marker designates the limit for resheathing, which is feasible until 90% of the FDs remain unsheathed. Lastly, it can expand to a maximum of 0.2 mm beyond its nominal diameter.[11]

The implantation of the SE was performed following the established protocols as outlined in existing literature and in accordance of the manufacturer's directions (Tables S1 and S2), with minor potential deviations dependent on the specific treating center and proceduralist's preferences.[11,13,14] All procedures were performed under general anesthesia, and the choice of access (femoral or radial) and intraprocedural heparinization or administration of IIb/IIIa inhibitors was as per the operator's preference. The use of adjunctive treatments including coiling, balloon-assisted angioplasty, or stenting was based on the individual treating operator's preference.

Dual Antiplatelet Therapy and Follow-Up Assessments

The preprocedural and postprocedural administration of antiplatelet and anticoagulation regimens were left to the discretion of the interventionalists (Table S3). In most cases, patients would initiate a dual antiplatelet therapy regimen before the procedure (5–7 days). This regimen included aspirin (maintained for at least

6 months postprocedure), in addition to either clopidogrel, prasugrel, or ticagrelor (maintained at least 6 months postprocedure).

The follow-up time for clinical and angiographic outcomes was determined according to the protocol of each center. Clinical assessments for ischemic/hemorrhagic events and mRS score were performed at discharge, 3 months, 6 months, and 1 year. Angiographic evaluations were performed with digital subtraction angiography (DSA), magnetic resonance angiography, or computed tomography angiography at 6 months and 1 year as per the usual practice at each center. Retreatment of the target IAs was also collected. The decision to retreat was at the discretion of the operator.

Study Outcomes

The primary effectiveness outcome was IA occlusion (without retreatment) at the last follow-up, adjudicated by neuroimaging experts at the core laboratory. Complete occlusion was considered by Raymond-Roy class 1.[15] Secondary effectiveness outcomes included final follow-up mRS score, worsening in mRS score between baseline and final follow-up, and occlusion using the O'Kelly-Marotta (OKM) class D[16] on patients with DSA only at follow-up. Additionally, the parent vessel flow status at follow-up was extracted by the core laboratory and classified as no stenosis, <50% stenosis, ≥50% stenosis, and complete occlusion.

The primary safety end point was the occurrence of major strokes (ischemic or hemorrhagic) within the territory supplied by the target vessel or procedure-related deaths within a 1-year timeframe. A major stroke was defined as an increase of at least 4 points on the National Institutes of Health Stroke Scale score. Secondary safety outcomes encompassed minor procedure-related incidents within 30 days postimplantation, including complications at the access site and minor neurological events characterized by a transient change of <4 points on the National Institutes of Health Stroke Scale score within 24 hours. Moreover, mortality related and unrelated to the SE implantation was also collected.

Statistical Analysis

Statistical analysis was conducted using the packages table 1 and lme4 through R version 4.3.2 (R Foundation for Statistical Computing) software. Continuous variables were expressed by the median and interquartile range (IQR) and compared using the Mann-Whitney *U* test. Categorical variables were presented as frequencies with percentages and compared using the χ^2 or Fisher exact test, as appropriate. Univariable and multivariable mixed effects binary logistic regression models to account for treatment heterogeneity between centers were used to identify IA characteristics that were significantly associated with incomplete occlusion and to calculate the adjusted odds ratio (aOR) and 95% CI. Variables that were significant to $P<0.15$ in the univariable analysis were included in the multivariable model. Detection of multicollinearity was done using the Spearman rank correlation and variance inflation factors, and variables that had high variance inflation factors were excluded from the final model. All tests were 2-sided, and *P* values <0.05 were considered statistically significant.

RESULTS

Characteristics of Patients and IAs

This study included 129 patients with 135 unruptured small/medium-sized wide-necked IAs. The median age of patients was 59 years (IQR, 51–67 years), 85.3% (110/129) were women, 39.1% were smokers, and 40.6% had hypertension. Table 1 describes the details of the patient and IA characteristics. The majority of the patients had a baseline mRS score 0 to 2 (122/127, 96.1%), and only 6 (4.7%) patients had 2 IAs in the parent vessel.

The SE was most used to treat IAs located in the C6 ophthalmic artery (65.9%, 89/135), followed by the C7 communicating artery (14.1%, 19/135). The median maximum sizes of the IAs, along with the sizes of the neck and dome to neck ratio, were 5.1 mm (IQR, 3.6–7.2 mm), 3.9 mm (IQR, 2.9–5.1 mm), and 1.2 mm (IQR, 1.0–1.6 mm), respectively. A vessel branch arising from the IAs' neck or dome was found in 3 (2.3%) and 7 (5.4%) IAs, respectively. The vessel diameters are presented in Table S4.

SE Procedures

Details of the SE procedures are reported in Table 2. Successful implantation of the SE was done in 100% (129/129) of patients. A single SE was deployed in most of the patients (93.8%, 121/129) through the femoral access (75.2%, 97/129). Of those who had >1 SE deployed, all patients had a single IA that was mostly located in the C6 ophthalmic artery (75.0%, 6/8). Balloon-assisted angioplasty was performed in 58 (45.0%) patients. A comparison of baseline characteristics and outcomes between those who had balloon-assisted angioplasty and those who did not is shown in Table S5. In addition, adjunctive coiling was done in 6 (4.7%) patients, whereas 3 (2.3%) patients had stenting. Of those who had stenting, 2 had poor wall apposition in the midportion that did not respond to angioplasty, whereas 1 had proximal braid collapse. All patients continued to receive a dual antiplatelet regimen for up to 6 months postprocedure, with the most common combination being aspirin and clopidogrel (65.6%, 84/129).

Table 1. Patient and Aneurysm Characteristics

Characteristics	Values
Patients (n=129)	
Age, y, median [IQR]	59.0 [51.0–67.0]
Women	110 (85.3%)
Baseline mRS score	
0–2	122 (96.1%)
3–4	5 (3.9%)
Comorbidities	
Hypertension	52 (40.6%)
Hyperlipidemia	43 (33.6%)
Diabetes	11 (8.6%)
Coronary arterial disease	5 (3.9%)
Stroke or transient ischemic attack	19 (14.8%)
Smoking (current or past)	50 (39.1%)
Patients with >1 aneurysm	6 (4.7%)
Aneurysms (n=135)	
Location	
Anterior circulation	
ICA C6 ophthalmic segment	89 (65.9%)
ICA C7 communicating segment	19 (14.1%)
ICA C4 cavernous segment	15 (11.1%)
ICA C5 clinoid segment	8 (5.9%)
ICA C2 petrous segment	2 (1.5%)
Vertebrobasilar	2 (1.5%)
Dimensions, mm, median [IQR]	
Maximum size	5.1 [3.6–7.2]
Aneurysm neck	3.9 [2.9–5.1]
Dome-to-neck ratio	1.2 [1.0–1.6]
Branch arising from aneurysm	
Neck	3 (2.3%)
Dome	7 (5.4%)

ICA indicates internal carotid artery; IQR, interquartile range; and mRS, modified Rankin Scale.

Effectiveness Outcomes and Predictors of Incomplete Occlusion

The primary and secondary outcomes are summarized in Table 3. In regard to the primary effectiveness outcome, of the 125 patients who had imaging follow-up at a median time of 10.2 months (IQR, 6.4–12.8 months), the core laboratory-adjudicated complete occlusion rate was 77.1% (101/131, Figure 2). In terms of the secondary effectiveness outcome, the complete occlusion rate measured by the OKM class D on DSA exclusively was 75.5% (74/98). The majority of patients exhibited an mRS score of 0 to 2 (96.8%, 122/126) during their last clinical follow-up, and worsening in mRS baseline score was only observed in 2.4% (3/125).

IA characteristics and their association with occlusion status at the last follow-up are illustrated in Table 4. After adjusting for confounders, larger size was significantly associated with higher odds of incomplete occlusion at follow-up (aOR, 1.2 [95% CI, 1.02–1.5]; P=0.03). For every 0.1-mm increase in IA diameter, the odds of experiencing incomplete occlusion increased by 1.2 times.

Safety Outcomes

Major stroke (ischemic/hemorrhagic) was observed in 2 (1.6%) patients. One of those afflicted patients received aspirin and prasugrel and had left-sided embolic strokes with right-sided weakness during hospitalization, whereas the other had an ischemic stroke in the territory of the parent vessel of the target IA. The latter patient was on aspirin and clopidogrel and died 33 days after the SE procedure. The overall procedure-related mortality rate in this study was 0.8%.

Other secondary complications included access-site complications (1, 0.8%), minor stroke (5, 4.0%), and unrelated mortality (1, 0.8%) due to lung cancer. Retreatment was needed in 1 (0.8%) patient, whereas 11 (8.8%) had ≥50% stenosis and 7 (5.6%) had fish-mouthing at follow-up. A comparison of the rates of stenosis between the antiplatelet regimens is shown in Table S6. There were no significant differences in rates of stenosis on the antiplatelet regimen.

DISCUSSION

Our study presents a focused subanalysis of the SEASE registry, an international, multicenter, real-world investigation into the angiographic and clinical

Table 2. Procedural Characteristics

Characteristics	Values
Successful SE implantation	129 (100%)
Access	
Femoral	97 (75.2%)
Radial	32 (24.8%)
Cases with >1 SE implanted	8 (6.2%)
Balloon-assisted angioplasty	58 (45.0%)
Adjunctive treatments	
Coils	6 (4.7%)
Stent	3 (2.3%)
Intraprocedural IIb/IIIa inhibitor use	10 (7.8%)
Postprocedural antiplatelet regimens*	
Aspirin + clopidogrel	84 (65.6%)
Aspirin + prasugrel	12 (9.4%)
Aspirin + ticagrelor	31 (24.2%)
Other (clopidogrel + cilostazol)	1 (0.8%)

SE indicates Surpass Evolve.

*Anticoagulation was additionally given to 4 patients due to other medical reasons.

Table 3. Safety and Effectiveness Outcomes

Characteristics	Values
Primary outcomes	
Effectiveness	
Complete occlusion (RR 1)*	101 (77.1%)
Safety	
Major stroke (ischemic/hemorrhagic)	2 (1.6%)
Procedure-related mortality	1 (0.8%)
Secondary outcomes	
Effectiveness	
Follow-up mRS score	
0–2	122 (96.8%)
3–6	4 (3.2%)
Worsening from mRS score from baseline	3 (2.4%)
Complete occlusion on DSA (OKM D)†	74 (75.5%)
Safety	
Access site complications	3 (2.3%)
Minor stroke	5 (3.9%)
Unrelated mortality	1 (0.8%)
Additional outcomes	
Retreatment	1 (0.8%)
Parent vessel stenosis at follow-up	
No stenosis	91 (72.8%)
<50% stenosis	23 (18.4%)
≥50% stenosis	11 (8.8%)
Fish-mouthing	
Intraoperative‡	11 (8.5%)
At follow-up‡	7 (5.6%)
Follow-up characteristics	
Time to follow-up, mo, median [IQR]	10.2 [6.4–12.8]
Type of imaging modality	
DSA	94 (75.2%)
MRA	19 (15.2%)
CTA	12 (9.6%)

CTA indicates computed tomography angiography; DSA, digital subtraction angiography; IQR, interquartile range; MRA, magnetic resonance angiography; mRS, modified Rankin Scale; OKM, O'Kelly-Marotta; and RR, Raymond-Roy.

*N=131 aneurysms from 125 patients.

†N=98 aneurysms from 94 patients had DSA at follow-up.

‡Proximal/distal flow diverter end ≥50%: 1 intraoperatively and 2 at follow-up.

outcomes associated with the use of the new 64-wire SE for the treatment of IAs. This analysis specifically evaluates the effectiveness and safety of the 64-wire SE in treating small/medium-sized wide-necked IAs located at the ICA or the vertebrobasilar system. Our results demonstrate that the 64-wire SE is associated with high rates of complete occlusion, confirming its effectiveness in occluding IAs and preventing further blood flow into the IA sac. Equally important, the device exhibited a favorable safety profile, characterized by low rates of major ischemic/hemorrhagic stroke, mortality, and the need for retreatment.

Our effectiveness outcomes suggest that the 64-wire SE is a highly effective option for patients with small/medium-sized wide-necked IAs in critical intracranial locations. Our overserved core laboratory-adjudicated complete occlusion rate of 77.1% notably surpasses the initial self-adjudicated rate of 57% reported by Orru et al[11] and underscores the 64-wire SE's effectiveness. This high occlusion rate is attributed to the treatment of smaller IAs (average size 5.1 versus 7.5 mm in previous reports) and a longer duration of angiographic follow-up (10.2 months), which provides a more comprehensive assessment of the device's effectiveness. More importantly, our results remain consistent when obliterations are evaluated in patients with DSA follow-up exclusively using the dynamic OKM class D scale.[16] In those patients, the complete occlusion rate measured by the OKM class D scale on DSA exclusively was 75.5% (74/98), confirming that results are consistent, independent of the methodology used, and suggesting that noninvasive imaging might be suitable to evaluate effectiveness in those patients.

Our study's occlusion rate slightly exceeds the rate reported by a previous meta-analysis (75%) for different FDs in small/medium-sized IAs.[17] Additionally, the SE's effectiveness is consistent with previous studies using a pipeline embolization device to treat small/medium-sized IAs (70%–91.7%).[2,18–24] A particular noteworthy comparison is with the PREMIER study, a prospective core laboratory-adjudicated single-arm study with the exact inclusion criteria, where we found similar complete occlusion rates between our 64-wire SE and the 48-wire pipeline embolization device (77.1% versus 76.8%).[6] Moreover, when examining studies involving nitinol-based FD studies that included a similar population of predominantly small/medium-sized wide necked IAs, our observed complete obliteration rates were higher than in the SAFE (Safety and efficacy Analysis of FRED Embolic device in aneurysm treatment) trial)[10] (77.1% versus 73.3%), which studied the outcomes for the flow direction endoluminal device, and lower than the Diversion-p64 trial[25] (76.5% versus 83.7%), which studied the outcomes for the p64 device (Table 5). Finally, our study also reinforces the concept that among small/medium-sized IAs, the greater the size, the lower the chances of complete occlusion rate, regardless of their location, when using the SE.

The low rates of major ischemic/hemorrhagic stroke (1.6%) as well as mortality (0.8%) underscore the safety profile of the SE for treating small/medium-sized wide-necked IAs, aligning with previously reported findings in the literature.[11] These rates were also similar to the combined major morbidity and mortality rate reported

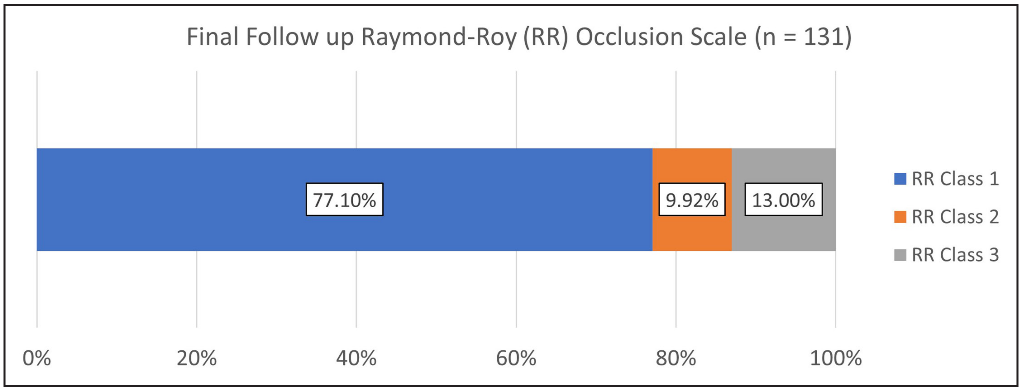

Figure 2. RR occlusion scale.
RR indicates Raymond-Roy.

by the PREMIER[6] study for the pipeline embolization device (2.1%) and was lower than the composite safety outcome (7.8%) reported by Fiorella et al.[17] Compared with the SCENT (Surpass Intracranial Aneurysm Embolization System Pivotal Trial to Treat Large or Giant Wide Neck Aneurysms) trial for the Surpass Streamline device, which included larger (>12 mm) IAs,[26] our study's safety outcomes were more favorable, further emphasizing the SE's applicability to a broader range of IA sizes with a high safety margin. As compared with the p64 device in the Diversion-p64 trial, our SE was associated with similar rates of major stroke (1.6% versus 1.9%) and mortality (0.8% versus 1.0%).[25] This supports not only an adequate effectiveness but also the high safety profile of the 64-wire SE for the treatment of small/medium-sized IAs comparable with other available flow diverters.

Notably, our study observed higher rates of parent vessel stenosis, with <50% and ≥50% stenosis occurring in 18.4% and 8.8% of patients, respectively. The rates of the ≥50% stenosis of the parent vessel

Table 4. Aneurysm Characteristics of Incompletely Occluded Aneurysms at Last Follow-Up

Characteristics	Complete	Incomplete		Univariable	Multivariable*
Aneurysms (n=131)	(n=101)	(n=30)	*P* value	Odds ratio (95% CI), *P* value	Odds ratio (95% CI), *P* value
Location					
Anterior circulation					
ICA C6 ophthalmic segment	63 (62.4%)	24 (80.0%)	0.506	Reference	
ICA C7 communicating segment	14 (13.9%)	4 (13.3%)		0.8 (0.2–2.3), *P*=0.64	
ICA C4 cavernous segment	12 (11.9%)	2 (6.7%)		0.4 (0.1–1.8), *P*=0.30	
ICA C5 clinoid segment	8 (7.9%)	0 (0%)		NA	
ICA C2 petrous segment	2 (2.0%)	0 (0%)		NA	
Basilar	2 (2.0%)	0 (0%)		NA	
Dimensions, mm, median [IQR]					
Maximum size	4.7 [3.4–6.5]	6.4 [4.2–9.3]	0.01	1.3 (1.1–1.5), *P*<0.001	1.2 (1.02–1.5), *P*=0.03
Aneurysm neck	3.4 [2.72–4.7]	4.4 [3.6–6.6]	0.002	1.4 (1.1–1.80), *P*=0.003	
Dome-to-neck ratio	1.2 [1.0–1.6]	1.2 [1.1–1.5]	0.523	2.10 (0.7–6.0), *P*=0.16	
Branch arising from aneurysm					
No	93 (93.9%)	22 (84.6%)	0.214	Reference	Reference
Yes	6 (6.1%)	4 (15.4%)		2.8 (0.7–10.7), *P*=0.13	2.4 (0.6–9.8), *P*=0.21

ICA indicates internal carotid artery; IQR, interquartile range; and NA, not applicable.
*Mixed-effects binary logistic regression was conducted for variables significant to *P*<0.15. Aneurysm neck was not included due to collinearity.

Table 5. Comparison With Other Reports That Studied Flow Diversion for Predominantly Small and Medium-Sized Wide-Necked Intracranial Aneurysms

Characteristics	Meta-analysis (Fiorella et al)[17]	PREMIER (Hanel et al)[6]	SAFE (Pierot et al)[10*]	Our results
No. of patients/aneurysms	2614 patients	141/141	103/103	129/135
Device	Multiple	PED	FRED	SE
Follow-up time, mo	12	12	Mean: 14.7	Median: 10.2
Complete occlusion	74.9%	76.8%	73.3%	77.1%
Composite safety (major stroke/mortality)	7.8%	2.1%	4.9%	2.3
In-stent stenosis 50%	NA	2.9%	2.2%	8.8%

*31% of the aneurysms had size >10 mm.

FRED indicates flow direction endoluminal device; NA, not applicable; PED, pipe embolization device; PREMIER, Prospective Study on Embolization of Intracranial Aneurysms With the Pipeline Device; SAFE, Safety and efficacy Analysis of FRED Embolic device in aneurysm treatment; and SE, Surpass Evolve.

in this study were higher than what is reported in the PREMIER (2.9%)[6] and SAFE (2.2%)[10] trials. Of importance, none of those patients who had ≥50% stenosis of the parent vessel in this study were reported to have major stroke or required additional endovascular treatments at follow-up. Only 3 patients with stenosis of the parent vessel had minor strokes. However, this is a finding that might require further investigation. We hypothesize that the increased use of balloon-assisted angioplasty following SE deployment (45.0%) might explain the increased occurrences of parent vessel stenosis in this study.[27] Of note, the high rate of angioplasty in this study may be attributed to varying practices at each of the enrolled centers, where in some of these centers, balloon angioplasty is routinely performed as a supplementary procedure following SE deployment. Alternatively, it can also be reasoned back to the relationship between the vascular characteristics (tortuosity, diameter, aneurysm location) and the mechanical properties of the SE (wires, navigability, radial force).[7,28] To date, there has not been any research that has compared the radial force among various FDs and its correlation with the most effective implantation.[28] Moreover, we could not reliably differentiate the cause due to the retrospective nature of our data. Nevertheless, when comparing those who had balloon-assisted angioplasty to those who did not, we found no significant difference in rates of stenosis of the parent vessel between the 2 groups. Future studies are warranted to explore if the higher occurrence of stenosis could be linked to the inherent traits of the SE and Surpass Streamline (both featuring a greater number of wires, which theoretically increases the endothelium-metal surface reaction after implantation), or if it is caused by the supplementary postinflammatory reaction to balloon angioplasty.

LIMITATIONS

This study is limited by its nonrandomized design, lack of a control arm, and its retrospective direction. The selection of patients with IAs for inclusion was left to the interventionalists and was not influenced by the authors, which is intended to produce a real-world experience. Although the cases presented in this study were consecutive, treatment with other FDs for specific cases could have been encountered during the period of this study. Furthermore, the inclusion of multiple centers resulted in variability in the management of patients on antiplatelet regimens, adjunctive treatments, and follow-up timings. Also, most of the included IAs were in the C6 segment of the ICA, which calls for future studies to investigate in more depth the use of the SE for small/medium-sized wide-necked IAs of the other ICA segments. Similarly, the extrapolation of our findings to the vertebrobasilar system is limited because we only included 2 (1.5%) vertebrobasilar system IAs. Although a central core laboratory was used to ensure consistency in imaging interpretations, there was no established protocol on the minimum angiographic follow-up. Considering that 25% of the patients had noninvasive imaging follow-ups, we note that the rate of complete occlusion could be overstated due to the inadequate assessments of small remnants that may only be visualized during a late venous phase on DSA. Nevertheless, the rate of complete occlusion at follow-up remained consistent when exclusively assessed on DSA using the OKM scale. Most importantly, the safety clinical outcomes were self-adjudicated by the principal investigator at each center, which might result in an underestimation of all safety events compared with those reported in a prospective study. Also, magnetic resonance imaging was only performed during the hospitalization or at follow-up when there was a clinical suspicion of major or minor stroke. In addition to the 1.6% rate of major stroke, only 3 had minor strokes, and for that no treatment was needed. Unfortunately, we did not perform follow-up magnetic resonance imaging postprocedure or at follow-up in patients without clinical symptoms and therefore cannot evaluate the incidence of silent strokes in that subgroup. Finally, the rationale for angioplasty was not collected; therefore, it was not possible to differentiate whether the use of angioplasty was related to routine postimplantation maneuver or impaired device wall apposition.

CONCLUSIONS

Our findings underscore the 64-wire SE's effectiveness and safety in managing small/medium-sized wide-necked IAs. The device demonstrates a favorable profile for achieving complete occlusion and maintaining a high safety margin, even in the context of higher stenosis rates associated with balloon-assisted angioplasty. These insights contribute to the growing body of evidence supporting the SE's role in neurointerventional surgery and underline the need for continued evaluation of procedural techniques to optimize patient outcomes.

ARTICLE INFORMATION

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Supplemental Material

Data S1

REFERENCES

1. Nurminen V, Raj R, Numminen J, Kivisaari R, Niemela M, Lehecka M. Flow diversion for internal carotid artery aneurysms: impact of complex aneurysm features and overview of outcome. *Clin Neurol Neurosurg*. 2020;193:105782. doi: 10.1016/j.clineuro.2020.105782
2. Chalouhi N, Zanaty M, Whiting A, Yang S, Tjoumakaris S, Hasan D, Starke RM, Hann S, Hammer C, Kung D, et al. Safety and efficacy of the pipeline embolization device in 100 small intracranial aneurysms. *J Neurosurg*. 2015;122:1498–1502. doi: 10.3171/2014.12.JNS14411
3. FDA. *P100018 PipelineTM Embolization Device*. 2011. https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100018A.pdf.
4. International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms—risk of rupture and risks of surgical intervention. *N Engl J Med*. 1998;339:1725–1733. doi: 10.1056/NEJM199812103392401
5. Wiebers DO, Whisnant JP, Huston J 3rd, Meissner I, Brown RD Jr, Piepgras DG, Forbes GS, Thielen K, Nichols D, O'Fallon WM, et al. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. *Lancet*. 2003;362:103–110. doi: 10.1016/s0140-6736(03)13860-3
6. Hanel RA, Kallmes DF, Lopes DK, Nelson PK, Siddiqui A, Jabbour P, Pereira VM, Szikora Istvan I, Zaidat OO, Bettegowda C, et al. Prospective study on embolization of intracranial aneurysms with the pipeline device: the PREMIER study 1 year results. *J Neurointerv Surg*. 2020;12:62–66. doi: 10.1136/neurintsurg-2019-015091
7. Dandapat S, Mendez-Ruiz A, Martinez-Galdamez M, Macho J, Derakhshani S, Foa Torres G, Pereira VM, Arat A, Wakhloo AK, Ortega-Gutierrez S. Review of current intracranial aneurysm flow diversion technology and clinical use. *J Neurointerv Surg*. 2021;13:54–62. doi: 10.1136/neurintsurg-2020-015877
8. Briganti F, Leone G, Ugga L, Marseglia M, Macera A, Manto A, Delehaye L, Resta M, Resta M, Burdi N, et al. Mid-term and long-term follow-up of intracranial aneurysms treated by the p64 Flow Modulation Device: a multicenter experience. *J Neurointerv Surg*. 2017;9:70–76. doi: 10.1136/neurintsurg-2016-012502
9. Lubicz B, van der Elst O, Collignon L, Mine B, Alghamdi F. Silk flow-diverter stent for the treatment of intracranial aneurysms: a series of 58 patients with emphasis on long-term results. *AJNR Am J Neuroradiol*. 2015;36:542–546. doi: 10.3174/ajnr.A4143
10. Pierot L, Spelle L, Berge J, Januel AC, Herbreteau D, Aggour M, Piotin M, Biondi A, Barreau X, Mounayer C, 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. doi: 10.1136/neurintsurg-2018-014261
11. Orru E, Rice H, de Villiers L, Klostranec JM, Wakhloo AK, Coon AL, Radovanovic I, Kortman H, Bhatia KD, Krings T, et al. First clinical experience with the new Surpass Evolve flow diverter: technical and clinical considerations. *J Neurointerv Surg*. 2020;12:974–980. doi: 10.1136/neurintsurg-2019-015734
12. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational

Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008;61:344–349. doi: 10.1016/j.jclinepi.2007.11.008
13. Rautio R, Alpay K, Sinisalo M, Numminen J. Treatment of intracranial aneurysms using the new Surpass Evolve flow diverter: safety outcomes and six-month imaging follow-up. *J Neuroradiol*. 2022;49:80–86. doi: 10.1016/j.neurad.2021.03.003
14. Maus V, Weber W, Berlis A, Maurer C, Fischer S. Initial experience with surpass evolve flow diverter in the treatment of intracranial aneurysms. *Clin Neuroradiol*. 2021;31:681–689. doi: 10.1007/s00062-020-00972-5
15. Raymond J, Guilbert F, Weill A, Georganos SA, Juravsky L, Lambert A, Lamoureux J, Chagnon M, Roy D. Long-term angiographic recurrences after selective endovascular treatment of aneurysms with detachable coils. *Stroke*. 2003;34:1398–1403. doi: 10.1161/01.Str.0000073841.88563.E9
16. O'Kelly CJ, Krings T, Fiorella D, Marotta TR. A novel grading scale for the angiographic assessment of intracranial aneurysms treated using flow diverting stents. *Interv Neuroradiol*. 2010;16:133–137. doi: 10.1177/159101991001600204
17. Fiorella D, Gache L, Frame D, Arthur AS. How safe and effective are flow diverters for the treatment of unruptured small/medium intracranial aneurysms of the internal carotid artery? Meta-analysis for evidence-based performance goals. *J Neurointerv Surg*. 2020;12:869–873. doi: 10.1136/neurintsurg-2019-015535
18. Chalouhi N, Daou B, Barros G, Starke RM, Chitale A, Ghobrial G, Dalyai R, Hasan D, Gonzalez LF, Tjoumakaris S, et al. Matched comparison of flow diversion and coiling in small, noncomplex intracranial aneurysms. *Neurosurgery*. 2017;81:92–97. doi: 10.1093/neuros/nyw070
19. Chalouhi N, Starke RM, Yang S, Bovenzi CD, Tjoumakaris S, Hasan D, Gonzalez LF, Rosenwasser R, Jabbour P. Extending the indications of flow diversion to small, unruptured, saccular aneurysms of the anterior circulation. *Stroke*. 2014;45:54–58. doi: 10.1161/STROKEAHA.113.003038
20. Deutschmann HA, Wehrschuetz M, Augustin M, Niederkorn K, Klein GE. Long-term follow-up after treatment of intracranial aneurysms with the pipeline embolization device: results from a single center. *AJNR Am J Neuroradiol*. 2012;33:481–486. doi: 10.3174/ajnr.A2790
21. Griessenauer CJ, Ogilvy CS, Foreman PM, Chua MH, Harrigan MR, He L, Fusco MR, Mocco JD, Stapleton CJ, Patel AB, et al. Pipeline embolization device for small intracranial aneurysms: evaluation of safety and efficacy in a multicenter cohort. *Neurosurgery*. 2017;80:579–587. doi: 10.1227/NEU.0000000000001377
22. Griessenauer CJ, Ogilvy CS, Foreman PM, Chua MH, Harrigan MR, Stapleton CJ, Patel AB, He L, Fusco MR, Mocco J, et al. Pipeline embolization device for small paraophthalmic artery aneurysms with an emphasis on the anatomical relationship of ophthalmic artery origin and aneurysm. *J Neurosurg*. 2016;125:1352–1359. doi: 10.3171/2015.12.JNS152499
23. Lin LM, Colby GP, Kim JE, Huang J, Tamargo RJ, Coon AL. Immediate and follow-up results for 44 consecutive cases of small (<10 mm) internal carotid artery aneurysms treated with the pipeline embolization device. *Surg Neurol Int*. 2013;4:114. doi: 10.4103/2152-7806.117711
24. Pumar JM, Mosqueira A, Cuellar H, Dieguez B, Guimaraens L, Masso J, Miralbes S, Blanco-Ulla M, Souto-Bayarri M, Vazquez-Herrero F. Expanding the use of flow diverters beyond their initial indication: treatment of small unruptured aneurysms. *J Neurointerv Surg*. 2018;10:245–248. doi: 10.1136/neurintsurg-2017-013062
25. Bonafe A, Perez MA, Henkes H, Lylyk P, Bleise C, Gascou G, Sirakov S, Sirakov A, Stockx L, Turjman F, 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. doi: 10.1136/neurintsurg-2021-017809
26. Meyers PM, Coon AL, Kan PT, Wakhloo AK, Hanel RA. SCENT trial. *Stroke*. 2019;50:1473–1479. doi: 10.1161/STROKEAHA.118.024135
27. Gui S, Chen X, Wei D, Deng D, You W, Meng X, Lv J, Feng J, Tang Y, Yang S, et al. Long-term outcomes and dynamic changes of in-stent stenosis after pipeline embolization device treatment of intracranial aneurysms. *J Neurointerv Surg*. 2023;15:1187–1193. doi: 10.1136/jnis-2022-019680
28. Maragkos GA, Dmytriw AA, Salem MM, Tutino VM, Meng H, Cognard C, Machi P, Krings T, Mendes PV. Overview of different flow diverters and flow dynamics. *Neurosurgery*. 2020;86:S21–S34. doi: 10.1093/neuros/nyz323