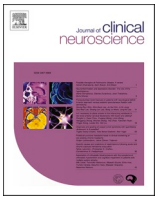
Journal of Clinical Neuroscience 130 (2024) 110909

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.journals.elsevier.com/journal-of-clinical-neuroscience



# Evaluating the efficacy and safety of flow diverter in pediatric cerebral aneurysm treatment: A systematic review and meta-analysis

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ARTICLE INFO

*Keywords:*
Flow diverter
Pipeline
Endovascular
Pediatric
Aneurysm cerebral

ABSTRACT

*Background:* Intracranial aneurysms are uncommon in pediatric patients, accounting for less than 5% of all intracranial aneurysms. Despite their rarity, they present notable challenges because of their non-saccular morphology. Given the rising utilization of flow-diverter (FD) devices such as the Pipeline Embolization Device (PED), there's a significant need for a systematic review and *meta*-analysis to evaluate their applicability for pediatric populations and assess their safety and efficacy.

*Methods:* Medline, Embase, and Web of Science databases following PRISMA guidelines. We used single proportion analysis with 95 % confidence intervals under a random-effects model, $I^2$ to assess heterogeneity, and Baujat and sensitivity analysis to address high heterogeneity. Eligible studies included those with ≥3 patients and focused on outcomes such as immediate and final occlusion, good clinical outcomes, complications, and mortality.

*Results:* The analysis comprised seven studies involving 80 patients with a total of 91 aneurysms. Immediate occlusion was observed in 49 out of 62 cases with a rate of 90 % (95 % CI: 74 % to 100 %). Final occlusion was achieved 71 out of 87 aneurysms a rate of 88 % (95 % CI: 78 % to 98 %). Notably, good clinical outcomes were reported for 59 out of 67 patients, representing a rate of 92 % (95 % CI: 83 % to 100 %). Complications occurred in 5 out of 73 patients, with an incidence rate of 3 % (95 % CI: 0 % to 11 %). The total mortality analysis revealed that 5 out of 72 patients died, resulting in a rate of 6 % (95 % CI: 0 % to 12 %). However, when examining mortality related to the FD, no patients died, resulting in a mortality rate of 0 % (95 % CI: 0 % to 3 %).

*Conclusion:* Our systematic review and *meta*-analysis reveal promising outcomes for FD treatment in pediatric intracranial aneurysms. We observed high occlusion rates and favorable clinical results, suggesting that the technique is safe and effective in the short term. However, further studies are necessary to validate and expand upon these findings.

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https://doi.org/10.1016/j.jocn.2024.110909
Received 23 July 2024; Accepted 31 October 2024
Available online 9 November 2024

## 1. Background

Intracranial aneurysms are rare among pediatric patients, representing less than 5 % of all intracranial aneurysms [1]. Different from adults, pediatric cerebral aneurysms have a greater tendency to present with a non-saccular morphology, which represents a surgical challenge to both the endovascular and open techniques. [2] Furthermore, a male predominance, a higher proportion of posterior circulation aneurysms, and a higher proportion of complex aneurysms are other differences between the pediatric and adult populations.

The choice of the most appropriate therapeutic technique is crucial for the treatment of intracranial aneurysms, as it directly impacts the outcomes. Although both endovascular and surgical methods are used to address this rare condition, the less invasive approach has become increasingly common. [3] In the literature, various endovascular procedures have been specifically described for the management of pediatric intracranial aneurysms, including coil embolization, pipeline embolization, liquid embolization, and endovascular vessel sacrifice [3].

Flow-diverter devices are a feasible and effective technique for unruptured complex aneurysms, where coiling and clipping are highly challenging, especially in cases of aneurysms with complex anatomy, such as blister-like, fusiform, giant, and dissecting aneurysms. [4] However, the pipeline embolization device (PED; Medtronic) was originally approved for endovascular treatment of intracranial aneurysms in adults (22 years and above), but it can also be used off-label in pediatric patients with aneurysms that cannot be treated with conventional endovascular methods [5,6].

Due to the low percentage of cerebral aneurysms in pediatric patients and also to the lack of large series evaluating FD devices in children, it is a complex task to analyze this specific treatment method. [1] Aiming to verify the safety and efficacy of FD devices in managing cerebral aneurysms in pediatric patients, we performed a systematic review and *meta*-analysis to clarify this important topic.

## 2. Methods

This systematic review and *meta*-analysis adhered to the guidelines established by the Cochrane Handbook and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement. [7,8].

### 2.1. Eligibility criteria

In this systematic review, we encompassed all studies documenting using the FD for treating aneurysms in pediatric patients. Moreover, non-English papers, reviews, letters to the editor, abstracts of confidence, and commentaries were excluded during the initial assessment.

### 2.2. Search strategy and data extraction

The comprehensive search was conducted in multiple databases, including Medline, Embase, and Web of Science, utilizing a search strategy with keywords such as: “aneurysm”, “pediatric”, “child”, “infant”, “cerebral”, “intracranial”, “brain”, “flow diversion”, “diverter”, “flow-diverter”, “pipeline”, “PED”, “endovascular”. Two researchers (S.B. and M.A.P.B.) autonomously conducted the bibliographic search and study selection process. Discrepancies were resolved through deliberations and consultations with the senior author (R.B.). Two authors independently assessed the studies for data extraction (P.C.A.R. and M.Y.F.), and any conflict was resolved by a third author (M.P.S.).

### 2.3. Endpoints

The data extraction encompassed several key metrics, including final occlusion, immediate occlusion, good clinical outcomes, complications, and mortality. Good clinical outcomes were defined as patients scoring between 0 and 2 on the Modified Rankin Scale (MRS) or between 4 and 5 on the Glasgow Outcome Scale (GOS). Related mortality was defined as deaths directly attributable to the FD. Immediate occlusion was identified when complete aneurysm occlusion was observed in postoperative angiography, classified as either OKM D (O’Kelly-Marotta D) or reported as complete occlusion by the studies. Final occlusion was determined similarly, based on the OKM D classification and the indication of complete occlusion during follow-up angiography.

### 2.4. Risk of bias assessment

Cochrane’s “Risk of Bias in Non-Randomized Studies – of Interventions” (ROBINS-I) tool was adopted to evaluate the risk of bias in the included studies. [9] Following this tool, each study was scrutinized across seven domains and categorized as having low, moderate, serious, or critical bias. Two authors independently assessed the quality of the studies (S.B. and C.K.F.), and any conflict was resolved by a third author (M.P.S).

### 2.5. Statistical analysis

A single proportion analysis under the random-effects model, along with 95 % confidence intervals (CI), was employed to pool the data. Heterogeneity was assessed using the $I^2$ statistic, where $I^2 > 40$ % was considered significant, and outlier studies were identified using Baujat analysis. Sensitivity analysis was conducted to address high heterogeneity. Random-effects model was adopted. Statistical analysis was conducted using R Studio software (version 4.2.3, R Foundation for Statistical Computing, Vienna, Austria).

## 3. Results

### 3.1. Study selection

The investigation yielded 1,621 articles, 318 from Medline, 967 from Embase, and 336 from Web of Science. After the elimination of 229 duplicated reports, 1392 citations underwent screening. Next, the exclusion of 1368 articles based on title or abstract sorting was performed. 24 studies underwent a full-text assessment. Subsequently, 17 articles were excluded during the full-text screening. Finally, a total of 7 studies were included. The study selection process is depicted in Fig. 1.

### 3.2. Risk of bias assessment

We employed the ROBINS-I tool to evaluate seven distinct scientific articles across seven domains. Additionally, employing this methodology, the overall risk of bias was categorized as moderate in three studies and serious in four studies. The graphical representation of these classifications can be observed in Supplementary Figs. 2 and 3.

### 3.3. Patients’ baseline characteristics

Our comprehensive analysis of 7 studies identified 80 patients with 91 aneurysms. Six studies were retrospective. The available demographic data indicated that ages ranged from 3 to 21 years among the patients in the studies, with a median mean age of 9.6 years reported across five studies. Three studies reported the state of the aneurysm with a total of 63, of which 55 were ruptured at presentation (87.3 %), while 8 were unruptured (12.7 %). The median of the means for the angiographic follow-up reported by six studies is 10.3, and the range is 6 to 22.6 months. Seven studies reported on a total of 75 treated aneurysms, with 60 located in the anterior circulation and 15 in the posterior circulation. The vessels most frequently involved in the anterior circulation include the internal carotid artery (ICA), the middle cerebral artery (MCA), and the anterior cerebral artery (ACA). In the posterior circulation, the most commonly affected vessels include the basilar artery

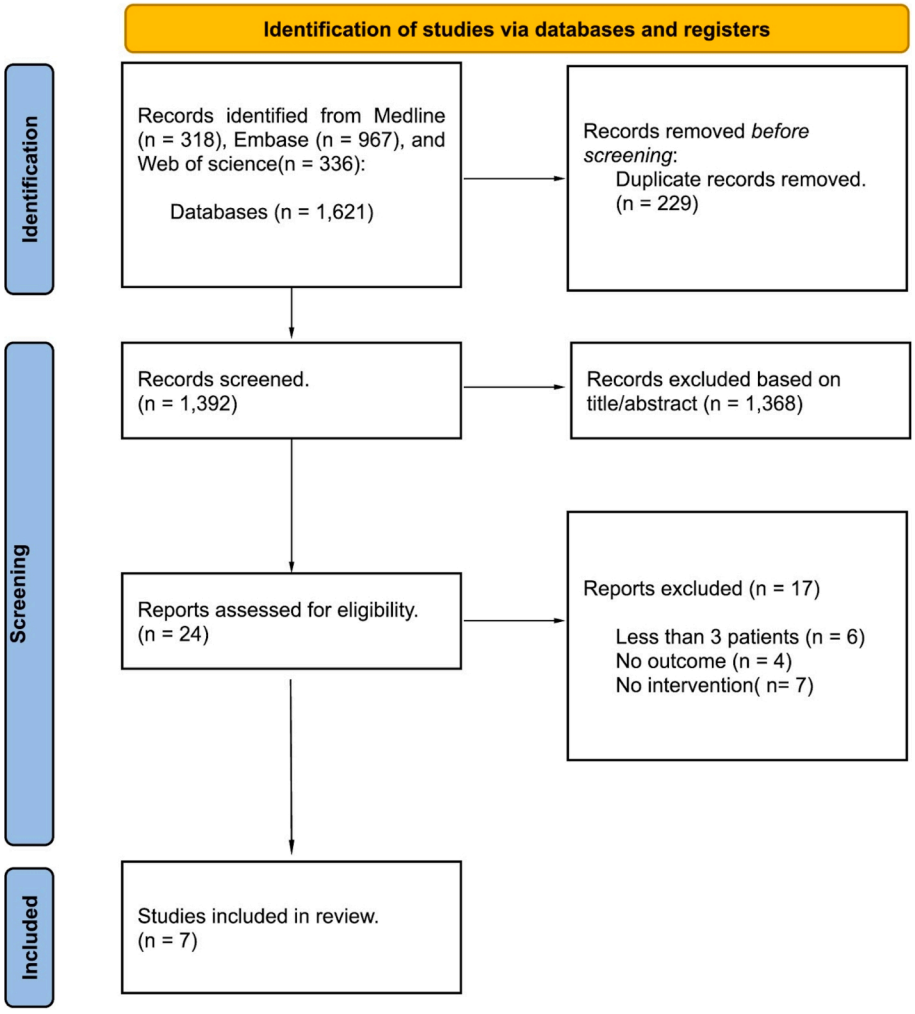


**Fig. 1.** PRISMA Flow Diagram.

(BA), the posterior cerebral artery (PCA), and the vertebral artery (VA). The median mean follow-up duration is approximately 15 months, ranging from 0.5 to 57 months. PED, FRED, and Silk were the most utilized FD. More information about clinical presentation, localization, and diameter is provided in Table 1.

Among the five studies that reported complications, only two of them documented occurrences, while the others did not report any. The complications were intra-stent thrombosis, mass effect, major ischemic stroke, and stent foreshortening. We analyzed the studies that reported immediate and final occlusion, with five and six studies available, respectively. Immediate occlusion was observed in 51 out of 64 aneurysms, while final occlusion was achieved in 68 out of 84. Mortality data were available from six studies, indicating five deaths. Data were only reported in five studies when evaluating good clinical outcomes based on the MRS and GOS scale. Additional details can be found in Table 2.

## 4. Outcomes

### 4.1. Immediate occlusion

In examining immediate occlusion across four studies involving 62 aneurysms, 49 achieved complete occlusion post-surgery, resulting in a combined resolution rate of 90 % (95 % CI: 74 to 100 %, $I^2 = 57$ %, Fig. 2). Leave-one-out sensitivity analysis revealed an immediate occlusion rate ranging from 87 % to 100 %, with just the omitting of Cherian et al. [5] resulting in observed heterogeneity at 0 %, in Fig. 3. Baujat analysis demonstrated that Cherian et al. [5] was the most significant contributor to heterogeneity, as shown in Supplementary Fig. 3.

### 4.2. Final occlusion

In the comprehensive examination of final occlusion, 71 out of 87 aneurysms were found to be occluded, reflecting an occlusion rate of 88 % (95 % CI: 78 % to 98 %; $I^2 = 28$ %, as illustrated in Fig. 4). The angiographic follow-up median across six studies is 10.3 months, with a range of 6 to 22.6 months. However, upon conducting sensitivity analysis, it was noted that omitting Cherian et al. [5] from the study led to a decrease in heterogeneity to 0 % and an increase in the rate of final occlusion to 93 % (95 % CI: 83 % to 100 %), as depicted in Fig. 5. Baujat's analysis Cherian et al. [5] as the primary contributor to both the outcome and the observed heterogeneity, in supplementary Fig. 4.

### 4.3. Good clinical outcomes

Information regarding favorable clinical outcomes was accessible for 67 individuals, with 59 experiencing good clinical outcomes. The median follow-up duration is 15 months, with a range of 0.5 to 57 months. This yielded a rate of 92 % (95 % CI: 83 % to 100 %; $I^2 = 15$ %, in Fig. 6).

### 4.4. Complications

Across the studies, data from 73 patients were deemed eligible for

**Table 1**
Patients baseline characteristics.

| Study | Type of Study | N° patients | N° aneurysm | Rup/ Unrup | Mean age (years) | Mean aneurysm diameter (mm) | Aneurysm location | Clinical Presentation | Antiplatelet management | Type of FD | Mean angiographic follow-up |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Barburoglu 2017 [10] | R | 5 | 5 | N/A | N/A | N/A | (1)ACA; (1) MCA; (2) ICA; (1) VA | N/A | Clopidogrel: 75 mg/day for patients weighing 45 kg; aspirin: 300 mg/day for children weighing 45 kg or 100 mg/ day for smaller children, both for at least 5 days before endovascular treatment. | N/A | 22.3 ((range 7–52) |
| Cherian 2020 [5] | R | 39 | 50 | 45U/ 5R | (range 3–21) | 10 | (29)ICA; (7) MCA; (2) ACA; (1) VA; (1) AICA; (2) PICA; (8) BA; (3) PCA | (5) Subarachnoid hemorrhage; (14) Headache; (10)Recurrent aneurysm | Clopidogrel and aspirin | N/A | 15 (median 11) |
| Fry 2023 [11] | R | 3 | 3 | 2U/1R | 13 (range 3–18) | 7.9 | (1)ACA; (2) ICA | (1) patient: SAH, IVH, subdural hematoma | Clopidogrel: 75 mg/day and aspirin: 100 mg/ day. | PED; FRED | 1; 0.5; N/A |
| Han 2023 [12] | R | 16 | 16 | N/A | 13 | N/A | (5) ICA; (1) MCA; (2) VA; (3)VBJ; (3) BAT; (2)PCA | (4) Incidental; (8) Headache; (1) Epilepsy; (1) Diplopia; (1) Numbness in the left limb; (1) Dizziness | N/A | PED | 8.2 (range 5.7–15.3) |
| Shirani 2020 [13] | N/A | 3 | 3 | N/A | 9.7 range 5–12) | N/A | (2) VA; (2) ICA | (1) Seizure; (1) headache; (1) blurred vision | Clopidogrel: 0.2–1.0 mg/kg/ day (maximum 75 mg/day); aspirin: 81 mg/day, both for 5 days prior to the procedure. | PED | 8.6 (range 6–12) |
| Santos −Franco 2022 [14] | R | 10 | 10 | 8U/2R | 9.5 (range 7–15) | 3,175 | (1) V4; (4) MCA; (3)ICA; (5) BA; (6) PCA | (2) SAH; (3) epilepsy; (3) cranial nerve compression; (4) headache | Clopidogrel: 37.5 mg and aspirin: 100 mg for children weighing <45 kg; clopidogrel: 75 mg and aspirin: 100 mg for children weighing >45 kg. | FRED, PED, silk | 12 |
| Wang 2019 [15] | R | 4 | 4 | N/A | 9.25 (range 8–11) | 15 | (1) LVA; (2) VBJ; (2) BA | (3) Headache; (1) Intermittent headache; (1) diplopia; (1) dysphagia; (1) vertigo | Clopidogrel: 1 mg/ kg and aspirin: 100 mg for 5 days prior to treatment. | N/A | 6 |

**N**/A: not available; R: retrospective; U: unruptured; R: ruptured; ICA:Internal Carotid Artery; MCA:Middle Cerebral Artery; ACA:Anterior Cerebral Artery; VA: Vertebral Artery; AICA:Anterior Inferior Cerebellar Artery; PICA:Posterior Inferior Cerebellar Artery; BA:Basilar Artery; PCA:Posterior Cerebral Artery; LVA:Labyrinthine Artery; VBJ:Bulbopontine Junction; OA: Ophthalmic artery; SHA: Superior hypophyseal; AChA: Anterior choroidal; SCA: Superior cerebellar artery; BAT: Basilar trunk; PED: Pipeline; FRED: Flexible Retrievable Endovascular Device; FD: Flow-diverter.

analysis, revealing complications in only five cases. The incidence rate of these complications was estimated at 3 % (95 % CI: 0 % − 11 %; $I^2 =$ 40 %), as depicted in Fig. 7. Upon conducting a leave-one-out analysis, it was discovered that omitting Han et al. [12] resulted in a decrease in heterogeneity to 0 %, as shown in Fig. 8. Baujat's analysis indicated that Han et al. [12] contributed slightly to the overall results and was primarily responsible for the observed heterogeneity in the analysis, as visualized in the Supplementary Fig. 5. Furthermore, the asymmetry observed in the funnel plot suggested a potential publication bias, with additional details available in Supplementary Fig. 8 (Fig. 9).

### 4.5. Mortality

Among the 72 patients, five deaths occurred. As shown in Fig. 10, the pooled analysis confirmed a total mortality rate of 6 % (95 % CI: 0 % to 12 %, $I^2 = 0$ %).

### 4.6. Related mortality associated with the FD

Concerning mortality associated with the FD, there were no reported deaths among the studies. After analysis, a related mortality rate of 0 %,

**Table 2**
Outcomes.

| Study | N° patients | N° aneurysm | Follow-up months | Complications | Immediate Occlusion | Final Occlusion | Final mRS/ GOS | Total Mortality |
|---|---|---|---|---|---|---|---|---|
| Barburoglu 2017 [10] | 5 | 5 | 22.3 | 0 | 5 | 5 | N/A | N/A |
| Cherian 2020 [5] | 39 | 50 | 15 | 0 | (37/50) | 37/50 | MRS = (25) 0; (2) 1; (1) 2; (1) 3;(2) 4; (3) 6; Unknown 5 | 3 |
| Fry 2023 [11] | 3 | 3 | 0.5; 1; N/A | (1) In-stent thrombosis | 2/2 | N/A | (1)No neurological deficits; (1) Ambulating with assistance; (1) N/A | 0/2 |
| Han 2023 [12] | 16 | 16 | 45,9 median range 37,8–57 | (2)mass effect; (1) major ischemic stroke; (1) stent foreshortening | N/A | 14 | MRS= (15) 0–2; (1) 6 | 1 |
| Shirani 2020 [13] | 3 | 3 | 8.6 | N/A | 3 | 3 | (3) GOS 5 | 0 |
| Santos-Franco 2022 [14] | 10 | 10 | 15,4 | 0 | N/A | 9 | (9) GOS 5; (1) GOS 4 | 0 |
| Wang 2019 [15] | 4 | 4 | 6 | N/A | 4 | 3/3 | (3) 0, (1) 6 | 1 |

MRS: Modified ranking scale; GOS: Glasgow outcome scale; N/A: Not available;

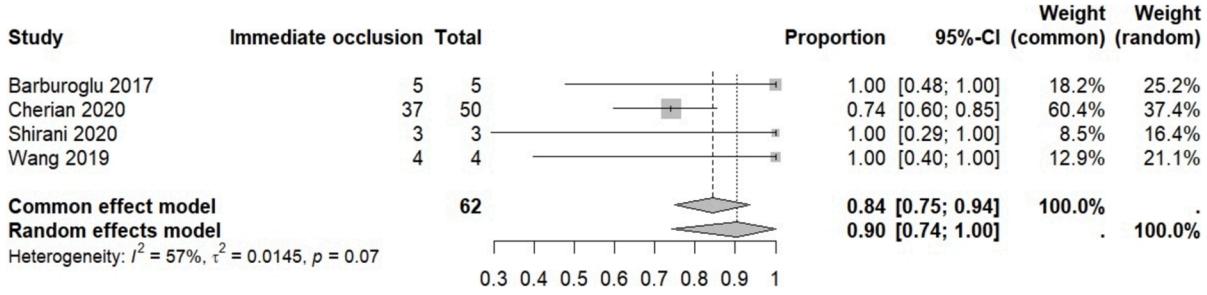


**Fig. 2.** Immediate occlusion.

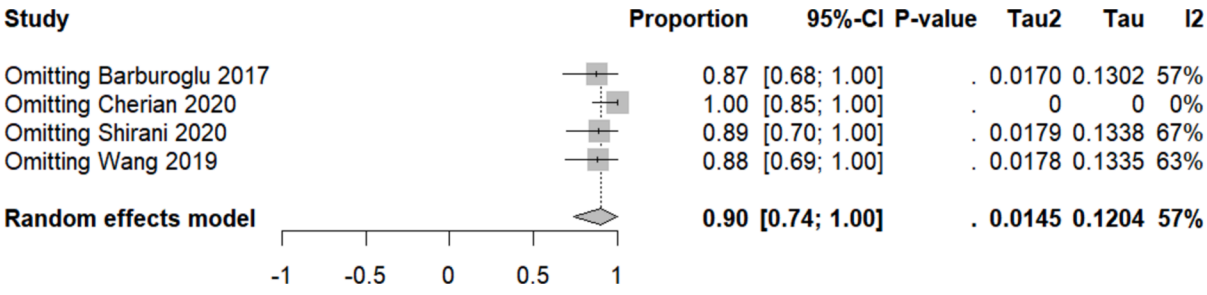


**Fig. 3.** Immediate occlusion – Leave-one-out.

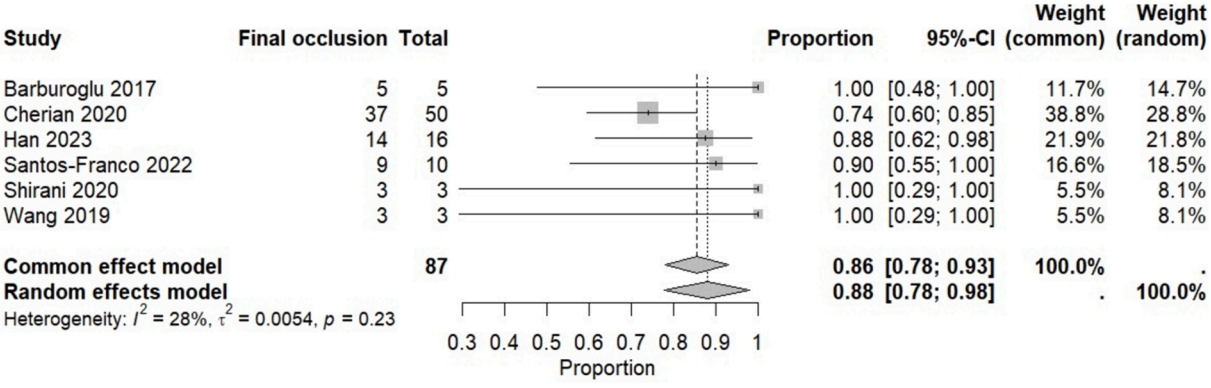


**Fig. 4.** Final Occlusion.

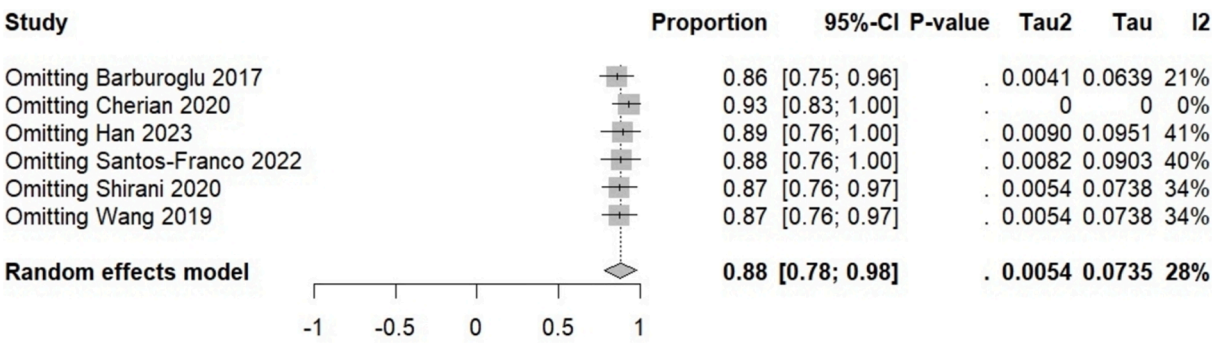


**Fig. 5.** final occlusion – Leave-one-out.

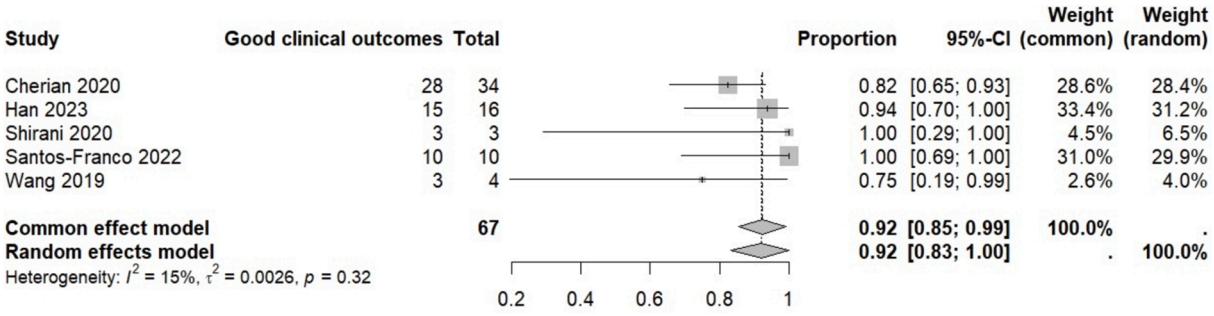


**Fig. 6.** Good Clinical Outcomes.

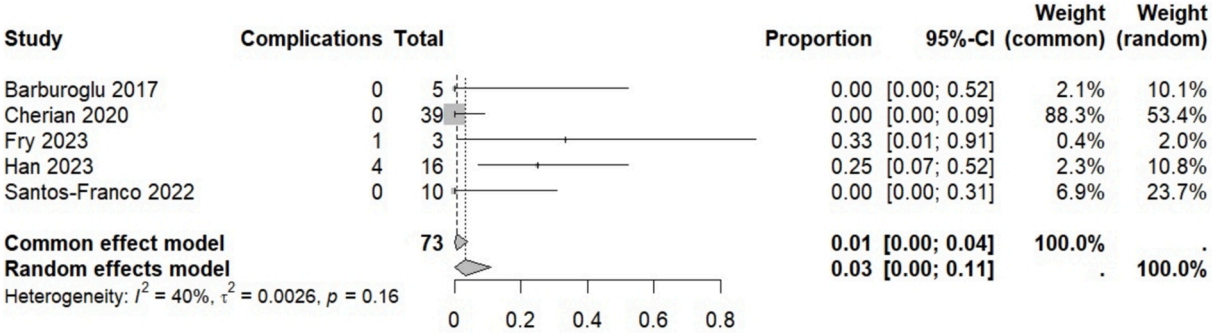


**Fig. 7.** Complications.

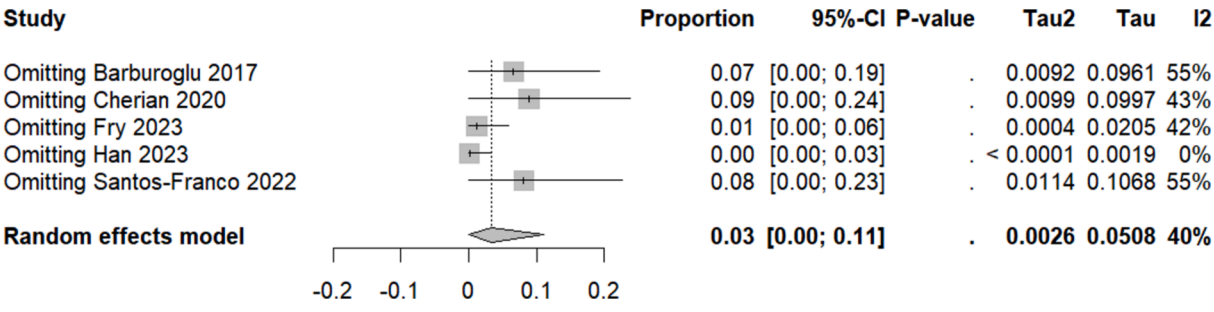


**Fig. 8.** Complications – Leave-one-out.

with a confidence interval of 0 % to 3 % and a heterogeneity value of $I^2$ = 0 %. The results of the pooled analysis are presented in Fig. 10.

## 5. Discussion

This *meta*-analysis aimed to assess the safety and efficacy of the FD in treating intracranial aneurysms among pediatric patients, focusing on outcomes such as final occlusion, favorable clinical outcomes, mortality, related mortality, and postoperative complications.

Pediatric intracranial aneurysms represent a rare condition, accounting for 0.5 %–4.6 % of all intracranial aneurysms. [16–19] Unlike adults, children lack typical risk factors, and the likelihood of an

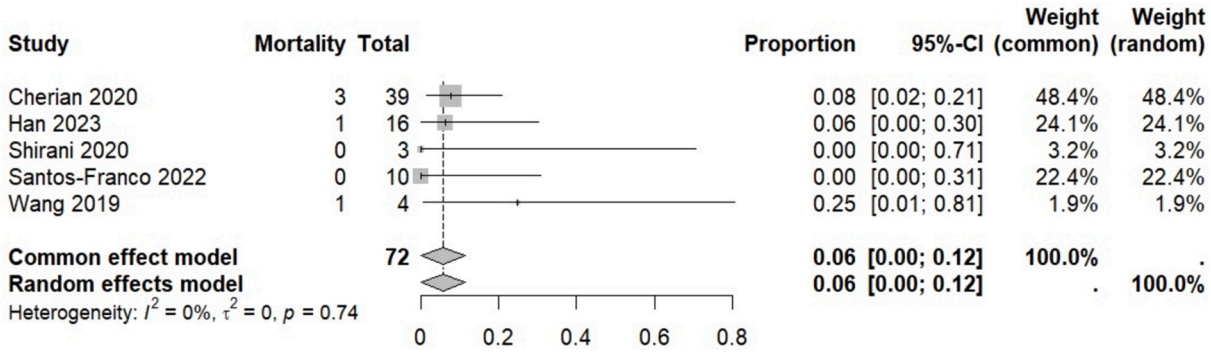


**Fig. 9.** Mortality.

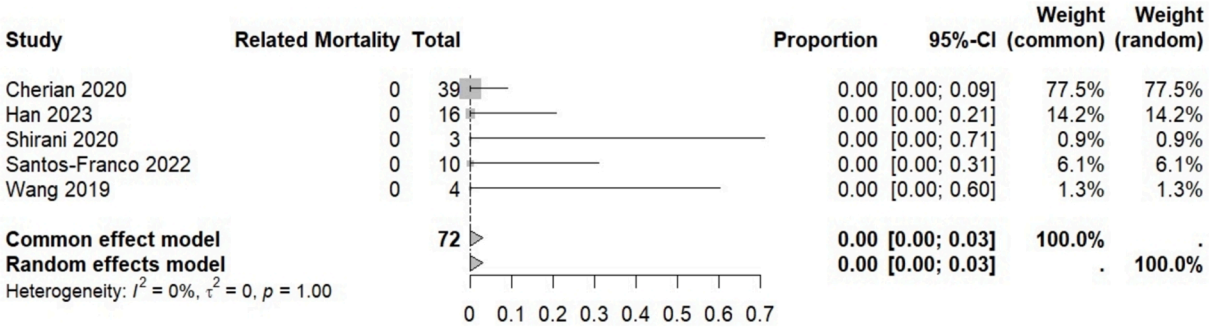


**Fig. 10.** Related Mortality.

aneurysm depends on intrinsic vessel integrity and external insults. [19] Pediatric aneurysms, often fusiform, giant, and complex, are typically found in the posterior circulation. [20] Clinical manifestations include subarachnoid hemorrhage, headache, neck stiffness, vomiting, seizures, coma, hydrocephalus, or focal neurological deficits, with a higher prevalence in male patients. [20] FD has gained attention in the endovascular treatment of intracranial aneurysms in adults, with increasing evidence suggesting its efficacy in pediatric cases, especially in managing complex aneurysms. [21].

The anatomy of an aneurysm plays a crucial role in determining the most appropriate therapeutic approach. The use of FD in treating intracranial aneurysms is crucial for complex anatomies, such as blister-like, fusiform, giant, and dissecting aneurysms, where other approaches may fail to obliterate the aneurysm completely. [4] FD stands out for its ability to promote blood flow within the vessel lumen, preventing hemorrhagic complications. It is important to emphasize that, following FD placement, the patient must undergo dual antiplatelet therapy to prevent thromboembolic events [4].

We evaluated the antiplatelet management adopted by the included studies, which presented a variety of approaches. Most utilized clopidogrel in doses ranging from 0.2 to 1.0 mg/kg per day, with a maximum of 75 mg/day, while aspirin was administered in doses varying from 81 mg to 300 mg per day, depending on the children's weight. [10,13] For patients weighing less than 45 kg, clopidogrel was often given at 37.5 mg and aspirin at 100 mg, while for those above 45 kg, clopidogrel was typically prescribed at 75 mg and aspirin at 100 mg. [5,10–15] The regimens were implemented at least five days prior to endovascular treatment, aiming to optimize platelet inhibition and minimize thrombotic risks. This diversity in dosing and protocols underscores the importance of a personalized approach, taking into account the weight and individual characteristics of pediatric patients.

Our study investigated the immediate occlusion of aneurysms, as reported in the analyzed studies. Out of the 64 aneurysms examined, 49 were completely occluded, resulting in a complete occlusion rate of 90 % postoperatively, according to our analysis. Additionally, the studies assessed the final occlusion of the aneurysms; of the 87 aneurysms analyzed, 71 remained occluded, resulting in a success rate of 88 % in a period of median mean follow-up of 8.66 months across the studies. The heterogeneity in the analysis of final or immediate occlusion was considered high. Studies contributing to this heterogeneity in sensitivity analysis were identified. Upon ommiting Cherian et al. [5], it was observed that the heterogeneity value was reduced to $I^2 = 0$ in both analyses. The study conducted by Barburoglu et al. (2017) [10] reported a complete occlusion rate in all cases, although the sample size was limited. In contrast, Fry et al. [11] observed a complete occlusion rate of 89.61 %, compared to the lower rate reported by Cherian et al. [5] of 74 %. It is important to note that previous studies that did not use FD reported occlusion rates ranging from 89 % to 100 % for microsurgical treatment [22].

Recently, there has been a notable shift from microsurgical treatment to endovascular management due to superior outcomes and reduced procedural complication rates. [23] The most common post-operative complications in endovascular treatment are bleeding and stent thrombosis. In the data collected for analysis, five complication cases were identified out of the 73 examined patients. When analyzing Fry et al. [11], the main complication with stenting or FD was the risk of stent vessel thrombosis, which occurred in 9.76 % of patients. Our study identified a complication rate of 3 %, with a confidence interval ranging from 0 % to 11 %. In the sensitivity analysis, it was observed that when excluding the study by Han et al. [12], the heterogeneity decreased to $I^2 = 0$. However, it is essential to recognize that risks still exist even with a low complication rate and should be considered when evaluating treatment options.

There are notable discrepancies in the clinical description and outcomes following the treatment of aneurysms in children. In the literature, favorable results have been documented with significant variations, ranging between 40 % and 95 %. [24] This diversity intrinsically relates to factors such as the surgical technique employed, patient characteristics, and lesion specificities. [24] In our study, despite the majority of patients experiencing aneurysm rupture, it was observed

that many achieved satisfactory clinical outcomes following the procedure. In the data collected regarding clinical outcomes related to FD, a positive clinical evolution was noted for 59 out of 67 individuals, representing a 92 % rate of good clinical outcomes. Notably, in the study by Cherian et al. [5], 82.3 % of patients exhibited favorable outcomes, while 7.69 % experienced early mortality due to rerupture. Studies such as that by Wang et al. [15] reported a post-procedure mortality rate of 25 %. Our research revealed a mortality rate of 6 %, with a confidence interval ranging from 0 % to 12 %. However, when analyzing deaths related with the FD, the rate was found to be 0 %.

In comparing the findings from our *meta*-analysis with those of the previous systematic review by Scoville et al. [25][25], both studies demonstrated high rates of immediate and final occlusion following the use of flow-diverting stents in pediatric patients. The prior review analyzed 37 pediatric patients and reported a complication rate of 21.6 % and an associated mortality rate of 5.4 %. In contrast, our *meta*-analysis, which included 80 patients, found a significantly lower complication rate (3 %) and no mortality directly related to the device. These findings suggest that the use of flow-diverting stents may be safe for children, although further studies are required to validate these results.

## 6. Limitations

A key limitation of our study is the relatively small patient sample, which may limit the generalizability of the findings. Additionally, the retrospective nature of the included studies introduces potential biases that could affect the accuracy of the results. Variability in outcome measures and follow-up durations among the studies also introduces heterogeneity, complicating the interpretation of the pooled results. Another significant limitation is the short-term follow-up period, which may not be sufficient to fully evaluate the long-term safety and efficacy of the treatment. Furthermore, although most intracranial aneurysms in the general population are located in the posterior circulation, the majority of aneurysms in our study were located in the anterior circulation. These limitations underscore the need for future prospective studies with larger, more representative patient samples, standardized methodologies, and longer follow-up durations to provide more conclusive evidence regarding the safety and effectiveness of endovascular treatment for pediatric intracranial aneurysms.

## 7. Conclusions

In conclusion, our study reveals the potential of FD as a promising alternative for treating pediatric intracranial aneurysms, with demonstrated safety, feasibility, and positive clinical outcomes. Despite the challenges posed by complex lesions, FD exhibits high final occlusion rates and relatively low mortality and complication risks. However, exercising caution, carefully evaluating each case, meticulously selecting patients before opting for this approach, and considering individual patient factors and potential associated risks are imperative. Future research should focus on clinical trials for this specific patient population to optimize outcomes and further enhance patient safety.

## CRediT authorship contribution statement

**Marcelo Porto Sousa:** Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Filipe Virgilio Ribeiro:** Formal analysis, Data curation. **Sávio Batista:** Writing – original draft. **Marcelo Antonio Pinheiro Braga:** . **Jairo Porfírio de Oliveira Júnior:** Methodology. **Pedro Cotta Abrahão Reis:** . **Christian Ken Fukunaga:** Data curation. **Gabriel Verly:** Writing – original draft. **Hugo Nunes Pustilnik:** Formal analysis. **Chiara Donnangelo Pimentel:** Methodology. **Felippe Figueiredo Torres Ribeiro:** . **Herika Negri Brito:** Supervision. **Raphael Bertani:** Supervision.

## Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgments

None.

*Ethical approval*

Not applicable.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jocn.2024.110909.

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