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Spotting Hemorrhagic Stroke

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Disclosures

- None

Presenter

Adam Oostema, MD

Goals and Objectives

- Discuss the epidemiology and clinical presentation of hemorrhagic stroke
- Review current guideline recommendations for the diagnostic evaluation of spontaneous intracerebral hemorrhage and subarachnoid hemorrhage

Hemorrhagic Stroke

https://commons.wikimedia.org/wiki/File:Parachemableedwithedema.png

https://commons.wikimedia.org/wiki/File:SubarachnoidP.png

Pathophysiology of Hemorrhagic Stroke

Intracerebral hemorrhage

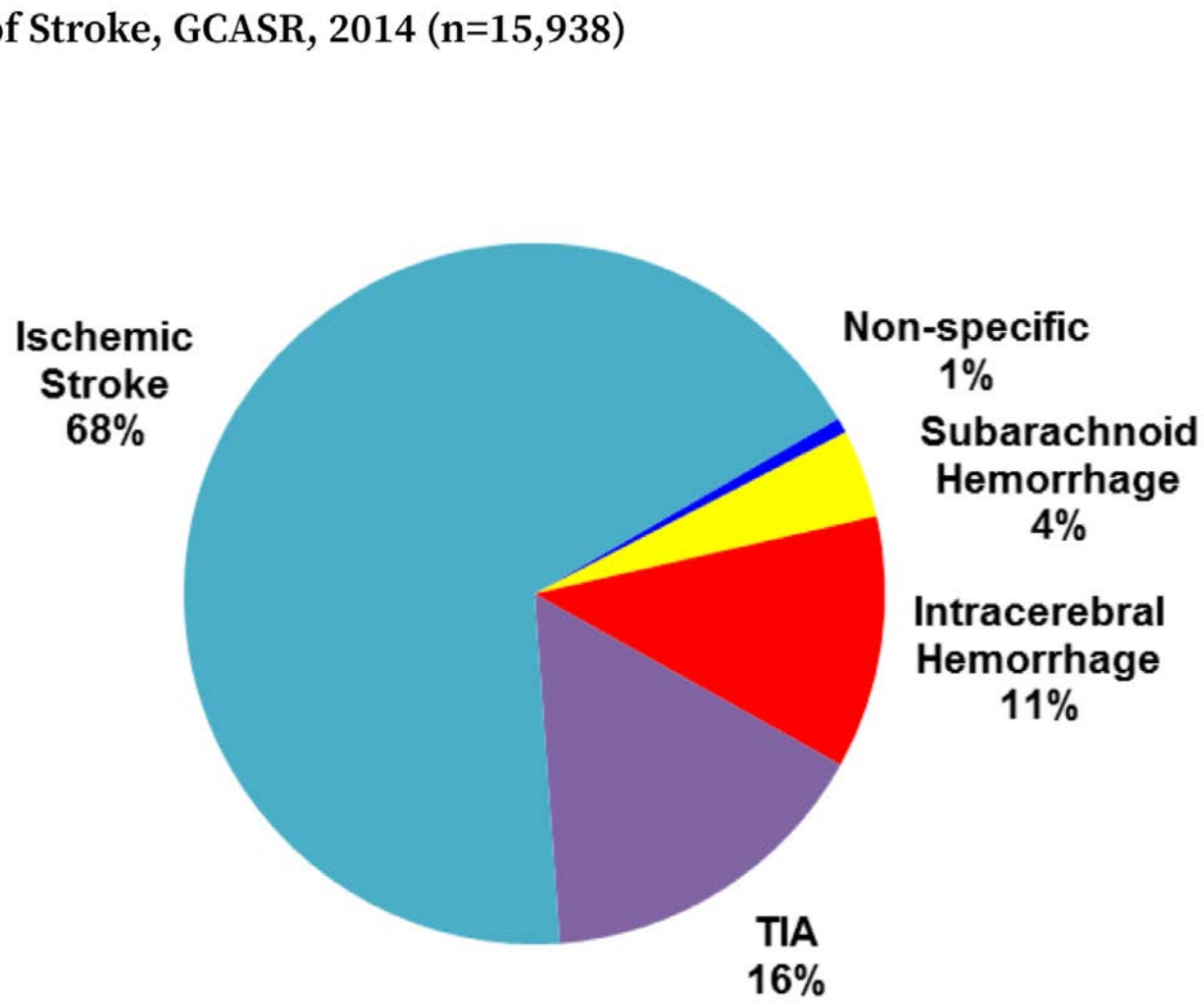
- Hypertensive angiopathy
- AVM
- Tumor
- Amyloid angiopathy
- Septic emboli
- Moyamoya
- Vasculitis

Subarachnoid hemorrhage

- Saccular aneurysms in the cerebrovascular circulation
  - Inciting event such as physical exertion (sometimes)
- Non-aneurysmal (perimesencephalic) bleeding from perforating vessels or veins

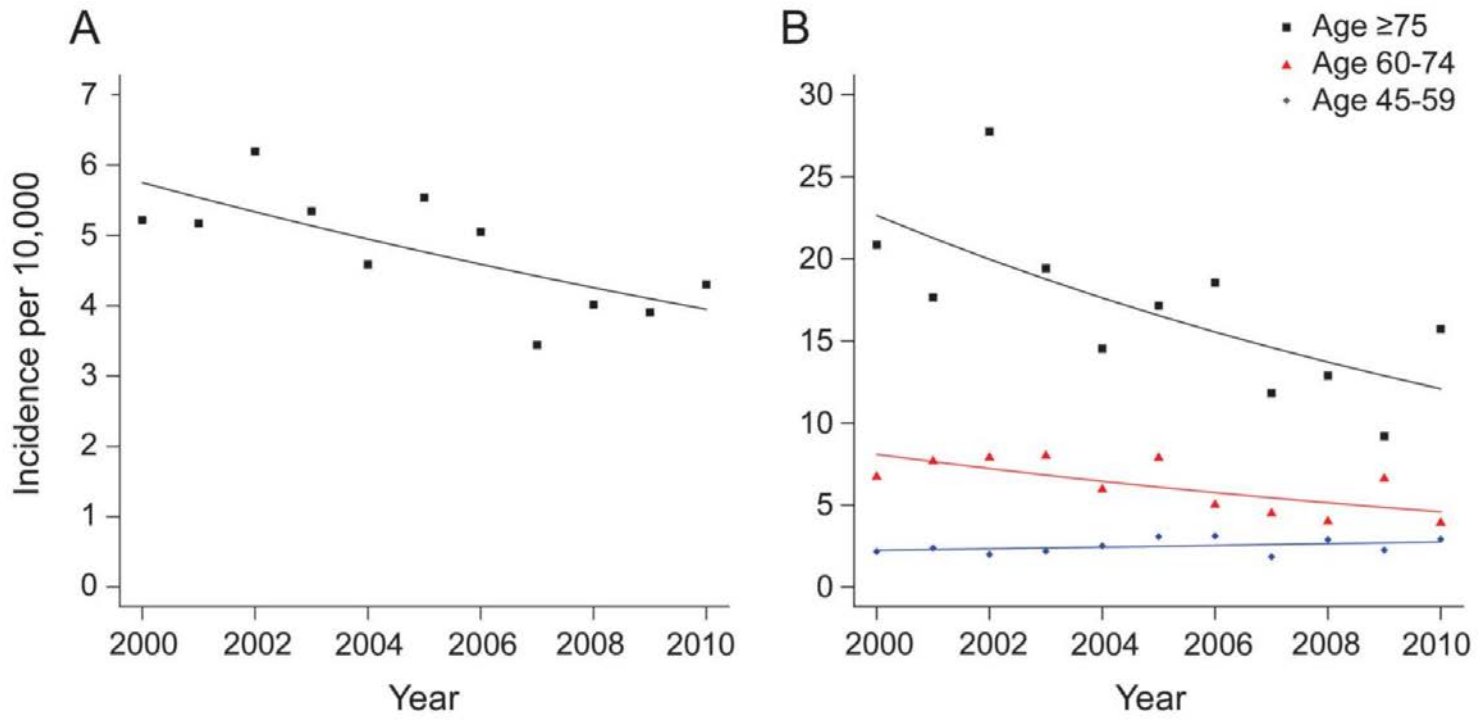
Epidemiology

Relative Proportions of Cerebrovascular Diseases



https://dph.georgia.gov/stroke

Figure 1 Trend in adjusted intracerebral hemorrhage incidence rate



Points represent the model-predicted incidence treating year as a categorical variable. Smoothed lines represent the model-predicted incidence assuming a linear trend. (A) Overall age-, sex-, and ethnicity-adjusted rates for all individuals 45 and older. (B) Sex- and ethnicity-adjusted rates by age group.

Incidence of Hemorrhagic Stroke

Risk Factors

ICH

- **Genetics**
- Age
- Race
  - Black
  - **Asian**
- Medical history
  - **Hypertension**
  - Anticoagulation
  - Low cholesterol
- Behaviors
  - High alcohol intake
  - Methamphetamine/cocaine

SAH

- Genetics
- Female (especially >50 years)
- Medical history
  - **Hypertension**
  - Anticoagulation
  - Statins?
- Behaviors
  - **Cigarette Smoking**
  - High alcohol
  - Methamphetamine/cocaine

ICH Incidence by Age

	Patients with intracerebral haemorrhage (n)	Person-years	Incidence per 100 000 person-years (95% CI)	Number of time periods	Incidence ratio (95% CI)
≤44 years[13,19,23,26,27,30,32,39–41,43,46–48,52,56]	119	5 958 646	1·9 (1·6–2·2)	16	0·10 (0·06–0·14)
45–54 years[19,23,26,27,30,32,33,39–41,43,46–48,52]	164	725 660	19·1 (13·4–27·4)	15	Reference
55–64 years[19,20,23,26,27,30,32,33,38–40,43,46–48,52]	305	865 173	36·5 (28·4–46·7)	16	1·8 (1·3–2·6)
65–74 years[19,23,26,27,29,30,32–34,38–41,43,46–48,52]	597	812 077	77·1 (65·0–91·5)	18	3·8 (2·7–5·4)
75–84 years[19,23,26,27,29,30,32–34,38–41,43,46–48,52]	665	531 845	136·9 (111·3–168·4)	18	6·8 (4·8–9·6)
≥85 years[19,23,26,27,29,30,32–34,38–41,46–48,52]	274	170 580	196·0 (148·3–259·1)	17	9·6 (6·6–13·9)

Because intracerebral haemorrhage is rare in people under age 45 years, the incidence ratios were calculated with the 45–54 years age group as the reference.

Table 2: **Incidence of intracerebral haemorrhage according to age**

van Asch C et al. Lancet Neurol. 2010;9(2):167-76

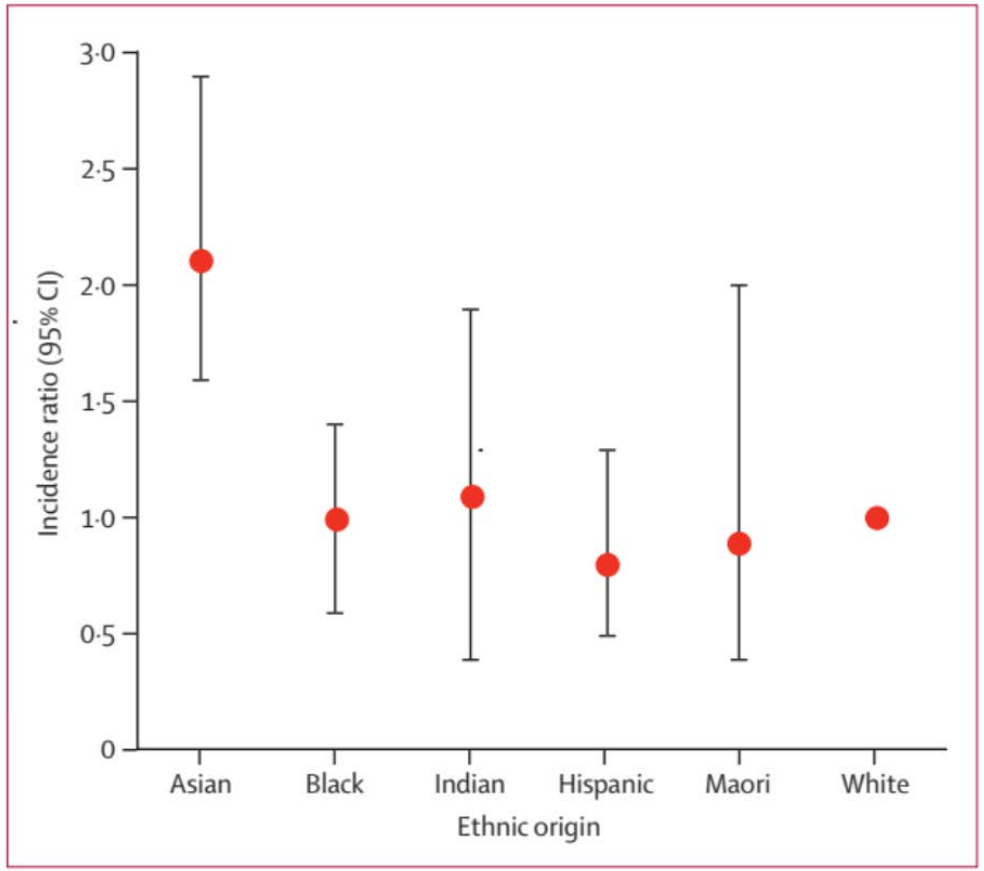


***Figure 3*: Intracerebral haemorrhage incidence ratios in ethnic groups**
White ethnic origin was taken as reference because it was the ethnic group with the largest number of patients with intracerebral haemorrhage. Circles are means and bars are 95% CI.

Intracerebral Hemorrhage by Race

van Asch C et al. Lancet Neurol. 2010;9(2):167-76

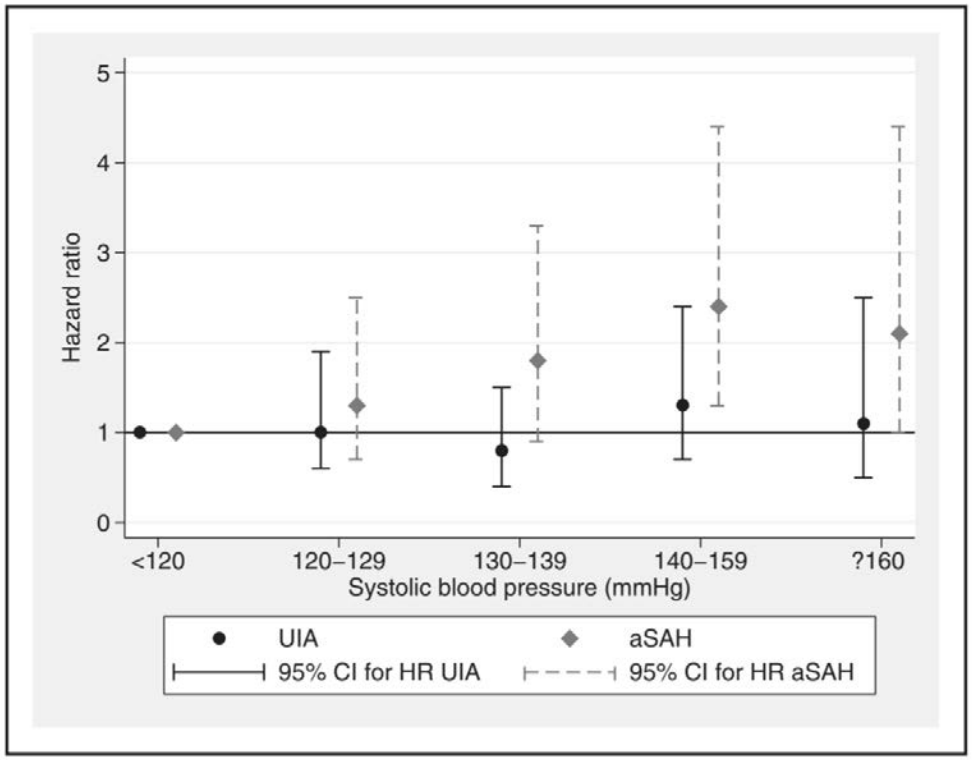


Figure 2. Risk of unruptured intracranial aneurysm (UIA) and aneurysmal subarachnoid hemorrhage (aSAH) according to systolic blood pressure.

Table. Risk Factors for Unruptured Intracranial Aneurysms and Aneurysmal Subarachnoid Hemorrhage in the HUNT Population

	Unruptured Intracranial Aneurysms		Subarachnoid Hemorrhage	
	No. Cases/ No. Participants*	HR (95% CI) Adjusted†	No. Cases/ No. Participants*	HR (95% CI) Adjusted†
Sex				
Male	23/39 402	1	36/39 402	1
Female	69/44 308	2.8 (1.7–4.5)	75/44 308	1.8 (1.2–2.7)
Smoking				
Never	17/36 423	1	27/36 423	1
Former	19/21 574	1.7 (0.9–3.3)	17/21 574	1.0 (0.5–1.9)
Current	56/25 713	4.1 (2.4–7.1)	67/26 713	3.4 (2.2–5.4)
P for trend		<0.001		<0.001

Aneurysmal SAH Risk Factors

Muller TB et al. Stroke. 2019;50(10):2952-5

Clinical Presentation

Hemorrhagic Stroke vs. Ischemic Stroke

Table 2. Accuracy of Findings for Diagnosing Hemorrhagic Stroke[a]

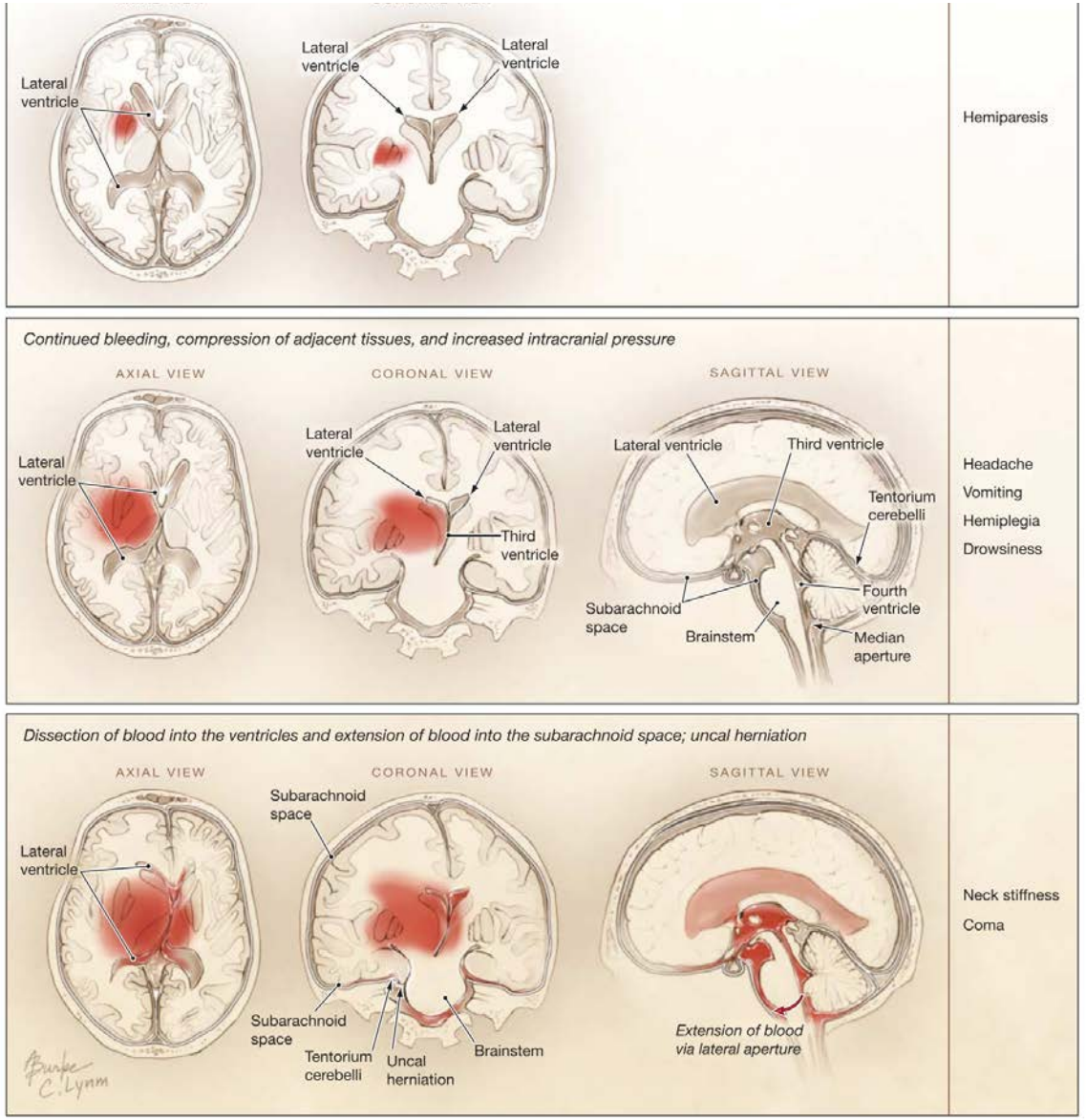
Finding	No. of Patients	Hemorrhage, No. (%)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive LR (95% CI)	Negative LR (95% CI)
Symptoms						
Seizures accompanying neurologic deficit[11,18,35]	2497	385 (15)	9 (6-12)	98 (97-100)	4.7 (1.6-14)	0.93 (0.9-0.96)
Vomiting[13,16-18,29,35]	2947	577 (20)	34 (17-52)	93 (90-96)	3.0 (1.7-5.5)	0.73 (0.59-0.91)
Headache[10,11,13,16-18,29,35]	3974	708 (18)	46 (41-52)	82 (75-89)	2.9 (1.7-4.8)	0.66 (0.56-0.77)
Loss of consciousness[17]	174	75 (43)	47 (35-58)	82 (74-89)	2.6 (1.6-4.2)	0.65 (0.52-0.82)
Acute onset of deficit[11]	887	109 (12)	44 (35-53)	32 (29-35)	0.65 (0.52-0.81)	1.7 (1.4-2.1)
Physical signs						
Kernig sign, Brudzinski sign, or both[29]	50	23 (46)	15 (0-29)	98 (93-100)	8.2 (0.44-150)	0.87 (0.73-1.0)
Level of consciousness: coma[11,17,18]	1161	223 (19)	35 (19-50)	94 (89-99)	6.2 (3.2-12)	
Neck stiffness[17,29]	223	97 (43)	20 (12-28)	97 (93-100)	5.0 (1.9-12.8)	0.83 (0.75-0.92)
Diastolic blood pressure >110 mm Hg[29]	50	23 (46)	48 (27-68)	89 (77-100)	4.3 (1.4-14)	0.59 (0.39-0.89)

Runchey S et al. JAMA 2010;303(22):2280-6

Intracerebral Hemorrhage

- Symptoms driven by size and location
  - Focal neurological deficit
  - Headache/vomiting
  - Depressed mental status/coma

- Progression over time
  - Abrupt onset
  - Deterioration common



Runchey S et al. JAMA 2010;303(22):2280-6

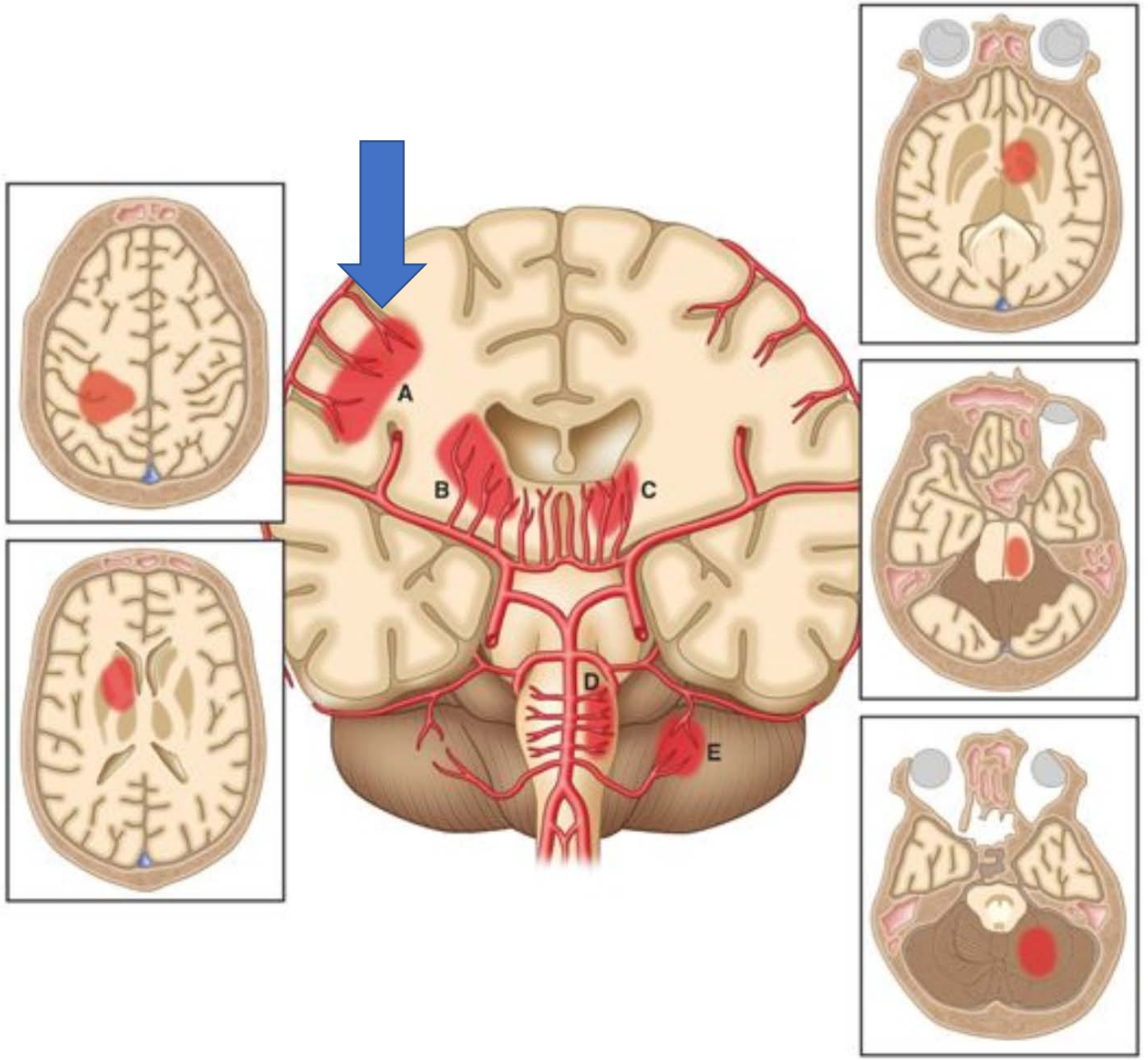
TABLE 4. Clinical Features Related to Selected Etiologies—Lausanne Stroke Registry

Clinical features	Cerebral infarction ($n=778$)			
	Atherosclerosis ($n=427$)	Emboligenic heart disease ($n=204$)	Hypertensive arteriolopathy ($n=147$)	Cerebral hemorrhage ($n=109$)
Transient ischemic attack(s)				
Previous	29	30	18	8
Ipsilateral	23	23	14	6
Deficit				
Immediately complete	66	82	54	44
Progressive	27	13	40	52
Fluctuating	7	5	6	4
At onset				
Convulsions	1	0	0	7
Syncope	2	3	1	2
Headaches	17 (17)	18 (19)	7 (7)	40 (51)
Decreased consciousness				
Somnolence	10	9	3	28
Coma	3	3	0	22

Bogousslavsky J et al. Stroke. 1988;19(9):1083-92

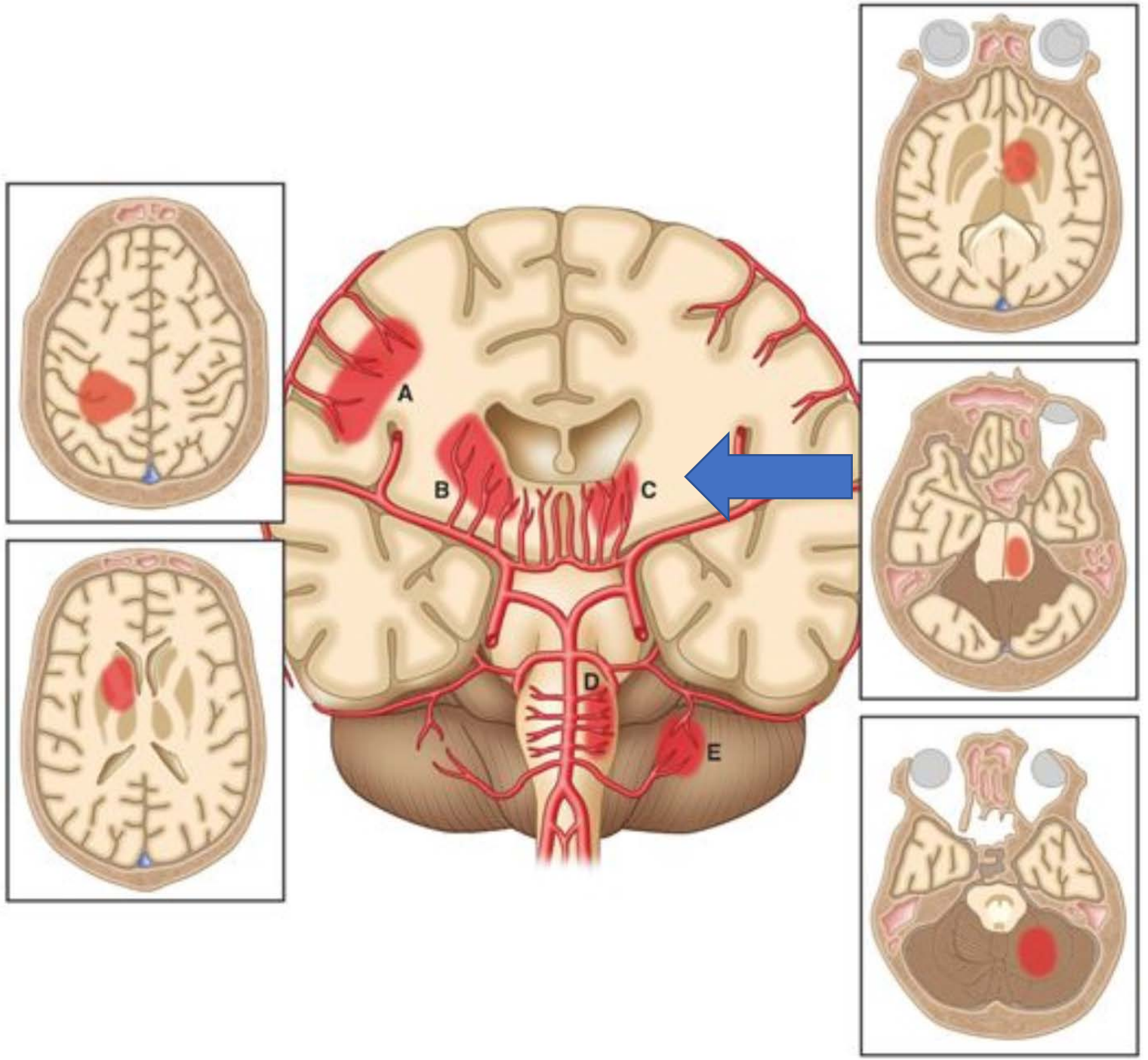
Clinical Presentation of Intracerebral Hemorrhage

- Subcortical (15%)
  - ➢ Similar to ischemic stroke in same location



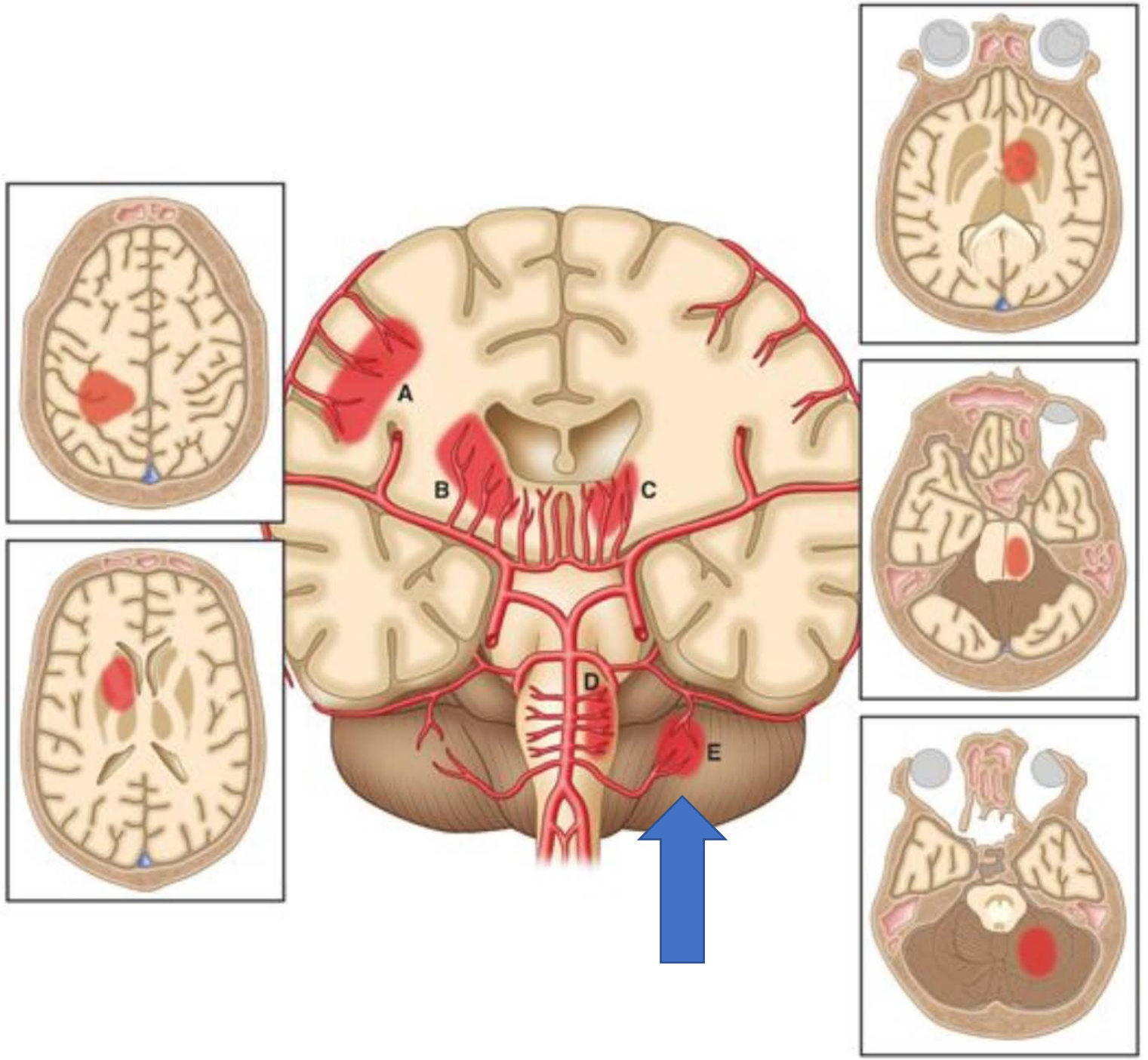
Clinical Presentation of Intracerebral Hemorrhage

- Deep brain (putamen, caudate internal/external capsule, thalamus) >50%
  - Hemiplegia
  - Hemisensory loss
  - Homonomous hemianopsia
  - Gaze palsy
  - Stupor
  - Coma



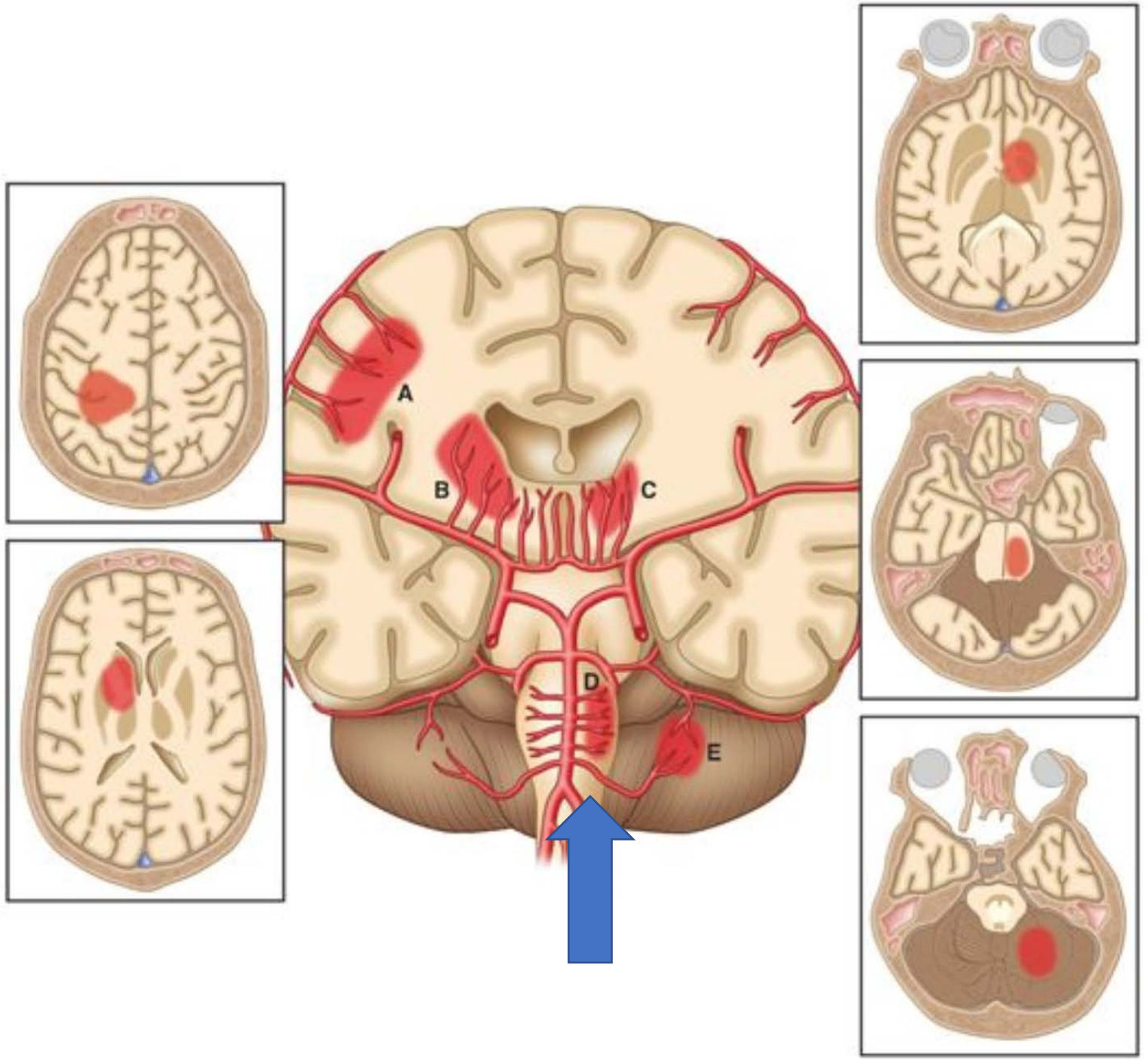
Clinical Presentation of Intracerebral Hemorrhage

- Cerebellum (15%)
  - ➢ Imbalance
  - ➢ Worsening occipital headache and vomiting
  - ➢ Generally no hemiparesis
  - ➢ Progressive somnolence due to obstructive hydrocephalus
    - ➢ Develops late



Clinical Presentation of Intracerebral Hemorrhage

- Pons (5%)
  - ➢Coma
    - Develops early
  - ➢Complete paralysis
  - ➢Pinpoint pupils



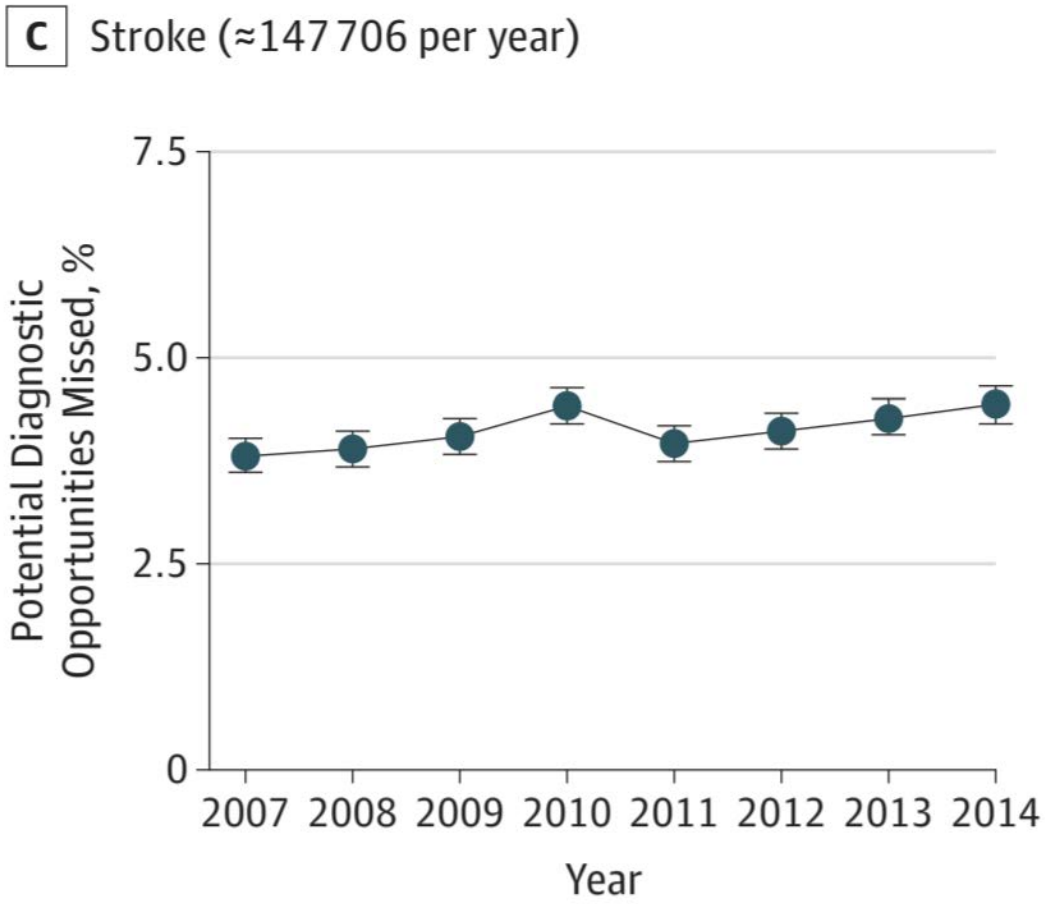
Clinical Presentation of Subarachnoid Hemorrhage

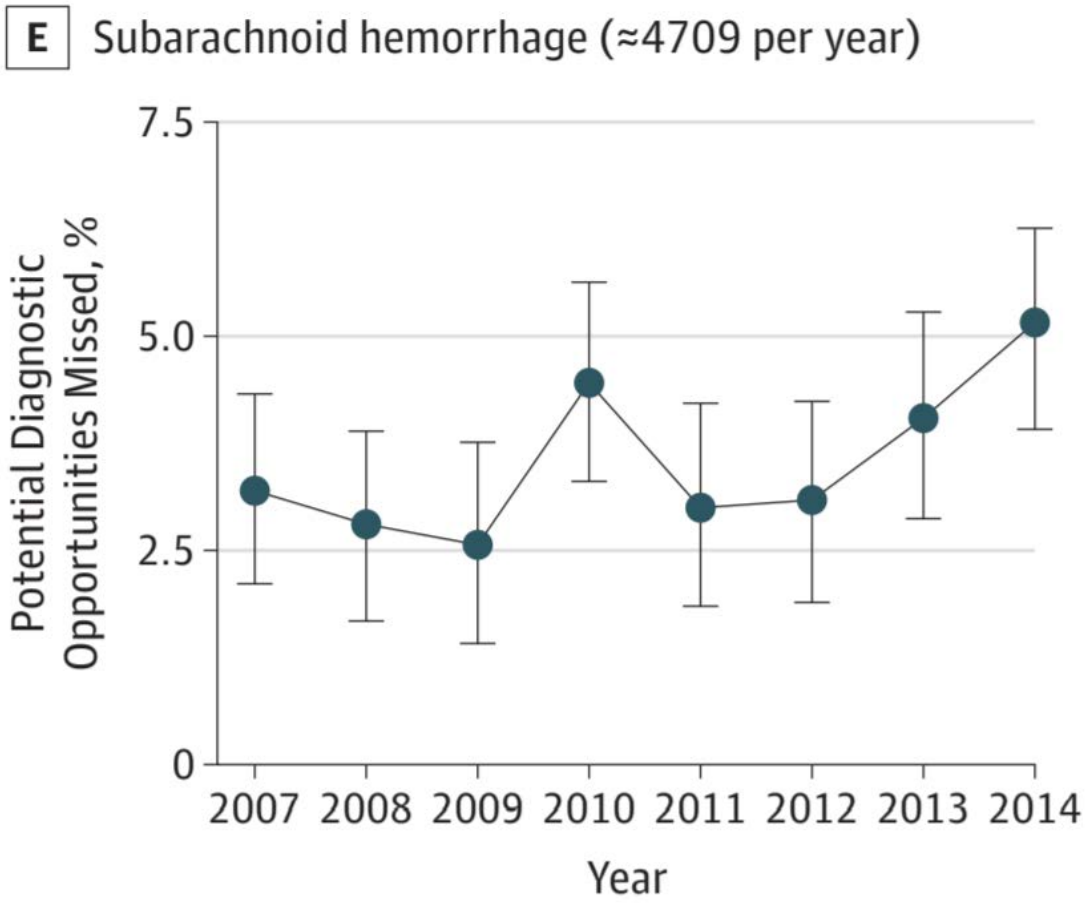
- 94% “Worst headache of life”
- 84% Thunderclap headache
-  75% Subjective neck stiffness
-  61% Vomiting
- 9% Transient loss of consciousness

Perry JJ et al. CMAJ. 2017;189(45):E1379-e85

Diagnostic Evaluation

Missed Diagnosis





Waxman DA et al. JAMA internal medicine. 2018;178(4):477-84

Consequences of Missed SAH Diagnosis

Table 2. Univariate and Multivariate Analysis of Indicators Related to Poor Outcome (n=401)

Variable, No. (%)	Poor Outcome, n=167	Good Outcome, n=234	Univariate, *P* Value	Multivariate, OR (95% CI)
Age* (mean±SD)	62.59±15.88	51.33±12.43	<0.001	1.05 (1.03–1.07)
Male sex	59 (35.3)	97 (41.5)	0.215	
Arterial hypertension*	92 (55.1)	86 (36.8)	<0.001	1.43 (0.81–2.5)
Diabetes mellitus*	20 (12)	11 (4.7)	0.007	1.15 (0.39–3.44)
Current smoking*	41 (24.6)	98 (41.9)	<0.001	0.59 (0.33–1.1)
Antithrombotic treatment*	26 (15.6)	15 (6.4)	0.003	1.36 (0.52–3.57)
Misdiagnosis* (n=400)	37 (22.3)	67 (28.6)	0.154	3.62 (1.87–7)

Ois A et al. Stroke. 2019;50(11):3072-6

Initial Evaluation of Suspected Hemorrhagic Stroke

History

- Time of onset
- Timing of onset
- Associated symptoms
- Anticoagulants
- Family history

Physical exam

- Primary survey
- Structured neuro exam
- NIHSS/GCS

Laboratory evaluation

- CBC
- Coagulation studies
- Drug screen
- Troponin

Hemphill, J. C., et al. Stroke 2015:46(7): 2032-206

Imaging

- CT Scan is the cornerstone imaging modality for ED evaluation of hemorrhagic stroke
- SAH
  - AHA Class I, Level of Evidence B[1]
  - ACR Appropriateness 9[2]
- ICH
  - Rapid neuroimaging with CT or MRI is recommended to distinguish ischemic stroke from ICH (Class I; Level of Evidence A) [3]
  - ACR Appropriateness 8-9[2]

1. Connolly, E. S., et al. Stroke 2012:43(6): 1711-1737
2. Salmela, M. B., et al. Radiology 2017:14(5, Supplement): S34-S61
3. Hemphill, J. C., et al. Stroke 2015:46(7): 2032-2060.

Importance of Early Recognition

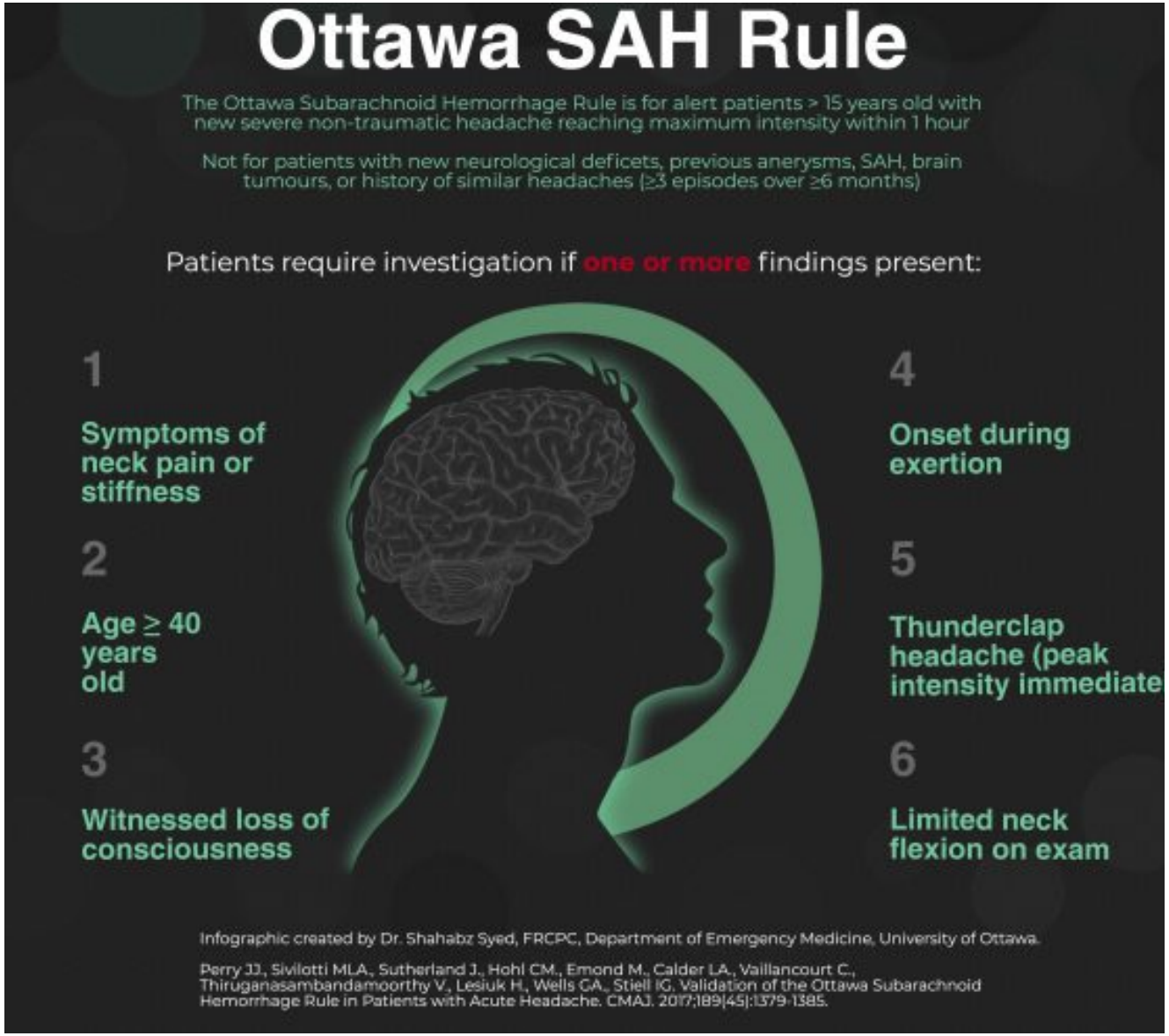
- Early deterioration is common
  - 22% of ICH patients transported by EMS experience a decrease in GCS of ≥2 during transport[1]
  - 22.6% of ICH who present with GCS 13-15 experience a drop in GCS of ≥ 2 points while in the ED[2]

	No Stroke Code	Stroke Code	P-value
Door-to-CT	48	24	<0.001
Door-to Coagulation test results	69	39	<0.001
Door-to-hemostatic medication	99	63	0.005
Door-to-ICU	228	176	<0.001

1. Moon, J. S., et al. Crit Care Med 2008:36(1): 172-175.
2. Fan, J. S., et al. Acad Emerg Med 2012:19(2): 133-138.
3. Colton, K., et al. J Stroke Cerebrovasc Dis 2020:29(2): 104552.

Are there situations where CT can be avoided?

- Several validation studies (mostly from same group in Canada)
- Sensitivity 100% (95% CI 94.6% to 100%)
- Specificity 13.6% (95% CI 13.1% to 15.8%)
- ACEP Clinical Policy on Headache:
  - Level B recommendations. Use the Ottawa Subarachnoid Hemorrhage Rule as a decision rule that has high sensitivity to rule out SAH, but low specificity to rule in SAH, for patients presenting to the ED with a normal neurologic examination result and peak headache severity within 1 hour of onset of pain symptoms.



What if CT is Negative?

- CT + LP is safe and sensitive to exclude diagnosis of SAH[1]

- Within 6 hours of symptom onset
  - Sensitivity of CT approaches 100%
    - Negative Likelihood Ratio 0.01 [0.0-0.04])[2]
  - ACEP Clinical Policy on Headache:
    - **"Level B recommendations**. Use a normal non-contrast head CT performed within 6 hours of symptom onset in an ED headache patient with a normal neurologic examination, to rule out nontraumatic SAH"[3]

- Beyond 6 hours of symptom onset
  - CT still fairly sensitive
  - LP is invasive and can be inconclusive
  - ACEP Clinical Policy on Headache:
    - **"Level C recommendations**. Perform LP or CTA to safely rule out SAH in the adult ED patient who is still considered to be at risk for SAH after a negative non-contrast head CT result." [3]
    - Benefit: eliminate painful, time-consuming procedure
    - Risk: Incidental aneurysm identification, increase testing/costs/radiation

1. Connolly, E. S., et al. Stroke 2012:43(6): 1711-1737.
2. Carpenter, C. R., et al. Acad Emerg Med 2016:23(9): 963-1003.
3. Godwin, S. A., et al. Ann Emerg Med 2019:74(4): e41-e74.

Thank You

Disclaimer

The Emergency Quality Network (E-QUAL) Stroke Initiative is sponsored through a research collaboration with Genentech, Inc. The sponsor is an active research collaborator in the E-QUAL Network Stroke Initiative but has no ownership in the Emergency Quality Network. The design and dissemination of this research, as well as the selection of content, the use of the Emergency Quality Network, and the selection of findings for publication are ultimately at the discretion of the American College of Emergency Physicians.

Factors Predictive of Hemorrhagic Stroke (vs. Ischemic Stroke)

Table 2. Accuracy of Findings for Diagnosing Hemorrhagic Stroke[a]

Finding	No. of Patients	Hemorrhage, No. (%)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive LR (95% CI)	Negative LR (95% CI)
Risk factors						
Age ≤60 y[35]	1510	237 (16)	50 (43-56)	70 (68-73)	1.7 (1.4-1.9)	0.71 (0.63-0.82)
Alcohol consumption[10]	178	27 (15)	48 (29-67)	70 (62-77)	1.6 (1-2.5)	0.75 (0.51-1.1)
Male[16-18,28,35]	3107	635 (20)	57 (53-61)	51 (47-54)	1.2 (1.1-1.3)	0.85 (0.77-0.94)
Hypertension[10,11,16-18,28,35]	4193	776 (19)	68 (60-75)	40 (33-47)	1.1 (1.0-1.2)	0.88 (0.77-1.01)
Cigarette smoking[11,28]	1187	216 (18)	38 (22-55)	52 (45-79)	0.79 (0.45-1.4)	1.2 (0.79-1.8)

Runchey S et al. JAMA 2010;303(22):2280-6

Final Diagnosis Among ED Patients with Worst Headache of Life Among Patients with and without history of Migraine

Study Group (n = 132)		Comparison Group (n = 92)	
Diagnosis	Frequency (%)	Diagnosis	Frequency (%)
Migraine	103 (78.0%)	Migraine	47 (51.1%)
Sinusitis	8 (6.1%)	Contusion	11 (13.0%)
Meningitis	5 (3.8%)	Sinusitis	4 (4.3%)
Tension	3 (2.3%)	Brain metastases	2 (2.2%)
Occipital neuralgia	2 (1.5%)	Meningitis	2 (2.2%)
Influenza	2 (1.5%)	ICP rise	2 (2.2%)
Acidosis	1 (0.8%)	Concussion	2 (2.2%)
Blood pressure rise	1 (0.8%)	Subcortical hemorrhage	2 (2.2%)
Chiari syndrome	1 (0.8%)	Subdural hematoma	2 (2.2%)
Giant cell arteritis	1 (0.8%)	Aneurysm	1 (1.1%)
Marijuana-induced headache	1 (0.8%)	Benign paroxysmal vertigo	1 (1.1%)
Pseudotumor cerebri	1 (0.8%)	Brain tumor	1 (1.1%)
Postpartum headache	1 (0.8%)	Cephalgia	1 (1.1%)
		CVA	1 (1.1%)
		Gunshot	1 (1.1%)
		Hypoxia	1 (1.1%)
		Intraparenchymal hematoma	1 (1.1%)
		Intraventricular hemorrhage	1 (1.1%)

Prospective Implementation of the Ottawa Subarachnoid Hemorrhage Rule and 6-Hour Computed Tomography Rule

Jeffrey J. Perry, MD, MSc; Marco L.A. Sivilotti, MD, MSc; Marcel Émond, MD, MSc; Corinne M. Hohl, MD, MHSc; Maryam Khan, MSc; Howard Lesiuk, MD; Kasim Abdulaziz, MSc; George A. Wells, PhD; Ian G. Stiell, MD, MSc

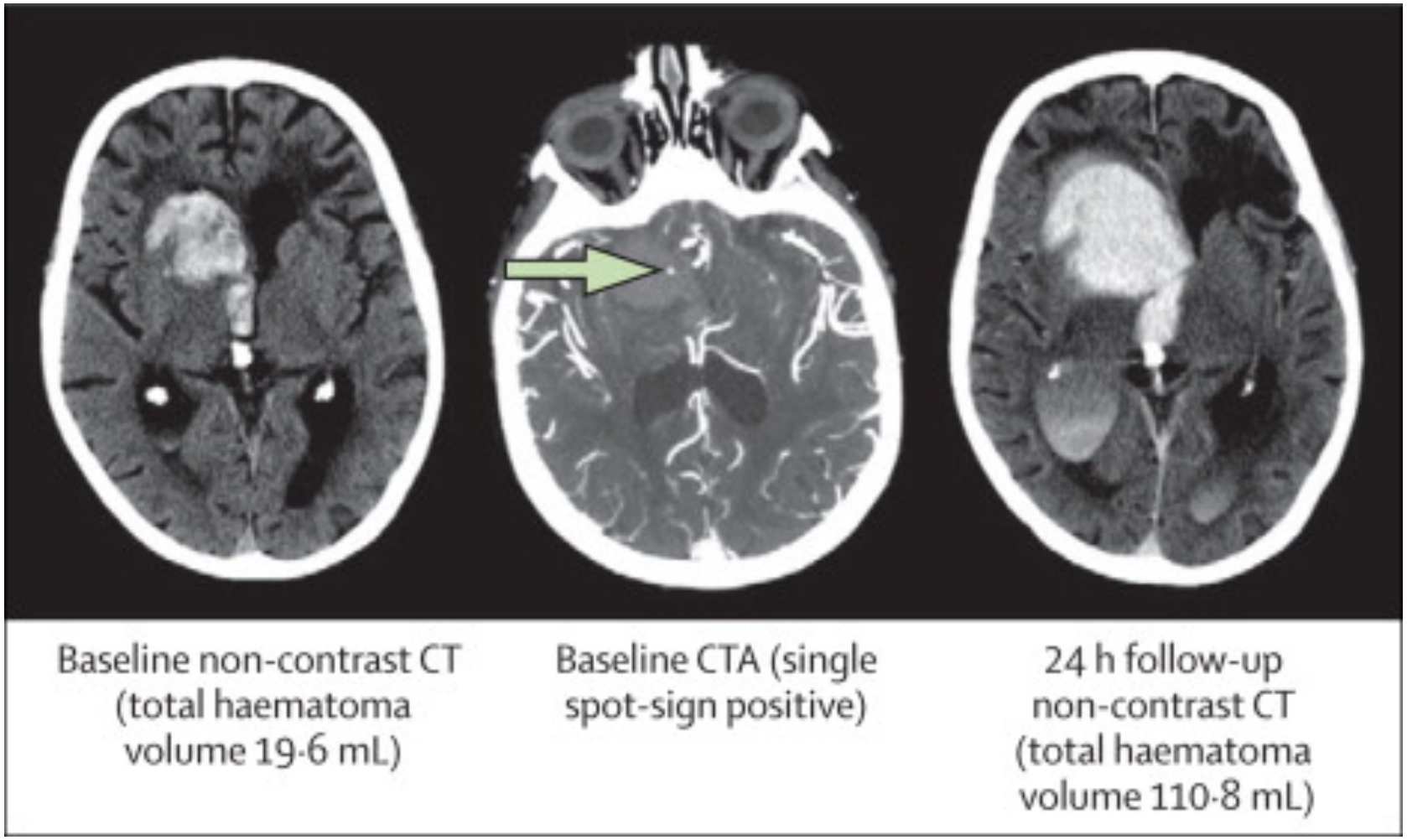
Background and Purpose—The Ottawa subarachnoid hemorrhage (SAH) rule identifies patients with headache requiring no testing for SAH, while the 6-hour computed tomography (CT) rule guides when to forgo a lumbar puncture. Our objectives were to: (1) estimate the clinical impact of the Ottawa SAH rule and the 6-hour-CT rule on testing rates (ie, CT, lumbar puncture, CT angiography); (2) validate the 6-hour-CT rule for SAH when applied prospectively in a new cohort of patients.

Methods—We conducted a multicenter prospective before/after implementation study from 2011 to 2016 with 6 months follow-up at 6 tertiary-care Canadian Academic Emergency Departments. Consecutive alert, neurologically intact adults with headache were included. For intervention period, physicians were given a 1-hour lecture, pocket cards, posters were installed, and physicians indicated Ottawa SAH rule criteria when ordering CTs. SAH was defined by blood on CT, xanthochromia in cerebrospinal fluid, or $>1\times10^6$/L red blood cells in cerebrospinal fluid with aneurysm.

Results—We enrolled 3672 patients, 1743 before and 1929 after implementation, including 188 with SAH. Proportions undergoing CT was unchanged (88.0% versus 87.5%; P=0.643). Lumbar puncture use decreased (38.9% versus 25.9% ; P<0.0001). Additional testing following CT (ie, lumbar puncture or CT angiography) decreased (51.3% versus 42.2%; P<0.0001). Admissions declined (9.8% versus 7.4%; P=0.011). Mean emergency department stay was unchanged (6.3±4.0 versus 6.4±4.2 hours; P=0.685). The Ottawa SAH rule was 100% (95% CI, 98.1%–100%) sensitive, and the 6-hour-CT rule was 95.5% (95% CI, 89.8–98.5) sensitive for SAH. The 6-hour-CT rule missed 5 SAHs: 1 radiology misread, 2 incidental aneurysms, 1 nonaneurysmal cause, and 1 profoundly anemic patient.

Conclusions—The Ottawa SAH rule and the 6-hour-CT rule are highly sensitive and can be used routinely when SAH is considered in patients with headache. Implementing both rules was associated with a meaningful decrease in testing and admissions to hospital. **(*Stroke*. 2020;51:424-430. DOI: 10.1161/STROKEAHA.119.026969.)**

CT Angiogram in ICH: Spot Sign



Baseline non-contrast CT (total haematoma volume 19·6 mL)

Baseline CTA (single spot-sign positive)

24 h follow-up non-contrast CT (total haematoma volume 110·8 mL)

https://www.thelancet.com/cms/attachment/2005796342/2025318374/gr1.jpg