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## Doppler Sonographic Evaluation of Shunts in Patients with Dural Arteriovenous Fistulas

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**BACKGROUND AND PURPOSE:** Doppler sonography has been used to assess global cerebral circulation time (CCT) in healthy volunteers and a small number of patients with cerebral arteriovenous malformations. We evaluated the effect of arteriovenous shunts on global CCT in patients with dural arteriovenous fistulas (DAVFs) by using this Doppler echo contrast-bolus tracking test.

**METHODS:** We measured CCT as the time delay in a contrast bolus to the internal carotid artery (ICA) and internal jugular vein (IJV) in 13 patients with DAVF and 30 age-matched control subjects. Mean CCT and mean arterial and venous rise times ( $\Delta t = 80\%$  of total signal-intensity increase) were compared. Posttreatment follow-up measurements were performed in five patients.

**RESULTS:** Mean CCT and venous  $\Delta t$  were significantly different between patients and controls (CCT,  $1.1 \pm 0.9$  vs  $6.9 \pm 1.2$  seconds,  $P < .0001$ ; venous  $\Delta t$ ,  $5.2 \pm 2.0$  vs  $7.0 \pm 2.6$  seconds,  $P = .024$ ), but arterial  $\Delta t$  values were not ( $4.4 \pm 1.8$  vs  $4.7 \pm 2.0$  seconds). Posttreatment follow-up of two occluded fistulas showed CCT normalization. One near-occlusion showed a two-step increase in signal intensity, and incomplete occlusion in two patients left the CCT unchanged. One patient with an extracranial, highly vascularized glomus tumor draining into the IJV had a CCT of 1.8 seconds.

**CONCLUSION:** In DAVF patients, sonographic CCT is significantly shortened. Our test is highly sensitive for arteriovenous shunts but not specific for DAVF alone. Follow-up measurements in DAVF patients are well correlated with results of angiographic treatment. CCT assessment might become an additional tool for evaluating these patients and monitoring their treatment.

Dural arteriovenous fistulas (DAVFs) are a subtype of vascular malformations related to the dura mater that show a shunt between the extracranial arteries (eg, branches of the external carotid artery) and the intracranial venous sinus (transverse or sigmoid sinus). Cerebral digital subtraction angiography (DSA) is a well-established method for establishing diagnosis and treating patients with DAVF and also for evaluating vascular morphology, the hemodynamic characteristics of a fistula, and results of endovascular treatment (1, 2). Other diagnostic imaging procedures, such as cerebral CT or MR imaging, depict only a

limited proportion of these malformations, and in some cases, they may even fail to show any pathologic finding (3–5).

At best, conventional sonography contributes indirect information about the hemodynamic effects of malformations by showing the flow pattern of feeding or draining vessels (6, 7). The introduction of intravenous sonographic enhancing substances such as Levovist (Schering AG, Berlin, Germany), which was originally designed to improve insonating conditions for transcranial sonography, opened new opportunities to study the intracranial circulation by echo contrast-bolus tracking. Levovist consists of 2- to 8- $\mu\text{m}$  air microbubbles stabilized by galactose and palmitic acid. The bubbles can pass through the microcirculation, and the sonographic enhancement can usually be seen for several minutes.

Two approaches have been reported: the analysis of arteriovenous circulation times by the insonation of brain vessels, similar to angiography, and the analysis of brain perfusion by the insonation of brain parenchyma, similar to MR or CT perfusion studies

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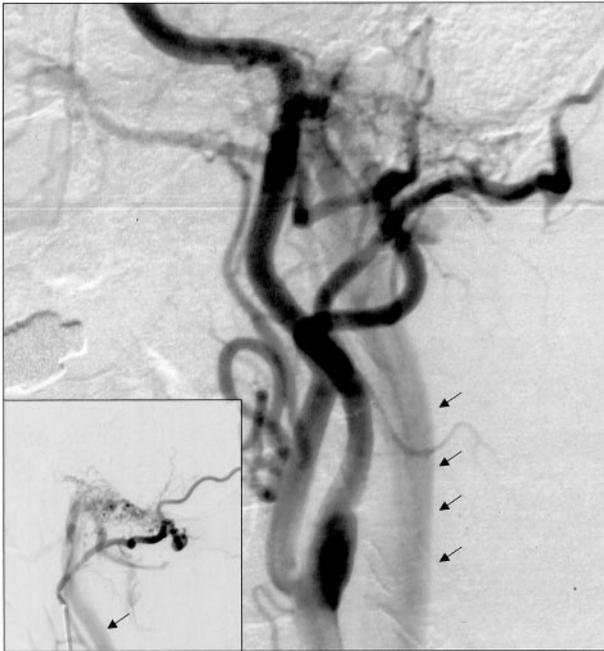


FIG 1. Lateral angiogram with common carotid artery contrast material injection shows an occipital DAVF (patient 1). *Inset*, Image shows selective contrast material filling of the occipital artery. Note early venous filling of the IJV (*arrows*).

(8–13). Using the former approach, a reliable Doppler sonography method to assess the global cerebral circulation time (CCT) has recently been described (14). In that report, CCT was measured extracranially as the time delay between enhancement in the distal internal carotid artery (ICA) and enhancement in the contralateral internal jugular vein (IJV). So far, the method has been used only to determine normal physiologic values in healthy volunteers. In a preliminary small group of patients with cerebral arteriovenous malformations (AVMs), shortening of CCT was demonstrated (14).

In this study, we applied an extracranial Doppler technique in patients with angiographically diagnosed occipital DAVF to analyze its value in diagnosis and treatment monitoring. We discuss the possible diagnostic pitfalls for future application of this technique.

## Methods

### *Patients and Control Group*

We applied the Doppler test to 14 untreated patients (six male, eight female; age range, 29–74 years; mean  $\pm$  SD, 53  $\pm$  14 years). The main presenting complaints and DAVF classification according to the criteria of Cognard et al (15) are summarized in Table 1. Prior diagnostic angiography had shown an occipital DAVF in 12 cases (Fig 1). Two patients (12 and 14) who presented with pulsatile tinnitus were prospectively included before DSA was performed. Results were compared with those of 30 age-matched control subject (age range, 39–67 years; mean  $\pm$  SD, 52  $\pm$  8 years) who were free of relevant atherosclerosis or carotid artery disease. Follow-up investigations were performed in five patients, and the results were correlated with those of postinterventional angiography. Patients with contraindications to Levovist (eg, galactosemia, severe cardiac failure

of New York Heart Association grade III or IV, severe chronic obstructive airway disease) were excluded. All patients and control subjects provided informed consent. The local ethics committee approved the study protocol.

### *Doppler Setup*

CCT measurements were performed by using a commercially available dual-channel Doppler system (TCD X4; DWL, Sipplingen, Germany), as described previously (14). Two pulsed, 2-MHz probes were fixed near the mandibular angle (with the subject lying in the supine position) to monitor the Doppler spectra of the IJV and ICA on opposite sides at an insonation depth of 30–50 mm. Doppler signals were continuously recorded and stored on a computer (Fig 2). Signal intensity in the ICA was chosen instead of that of the external carotid artery (ECA) because the numerous anatomic variations of ECA branches would have limited an exact determination of the insonated vessel. At the measured level, which was about 3–5 cm distal to the carotid bifurcation, equal arrival of the bolus was assumed for the ECA and ICA. In patients, the venous signal intensity was recorded on the side of the malformation. In case of ipsilateral transverse sinus occlusion or insufficient IJV flow, the contralateral side was used for venous insonation. In cases of arterialized venous flow, we performed a short compression test by applying mild manual pressure about 4–5 cm below the Doppler probe to stop the signal intensity due to IJV flow; this was done to ensure a venous origin of the signal intensity. In control subjects, we used the side of the dominant IJV, as assessed in a prior extracranial duplex scan (Powervision 6000, SSA-370A; Toshiba, Tokyo, Japan). If no IJV difference was found, the right IJV was chosen in the control subjects.

For CCT registration, a 4-mL bolus of contrast material (Levovist, 300 mg/mL) was injected into a cubital vein by using an infusion pump (Pulsar, 3 mL/s; Medrad, Indianola, IN). Heart and breath rates were monitored during the measurements. For data evaluation, peak intensity values of the Doppler spectra were exported, resulting in time-intensity curves with a 0.04-second time resolution (TCD8 software, modified by D.W.L.). Raw data were fitted by using a 20th-order polynomial function, and CCT was calculated as the interval between turning points (ie, the points of the steepest rise of the ICA and IJV curves). In addition, the arterial and venous rise time,  $\Delta t$ , was determined as 80% of the total signal intensity increase (Fig 3).

### *Statistical Analyses*

Welch-corrected unpaired *t* tests were used to compare CCT and mean  $\Delta t$  values between control subjects and patients. A *P* value  $<$ .05 was considered to indicate a significant difference. Sensitivity and specificity testing was performed with a 95% confidence interval. All tests were performed by using the SPSS software (version 10.0.7; SPSS, Chicago, IL) for Windows (Microsoft, Redmond, WA).

## Results

We achieved successful sonographic measurements (ie, test duration of approximately 20–30 minutes and no reported adverse effects to Levovist) and analyzed time-intensity curves in all patients and controls. In 12 patients, the diagnosis of DAVF had already been established by means of DSA before CCT analysis. Angiography in the two prospectively investigated cases confirmed a right-sided DAVF in one but showed a greatly vascularized glomus tumor draining into the right IJV in the other.

## Patient Characteristics

Patient No.	Age (y)/ Sex (M/F)	Presentation	Type	Feeder	Venous Drainage	Venous Insonation Side	CCT (s)
1	45/F	Tinnitus, headache, dizziness	Ila: L occipital DAVF	L ECA via OA, L VA	R SS and SSS via retrograde Lt SS, L jugular bulb occlusion	R	1.6
2	53/M	Tinnitus, dizziness, impaired memory	Ila: L occipital DAVF	Both ECA, R VA	L > R SS and SSS	L	0.4
3	58/M	Tinnitus, papilloedema	III: R occipital and confluens sinuum DAVF	Both ECA via OA, both VA	R SS and SSS, cortical bridging veins, SPS and CS	R	2.0
4	44/M	Tinnitus, headache, dizziness, depression (7 months after L TS and partial SSS thrombosis)	III: L occipital DAVF	L ECA via OA	R SS and SSS, cortical bridging veins	R	0.1
5	67/F	Tinnitus	III: R occipital DAVF	R ICA via OA, R ECA via OA, R VA, R APA	R SS and R IPS, CS	R	0.5
6	31/F	Tinnitus	Ila: R occipital DAVF	R ECA via OA	L SS via retrograde R SS, R jugular bulb occlusion	L	1.2
7	57/M	Complex-partial seizure	III: tentorium	R ECA via MMA	Cortical bridging veins, R > L SS	R	2.6
8	71/F	Headache, hydrocephalus	IV: cerebral falx	Both ECA via OA, both MMA, PCA and SCA, both VA	R > L SS via STS	R	2.4
9	29/F	Tinnitus	Ila: R occipital DAVF	R ECA via OA, R VA, R ICA via tentorial branch	Both SS	R	0.3
10	57/M	Tinnitus	Ila: L occipital DAVF	L ECA via OA and superficial temporal artery	L > R SS	L	0.4
11	74/M	Tinnitus	I: L occipital DAVF	L ECA via OA	L > R SS	L	0.5
12	58/F	Tinnitus	Ila: R occipital DAVF	R ECA via OA	R > L SS	R	1.5
13	40/F	Tinnitus	Ila: L occipital DAVF	L ECA via OA, L VA	L > R SS	L	0.6
14	60/F	Tinnitus, impaired L lateral visual field	Highly vascularized R glomus tumor	R APA	R SS	R	1.8

Note.—R = right, L = left, OA = occipital artery, SSS = sagittal superior sinus, SPS = sphenoparietal sinus, IPS = inferior petrosal sinus, TS = transverse sinus, STS = straight sinus, ICA = internal carotid artery, OV = ophthalmic vein, SS = sigmoid sinus, CS = cavernous sinus, APA = ascending pharyngeal artery, MMA = middle meningeal artery, PCA = posterior cerebral artery, SCA = superior cerebellar artery, L > R = predominantly left, L < R = predominantly right, I-IV = DAVF grades according to Cognard et al (15), ECA = external carotid artery, ICA = internal carotid artery, VA = vertebral artery

Mean CCT was  $1.1 \pm 0.9$  seconds (range, 0.1–2.6;  $n = 13$ ) in the DAVF group and  $6.9 \pm 1.2$  seconds (range, 4.8–11.1;  $n = 30$ ) in the control group. Mean arterial  $\Delta t$  was  $4.4 \pm 1.8$  seconds (range, 1.8–7.4 seconds) in patients with DAVF and  $4.7 \pm 2.0$  seconds (range, 2.7–10.9 seconds) in control subjects, and mean venous  $\Delta t$  was  $5.2 \pm 2.0$  seconds (range, 2.2–7.9 seconds) and  $7.0 \pm 2.6$  seconds (range, 2.6–13.5 seconds), respectively.

Mean CCT values were significantly different between patients and control subjects ( $P < .0001$ ). No difference was found in arterial rise times between the groups. However, a significant difference in venous  $\Delta t$  was found ( $P = .024$ ) (Fig 4). CCT did not correlate with the angiographically determined grade of the malformation.

Endovascular intervention in seven patients led to a complete occlusion of the fistula in four, one partial occlusion, and two remaining fistulas. Treatment in patients 9 and 10 led to a complete occlusion of the involved transverse sinus and the distal IJV; there-

fore, a comparative control CCT measurement was not possible. Fistula occlusion led to CCT normalization from 0.4 to 7.5 seconds in patient 2 and from 2.6 to 9.1 seconds in patient 7. Patient 5 had a remaining, small, angiographic shunt after arterial embolization, as the patient refused the continuation of treatment via a transvenous endovascular approach. Posttreatment Doppler spectrum analysis in this patient revealed a two-step pattern of contrast-bolus arrival. The first step represented the remaining shunt (CCT = 1.3 seconds), and the second probably corresponded to the normalized main blood flow via the physiologic vessel pathways (CCT = 6.8 seconds) (Fig 2).

In patients 8 and 11, angiographic flow reduction of the malformation was achieved, but without complete occlusion, despite repeated endovascular interventions. In patient 8, according to each treatment step, CCTs of 3.2, 3.8, and 3.1 seconds were found after 1 week, 5 months, and 7 months. Patient 11 had follow-up CCTs of 2.3 and 1.3 seconds after 4 and 5 weeks, respectively. Because of the small number of

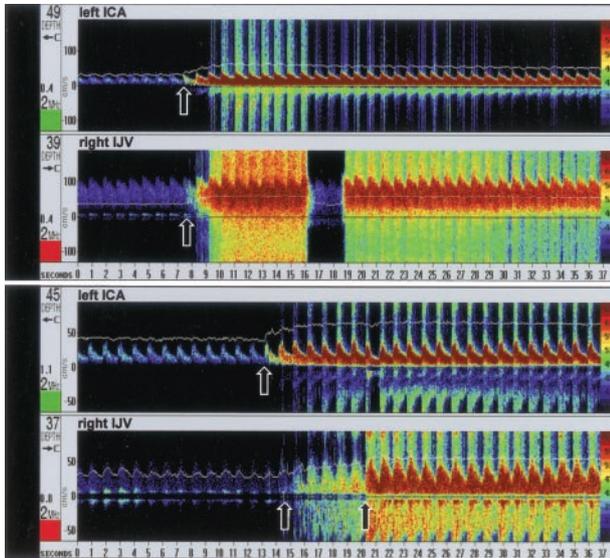


FIG 2. Sample Doppler spectra during the arrival of the contrast-agent bolus in two patients. Intravenous injection occurred at 0 seconds. Color change of the Doppler spectrum from blue to orange (arrows) indicates arrival of the bolus. The superimposed transient, high-frequency signals that fill the complete frequency range of the Doppler are artifacts caused by echo contrast-induced overmodulation (blooming effect). White lines in each spectrum represent the computer-generated graph of the calculated peak intensity values of the spectrum. Top: Spectra in patient 9, who was untreated. Note the typical, pulsatile, flow signal intensity in the ICA and the arterialized flow in the IJV. Moderate jugular vein compression at 16–19 seconds leads to a marked reduction in signal intensity. Bottom: Spectra in patient 5 after incomplete occlusion of the malformation. Note the still-prevailing, arterialized flow and the two-step pattern of intensity rise in the IJV; the moderate increase in venous intensity increase between 14.5 and 20.2 seconds; and the second, sharp intensity rise at 20.2 seconds.

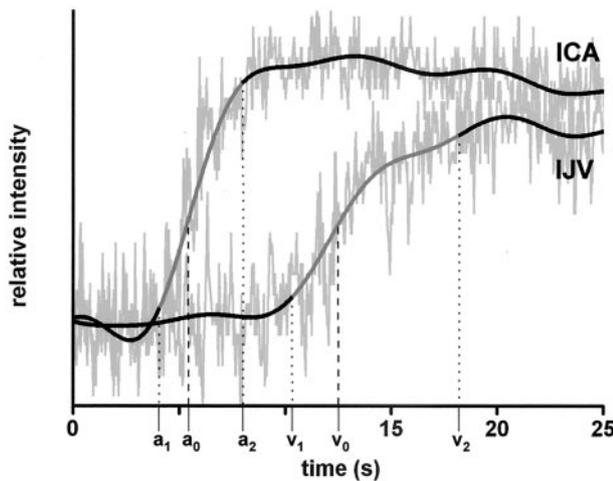


FIG 3. Sample time-intensity curves and data analysis in a healthy control subject. Vertical gray lines are the raw data. Black and gray curves are polynomial fit, where gray indicates 80% of total signal-intensity increase, CCT =  $v_0 - a_0 = 7.3$  seconds, where  $v_0$  and  $a_0$  = turning point of the venous and arterial polynomial fit. Venous rise time  $\Delta t = v_2 - v_1 = 8.2$  seconds. Arterial rise time  $\Delta t = a_2 - a_1 = 4.2$  seconds.  $a_1$  and  $v_1$  = point at 10% total intensity increase, and  $a_2$  and  $v_2$  = point at 90% total intensity increase.

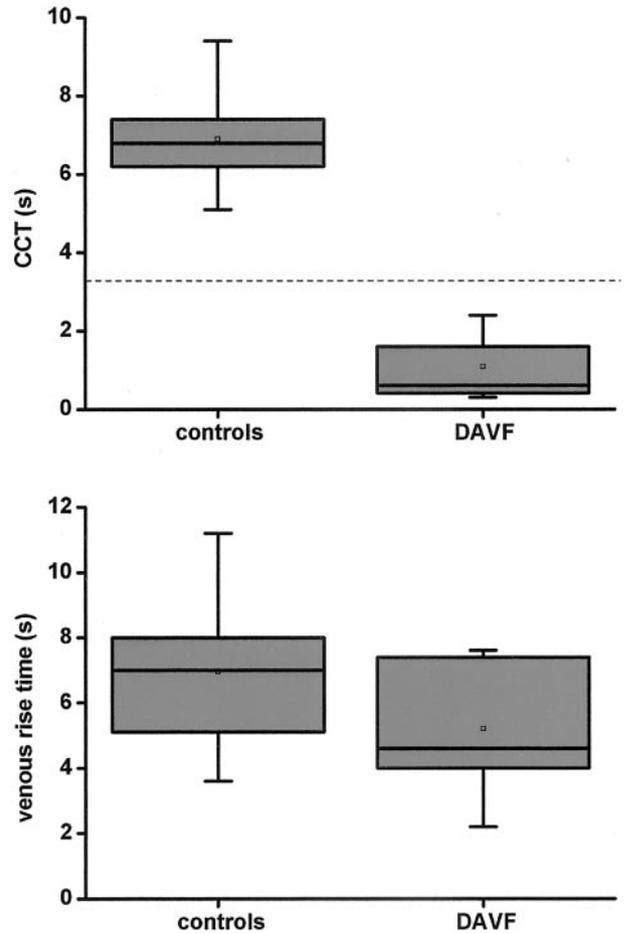


FIG 4. Box-plot analysis of the results, including the mean, median, 25/75 percentiles (box) and 5/95 percentiles (whisker). Top: Plots of CCT results in control subjects ( $n = 30$ ) and patients with DAVF ( $n = 13$ ). Dotted line represents the cutoff value of 3.3 seconds [ $\text{mean CCT}_{\text{controls}} - (3 \times \text{SD}_{\text{controls}})$ ] chosen for sensitivity and specificity analysis. Bottom: Plots of venous  $\Delta t$  in control subjects and patients.

cases, no statistical correlation analysis between radiologic and CCT findings was attempted.

Calculation of sensitivity and specificity for the detection of a DAVF was performed with a CCT cutoff value of 3.3 seconds [ $\text{mean}_{\text{controls}} - (3 \times \text{SD}_{\text{controls}})$ ]. Sensitivity of the test was 1, and its specificity was 0.97 with a positive predictive value of 0.93 and a negative predictive value of 1.

### Discussion

So far, the detection or exclusion of a clinically suspected DAVF relies on diagnostic DSA exclusively. In most cases of DAVF, conventional CT or MR imaging of brain tissue allows us to detect only the hemodynamic adverse effects of venous outflow obstruction, such as brain edema, hydrocephalus, or intracranial bleeding (3–5). More recently, MR and CT angiography techniques have been reported. However, they have not yet found their place in routine diagnostic practice (16, 17). Past sonographic methods could strongly suggest a DAVF on the basis

of a pathologic Doppler spectrum, if an increased flow velocity or an increased diastolic flow proportion in the ECA or occipital artery were found on the side of the malformation. Sometimes, a pseudoarterialized flow pattern can be detected by means of extracranial duplex sonography in the draining IJV (6, 7), which was present in nine of our 14 patients and in none of the controls. However, as jugular venous flow is known to vary between individuals, even under physiologic conditions, clear differentiation of a DAVF based on this characteristic alone seems problematic.

Similar to cerebral angiography, our sonographic approach for CCT measurement by echo contrast-bolus tracking was set up to detect the hemodynamic effect of the arteriovenous shunts in patients with DAVF. The frequent angiographic finding of early contrast medium arrival in the draining IJV suggests a drastic reduction in the measured circulation time (18). In a previous report using the same sonographic setup, CCT was significantly reduced in nine patients with cerebral AVMs (14). The AVM group had a mean CCT of  $3.0 \pm 1.3$  seconds compared with  $7.0 \pm 1.3$  seconds in controls. However, no defined cutoff value could be obtained because of an overlap of CCT ranges between patients (1.4–5.1 seconds) and controls (4.8–11.1 seconds).

The present study of 13 DAVF patients revealed highly significant shortening of CCT compared with the controls ( $1.1 \pm 0.9$  vs  $6.9 \pm 1.2$  seconds) and no overlap between individually measured values. Although the number of cases was relatively small, our results suggest a test sensitivity as high as 100% for detecting an arteriovenous shunt at the skull-base level. However, in all of our cases, venous drainage occurred via at least one of the IJVs. A vascular malformation exclusively draining via the vertebral veins or the paraspinal venous system would probably not be detected with our method. Regarding the specificity analysis for diagnosing a DAVF, only preliminary conclusions can be drawn, as only two of our patients were prospectively evaluated. Interestingly, one of these patients did not have the expected DAVF but a highly vascularized glomus tumor, which is well known to cause pulsatile tinnitus (19). Furthermore, other studies in patients with intracerebral AVM show that Doppler sonographic CCT may be as short as 1.4 seconds (14). However, these facts reduce the specificity of the test only for the exclusive detection of a DAVF and not for the detection of a pathologic arteriovenous shunt. Therefore, the actual positive predictive value of a relevant arteriovenous shunt in our study is 100%. This is a promising result, considering the potential application of the technique as a noninvasive screening tool in cases of suspected DAVF before a more invasive angiography is performed.

In five of our patients, sonographic control measurements could be performed in the course of treatment. Because this number was small and because tests were not performed in a consistently blinded design, no statistical correlation between interventional angiographic results and CCT values was at-

tempted. Our data nevertheless indicate a possible role of this sonographic test in the evaluation of individual treatment courses. We found no discrepancies between the treatment evaluations of the interventional radiologist and our CCT data. The two cases with complete occlusion of the malformation led to CCT normalization. In the two cases of a relevant shunt volume that remained despite repeated interventional sessions, no significant CCT change was seen. Finally, in our fifth case with a minimal residual shunt (as shown angiographically), CCT showed a two-step increase in signal intensity. This finding seems especially interesting when we consider the frequent clinical question of permanent posttreatment occlusion or the development of newly emerging collaterals. Sonographic CCT assessment could potentially serve as an additional diagnostic step before repeat DSA, which is the only established diagnostic tool that can address these issues at present. However, as a frequent therapeutic step, occlusion of the draining transverse sinus limits applicability of this test. This problem might be solved if pretreatment CCTs to both IJVs can be obtained.

Because of the limited numbers of patients, the present study did not allow us to document how small an arteriovenous shunt can be and still be detected. However, the extremely high sensitivity of the sonographic technique in showing even single microbubbles—as in testing the foramen ovale—suggests a sensitivity at least comparable to that of DSA.

Our data allowed us to analyze rise time ( $\Delta t$ ), which was defined as the interval between 10% and 90% of the total increase in Doppler signal intensity. As expected, no difference was found between the arterial  $\Delta t$  values in patients with DAVF and control subjects ( $4.4 \pm 1.8$  vs  $4.7 \pm 2.0$  seconds). However, comparing venous  $\Delta t$ , we found a significant difference ( $5.2 \pm 2.0$  vs  $7.0 \pm 2.6$  seconds), which we attribute to the different extents of echo contrast-bolus dispersion. Physiologic brain perfusion in the control subjects led to a mean  $\Delta t$  difference of  $>2$  seconds between arterial and venous signal intensities, whereas the shunt caused by a DAVF reduced bolus dispersion and consequently led to  $\Delta t$  values within the arterial range. As the venous  $\Delta t$  in our patient group was not correlated with the CCT, it might be an additional parameter for characterizing arteriovenous shunts.

In conclusion, we found marked shortening of Doppler sonographic CCT in patients with DAVF. Our test had high diagnostic sensitivity and specificity for arteriovenous shunts but not for DAVF alone, as a pathologic CCT shortening can also be found in other vascular malformations causing arteriovenous shunts. Our simple, minimally invasive test has the potential to be applied as a diagnostic screening tool in patients with clinically suspected DAVF; however, it provides no direct information about the anatomic structure of a vascular malformation itself, unlike the criterion standard DSA. Our technique could be a useful additional step in follow-up and treatment monitoring in patients with DAVF.

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