Treatment of Ethmoidal Dural Arteriovenous Fistulas: A Meta-analysis Comparing Endovascular versus Surgical Treatment

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Key words
- eDAVF
- Endovascular therapy
- Ethmoidal dural arteriovenous fistula
- Surgical disconnection

Abbreviations and Acronyms
CI: Confidence interval
DAVF: Ethmoidal dural arteriovenous fistula
EVT: Endovascular therapy
OR: Odds ratio
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
TIA: Transient ischemic attack

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BACKGROUND: **Dural arteriovenous fistulas (DAVFs) in the anterior cranial fossa constitute approximately 1%–1.5% of intracranial vascular malformations. Depending on the drainage patterns, the diagnosis of ethmoidal DAVFs should prompt treatment because of the high risk of bleeding. Available treatments strategies are surgical treatment and the endovascular approach.**

OBJECTIVE: **To compare the surgical treatment with the endovascular therapy in terms of complete obliteration and perioperative adverse events.**

METHODS: **This study was performed according to the PRISMA guidelines. Eligible studies were identified through a search of PubMed and Cochrane until February 2019. A random effects model meta-analysis of odds ratios (OR) was conducted and the I-square was used to assess heterogeneity. Good outcome was defined as no neurologic deterioration within 30 days after the procedure.**

RESULTS: **Five studies comprising 81 patients were included in the meta-analysis. Surgical disconnection was superior to endovascular therapy in terms of postprocedural complete obliteration rate (surgery group, 100% [n = 65/65]; endovascular therapy, 47% [n = 15/32]; OR, 32.19; 95% confidence interval, 5.46–189.72; I^2 = 9.9%) and 30-day good outcome (surgery group, 98% [n = 63/64]; endovascular therapy, 47% [n = 15/32]; OR, 21.90; 95% confidence interval, 1.94–247.27; I^2 = 53.6%). No significant differences in terms of 30-day stroke, transient ischemic attack; visual deficit, new-onset seizure, and intracranial hemorrhage were identified.**

CONCLUSIONS: **Surgical treatment was superior to endovascular therapy in terms of complete obliteration and overall good outcome. Adverse event rates were similar between the 2 groups. Future studies should be conducted to validate our results.**

INTRODUCTION

Dural arteriovenous fistulas (DAVFs) account for approximately 10%–15% of intracranial vascular malformations.[1,2] DAVFs occur in the anterior ethmoidal region with an incidence of about 10% of DAVFs overall.[3,4] Patients may be asymptomatic or experience symptoms ranging from headaches to fatal hemorrhage.[5-7] Ethmoidal DAVFs tend to have more malignant drainage patterns and are accordingly treated regardless of whether they are symptomatic because of their high bleeding risk and associated neurologic morbidity.[8-11]

Ethmoidal DAVFs are usually managed with surgical disconnection or endovascular therapy (EVT).[12,13] Although the surgical disconnection or resection of ethmoidal DAVFs is an effective approach, it exposes patients to peri- and postoperative risks associated with craniotomy and major surgery.[14] An increasing interest in endovascular embolization of DAVFs to mitigate the risk of bleeding and avoid the unfavorable perioperative risk of major surgery can be demonstrated by the increasing number of case reports and reviews that have investigated periprocedural outcomes in endovascular procedures.[4,13,15-17] There is conflicting evidence with regard to the safety and efficacy of the endovascular approach, with several reports highlighting an increased incidence of complications and questionable prognosis.[12-14,16,18,19]

The present work aimed to systematically review the literature and identify the comparative safety and efficacy of the surgical versus endovascular approach for the treatment of ethmoidal DAVFs.

METHODS

Search Strategy and Selection Criteria

Systematic searches were conducted in PubMed, Scopus, and Cochrane Central. The algorithm used for the database searches was ("dural arteriovenous" OR DAVF) AND fistula* AND ethmoidal. The search was conducted by 2 independent investigators (P.T., S.G.). The references of the included studies were manually reviewed to identify further eligible articles.

A study was included in this meta-analysis if it fulfilled 2 predefined criteria: 1) randomized controlled trials or prospective or retrospective observational analyses reporting on clinical outcomes of interest, and 2) studies published in English up to February 2019. Studies with a high risk of bias or studies reporting on irrelevant outcomes were excluded.

Data Extraction and Outcomes

Two reviewers (P.T., S.G.), blind to each other, extracted the relevant data from the eligible studies independently. All disagreements were resolved following discussion, and a final decision was reached by consensus. The primary outcome was obliteration of the ethmoidal DAVF. Secondary outcomes were favorable postoperative outcome, defined as no neurologic deterioration, new-onset seizures, stroke, transient ischemic attack (TIA), any new visual deficit, and intracranial hemorrhage.

Risk of Bias Assessment

Risk of bias was assessed by 2 investigators (P.T., S.G.) with the Robins-I tool for nonrandomized studies.[20] The following domains for the nonrandomized studies were evaluated: confounding, selection of participants, departure from intended interventions, missing data, measurement of outcomes, and selective reporting. Discrepancies in quality assessment were resolved via consensus (**Supplementary Table 1**).

Statistical Synthesis and Analysis

Odds ratios (OR) with the corresponding 95% confidence intervals (CIs) were used for the outcomes. A random effects model was used to account for heterogeneity among studies. Heterogeneity was assessed with the Higgins I^2 statistic.[21] I^2 greater than 50% indicated significant heterogeneity.[21] Forest plots were used to graphically display the effect size in each study and the pooled estimates. A P value <0.05 was considered significant. STATA 14.1 (StataCorp, College Station, Texas, USA) was used as statistical software.

RESULTS

Search Results

The literature search yielded 78 potentially relevant records after duplicates were removed. After screening titles and abstracts, 39 articles were retrieved for full-text evaluation and 5 studies satisfied the predetermined search criteria and were included in this meta-analysis as shown in the PRISMA flow diagram (**Figure 1**).

Characteristics of the Studies and Patients

All the included studies were retrospective observational cohort analyses.[4,9,12,22,23] In total, 81 patients were included in this meta-analysis. Overall, 2 studies were assessed as having low and 3 as having moderate risk of bias (**Supplementary Table 1**). Detailed patient and study characteristics are presented in **Table 1**.

All studies used angiography to confirm the diagnosis of ethmoidal DAVF.[4,9,12,22,23] The main arterial supply of the DAVFs in all cases was the ethmoidal branches of the ophthalmic artery. Two studies reported minimal contribution by other arteries, mostly branches of the external carotid artery, to the arterial supply of the DAVF.[4,12] Detailed anatomic and procedural characteristics are summarized in **Table 2**. Polyvinyl alcohol particles were used as the sole embolization material in 6 patients.

Four studies reported the symptoms at hospital admission. Overall, 69% (n = 54/78) of patients were symptomatic at baseline. The most common presentation was intracranial hemorrhage, which was documented in 37% of the patients (n = 29/78). Other symptoms were headache in 9% (n = 7/78), vision impairment in 9% (n = 7/78), and seizures in 4% of the patients (n = 3/78). The endovascular procedure was the therapy of choice in 32 patients. Surgical disconnection was performed in 49 patients as a primary intervention. Four studies reported that surgery was reserved for 16 cases in which the endovascular approach had previously failed.[4,9,12,23] One study did not report the exact number of patients in the surgical disconnection group in which EVT had previously failed.[22]

Periprocedural 30-Day Outcomes

Surgical disconnection was superior to EVT in terms of postprocedural complete obliteration rate (surgery group, 100% [n = 65/65]; EVT, 47% [n = 15/32]; OR, 32.19; 95% CI, 5.46–189.72; I^2 = 9.9%) (**Figure 2**). One patient from the surgery group had cerebral edema as a result of thrombosis of the venous pouch after disconnection. The patient was successfully treated with steroids, and he was discharged to rehabilitation with mild confusion.[12] A second patient had transient dysarthria, secondary to a small postoperative venous infarct[9]; another patient developed visual deficit that persisted after 30 days postoperatively.[22]

Surgical disconnection was associated with superior 30-day good outcome compared with EVT (surgery group, 98% [n = 63/64]; EVT, 47% [n = 15/32]; OR, 21.90; 95% CI, 1.94–247.27; I^2 = 53.6%). The cumulative risk of hemorrhage was 3% in the surgery group (n = 2/62) and 7% in the EVT group (n = 2/29), without statistically significant differences (OR, 0.66; 95% CI, 0.12–3.58; I^2 = 0%). Postoperative stroke rates were similar and occurred in 2% (n = 1/62) and 3% (n = 1/29) of patients in the surgery and EVT groups, respectively (OR, 0.92; 95% CI, 0.13–6.71; I^2 = 0%). The single stroke in the surgery group occurred as a result of occipital ischemia, secondary to an acute subdural hematoma, whereas the stroke in patient from the EVT group was caused by a frontal hemorrhage.[22] The risks for TIA (surgery group, 0% [n = 0/62]; EVT, 0% [n = 0/29]; OR, 1.00; 95% CI, 0.11–9.11; I^2 = 0.0%), visual deficits (surgery group, 2% [n = 1/62]; EVT, 0% [n = 0/29]; OR, 1.55; 95% CI, 0.19–12.58; I^2 = 0.0%), and new-onset seizures (surgery group, 3% [n = 2/62]; EVT, 0% [n = 0/29]; OR, 1.50; 95% CI, 0.17–12.82; I^2 = 0.0%) were similar between the 2 study groups.

Late Outcomes During Follow-Up

Four studies reported that during a mean follow-up of 10 months, occlusion of ethmoidal DVAFs was complete in all patients who underwent surgical

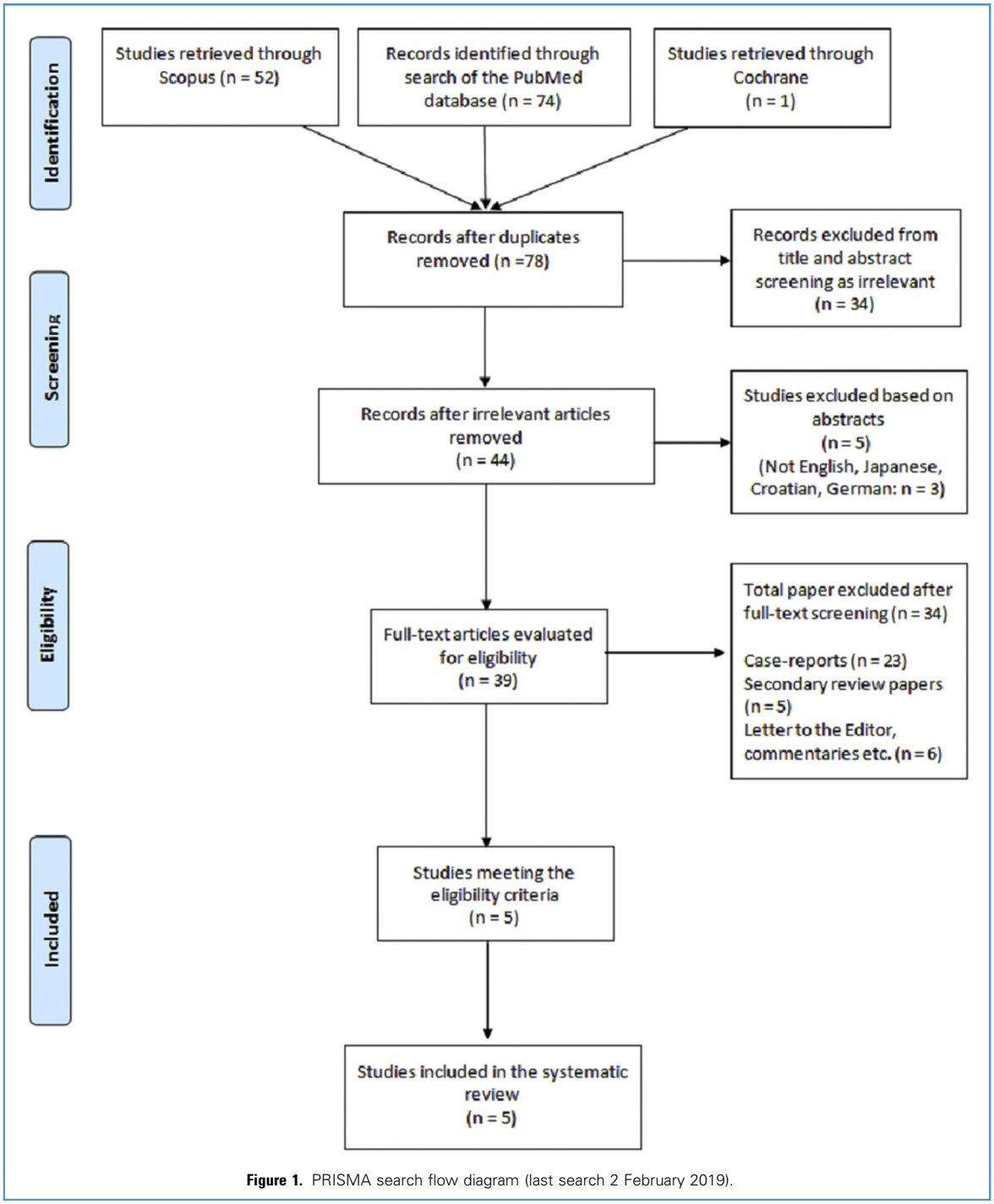

Figure 1. PRISMA search flow diagram (last search 2 February 2019).

disconnection (n = 62), including those who had undergone EVT that had previously failed. All the ethmoidal DAVFs that were obliterated completely after endovascular embolization (n = 15) remained as such during the follow-up. One patient with postoperative confusion due to cerebral edema, which was treated with corticosteroids, showed slow resolution of the edema within a year together with a residual area of postsurgical gliosis. Two years after treatment, the patient began to experience seizures, which were controlled by anticonvulsive medication.[12]

DISCUSSION

This meta-analysis investigated the differences between surgical disconnection and ETV of ethmoidal DAVFs. Our results showed that surgery is associated with an increased rate of complete obliteration and 30-day good outcome when compared

Table 1. Study and Patient Characteristics

Study	Design	Patients		Procedures		Mean Age (years)		No. of Men		Symptomatic		Other Vascular Malformations		Failed EVT, Undergone Surgery, n
		Surgery Group, n	EVT group, n	Surgery Group, n	EVT Group, n	Surgery Group	EVT Group	Surgery Group	EVT Group	Surgery Group, n	EVT Group, n	Surgery Group, n	EVT Group, n	
Lefkowitz et al., 1998[4]	Retrospective	0	3	3	3	61		0	3	NR	NR	None	None	3
Lawton et al., 1999[4]	Retrospective	13	3	16	3	62	62	11	2	11	2	None	None	3
Agid et al., 2009[12]	Retrospective	11	11	15	11	59	59	22 total		18 total		AVM	AVM	4
Cannizzaro et al., 2018[22]	Retrospective	7	6	7	6	57	57	6	5	5	4	None	None	Yes (number not reported)
Gross et al., 2016[9]	Retrospective	18	9	24	9	62		18 total		14 total		None	None	6

EVT, endovascular therapy; AVMs, arteriovenous malformation.

with EVT. However, no significant differences in terms of 30-day stroke, TIA, visual deficit, new-onset seizure, and intracranial hemorrhage were identified.

In this meta-analysis, 83% of patients (n = 67/81) were male. As previously reported, the population of patients with anterior cranial fossa DAVFs is predominantly male.[1,24,25] Furthermore, 69% (n = 54/78) of patients were symptomatic at presentation, most commonly due to hemorrhage, which is in accordance with the existing literature.[1,5,7,9,12,22,26] Our study reported that approximately 62% of the symptomatic patients presented at admission with vision deficits, seizures, or headaches. As the bleeding risk of ethmoidal DAVFs is high and bleeding occurs in up to 91% of cases,[13,27] the existence of ethmoidal DAVFs is considered particularly dangerous and warrants further intervention,[28-31] regardless of the patient status.[9,10,32]

Three kinds of interventions are proposed for the treatment of the ethmoidal DAVFs: stereotactic radiosurgery, surgical disconnection, and EVT.[12,13] A combination of EVT and surgery is also considered an available option for ethmoidal DVAF treatment.[18] As DVAFs are relatively simple lesions, the combined surgical and EVT approach is rarely necessary.[22] Furthermore, Cognard et al.[33] and Barnwell et al.[34] previously reported that in selected cases, an aggressive open surgical treatment strategy may expose patients to unnecessary risks and EVT might be preferable. The embolization of DAVFs is a challenging procedure for a number of reasons. First, there is a risk of nontarget embolization of vessels, including the central retinal artery, which could lead to neurologic or visual deficits.[4,23] Second, the caliber of the vessels that have to be catheterized is small, which hinders the positioning of the catheter.[10,12,35] Third, when using embolic agents, there is always a risk of systemic diffusion of these materials that could harm the patient.[4,10] In order to overcome the above restrictions of endovascular surgery and achieve higher obliteration rates with fewer complications, new microcatheter, balloon catheter, and microguidewire technologies have been developed.[12,32,35] Although EVT has become more promising,[36] embolization may still not be sufficient to achieve complete obliteration of the fistula in approximately 50% of patients,[37] which is

Table 2. Anatomic and Procedural Characteristics

Study	Venous Drainage	DAVFs with Venous Varices	Surgical Approach	EVT Approach	EVT Embolization Site	Embolization Material	Diagnostic Modality
Lefkowitz et al., 1998[4]	NR	NR	NR	Transarterial (n = 3)	×2 OA, ×1 IMA, ×1 MMA, ×1 ethmoidal branches	×3 PVA + platinum coils	DSA
Lawton et al., 1999[4]	×16 frontal veins, ×7 SSS, ×4 cavernous sinus, ×3 both sinuses, ×1 vein of Galen, ×1 vein of Labbe	11	×9 low bifrontal, ×6 unilateral, ×1 pterional	Transarterial (n = 3)	×3 IMA	×3 PVA	Angiography
Agid et al., 2009[12]	×22 cortical veins, ×19 SSS, ×5 sylvian veins, ×2 transverse-sigmoid sinus, ×1 basal vein of Rosenthal, ×1 contralateral superior petrosal sinus	NR	NR	Transarterial (n = 11)	×11 OA	×9 NBCA glue, ×1 NCBA glue + PVA, ×1 NCBA glue + PVA + Onyx	Preferably DSA, MRA
Cannizzaro et al., 2018[22]	Frontal cortical veins (not determined)	NR	All basal frontal	Transarterial (n = 4), transvenous (n = 2)	NR	×4 Onyx + cyanoacrylate glue, ×2 clips + cyanoacrylate glue	DSA
Gross et al., 2016[9]	×19 orbitofrontal or frontopolar veins, 8 posterior orbitofrontal or olfactory veins, ×5 basal vein of Rosenthal, ×3 superficial sylvian veins and vein of Trolard or Labbe	16	Modified orbitocranial, bifrontal interhemispheric, supraorbital craniotomy	Transarterial (n = 8), transvenous (n = 1)	Ethmoidal branches of OA or IMA, ACA dural branches	×7 Onyx, ×2 Onyx + cyanoacrylate glue	Diagnostic cerebral angiography, postprocedural angiography ± CT, follow-up MRI

DAVF, dural arteriovenous fistula; EVT, endovascular therapy; NR, not reported; OA, ophthalmic artery; IMA, inferior mesenteric artery; MMA, medial meningeal artery; PVA, polyvinyl alcohol particles; DSA, digital subtraction angiography; SSS, superior sagittal sinus; NBCA, N-butyl cyanoacrylate; MRA, magnetic resonance angiography; CT, computed tomography scan; MRI, magnetic resonance imaging.

also demonstrated by the present meta-analysis, in which 17 patients (53%) who underwent EVT did not achieve complete obliteration.

Ethmoidal DAVFs are rare vascular abnormalities[3,36] and express a high variability in exact location, size, arterial supply, venous drainage, and clinical presentation.[13,38] Thus, the choice of the optimal surgical technique depends on the anatomic and hemodynamic characteristics of the lesion and on the preference of the surgeon.[4,30,39-43] Despite the fact that a variety of surgical techniques were used in the included studies, all lesions in the surgery group were completely obliterated and remained as such during the follow-up. Furthermore, even though in some cases, open surgical disconnection was performed after EVT had previously failed, it was associated with statistically significantly higher rates of 30-day good outcome (surgery group, 98% [n = 63/64]; EVT, 47% [n = 15/32]; OR, 21.90; 95% CI, 1.94–247.27; I^2 = 53.6%). Thus, this meta-analysis showed that surgical management of ethmoidal DAVFs carries a low morbidity rate overall, regardless of the technique used, which is in accordance with the existing literature.[4,10] Consequently, our results favor the use of surgical disconnection as the therapy of choice for patients with ethmoidal DAVFs. Although surgical treatment of ethmoidal DAVFs in our study yielded complete obliteration in 100% of cases, it can expose the patients to the risks of a craniotomy (eg, blood loss, infection, postoperative hemorrhage, more discomfort for the patient compared with EVT).[44] Moreover, an injury to the adjacent fragile vessels of the brain parenchyma could lead to significant blood loss and cerebral damage.[44,45] Thus, the angiographic architecture of each DAVF plays an important role in the prognosis of the patient, especially if it has a complex cortical venous pathology, when the bleeding risk with any manipulation is extremely high.[32,46] Collice et al.[46] suggested that careful preoperative identification of the venous drainage of the DVAF is critical for the optimal choice of treatment and good outcome.[46] Consequently, the choice of open surgery versus EVT as the therapeutic modality for a patient with ethmoidal DAVF should be individualized, and the risks and benefits of each procedure should be discussed.[47]

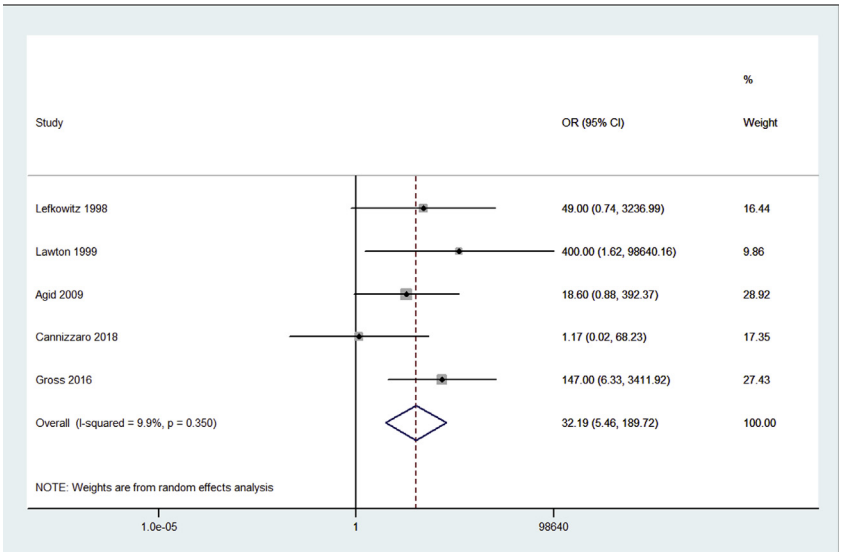

Figure 2. This forest plot presents the comparison between the surgery group and the endovascular therapy group in terms of perioperative complete obliteration. CI, confidence interval; EVT, endovascular therapy; OR, odds ratio.

In general, surgery is considered for ethmoidal DAVFs after failed EVT or radiosurgery, for ethmoidal DAVFs with numerous or tortuous arterial feeders, when the feeding main artery is difficult to navigate with endovascular surgery, and when the main artery of the ethmoidal DAVF has many branches into adjacent structures of brain parenchyma.[39,45,47-50]

Both EVT and surgical disconnection are associated with procedure-related complications.[10,12,22,35,45,47] However, no differences were identified in terms of risk for perioperative stroke, TIA, visual deficits, intracranial hemorrhage, and new-onset seizures between the 2 groups. Two cases of intracranial hemorrhage and 1 stroke were reported in the EVT group. Although EVT can be complicated by inadvertent embolization of the central retinal artery, no visual deficits were observed in the EVT group.[12,51-53] In contrast, 2 intracranial hemorrhages, 1 stroke, 1 permanent visual deficit, and 2 cases of new-onset seizures were reported in patients who had surgery.[9,22] All adverse events in the surgery group were reported by 2 studies, and it was not determined whether these complications occurred in patients in whom EVT had previously failed. As a result, no conclusions can be made with regard to the efficacy of surgery as a primary or rescue procedure; however, this meta-analysis showed that surgery was as safe as EVT in terms of periprocedural adverse events.

Because of the high variability in presentation, location, arterial supply, venous drainage, and tortuosity of ethmoidal DAVFs,[13,38] an individualized approach should be considered.[54] Thus, although surgical disconnection had the highest complete obliteration rate in this meta-analysis, with an OR of 32.19, it might not always be the optimal treatment method. A careful angiographic evaluation of ethmoidal DAVFs and appropriate patient selection are required to achieve excellent outcomes.

Limitations

Our results should be interpreted in the context of several limitations. First, this meta-analysis is limited by the small number of patients and the observational design of the included studies. Second, individual centers or surgeons might have caused heterogeneity in our results, which could not be accounted for. Third, this meta-analysis is limited by the small sample size of articles.

CONCLUSIONS

This meta-analysis showed that surgical treatment was superior to EVT in terms of complete obliteration and overall good outcome within 30 days after the procedure. Further studies with appropriate long-term follow-up are needed to validate our results and evaluate the late outcomes of the 2 approaches.

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APPENDIX

Supplementary Table 1. Risk of Bias Assessment for Observational Studies (Robins-I Tool)

Study	Confounding	Selection	Measurement of Interventions	Deviations from Intended Interventions	Missing Data	Measurement of Data	Selection of the Reported Result
Lefkowitz et al., 1998[4]	Moderate	Moderate	Low	Moderate	Moderate	Low	Low
Lawton et al., 1999[4]	Low	Low	Low	Moderate	Low	Low	Low
Agid et al., 2009[12]	Moderate	Moderate	Low	Moderate	Low	Low	Low
Cannizzaro et al., 2018[22]	Moderate	Low	Low	Moderate	Moderate	Low	Low
Gross et al., 2016[9]	Low	Low	Low	Moderate	Low	Low	Low