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BRIEF REPORT

Outcome Following Hemorrhage From Cranial Dural Arteriovenous Fistulae

Analysis of the Multicenter International CONDOR Registry

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BACKGROUND AND PURPOSE: Dural arteriovenous fistulae can present with hemorrhage, but there remains a paucity of data regarding subsequent outcomes. We sought to use the CONDOR (Consortium for Dural Arteriovenous Fistula Outcomes Research), a multi-institutional registry, to characterize the morbidity and mortality of dural arteriovenous fistula–related hemorrhage.

METHODS: A retrospective review of patients in CONDOR who presented with dural arteriovenous fistula–related hemorrhage was performed. Patient characteristics, clinical follow-up, and radiographic details were analyzed for associations with poor outcome (defined as modified Rankin Scale score ≥3).

RESULTS: The CONDOR dataset yielded 262 patients with incident hemorrhage, with median follow-up of 1.4 years. Poor outcome was observed in 17.0% (95% CI, 12.3%–21.7%) at follow-up, including a 3.6% (95% CI, 1.3%–6.0%) mortality. Age and anticoagulant use were associated with poor outcome on multivariable analysis (odds ratio, 1.04, odds ratio, 5.1 respectively). Subtype of hemorrhage and venous shunting pattern of the lesion did not affect outcome significantly.

CONCLUSIONS: Within the CONDOR registry, dural arteriovenous fistula–related hemorrhage was associated with a relatively lower morbidity and mortality than published outcomes from other arterialized cerebrovascular lesions but still at clinically consequential rates.

GRAPHIC ABSTRACT: An online graphic abstract is available for this article.

Key Words: anticoagulant ■ arteriovenous fistula ■ fistula ■ hemorrhage ■ morbidity ■ mortality ■ registry

Outcomes following intracranial hemorrhage are dependent on underlying pathology, with variable outcomes in the setting of aneurysmal subarachnoid hemorrhage, arteriovenous malformations (AVM), cavernous malformations, and primary intracerebral hemorrhage.[1–4] Such outcome data aids in the understanding of the natural history of the disease and prognostication, as well as informing treatment decisions. Dural arteriovenous fistulae (dAVF) represent only 10% to 15% of all cerebral vascular malformations,[5] but can present with hemorrhage, in addition to nonhemorrhagic neurological manifestations and other

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Nonstandard Abbreviations and Acronyms

AVM	arteriovenous malformation
CONDOR	Consortium for Dural Arteriovenous Fistula Outcomes Research
dAVF	dural arteriovenous fistula

benign symptoms.[6] Regarding hemorrhage, studies have focused on the risk of initial or recurrent bleeding, but clinical outcomes following hemorrhage are less well characterized.[6–9] Presently, our understanding of outcomes after dAVF-related hemorrhage is limited to smaller case series and a single meta-analysis.[10] Without a clear assessment of morbidity and mortality associated with dAVF hemorrhage, prognosticating outcomes and balancing the risks of treatment for lesions at risk for hemorrhage remain difficult.

CONDOR (Consortium for Dural Arteriovenous Fistula Outcomes Research), an international multi-institutional database, was created with the intent of studying dAVFs. We sought to use this dataset to better characterize the morbidity and mortality of intracranial hemorrhage secondary to dAVF.

METHODS

The details of the CONDOR retrospective registry have been previously described.[11] In brief, with the approval of each participating institution's Institutional Review Board, and with waiver of consent, data from patients with dAVF were collected, deidentified, and maintained within a central registry. Patients were required to have dural arteriovenous fistula on digital subtraction angiography for inclusion in the registry. Twelve centers contributed a total of 1077 patients presenting between 1990 and 2017. From this dataset, those presenting with hemorrhage were selected for further review, yielding 264 patients. One neonate and one patient with inadequate data recorded were excluded (see flow diagram in Figure I in the Data Supplement). All but one patient was diagnosed with dAVF following hemorrhage presentation. The data that support the findings of this study can be requested from the CONDOR registry central repository (Dr Zipfel, zipfelg@wustl.edu); data requests are subject to approval of the CONDOR consortium. The RECORD reporting guideline checklist (Reporting of Studies Conducted Using Observational Routinely-Collected Data) was utilized for this article.

Patient characteristics, radiological data (including Cognard grade, as outlined in Table I in the Data Supplement), clinical data, and follow-up data were reviewed for inconsistencies and any issues were reconciled with the central database and/or the contributing institutions. Modified Rankin Scale (mRS) score at follow-up was dichotomized as good (mRS score 0–2) versus poor (mRS score ≥3). Univariate analyses was performed using χ^2, Fisher exact test, *t* test, and Freeman-Halton test, as appropriate, using SPSS. Using backward stepwise selection, variables with $P<0.2$ on univariable analysis were included in multivariable analysis; $P<0.05$ was marked as the level for statistical significance.

RESULTS

The CONDOR dataset yielded 262 dAVF patients who presented with hemorrhage. The mean age of the included cohort (n=262) was 59±13 years, with 70% male. Cohort characteristics are summarized in Table 1. 131 (52%) patients presented with isolated parenchymal hemorrhage, 55 (22%) with isolated subarachnoid hemorrhage, and 58 (23%) with both. The remaining 13 patients presented with intraventricular hemorrhage. All but one patient's dAVF was Cognard grade ≥IIb, indicating the presence of cortical venous reflux.

Median follow-up was 1.4 years (interquartile range, 0.4–4.4 years); follow-up mRS data were available for 247 patients, 94.3% of the cohort. Poor mRS was evident at follow-up in 42 (17.0% [95% CI, 12.3%–21.7%]) patients, of which 9 (3.6% [95% CI 1.3%–6.0%]) represented mortality. All but 4 patients received treatment with the majority, 134 (51%), undergoing embolization as the treatment modality.

Univariate analysis demonstrated an association of age, hypertension, anticoagulant use, Cognard grade, type of treatment, length of follow-up, and recurrent hemorrhage with poor outcome at the prespecified $P<0.2$ (Table II in the Data Supplement). Multivariable regression demonstrated older age, anticoagulation use at presentation and recurrent hemorrhage as significantly associated with poor outcome (Table 2). Outcomes did not change significantly over the three decades of the study period ($P=0.25$).

DISCUSSION

Within the CONDOR database, we demonstrate a morbidity and mortality associated with dAVF hemorrhage of 13.4% (95% CI, 9.1%–17.6%) and 3.6% (95% CI, 1.3%–6.0%), respectively. Before this study, our knowledge of outcomes following dAVF hemorrhage has been limited to small case series and one meta-analysis, as well as extrapolation from experience with other pathologies causing intracranial hemorrhage. The meta-analysis, by Jolink et al,[10] compiled results from case series with >10 patients suffering dAVF-related hemorrhage, comprising 326 patients in total from 17 studies; however, only 9 studies (n=193) reported some form of functional outcome beyond case fatality. They observed poor outcomes, defined as mRS score ≥3 or Glasgow Outcome Scale score ≤3, in 8.3% (95% CI, 3.1%–15.7%) of patients and a mortality of 4.7% (95% CI, 2.5%–7.5%), similar to our observed rates. Also, similar to our findings, there with no association found between type of hemorrhage and outcomes.

Unlike our study which demonstrates an association of age with poor outcome, the previously published meta-analysis did not identify age as a predictor outcome, despite a similar median age (54 years) and gender profile (73%). Age plays a strong association with

Table 1. Patient Clinical, Lesional and Treatment Characteristics Within CONDOR Cohort of Patients (n=262) Presenting With dAVF Hemorrhage

	N (%)*
Age (mean±SD years)	59±13
Male	183 (70)
HTN	108 (42)
Ever smoker	76 (39)
Anticoagulation	10 (3.9)
Follow-up (median days)	502
Cognard grade	
I	1 (0.4)
II b	11 (4)
II a+b	19 (8)
III	101 (40)
IV	118 (46)
V	5 (2)
Hemorrhage subtype	
Only ICH	131 (52)
Only SAH	55 (22)
Combination	58 (23)
IVH	13 (5)
Recurrent hemorrhage†	7 (3)
Treatment type	
None	4 (2)
Embo	134 (51)
Surgery	57 (22)
Embo+surgery	45 (17)
Radiosurgery	7 (3)
Embo+radiosurgery	11 (4)
Surgery+radiosurgery	2 (1)
Embo+surgery+radiosurgery	2 (1)
Fistula location	
Cavernous	2 (1)
Tentorial/petrosal/foramen magnum/torcular/ transverse sinus	172 (66)
Sylvian/convexity/anterior fossa/falcine	66 (25)
Other	19 (7)

CONDOR indicates Consortium for Dural Arteriovenous Fistula Outcomes Research; dAVF, dural arteriovenous fistula; HTN, hypertension; ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage; and SAH, subarachnoid hemorrhage.

*As percentage of available data (excluding missing data).

†Recurrent hemorrhage attributable to the dAVF.

outcome for a variety of vascular pathologies, and our findings follow this expected trend.[4] Our cohort also identified recurrent hemorrhage and anticoagulant use as being is associated with worse outcomes, as has been noted in other settings of lesional hemorrhage, such as aneurysmal subarachnoid hemorrhage.[12]

Among cerebrovascular lesions, dAVF hemorrhage could be expected to have outcomes most comparable to AVM hemorrhage, as opposed to the more severe outcomes

Table 2. Multivariable Analysis of Poor Outcome

	OR (95% CI)	*P* value
Age (per year)	1.04 (1.01–1.08)	0.008
>65 yo	2.3 (1.1–4.8)	0.02
Anticoagulation use	5.1 (1.2–22.2)	0.03
Recurrent hemorrhage	7.6 (1.6–36.8)	0.01

OR indicates odds ratio; and yo, years old.

associated with hemorrhage from purely arterial lesions like aneurysms. AVMs carry an approximately 10-15% mortality and 30% morbidity (defined as mRS score ≥3) from incident hemorrhage,[2,3] roughly 2- to 3-fold higher than the rates we observed with dAVF hemorrhage. This could be due to the potentially lower flow and extraparenchymal nature of dAVFs when compared with AVMs. Although dAVF hemorrhage may have a lower morbidity and mortality compared with more lethal sources such as aneurysmal subarachnoid hemorrhage and primary intracerebral or AVM hemorrhage, still one in six patients will be dependent or worse as a consequence of bleeding. At the same time, available data generally indicate a low morbidity associated with dAVF treatment, and thus, treatment of dAVFs at elevated risk for hemorrhage remains advisable.[13–15]

As an analysis of a multicenter retrospective registry, our study has several limitations. There is an inherent selection bias in the inclusion of only tertiary referral centers. Although the high rate of dAVF treatment, at >95% of the cohort, suggests that failure to offer active therapy/withdrawal of care was not a contributor to the outcomes in the included cohort, the observed mortality and morbidity may be artificially low if more severely affected patients suffered prehospital mortality or were judged too moribund for transfer to a tertiary center. When considering the natural history of dAVF, it is also important to note that hemorrhage-related morbidity is not the only dAVF associated morbidity. Approximately 13% of dAVFs present with nonhemorrhagic neurological deficit, a potential morbidity that is not addressed in this paper.[8]

CONCLUSIONS

We present the largest individual patient data series characterizing the outcome of dAVF hemorrhage. Overall, these hemorrhages have a morbidity and mortality lower than cerebral AVMs, but are still clinically consequential, especially with older age. This data provides valuable information towards prognostication and considerations for prophylactic intervention.

ARTICLE INFORMATION

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The podcast and transcript are available at https://www.ahajournals.org/str/podcast.

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Dr Lanzino reported financial relationships with Superior Medical Experts and Nested Knowledge; Dr Alaraj reported financial relationships as a consultant for Cerenovus; Dr Gross reported financial relationships as a consultant for Medtronic and Microvention; and Dr Polifka reported financial relationships as a consultant for Depuy Synthes. The other authors report no conflicts.

Supplemental Materials

Online Tables I and II
Online Figure I
Appendix

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