

Diagnostic Performance of Superior Ophthalmic Vein Doppler Ultrasonography for Carotid-Cavernous Fistula and Cavernous Sinus Dural Arteriovenous Fistula

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Abstract

Background: Carotid-cavernous fistula (CCF) and cavernous sinus dural arteriovenous fistula (dAVF) often present with ocular symptoms and may increase intraocular pressure (IOP). Cerebral angiography is the reference standard; however, noninvasive tools are needed to support diagnostic triage and treatment decision-making.

Objectives: To evaluate the diagnostic performance of superior ophthalmic vein (SOV) Doppler ultrasonography (DUS) for CCF/cavernous dAVF, to compare its performance with magnetic resonance angiography (MRA), and to assess the relationship between Doppler parameters and elevated IOP.

Methods: This retrospective diagnostic accuracy study included 67 eyes from 51 patients who underwent SOV DUS and cerebral digital subtraction angiography for suspected CCF/cavernous dAVF. Analyses were performed at the eye level. Diagnostic performance of DUS, MRA, and an either-positive combined strategy was calculated using cerebral angiography as the reference standard. Doppler parameters, clinical features, and IOP were analyzed, and receiver operating characteristic analysis was used to evaluate the ability of the resistive index (RI) to identify elevated IOP (≥ 20 mmHg).

Results: Cerebral angiography confirmed fistulas in 59/67 eyes (88.1%). DUS had a sensitivity of 72.9% (95% CI, 60.4%-82.6%) and specificity of 75.0% (95% CI, 40.9%-92.9%), whereas MRA had a sensitivity of 79.7% (95% CI, 67.7%-88.0%) and specificity of 87.5% (95% CI, 52.9%-97.8%). The combined DUS-or-MRA strategy increased sensitivity to 81.4% (95% CI, 69.6%-89.3%). RI showed limited discrimination for elevated IOP, with an area under the curve of 0.65 (95% CI, 0.46-0.79). At an RI cutoff of 0.62, sensitivity was 46.4% and specificity was 84.2%.

Conclusions: SOV DUS demonstrated moderate diagnostic performance for CCF/cavernous dAVF and may complement MRA in clinical triage. However, a negative DUS finding does not exclude the condition. RI should be interpreted as a supportive Doppler parameter rather than a standalone marker of elevated IOP.

Keywords: Superior ophthalmic vein, Doppler ultrasonography, Carotid-cavernous fistula, Dural arteriovenous fistula, Intraocular pressure

Citation: Apirakkan M, Krisem M, Chanthanaphak E. Diagnostic performance of superior ophthalmic vein Doppler ultrasonography for carotid-cavernous fistula and cavernous sinus dural arteriovenous fistula. *Res Med J.* 20XX;XX(X):e280317. doi:10.33165/rmj.2027.e280317

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Received: 7 February 2026

Revised: 7 July 2026

Accepted: 20 July 2026

Published Online:
11 August 2026



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Introduction

Carotid-cavernous fistula (CCF) and cavernous sinus dural arteriovenous fistula (dAVF) are abnormal arteriovenous shunts that can cause venous hypertension and abnormal

venous drainage. These lesions may present with ocular congestion, diplopia, eye pain, visual impairment, secondary glaucoma, and, in some patients, serious neurologic complications.^{1, 2}

Digital subtraction angiography (DSA) is the reference standard because it demonstrates the shunt point, arterial feeders, and venous drainage pattern and is also used for treatment planning.³ However, angiography is invasive and may not be immediately available. Therefore, noninvasive imaging, including computed tomography (CT) angiography and magnetic resonance angiography (MRA), is commonly used for initial evaluation, although diagnostic performance varies according to flow dynamics and the venous drainage pattern.^{4, 5}

Doppler ultrasonography (DUS) of the superior ophthalmic vein (SOV) is a simple, noninvasive, bedside tool that provides physiological information. Because the SOV drains into the cavernous sinus, cavernous sinus hypertension can result in SOV dilatation, retrograde flow, and an arterialized venous waveform. These Doppler findings have been described in CCF and intracranial dAVF.^{6, 7} Doppler-based hemodynamic assessment has also been used for diagnosis and follow-up after treatment.^{8, 9} Recent reports continue to emphasize orbital color Doppler ultrasound as a noninvasive adjunct for identifying SOV dilatation and arterialized venous pulsation in suspected CCF, while also confirming the role of angiography for definitive diagnosis and treatment planning.^{10, 11}

Patients may present with nonspecific ocular symptoms in clinical practice, and clinicians need a rapid method to support diagnosis and decide which patients should proceed to angiography. Although qualitative Doppler signs are well described, the diagnostic performance of SOV DUS compared with DSA and MRA remains incompletely defined, particularly in patients evaluated at the eye level. In addition, the clinical value of quantitative parameters, such as peak systolic velocity (PSV), end-diastolic velocity (EDV), SOV diameter, and resistive index (RI) remains uncertain.

Therefore, this study aimed to evaluate the diagnostic accuracy of SOV DUS for CCF/cavernous dAVF using cerebral angiography as the reference standard, to compare its performance with MRA and an either-positive combined strategy, and to assess the association between SOV Doppler parameters and clinical findings, with particular attention to elevated intraocular pressure (IOP).

Methods

Study Design and Patient Selection

This retrospective diagnostic accuracy study was conducted at the Department of Diagnostic and Therapeutic Radiology, Ramathibodi Hospital, Mahidol University, Thailand. Eligible diagnostic episodes occurred between August 2011 and May 2019. The clinical cohort included patients aged > 18 years with ocular signs or symptoms suspicious for CCF or cavernous sinus dAVF who underwent SOV DUS and cerebral DSA during the same diagnostic work-up. MRA was reviewed for all included eyes. The study was reported in accordance with the Standards for Reporting of Diagnostic Accuracy (STARD) recommendations.¹²

Eyes were eligible when ocular manifestations led to clinical suspicion of CCF/cavernous dAVF, SOV DUS was performed as part of the diagnostic work-up, and DSA was available for final classification. Eyes were excluded if DSA reports or images were unavailable, if SOV DUS images were insufficient to classify the DUS result, or if prior endovascular or surgical treatment for CCF/dAVF had been performed before the index

DUS/DSA evaluation. Eyes with missing DSA outcomes were excluded; eyes with missing secondary variables were retained for analyses using available data.

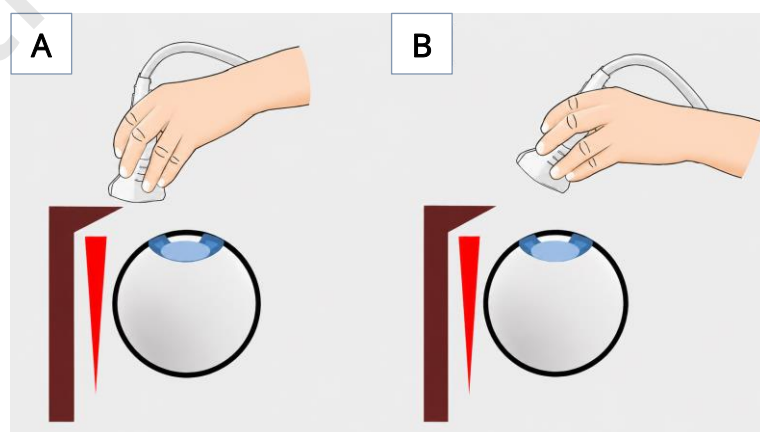
The final dataset included 51 patients (67 eyes). Analyses were performed at the eye level because clinical findings and imaging results were recorded separately for each eye. The potential nonindependence of eyes from the same patient was considered in sensitivity analyses and in the interpretation of the regression findings.

The study was approved by the Institutional Review Board (IRB) of the Faculty of Medicine Ramathibodi Hospital, Mahidol University (MURA2019/36). Medical records and imaging data were retrospectively reviewed after IRB approval and within the approved study period. SOV DUS was performed in the outpatient setting as a noninvasive adjunct clinical assessment during the routine diagnostic work-up. Separate written informed consent for the Doppler examination was not routinely obtained in this clinical setting. All data were analyzed after deidentification.

Assessment of the SOV DUS

SOV DUS was performed using a Philips iU22 scanner (Andover, MA, US) with a high-frequency linear-array transducer at 9 MHz. Patients were examined in the supine position with the eyes closed. Minimal transducer pressure was applied to avoid ocular injury or collapse of the SOV (Figure 1). Gray-scale imaging was used to identify the SOV in the superior-medial orbit, followed by color or power Doppler and spectral Doppler assessment. SOV diameter, flow direction (anterograde or retrograde), waveform pattern (arterialized or nonarterialized), PSV, EDV, and RI were recorded. RI was calculated from spectral Doppler measurements as $(PSV - EDV)/PSV$. When reversed diastolic flow was present, EDV was recorded as a negative value. A DUS result was considered positive for CCF/cavernous dAVF if any of the following were present: SOV dilatation, retrograde SOV flow, or an arterialized pulsatile venous waveform (Figure 2).

Figure 1. Manipulation of the Ultrasound Transducer to Demonstrate the Superior Ophthalmic Vein



A, The high-frequency linear-array transducer is gently placed over the closed upper eyelid with minimal pressure.
B, The transducer is tilted and adjusted to align the ultrasound beam with the superior ophthalmic vein (SOV) in the superomedial orbit.

Figure 2. A 72-Year-Old Woman with Ocular Symptoms Suspicious for Intracranial Arteriovenous Fistulas



A, Color Doppler ultrasonography (DUS) shows dilatation of the right superior ophthalmic vein (SOV) with retrograde flow direction.

B, Spectral DUS shows an arterialized venous waveform with peak systolic velocity (PSV), end-diastolic velocity (EDV), and resistive index (RI) measurements.

Determination of MRA

MRA was reviewed from the clinical imaging study and radiology report. MRA protocols included T1-weighted imaging, T2-weighted imaging, and time-of-flight sequences with multiplanar reconstruction in axial, coronal, and sagittal planes. MRA was considered positive when findings were consistent with CCF/cavernous dAVF, including abnormal early enhancement of the cavernous sinus, abnormal venous drainage, a dilated SOV, or a radiology impression of a fistula.

Combined Diagnostic Strategy

For the combined strategy, the result was considered positive if either SOV DUS or MRA was positive.

Reference Standard

Cerebral DSA served as the reference standard. DSA was performed using a Toshiba Infinix VF-I (Toshiba Medical Systems Corporation, Otawara, Tochigi, Japan) biplane angiography system. Catheterization was performed by the modified Seldinger technique with a 5- or 6-French catheter through common femoral arterial and/or venous approaches. Diagnostic angiography included bilateral external carotid artery, internal carotid artery, and dominant vertebral artery injections at 3 frames per second. Angiography was considered positive if a fistula was demonstrated and negative if no fistula was identified.

Image Review and Interobserver Agreement

Two neurointerventionists independently reviewed DUS, MRA, and angiography and classified each modality as positive or negative. Reviewers were blinded to other clinical information during the independent review. Disagreements were resolved by consensus, and the consensus interpretation was used for analysis. Interobserver agreement was assessed using Cohen κ .¹³

Clinical Data and Outcomes

Demographic data (age, sex), clinical variables (laterality, trauma history, ocular signs and symptoms), and IOP were extracted from medical records. Imaging parameters and angiographic results were recorded per eye. The primary outcome was the diagnostic performance of SOV DUS compared with DSA. Secondary outcomes were the diagnostic performance of MRA and the DUS-or-MRA combined strategy, associations between Doppler parameters and clinical findings, and the ability of RI to identify elevated IOP.

Statistical Analysis

Continuous variables are presented as mean (SD), median, and range. Categorical variables are presented as numbers and percentages. Diagnostic accuracy measures were calculated from 2×2 tables and included sensitivity, specificity, positive predictive value, negative predictive value, and accuracy. Proportions were reported with 95% CIs using the Wilson score interval where appropriate.¹⁴ Receiver operating characteristic (ROC) analysis was used to evaluate RI for identifying elevated IOP (≥ 20 mmHg), including the area under the ROC curve (AUC) and 95% CI.¹⁵

Linear regression was used for continuous outcomes and logistic regression for binary outcomes. Patient-cluster robust standard errors were used in sensitivity analyses for selected regression models to address the potential correlation between 2 eyes from the same patient. Stata version 16.0 (StataCorp LP) was used for statistical analyses. A 2-sided P value $< .05$ was considered statistically significant.

Results

Interobserver Agreement

Interobserver agreement between the 2 neurointerventionists was almost perfect for DUS interpretation ($\kappa = 0.92$) and MRA interpretation ($\kappa = 0.83$), and substantial for cerebral angiography diagnosis ($\kappa = 0.80$).

Baseline Characteristics and Imaging Findings

A total of 51 patients (67 eyes) were included (Table 1). There were 39 women (76.5%) and 12 men (23.5%). The mean (SD) age was 56.4 (18.3) years. A history of trauma was present in 13/67 eyes (19.4%). The mean (SD) IOP was 19.8 (6.2) mmHg (IOP available in 64 eyes).

For SOV DUS, intracranial AVFs were classified as positive in 45/67 eyes (67.2%). Quantitative Doppler parameters were available in 49 eyes: median (range) SOV diameter was 4.1 (1.5-7.3) mm, mean (SD) PSV was 18.5 (3.1-73.9) cm/s, median (range) EDV was 7.1 (0.8-24.5) cm/s, and median (range) RI was 0.5 (0.2-2.1). Waveform characterization was available in 55 eyes, with an arterialized waveform in 46/55 eyes (83.6%). Flow direction was available in 51 eyes, with retrograde flow in 45/51 eyes (88.2%).

Cerebral angiography confirmed intracranial AVFs in 59/67 eyes (88.1%). MRA demonstrated findings consistent with intracranial AVFs in 48/67 eyes (71.6%).

Diagnostic Performance of DUS and MRA

Among 67 eyes, the diagnostic performance of SOV DUS, MRA, and the combined DUS-or-MRA strategy was determined (Table 2). For DUS, the sensitivity was 72.9% (95% CI, 60.4%-82.6%) and specificity was 75.0% (95% CI, 40.9%-92.9%). For MRA, the sensitivity was

79.7% (95% CI, 67.7%-88.0%) and specificity was 87.5% (95% CI, 52.9%-97.8%). The combined DUS-or-MRA strategy yielded a sensitivity of 81.4% (95% CI, 69.6%-89.3%) and specificity of 75.0% (95% CI, 40.9%-92.9%).

Associations Between Doppler Parameters and Clinical Features

SOV diameter on ultrasound was positively associated with a history of trauma and negatively associated with eye pain (Table 3). These findings remained similar in the sensitivity analysis using patient-cluster robust standard errors. In the cluster-robust model, the coefficient for eye pain was -1.32 mm (95% CI, -2.10 to -0.54; $P = .002$), and the coefficient for trauma history was 1.07 mm (95% CI, 0.11-2.02; $P = .031$).

RI and Identification of Elevated IOP

RI showed limited discrimination for elevated IOP (≥ 20 mmHg). The AUC was 0.65 (95% CI, 0.46-0.79) (Figure 3). Using an RI cutoff of 0.62, sensitivity was 46.4% and specificity was 84.2% (Table 4). Combined rules using RI with clinical signs or SOV diameter increased sensitivity in some scenarios but reduced specificity. The rule of $RI \geq 0.62$ or SOV diameter ≥ 5.2 mm produced a sensitivity of 71.4% and specificity of 83.3% in 46 eyes with available data.

Table 1. Demographics, Clinical Features, and Imaging Findings

Variable	No./Total No. (%)
Patients, No.	51
Eyes, No.	67
Female, No. (%)	39 (76.5)
Age, mean (SD) [range], y	56.4 (18.3) [22-88]
Intraocular pressure, mean (SD) (range), mmHg (n = 64)	19.8 (6.2) [8-37]
Trauma history	13/67 (19.4)
Clinical signs and symptoms (eye-level)	
Exophthalmos	42/67 (62.7)
Chemosis	15/67 (22.4)
Orbital bruit	17/67 (25.4)
Diplopia	33/67 (49.3)
Eye pain	14/67 (20.9)
Headache	11/67 (16.4)
Episcleral vein dilatation	37/67 (55.2)
Visual impairment	28/67 (41.8)
Alteration of consciousness	1/67 (1.5)
Imaging findings (eye-level)	
DUS positive (SOV Doppler)	45/67 (67.2)
SOV diameter on DUS, mean (SD), mm (n = 49)	4.1 (1.4)
Arterialized waveform	46/55 (83.6)
Retrograde SOV flow	45/51 (88.2)
PSV, median (range), cm/s (n = 49)	18.5 (3.1-73.9)
EDV, median (range), cm/s (n = 49)	7.1 (0.8-24.5)
RI, median (range), (n = 49)*	0.5 (0.2-2.1)

Table 1. Demographics, Clinical Features, and Imaging Findings (Continued)

Variable	No./Total No. (%)
MRA positive	48/67 (71.6)
Cerebral angiography positive	59/67 (88.1)
SOV diameter on angiography, mean (SD) [range], mm (n = 54)	3.2 (1.2) [1.4-6.0]
Fistula size (angiography)	
Small	44/54 (81.5)
Large	10/54 (18.5)

Abbreviations: DUS, Doppler ultrasonography; EDV, end-diastolic velocity; MRA, magnetic resonance angiography; PSV, peak systolic velocity; RI, resistive index; SOV, superior ophthalmic vein.

* Resistive index (RI) values greater than 1.0 reflect reversed diastolic flow.

Table 2. Diagnostic Performance Using Cerebral Angiography as the Reference Standard

Test	True Positive	False Positive	False Negative	True Negative	Sensitivity (95% CI)	Specificity (95% CI)	Positive Predictive Value	Negative Predictive Value	Accuracy (95% CI)
DUS	43	2	16	6	72.9 (60.4-82.6)	75.0 (40.9-92.9)	95.6	27.3	73.1 (61.5-82.3)
MRA	47	1	12	7	79.7 (67.7-88.0)	87.5 (52.9-97.8)	97.9	36.8	80.6 (69.6-88.3)
DUS or MRA	48	2	11	6	81.4 (69.6-89.3)	75.0 (40.9-92.9)	96.0	35.3	80.6 (69.6-88.3)

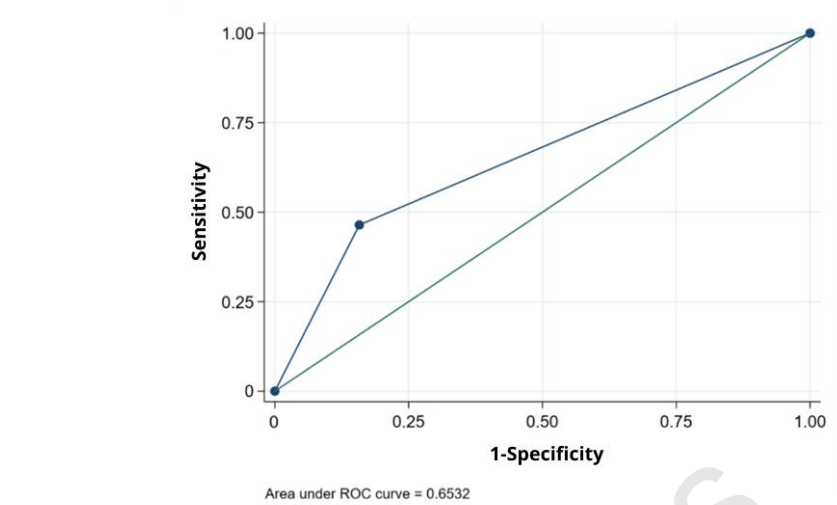
Abbreviations: DUS, Doppler ultrasonography; MRA, magnetic resonance angiography;

Table 3. Linear Regression of Factors Associated With the Superior Ophthalmic Vein Diameter on Ultrasound and Intraocular Pressure

Outcome	Predictor	Univariate (95% CI)	P Value	Multivariate (95% CI)	P Value
SOV diameter, mm	Trauma history (yes vs no)	0.98 (0.06 to 1.91)	.038	1.07 (0.21 to 1.92)	.016
SOV diameter, mm	Eye pain (yes vs no)	-1.25 (-2.15 to -0.35)	.007	-1.32 (-2.17 to -0.46)	.003
IOP, mmHg	Orbital bruit (present vs absent)	-3.77 (-7.16 to -0.38)	.030	-2.87 (-6.45 to 0.71)	.115
IOP, mmHg	Episcleral vein dilatation (present vs absent)	3.23 (0.19 to 6.27)	.038	2.34 (-0.86 to 5.54)	.149

Abbreviations: IOP, intraocular pressure; SOV, superior ophthalmic vein.

Figure 3. Receiver Operating Characteristic Analysis



Abbreviation: ROC, receiver operating characteristic.

Table 4. Resistive Index-Based Criteria for Identifying Elevated Intraocular Pressure (≥ 20 mmHg)

Rule (Positive If)	No.	True Positive	False Positive	False Negative	True Negative	Sensitivity	Specificity
RI ≥ 0.62	47	13	3	15	16	46.4	84.2
RI ≥ 0.62 or chemosis	47	17	6	11	13	60.7	68.4
RI ≥ 0.62 or diplopia	47	23	12	5	7	82.1	36.8
RI ≥ 0.62 or eye pain	47	14	8	14	11	50.0	57.9
RI ≥ 0.62 and chemosis	47	5	0	23	19	17.9	100.0
RI ≥ 0.62 and eye pain	47	5	0	23	19	17.9	100.0
RI ≥ 0.62 or SOV diameter ≥ 5.2 mm	46	20	3	8	15	71.4	83.3

Abbreviations: RI, resistive index; SOV, superior ophthalmic vein.

Discussion

In this retrospective diagnostic accuracy study of 51 patients (67 eyes) evaluated for suspected CCF/cavernous sinus dAVF, SOV DUS showed moderate diagnostic performance when compared with cerebral angiography. MRA had higher specificity and overall accuracy than DUS. The combined DUS-or-MRA strategy increased sensitivity, supporting its potential role as a practical triage approach when the clinical goal is to reduce the risk of missing a fistula before proceeding to DSA.

The diagnostic value of SOV DUS is biologically plausible because CCF/cavernous dAVF can transmit arterialized pressure into the cavernous sinus and orbital venous drainage pathways. Prior Doppler reports demonstrated that affected eyes may show SOV dilatation, retrograde flow, and arterialized venous waveforms.^{6,7} These Doppler findings can also change after treatment.^{8,9} However, most previous studies focused on descriptive Doppler findings or follow-up, whereas the present study directly estimated diagnostic performance against cerebral angiography at the eye level.

The sensitivity of DUS in this study was lower than that reported in some earlier Doppler descriptions. Several factors may explain this finding. First, this was a referral cohort with high clinical suspicion and high disease prevalence, which may have enriched the dataset with complex or chronic fistulas. Second, indirect cavernous sinus dAVFs may have lower-flow or variable drainage patterns, reducing the conspicuity of SOV Doppler abnormalities. Third, DUS is operator dependent, and SOV visualization can be affected by orbital anatomy, transducer pressure, venous thrombosis, and drainage through alternative venous pathways. Therefore, a negative DUS finding should not be used to rule out CCF/cavernous dAVF when clinical suspicion remains high.

Interpretation of SOV findings should also consider that SOV dilatation is not specific to CCF/cavernous dAVF and may occur in several orbital and cranial venous conditions.¹⁶ Angiographic assessment remains the standard for pretreatment planning.¹⁷ Registry-level data have shown that dAVF epidemiology and drainage patterns vary by population and fistula site.¹⁸ Quantitative Doppler indices outside the SOV, such as external carotid artery RI, have also been explored for cavernous sinus dAVF assessment.¹⁹ CT angiography-based screening studies further support the role of noninvasive vascular imaging in selected suspected dAVF populations.²⁰

Clinical series and reviews also highlight the heterogeneity of dAVF/CCF presentation, imaging findings, and outcomes.²¹⁻²³ The classic Barrow classification and later clinical-imaging correlations emphasize that shunt type and venous drainage determine ocular manifestations.^{24, 25} Imaging reviews of dural/direct cavernous fistulae and CT angiographic venous findings provide additional context for interpreting noninvasive imaging signs.^{26, 27}

MRA showed higher specificity and accuracy than DUS, which is expected because MRA can depict indirect signs of a fistula, including cavernous sinus enlargement, early venous enhancement, dilated venous drainage, and associated intracranial vascular abnormalities. Nevertheless, MRA may not be immediately available in all outpatient or emergency settings. SOV DUS is inexpensive, noninvasive, repeatable, and can be performed in ophthalmology clinics, emergency departments, or radiology units as an adjunct to clinical examination. In this context, DUS is best considered a supportive screening or triage tool rather than a definitive test.

The combined DUS-or-MRA strategy is clinically relevant because it improved sensitivity compared with DUS alone and may help identify patients who should undergo angiography. This approach could be useful when ocular findings are concerning but initial imaging is equivocal. However, the combined strategy did not improve specificity, and a positive screening result still requires clinical correlation and, when appropriate, cerebral angiography for definitive diagnosis and treatment planning. Its cost-effectiveness and ability to reduce unnecessary angiography should be evaluated prospectively.

RI showed limited discrimination for elevated IOP. The AUC confidence interval was wide and included values close to those of nondiscrimination, and sensitivity at the selected cutoff was low. Therefore, RI should not be interpreted as a stand-alone marker of elevated IOP. Rather, RI may be used as one supportive parameter together with waveform morphology, SOV diameter, ocular signs, and direct ophthalmologic assessment. RI values also depend on the direction and morphology of diastolic flow, so interpretation should consider the underlying waveform pattern and venous outflow status.

This study has several strengths. It used cerebral angiography as the reference standard, included both DUS and MRA comparisons, evaluated eye-level clinical and imaging findings, and demonstrated high interobserver agreement for imaging interpretation. The study also

examined quantitative Doppler parameters and their relationship with ocular findings, which may be relevant for clinical triage and follow-up. In addition, because it is noninvasive and repeatable, SOV DUS may also be useful for follow-up after embolization when serial assessment of SOV flow and waveform is clinically needed.

This study also has limitations. The retrospective design may introduce selection and verification bias because angiography was performed mainly in clinically suspicious cases. The number of angiography-negative eyes was small, resulting in wide confidence intervals for specificity. Quantitative Doppler variables were not available in all eyes. DUS is operator dependent, and the study was conducted at a single tertiary center, which may limit generalizability. Finally, analyses were performed at the eye level, and eyes from the same patient may not be fully independent. Sensitivity analyses using patient-cluster robust standard errors showed similar conclusions for the main regression findings, but the modest sample size limited more complex mixed-effects modeling.

Conclusions

SOV DUS demonstrated moderate diagnostic performance for CCF/cavernous dAVF and may complement MRA in clinical triage. However, a negative DUS finding does not exclude the disease. RI showed limited discrimination for elevated IOP and should be interpreted as a supportive Doppler parameter together with clinical and imaging findings.

Additional Information

Ethics Approval: The study was approved by the Institutional Review Board of the Faculty of Medicine Ramathibodi Hospital, Mahidol University, Thailand (MURA2019/36 on 24 January 2019).

Clinical Trial Consideration: This study does not report on a clinical trial.

Financial Support: No specific funding was received for this study.

Conflict of Interest: The authors declare no conflict of interest.

Declaration of AI Assistance: Grammarly was used for language editing, grammar checking, spelling correction, and clarity improvement during manuscript revision. The authors reviewed and verified all edited content and take full responsibility for the accuracy, validity, and integrity of the final manuscript.

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