THE WARREN ALPERT
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Rhode Island STROKE SYMPOSIUM

Advanced Neuroimaging in ICH – who, when and why?

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DISCLOSURE

- I have the following funding to disclose, which is not connected to this talk:
  - MGH/BSC -> the Neuro-Afib study
  - AHA (24SCVNCFRE1401274)
  - Duke University Medical Center/NIH (30200478/5K23HL161426-02)
- My talk will not include any off-label discussion.

Objectives

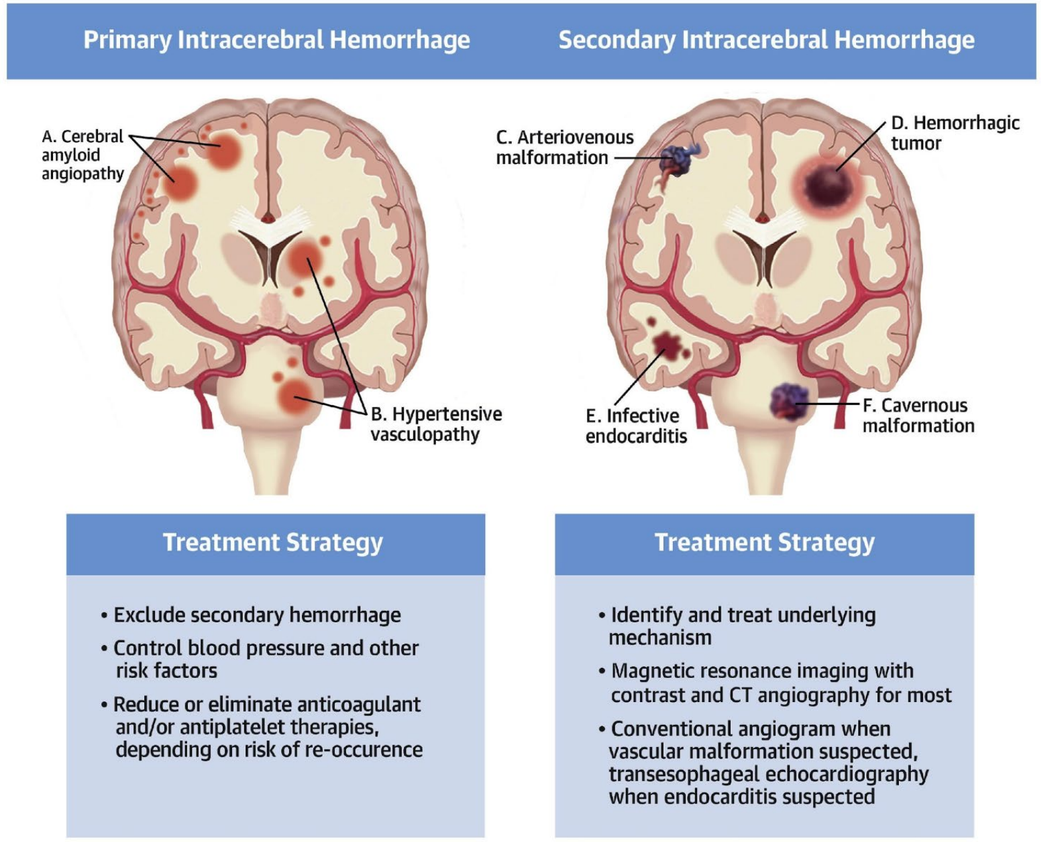
- Discuss the concept of primary vs secondary ICH
- Select patients for vascular imaging in the workup of ICH
- Review role of MRI for evaluation, treatment and prognosis of ICH

Introduction

- Spontaneous ICH (sICH) – brain injury due to acute hemorrhage from ruptured cerebral blood vessel
- Neurologic emergency
- Epidemiology [1-3]
  - About 10 – 15% of all strokes in the US
  - Incidence increases with age; use of anticoagulation is growing
  - Incidence 1.6 - fold higher in Black>White and 1.6 -fold higher in Mexican Americans > non -Hispanic White people
- Morbidity & Mortality
  - Great public health burden [4]
  - Mortality up to 33% at 30 days and 50 -55% at one year [5]

[1] Tsao CW, et al. Circulation 2022; 145(8): e153 -639, [2] Poon MT, et al. Front Neurol Neurosci. 2015; 37:1 -12, [3] Morgenstern LB, et al. Am J Epidemiol. 2004; 160: 376 -383, [4] Greenberg SM, et al. Stroke. 2022; 53:e282 -361, [5] Jolink WMT, et al. Neurology 2015; 85(15): 1318 -1324

CENTRAL ILLUSTRATION: Differential Diagnosis and Diagnostic Features of Primary and Secondary Intracerebral Hemorrhages

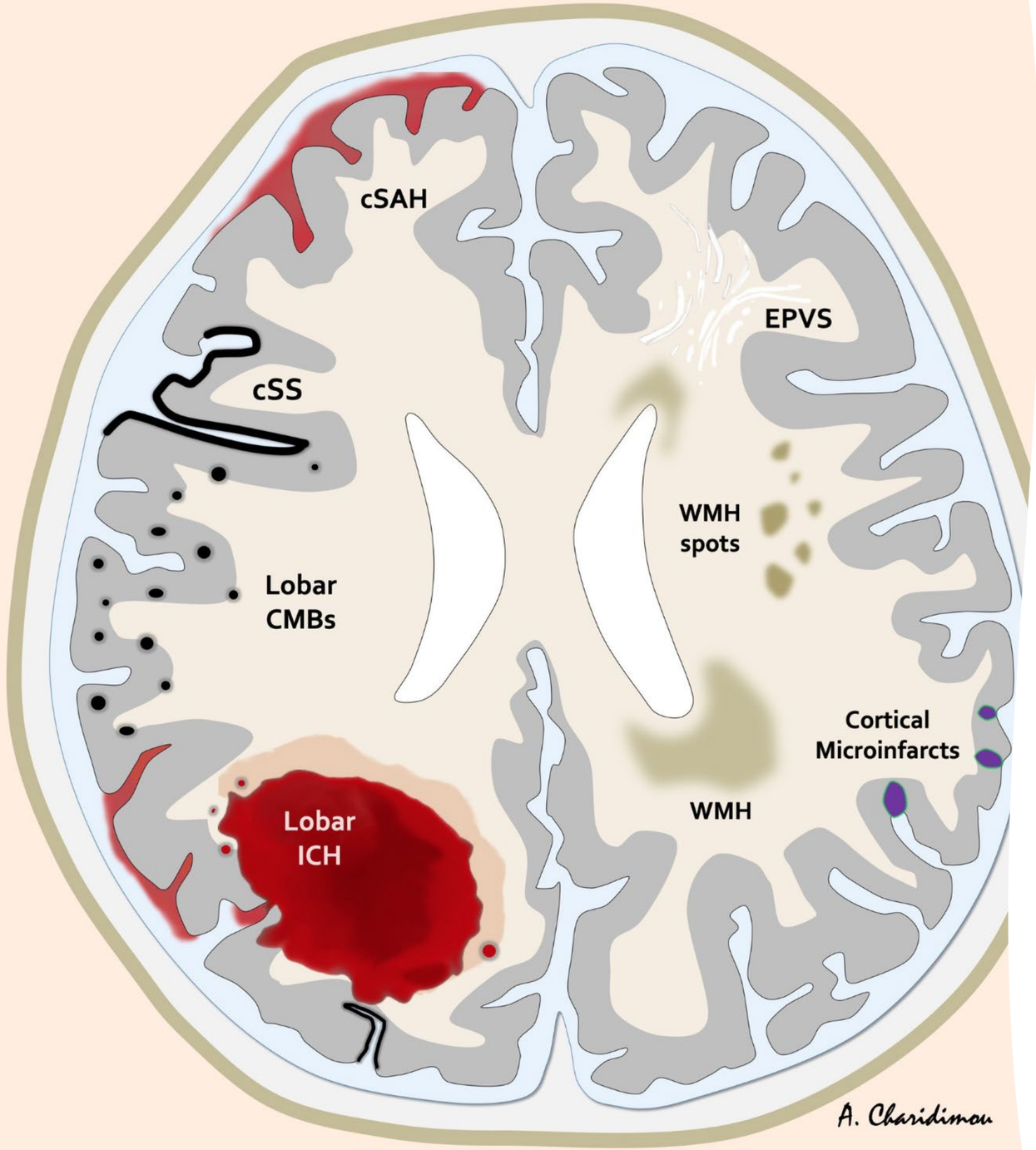


Schrag, M. et al. J Am Coll Cardiol. 2020;75(15):1819-31.

ICH Etiologies

- primary (spontaneous) ICH not truly primary but result of defined underlying (often co - occurring) common cerebral small vessel disease pathologies [1]
- Primary ICH accounts for about 80% of cases [2]

[1] Greenberg SM, et al. Stroke. 2022; 53:e282 -361
[2] Macellari F, et al. Stroke. 2014;45(3):903 –908e

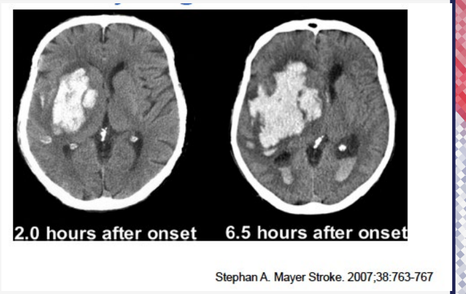


Primary ICH

- Result of 2 common cerebral small vessel pathologies, age-related
  - Arteriolosclerosis (= lipohyalinosis)
    - Concentric vascular wall thickening of penetrating arterioles in deep territories
    - RF: hypertension, diabetes, age
  - Cerebral amyloid angiopathy (CAA)
    - Deposition of b-amyloid peptide in arteriolar walls and capillaries in leptomeninges, cortex and cerebellar hemispheres
    - RF: age, apolipoprotein E genotypes of e2 or e4 alleles

Greenberg SM, et al. Stroke. 2022;53:e282-361
https://twitter.com/a_charidimou/status/1498162581399293953

Neuroimaging - ICH Diagnosis



Stephan A. Mayer Stroke. 2007;38:763-767

- Emergent neuroimaging with **CT** (MRI)
- Serial imaging at 6 h to assess for HE, until ICH stable and in case of neurologic worsening
  - 20-25% of ICH have HE[1], most w/in 6 h (peak w/in 3 h)[2]
  - Shorter time from onset to baseline imaging, higher ICH volume, anti-thrombotic use, spot sign on CTA associate with HE[2]
- CTA w/in first hours of ICH onset can help identify patients at high risk for HE

[1] Morotti A, et al. Lancet Neuro 2023;22(2):159-171
[2] Al-Shadi Salman R, et al. Lancet Neurol 2018;17(10):885-894

Multicenter Study > BMJ. 2015 Nov 9:351:h5762. doi: 10.1136/bmj.h5762.

Diagnostic yield and accuracy of CT angiography, MR angiography, and digital subtraction angiography for detection of macrovascular causes of intracerebral haemorrhage: prospective, multicentre cohort study

Charlotte J J van Asch [1], Birgitta K Velthuis [2], Gabriël J E Rinkel [3], Ale Algra [4], Gérard A P de Kort [2], Theo D Witkamp [2], Johanna C M de Ridder [3], Koen M van Nieuwenhuizen [3], Frank-Erik de Leeuw [5], Wouter J Schonewille [6], Paul L M de Kort [7], Diederik W Dippel [8], Theodora W M Raaymakers [9], Jeannette Hofmeijer [10], Marieke J H Wermer [11], Henk Kerkhoff [12], Korné Jellema [13], Irene M Bronner [14], Michel J M Remmers [15], Henri Paul Bienfait [16], Ron J G M Witjes [17], Jacoba P Greving [18], Catharina J M Klijn [19]; DIAGRAM Investigators

Study question: What are the diagnostic yield and accuracy of early computed tomography (CT) angiography followed by magnetic resonance imaging/angiography (MRI/MRA) and digital subtraction angiography (DSA) in patients with non-traumatic intracerebral hemorrhage?

Results: **A macrovascular cause was identified in 69 patients (23%).** 291 patients (98%) underwent CT angiography; 214 with a negative result underwent additional MRI/MRA and 97 with a negative result for both CT angiography and MRI/MRA underwent DSA. Early CT angiography detected 51 macrovascular causes (yield 17%, 95% confidence interval 13% to 22%). CT angiography with MRI/MRA identified two additional macrovascular causes (18%, 14% to 23%) and **these modalities combined with DSA another 15 (23%,** 18% to 28%).

Macrovascular causes of ICH

- Depending on age category, in those <70 years of age without hypertension-related deep ICH, **1 of 4 to 1 of 7 patients had an underlying macrovascular cause in the DIAGRAM study** [1]
- Rapid identification is important and influences treatment and outcome [1,2]

[1] Van Asch CJJ, et al. BMJ. 2015 Nov 9:351:h5762
[2] Fam MD, et al. Cerebrovasc Dis. 2017;43:223-230

Neurovascular imaging for ICH pathogenesis (2022)

- CTA ± CTV (MRI/MRV) on admission to acutely exclude macrovascular cause or CVT
- CTA ± CTV recommended and highest yield of DCA* as **adjunct/alternative imaging** in
  - < 70 years with lobar ICH
  - < 45 years with deep or posterior fossa ICH
  - 45 – 70 years with deep or posterior fossa ICH and no h/o hypertension and signs of small vessel disease
  - ICH with CTA/MRA and macrovascular lesion*
  - Patients with primary IVH*
- Primary IVH -> DSA recommended to r/o macrovascular cause
- If CTA/MRA suggestive of macrovascular cause -> obtain DSA
- MRI/MRA reasonable to assess for non-macrovascular etiology if CTA/CTV negative
- If initial DCA negative and no clear cause, consider repeat DCA in 3-6 months

Greenberg SM, et al. Stroke. 2022;53:e282-361

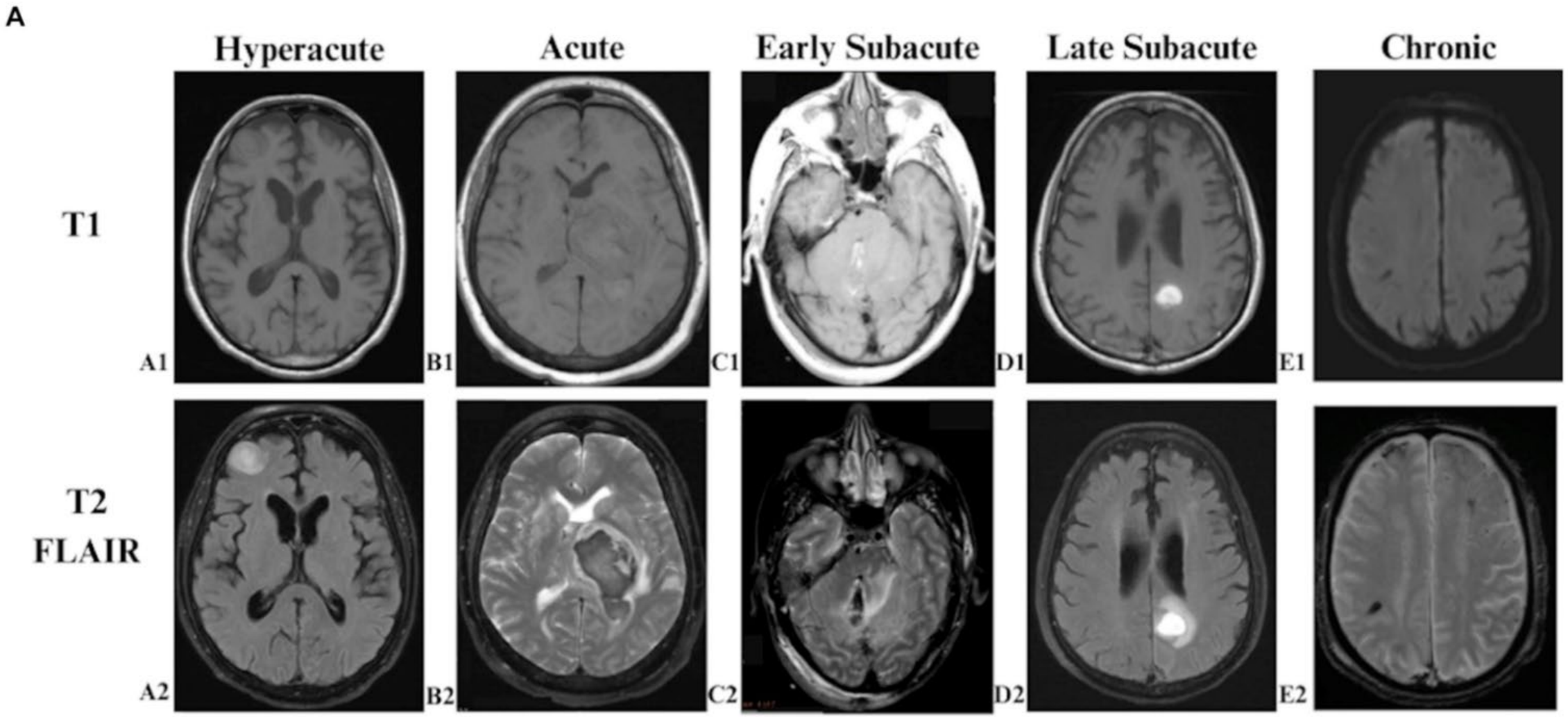
Role of MRI – ICH Diagnosis

- ICH diagnosis in hyperacute & acute settings[1-2]
- Determining the acuity of ICH[3-5]

TABLE 1 Stages of hemorrhage on MRI.

	T1 Sequence MR	T2 Sequence MR	Gradient-echo sequence MR
Hyperacute (<24 h)	Hypointense/isointense	Isointense/hyperintense center with peripheral hypointensity and hyperintense rim of vasogenic edema	Marked hypointensity
Acute (1–3 days)	Isointense/slightly hypointense	Hypointense with hyperintense rim	Marked hypointensity
Early subacute (3–7 days)	Hyperintense	Hypointense	Hypointense
Late subacute (7–28 days)	Hyperintense	Hyperintense	Hypointense
Chronic (>1 month)	Hypointense	Hypointense	Hyperintense/Isointense core with hypointense rim

[1] Fiebach J, et al. Stroke. 2004 Feb;35(2):502-6, [2] Romanova AL, et al. J Stroke Cerebrovasc Dis 2014 Sep;23(8):2036-2040, [3] Bradley WG. Radiology. 1993 Oct;189(1):15-26, [4] Weerink LB, et al. Br J Radiol. 2023 Aug;96(1148):20220304, [5] Penckhofer M, et al. Front Neurosci. 2024 May 9:18:1408288



From: Penckhofer M, et al. Front Neurosci. 2024 May 9:18:1408288

Role of MRI – ICH Etiology

- Timing of study
- Primary etiologies
- **Secondary etiologies**

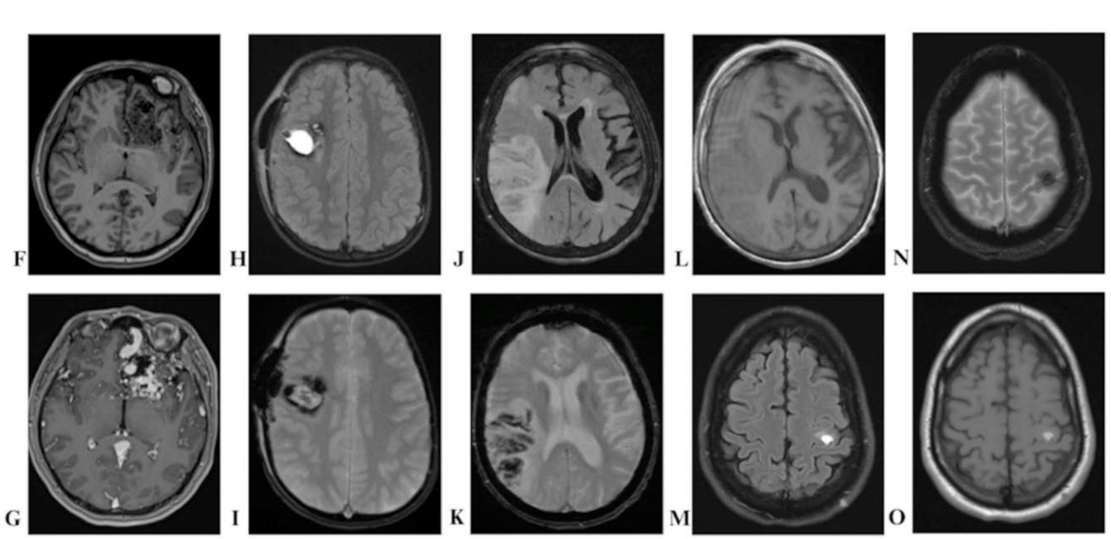
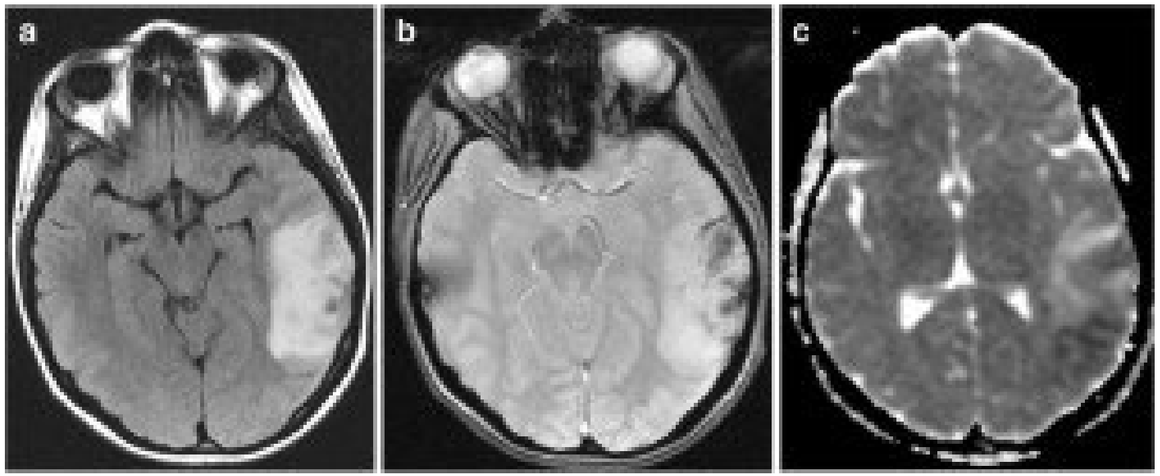


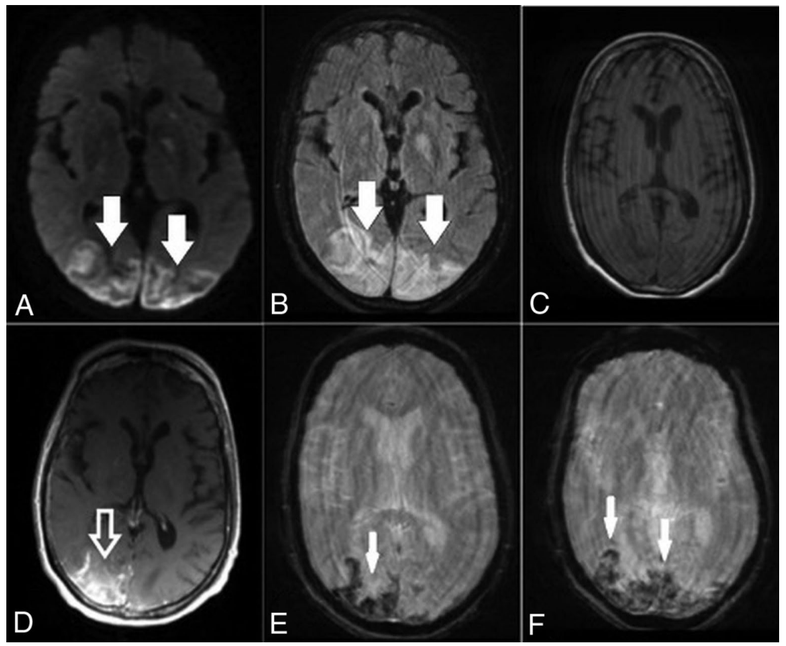
FIGURE 1
ICH stages of blood over time on MRI and common Etiologies of ICH on MRI. **(A)** Stages of blood in ICH: **(A1)** ICH hyperacute blood on T1, **(A2)** ICH hyperacute blood on T2 FLAIR, **(B1)** ICH acute blood on T1, **(B2)** ICH acute blood on T2 FLAIR, **(C1)** ICH early subacute blood on T1, **(C2)** ICH early subacute blood on T2 FLAIR, **(D1)** ICH late subacute blood on T1, **(D2)** ICH late subacute blood on T2, **(E1)** ICH chronic blood on T1. **(E2)** ICH chronic blood on GRE. **(B)** Common ICH etiologies on MRI: **(F)** AVM on T1 Pre-Contrast, **(G)** AVM on T1 Post-Contrast, **(H)** Cavernous hemangioma on T2 FLAIR, **(I)** Cavernous hemangioma on GRE, **(J)** Hemorrhagic conversion of ischemic stroke on T2 FLAIR, **(K)** Hemorrhagic conversion of ischemic stroke on GRE, **(L)** Hemorrhagic conversion of ischemic stroke on T1, **(M)** Hemorrhagic metastasis on T2 FLAIR, **(N)** Hemorrhagic metastasis on GRE, **(O)** Hemorrhagic metastasis on T1. ICH=Intracerebral hemorrhage, FLAIR=fluid-attenuated inversion recovery, GRE=gradient-echo, AVM=arteriovenous malformation.

From: Penckhofer M, et al. Front Neurosci. 2024 May 9:18:1408288

Role of MRI – Secondary causes of ICH



Vein of Labbe hemorrhagic infarct



Hemorrhagic PRES

[1] Boukobza M, *et al. Neuroradiology* **62**, 935–945 (2020)
[2] Franceschi AM, et al. AJNR Am J Neuroradiol. 2020 Jul;41(7):1173-1176

Role of MRI – Risk stratification & prognosis

- ICH etiology associates with recurrence risk
  - CAA-related ICH 7.39%/y vs 1.11%/y arteriolosclerosis-related ICH[1]
- Imaging biomarkers
  - cSS associates with higher risk of HE, independent marker of poor prognosis and higher recurrence risk of ICH in lobar ICH[2,3]
  - DWI+ punctate lesions, while often subclinical, associate with increased risk by 2.5 of subsequent ischemic stroke[3]

[1] Charidimou A, et al. Neurology. 2017;89:820-829, [2] Boulois G, et al. Jama Neurol. 2016;73:1440-1447, [3] Sporns PB, et al. J Clin Med. 2021;10:1086

Role of MRI – Treatment

- Acute management informed by MRI(MRA/MRV)
  - CVST: anticoagulation, even in presence of hemorrhage
  - Vascular malformations -> endovascular/neurosurgery evaluations
  - Hemorrhagic mass -> neuro/oncology/neurosurgery consultations
  - Hemorrhagic abscess -> ID/neurosurgery evaluations
- Secondary stroke prevention
  - Antiplatelet/anticoagulation therapy guided by ICH etiology and recurrence risk, weighing risk of hemorrhage vs ischemia[1]

[1] Greenberg SM, et al. Stroke. 2022;53:e282-361

Summary

- About 1 in 5 patients with ICH have a secondary etiology.
- CTA +/- CTV (MRA/V) imaging on admission can help exclude macrovascular cause or CVT.
- MRI brain can guide diagnosis, etiology, risk stratification & prognosis and treatment decisions.
- DSA with highest yield as adjunct/alternative to CTA/MRA in select patients
  - <70 with lobar ICH
  - <45 with deep or posterior fossa ICH
  - 45 -70 with deep or posterior fossa ICH w/o HTN or SVD
  - ICH with CT or MR evidence of macrovascular etiology
  - Primary IVH
- Repeat neuro -imaging via MRI brain and/or DSA if previous imaging inconclusive.