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INTERVENTIONAL RADIOLOGY

REVIEW ARTICLE

Short to mid-term outcomes of flow re-direction endoluminal device X (FRED™ X) in the management of intracranial aneurysms: a meta-analysis

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ABSTRACT

This meta-analysis evaluates the clinical and angiographic outcomes of the flow re-direction endoluminal device X (FRED™ X) in treating intracranial aneurysms. A systematic review was performed across Medline, Scopus, and Web of Science databases from inception to March 2025. Eligible studies included those reporting clinical and angiographic results of FRED X treatment. Favorable outcomes were defined as those stated explicitly in the studies or a modified Rankin scale score of 0–2. Pooled estimates were calculated using a random-effects model in R. A total of nine studies encompassing 780 patients with 869 aneurysms were included. The weighted mean age was 56.28 years, with 19.1% of patients being men. Most aneurysms were saccular (85.7%), unruptured (92.52%), and located in the anterior circulation (73.6%), primarily in the internal carotid artery. The average aneurysm size was 13.12 mm. All studies employed dual antiplatelet therapy, with antiplatelet response testing performed in eight studies. The mean clinical follow-up period was 9.27 months. The meta-analysis demonstrated favorable neurological outcomes in 97.71% of cases and complete or near-complete occlusion in 86.9%. Procedure-related complications were reported in 9.28% of cases, while in-stent thrombosis or intimal hyperplasia occurred in 4.29%. Overall mortality was low at 0.60%. Subgroup analysis revealed that unruptured aneurysms had a 100% rate of favorable neurological outcomes and an 84.76% rate of complete or near-complete occlusion. Complication and mortality rates were 7.76% and 0.25%, respectively. In addition, favorable outcomes were seen in 100% of ruptured aneurysm cases; however, complete occlusion was achieved in only 59.65%, and the mortality rate was higher at 9.19%. Therefore, FRED X demonstrated high efficacy and procedural safety in the treatment of intracranial aneurysms, offering improved outcomes compared with earlier-generation flow diverters.

KEYWORDS

Intracranial aneurysms, flow re-direction endoluminal device X (FRED X), flow diverter, X technology

In 2011, the approval of a pipeline embolization device by the United States (US) Food and Drug Administration (FDA) marked a significant milestone in the treatment of intracranial aneurysms. Following the success of the pipeline embolization device, flow diverter (FD) stents have become an increasingly integral part of clinical practice. The flow re-direction endoluminal device (FRED™) and its smaller counterpart, FRED junior (FRED Jr), manufactured by MicroVention, now Terumo Neuro (Aliso Viejo, CA, USA), are notable examples of these devices. Designed with a dual-layer construction, they employ a self-expanding braided nitinol mesh to ensure superior wall apposition and facilitate safe delivery to distal aneurysms.[1,2]

An important advancement in flow-diversion technology has been the development of antithrombotic coatings, which aim to reduce the risk of thrombus-related complications. Building on this trend and the original FRED system, FRED X represents the latest generation of FDs. While retaining the structural design of its uncoated predecessor, the FRED X incorporates innovative X technology surface coating. This coating consists of an amphiphilic polymer, poly

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(2-methoxyethyl acrylate), which features a hydrophobic segment facing the device's surface and a hydrophilic segment oriented toward the vascular lumen.[3,4] This unique design creates a boundary layer along the stent struts, minimizing protein denaturation and subsequent platelet adhesion. These attributes suggest a potentially improved safety profile for the device. The FRED X received FDA premarket approval in September 2021, and the first clinical use was reported in February 2022. However, while preliminary studies suggest high procedural safety with the FRED X, the clinical benefits of these surface coatings remain uncertain and warrant further investigation.[5]

To address this gap, this study provides a comprehensive systematic review and meta-analysis of the existing literature on the clinical outcomes of using FRED X in the treatment of intracranial aneurysms. This meta-analysis aims to identify knowledge gaps and offer valuable insights to inform clinical decision-making regarding this novel therapeutic approach by synthesizing the current evidence and critically analyzing the findings.

Methods

This systematic review and meta-analysis followed the recommendations of the Cochrane Collaboration Handbook for Systematic Review of Interventions[6] and the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) 2020 statement guidelines.[7] The NeuroComp Meta-Analysis Checklist was adopted to assess the outcomes related to complications.[8]

Eligibility criteria

This meta-analysis included studies that met the following criteria: (1) case series, prospective, or retrospective cohort studies, or randomized controlled trials; (2) studies providing follow-up data on clinical and angiographic outcomes; and (3) studies specifically involving the FRED X. Studies using other FRED stents (e.g., FRED, FRED Jr) were excluded from this analysis. There were no restrictions regarding aneurysm type, location, rupture status, or other related factors.

Main points

- The flow re-direction endoluminal device X (FRED™ X) device demonstrated favorable neurological outcomes in 97.71% of cases, with a low overall mortality and complication rate of 0.6% and 9.28%, respectively, highlighting its safety and efficacy in treating intracranial aneurysms.
- Complete or near-complete aneurysm occlusion was achieved in 86.9% of cases, indicating strong angiographic efficacy, even with relatively short follow-up periods.
- The study highlights the potential benefits of FRED X's surface-modifying X technology coating in reducing platelet adhesion and thrombogenicity, although its direct clinical impact remains under investigation.

Search strategy, data extraction, and quality assessment

A comprehensive literature search was conducted in the Medline, Scopus, and Web of Science databases from inception to March 8, 2025. The search strategy employed keywords such as "FRED X," "FREDX," and "FRED™" in various combinations using "AND" and "OR" to ensure a broad capture of relevant studies.

Two independent researchers performed the data extraction and quality assessment; any discrepancies were resolved through consensus with two of the study's researchers. The risk of bias was evaluated using a modified Newcastle–Ottawa Scale.[9-11] Studies were classified as having a "low risk of bias" if they provided satisfactory angiographic and clinical follow-up data together with clear outcome reporting. Studies with unsatisfactory follow-up were categorized as "medium risk of bias," while those lacking satisfactory follow-up and clear outcome reporting were deemed to have a "high risk of bias" (Supplementary Table 1).

Endpoints, subanalysis, and definitions

Clinical and angiographic outcomes assessed included the following: (1) favorable neurological outcomes; (2) minor and major complications; (3) occlusion rate; (4) adjunctive coiling; (5) aneurysm presentation (ruptured or unruptured); (6) technical success; and (7) mortality. Additional subanalyses examined outcomes specifically for ruptured and unruptured aneurysms. Favorable neurological outcomes were defined as either those reported directly or as a modified Rankin scale score of 0–2 for aneurysms. Complete occlusion was directly reported or, if not, classified as Raymond–Roy class 1 (indicating complete obliteration) or O'Kelly–Morata grade D. Near-complete occlusions were defined as Raymond–Roy class 2 or O'Kelly–Morata grade C, with other outcomes classified as incomplete occlusions.

Statistical Analysis

Analyses were conducted using pooled estimates with a 95% confidence interval (CI) under a random-effects model. Heterogeneity was assessed using the I^2 statistic, with values above 50% indicating substantial heterogeneity. To explore the robustness of the pooled estimates and identify potential sources of heterogeneity, leave-one-out sensitivity analyses were performed. Assessment of publication bias was not performed using funnel plots or Egger's regression tests because the meta-analysis comprised fewer than 10 studies, as these methods are considered unreliable with a small sample size. Pearson's χ^2 test examined the relationship between aneurysm localizations. A P value <0.05 was considered statistically significant. All statistical analyses were performed using R (version 4.2.3, R Foundation for Statistical Computing, Vienna, Austria), applying inverse variance and restricted maximum likelihood methods.

Results

Literature review

Nine studies were included in the final analysis.[1-5,12-15] The search process is illustrated in Figure 1. Two studies employed a prospective design,[2,12] whereas the remaining seven were conducted retrospectively. Additionally, two studies were conducted at a single center,[12,13] while the other seven were multicenter studies.

Patient population and study characteristics

The nine studies included in the final analysis represented 780 patients with a weighted mean age of 56.28 years and encompassed 869 aneurysms. Among the 780 patients with reported sex information, 149 (19.1%) were men.

Morphologically, saccular aneurysms were the most common type, comprising 680 of 793 aneurysms (85.7%). The mean aneurysm size across the studies was 13.12 mm. Analysis of the rupture status of the 869 aneurysms evaluated determined that 65 (7.4%) were ruptured and 804 (92.5%) were unruptured. The mean clinical follow-up duration of the nine studies included was 9.27 months (Table 1). Detailed information for each study is provided in Table 2.

Aneurysms were predominantly located in the anterior circulation (n = 640, $P < 0.001$), with the internal carotid artery (n = 542) being the most common site. Among posterior circulation aneurysms (n = 103), the vertebral (n = 42) and basilar (n = 26) arteries were the primary locations. Additionally, 126 aneurysms lacked specific location information (Table 3).

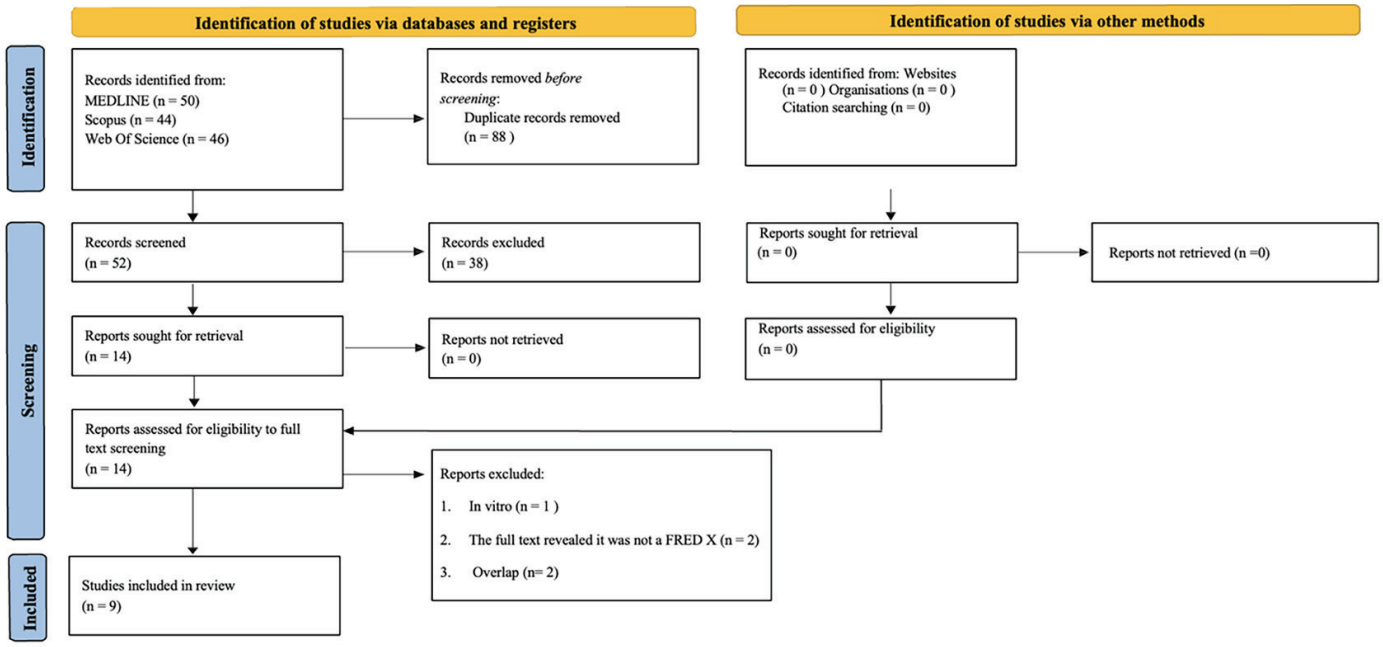


Figure 1. Prisma flow diagram.

Table 1. Baseline clinical and aneurysm characteristics*

Variable	Raw number (%)*	Number of studies
Number of patients	780	9
Number of aneurysms	869	9
Mean age†	56.28	9
Proportion of men	149/780 (19.1%)	9
Previous treatment history	125/772 (16.1%)	7
Mortality	11/780 (1.4%)	9
Clinical status at presentation		
mRS ≤2/good neurologic	594/780 (76.1%)	6
mRS >2/bad neurologic	14/780 (1.79%)	6
NA	87	3
Morphology		
Saccular	680/793 (85.7%)	9
Fusiform	40/793 (5%)	8
Other	73/793 (9.2%)	8
Mean aneurysm size (mm)	13.12	9
Ruptured	65/869 (7.4%)	6
Unruptured	804/869 (92.5%)	9
Mean follow-up (in months)††	9.27	9

*Reported as pooled aggregate data and not based on random-effects inverse-variance meta-analysis. †Represents weighted average. ††Based on the last longitudinal clinical follow-up scan. mRS, modified Rankin scale.

Antiplatelet regiment

Dual antiplatelet therapy was utilized in all nine studies. The antiplatelet response was assessed in eight studies, with five using the VerifyNow™ system (Werfen, Bedford, MA, USA), while the method of assessment was not specified in three studies (Supplementary Table 2).

Angiographic, clinical outcomes, and complications

The meta-analysis of the nine studies demonstrated favorable neurological outcomes in 97.7% of cases (95% CI 95.42–100). Complete or near-complete occlusion was achieved in 86.9% of aneurysms (95% CI 79.84–93.60), based on the data reported in eight studies. Complications occurred in 9.2% of cases (95% CI 4.94–13.61), based on the data derived from nine studies. In-stent thrombosis or intimal hyperplasia was observed in 4.2% of cases (95% CI 1.16–7.42) in eight of the studies. Mortality was low, at 0.60% (95% CI 0.00–1.31), based on nine studies (Figure 2).

Subanalysis of ruptured and unruptured aneurysms

For unruptured aneurysms, five studies representing 379 patients reported favorable neurological outcomes in 100% of cases (95% CI 99.31–100) (Supplementary Figure 1). Complete or near-complete occlusion was achieved in 84.7% of cases (95% CI 78.81–90.71), based on five studies representing 331 patients. Complications occurred in 7.7% of cases (95% CI 4.09–11.43), derived from seven studies involving 581 patients. In-stent thrombosis or intimal hyperplasia occurred in 2.1% of cases (95% CI 0–4.21), based on five studies. Mortality was 0.25% (95% CI 0–0.85), based on data from eight studies (Table 4).

For ruptured aneurysms, two studies with 13 patients reported favorable neurological outcomes in 100% of cases (95% CI 87.61–100) (Supplementary Figure 2). Complete or near-complete occlusion was observed in 59.6% of cases (95% CI 25.17–94.13), based on two studies with 23 patients. Procedure-related complications occurred in 0.52% of cases (95% CI 0–6.18), based on four studies involving 41 patients. Mortality was 9.19% (95% CI 0–25.95), based on five studies (Table 4). Details of complications and their

Table 2. Summary of included studies

Study and patient characteristics				Aneurysm characteristics						Follow-up	
Study	Design	Patients/ aneurysms (n)	Sex (M/W)	Aneurysm location (n)	Covered branches (n)	Type (n)	Mean diameter (range), mm	Mean neck width (range), mm	Parent vessel diameter (range), mm	Clinical mean (range), months	Radiological mean (range), months
Abbas et al.[3]	RMC	44/44	7/37	ICA (34), MCA (2), ACA (6), PCOM (2), AICA (1)	15, arising from SAC/ neck of aneurysm	SAC (41) Blister (2) DIS (2)	5.6 ± 4.6	5.6 ± 4.6	NA	6 (1–12)	6 (1–12)
Goertz et al.[1]	RMC	156/156	31/125	ICA (121), ACOM (3), ACA (2), MCA (9), VA (10), BA (7), PICA (3), PCA (1)	4	SAC (138) FU (10) DIS (3) Blister (5)	8.1*5.0	5.0 ± 3.8	Proximal 3.6 ± 0.7 Distal 3.2 ± 0.7	6 (1–12)	6 (1–12)
Hendrix et al.[4]	RMC	101/117	21/90	ICA (102), MCA (3), ACA (8), VA (4)	NA	SAC (112) FU (3) DIS (2)	4.6*3.5	3.5	3.3	6 (1–12)	6 (1–12)
Wen et al.[15]	RMC	22/24	2/20	ICA (10), PCOM (5), ACOM (3), MCA (2), others (4)	NA	SAC (24)	5.7	3.6	NA	21.5 (18–30)	21.5 (18–30)
Clausen et al.[13]	RSC	77/85	21/56	VA (19), ICA (24), BA (3), SHA (5), PCOM (18), Opht (7), ACOM (4), ACA (1) MCA (1), PICA (2), PCA (1)	NA	Saccular (42) Side wall (16) FU (8) DIS (6) Pseudoaneurysm (4) Blister (2) Multiple (2)	0–5 (28) 5–1 (26) >10 (19)	NA	NA	6 (1–6)	6 (1–6)
Roy et al.[14]	RMC	154/162	28/126	ICA (122), MCA (5), ACA (17) V4 (5), basilar (3), P1 (4), AICA (1), SCA (1)	38, arising from SAC/ neck of aneurysm	SAC (140) FU (6) Blister (8) DIS (8)	5.9	3.8	Proximal 3.5 ± 0.9 Distal 3.1 ± 0.7	6 (1–12)	6 (1–12)
Vollherbst et al.[5]	RMC	161/184	36/125	ICA (117), BA (13), MCA (10), VA (9), other (12)	NA	SAC (131) Blister (14) FU (11) DIS (5)	7.8 × 4.7 × 1.7	4.7	Proximal 3.5 ± 0.8 (1.5–7.0) Distal 3.1 ± 0.7 (1.2–5.2)	7 (1–2)	7 (1–12)
Cherednychenko et al.[12]	PSC	7/12	3/4	ICA (12)	NA	SAC (2) Blister (2) FU (1) NS (7)	6 × 8 × 5	NA	NA	7 (1–12)	7 (1–12)
Guimaraens et al.[2]	PMC	58/85	10/48	Carotid artery (44), ACA (5), MCA (13), PCA (3), choroidal artery (6), posterior (14)	NA	Blister (6) DIS (4) FU (2) SAC (60) Pre-treated (13)	7 × 13 × 52	NA	NA	6 (1–12)	6 (1–12)

ACA, anterior cerebral artery; ACOM, anterior communicating artery; BA, basilar artery; CMA, callosal marginal artery; DACA, distal anterior cerebral artery; DIS, dissecting; FU, fusiform; ICA, internal carotid artery; Inf, inferior; IQR, interquartile range; MCA, middle cerebral artery; PCA, posterior cerebral artery; PCOM, posterior communicating artery; PICA, posterior inferior cerebellar artery; M, men; NA, not available; NS, not specified; Opht, ophthalmic artery; RMC, retrospective multicenter; RSC, retrospective single-center; PSC, primary sclerosing cholangitis; SAC, saccular; SHA, superior hypophyseal artery; Sup, superior; VA, vertebral artery; W, women.

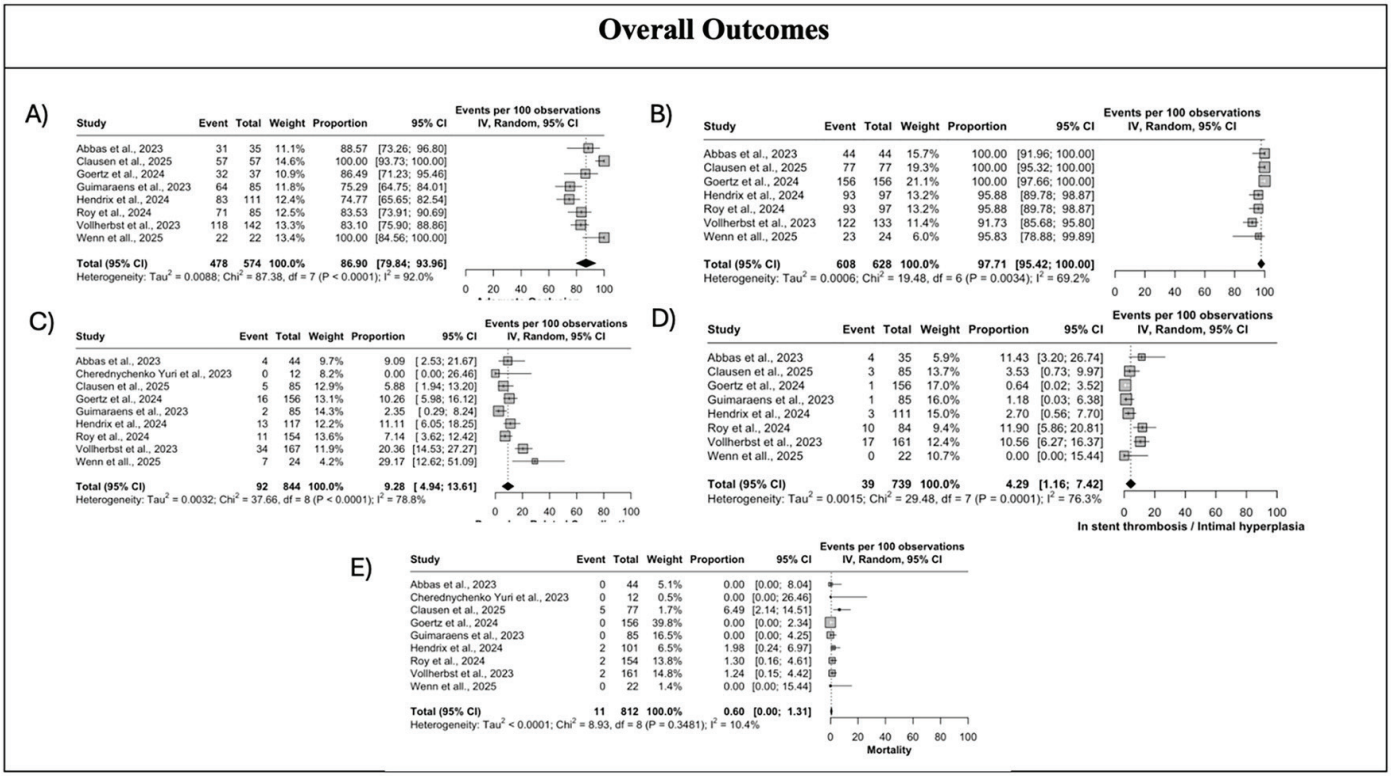


Figure 2. Summary of meta-analysis of single-arm studies. Forest plots show event proportions per 100 observations (95% CI). Heterogeneity was assessed using Tau^2, Chi^2, and I^2 values. CI, confidence interval; IV, intravenous.

management are presented in Supplementary Tables 3, 4. Leave-one-out results are presented in Supplementary Figures 3-5.

Discussion

This meta-analysis, encompassing data for 780 patients with 869 aneurysms reported in nine studies, underscores several key findings. Favorable neurological outcomes were achieved in 97.71% of cases, with a low overall mortality rate of 0.60%. Most aneurysms were unruptured (92.52%) and predominantly located in the anterior circulation, especially in the internal carotid artery. Complete or near-complete occlusion was achieved in 86.9% of aneurysms, while complications occurred in only 9.28% of cases. Although outcomes for ruptured and unruptured aneurysms were generally comparable, unruptured aneurysms exhibited significantly lower complication rates. Despite the relatively short follow-up periods reported in the nine studies, their findings highlight the efficacy and safety of the FRED X device, particularly in achieving high rates of complete occlusion.

While FD technology has revolutionized the treatment of intracranial aneurysms, its use is not without limitations and potential complications. Since FDA approval, multiple studies have assessed the safety and efficacy of FDs, frequently reporting high occlusion rates. However, the overall complication rate, including major and minor events, has been reported to reach up to 17%, with ischemic complications being the most prevalent.[16] Notably, compared with the pipeline embolization device, the FRED device has been associated with higher rates of in-stent stenosis, potentially elevating the risk of ischemic events.[17]

To address these concerns, MicroVention, now Terumo Neuro, developed the next-generation FRED X, incorporating advanced X technology. This technology introduces a protective hydration layer across the stent's surface, aiming to reduce platelet adhesion and enhance endothelialization. By minimizing thrombogenicity and promoting natural vascular healing, the FRED X endeavors to improve safety and clinical outcomes. Furthermore, the novel surface coating facilitates improved device delivery without altering the core stent design. Importantly, the FRED X retains the same dual-layer design as the FRED, which features 16 + 48 wires, achieving 35%–40% metal coverage. In contrast, the FRED Jr, another variant, uses 16 + 36 wires with approximately 30% metal

Table 3. Distribution of aneurysms by location

	Location	*P* value
Anterior circulation (n = 640)	Middle cerebral artery (MCA) (n = 44)	**<0.001***
	Internal carotid artery (ICA) (n = 542)	
	Choroidal artery (n = 6)	
	Anterior cerebral artery (ACA) (n = 38)	
	Anterior communicating artery (AcomA) (n = 10)	
	Posterior cerebral artery (PCA) (n = 5)	
Posterior circulation (n = 103)	Basilar artery (n = 26)	**<0.001****
	Vertebral artery (n = 42)	
	Posterior inferior cerebellar artery (PICA) (n = 5)	
	Posterior communicating artery (PcomA) (n = 25)	

*Within the anterior circulation, the number of internal carotid artery aneurysms is significantly higher. **Within the posterior circulation, the number of vertebral artery aneurysms is significantly higher.

Table 4. Meta-analysis outcome findings

Overall					
Outcomes	Proportion (95% CI)	I^2 (%)	Q statistic, *P* value	Number of studies	Events/total
Adequate occlusion	86.90 (79.84–93.60)	92	97.38, $P < 0.001$	8	478/574
Favorable neurological outcomes	97.71 (95.42–100)	69.2	19.48, $P = 0.003$	7	608/628
Procedure-related complications	9.28 (4.94–13.61)	78.8	37.66, $P < 0.001$	9	92/844
In-stent thrombosis/intimal hyperplasia	4.29 (1.16–7.42)	76.3	29.48, $P < 0.001$	8	39/739
Mortality	0.60 (0.00–1.31)	10.4	8.93, $P = 0.348$	9	11/812
Adequate occlusion	84.76 (78.81–90.71)	51.6	8.27, $P = 0.082$	5	273/331
Favorable neurological outcomes	100 (99.31–100)	0	0, $P = 1$	5	379/379
Procedure-related complications	7.76 (4.09–11.43)	67.9	18.70, $P = 0.005$	7	49/581
In-stent thrombosis/intimal hyperplasia	2.10 (0–4.21)	44	7.14, $P = 0.129$	5	11/387
Mortality	0.25 (0–0.85)	0	2.36, $P = 0.937$	8	3/633
Subanalysis of ruptured aneurysms					
Adequate occlusion	59.65 (25.17–94.13)	63.8	2.17, $P = 0.096$	2	12/23
Favorable neurologic outcomes	100 (87.61–100)	0	0, $P = 1$	2	13/13
Procedure related complications	0.52 (0–6.18)	0	1.22, $P = 0.748$	4	1/41
Mortality	9.19 (0–25.95)	69.4	13.07, $P = 0.012$	5	6/56

CI, confidence interval.

coverage. The specific impact of the surface coating, however, remains a subject of ongoing investigation.

Retrospective analyses, such as that by Cortez et al.[18], comparing the Pipeline™ Flex with and without Shield Technology™, found no significant differences in diffusion-weighted imaging lesions. However, the study's small sample size and retrospective design limit the generalizability of these findings, emphasizing the need for further research. An *in vitro* blood loop model study by Yoshizawa et al.[19] demonstrated reduced platelet adhesion on the FRED X surface compared with the uncoated FRED. Additionally, multicenter trials suggest that the FRED X may have a lower complication rate than the uncoated FRED. For example, the SAFE study[20] reported thromboembolic events in 4.9% of cases and a morbidity rate of 3.0%. Moreover, Guimaraens et al.[2] highlighted that the FRED X achieved higher medium-term occlusion rates while maintaining a favorable safety profile.

Despite the widely accepted necessity of dual antiplatelet therapy (typically aspirin and clopidogrel/prasugrel/ticagrelor) following FD implantation, the optimal dosage and duration of post-treatment antiplatelet therapy remain unstandardized when using surface-modified FDs. The reduced thrombogenicity of surface-modified FDs compared with uncoated FDs raises the question of whether adjustments to antiplatelet regimens are warranted. The study by Goertz et al.[21] investigated single therapy following surface-modified FD implantation; aspirin, ticagrelor, and prasugrel were utilized as monotherapies, with prasugrel being the most frequently chosen agent. Evidence suggests that prasugrel and ticagrelor have a superior safety profile for ischemic events compared with aspirin in single antiplatelet therapy (SAPT) regimens. According to a meta-analysis by Ma et al.[22], the rate of thromboembolic complications following surface-modified FD implantation was reported as 20% for aspirin, compared with 2% and 4% for prasugrel and ticagrelor monotherapies, respectively. These findings suggest that SAPT with prasugrel or ticagrelor is favored over aspirin in specific clinical scenarios when using surface-modified FDs.

Current evidence supports the reasonable safety and efficacy of SAPT in treating aneurysms with modified FDs; however, the lack of studies directly comparing modified FDs with dual antiplatelet therapy and uncoated FDs with SAPT, coupled with the scarcity of large, prospective trials, precludes definitive conclusions. The studies included in this meta-analysis reveal a persistent tendency to favor dual therapy. Results from registries and trials investigating new-generation FDs, such as the coating study,[23] have aimed to optimize aneurysm treatment and contribute valuable insights to refine treatment strategies. Notably, most studies included in this meta-analysis assessed platelet function before the procedure. However, no consensus exists on whether such evaluations are necessary for modified FDs. Further research is required to address this uncertainty.

Despite the short follow-up periods, the meta-analysis established that the FRED X had a satisfactory occlusion rate, with a combined major and minor complication rate of 9.2%. The average aneurysm size was 13.12 mm, a noteworthy finding given that the FRED X was used in small parent vessels and more proximal aneurysms, achieving relatively low complication rates. Larger aneurysms are generally associated with higher complication risks, as demonstrated by the study from Sweid et al.[24], which identified aneurysm size >10–15 mm as a statistically significantly independent predictor of major ischemic stroke. Additionally, Sweid et al.[24] reported a statistically significant association between the time from treatment and the development of in-stent stenosis.

This meta-analysis did not include sufficient data to directly compare outcomes between FRED X with and without adjunctive coiling. However, Goertz et al.[25] investigated the impact of coiling in their study and found no significant differences in clinical or angiographic outcomes between coiled and non-coiled cases. In the studies included in this meta-analysis, only one patient experienced technical failure.

Although the preliminary safety and efficacy results for FRED X are promising, long-term follow-up studies, particularly those comparing coated and uncoated FDs, are

needed to further evaluate its clinical performance.

This meta-analysis has several limitations, despite efforts to address heterogeneity and publication bias. The retrospective design of the included studies introduces inherent constraints, such as selection bias, missing data, and variability in reporting practices, which may affect the reliability and generalizability of the findings. In comparing ruptured and unruptured aneurysms, differences in aneurysm characteristics, such as location and morphology, and variations in treatment approaches, including the use of adjunctive coiling, may further complicate interpretations and reduce comparability. Additionally, the short- to mid-term follow-up periods in most of the included studies may not sufficiently capture long-term treatment outcomes. These factors should be carefully considered when interpreting the conclusions of this analysis.

In conclusion, this study demonstrates that the FRED X offers high feasibility and procedural safety, surpassing the performance of first-generation devices. While the short-term occlusion rates appear satisfactory, long-term and comparative studies are needed to fully evaluate the potential of the FRED X and other coated FDs.

Footnotes

Conflict of interest disclosure

The authors declared no conflicts of interest.

References

1. Goertz L, Hohenstatt S, Vollherbst DF, et al. Lower-ischemic-risk profile of coated flow redirection endoluminal device x compared with uncoated flow redirection endoluminal device flow diverter in the treatment of unruptured intracranial aneurysms. *Neurosurgery*. 2024. [Crossref]
2. Guimaraens L, Saldaña J, Vivas E, et al. Flow diverter stents for endovascular treatment of aneurysms: a comparative study of efficacy and safety between FREDX and FRED. *J Neurointerv Surg.* 2024;17(e1):e159-e165. [Crossref]
3. Abbas R, Lan M, Naamani KE, et al. First United States multicenter experience with the new-generation FRED X surface-modified flow diversion stent: feasibility, safety, and short-term efficacy. *J Neurosurg*. 2023;140(4):1054-1063. [Crossref]
4. Hendrix P, Hemmer S, Sioutas GS, et al. FRED X flow diversion stenting for unruptured intracranial aneurysms: US multicenter post-market study. *J Neurointerv Surg.* 2025:jnis-2024-022523. [Crossref]
5. Vollherbst DF, Lücking H, DuPlessis J, 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(4):474-480. [Crossref]
6. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.5. Cochrane, 2024. Available from: www.training.cochrane.org/handbook. [Crossref]
7. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. [Crossref]
8. Ferreira MY, Cardoso LJC, Günkan A, et al. Challenges and limitations in meta-analyses of complications in neurosurgery: systematic review with proposed approach and checklist to mitigate errors and improve the assessment of the real-world experience. *Neurosurg Rev.* 2024;47(1):722. [Crossref]
9. Cinar C, Elek A, Allahverdiyev I, et al. Comprehensive evaluation of serpentine aneurysms: a systematic review and meta-analysis with a subanalysis for treatment approaches. *Clin Neuroradiol.* 2024;34(4):749-760. English. [Crossref]
10. Elek A, Allahverdiyev I, Ozcinar KK, et al. Comprehensive evaluation of management strategies and rupture status in partially thrombosed aneurysms: a systematic review and meta-analysis. *J Neurointerv Surg*. 2024:jnis-2024-022571. [Crossref]
11. Elek A, Karagoz S, Dindar GN, et al. Safety and efficacy of low profile flow diverter stents for intracranial aneurysms in small parent vessels: systematic review and meta-analysis. *J Neurointerv Surg.* 2025:jnis-2024-022834. [Crossref]
12. Cherednychenko YV, Armonda RA, Sirko AH, Zorin MO, Miroshnychenko AY, Perepelytsia VA. Intracranial aneurysms treatment using new generation FRED X flow diverters with antithrombotic coating and preoperative PreSize Neurovascular software simulation: literature review and own clinical observations analysis. *Ukr Neurosurg J.* 2023;29(3):43-57. [Crossref]
13. Clausen TM, Nakamura R, Conching A, et al. Flow diversion in the treatment of intracranial aneurysms using the novel FRED X device: An early experience from a single high-volume center. *Interv Neuroradiol.* 2025:15910199251319059. [Crossref]
14. Roy JM, El Naamani K, Amaravadi C, et al. Long-term safety and efficacy of the FRED X flow diverter for intracranial aneurysms: a multicenter study of 154 patients. *J Neurosurg*. 2025;1-11. [Crossref]
15. Wen DW, Ayre J, Puthuran M, et al. Treatment of intracranial aneurysms with the FRED X flow diverter stent: mid-term angiographic and safety results. *Clin Neuroradiol*. 2025. [Crossref]
16. Cagnazzo F, Lefevre PH, Derraz I, et al. Flow-diversion treatment for unruptured nonsaccular intracranial aneurysms of the posterior and distal anterior circulation: a meta-analysis. *AJNR Am J Neuroradiol*. 2020;41(1):134-139. [Crossref]
17. El Naamani K, Saad H, Chen CJ, et al. Comparison of flow-redirection endoluminal device and pipeline embolization device in the treatment of intracerebral aneurysms. *Neurosurgery*. 2023;92(1):118-124. [Crossref]
18. Cortez GM, Benalia VHC, Sauvageau E, Aghaebrahim A, Pederson JM, Hanel RA. Diffusion-weighted imaging lesions after intracranial aneurysm treatment with pipeline flex and pipeline flex with shield technology: a retrospective cohort analysis. *J Neurointerv Surg*. 2024;16(4):385-391. [Crossref]
19. Yoshizawa K, Kobayashi H, Kaneki A, et al. Poly(2-methoxyethyl acrylate) (PMEA) improves the thromboresistance of FRED flow diverters: a thrombogenic evaluation of flow diverters with human blood under flow conditions. *J Neurointerv Surg*. 2023;15(10):1001-1006. [Crossref]
20. Pierot L, Spelle L, Berge J, et al. Feasibility, complications, morbidity, and mortality results at 6 months for aneurysm treatment with the flow re-direction endoluminal device: report of SAFE study. *J Neurointerv Surg*. 2018;10(8):765-770. [Crossref]
21. Goertz L, Hohenstatt S, Vollherbst DF, et al. Safety and efficacy of coated flow diverters in the treatment of cerebral aneurysms during single antiplatelet therapy: a multicenter study. *Interv Neuroradiol.* 2024;30(6):819-826. [Crossref]
22. Ma Y, Madjidyar J, Schubert T, Thurner P, Barnaure I, Kulcsar Z. Single antiplatelet regimen in flow diverter treatment of cerebral aneurysms: the drug matters. a systematic review and meta-analysis. *Interv Neuroradiol*. 2023:15910199231177745. [Crossref]
23. Pierot L, Lamin S, Barreau X, et al. Coating (coating to optimize aneurysm treatment in the new flow diverter generation) study. The first randomized controlled trial evaluating a coated flow diverter (p64 MW HPC): study design. *J Neurointerv Surg*. 2023;15(7):684-688. [Crossref]
24. Sweid A, Starke RM, Herial N, et al. Predictors of complications, functional outcome, and morbidity in a large cohort treated with flow diversion. *Neurosurgery*. 2020;87(4):730-743. [Crossref]
25. Goertz L, Styczen H, Siebert E, et al. FRED X flow diverter for the treatment of intracranial aneurysms: two-center experience and mini-review of the literature. *Interv Neuroradiol.* 2024:15910199241246018. [Crossref]

Supplementary Table1. Quality assessment of included studies

Study	Retrospective (R) or prospective (P)	Included all patients (A), consecutive patients (B), or selected sample (C)	Angiographic/ clinical follow-up confirmed all outcomes (Yes/No)	Clearly reported outcomes (Yes/No)	Interventionalists treated patients and assessed angiographic outcomes (Yes/No)	Interventionalists treated patients and assessed clinical outcomes (Yes/No)	Multicenter (M) or single center (S) study
Abbas et al.[3]	R	A	Y	Y	Y	Y	M
Goertz et al.[1]	R	C	Y	Y	Y	Y	M
Hendrix et al.[4]	R	A	Y	Y	Y	Y	M
Wen et al.[15]	R	A	Y	Y	Y	Y	M
Clausen et al.[13]	R	A	Y	Y	Y	Y	S
Roy et al.[14]	R	A	Y	Y	Y	Y	M
Vollherbst et al.[5]	R	A	Y	Y	Y	Y	M
Cherednychenko.[12]	P	A	Y	N	N	N	S
Guimaraens et al.[2]	P	C	Y	Y	Y	N	M

Supplementary Table 2. Antiaggregation and antiplatelet therapies of studies

Study, year	Pre-procedure antiplatelets	Antiaggregation test	Intra-procedure anticoagulants/antiplatelets	Post-procedure antiplatelets
Abbas et al.[3]	Patients were started on dual antiplatelet therapy (DAPT) of aspirin 81 mg and clopidogrel 75 mg once daily for 10 days prior to the procedure	VerifyNow (accumetrics)	Activated clotting time was preserved at 2–3 times the patient's baseline through heparin flushes (100 U/kg)	DAPT was maintained for at least 6 months postoperatively
Goertz et al.[1]	Dual antiplatelet therapy was initiated 5–7 days before the procedure with 100 mg aspirin and 75 mg clopidogrel, 5 mg prasugrel, or 2 × 90 mg ticagrelor	VerifyNow (accumetrics) light transmission aggregometry	Heparin was administered with an initial bolus of 5000 IU followed by subsequent aliquots of 1000 IU/h	DAPT was maintained for at least 6 months postoperatively
Hendrix et al.[4]	Dual antiplatelet therapy (aspirin and a P2Y12 inhibitor) for 6months with pre-procedure platelet function testing was standard of care	Yes (not specified)	All patients received intraprocedural intravenous heparin, with 78.2% guided by activated clotting time	DAPT was maintained for at least 6 months postoperatively
Wen et al.[15]	NA	Yes (not specified)	NA	DAPT was maintained for at least 6 months postoperatively
Clausen et al.[13]	Scheduled surgery for incidental non-ruptured aneurysms involved pre-treatment with DAPT (ASA and ticagrelor) for 1 week prior to intervention. Patients with ruptured aneurysms received a DAPT loading dose after EVD stabilization (24–48 hours). For patients requiring thrombectomy, ASA was administered per rectum, and a cangrelor drip was started upon ICU arrival	Yes (not specified)	The procedure was performed under systemic heparinization (target ACT 250–300 s) and general anesthesia administered by a anesthesiologist	DAPT was maintained for at least 6 months postoperatively
Roy et al.[14]	Patients started on DAPT with aspirin 81 mg and clopidogrel 75 mg once daily for 10 days prior to the procedure	P2Y12 assay (VerifyNow, accumetrics)	Activated clotting time was preserved at 2–3 times the patient's baseline through heparin flushes (100 U/kg)	DAPT was maintained for at least 6 months postoperatively
Vollherbst et al.[5]	In all patients, the flow diverter was implanted on the DAPT	Platelet reactivity testing	NA	DAPT was maintained for at least 6 months postoperatively
Cherednychenko et al.[12]	In all patients, the flow diverter was implanted on the DAPT (ticagrelor and acetylsalicylic acid)	NA	NA	DAPT was maintained for at least 6 months postoperatively
Guimaraens et al.[2]	Patients were initiated on dual antiplatelet therapy (DAPT) comprising aspirin (300 mg once daily) and clopidogrel (75 mg once daily), starting 5 days before the intervention	VerifiyNow	At the beginning of the procedure, all patients received IV heparin (50IU/kg), followed by an additional bolus of 1000 IU during the intervention to maintain a clotting time >250–300 s	After the procedure, patients continued DAPT for 6 months, consisting of aspirin (300 mg once daily) and clopidogrel (75 mg once daily). Subsequently, the aspirin dosage was adjusted to 100 mg once daily while the clopidogrel dosage remained at 75 mg once daily up to the 1-year follow-up

All antiplatelet doses were administered orally and reported as daily amounts. ASA, acetylsalicylic acid (aspirin); IV, intravenous; NA, not applicable; EVD, external ventricular drainage; ICU, intensive care unit; ACT, activated clotting time; IU, international unit.

Supplementary Table 3. Summary of complications

Study	Procedure-related complications (n)	Device deployment complications (n)	Major complications (n)	Minor complications (n)	Ischemic/ thrombotic complications (n)	Hemorrhagic complications (n)
Abbas et al.[3]	Access site complication (1), transient ischemic attack (2), ischemic stroke in the treated territory (1)	Access site complication (1)	Ischemic stroke in the treated territory (1)	TIA (2)	TIA (2), ischemic stroke (1)	None
Goertz et al.[1]	Access site complication (3), contrast related complication (1), thromboembolic event (4), hemorrhagic event (1), vasospasm (2), ischemic event (1), minor stroke (1)	Access site complication (3), contrast related complication (1)	Vasospasm (2)	Minor stroke (1), ischemic event (1)	Minor stroke (1)	Hemorrhagic events (1)
Hendrix et al.[4]	Intraprocedural stent thrombosis (1), stent thrombosis <24 hours (1), periprocedural minor stroke (<30 days) (3), delayed stent thrombosis (>180 days) (1), microwire vessel perforation (1), delayed subarachnoid hemorrhage (1), periprocedural seizure (<30 days) (1), device related events (2), access site complications (2)	Device related events (2), access site complications (2)	Intraprocedural stent thrombosis (1), stent thrombosis <24 hours (1)	Delayed SAH (1)	Intraprocedural stent thrombosis (1), stent thrombosis <24 hours (1), periprocedural minor stroke (<30 days) (3), delayed stent thrombosis (>180 days) (1)	Microwire vessel perforation (1), delayed subarachnoid hemorrhage (1)
Wen et al.[15]	Left MCA infarction (1), asymptomatic events (2), ICA dissection during the procedure (1), femoral pseudoaneurysm (1), transient neurological symptoms (2)	ICA dissection during the procedure (1)	Left MCA infarction (1)	Femoral pseudoaneurysm (1), transient neurological symptoms (2)	Left MCA infarction (1)	None
Clausen et al.[13]	Acute stent narrowing (1), radial oozing/hematoma (4)	None	Acute stent narrowing (1)	Radial oozing/ hematoma (4)	None	None
Roy et al.[14]	The total number of complications was 16 (10.6%), 11 (68.8%) of which occurred on the day of the procedure and 4 (25%) within 6 months of the postoperative period	1 failed deployment (0.7%)	5 neurological complications (4.1%), including 2 deaths	6 access site complications (4.0%), 2 TIAS (1.3%)	4 ischemic strokes in treated territory (3.2%)	2 intracranial hemorrhages (1.3%)
Vollherbst et al.[5]	5 technical complications (3.1%) including stent shortening, kinking, insufficient opening, and coil migration	None reported, 100% successful implantation	5 major adverse events (3.1%) including 2 ischemic strokes, 1 intracerebral hemorrhage, 1 mass effect, and 1 vasospasm	21 minor adverse events (13.0%) including 9 neurological events (5.6%)	8 thrombotic events in 7 patients (4.3%), including 4 intra-procedural and 4 post-procedural in-stent thromboses	1 intra cerebral hemorrhage
Cherednychenko et al.[12]	No major technical difficulties reported in FRED X deployment	One case required balloon angioplasty for FD opening optimization	Not reported	Not reported	Not reported	Not reported
Guimaraens et al.[2]	2 complications (2.35%), both non-symptomatic	NA	None reported in the FREDX group	None reported in the FREDX group	None reported in the FREDX group	None reported in the FREDX group

TIA, transient ischemic attack; SAH, subarachnoid hemorrhage; MCA, middle cerebral artery; ICA, internal carotid artery; FRED, flow re-direction endoluminal device.

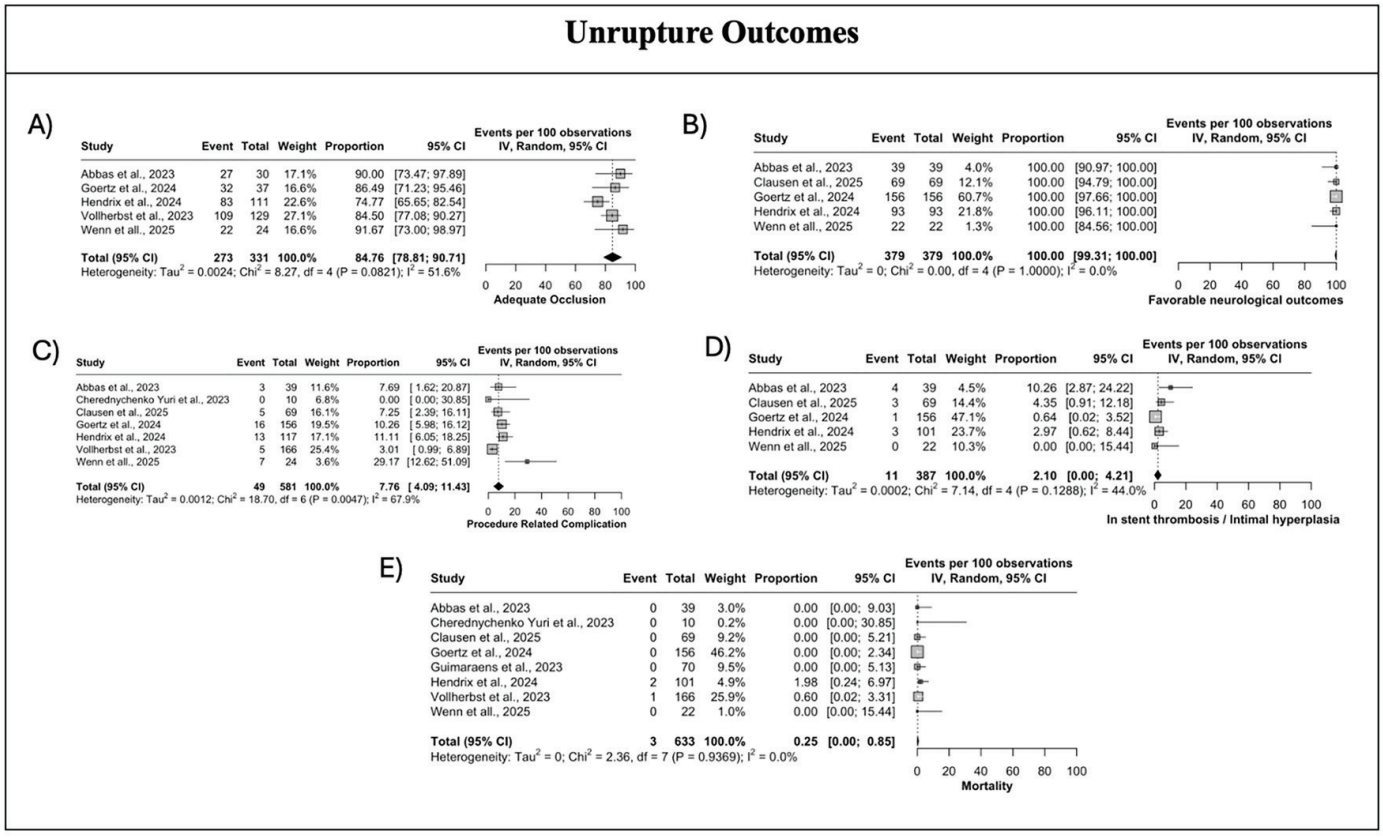
Supplementary Table 4. Management and outcomes of complications

Study	Description of complications (n)	Management of complications	Outcome of complication	Immediate angiographic outcome of covered vessel by FD (n)	Angiographic outcome of covered vessels by FD at last follow-up (n)
Abbas et al.[3]	Access site complication (1), transient ischemic attack (2), ischemic stroke in the treated territory (1)	NA	Patients discharged with mRS scores 0	Patent (28/46)	15 branches arising from the aneurysm sac/neck, without angiographic follow-up mentioned
Goertz et al.[1]	Access site complication (3), contrast related complication (1), thromboembolic event (4), hemorrhagic event (1), vasospasm (2), ischemic event (1), minor stroke (1)	IV tirofiban	Patients fully recovered	Patent (69/156)	4 branch involvement with adjunctive coiling and jailing, without angiographic follow-up mentioned
Hendrix et al.[4]	Intraprocedural stent thrombosis (1), stent thrombosis <24 hours (1), periprocedural minor stroke (<30 days) (3), delayed stent thrombosis (>180 days) (1), microwire vessel perforation (1), delayed subarachnoid hemorrhage (1), periprocedural seizure (<30 days) (1), device related events (2), access site complications (2)	IV tirofiban, IV eptifibatide	The symptoms resolved spontaneously; however, two deaths occurred due to parent vessel occlusion	Patent (1/101)	NA
Wen et al.[15]	Left MCA infarction (1), Asymptomatic events (2), ICA dissection during the procedure (1), femoral pseudoaneurysm (1), Transient neurological symptoms (2)	ICA dissection was managed with the insertion of an additional stent, while femoral pseudoaneurysm was treated with manual compression	The symptoms resolved in all patients except for one, who experienced a persistent symptom	NA	NA
Clausen et al.[13]	Acute stent narrowing (1), radial oozing/hematoma (4)	Angioplasty	The mean mRS score at discharge was 0 (IQR; 0, 0), with no worsening in condition attributed to the procedure performed	NA	NA
Roy et al.[14]	Ischemic stroke in treated territory (n = 4)-transient ischemic attack (= 2)-intracranial hemorrhage (n = 2)-access site complications (n = 6)-two deaths due to complications (one from ICH, one from aneurysm rupture post-treatment)	Balloon angioplasty and stenting for vessel occlusion, decompressive hemicraniectomy for ICH, conservative management for mild in-stent stenosis, and comfort care for severe cases	Most neurological complications resolved within 3 months. Two in-hospital deaths 95.9% of patients functionally independent at 12 months	66% of aneurysms showed >90% contrast stasis -100% had good wall apposition and complete neck coverage	Complete occlusion (RROC I) in 63.5% of cases at 12 months residual neck (RROC II) in 20% Residual aneurysm (RROC III) in 16.5% - in-stent stenosis reduced over time (mild 9.5%, moderate 1.2%, severe 1.2%)
Vollherbst et al.[5]	Minor adverse events occurred in 13.0% of the patients. Nine of 21 of these events were neurologic, resulting in a minor neurologic adverse event rate of 5.6%. Major adverse events (2 ischemic strokes, 1 intracerebral hemorrhage, 1 mass effect of the aneurysm, and 1 case of vasospasms caused by a pre interventional aneurysmal SAH) were observed in 5 patients (3.1%), leading to neurologic morbidity in 3 (1.9%) and death in 2 patients (1.2%)	Tirofiban administered for thrombotic events-balloon angioplasty for in-stent stenosis conservative management for mild cases	3 patients had neurological morbidity (1.9%) - 2 deaths (1.2%) due to mass effect and stent occlusion following SAH	Successful deployment in all cases-good or very good vessel wall apposition in 98.8% of cases	Complete occlusion (RROC I) in 66.2% of cases -residual neck (RROC II) in 16.9% - residual aneurysm (RROC III) in 16.9% in-stent stenosis observed in 10.6% of patients (mostly mild)

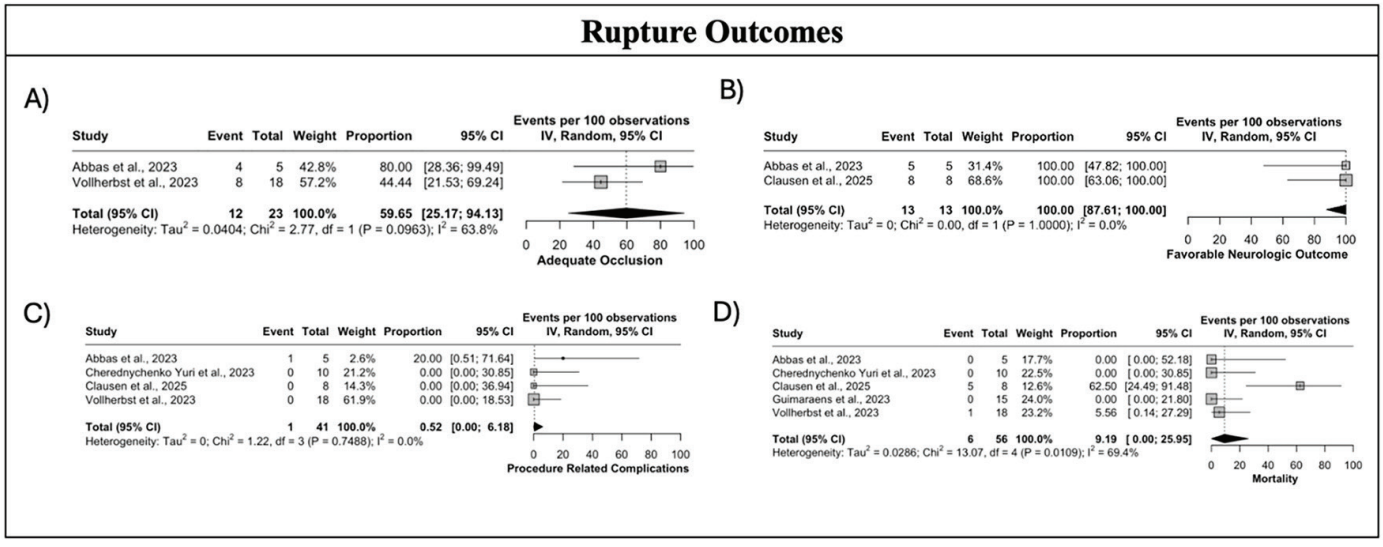
Supplementary Table 4. Continued

Study	Description of complications (n)	Management of complications	Outcome of complication	Immediate angiographic outcome of covered vessel by FD (n)	Angiographic outcome of covered vessels by FD at last follow-up (n)
Cherednychenko et al.[12]	In our study, we managed to avoid thrombotic complications, postoperative neurological morbidity and mortality	NA	No neurological morbidity or mortality reported in the FRED X group-all patients discharged in stable condition with no neurological deficits	100% successful implantation with good vessel wall apposition in FRED X cases	No ischemic events observed in FRED X patients Follow-up imaging confirmed satisfactory FD positioning and aneurysm occlusion
Guimaraens et al.[2]	2 cases of non-symptomatic complications: 1 stent misplacement and 1 intimal hyperplasia-induced stenosis	Conservative management for the cases of stenosis and stent misplacement	No neurological morbidity or mortality in the FRED X group	100% successful deployment with good vessel wall apposition	79.4% complete occlusion at 1-year follow-up, significantly higher than FRED (59.3%)

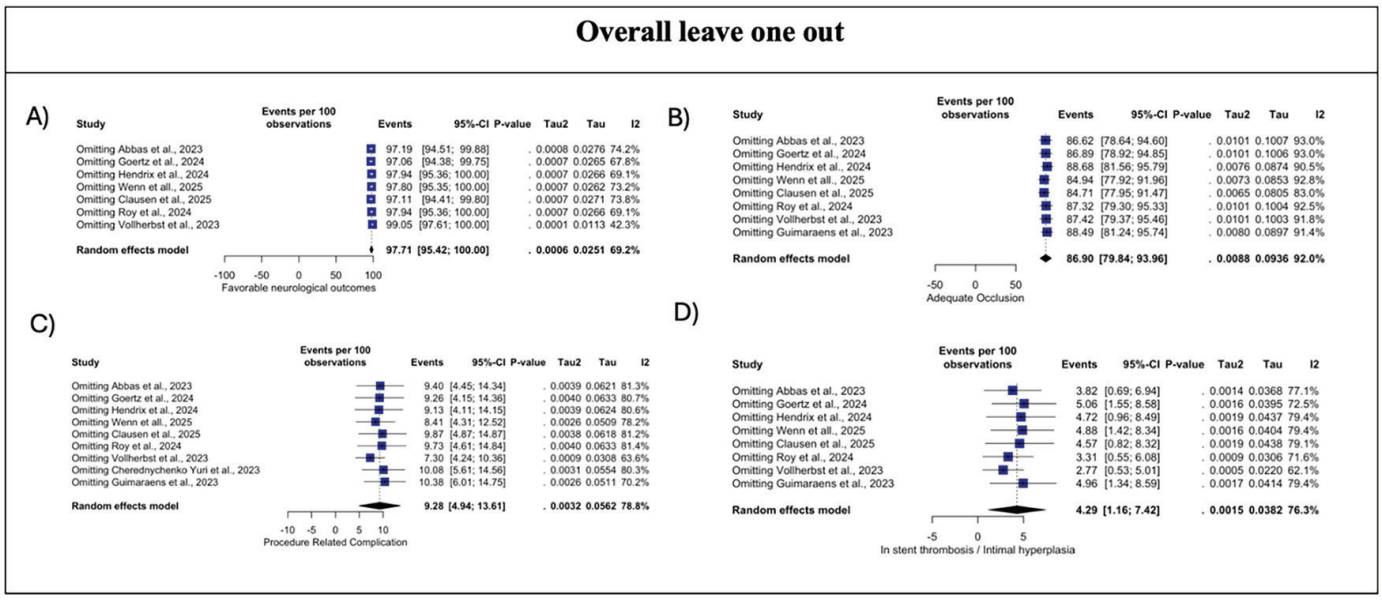
NA, not applicable; mRS, modified Rankin Scale; MCA, middle cerebral artery; ICA, internal carotid artery; IQR, interquartile range; FRED, flow re-direction endoluminal device; FD, flow diverter; IV, intravenöz; ICH, intracerebral hemorrhage; RROC, raymond-roy occlusion classification; SAH, subarachnoid hemorrhage.



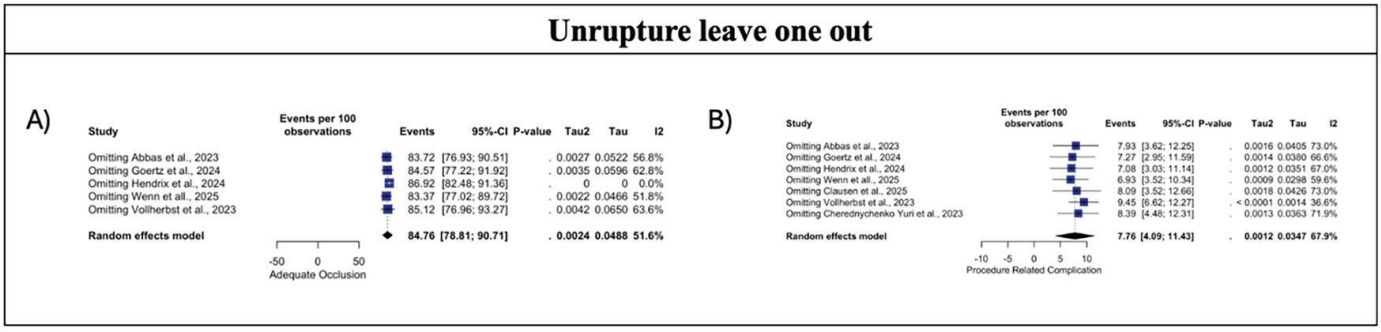
Supplementary Figure 1. Unruptured aneurysms subanalysis–outcomes. CI, confidence interval; IV, intravenous.



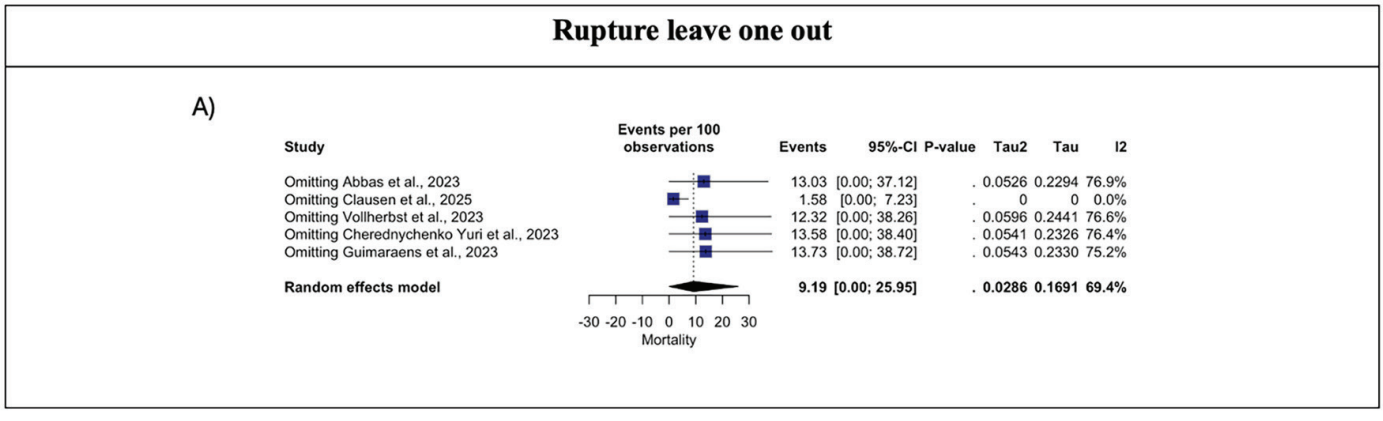
Supplementary Figure 2. Ruptured aneurysms subanalysis-outcomes. CI, confidence interval; IV, intravenous.



Supplementary Figure 3. Leave-one-out sensitivity analysis. CI, confidence interval.



Supplementary Figure 4. Leave-one-out sensitivity analysis. CI, confidence interval.



Supplementary Figure 5. Leave-one-out sensitivity analysis. CI, confidence interval.