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# Dural Arteriovenous Fistulas: Baseline Cognitive Changes and Changes following Treatment: A Prospective Longitudinal Study

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#### **ABSTRACT**

**BACKGROUND AND PURPOSE**: Dural arteriovenous fistulas (DAVFs) exhibit varied clinical manifestations, and high-grade cases are associated with both a risk of hemorrhage and (in certain cases) dementia. Less known, however, is the association between DAVF and more subtle cognitive changes, which might not be clinically apparent without formal neurocognitive testing. This study prospectively assesses baseline cognitive changes in patients with unruptured DAVFs and looks at the effects of treatment on any such changes.

MATERIALS AND METHODS: A longitudinal prospective study was conducted to formally evaluate the neurocognitive status of patients with unruptured DAVFs undergoing embolization. Pre- and posttreatment assessments included neurologic examinations and cognitive tests (Repeatable Battery for the Assessment of Neuropsychological Status and Trail-Making Test [TMT]).

**RESULTS:** A total of 23 patients were treated, with 78% demonstrating cortical venous reflux at baseline. At baseline, 50% of patients demonstrated cognitive impairment in at least 1 cognitive domain, and this was significantly associated with cortical venous reflux (P < .05). Following treatment, significant improvements were observed in several cognitive domains. The mean change in Immediate Memory was an increase of 10.5 points (95% CI, 6.2–14.8, P < .001). Visuospatial/Constructional abilities showed a mean increase of 3.8 points (95% CI, 1.1–6.5, P = .008), while Language improved by a mean of 4.2 points (95% CI, 0.9–7.5, P = .015). Attention scores increased by a mean of 6.1 points (95% CI, 2.7–9.5, P < .001). Delayed Memory demonstrated a mean improvement of 7.4 points (95% CI, 3.5–11.3, P < .001), and the Total Repeatable Battery for the Assessment of Neuropsychological Status Score increased by a mean of 8.6 points (95% CI, 5.0–12.2, P < .001). For the TMT, the mean change in TMT-A was a decrease of 9.2 seconds (95% CI, 5.6–12.8, P < .001), indicating faster completion times. TMT-B scores decreased by a mean of 12.7 seconds (95% CI, 8.4–17.0, P < .001). The TMT B-A difference decreased by a mean of 3.5 seconds (95% CI, 0.5–6.5, P = .023), and the TMT B/A ratio showed a mean decrease of 0.18 (95% CI, 0.10–0.26, P = .002). Overall, among the patients with baseline cognitive impairment, 70% showed significant cognitive improvement following endovascular treatment, particularly in memory domains.

**CONCLUSIONS:** In our study, 50% of patients with DAVFs had cognitive impairment when assessed with formal neurocognitive testing, with a significant link to cortical venous reflux. This cognitive impairment improved in 70% of those patients following treatment. These findings expand our understanding of how DAVF affects the brain, highlighting cognitive impairment as a critical factor. Consequently, the treatment of DAVFs should perhaps not only focus on hemorrhagic risk but also consider cognitive outcomes as a potential indicator for intervention.

**ABBREVIATIONS:** CVR = cortical venous reflux; DAVF = dural arteriovenous fistula; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status; TMT = Trail-Making Test

**D** ural arteriovenous fistulas (DAVFs) present with a spectrum of clinical manifestations, often correlating with their angiographic grade. The prevailing literature emphasizes the association

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of "high-grade" DAVFs with an increased risk of intracranial hemorrhage. However, venous hypertension, a hallmark of DAVF, has also been implicated in neurodegenerative presentations, including cognitive decline, dementia, and parkinsonism.<sup>1-2</sup> High-grade

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DAVFs (ie, those with significant cortical venous reflux [CVR]) are often associated with significant cognitive and neurologic deficits and can necessitate treatment due to the concomitant risk of intracranial hemorrhage.<sup>3-10</sup>

Conversely, treatment of low-grade DAVFs is more variable and can be indicated in some cases by disabling tinnitus, and, rarely, headaches. Relatively little attention has been paid in the literature to cognitive changes in these patients, specifically in those who do not exhibit frank cognitive impairment or dementia. Could there be a significant and largely unrecognized burden of "subclinical" cognitive impairment in these patients? It appears so, and recent research has shown that surgical or endovascular treatment can halt and potentially reverse the trajectory of neurologic and cognitive deterioration in these patients, with a substantial proportion achieving complete clinical recovery. <sup>11,12</sup>

Nevertheless, the specific nature of cognitive impairment at baseline in patients with DAVFs, particularly in distinct domains, requires further exploration. Additionally, while cognitive improvements posttreatment may be demonstrable via psychometric evaluations, there are nuances to these evaluations and the influence of practice effects must be carefully considered. (Practice effects refer to the phenomenon in which repeat testing leads to improved scores due to familiarity with the test material rather than genuine cognitive improvements, presenting a potential confound in longitudinal assessments of neuropsychological function. 13-15) This article presents findings from a prospective longitudinal study of a cohort of patients who presented with unruptured DAVFs and underwent treatment. We aimed to further investigate the incidence of cognitive impairment in patients with unruptured DAVFs and assess the effects of treatment on these changes. By using reliable change indices within a standardized neuropsychological battery, we aimed to meticulously assess treatment impacts, delineating the cognitive and neurologic statuses of patients with unruptured DAVFs both pre- and postintervention.

#### **MATERIALS AND METHODS**

#### Study Design

This study was conducted following the guidelines provided by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist, which is included as Online Supplemental Data. A longitudinal prospective study was designed to assess the baseline and posttreatment neurocognitive statuses of patients with DAVFs. Detailed methodology regarding neurocognitive testing is outlined in the Online Supplemental Data.

#### **Participants**

Inclusion criteria for the study:

- Patients older than 18 years of age
- Diagnosed and treated for nonacute DAVF by endovascular embolization
- Baseline mRS of  $\leq 3$
- Signed informed consent provided by the participant or the next of kin (depending on baseline cognitive status).

Exclusion criteria:

- A significant language barrier impairing reliable cognitive evaluation
- Active neuroleptic or psychoactive treatment (eg, antipsychotic or antiepileptic medications affecting cognitive status)
- Baseline mRS of 4 or 5, indicating severe baseline cognitive impairment
- Severe complications postprocedure leading to long-term cognitive impairment (eg, ischemic stroke or intracerebral hemorrhage).

Detailed inclusion and exclusion criteria are provided in the Online Supplemental Data.

### Cognitive and Neurologic Assessment

Pretreatment and posttreatment assessments included complete neurologic examinations and validated neurocognitive testing using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) and the Trail-Making Test (TMT). Both were assessed by a fellowship-trained neurologist. The neurocognitive testing strategy was designed by an experienced clinical neuropsychologist and cognitive neuroscientist. Different forms of RBANS were used for pre- and posttreatment assessments to minimize practice effects. Standard scores for the global index and each of the 5 domain scales (Immediate Memory, Delayed Memory, Attention, Language, and Visuospatial Function) were calculated using agespecific normalization tables.

#### Imaging and Classification

Pre- and posttreatment imaging included classification of fistula location and DAVF grading (using both the Borden and Cognard classifications). The presence or absence of CVR on a cerebral angiogram was also documented.

#### Statistical Analysis

Descriptive statistics were used to characterize baseline demographics, cognitive status, and clinical characteristics of the treated patients. The Pearson correlation analysis was performed to quantify correlations between RBANS scores and continuous variables such as patient age and the duration of symptoms. Paired t tests were used to identify statistically significant changes in test scores from pre- to posttreatment, with a threshold for statistical significance set at P < .05.  $^{16-20}$ 

#### RESULTS

We prospectively enrolled 23 patients, each presenting with an unruptured brain DAVF. These patients underwent endovascular embolization aimed at curing the DAVF. Posttreatment cognitive function was assessed in 21 patients. Two patients were excluded from the posttreatment evaluation due to significant treatment-related complications: one with a large ischemic stroke and the other with a substantial intracerebral hemorrhage, both of whom required extended rehabilitation. Notably, 1 patient who experienced a mild-to-moderate venous infarct postprocedure was included in the posttreatment cognitive assessment.

### **Baseline Characteristics**

Patient demographics and baseline clinical characteristics are detailed in the Online Supplemental Data. The cohort's mean age

Cognitive performance of patients with DAVF, before and after endovascular embolization, stratified according to presence of CVR<sup>a</sup>

		Patients with CVR		Patients without CVR					
	Baseline (mean) (SD)% Impaired	Posttreatment (mean) (SD)% Impaired	Reliable Change% above Cutoff	Baseline (mean) (SD)% Impaired	Posttreatment (mean) (SD)% Impaired	Reliable Change% above Cutoff			
RBANS total	87.7	95.5		86.8	103.3				
	14.98	13.46		14.89	10.50				
	28%	23%	24%	20%	0%	25%			
RBANS Immediate Memory	82.9	94.6		79.0	103.5				
	18.72	15.03		15.60	11.79				
	39%	23%	35%	40%	0%	75%			
RBANS Delayed Memory	87.3	95.8		86.0	101.8				
	22.49	16.14		24.46	14.17				
	33%	18%	24%	20%	0%	0%			
RBANS Visuo spatial	94.3	91.6		93.8	100.8				
·	11.58	18.04		18.05	3.77				
	22%	41%	0%	40%	0%	0%			
RBANS Language	91.1	98.2		95.8	100.5				
	9.63	14.75		13.92	16.60				
	22%	6%	12%	20%	25%	0%			
RBANS Attention	97.4	102.5		97.6	106.8				
	21.26	14.05		6.84	8.26				
	28%	6%	18%	0%	0%	25%			
TMT A (raw/z score)	52.7/—1.5	50.6/-1.1	NA	52.4/-1.6	43.8/-1.2	NA			
•	29.52/3.16	28.75/2.10		24.31/1.38	14.75/1.83				
	44%	35%		60%	50%				
TMT B (raw/z score)	164.2/-3.1	157.5/-2.7	NA	132.2/-2.6	146.8/-3.0	NA			
	113.89/4.39	114.04/4.43		95.93/2.09	105.16/2.19				
	50%	53%		60%	75%				
TMT B-A (raw/z score)	111.6/-2.6	106.9/-2.5	NA	79.8/-1.8	103.0/-2.4	NA			
, , ,	96.64/4.23	95.58/4.49		74.50/2.08	111.41/3.12				
	50%	41%		60%	50%				

Note:—NA indicates not applicable

a RBANS data are presented as scaled scores, which have a mean of 100 (SD, 15). Higher scores indicate better cognitive performance. The RBANS assesses 5 cognitive domains: Immediate Memory, Visuospatial/Constructional Abilities, Language, Attention, and Delayed Memory. TMT A and B scores and their contrasts (B-A, B/a) are presented as raw scores in seconds, which measure the time taken to complete the test. Lower scores indicate faster performance and better cognitive function. These raw scores are also converted into z scores, which have a mean of 0 (SD, 1). Z scores allow comparison across different tests and populations, with higher z scores indicating better performance relative to the normative sample. Sample interpretation: RBANS Immediate Memory: a scaled score of 85 would indicate performance below the average (mean of 100) for the general population, suggesting some impairment in this cognitive domain. TMT: a raw score: 35 seconds would be converted to a z score for comparison. If this z score is -1.5, it indicates that the performance is 1.5 SDs below the mean, suggesting slower processing speed compared with the normative sample.

was 60.5 (SD, 11.7) years. Men represented 52.1% of the study participants. Nearly all patients exhibited minimal disability, having a baseline mRS score of 0 or 1, except for 1 individual who had an mRS score of 3, attributed to a prior and unrelated ischemic stroke. Two patients presented with previous cerebral venous thrombosis affecting a major dural sinus. Symptomatic DAVF presentations were confirmed in 18 patients, manifesting as tinnitus, headaches, and cognitive decline. Three patients were asymptomatic and were incidentally diagnosed with highgrade DAVFs. The average symptom duration before intervention was 6.6 (SD 10) months.

#### Fistula Details

The anatomic distribution of DAVFs was diverse among the cohort, spanning the full spectrum of venous shunts as cataloged in the accompanying Table and in more detail in the Online Supplemental Data. Notably, this included 2 instances of indirect carotid cavernous fistulas and a singular case of direct shunting into the deep venous system. Bilateral shunts were observed in 3 patients, while 10 and 9 patients had right- and left-sided shunts, respectively.

In terms of classification, 15% of patients had Borden type I, 5% had Borden type II, and 65% had Borden type III DAVFs. By means of the Cognard classification, 5% were type I, 20% were type 2IIa, 15% were type IIa+b, 15% were type III, and 40% were type IV (Online Supplemental Data).

Notably, 78% of the cohort (18 patients) demonstrated CVR. Of those, nearly one-half (44%) had multiple cerebral lobes impacted by venous reflux. Baseline MRI was performed on 18 patients, revealing signs of cerebral venous congestion in 13 of them, which, intriguingly, included 2 patients classified as having benign Borden type DAVFs (ie, Borden types I and II).

Four patients overall (17% of the cohort) had either a Borden type I or II fistula, without CVR. Three patients had symptomatic carotid cavernous fistulas, 2 of whom had CVR. Another patient presented with a complex DAVF of the right petrous ridge, which was secondary to prior radiation therapy leading to chronic venous occlusion and venous congestion on MRI, yet without CVR. None of the patients had bithalamic edema.

Of the 18 patients with CVR, all except one underwent postprocedural neurocognitive reassessment. The remaining patient

	Age range	Cortical venous reflux	Affected cortical regions	Laterality of the shunt	Baseline RBANS Immediate Memory	Baseline RBANS Visuospatial/C onstructional function	Baseline RBANS Language	Baseline RBANS Attention	Baseline RBANS Delayed Memory	Baseline Total Scale	Post treatment RBANS Immediate Memory	Post treatment RBANS Visuospatial/ Construction al function	Post treatment RBANS Language	Post treatment RBANS Attention	Post treatment RBANS Delayed Memory	Post treatment Total Scale	
1	30s	no	none	left	-1.6	0.2	-1.5	-0.2	-0.6	-1.0	-1.4	0.0	-1.3	-0.4	-0.1	-1.1	2 and more deviations above average
2	70s	no	none	bilateral	-1.6	-1.4	-0.7	-1.1	0.1	-1.3	0.5	0.1	-0.4	0.2	1.3	0.6	
3	40s	no	none	right	-0.9	0.4	0.9	-1.1	-1.2	-0.6	0.5	0.3	1.3	0.5	-0.7	0.6	
4	50s	no	none	left	-2.1	0.9	-0.6	0.0	-0.8	-0.8	-0.2	-0.3	0.0	-0.9	-0.2	-0.5	
5	50s	no	none	right	-4.1	-2.3	-1.6	-0.7	-4.4	-3.3	not tested						
6	30s	yes	temporal	right	-2.5	0.9	+0.3	-1.3	-1.2	-1.2	-1.9	1.6	-3.2	-1.5	+0.4	-1.7	1 and more deviations above average
7	50s	yes	parietal	left	-4.8	0.0	-2.2	-3.8	-6.5	-4.1	-3.1	-1.3	-0.8	-1.1	-2.1	-2.3	
8	50s	yes	temporal	left	-1.6	0.4	-0.3	-1.3	-2.2	-1.4	0.0	-1.0	-0.2	-1.3	-2.3	-1.5	
9	60s	yes	cerebellar	left	-2.5	0.9	-1.0	-0.2	-0.7	-1.0	-0.2	0.9	-0.3	-1.8	0.6	-0.3	
10	50s	yes	multiple cortical regions	right	-0.4	0.7	-0.6	1.8	0.0	0.4	0.9	1.2	0.5	0.2	1.2	1.2	
11	70s	yes	occipital	bilateral	-1.6	-0.6	-1.5	-0.2	-0.3	-1.2	-2.1	-0.3	-0.4	-0.2	0.1	-0.4	
12	70s	yes	cerebellar	right	-3.1	-1.6	-1.7	-1.7	-2.9	-2.8	-1.4	-2.4	-0.9	-0.9	-0.4	-1.7	average
13	70s	yes	frontal	right left	0.7	-1.6	0.2	1.5	0.3	0.3	1.3	-0.7	0.7	2.2	0.0	1.1	
14	60s	yes	temporal		-0.4	-0.8	-0.7	-0.9	-2.4	-1.5	0.0	-1.5	-0.1	-2.0	-1.9	-1.6	
15 16	70s	yes	multiple cortical regions multiple cortical regions	bilateral	-0.9	0.0	-1.0 -0.7	-0.5 0.4	0.1 -1.2	-0.7	-1.2	-0.9 -2.4	0.4 -0.7	-0.6	-0.6	-0.7	
16	30s 70s	yes	multiple cortical regions multiple cortical regions	left right	-1.6 -3.8	-1.6 -1.6	-1.0	-1.9	-1.2 -0.3	-1.3 -2.1	-0.7 -1.6	-2.4 -2.0	-0.7	0.2	+0.6 0.0	-1.3 -1.1	2 and more deviations below average
18	70s 60s	yes ves	multiple cortical regions multiple cortical regions	ngnt left	-3.8 -2.1	-1.6	-1.0	-2.7	-0.3	-2.1 -2.3	not tested	-2.0	-0.2	0.0	0.0	-1.1	z and more deviations below average
19	50s	yes ves	multiple cortical regions multiple cortical regions	right	-1.4	-0.8	-1.1	0.4	-1.7	-2.5	-0.9	-1.5	-0.2	-0.2	-0.4	-1.0	
20	60s	yes yes	multiple cortical regions temporal	left	-3.8	0.4	-1.1	-2.4	-1.0	-2.3	-0.9	0.1	-0.2	-0.2	0.0	-0.8	
21	50s	ves	deep venous system	right	-1.2	-0.6	-2.2	0.8	-0.6	-2.5	-0.4	0.7	-0.2	1.0	1.2	0.7	
22	70s	yes ves	temporal	right	-0.2	-0.6	0.0	0.0	-0.5	-0.4	-1.7	-3.0	1.8	-0.6	-0.9	-1.3	
23	50s	yes ves	multiple cortical regions	left	-0.2	-0.6	-1.7	0.6	0.0	-0.5	0.3	0.9	-0.3	-0.2	0.7	0.3	4 and more deviations below average

**FIG 1.** The heat map shows individual patient cognitive performance pre- and posttreatment across various RBANS domains. *Green shades* indicate improvement, while *red shades* indicate declines. Darker colors represent more significant changes. The numeric values reflect deviations from average standardized scores, with positive values indicating above-average performance and negative values indicating below-average performance. These provide a visual representation for baseline values and outcomes for each patient pre- and posttreatment, as well as for the entire cohort.

had a disabling periprocedural ischemic stroke and was thus unable to attend the postprocedural evaluation.

#### **Treatment Details**

Transarterial embolization was performed in 9 patients (39.1%); a transvenous approach, in 11 patients (47.8%); and a combined transvenous and transarterial approach, in 3 patients (13.0%). Treatment involved a combination of liquid embolic agents and coils for 10 patients (43.5%), coil embolization exclusively for another 10 patients (43.5%), Onyx (Medtronic) embolization exclusively in 2 patients (8.7%), and a combination of Onyx and glue in 1 patient (4.3%).

On follow-up control cerebral angiography, a residual shunt was identified in 4 patients (17.4%), with a single patient (4.3%) having a high-grade residual shunt.

#### Neurocognitive Evaluation: Baseline and Posttreatment

Neurocognitive outcomes are detailed in the Table, which compares patients presenting with CVR (n = 18) with those without CVR (n = 5).

The RBANS is a standardized battery that evaluates multiple cognitive domains, including Immediate Memory, Delayed Memory, Attention, Language, and Visuospatial/Constructional abilities. Improvements in these domains posttreatment suggest a positive effect of DAVF intervention on cognitive function. The TMT, divided into TMT-A and TMT-B, measures processing speed and cognitive flexibility and executive function, respectively. To mitigate learning effects, we used alternate forms of the RBANS and the Reliable Change Index to ensure that observed changes were beyond what could be attributed to practice effects alone.

At baseline, across the entire cohort (n = 23), 26.1% (6 patients) displayed cognitive impairment on the RBANS Total Scale, indicating a decrease of >1 SD from age-adjusted norms. Within this subset, 1 patient with a benign DAVF without CVR had a compromised total scale performance.

Subdomain analysis of RBANS revealed additional baseline deficits: 39.1% (9 patients) in Immediate Memory (2 with benign DAVFs without CVR); 26.1% (6 patients) in Visuospatial/Constructional functions (2 with benign DAVFs

without CVR); 21.7% (5 patients) in Language (1 with benign DAVF without CVR); 21.7% (5 patients) in Attention (all with CVR); and 30.4% (7 patients) in Delayed Memory (1 with benign DAVF without CVR).

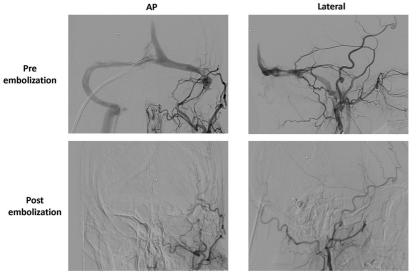
Following treatment, significant improvements were observed in several cognitive domains as measured by the RBANS. The mean change in Immediate Memory was an increase of 10.5 points (95% CI, 6.2–14.8, P < .001). Visuospatial/Constructional abilities showed a mean increase of 3.8 points (95% CI, 1.1–6.5, P = .008), while Language improved by a mean of 4.2 points (95% CI, 0.9–7.5, P = .015). Attention scores increased by a mean of 6.1 points (95% CI, 2.7–9.5, P < .001). Delayed Memory demonstrated a mean improvement of 7.4 points (95% CI, 3.5–11.3, P < .001), and the Total RBANS Score increased by a mean of 8.6 points (95% CI, 5.0–12.2, P < .001).

For the TMT, the mean change in TMT-A was a decrease of 9.2 seconds (95% CI, 5.6–12.8, P < .001), indicating faster completion times. TMT-B scores decreased by a mean of 12.7 seconds (95% CI, 8.4–17.0, P < .001). The TMT B-A difference decreased by a mean of 3.5 seconds (95% CI, 0.5–6.5, P = .023), and the TMT B/A ratio showed a mean decrease of 0.18 (95% CI, 0.10–0.26, P = .002).

These results indicate that endovascular treatment of DAVFs leads to significant improvement in cognitive function, particularly in memory, attention, and processing speed.

To account for test-retest reliability, we used the Reliable Change Index, revealing that 5 patients exhibited improvement in total scale performance; 9, in Immediate Memory; 2, in Language; 3, in Attention; and 4, in Delayed Memory. There were 2 instances of a tendency toward postprocedural decline, one associated with a periprocedural venous infarct.

Figure 1 depicts a "heat map" of cognitive performance of the individual patients of the cohort before and after treatment. The heat map uses color coding to represent changes in cognitive performance across various domains assessed by the RBANS. Green shades indicate improvement in cognitive function, with darker greens representing more significant improvement. Red shades indicate declines in cognitive function, with darker reds representing more significant declines. Numeric values reflect deviations from average standardized scores, with positive



Patient #4, (see Figure 1), impaired memory improved after transvenous embolization.

**FIG 2.** Diagnostic cerebral angiographies (left external carotid artery selective injections) showing a representative patient who presented with a low-grade DAVF (ie, no cortical venous reflux) and cognitive impairment, which improved following endovascular disconnection of the shunt. AP indicates anterior-posterior.

values indicating above-average performance and negative values indicating below-average performance. This visualization allows an at-a-glance understanding of the individual cognitive trajectories of patients before and after treatment, highlighting areas of improvement or decline. Figure 2 demonstrates representative imaging of a patient with a successfully embolized low-grade DAVF, who also exhibited cognitive improvement following the treatment.

The Pearson correlation analysis did not show significant associations between cognitive impairment and patient age, symptom duration, treatment technique, or extent of CVR involvement. (The more detailed results of the Pearson correlation analysis are presented in the Online Supplemental Data).

#### **DISCUSSION**

The present study looks into cognitive impairment associated with unruptured cranial DAVFs yields significant insights that warrant a reconsideration of current treatment paradigms. Our cohort comprised 23 patients, of whom 21 were subjected to cognitive assessment post-endovascular treatment. This revealed a high prevalence of pretreatment cognitive dysfunction, with 50% of individuals demonstrating deficits in at least 1 cognitive domain. This finding alone suggests that cognitive impairment is a much more common presentation in cases of unruptured brain DAVFs than was previously documented. This finding is also supported by other recent studies.

Following treatment, 70% of patients who had baseline cognitive impairment exhibited improvement in memory functions in particular. This improvement in cognitive faculties posttreatment is particularly compelling because it challenges the prevailing guidelines, which do not consider cognitive impairment as an isolated criterion for intervention in unruptured DAVFs. Our study highlights the necessity of integrating cognitive function

into the clinical evaluation of these patients, potentially expanding the indications for treatment beyond the traditional benchmarks of hemorrhage risk and symptomatic presentation.

Most interesting, the study demonstrated no statistical correlation between the extent of cognitive impairment and other variables such as the location of the DAVF, the age of the patients, or the Borden/Cognard classifications. This observation underscores the complexity of cognitive outcomes in patients with cranial DAVFs and suggests that other as yet unidentified factors may contribute to cognitive dysfunction. Most interesting, none of the patients in our study had bithalamic edema, a recognized pattern associated with neuropsychological changes in DAVFs.<sup>20,21</sup> This finding corresponds with none of the patients having frank dementia or severe cognitive impairment. It also indicates that we should consider assessment

for cognitive impairment in all patients with DAVFs, and not merely those with high-grade lesions.

Our findings align with the Neuropshchology in Dural Arterial Fistula (NAIF) study, 12 a multicenter prospective cohort investigation, which demonstrated significant cognitive improvement, particularly in attention, executive functions, memory, and language, following endovascular embolization of DAVFs. The use of a complete neuropsychological battery in the NAIF study parallels our approach, reinforcing the importance of comprehensive cognitive evaluation. While the NAIF study reported substantial improvement using specific cognitive tests, the broader assessment (using RBANS and TMT) of our study allows a more nuanced understanding of cognitive changes across multiple domains, providing robust evidence for the cognitive benefits of treating DAVFs. Moreover, the NAIF study found that cognitive improvement was independent of the risk of hemorrhage, suggesting that even patients with less severe fistulas can experience cognitive benefits from treatment. Our findings support this observation and emphasize the need for routine cognitive assessments in all patients with DAVFs.

Another recent study by the CONDOR Consortium (https://condorprogram.com/consortium) looked at patients who presented with frank cognitive impairment.<sup>22</sup> Unlike our study, this study did not use a standardized neuropsychological battery, which may limit the comparability and generalizability of their findings. By including all patients, regardless of symptomatic presentation, our study demonstrates that cognitive impairment is prevalent even among those not initially presenting with cognitive symptoms. This broader inclusion criterion underscores the need for routine cognitive assessment in all patients with DAVFs, because subclinical cognitive deficits can significantly impact quality of life and may clearly go undetected without a thorough evaluation. The CONDOR study was also retrospective, another significant limitation.

Previous publications on this topic revealed some discrepancies in the reported rates of cognitive impairment, potentially attributable to differences in assessment methodologies. The use of a Reliable Change Index in our study minimizes the impact of so-called practice effects associated with repeat cognitive testing, thereby lending credence to the modest improvement effect we observed posttreatment.

In this study, we have focused only on endovascular treatment, which, in our center, is generally a first-line treatment approach for many DAVFs. However, we must also consider other treatment modalities, including both surgery and radiosurgery, and their potential impact on cognitive outcomes. For example, compared with radiosurgery, surgery may offer quicker resolution of venous hypertension (and therefore potentially faster resolution of any cognitive impairment), but this must be balanced against the potentially negative effects of a craniotomy and surgery on any cognitive issues. We simply do not yet know the answers to these questions, and more research is needed in this area.

Our study has several important limitations. First, the relatively small sample size and its single-center design may limit the generalizability of the findings and introduce biases specific to the treatment protocols or patient-selection criteria of the center. Additionally, the absence of a control group—comprising untreated patients or those receiving alternative therapeutic interventionsmakes it challenging to definitively attribute observed cognitive and neurologic improvements to the endovascular treatment alone, without considering the natural disease progression or regression toward the mean. Moreover, the follow-up duration might not be sufficiently long to assess the long-term stability of the treatment-induced cognitive improvements or to detect late complications or recurrence of symptoms. However, we can state that our patient recruitment was consecutive, and all treatment decisions were recommended by a multidisciplinary team, emphasizing our methodic and unbiased approach.

The number of patients without CVR in our cohort was only 5. This small sample size warrants cautious interpretation of the findings related to this subgroup. The limited number of patients without CVR may not provide a fully representative view of cognitive outcomes in this population. Thus, further studies with larger cohorts are necessary to validate these observations and better understand the implications of CVR absence on cognitive function. Our study did not account for other potential confounding causes of cognitive dysfunction, such as microvascular disease or Alzheimer disease, which are particularly relevant given the mean age of 60 and the prevalence of hypertension among our patients. Our MRI work-up for DAVF includes relatively standard sequences in addition to MRA (ie, we do not acquire volumetric imaging to assess brain atrophy, nor do we perform perfusion studies). This limitation should be considered when interpreting our findings, and future studies should include a more comprehensive analysis of these factors to better isolate the impact of DAVF on cognitive function.

Last, we chose to exclude patients with severe posttreatment complications, such as large ischemic strokes or significant intracerebral hemorrhages, from the cognitive outcome analysis. This choice was because these outcomes independently affect cognitive function and including them could skew our results. This exclusion is a limitation, and larger studies should consider evaluating these subgroups separately to provide a more complete picture of treatment outcomes.

#### **CONCLUSIONS**

Our study shows that cognitive impairment, and in particular memory issues, are much more common in patients with DAVFs than was previously recognized. Indeed, looking at only those patients who present clinically with dementia or frank cognitive impairment almost certainly underestimates the burden of disease. This more subtle cognitive impairment can, however, be picked up through comprehensive neurocognitive assessment, and perhaps we are approaching the stage in which all such patients should be referred for neurocognitive assessment by a qualified specialist in this area. Treatment of cranial DAVFs can lead to cognitive improvements, and the presence of cognitive dysfunction, even in low-grade lesions, may warrant consideration of treatment in these patients.

It is time for a more nuanced approach to the management of DAVFs, one that prioritizes cognitive outcomes and recognizes the potential for cognitive recovery following appropriate intervention, irrespective of the angiographic grade of the DAVF. Treatment considerations for DAVFs should, therefore, be about more than just hemorrhage risk. Our findings indicate the need to reassess current management strategies for DAVFs, with further multicenter studies required to confirm these results.

Disclosure forms provided by the authors are available with the full text and PDF of this article at www.ajnr.org.

#### **REFERENCES**

- Brito A, Tsang AC, Hilditch C, et al. Intracranial dural arteriovenous fistula as a reversible cause of dementia: case series and literature review. World Neurosurg 2019:121:e543-53 CrossRef Medline
- Velz J, Kulcsar Z, Büchele F, et al. The challenging clinical management of patients with cranial dural arteriovenous fistula and secondary Parkinson's syndrome: pathophysiology and treatment options. Cerebrovasc Dis Extra 2020;10:124–38 CrossRef Medline
- Holekamp TF, Mollman ME, Murphy RK, et al. Dural arteriovenous fistula-induced thalamic dementia: report of 4 cases. J Neurosurg 2016;124:1752–65 CrossRef Medline
- Luo Y, Qi J, Cen Z, et al. Two cases of dural arteriovenous fistula presenting with parkinsonism and progressive cognitive dysfunction. J Neurol Sci 2014;343:211–14 CrossRef Medline
- Alexandratou A, Mah Y, Ramsey D, et al. Dural arteriovenous fistula causing reversible cognitive impairment. Pract Neurol 2022;23:82–84 CrossRef Medline
- Netravathi M, Pal PK, Bharath RD, et al. Intracranial dural arteriovenous fistula presenting as parkinsonism and cognitive dysfunction. J Clin Neurosci 2011;18:138–40 CrossRef Medline
- Han Z, Yang H, Du Y, et al. Progressive cognitive decline with bithalamic and basal ganglia lesions caused by dural arteriovenous fistula. Neurology 2021;97:738–39 CrossRef Medline
- 8. Xie J, Zhang T, Zhang Y, et al. **Dural arteriovenous fistula with progressive dementia and parkinsonism: two case reports and a literature review.** *Medicine (Baltimore)* 2023;102:E35782 CrossRef Medline
- 9. Racine CA, Lawton MT, Hetts SW, et al. Neuropyschological profile of reversible cognitive impairment in a patient with a

- dural arteriovenous fistula. Neurocase 2008;14:231–38 CrossRef Medline
- 10. Wilson M, Doran M, Enevoldson TP, et al. **Cognitive profiles associated with intracranial dural arteriovenous fistula.** *Age Ageing* 2010;39:389–92 CrossRef Medline
- Sekar S, Kannath SK, Ramachandran S, et al. Alterations in restingstate functional MRI connectivity related to cognitive changes in intracranial dural arteriovenous fistulas before and after embolization treatment. J Magn Reson Imaging 2022;55:1183–99 CrossRef Medline
- 12. Gramegna LL, Ortega G, Dinia L, et al. Cognitive improvement following endovascular embolization in patients with intracranial dural arteriovenous fistula: the Neuropsychology in dural ArterIal Fistula (NAIF) Study. *J Neurointerv Surg* 2023 Dec 7. [Epub ahead of print] CrossRef Medline
- Anokhin AP, Luciana M, Banich M, et al. Age-related changes and longitudinal stability of individual differences in ABCD neurocognition measures. Dev Cogn Neurosci 2022;54:101078 CrossRef Medline
- 14. Tröster AI, Woods SP, Morgan EE. Assessing cognitive change in Parkinson's disease: development of practice effect-corrected reliable change indices. Arch Clin Neuropsychol 2007;22:711–18 CrossRef Medline

- Slade PD, Townes BD, Rosenbaum G, et al. The serial use of child neurocognitive tests: development versus practice effects. Psychol Assess 2008;20:361–69 CrossRef Medline
- Shura RD, Brearly TW, Rowland JA, et al. RBANS validity indices: a systematic review and meta-analysis. Neuropsychol Rev 2018;28:269–84 CrossRef Medline
- Novitski J, Steele S, Karantzoulis S, et al. The repeatable battery for the assessment of neuropsychological status effort scale. Arch Clin Neuropsychol 2012;27:190–95 CrossRef Medline
- Speer DC. Clinically significant change: Jacobson and Truax (1991) revisited. J Consult Clin Psychol 1992;60:402–08 CrossRef Medline
- Sherman E, Hrabok M. A Compendium of Neuropsychological Tests. New York: Oxford University Press; 2006
- Tombaugh TN. Trail Making Test A and B: normative data stratified by age and education. Arch Clin Neuropsychol 2004;19:203–14 CrossRef Medline
- Chen PM, Olson SE, Handwerker J. Bithalamic lesions: cranial dural arteriovenous fistula manifesting as thalamic dementia. Stroke 2020;51:E355–58 CrossRef Medline
- Sanchez S, Wendt L, Hayakawa M, et al. Dural arteriovenous fistulas with cognitive impairment: angiographic characteristics and treatment outcomes. Neurosurgery 2023 Dec 14. [Epub ahead of print] CrossRef