THE WARREN ALPERT
Medical School
BROWN UNIVERSITY

Rhode Island STROKE SYMPOSIUM

Updates on the Evaluation and Management of Dural Arteriovenous Fistulae

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DISCLOSURE

Please list one:

- I have the following financial relationships to disclose: Consultant with CERENOVUS
- This lecture will include discussion of liquid embolic agents for cerebral dAVF obliteration (off-label use); only on-label use for AVMs.

What is a dural arteriovenous fistula?

Acquired direct abnormal connection between an artery and venous sinus or vein

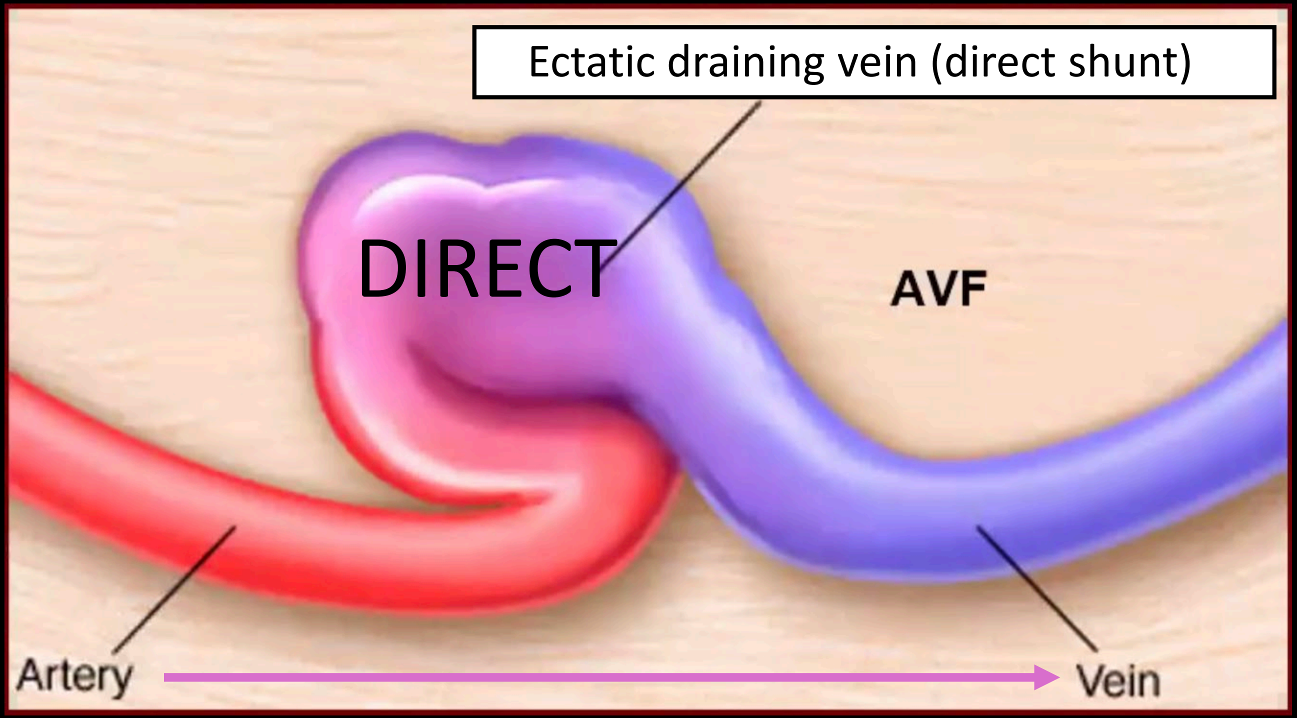
Abnormal connection (fistula) located within the dural leaflets

What is a dural arteriovenous fistula?

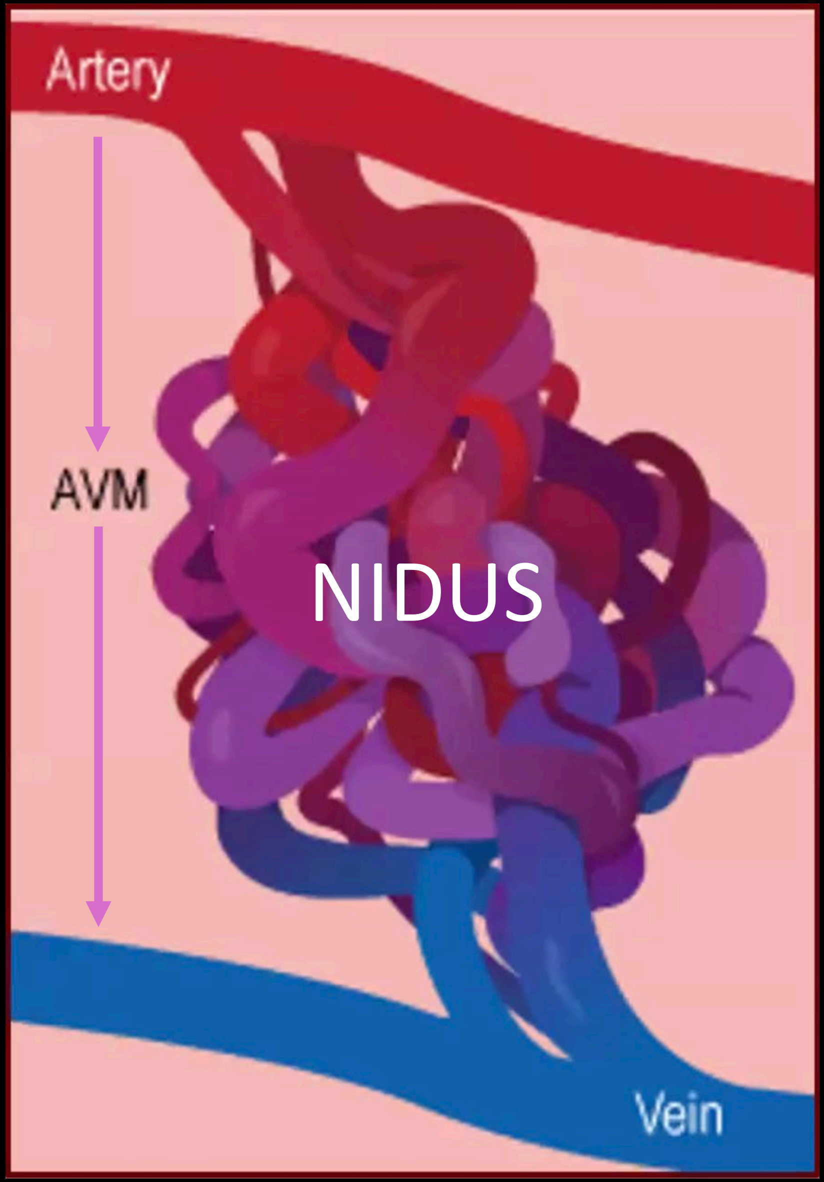
It’s NOT an arteriovenous malformation (AVM)

No nidus – dAVFs have a direct connection

Acquired – most AVMs are congenital



Dural arteriovenous fistula (dAVF)



Arteriovenous malformation (AVM)

Types of dural fistulae

<u>CNS AV Fistulae</u>

Pial AVF

- Idiopathic or acquired
- Congenital (pediatrics)
- HHT + Klippel-Trenaunay-Weber syndrome

Dural AVF

- Usually acquired
- Classified by drainage pattern
- Borden or Cognard classification

Spinal AVF

- Acquired
- Dural or epidural
- Mostly Type 1 (direct, single-hole)

Carotid-Cavernous Fistula

- Acquired
- Direct (A) or Indirect (B-D)
- Barrow classification

Pediatric AVFs

- Congenital
- VOG malformations
- Dural sinus malformations (jugular bulb or giant dural lakes)
- Infantile-type dAVFs (multifocal)
- Adult-type dAVFS

Types of dural fistulae

<u>CNS AV Fistulae</u>

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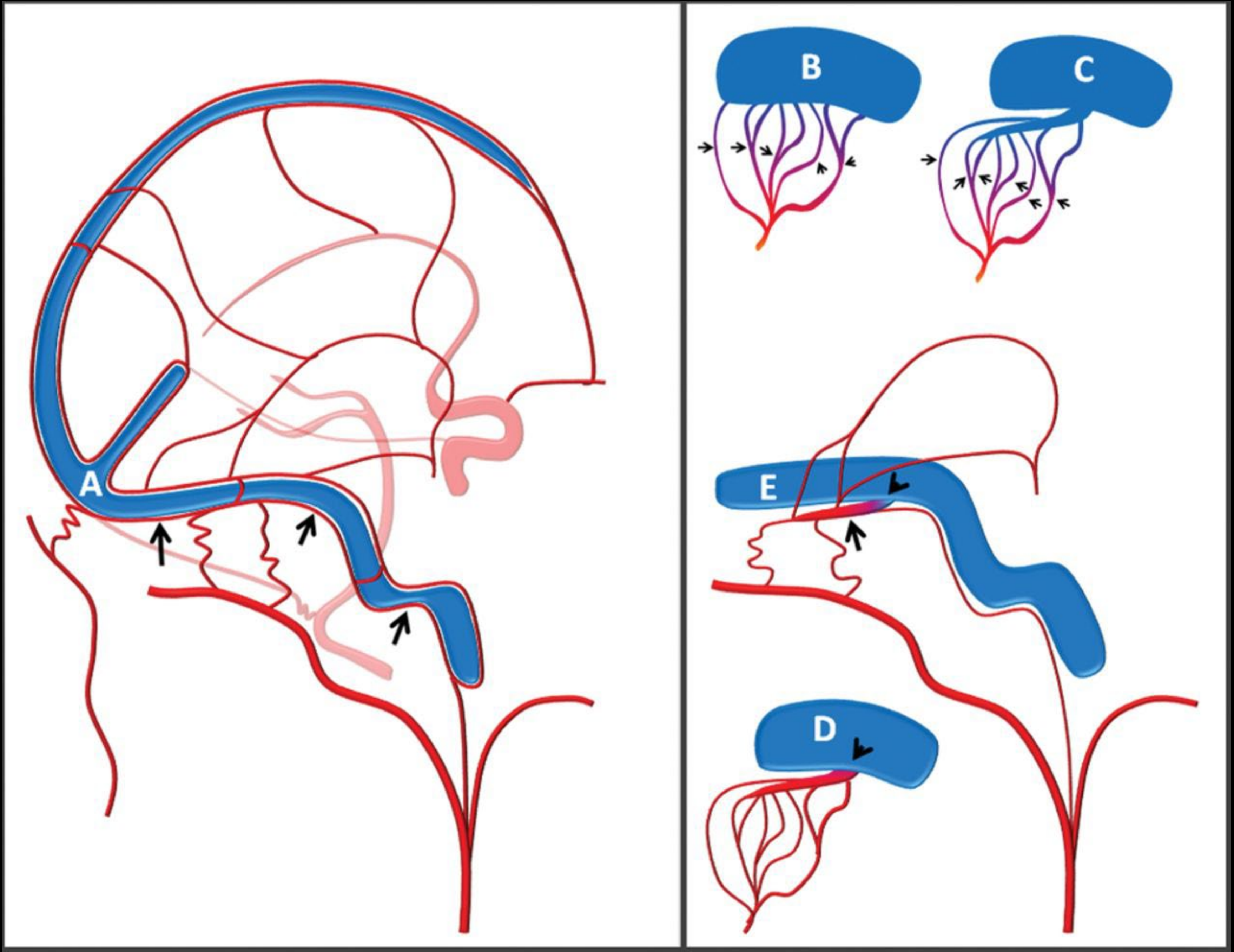
~~Carotid-Cavernous Fistula~~

- Acquired
- Direct (A) or Indirect (B-D)
- Barrow classification

~~Pediatric AVFs~~

- Congenital
- VOG malformations
- Dural sinus malformations (jugular bulb or giant dural lakes)
- Infantile-type dAVFs (slow flow)
- Adult-type dAVFS



Shapiro, M., Raz, E., Litao, M., et al. (2018) Toward a Better Understanding of Dural Arteriovenous Fistula Angioarchitecture. *AJNR* 39(9) 1682-1688.

Anatomic dAVF classification schema

Risks depend on presence of cortical venous drainage and ectasia

Venous hypertension leads to risk of ICH or non-hemorrhagic neurologic deficits (NHND)

Anatomic dAVF classification schema

Low-grade (-CVD) dAVFs:

All risks (hemorrhage, death, NHND) = <1%/yr

Risk of progression to high-grade = 0.8-2% overall

Ghandi, D., Chen, J., Pearl, M., et al. (2012) Intracranial Dural Arteriovenous Fistulas: Classification, Imaging Findings, and Treatment. *AJNR* 33(6) 1007-1013.
Satomi J, van Dijk JMC, Terbrugge KG, et al. (2002) Benign cranial dural arteriovenous fistulas: outcome of conservative management based on the natural history of the lesion. J Neurosurg 97:767–70.
Reynolds, M., Lanzino, G., Zipfel, G.J. (2017) Intracranial Dural Arteriovenous Fistulae. Stroke 48:1424-1431

Anatomic dAVF classification schema

High-grade (+CVD) dAVFs:

Hemorrhage risk = ~8.1%/yr

Mortality risk = ~10.4%/yr

NHND risk = ~6.9%/yr

Ghandi, D., Chen, J., Pearl, M., et al. (2012) Intracranial Dural Arteriovenous Fistulas: Classification, Imaging Findings, and Treatment. *AJNR* 33(6) 1007-1013.

Anatomic dAVF classification schema

	Cognard Grade	Venous Drainage	Flow Pattern	Cortical Venous Reflux	Cortical Venous Ectasia	ICH Risk	Mortality Risk	NHND Risk
Benign	I	Sinus	Antegrade	No	No	<1%/yr		
	IIa	Sinus	Retrograde	No	No			
Aggressive	IIb	Sinus	Antegrade	Yes	No	8.1%/yr	10.4%/yr	6.9%/yr
	III	Cortical	Antegrade	Yes	No			
	IV	Cortical	Antegrade	Yes	Yes			
	V	Perimedullary	Retrograde	Yes	Yes			

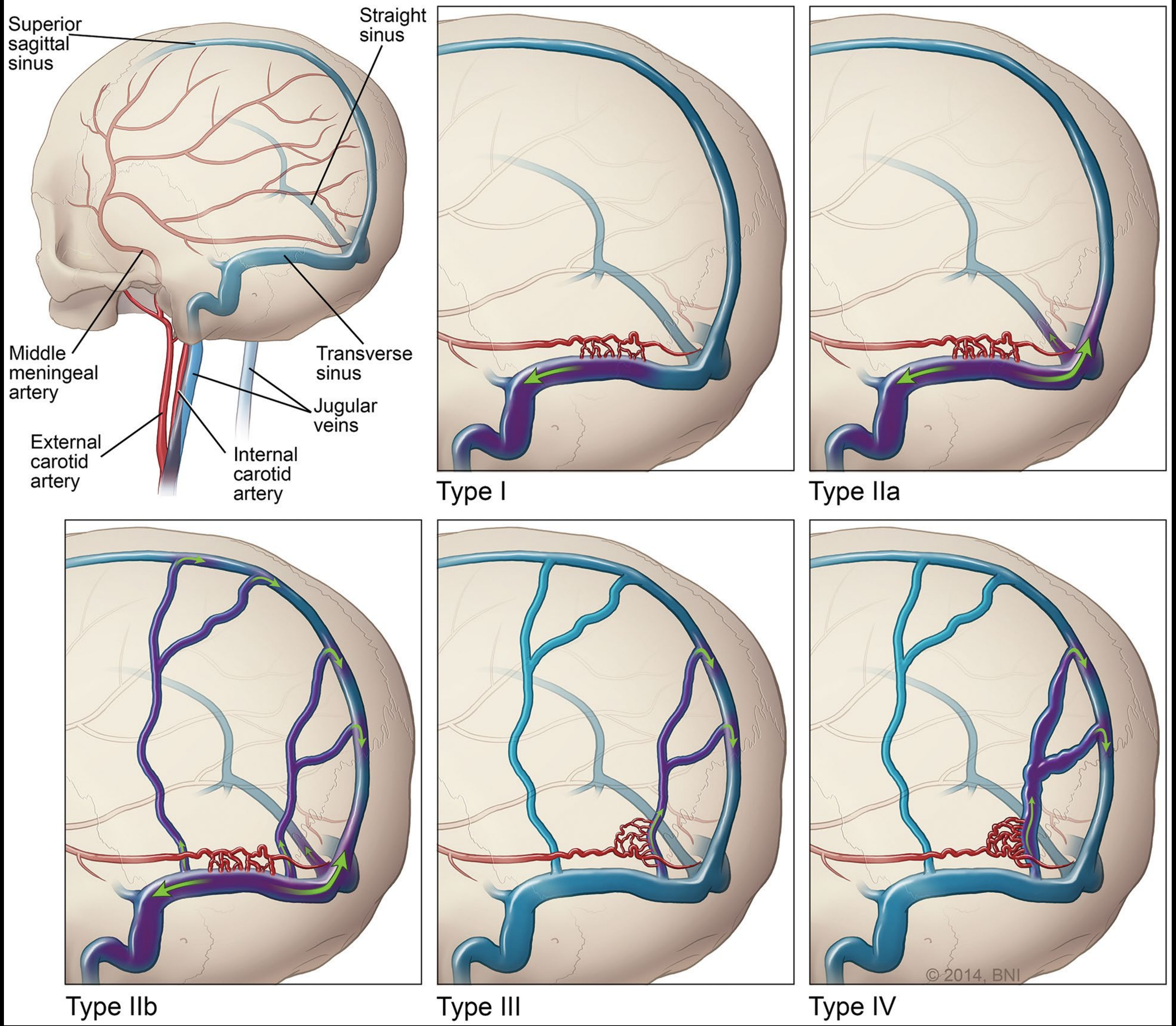
Reynolds, M., Lanzino, G., Zipfel, G.J. (2017) Intracranial Dural Arteriovenous Fistulae. *Stroke* 48:1424-1431; Cognard, C., Gobin, Y.P., Pierot, L., et al. (1995) *Radiology*. 194:671-680.

Anatomic dAVF classification schema

	Borden Grade	Cognard Grade	Venous Drainage	Flow Pattern	Cortical Venous Reflux	Cortical Venous Ectasia	ICH Risk	Mortality Risk	NHND Risk
Benign	I	I	Sinus	Antegrade	No	No	<1%/yr		
	I	IIa	Sinus	Retrograde	No	No			
Aggressive	II	IIb	Sinus	Antegrade	Yes	No	8.1%/yr	10.4%/yr	6.9%/yr
	III	III	Cortical	Antegrade	Yes	No			
	III	IV	Cortical	Antegrade	Yes	Yes			
	III	V	Perimedullary	Retrograde	Yes	Yes			

Reynolds, M., Lanzino, G., Zipfel, G.J. (2017) Intracranial Dural Arteriovenous Fistulae. *Stroke* 48:1424-1431; Cognard, C., Gobin, Y.P., Pierot, L., et al. (1995) *Radiology*. 194:671-680.

Cortical veins are the key!


Superior
sagittal
sinus
Straight
sinus
Middle
meningeal
artery
Transverse
sinus
Jugular
veins
External
carotid
artery
Internal
carotid
artery
Type I
Type IIa
Type IIb
Type III
Type IV
© 2014, BNI

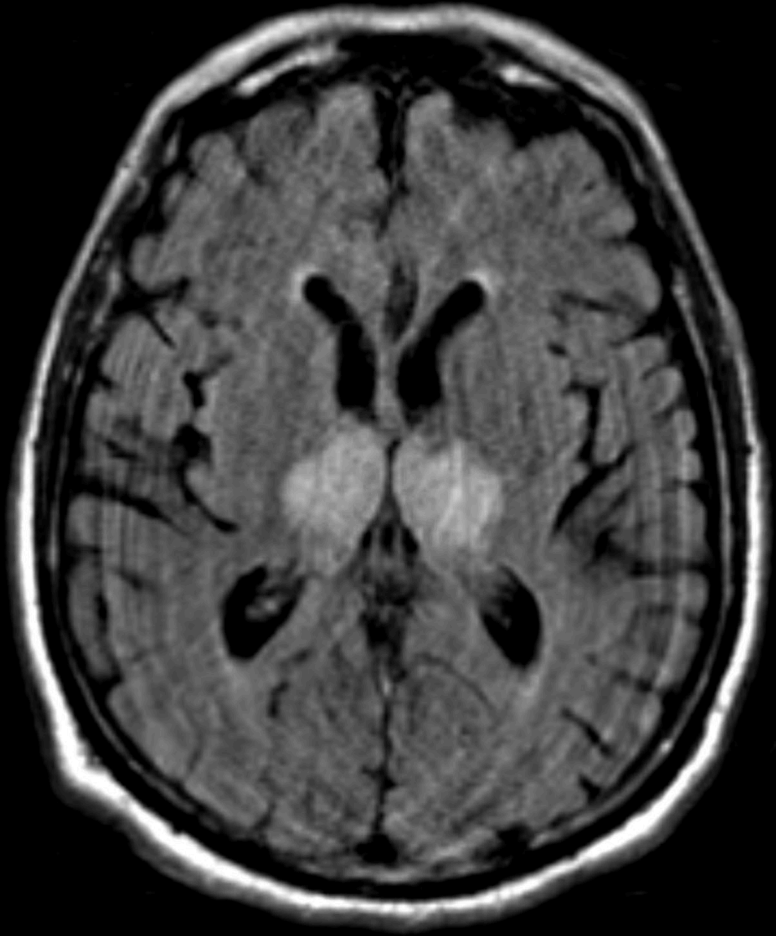
Epidemiology of dural fistulae

- Rare lesions (10-15% of all vascular malformations)
  - Limited incidence estimates; 0.15-0.29 per 100,000 person-yrs
- Typically present in middle age (50-60s)
- No sex predilection
- No strong direct genetic association
  - Indirect association with hereditary thrombophilias (Factor V Leiden, Protein C/S deficiency, etc.)

Murai, S., Hiramatsu, M., Suzuki, E., et al. (2021) Trends in Incidence of Intracranial and Spinal Arteriovenous Shunts. *Stroke* 52(4): 1455-1459.

Epidemiology of dural fistulae

- Presenting symptoms/syndromes:
  - Asymptomatic/incidental
  - Headache
  - Pulsatile tinnitus
  - Seizure
  - Cranial neuropathy
  - Ophthalmologic phenomena (palsy, proptosis,
  - Myelopathy
  - Intracranial hypertension
  - Early/rapid dementia (thalamic/cortical)
  - Focal neurologic deficits
  - Intracranial hemorrhage (12-18%)



Pathogenesis of dural fistulae

- Poorly understood
- Associations with trauma, thrombosis, prior surgery, and infection
- Suggestive of venous injury/thrombosis initiating a maladaptive angiogenic cascade
- Angiogenic factors enlarging pre-existing small physiological shunts or spurring neoangiogenesis
- Cortical reflux or direct cortical venous drainage results in venous hypertension and impaired venous drainage

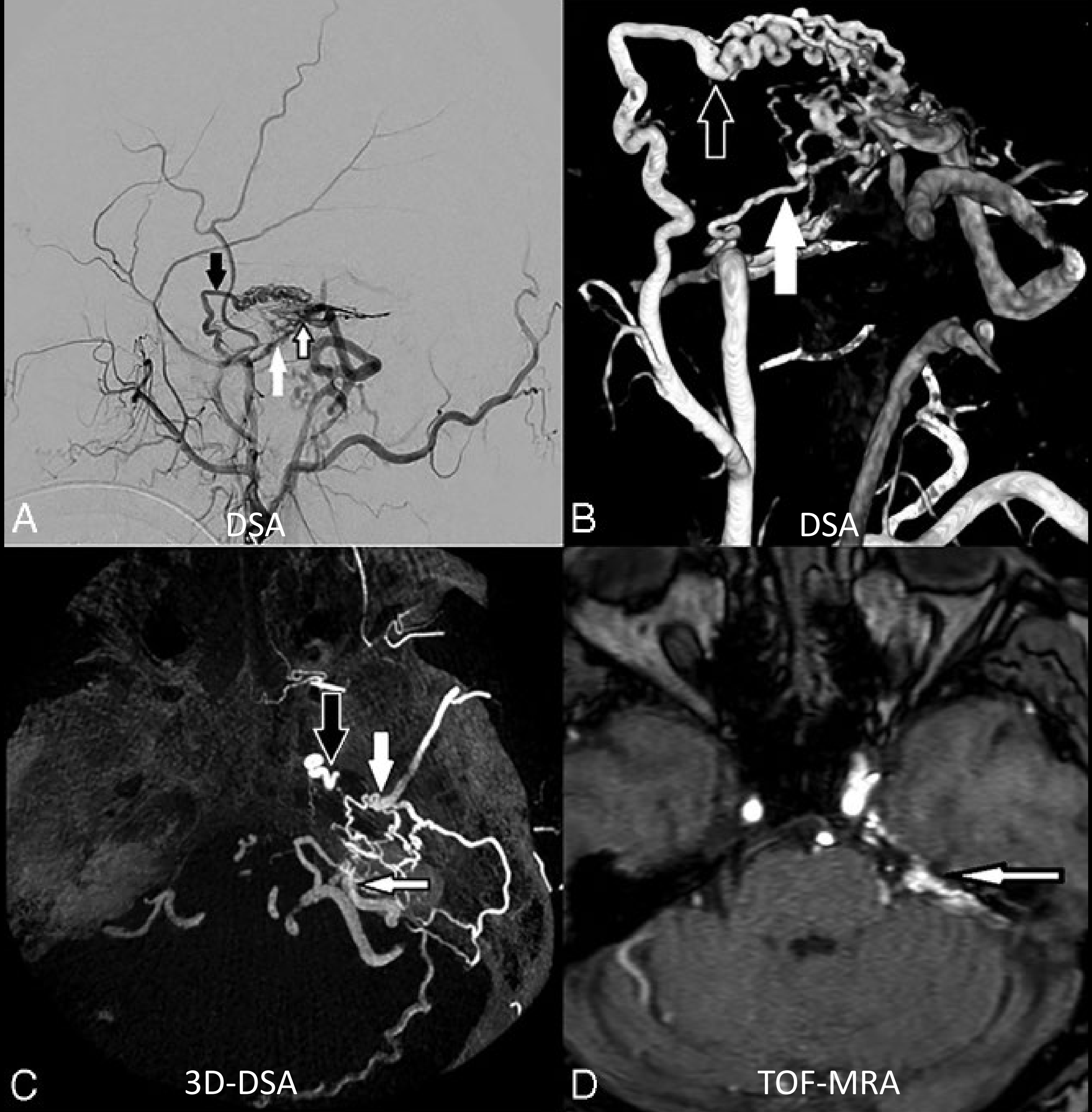
Imaging of dAVFs

- May be difficult to detect on structural imaging
- Noncontrast CT:
  - Sensitive to edema (due to venous hypertension) or hemorrhage
- Structural MRI:
  - **T2/FLAIR** sensitive to edema (due to venous hypertension)
  - **T2 flow voids**:
    - CVR/CVH in high-grade fistula = tortuous/dilated veins.
    - Loss of normal sinus flow voids when associated with thrombosis
  - **SWI**: Venous hyperintensity due to shunting with low deoxyhemoglobin concentration
  - **C+ SPGR**:
    - Deep parenchymal enhancement due to medullary venous engorgement
    - Dilated enhancing veins
- **ASL**: Arterial spin labeling
  - Non-contrast T1 labeling of blood-water protons (reflecting cerebral blood flow)
  - Normal ASL signal absent in cerebral veins due to T1 decay during capillary transit
  - ASL signal in cortical veins or dural sinuses is highly sensitive (94%) for shunting

Amukotuwa, S.A, Marks, M.P., Zaharchuk, G., et al. (2018) Arterial Spin-Labeling Improves Detection of Intracranial Dural Arteriovenous Fistulas with MRI. *AJNR* 39(4): 669-677.

Imaging of dAVFs

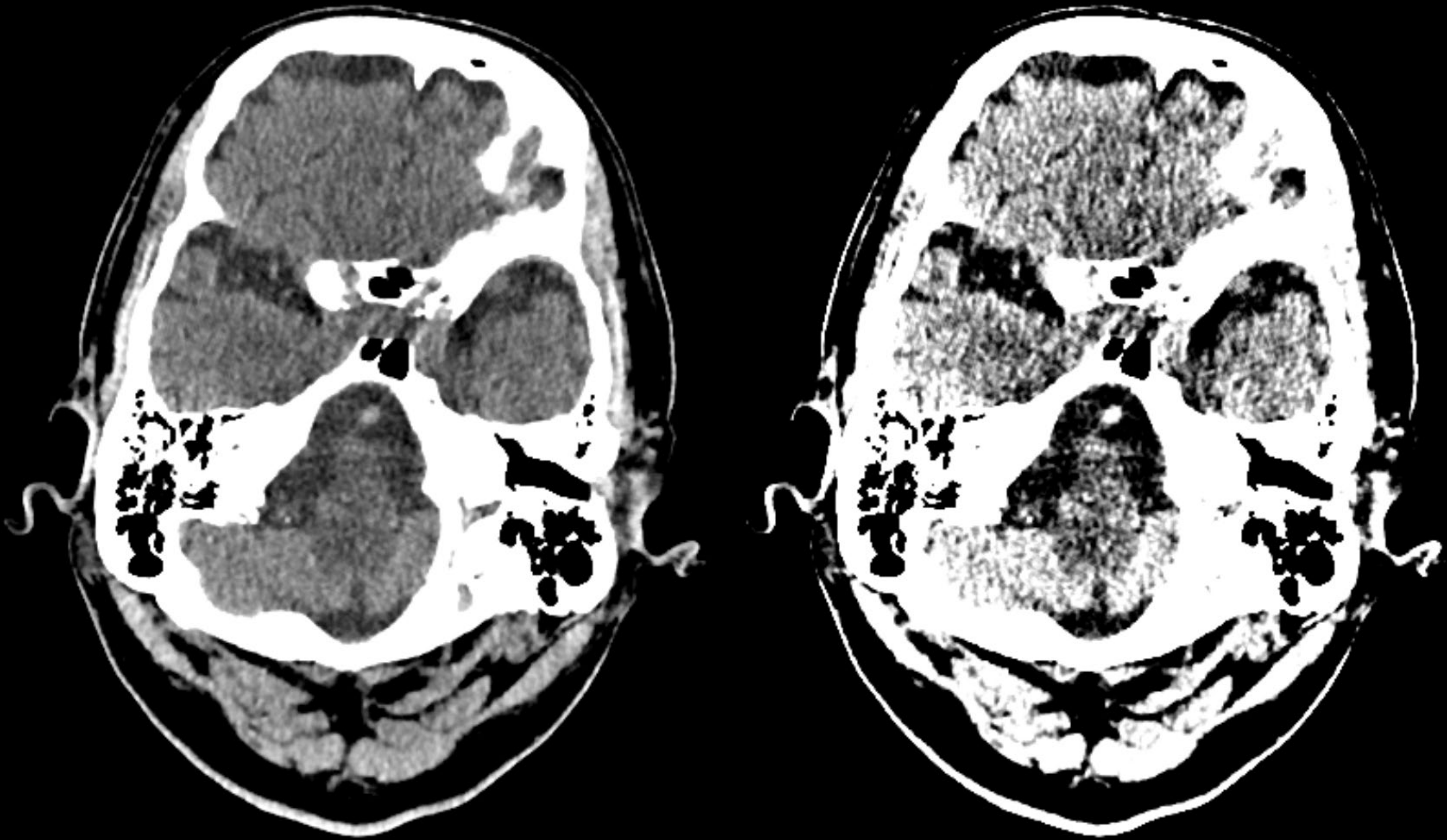
- Vessel imaging:
  - **CTA**:
    - Sensitive for detecting abnormally enlarged cortical veins or dilated feeding arteries, but insensitive for dural sinus involvement.
    - Extremely dependent on bolus timing
      - Early arterial phase CTA may fail to demonstrate shunting
      - Venous phase CTA will opacify all normal veins, making differentiation of the shunting vein difficult
  - **TOF-MRA**:
    - Highly sensitive to flow-related enhancement present in a vein
      - Suppression of caudally directed venous outflow allows for detection of venous opacification
  - **CE-MRA**:
    - Less sensitive than CTA due to tendency to be more delayed
    - May show dilated/tortuous veins well (like +C SPGR)
    - Time-resolved may demonstrate early venous opacification

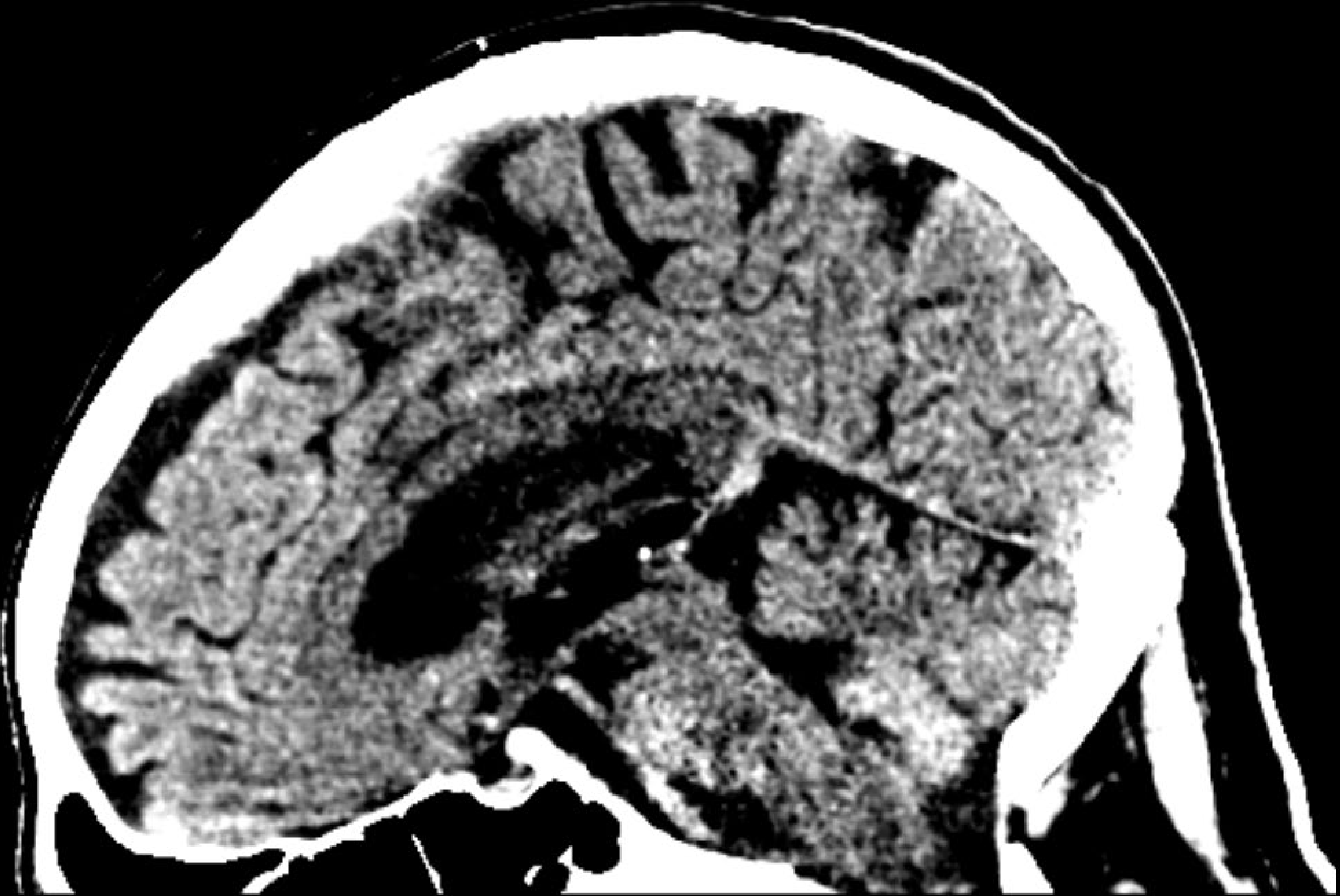


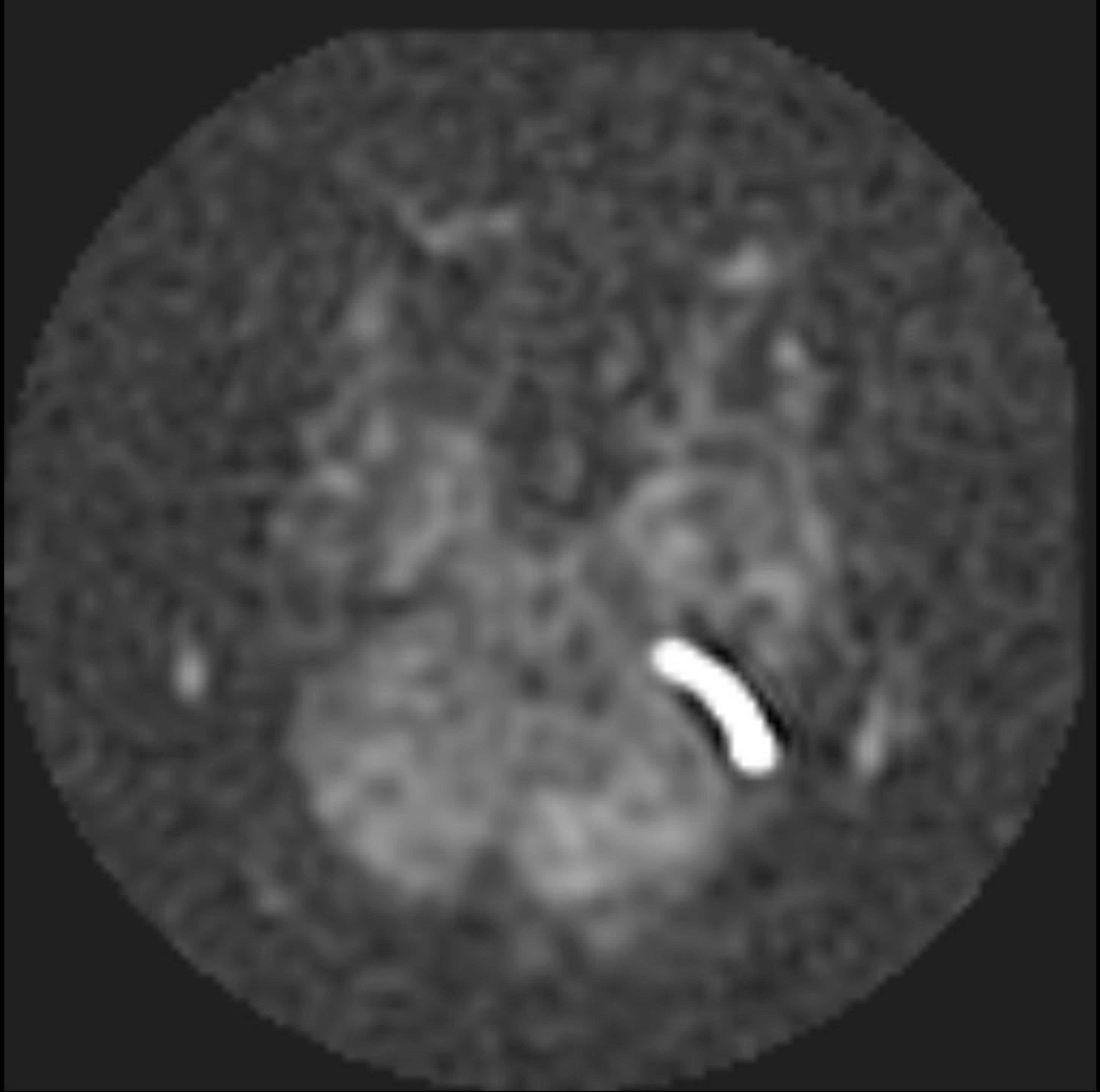
Bhatia, K.D., Lee, H., Kortman, H., et al. (2022). Endovascular Management of Intracranial Dural AVFs: Principles. *AJNR* 43(2): 160-166.

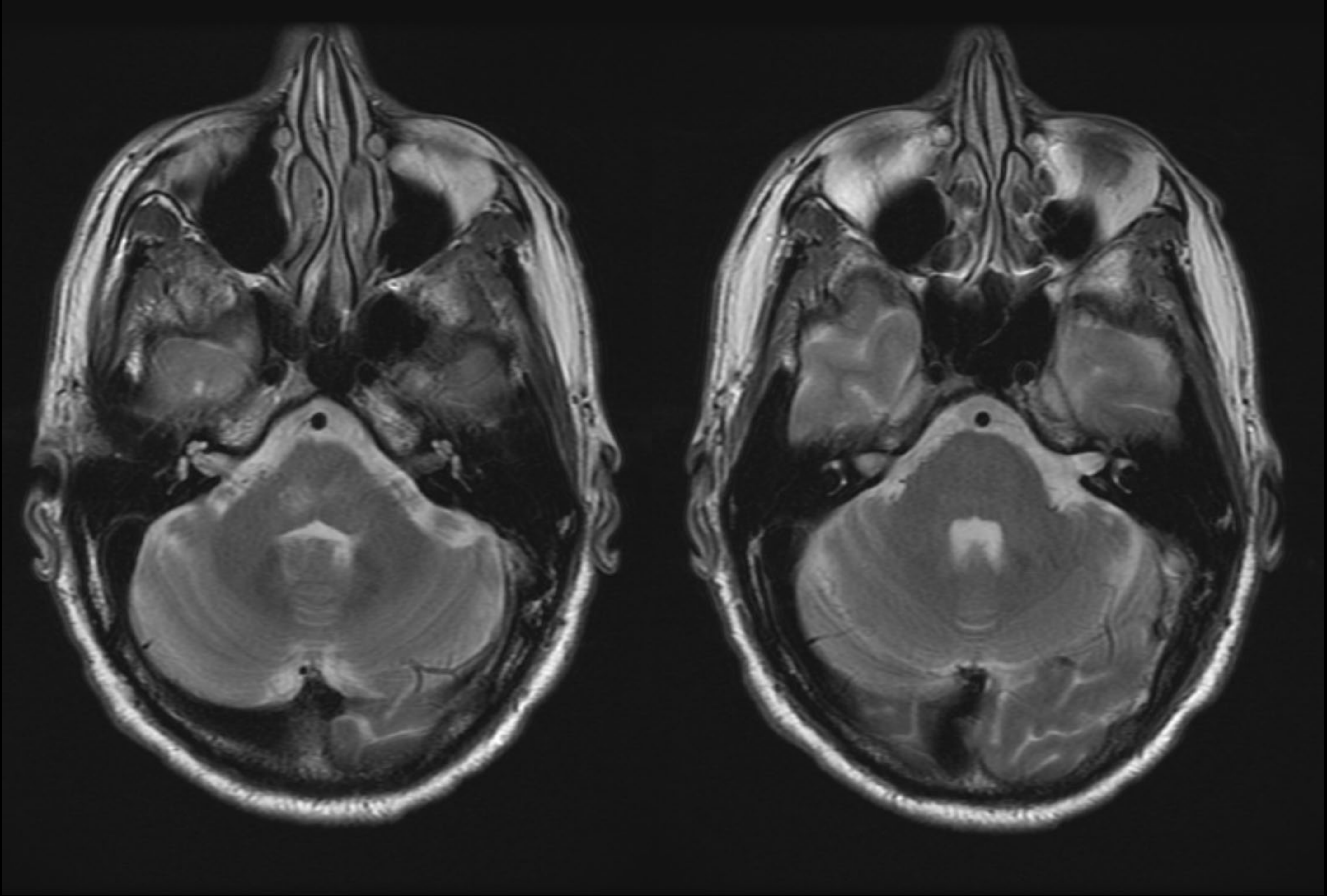
Example:

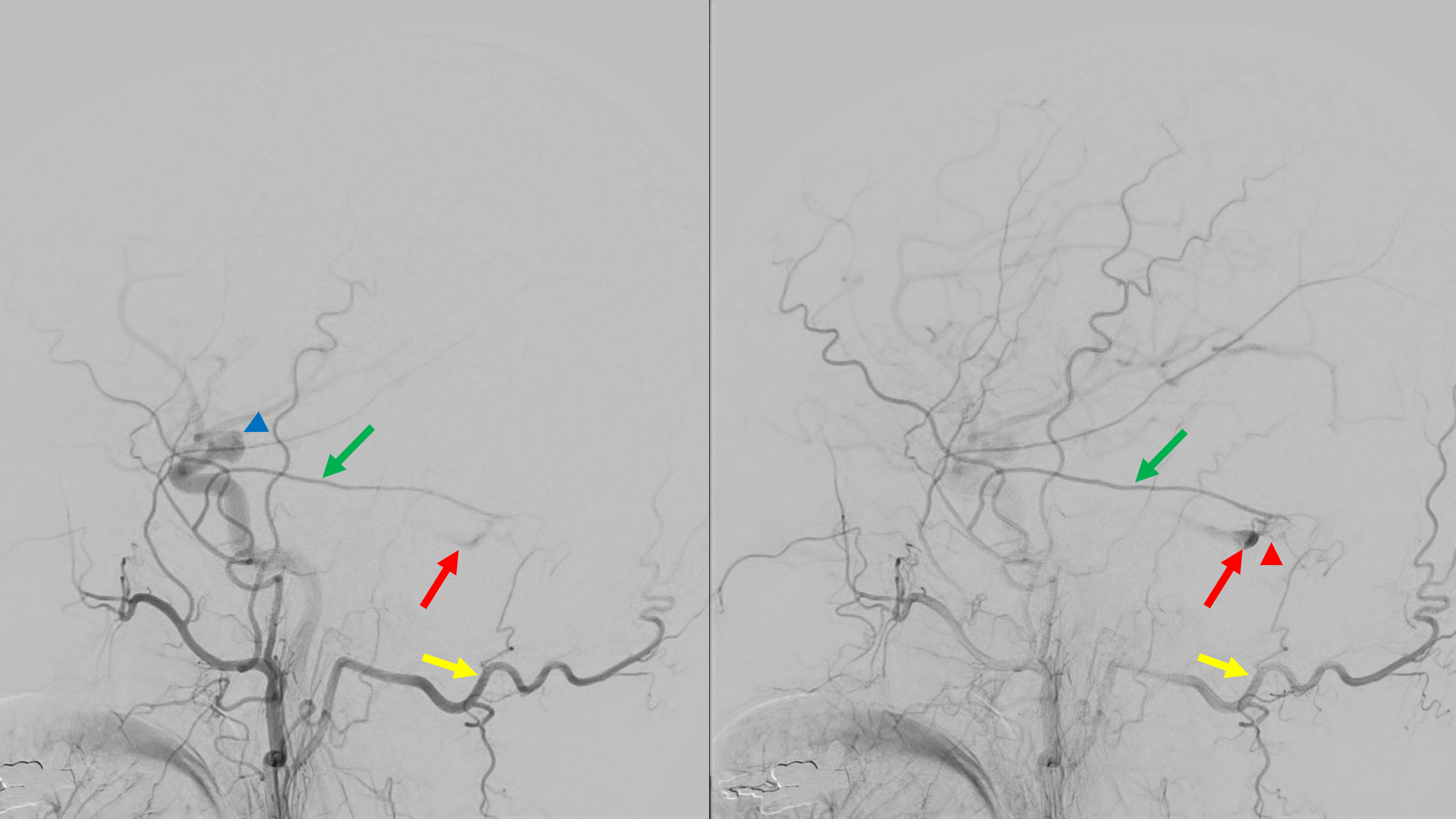
Bilateral upper and lower extremity weakness, altered mental status

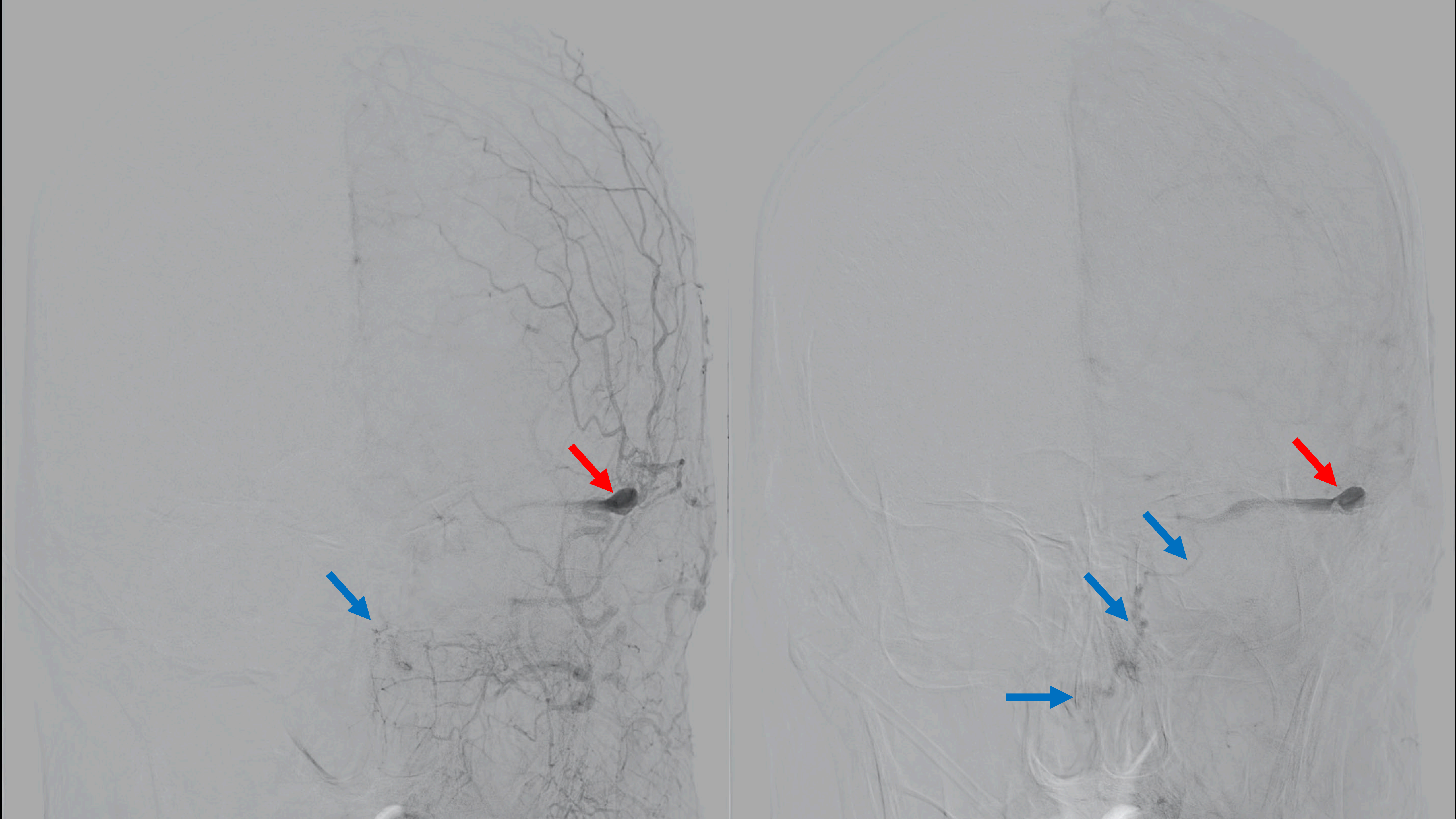










Cognard grade 5 left petrosal vein dAVF

Perimedullary drainage
Occluded left sigmoid sinus

Management paradigm

<u>Ruptured or Severe NHND</u>

↓

Diagnostic angiography
and embolization

Management paradigm

<u>Ruptured or Severe NHND</u>

↓

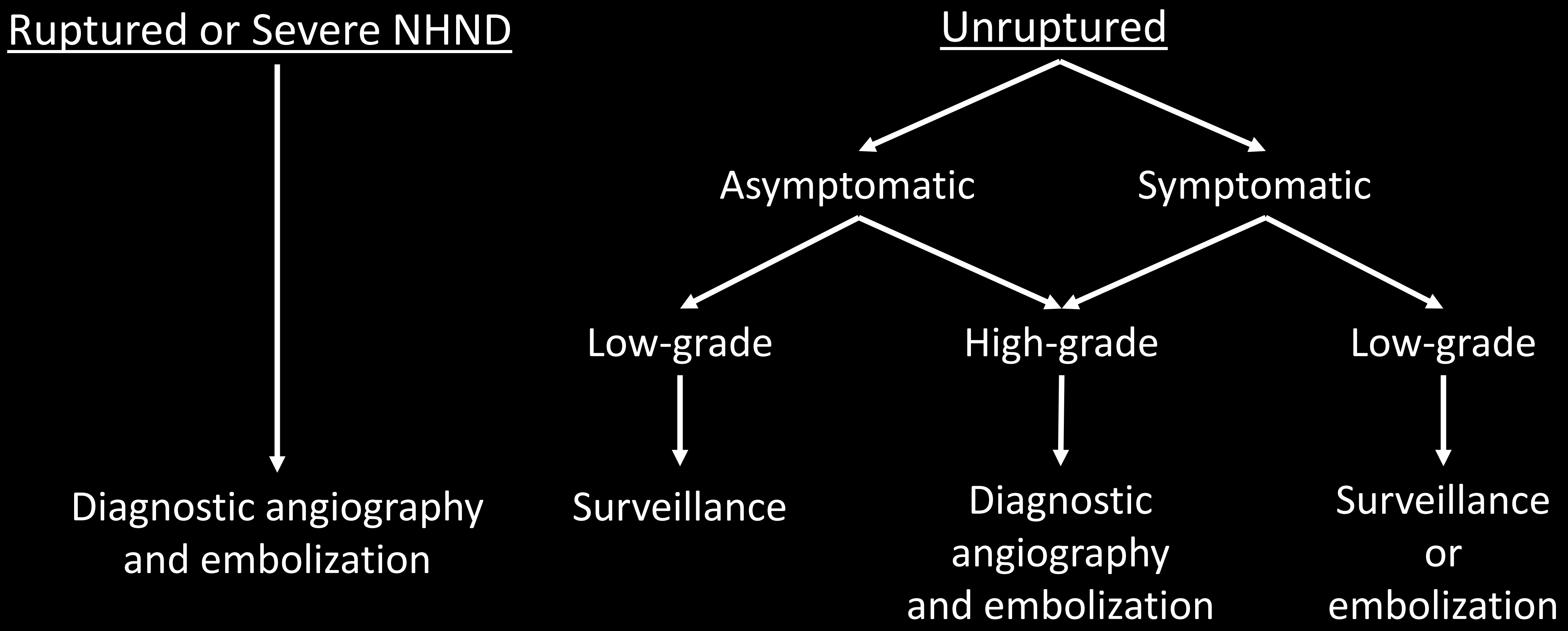
Treat within ~5 days
1.6%/14 days rebleed risk
5.3-7.3%/yr rebleed risk

↓

Diagnostic angiography
and embolization

Durnford, A.J., Akarca, D., Culliford, D. et al. (2022) Risk of early versus later rebleeding from dural arteriovenous fistulas with cortical venous drainage. *Stroke* 53(7): 2340-2345.

Management paradigm



Treatment methods

- Transarterial
- Transvenous
- Microsurgical ligation
- Gamma knife

Treatment principles

Close the fistula!

Treatment principles

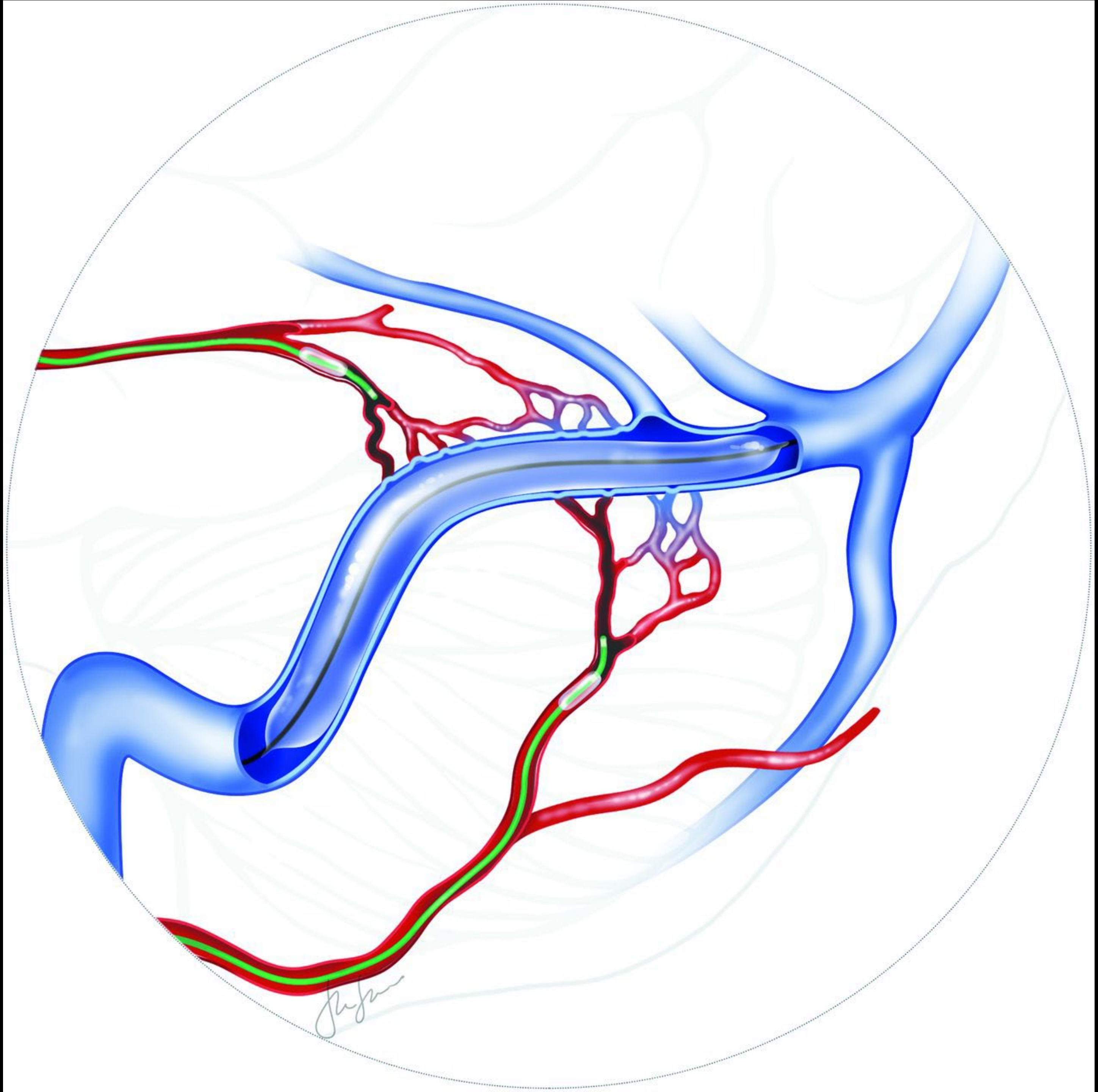
Close the fistula!

close the distal arterial inflow and the proximal draining vein

Treatment efficacy and risks

- Transarterial embolization:
  - Antegrade delivery of liquid embolic agents (nBCA glue or EvOH copolymers) to permeate through the supplying artery into the fistula and to the foot of the vein.
  - Improved efficacy in last 15 years due to three developments:
    - New embolic agents (Onyx, now PHIL, SQUID, ihtObtura)
    - More trackable microcatheters
    - Dual-lumen balloon microcatheters
  - Modern angiographic cure rate = 77%-95% (60-80% in single session)
    - Improved from pre-EvOH era: 23-26%
  - Complications: (Overall morbidity 6.9%; mortality 1.0%)
    - Liquid embolic penetration into feeding arteries, cranial nerve vasa nervorum, dangerous anastomoses = ~2.3-2.8%
    - Vessel perforation (0.9%) or rupture (0.3%)
    - Venous occlusion with NHND or hemorrhage = 1.1%
    - Microcatheter glued in = 0.2%

Bhatia, K.D., Lee, H., Kortman, H. et al. (2022) Endovascular management of intracranial dural arteriovenous fistulas: Transarterial approach. *AJNR* 43(3): 324-331.



Zamponi Jr, J.O., Trivelato, F.P., Rezende, M.T.S., et al. (2020) Transarterial treatment of cranial dural arteriovenous fistulas: The role of transarterial and transvenous balloon-assisted embolization. *AJNR* 41(11): 2100-2106.

Treatment efficacy and risks

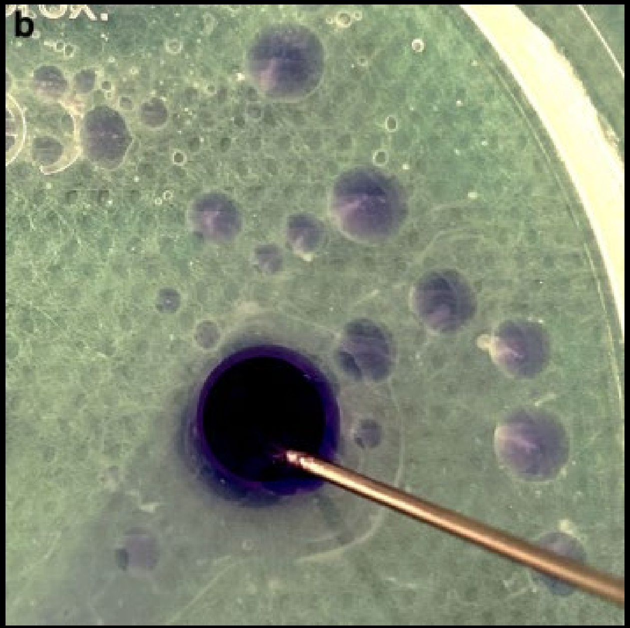
- Transvenous embolization:
  - Retrograde delivery of coils and/or liquid embolic agents (nBCA glue or EvOH copolymers) to permeate from the draining vein into the fistula.
  - Typically used when risk is high for:
    - Ischemic cranial neuropathy due to adjacent vasa nervorum
    - Infarction due to EC-IC anastomoses
    - Difficult transarterial access due to vessel tortuosity/caliber
  - Modern angiographic cure rate = 80-90% (60% in single session)
    - Particularly when EvOH is combined with coils
  - Complications:
    - Overall morbidity approximately 7-8%
      - Due to venous thrombosis, NHND, transient cranial neuropathy, arterial infarcts
    - Overall mortality approximately 0.7%
      - Due to vessel perforation/rupture, venous thrombosis and hemorrhage

Bhatia, K.D., Lee, H., Kortman, H. et al. (2022) Endovascular management of intracranial dural arteriovenous fistulas: Transvenous approach. *AJNR* 43(4): 510-516.

Liquid embolic agents

- Cyanoacrylates
  - N-butyl cyanoacrylate (nBCA) = ”glue”
- Ethylene vinyl alcohol-tantalum copolymers:
  - Onyx
  - Squid
- Triiodophenol-polylactide-polyhydroxyethylmethacrylate polymer
  - PHIL (precipitating hydrophobic injectable liquid)
- Ethylene vinyl alcohol-iodine copolymer:
  - $_{\text{iht}}$Obtura

Vollherbst, D.F., Chapot, R., Bendszus, M., Mohlenbruch, M.A. (2022) Glue, Onyx, Squid or PHIL? Liquid Embolic Agents for the Embolization of Cerebral AVMs and dAVFs. *Clin Neuroradiol* 32: 25-38.



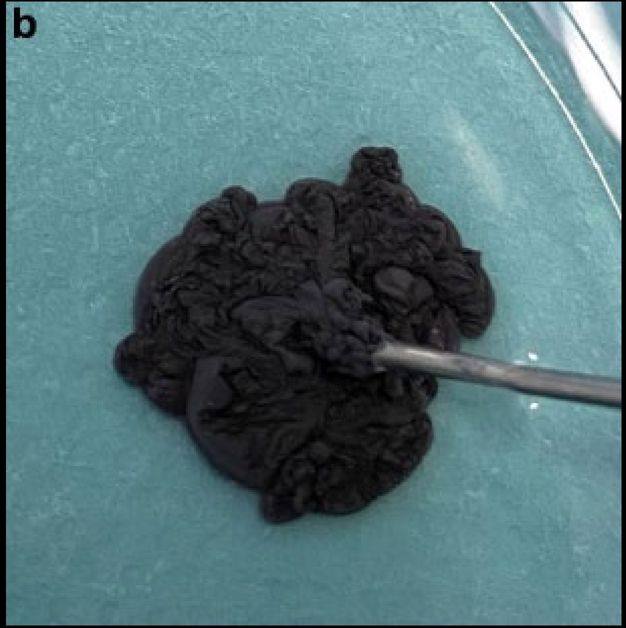
nBCA glue

Lipiodol
Tantalum powder

User customizable concentration

Short working time

Adhesive embolic agent

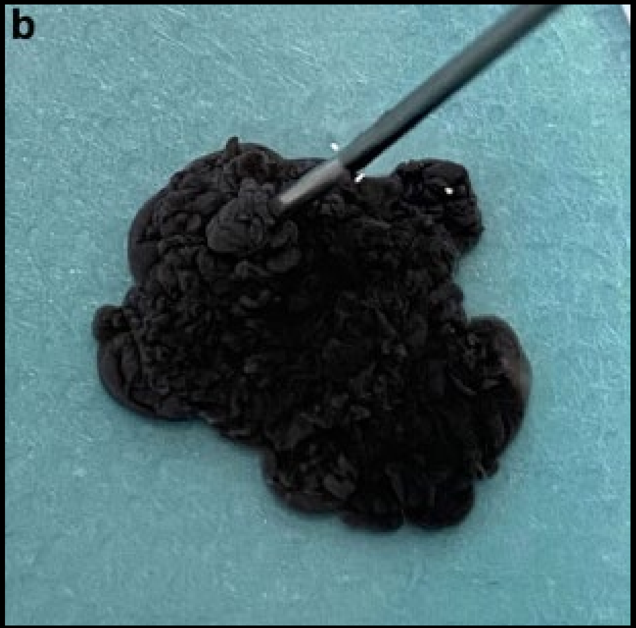


Onyx

DMSO solvent
Tantalum suspension

Most widely tested
Broad experience

Onyx 18, 34

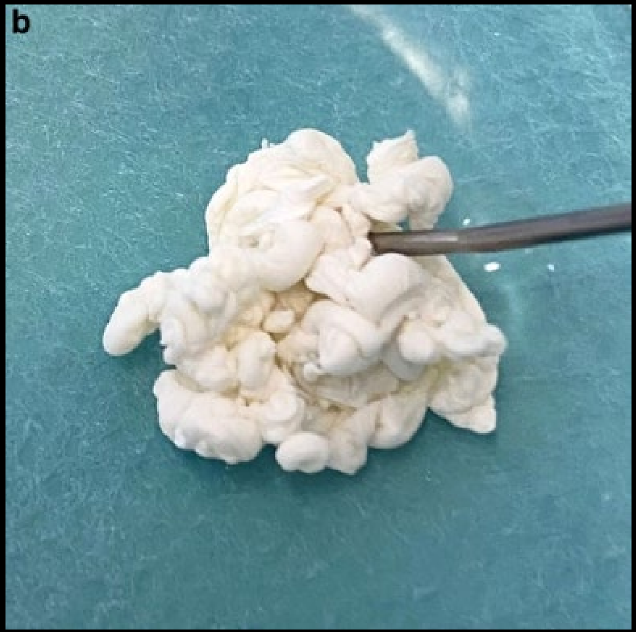


Squid

DMSO solvent
Tantalum suspension

Lower viscosity options
Smaller tantalum grain

Squid 12, 18, 34
Squid Low Density 12-34



PHIL

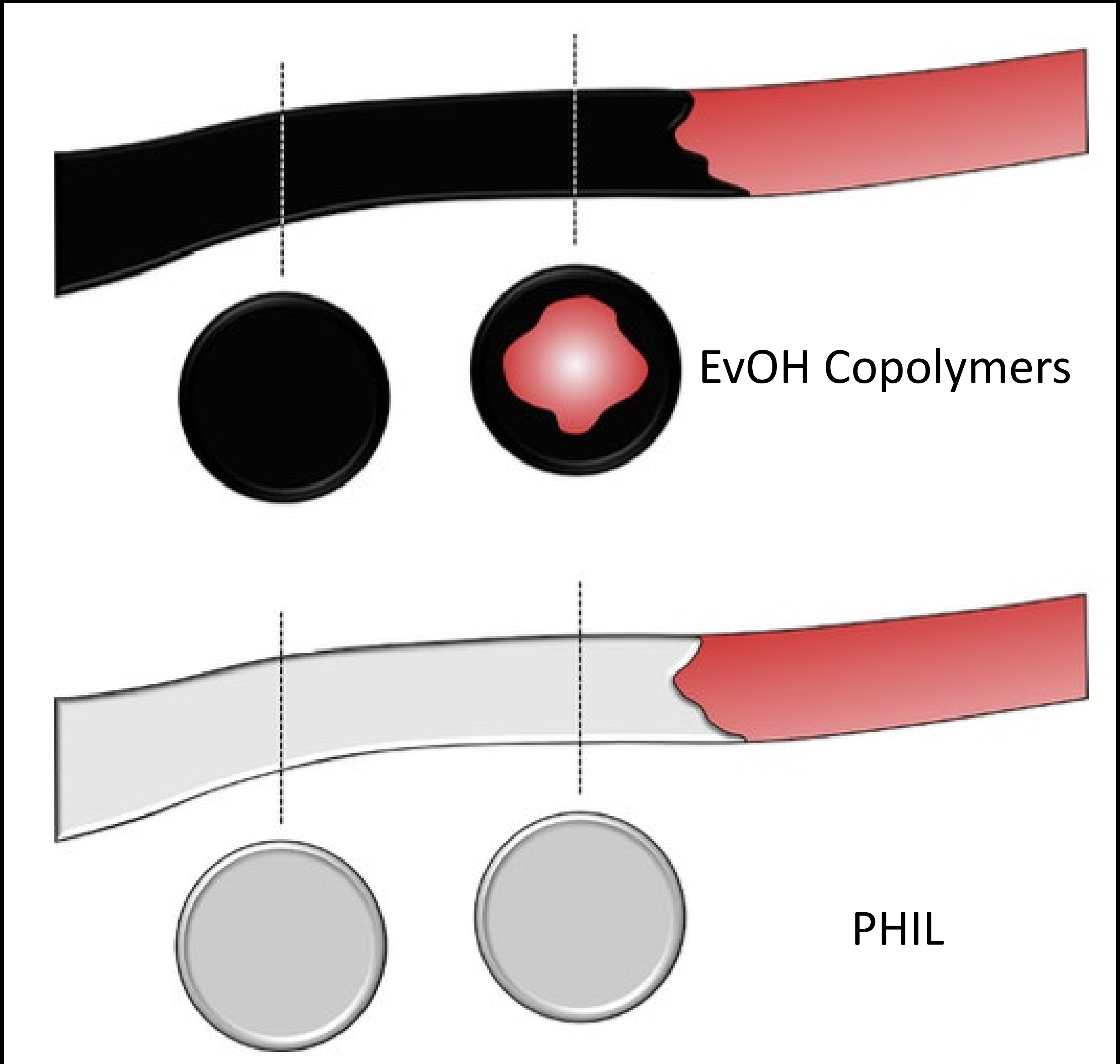
DMSO solvent
Covalently bound iodine

Lower viscosity options
No tantalum sedimentation

PHIL 25%, 30%, 35%
PHIL LV (Low viscosity)

Vollherbst, D.F., Chapot, R., Bendszus, M., Mohlenbruch, M.A. (2022) Glue, Onyx, Squid or PHIL? Liquid Embolic Agents for the Embolization of Cerebral AVMs and dAVFs. *Clin Neuroradiol* 32: 25-38.

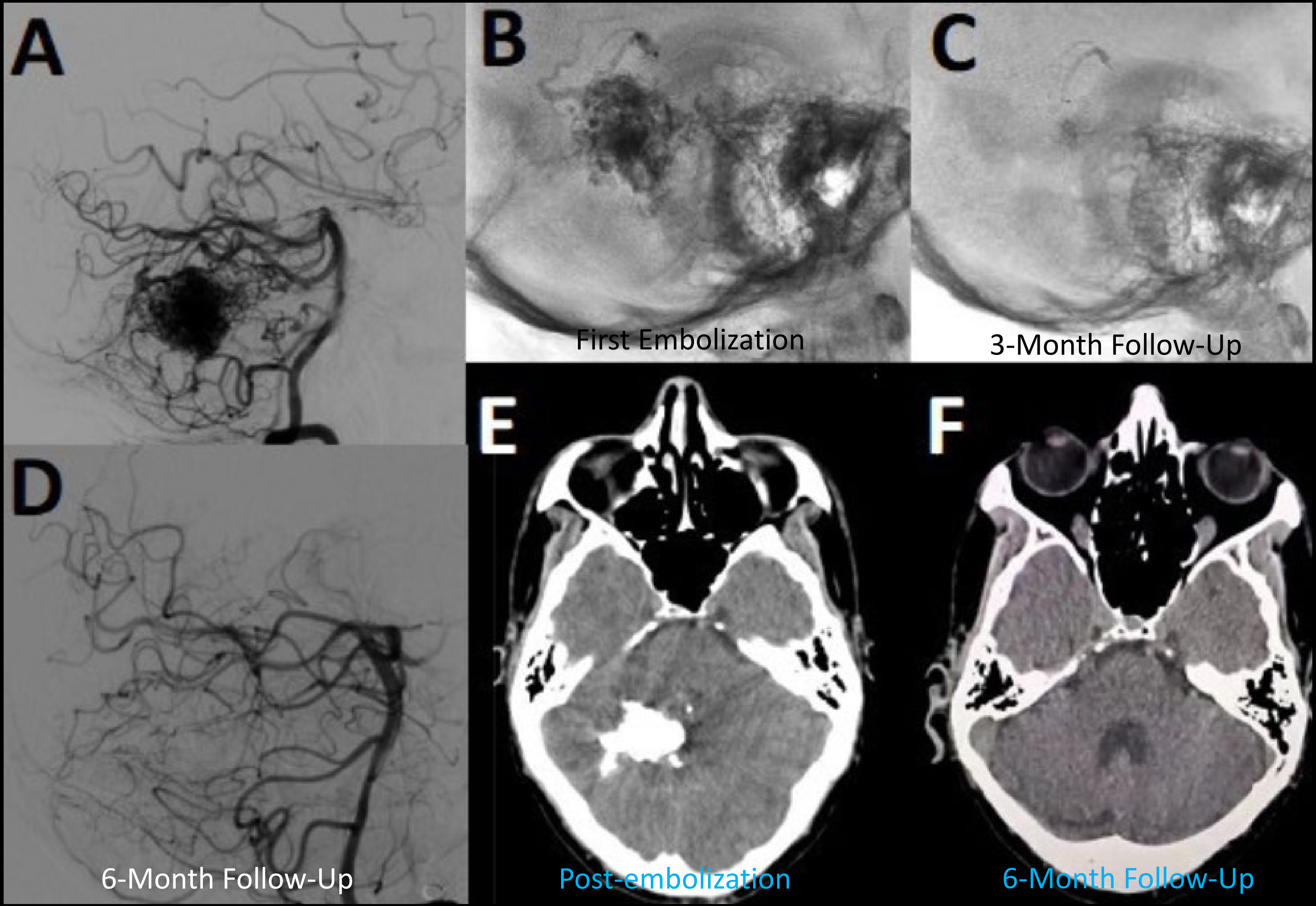
Cohesive, not adhesive



- Lava-like outside-to-inside polymerization
- Casts inside of vessel in layers
- Precipitates out of DMSO solvent

- Forms a solid column rather than layering outside-to-inside
- Precipitates out of DMSO solvent

Vollherbst, D.F., Chapot, R., Bendszus, M., Mohlenbruch, M.A. (2022) Glue, Onyx, Squid or PHIL? Liquid Embolic Agents for the Embolization of Cerebral AVMs and dAVFs. *Clin Neuroradiol* 32: 25-38.



Llibre-Guerra, J.C., Guimaraens, L., Kadziolka, K.B., et al. (2024) ihtObtura: A novel liquid embolic agent with post-embolization radiopacity loss in endovascular treatment of brain AVMs, dAVFs and tumors: CLARIDAD trial. *JNIS* 0:1-7.

Liquid embolic agents

- Newer agents with limited clinical experience
- Lower viscosity agents with potential for improved penetration
- Improved procedural visibility with iodine copolymers
- Finer tantalum grain may reduce imaging artifact or settling
- Reduced beam hardening artifact at follow-up with iodine copolymers

- Much more experience needed

Treatment efficacy

- Microsurgical ligation:
  - Open surgical disconnection by ligation or clipping
  - Angiographic cure achieved in up to 94%; or may convert high-grade to low grade fistulas by closure of cortical venous drainage route.

- Gamma knife radiosurgery:
  - Limited efficacy as stand-alone therapy; ~56% angiographic cure.
  - Best used as part of multimodality therapy (after incomplete endovascular or surgical treatment) with >75% cure.
  - Long interval from treatment to obliteration = prolonged risk exposure.

Bhatia, K.D., Lee, H., Kortman, H. et al. (2022) Endovascular management of intracranial dural arteriovenous fistulas: Transvenous approach. *AJNR* 43(4): 510-516.

Follow-up after treatment

- Recurrence risk:
  - ~4.5% recurrence risk overall
  - Increased risk of recurrence with radiosurgery or EvOH embolization
  - Delayed long-term angiography or screening MRA/ASL recommended at 1 year and 3-5 years.

Abecassis, I.J., Meyer, M.R., Levit, M.R., et al. (2022) Recurrence after cure in cranial dural arteriovenous fistulas: a collaborative effort by the Consortium for Dural Arteriovenous Fistula Outcomes Research (CONDO)R. *JNS* 136: 981-989.

Conclusions

- Unruptured dAVFs are divided into low- and high-grade on the basis of cortical venous reflux or hypertension.
- High-grade dAVFs have a high risk of hemorrhage, death, and NHND.
- dAVFs may present with hemorrhage, NHND, or be incidental.

- Endovascular embolization is the first-line therapy for dAVFs.
- Transarterial or transvenous approaches depend on particular anatomy
- Newer embolic agents and improved microcatheter technology allow superior obliteration rates, safety profiles, and endovascular access.

Thank you!

Questions?

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