High-signal venous sinuses on MR angiography: discrimination between reversal of venous flow and arteriovenous shunting using arterial spin labeling

（MRA における静脈洞内の高信号：Arterial spin labeling による生理的静脈逆流と動静脈瘻の鑑別）

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Abstract

Purpose: It is sometimes difficult to differentiate between high signals originating from a reverse flow on magnetic resonance angiography (MRA) and occult arteriovenous shunting. We attempted to determine whether arterial spin labeling (ASL) can be used to discriminate reversal venous flow from arteriovenous shunting for high-signal venous sinuses on MR angiography.

Methods: Two radiologists evaluated the signals of the venous sinus on MRA and ASL obtained from 364 cases without arteriovenous shunting. In addition, the findings on MRA were compared with those on ASL in an additional 13 patients who had dural arteriovenous fistula (DAVF).

Results: In the 364 cases (728 sides) without arteriovenous shunting, a high signal due to reverse flow in the cavernous sinuses (CS) was observed on 99 sides (13.6%) on MRA and none on ASL. Of these cases, a high signal in the sigmoid sinus, transverse sinus, and internal jugular vein was seen on 3, 3, and 8 sides, respectively. All of these venous sinuses showed a high signal from the reverse flow on MRA images.

Conclusions: ASL is a simple and useful MR imaging sequence for differentiating between reversal of venous flow and CS DAVF. In the sigmoid and transverse sinus, ASL showed false-positives due to the reverse flow from the jugular vein, which may be a limitation of which radiologists should be aware.

Keywords: Magnetic resonance angiography・Arterial spin labeling・Digital subtraction angiography・Cavernous sinuses・Venous reverse flow,・Dural arteriovenous fistulas

Abbreviations

- MRA, Magnetic resonance angiography
- ASL, Arterial spin labeling
- DSA, Digital subtraction angiography
- DAVF, Dural arteriovenous fistulas
- CS, Cavernous sinuses
- IPS, Inferior petrosal sinus
- PP, Pterygoid plexus
- EV, Emissary vein
- IJV, Internal jugular vein
- SS, Sigmoid sinus
- SSS, Superior sagittal sinus

- TS, Transverse sinus

Conflict of interest statement

We declare that we have no conflict of interest.

Introduction

Three-dimensional (3D) time-of-flight magnetic resonance angiography (MRA) is a noninvasive imaging technique that is widely accepted as a first-line diagnostic tool in magnetic resonance imaging (MRI) examinations of numerous cerebrovascular diseases. MRA has also been used to screen patients with dural arteriovenous fistula (DAVF) at the sigmoid sinus (SS), transverse sinus (TS), cavernous sinuses (CS), etc.[1,2]. The MRA characteristics of DAVF at the CS commonly include visualizing venous structures, such as the CS, inferior petrosal sinus (IPS), superior petrosal sinus, pterygoid plexus (PP), Sylvian veins, superior ophthalmic vein, and sphenoparietal sinus [3].

High signals originating from the reverse flow are frequently seen on 3-Tesla MRA [4]. Previous studies found a high signal in the CS on MRA in 43 (10.6%) of 406 healthy participants [4]. These findings are considered to indicate flow signals in the PP/emissary vein (EV) originating from the reverse flow, as in the internal jugular vein (IJV) and SS. Although previous investigators described the pathological and non-pathological imaging features of incidental high signal in the CS on MRA [5], it is sometimes difficult to differentiate a high signal originating from the reverse flow on MRA and occult CS-DAVF. In a clinical setting, a diagnosis of simply "suspected occult CS-DAVF" would indicate the need for long-term follow-up or further examinations with another imaging technique. The gold standard for the diagnosis of a DAVF, catheter-based digital subtraction angiography

(DSA), is invasive, uses radiation and iodinated contrast media, which sometime causes side effects of acute allergy and nephrotoxity, and carries a very small but not insignificant risk of permanent neurological injury [6]. Although time-resolved contrast-enhanced MRA and computed tomography angiography (CTA) techniques have been shown to have a high sensitivity and specificity for the identification of DAVF [7-9], they are limited by their invasiveness and use of contrast agents. Therefore, an accurate noninvasive imaging method of diagnosing DAVF would be valuable.

Arterial spin-labeling (ASL) is a completely noninvasive MRI technique that is now widely available on clinical MRI scanners. A high ASL signal is not observed in cerebral veins under normal conditions due to T1 decay during capillary transit and exchange with the extravascular space of labeled blood-water protons [10,11]. However, under conditions of arteriovenous shunting, such as with a DAVF, the rapid transit of labeled blood directly from feeding arteries to draining veins results in a high signal in venous structures [10,11]. This venous ASL signal is a conspicuous finding that can indicate the presence of arteriovenous shunting. Although a previous study showed that a venous high signal on ASL had a high sensitivity and specificity for detecting the presence of an intracranial DAVF [12], the effect of the venous reverse flow on the ASL signal has not been elucidated.

We aimed to determine whether ASL can be used to discriminate reversal of venous flow from arteriovenous shunting for high-signal venous sinuses on MRA.

Materials and Methods

Subjects

The ethics review committees of Aomori Prefectural Central Hospital approved this retrospective study, and the need to obtain informed consent from the patients was waived.

From the MRI database between January 2016 and April 2016, we selected 374 consecutive patients who underwent brain MRI with MRA and ASL. A total of 71 patients were excluded based on the following exclusion criteria: acute large territory infarction (n = 38), acute epilepsy (n = 6), acute cerebral hemorrhage (n = 20), and arteriovenous malformation (n = 7). Therefore, 303 patients (group A) were included in the evaluation. For group A, the specific diagnoses are shown in Table 1. Next, to identify cases who underwent brain MRA before or within 1 month after DSA, we performed a computerized search of the radiology data base (DSA files) at our hospital for a 3-year period from July 2017 through July 2020, with 74 cases meeting our criteria. We further divided these cases into two groups: group B, 61 patients without arteriovenous shunting; and group C, 13 patients with arteriovenous shunting (Table 1). For groups B and C, the specific diagnoses made according to the DSA images are shown in Table 1.

Magnetic resonance imaging (MRI)

MRI studies (MRA and ASL) were performed with a 3-Tesla MR system (Discovery

MR750w DV25 & DV26; GE Healthcare, Milwaukee, WI, USA) using a dedicated 8-channel phased array coil (GE Healthcare) and a 1.5-Tesla MR system (Optima MR 450w DV26; GE Healthcare) using a dedicated 8-channel phased array coil (GE Healthcare).

The parameters for 3D TOF-MRA were (1.5 T): TR/TE, 20/3.2 ms; field of view (FOV), 20 × 20 cm; flip angle, 15°; matrix, 288 ×192; slice thickness, 1.2 mm; number of slab, 4; sections per slab**,** 38; acquisition time, 4 min 43 s. For 3 T, they were TR/TE, 20/3.2 ms; FOV, 20 × 20 cm; flip angle, 15°; matrix, 416×224; slice thickness, 1.2 mm; number of slab, 4; sections per slab**, 38** acquisition time, 4 min 46 s.

3D pCASL imaging (TR/TE, 4800/11.5ms [1.5T], 4800/10.5 ms [3T]; 24-cm FOV) with background suppression was implemented using a labeling period of 1500 ms, a postlabel delay of 2000 ms, labeling plane at the level of the foramen magnum, and a segmented 3D stack-of-spirals FSE readout (spiral arms: 6 [1.5T and 3T]). The in-plane spatial resolution was 3 mm, and the through-plane spatial resolution was 3-4 mm, yielding 32-36 slices. The scan time was 4 min. No vascular crusher gradients were used. This acquisition complies with the consensus recommendations of the ASL community.

The angiography procedure was standard, and conventional digital subtraction angiography (DSA) was performed with an angiography system (Innova 3131 IQ; GE Healthcare, Chalfont St. Giles, UK). For bilateral common carotid or internal carotid studies, venous-phase DSA images, as well as arterial-phase DSA images, were obtained in all patients.

Image interpretations

All MRA examinations were independently evaluated by 2 neuroradiologists (M.I. and S.K., with 12 years and 23 years of experience in neuroradiology, respectively) by consensus. First, 364 MRA images (Group A and B), including MRA source and maximum intensity projection images, were evaluated. Then, according to a previous study [4], the radiologists subjectively rated the flow signals observed in the PP/EV and CS on the MRA images using a 5-point grading scale (Fig. 1a)as follows: grade 0 = all flow signals of the PP are less than or equal to the background signal; grade I = the flow signal in a part of the PP/ EV is higher than the background signal and lower than the arterial signal; grade II = the flow signal in a part of the PP/EV is equal to arterial signal; grade III = a high signal intensity is seen in less than or equal to one-third area of the CS; and grade IV = a high signal intensity is seen in more than one-third of the CS. In addition, the radiologists rated the flow signals observed in the IPS and CS using a 5-point grading scale(Fig. 1b): grade 0 = all flow signals of the IPS flow signal are less than or equal to the background signal; grade I = the flow signal in part of the IPS is higher than the background signal and lower than the arterial signal ; grade II = the flow signal in part of IPS is equal to the arterial signal; grade III = a high signal intensity is seen in less than or equal to one-third area of the CS; and grade IV = a high signal intensity is seen in more than one-third area of the CS. They also evaluated presence of a high signal intensity on MRA source images within the superior sagittal sinus (SSS), SS, TS, and IJV.

Next, for a high signal intensity in the CS and a venous sinus on ASL, two neuroradiologists rated as "presence" or "absence" by consensus. The ASL images were always reviewed in conjunction with MRA and conventional MR images. Finally, for the patients with arteriovenous shunting (group C), the two neuroradiologists evaluated the presence of a high signal intensity on MRA and ASL images and com- pared them with the DSA findings.

Statistical analyses

All of the statistical analyses were performed using the R software program [13]. For the grading of the flow signals in the PP/EV or IPS on MRA, a Mann–Whitney U test was performed to assess the statistical significance of the different scores assigned on 1.5 and 3 T. A *P* value of 0.05 was considered to indicate a statistically significant difference.

Results

Of the total 3-Tesla MRA images (148 cases, 296 sides) in Group A, the flow signal was rated as "grade I or II" on 56 sides (18.9%) and "grade III or IV" on 50 sides (16.9%) (Table 2). In the analysis of Group B, 1 (2.8%) of 36 sides on 1.5-Tesla MRA and 10 (11.6%) of 86 sides on 3-Tesla MRA were rated as “grade III or IV” (Table 2). The number of sides rated as “grade III or IV” in Group B was greater on 3-Tesla MRA than on 1.5-Tesla MRA (20.9% [10/86] vs. 5.5% [1/18]), although no statistically significant differences were identified (P=0.12). Among cases rated as “grade III or IV” in Group B, no DAVFs were seen at the CS on DSA images (Fig. 2). In the ASL analysis, no cases rated as “grade III or IV” (88 and 11 sides of groups A and B, respectively) showed a high signal in the CS (Fig. 2).

For the MRA analyses in groups A and B (364 cases, 728 sides), a high signal was seen in the SSS, SS, TS, and IJV in 23 cases, on 28 sides, on 29 sides, and on 41 sides, respectively (Table 3). For the SS, TS, and IJV, a high signal on MRA was more common on the left side than on the right. For the ASL analyses of groups A and B (364 cases, 728 sides), a high signal was seen in the SSS, SS, TS, and IJV in 0 cases, on 3 sides, on 3 sides, and on 8 sides, respectively (Table 3). A high ASL signal of the SS and TS was seen only on the left side, never on the right. For the IJV, a high ASL signal was more common on the left side than on the right (1 vs. 7 sides). For Group B, DAVFs were not seen at any sinus or vein on DSA images. For cases with a high ASL signal in the SS (n=3), TS (n=3), and IJV (n=7), the radiologists found a high signal originating from the reverse flow on MRA images (Fig. 3). For the ASL, the frequency of a high signal was significantly higher in the IJV than in the SSS (P = 0.04); however, among any other sinuses, the frequency of high signal on both MRA and ASL did not differ significantly.

For Group C (Table 1), in all patients with CS-DAVF (n=6), SSS-DAVF (n=1), TS-DAVF (n=5), and lateral tentorial sinus DAVF (n=1), arteriovenous shunting was able to be identified on MRA and ASL. In one case with low-flow CS-DAVF, arteriovenous shunting was able to be detected on ASL, although abnormality was subtle on MRA (likely due to signal saturation) (Fig. 4).

Discussion

While high signals originating from the reverse flow on the MRA were frequently seen in CS, these cases showed no ASL signal in the CS. Furthermore, all CS-DAVF patients identified on DSA showed a high ASL signal in the CS. Therefore, the detection of a high ASL signal in the venous sinus had perfect sensitivity and specificity for the presence of CS-DAVF. In contrast to the CS, as false-positive lesions, we found high signals in the TS, SS, or IJV that was identified by ASL.

Previous investigators speculated that the blood flow in the PP/EV might be easily reversed because of the anatomical characteristics, as venous valves, arteriovenous anastomoses, and blood-storable shapes were observed in the PP, all of which can easily cause a stagnant bloodstream [14]. On 3-Tesla MRA in Group A, 49 (17%) of 296 sides showed a high signal in the CS (grade III or IV). In Group B, MRA images also showed flow signals in the CS on 10 (12%) of 86 sides; no CS-DAVF were identified on DSA in any of these patients. Our results are consistent with the findings of a previous study that detected evidence flow signals (grade III or IV) in the CS of 68 (16%) of 406 cases on 3-Tesla MRA [4]. For both groups A and B, we found that a grade of III or IV was more common on 3-Tesla than on 1.5-Tesla MRA. This result may be due to the potential benefits of 3-Tesla MRA over 1.5-Tesla MRA, including increased T1 relaxation times and/or high signal-to-noise ratios [15].

It is important to note that, in the ASL analysis, no cases rated as “grade III or IV” in groups A or B showed a high signal in the CS. Interpreting MRA findings requires discriminating a high signal originating from the reverse flow from occult DAVF in order to avoid unnecessary further evaluation [4]. Our result indicates that, in cases with high signals in the CS on MRA, the detection of no ASL signal in CS improves the diagnostic accuracy and increases the confidence in the absence of a DAVF. ASL may be a simple, useful MRI sequence for differentiating these entities because ASL is becoming increasingly common in the clinical setting due to recent technical advances, including the use of spin-echo readout and background suppression [16]. Therefore, we recom- mend that the ASL sequence, which can be obtained with a relatively short acquisition time and wide anatomic coverage, should be employed in patients suspected of having DAVF.

Our study showed that a high ASL signal in the venous sinus had a perfect sensitivity for detecting the presence of a CS-DAVF. We also found one case of low-flow fistula in the

CS that was able to be detected on ASL despite being subtle on MRA. Our excellent results are consistent with the previous results [10,11]. Amukotuwa et al. demonstrated that a venous ASL signal had a high sensitivity for detecting the presence of a DAVF [12]. Our results also showed not only a high sensitivity but also an extremely high specificity with ASL for the diagnosis of CS-DAVF.

In contrast to the CS, for the ASL analyses of groups A and B, we found a high signal in the SS, TS, and IJV, which might have been false-positives due to the reverse flow. Although previous investigators detected a high ASL signal in the venous sinus in 11 (9.4%) of 117 controls without arteriovenous shunting [12], the mechanisms underlying the venous ASL signal could not be fully explained. We speculate that one possible explanation for these high ASL signals may be arti- facts due to the reverse flow from the jugular veins, as labeled blood-water protons within the jugular veins might backflow into the TS or SS. This hypothesis is supported by the results, as all of the TS, SS, and IJV specimens with a high ASL signal had a high signal originating from the reverse flow on MRA. Furthermore, a high ASL signal was seen only in the left TS and SS, not in the right TS or SS. Previous investigators suggested that a high signal originating from the reverse flow in the IJV and SS on MRI was significantly more common on the left side than on the right because of compression of the left brachiocephalic vein [17, 18]. In the present study, in contrast to findings in the TS and SS, we noted no high ASL signal in the CS as a false-positive, although reverse flow signals from the PP/EV and IPS to the CS were often seen on MRA. The main reason for this may be that intracranial vessel structures, such as the PP/EV and IPS, were unable to be labeled at the ASL examinations.

Several limitations associated with the present study warrant mention. First, there were a few cases of low-flow DAVF, which might have registered as occult on ASL. This likely affected our results, especially regarding the sensitivity for the detection of DAVF. Second, the study was retrospective and DSA was not performed in all cases.

In conclusion, none of the cases with high signals originating from the reverse flow in the CS on MRA showed an ASL high signal in the CS, suggesting that ASL is a simple and useful MRI sequence for differentiating between reversal of the venous flow and occult CS-DAVF. However, ASL did show some false-positives due to the reverse flow from the jugular vein, which may be a limitation that radiologists should be aware of when using ASL to screen for DAVF. Furthermore, to distinguish the true-positives from the false- positives by ASL, radiologists should always evaluate ASL in conjunction with source images obtained with MRA, because the source images are helpful for diagnosing subtle abnormal flows due to DAVF, such as draining veins.

Figure legends

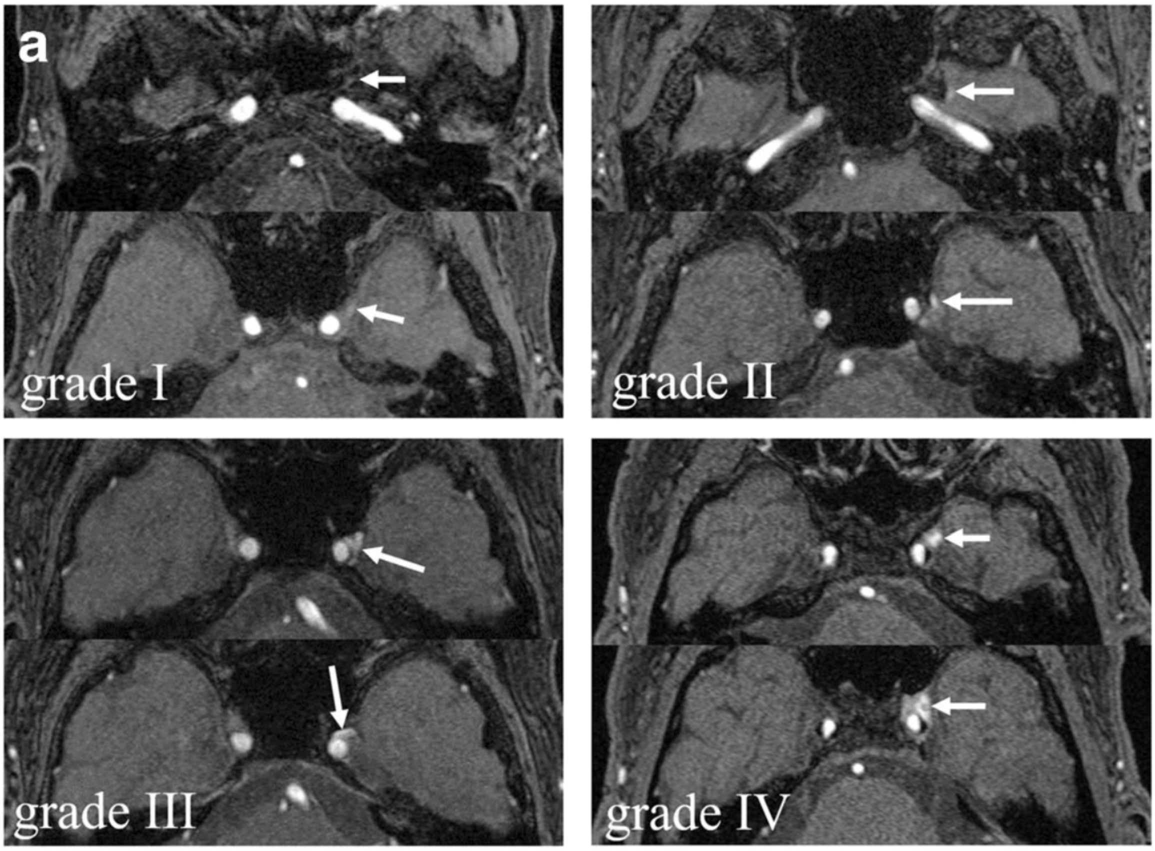

Figure. 1 a: Examples of the 5-point grading scale for the PP/EV and CS. Grade I = the flow signal (arrows) in a part of the PP/EV is higher than the background signal and lower than the arterial signal; grade II = the flow signal (arrows) in a part of the PP/EV is equal to arterial signal; grade III = a high signal intensity (arrows) is seen in less than or equal to one-third area of the CS; and grade IV = a high signal intensity (arrows) is seen in more than one-third of the CS.

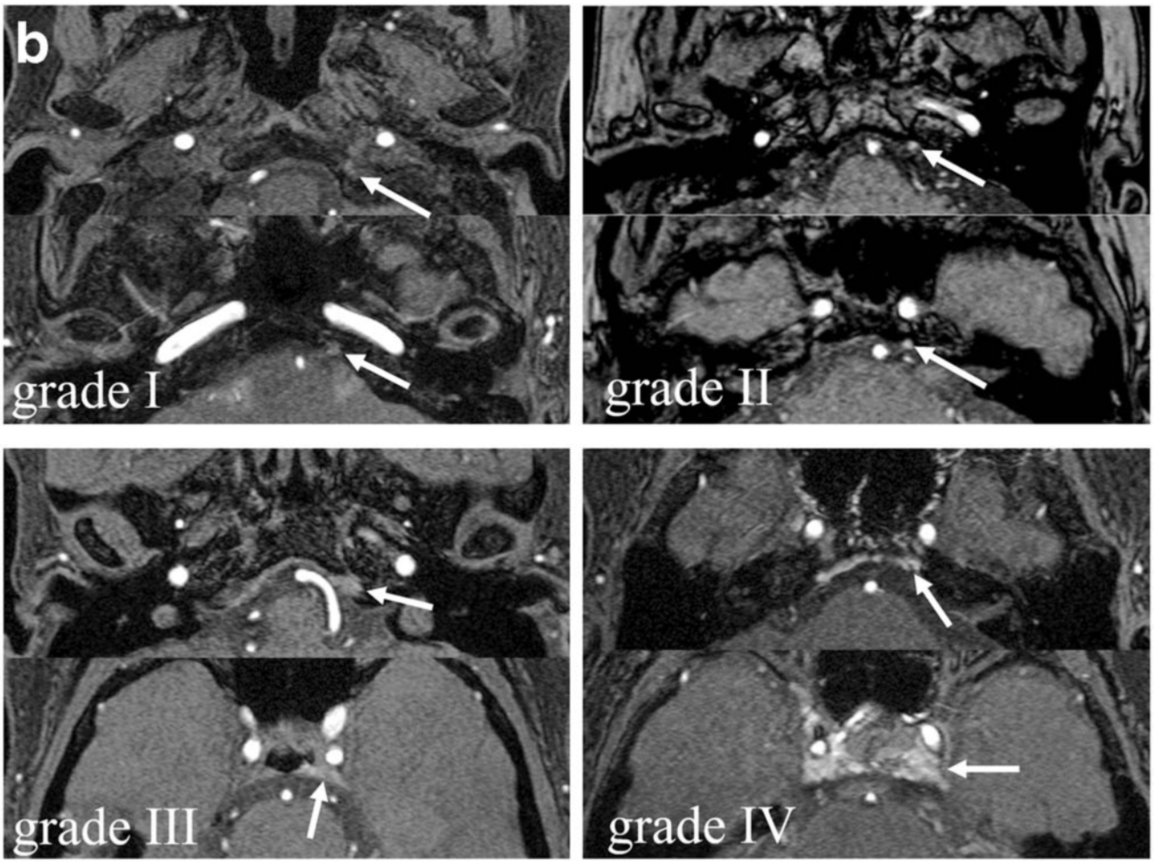

Figure.1 b: Examples of the 5-point grading scale for the IPS and CS. Grade I = the flow signal (arrows) in part of the IPS is higher than the background signal and lower than the arterial signal; grade II = the flow signal (arrows) in part of IPS is equal to the arterial signal; grade III = a high signal intensity (arrows) is seen in less than or equal to one-third area of the CS; and grade IV = a high signal intensity (arrows) is seen in more than one-third area of the CS.

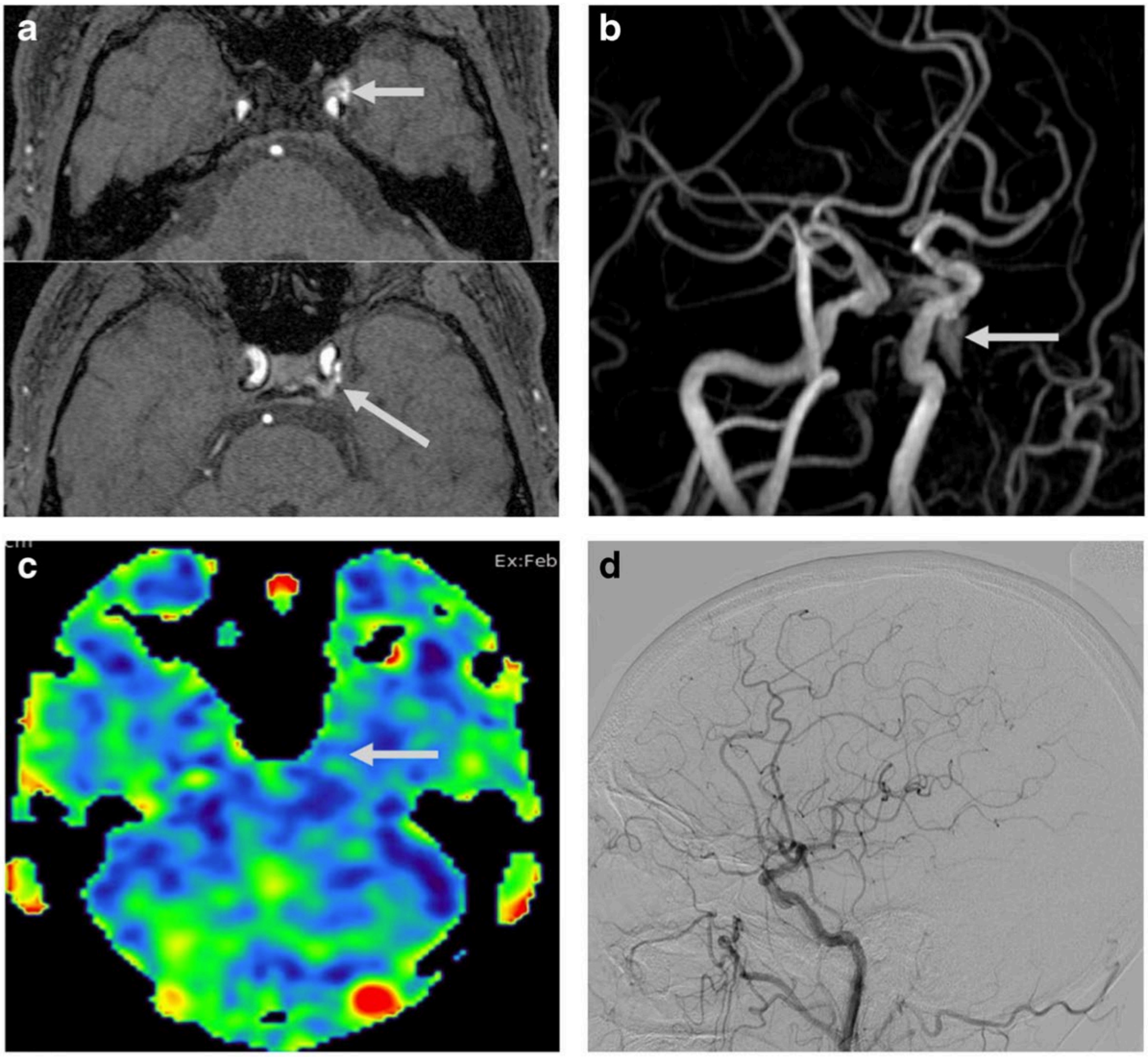

Figure. 2: A 72-year-old man rated as grade IV on the grading scale for the PP/EV. MRA source (a) and maximum intensity projection (b) images show a high signal intensity in the left PP/EV and CS (arrows). The ASL color map (c) image do not show a high signal in the left PP/EV or CS (arrow). DAVF at the CS is not seen on DSA (lateral view) with a left common carotid artery injection (d).

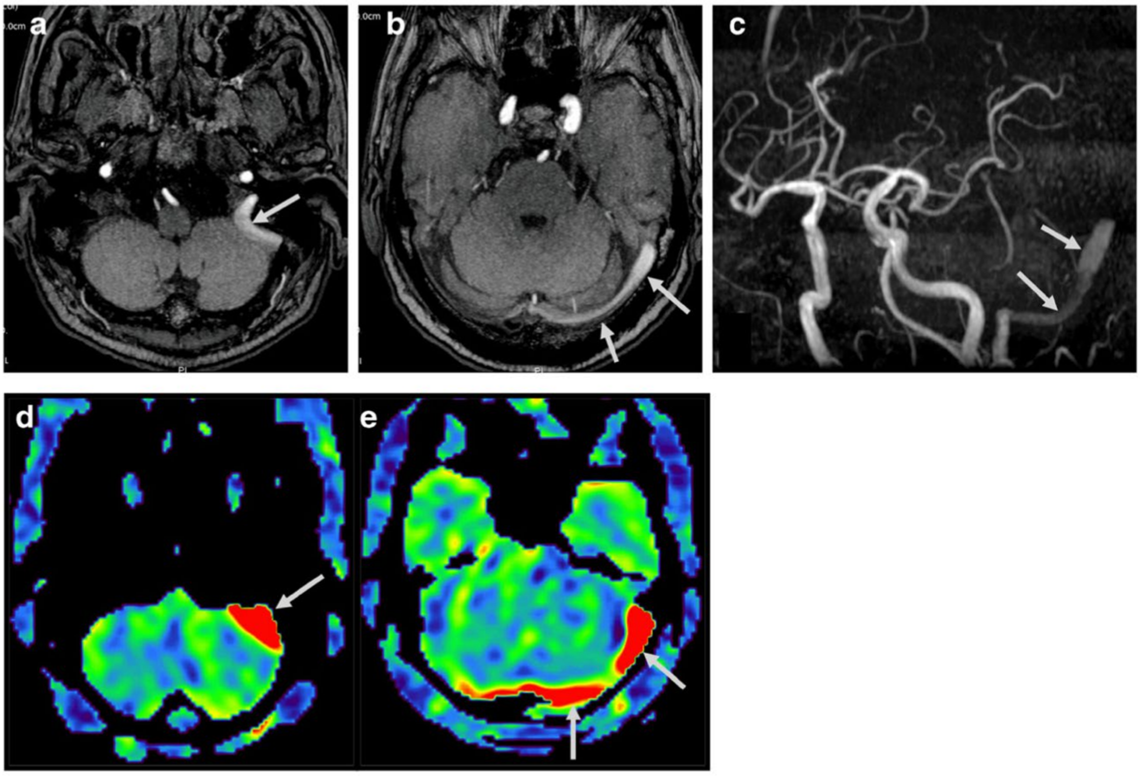

Figure. 3: A 72-year-old man without DAVF. The MRA source (a,b) and maximum intensity projection (c) images show a high signal intensity in the left transverse-sigmoid sinus and internal jugular vein (arrows). The ASL color map (d,e) shows a high signal in the left transverse-sigmoid sinus and internal jugular vein (arrows).

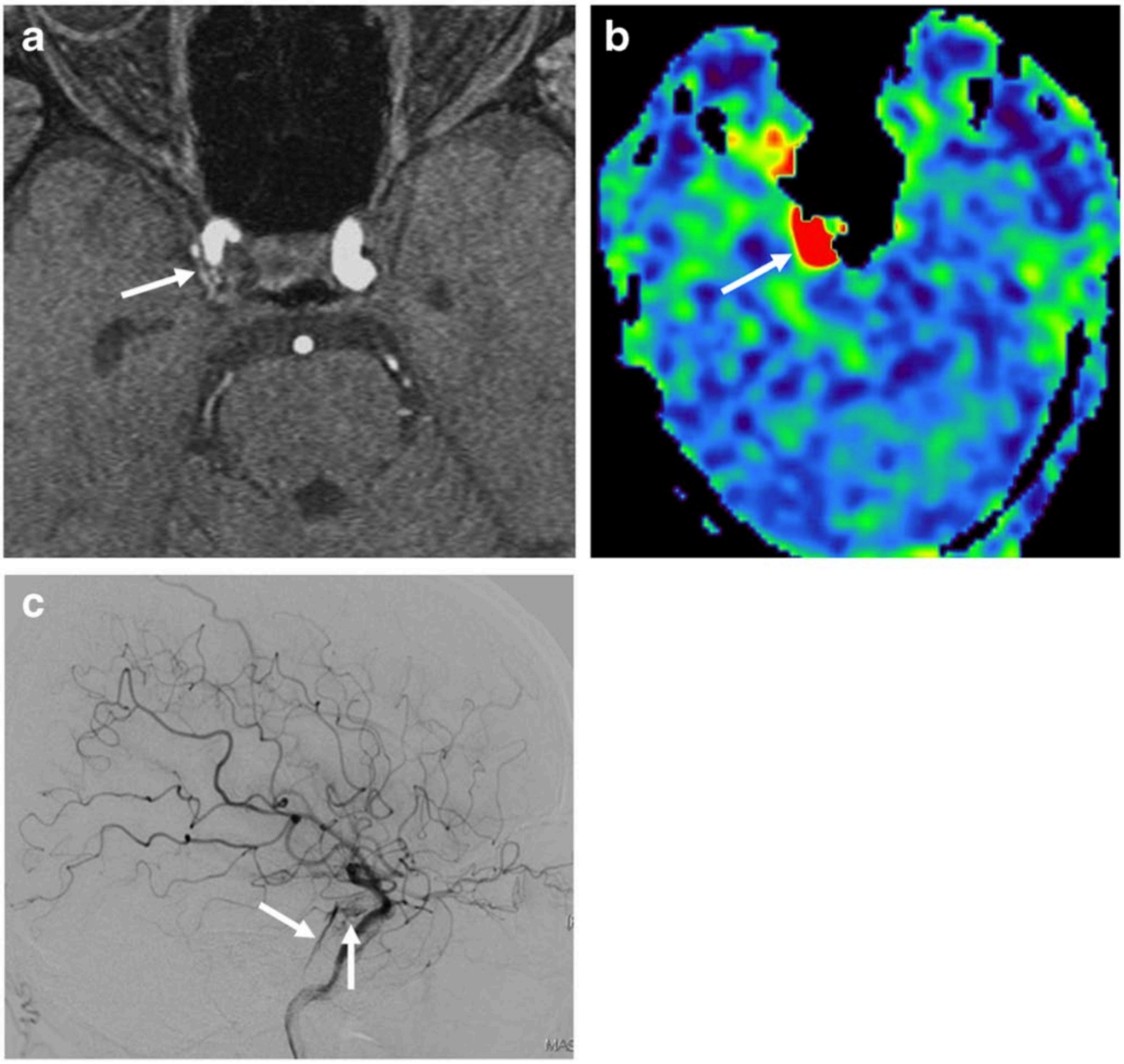

Figure. 4: A 67-year-old man with right CS DAVF (Cognard I). The MRA source image (a) shows a slight high signal intensity in the right CS (arrow). The ASL color map (b) shows a high signal in the right CS (arrow). This patient was rated as grade II. DAVFs at the CS were seen on DSA (lateral view) with a right internal carotid artery injection (c).

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Table 1: Patient characteristics

	Group A (n=303)	Group B (n=61)	Group C (n=13)
Mean age: years (range, SD)	62.8(16.71)	61.6(13.99)	69.3(12.31)
Sex: male/female	148/155	31/30	3/10
MRI: 1.5-Tesla/3-Tesla	155/148	24/37	1/12
Diagnoses	cerebrovascular disease (aneurysm, dissection, moyamoya disease, ICA stenosis or occlusion): n=97 (31.6%), small acute infarction: n=86 (28.4%), small acute multiple infarction: n=2 (0.7%), old cerebrovascular disease: n=16 (5.3%), extra-axial tumor: n=7 (2.3%), intra-axial tumor: n=5 (1.7%), leptomeningeal carcinoma: n=1 (0.3%), neurodegenerative disease: n=4 (1.3%), encephalitis: n=4 (1.3%), anomaly: n=1 (0.3%), and normal: n=80 (26.4%).	cerebrovascular disease (aneurysm, dissection, moyamoya disease, ICA stenosis or occlusion): n=39 (63.9%), extra-axial tumor: n=5 (8.2%), intra-axial tumor: n=5 (8.2%), dural sinus thrombosis: n=4 (6.6%), neurodegenerative disease: n=2 (3.3%), small infarction: n=1 (1.6%), and normal findings: n=5 (8.2%).	CS-DAVF (n=6), SSS-DAVF (n=1), TS-DAVF (n=5), and lateral tentorial sinus DAVF (n=1).

ICA = internal carotid artery, DAVF = dural arteriovenous fistula, CS = cavernous sinus, SSS = superior sagittal sinus, TS = transverse sinus.

Table 2: Frequency of the flow signal in the PP/EV and IPS on 1.5- and 3-Tesla MRA

	(case, side)	grade 0		grade I or II				grade III or IV			
				PP/EV	IPS	PP/EV+IPS	Total sides	PP/EV	IPS	PP/EV+IPS	Total sides
Group A	1.5-Tesla (155, 310)	67.1% (208/310)	45.1% (70/155)	3.9% (12/310)	8.4% (26/310)	8.4% (26/310)	20.6% (64/310)	3.2% (10/310)	0.3% (1/310)	8.7% (27/310)	12.3% (38/310)
	3-Tesla (148, 296)	64.2% (190/296)	43.2% (64/148)	5.7% (17/296)	7.1% (21/296)	7.1% (18/296)	18.9% (56/296)	6.1% (18/296)	2.4% (7/296)	8.4% (25/296)	16.9% (50/296)
	1.5-Tesla and 3-Tesla (303, 606)	65.7% (398/606)	44.2% (134/303)	4.8 % (29/606)	7.8% (47/606)	7.8% (44/606)	19.8% (120/606)	4.6% (28/606)	1.3% (8/606)	8.6% (52/606)	14.5% (88/606)
Group B	1.5-Tesla (18, 36)	52.8% (19/36)	55.6% (10/18)	11.1% (4/36)	8.3% (3/36)	25.0% (9/36)	44.4% (16/36)	0% (0/36)	0% (0/36)	2.8% (1/36)	2.8% (1/36)
	3-Tesla (43, 86)	60.5% (52/86)	34.9% (15/43)	7.0% (6/86)	11.6% (10/86)	9.3% (8/86)	27.9% (124/86)	2.3% (2/86)	0% (0/86)	9.3% (8/86)	11.6% (10/86)
	1.5-Tesla and 3-Tesla (25, 122)	58.2% (71/122)	41.0% (25/61)	8.2% (10/122)	10.7% (13/122)	13.9% (17/122)	32.8% (40/122)	1.6% (2/122)	0% (0/122)	7.4% (9/122)	9.0% (11/122)

Data represent the average (numbers of cases).

PP = pterygoid plexus, EV = emissary vein, IPS = inferior petrosal sinus.

Table 3: Frequency of a high signal on MRA and ASL

		SSS	SS R/L	TS R/L	IJV R/L	Total cases
MRA	Group A: 303 cases, 606 sides	20	1/23	2/23	3/32	17.5% (53/303)
	Group B: 61 cases, 122 sides	3	0/4	0/4	0/6	14.8% (9/61)
	Group A+B: 364 cases, 728 sides	6.3% (23/364)	3.8% (28/728)	4.0% (29/728)	5.6% (41/728)	17.0% (62/364)
ASL	Group A: 303 cases, 606 sides	0	0/3	0/3	1/7	2.6% (8/303)
	Group B: 61 cases, 122 sides	0	0	0	0	0
	Group A+B: 364 cases, 728 sides	0	0.4% (3/728)	0.4% (3/728)	1.1% (8/728)	2.2% (8/364)

ASL = arterial spin labeling, SSS = superior sagittal sinus, SS = sigmoid sinus, TS = transverse sinus, IJV = internal jugular vein.