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Review Article

# Cerebral dural arteriovenous fistulae presenting with acute hemorrhage: A systematic review

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ABSTRACT

*Background:* Cerebral dural arteriovenous fistulae (dAVFs) are rare connections between arteries and veins or sinuses in the brain. dAVFs have a higher risk of intracranial hemorrhages due to increased venous pressure. Endovascular treatment is considered the first line treatment. However, it is unknown if surgery improves outcomes for patients presenting with an acute hemorrhage. Therefore, this systematic review assesses complete obliterations and recurrences of surgery and endovascular treatment in hemorrhagic dAVFs patients.

*Methods:* A literature search in the PubMed and Web of Sciences database was conducted up till October 2021. Studies of surgical and endovascular treatments with hemorrhagic dAVFs were included. The Quality Assessment Tool for Before-After (Pre-Post) Studies with No Control Group and the JBI critical appraisal checklist for case reports were used for risk of bias assessment.

*Results:* Eleven articles were included. 681 dAVFs patients with 686 fistulae were reported. 245 (36 %) patients presented with an intracranial hemorrhage. Most fistulae were found in the transverse or sigmoid sinuses (n = 220; 32.1 %) and the majority were classified as Borden III. 571 endovascular treatments resulted in 390 (68.3 %) complete dAVF obliterations and there was a recurrence of 66 dAVFs (16.9 %). 183 surgeries resulted in the complete obliteration of 166 fistulae (91.8 %) with a recurrence of 2 dAVFs (1.2 %).

*Conclusions:* Due to the lack of literature on hemorrhagic dAVFs exclusively, we cannot make a statement on the effectiveness of surgical interventions compared to endovascular treatments. Future studies should report outcomes based on location, previous treatments, and patient presentation.

## 1. Introduction

Cerebral dural arteriovenous fistulae (dAVFs) are rare abnormal connections between arteries and veins or venous sinuses in the brain. They are specifically found in the dura mater or arachnoid covering the brain. The etiology of dAVFs is not completely understood but is associated with a variety of conditions such as trauma, cranial surgery, tumors, infections, venous thrombosis, and thrombophlebitis [1–3].

dAVFs allow high-pressure arterial blood to enter the veins or venous sinuses that drain blood from the brain. Consequently, there is an increased venous pressure around the brain and an increased risk of intracranial hemorrhage [1,4]. It is estimated that 10–15 % of all intracranial vascular malformations are dAVFs, however, many dAVFs remain clinically silent and therefore the true incidence may be higher [1,5]. Approximately 20–33 % of patients with dAVFs present with an intracranial hemorrhage [5–7].

Currently, digital subtraction angiography is the gold standard for identifying and assessing suspected dAVFs. Present classifications of dAVFs are based on the pattern of venous drainage and/or angioarchitecture. The Borden and Cognard classifications are the most often used grading systems [5]. Borden type I or Cognard type I or IIa are generally regarded as benign due to their lack of cortical venous reflux (CVR) [8].

*Abbreviations:* dAVFs, Cerebral dural arteriovenous fistulae; CVR, cortical venous reflux.

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On the other hand, Borden type III or Cognard type IIb-V show persistent CVR and are considered aggressive. One study estimated a 10.4 % annual mortality with an annual 8.1 % risk of hemorrhage [7]. However, it has been suggested that the incidence of intracranial hemorrhages resulting from dAVFs may not be as high as previously thought. According to one study, the annual incidence of an initial hemorrhage and mortality was 1.5 % and 1.7 % respectively [9]. Due to the small sample sizes of these studies, conclusions must be made with care.

For most dAVFs, endovascular treatment is the first line of therapy. The endovascular approach relies on embolization of the fistulous link and its venous components while avoiding adverse complications [1,10]. However, surgery can provide an effective and safe alternative. Surgery is often reserved for situations in which endovascular treatments have failed to cure the lesion entirely [10–12]. Although endovascular treatment is considered the standard for dAVFs, it is unknown if surgery improves complete obliteration and recurrence rates for patients presenting with an acute hemorrhage. The rate of rebleeding after a hemorrhage is considerable. One study has identified that in dAVFs that exhibit CVR, hemorrhage is a significant risk factor for further hemorrhagic events. In the study, patients presenting with intracranial hemorrhage had an annual incidence of approximately 7.4 % for subsequent hemorrhages [9]. Therefore, appropriate care is necessary to prevent initial and further hemorrhages with its clinical consequences.

Currently, there is no systematic review focusing on obliteration and recurrence rates of dAVFs with an acute hemorrhage. Therefore, the objective of this systematic review is to summarize current literature on complete obliteration and recurrence rates of surgical and endovascular approaches in dAVFs patients with an acute hemorrhage.

## 2. Materials and methods

### 2.1. Search strategy

A systematic search was performed on the 2nd of October 2021 using PubMed and Web of Sciences. The search encompassed studies published from November 2011 to November 2021. Only free terms were used as the algorithms of PubMed and Web of Sciences improve the search by creating synonyms and Mesh Terms (see Supplementary Table 1 for search details). A filter of 10 years was applied due to the advancements in surgical and endovascular approaches for treating dAVFs. The search results were combined, and duplicates were removed. Hereafter, articles were screened on title and abstract followed by full text review with predefined eligibility criteria. The literature was reviewed by one author (MV). The protocol and systematic review were not registered. This systematic review follows the PRISMA guidelines [13].

### 2.2. Eligibility criteria

The following inclusion criteria were used: (1) Retrospective or prospective cohort studies, randomized controlled trials (RCTs), case reports or case-series of dAVFs patients presenting with acute hemorrhage. (2) Studies using the Cognard or Borden classifications for dAVFs. (3) RCTs or cohort studies of endovascular and/or surgical treatments with angiographic follow-up of at least 1 month.

Studies were excluded if (1) there were less than 10 or 20 % dAVFs patients with acute hemorrhage in RCTs or cohort studies. (2) Studies exclusively analyzing non-cerebral dAVFs or pial arteriovenous fistulae. (3) Studies that exclusively use other treatments (e.g., Gamma knife surgery) or combined modalities (4) Studies in languages other than English or Dutch.

Acute intracranial hemorrhage was defined as occurring within a timeframe of less than 24 h.

### 2.3. Data extraction

The Cochrane data collection form was used for data extraction [14]. In case-series with less than 5 patients, information of dAVFs patients with acute hemorrhage were extracted. Demographic and angiographic features were extracted. Cognard classifications were converted to Borden classifications because not all studies utilized the Cognard classification. Furthermore, the treatment modalities, follow-up duration, number of complete obliterations and recurrences were extracted if possible. The mean and percentages of age, Borden classifications, number of hemorrhagic patients and follow-up duration were calculated. The mean proportion of men and was also calculated. The locations of the most prevalent fistulae were determined. Lastly, the total number of complete obliterations and recurrences were calculated per treatment. Missing data were excluded from the calculations. All extractions and calculations were performed by one author (MV). Due to the qualitative nature of this systematic review, a statistical analysis was not suitable.

### 2.4. Risk of bias assessment

Risk of bias was assessed using the Quality Assessment Tool for Before-After (Pre-Post) Studies with No Control Group [15,16]. This assessment tool was chosen because the included studies did not have control groups. This assessment tool consists of 12 items to evaluate and provide a quality rating of good, fair, or poor. Case-series and cohort studies were assessed with this tool. To assess case-reports, the JBI critical appraisal checklist for case reports was used [15,17]. This tool consists of 8 items. The quality of the case-reports was also rated good, fair, or poor. The JBI critical appraisal checklist for case reports was also used for the case extracted from the case-series. The risk of bias was assessed by one author (MV).

## 3. Results

A total of 145 articles were screened. 31 duplicates were removed. 99 articles were excluded. 10 articles met the inclusion criteria (Fig. 1). One study had a prospective design and was a case-series [18]. The other studies were retrospective cohorts, case-reports, or case-series [19–24]. There were no RCTs found. The following case-reports and studies appeared to meet inclusion criteria but were excluded on full assessment. Four case-reports were excluded because they did not report any dAVFs classification [25–28]. One study did not provide a clear follow-up duration and was excluded [10]. One study did not provide the number of hemorrhagic dAVFs patients and was thus excluded [24]. Lastly, two case-reports utilized combined treatment modalities exclusively and where therefore excluded [21,22].

Only one study, Daniels et al., analyzed hemorrhagic dAVFs patients exclusively [22]. Four studies analyzed treatment outcomes of endovascular treatment and surgery [18,19,21,22]. One study examined surgical outcomes exclusively [24]. Three studies also included other or combined treatment modalities [19,21,22]. All included studies provided complete obliteration and recurrence rates of endovascular and/or surgical treatment. All surgical treatments consisted of clipping the dAVF. Only the study of Westmaier et al. included a hemorrhagic patient in which cauterization was used for treatment [29]. Study characteristics including design, demographic, angiographic and classification data are summarized in Table 1.

The study of Daniels et al. examined hemorrhagic dAVFs patients exclusively. They did not provide separate data on obliteration and recurrence rates for endovascular or surgical treatment. After treatment or during follow-up, 21 of the 26 patients (75 % of all patients) achieved complete obliteration [22]. Furthermore, only the study of Abecassis et al. performed statistical evaluation between a cured group and a recurrence group [19]. For Borden type III dAVFs, surgery was more frequently performed and statistically resulted in less recurrence

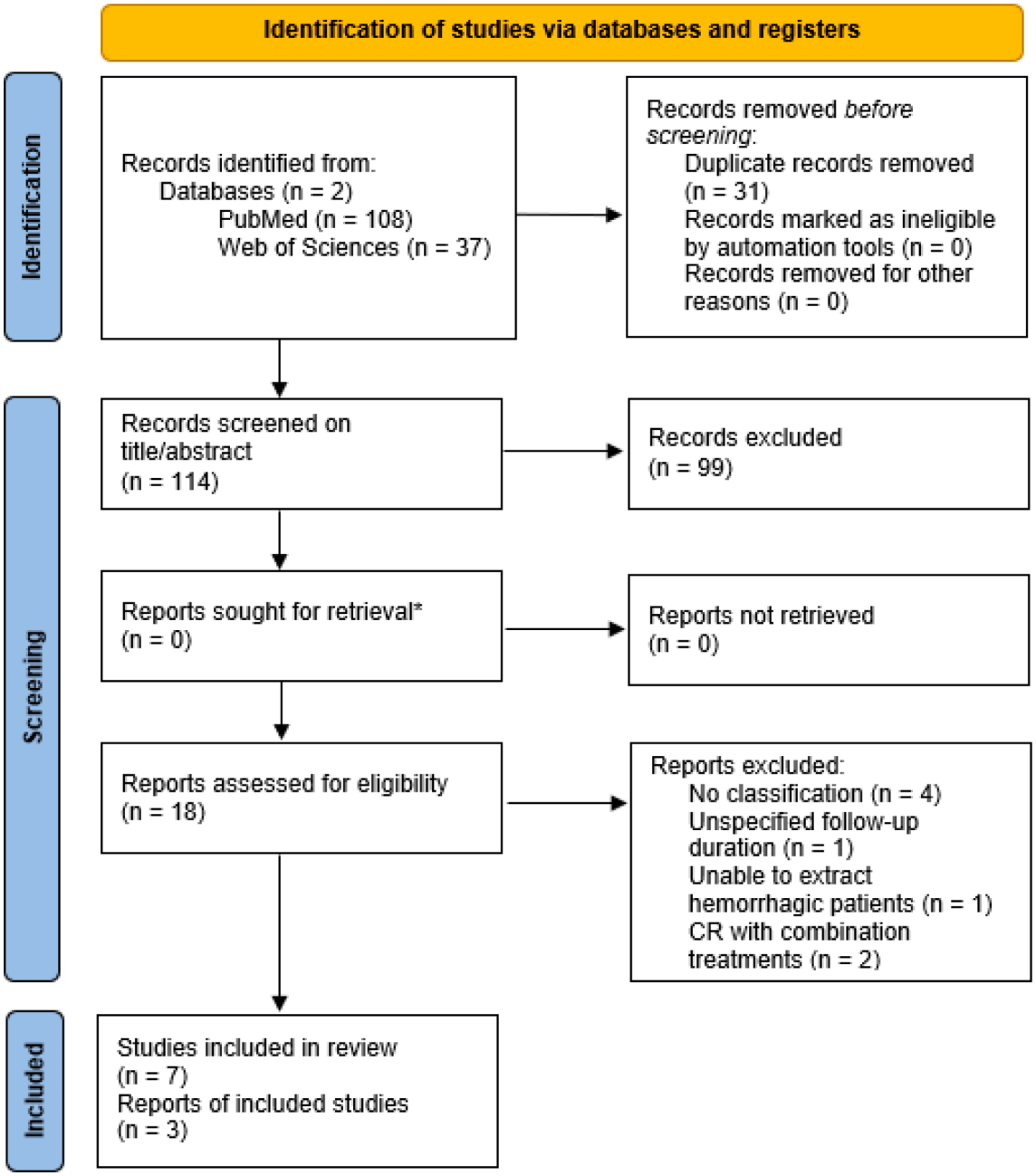


**Fig. 1.** Flowchart of study selection.

compared to endovascular treatment (0 vs. 13.3 %, p = 0.0001). The treatment for all 32 dAVFs patients who experienced recurrence was endovascular embolization. 67.6 % of recurrences occurred within 9 months of endovascular treatment. A calculation provided a recurrence rate of 4.5 %/year. However, dAVFs patients with recurrences had longer follow-up durations compared to the cured group [19].

A total of 681 dAVFs patients were included. 245 (36 %) patients presented with intracranial hemorrhage, thus not all patients had an acute hemorrhage. Not all included studies provided information on which dAVF classifications experienced hemorrhages. The mean age of the patients was 57.1 years. 323 men were included. The mean proportion of men was 47 %. There was a total of 686 fistulae. The majority of fistulae were found in the transverse or sigmoid sinuses (n = 220; 32.1 %). The second and third most common locations for the fistulae were the tentorium (n = 118; 17.2 %) and the cavernous sinus (n = 66; 9.6 %), respectively. The localization of 99 (14,4 %) fistulae were not specified or mentioned. 131 (19.1 %) fistulae were classified as Borden I. 146 (21.3 %) fistulae were classified as Borden II. The most prevalent classification was Borden III. 410 (59.8 %) fistulae were classified as Borden III.

Of the 681 dAVFs patients, 809 treatments were performed. 571 (70.6 %) of those were endovascular treatments and 183 (22.6 %) were surgical treatments. 55 (6.8 %) patients underwent other treatment modalities such as Gamma Knife Radiation or combined treatments. The mean follow-up duration was 27.7 months. A total of 571 endovascular treatments resulted in 390 (68.3 %) complete dAVF obliterations and there was a recurrence of 66 dAVFs (16.9 %). 168 fistulae were completely obliterated with 183 surgeries (91.8 %) and there was a recurrence of 2 dAVFs (1.2 %). Treatment modalities, follow-up duration, complete obliteration and recurrence rates are summarized in Table 2.

The overall risk of bias of each included study was assessed using the

**Table 1**
Summary of study characteristics for cerebral dural arteriovenous fistulae.

| References | Design | Patients (N) | Mean Age (years) | Men (%) | N ICH (%) | Angiographic data of fistulae (N) | Borden I (N) | Borden II (N) | Borden III (N) |
|---|---|---|---|---|---|---|---|---|---|
| Abecassis et al., 2021 | RS | 457 | 56.6 | 187 (41) | 143 (31) | Tent (76), SSS (52), Torc (22), Falc (3), ACF (30), MCF (9), TSS (151), PS (17), CS (51), Other (43) | 112 | 81 | 263 |
| Al-Mahfoudh et al., 2015 | Case-series | 25 | 55.7 | 19 (76) | 16 (64) | Tent (8), Torc (1), Parafalc (1), ACF (8), MCF (2), Other (5) | 0 | 1 | 24 |
| Chandra et al., 2013 | RS | 40 | 57 | 21 (53) | 13 (33) | N/A (41) | 8 | 7 | 26 |
| Cho et al., 2012 | RS | 38 | 49.4 | 21 (55) | 10 (26) | TSS (38) | 11 | 18 | 9 |
| Daniels et al., 2013 | RS | 28 | 56.5 | 24 (86) | 28 (100) | Tent (21), TSS (5), Other (2) | 0 | 5 | 23 |
| Mendez-Ruiz et al., 2021 | RS | 51 | 61* | 22 (43) | 12 (24) | Tent (8), SSS (7), Torc (6), ACF (3), MCF (1), TSS (15), PS (1), CS (15), Other (1) | 0 | 27 | 30 |
| Sugiyama et al., 2020 | RS | 39 | 64.2 | 27 (69) | 20 (51) | Tent (5), SSS (2), Torc (1), ACF (10), MCF (1), TSS (11), PS (2), Other (7) | 0 | 6 | 33 |
| Suyama et al., 2018 | CR | 1 | Early 60 s | 0 (0) | 1 (100) | Left occipital convexity near the confluence (1) | 0 | 0 | 1 |
| Ohara et al., 2012 | CR | 1 | Early 60 s | 1 (100) | 1 (100) | SSS (1) | 0 | 1 | 0 |
| Westmaier et al., 2012 | Case-series | 1 | Late 40 s | 1 (100) | 1 (100) | PS (1), medial margin of the left occipital lobe (1) | 0 | 0 | 1 |
| Total | | 681 | 57.1 | 323 (47) | 245 (36) | 686 | 131 | 146 | 410 |

RS, retrospective cohort study; CR, case-report; ICH, intracranial hemorrhage; Tent, tentorial; SSS, superior sagittal sinus; Torc, torcular; Falc, falcine; ACF, anterior cranial fossa; MCF, middle cranial fossa; TSS, transverse or sigmoid sinuses; PS, petrosal sinus; CS, cavernous sinus; Parafalc, parafalcine; N/A, not announced.
* Median.

**Table 2**
Summary of treatment outcomes for cerebral dural arteriovenous fistulae.

| Reference | Endovascular Treatments (N) | Surgeries (N) | Other treatments (N) | Complete obliterations endovascular treatments (%) | Complete obliterations Surgeries (%) | Mean Follow-up (months) | Recurrences endovascular treatments (%) | Recurrences Surgeries (%) |
|---|---|---|---|---|---|---|---|---|
| Abecassis et al., 2021 | 396 | 103 | 34 | 296 (75) | 102 (99) | 26.4 | 32 (11) | 0 (0) |
| Al-Mahfoudh et al., 2015 | 8 | 25 | 0 | N/A | 23 (92) | 67* | 8 | 0 (0) |
| Chandra et al., 2013 | 40 | 0 | 0 | 35 (88) | 0 | 28.2* | 16 (46) | 0 (0) |
| Cho et al., 2012 | 23 | 2 | 13 | 11 (48) | 2 (100) | 33.7 | 4 (37) | 1 (50) |
| Daniels et al., 2013 | 20 | 12 | 8 | N/A | N/A | 17 | N/A | N/A |
| Mendez-Ruiz et al., 2021 | 82 | 0 | 0 | 46 (56) | 0 | 26.7* | 6 (13) | 0 (0) |
| Sugiyama et al., 2020 | 0 | 39 | 0 | 0 | 38 (97) | 32.7 | 0 (0) | 1 |
| Suyama et al., 2018 | 1 | 0 | 0 | 1 (100) | 0 | 36 | 0 (0) | 0 (0) |
| Ohara et al., 2012 | 1 | 0 | 0 | 1 (100) | 0 | 3 | 0 (0) | 0 (0) |
| Westmaier et al., 2012 | 0 | 2 | 0 | 0 | 1 (100) | 6 | 0 (0) | 0 (0) |
| Total | 571 (70.6 %) | 183 (22.6 %) | 55 (6.8 %) | 390 (68.3 %) | 168 (91.8 %) | 27.7 | 66 (16.9 %) | 2 (1.2 %) |

Other treatments include Gamma Knife Surgery or a combination of modalities. N/A, not announced.
* Median.

appropriate tools mentioned in the methods (Table 3). The complete risk of bias assessments can be found in Supplementary Tables S2 and S3. Only one study blinded the assessors for the exposures/interventions [23]. One case-series was evaluated as a case-report because only one of the four cases was eligible and extracted from the paper [29].

## 4. Discussion

The low prevalence of dAVFs makes it a difficult topic to research. High grade dAVFs have an increased risk of hemorrhage and are thus in need of urgent care [1,30]. Early rebleeding can result in more serious consequences such as neurological deterioration into a coma and even death. Therefore, complete obliteration early-on and in the long run is necessary to avoid these complications [1,5,31].

The results of this systematic review suggest that more dAVFs patients undergo endovascular treatments (70.6 %) than surgeries (22.6 %). Yet, surgeries seem to be more successful in complete obliterations and recurrences compared to endovascular treatments in absolute numbers, although not statistically proven. 91.8 % of surgically treated dAVFs were completely obliterated and only 1.2 % recurrences occurred. While 68.3 % of endovascular treated dAVFs were completely obliterated and 16.9 % recurrences occurred. This difference in

**Table 3**
Risk of bias assessment for the included studies.

| References | Quality Rating |
|---|---|
| Abecassis et al., 2021 | Good |
| Al-Mahfoudh et al., 2015 | Fair |
| Chandra et al., 2013 | Fair |
| Cho et al., 2012 | Good |
| Daniels et al., 2013 | Fair |
| Mendez-Ruiz et al., 2021 | Good |
| Sugiyama et al., 2020 | Good |
| Suyama et al., 2018 | Good |
| Ohara et al., 2012 | Good |
| Westmaier et al., 2012 | Fair |

complete obliterations and recurrences could be explained by the locations of the dAVFs. Surgery is expected to be more effective than endovascular treatments in a few sites, such as anterior cranial fossa (ACF) dAVFs [1,32]. A recent meta-analysis of ACF dAVFs treatments by Giannopoulos et al. also reported surgical superiority compared to endovascular treatment in terms of complete obliteration and neurological deterioration [32]. Another review and series of ACF dAVFs showed that surgical ligation remains a beneficial procedure regarding the patient outcomes [33,34].

Surgery is normally reserved for patients when endovascular treatment has failed to completely obliterate the dAVFs [12]. Yet, there are multiple reasons why dAVFs might be ineligible for endovascular treatment. Surgery could be indicated when dAVFs are present with multiple arterial feeders and when a transvenous approach is limited [1]. Another reason could be an extensive thrombotic occlusion which can make catheterization impossible in case of a venous approach [35–37]. These limited indications and preference for endovascular treatments could explain the difference in the number of surgeries compared to endovascular treatments. Furthermore, the high number of complete obliterations and low number of recurrences for surgery could be explained by the fact that endovascular treatment is usually performed first.

While both approaches have demonstrated effectiveness, they are not without potential complications and drawbacks. During surgery, it is important to be cautious and prevent substantial blood loss, especially in intricate fistulas that have well-established and enlarged networks of arteries supplying blood. Surgery may result in other significant complications such as infection, hydrocephalus, leakage of cerebrospinal fluid, stroke, and paralysis of cranial nerves. For the endovascular approach, complications are dependent on the venous approach, the transarterial approach and the materials used for embolization. In general, the major risks of endovascular treatments can include vessel perforation, cerebral hemorrhage, and venous infarction. Furthermore, navigational issues or thrombosis in the involved venous region may result in cranial nerve injury [1].

There were multiple limitations in analyzing the studies. First, this systematic review consisted mainly of retrospective studies with one prospective study and a few case-reports. There were no RCTs included. Second, only one study examined hemorrhagic dAVFs patients exclusively and did not report separate data on the outcome of different treatment modalities [22]. Third, not all studies reported the exact location of the dAVFs or the arterial feeders. [1,35]. Although Borden I and II fistulae have a low chance of bleeding, their inclusion in the study may have affected the results [38,39]. It is unclear which Borden classification presented with a hemorrhage, as almost none of the studies provided this information. This limits our ability to draw conclusions about the bleeding risk of different dAVFs and the effectiveness of different treatment options for dAVFs with an acute hemorrhage. Furthermore, due to the heterogenous patient populations, there might be selection bias. Also, none of the studies included provided separate data of hemorrhagic dAVFs patients and their treatment modalities and outcomes. Lastly, only one author (MV) performed the search. Therefore, the results and implications for clinical practice should be interpreted with caution.

In conclusion, only one paper was published that analyzed hemorrhagic dAVFs exclusively, but there was a lack of data on the specific treatment outcomes [22]. Based on the above, we were limited in drawing clear conclusions. Therefore, we cannot make a statement about the effectiveness of surgery compared to endovascular treatment in hemorrhagic dAVFs patients.

However, surgical treatment could be considered with good obliteration and recurrence rates. Prompt treatment is crucial in cases of dAVFs with acute hemorrhage, as approximately half of the mortality occurs within the first 24 h [40]. Therefore, treating dAVFs with acute hemorrhage as quickly as possible is strongly recommended. Downgrading dAVFs from high bleeding risk to low bleeding risk with endovascular treatment can also be considered when choosing the treatment modality. There is a need for a multidisciplinary approach for the treatment of hemorrhagic dAVFs, given the variable presentation and localization. Treatment of dAVF with acute hemorrhage requires a multidisciplinary team, consisting of both a neuro-interventional radiologist and a neurosurgeon. Follow-up after obliteration remains of utter importance for the patient, but documentation of this follow-up will be important for our general knowledge. After the obliteration, structured follow-up is essential to monitor for any potential recurrence or complications. Follow-up should be tailored to the individual patient's clinical presentation and imaging findings. The follow-up protocol should include clinical examination and neuroimaging at regular intervals. The frequency and duration of follow-up depend on the location and severity of the dAVF, as well as the patient's clinical course. Generally, follow-up should be performed at 3 months, 6 months, and 12 months post-treatment, and then annually thereafter.

In light of the limitations and challenges identified in our systematic review, we propose specific areas of focus for future research:

Detailed Outcome Parameters by Treatment Type: Future studies should prioritize the thorough description of outcome parameters, stratified by treatment type (e.g., endovascular embolization, surgical intervention). This stratification is essential to provide a clearer understanding of the effectiveness and safety of each treatment modality. Specifically, studies should report on the rates of complete obliteration and recurrence, as well as potential complications associated with each treatment approach. These details are crucial for informing treatment decisions and guiding clinical practice.

Distinguishing Outcomes for Initial Surgeries and Sequential Treatments: To gain deeper insights into the outcomes of dural arteriovenous fistula (dAVF) management, future investigations should distinguish between outcomes for patients undergoing initial surgical interventions and those receiving surgery after prior endovascular treatment. This differentiation is particularly relevant given the evolving nature of dAVF management and the potential need for sequential therapies. A comprehensive analysis of outcomes in these distinct groups can offer valuable guidance on treatment sequencing and decision-making.

Prospective or Retrospective Cohort Studies: While the ideal study design would involve randomized controlled trials (RCTs) to minimize bias and provide objective results, the rarity of dAVFs and the ethical considerations surrounding their treatment make RCTs highly unlikely. Therefore, we recommend the inclusion of prospective or retrospective cohort studies in future research. These cohort studies can offer valuable insights into real-world treatment outcomes and provide a larger pool of data for analysis. Careful consideration of study design, data collection, and standardized reporting is crucial to enhance the quality and relevance of these cohort studies.

## 5. Conclusion

Due to a lack of data, we cannot determine the most effective treatment option for dAVFs with an acute hemorrhage. We recommend radiologic follow-up at 3, 6 and 12 months and then annually. Future

studies should describe outcomes based on location, previous treatments, and patient presentation.

## Ethical approval

This study does not involve human participants.

## Funding

There was no funding or sponsoring for this systematic review.

## 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.

## Data availability

All data is available on request to the first author (MV).

## Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.inat.2023.101853.

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