



RICORS - ICTUS



III Stroke Congress

NEW INSIGHTS AND PERSPECTIVES ON INTRACEREBRAL HEMORRHAGE:

A COMPREHENSIVE UPDATE

Ischemic Stroke Meeting. Spanish Stroke Research Network

**Imaging biomarkers:
what to look out for**

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DISCLOSURES

- Expert meeting honoraria for EMG-REG International
 - Expert meeting honoraria and consulting for AstraZeneca
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OUTLINE

ICH etiology

- Etiologic Classification
- Vascular Imaging
- Added Value of Magnetic Resonance Imaging (MRI)

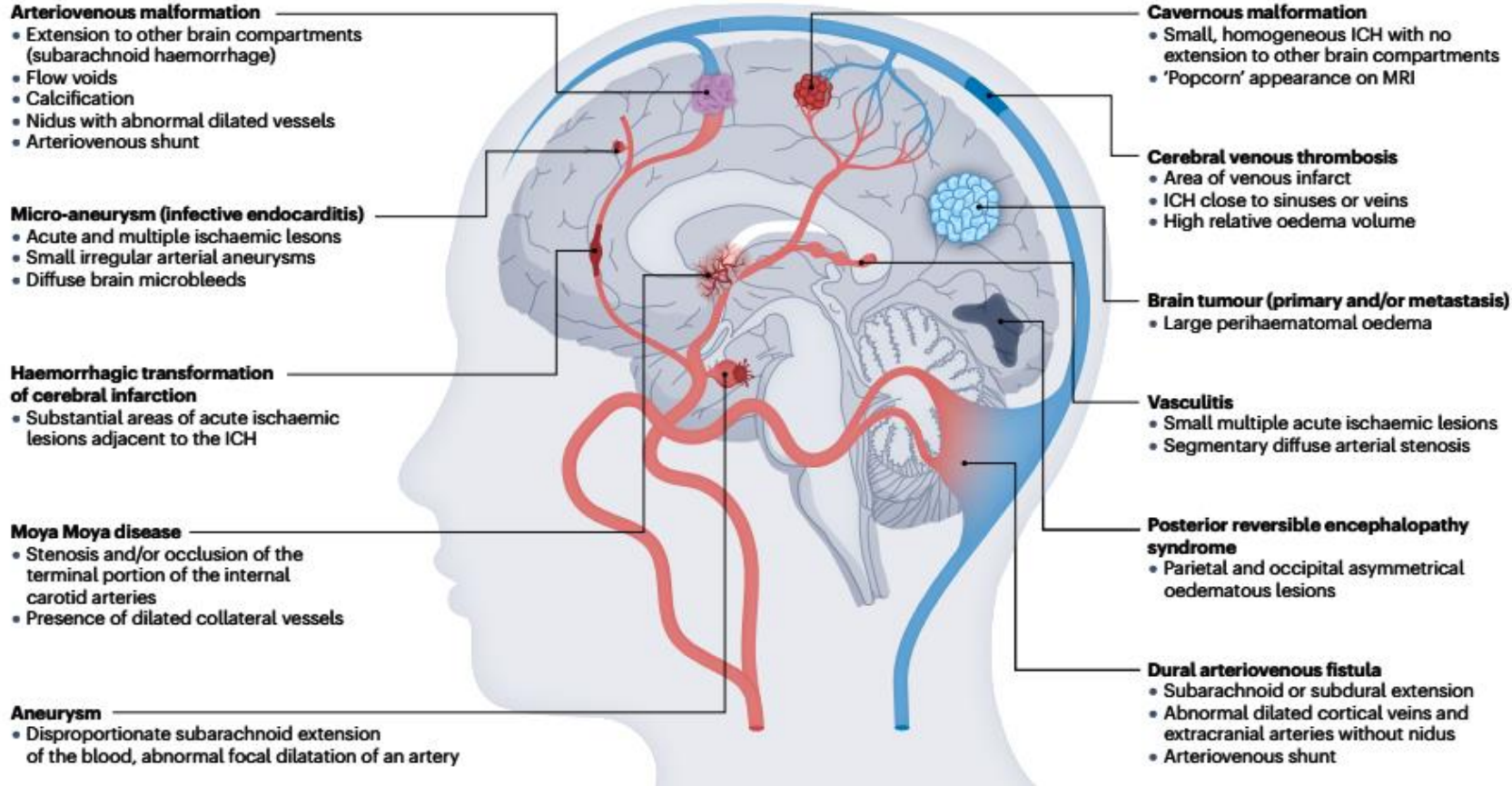
HEMATOMA EXPANSION (HE)

- CTA Spot Sign
- Non-contrast CT (NCCT) features

OUTCOME

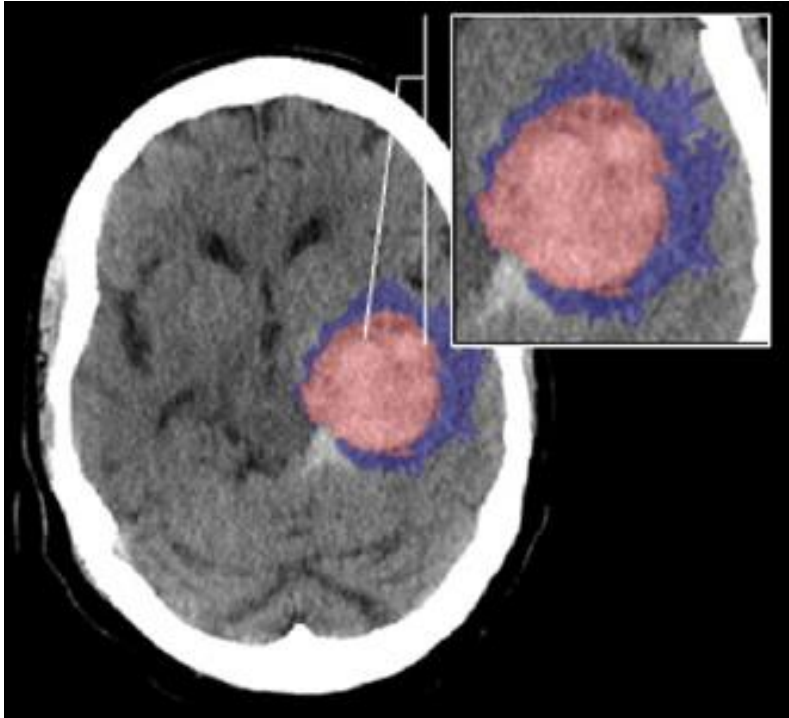
- Imaging predictors of poor outcome
 - Prognostication timing
-

ICH ETIOLOGY



**75 % “Primary”
CEREBRAL SMALL
VESSEL DISEASE**

**25% “Secondary”
MACROVASCULAR
NON-MACROVASCULAR**



Disproportionate Edema
→ Tumor



Hyperdense Veins
→ CVT



Calcification
→ AVM

NCCT – Cerebral Amyloid Angiopathy

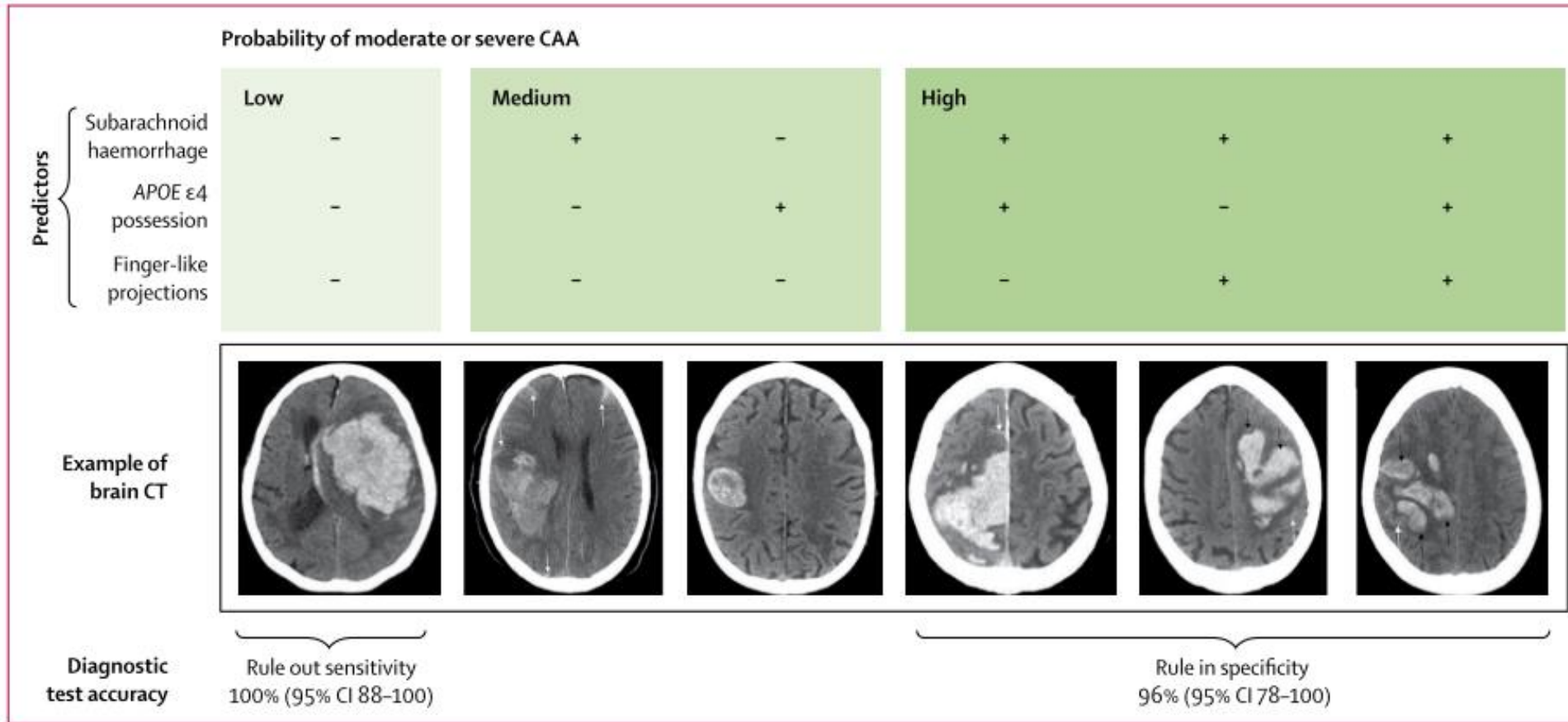


Figure 3: Categorisation of probability of lobar intracerebral haemorrhage associated with moderate or severe cerebral amyloid angiopathy according to the three predictor variables, with example CT images

RED FLAGS

Patient characteristics and NCCT (DIAGRAM score)							
Age 18-50 years			Age 51-70 years				
	Deep	Lobar	Posterior Fossa		Deep	Lobar	Posterior Fossa
SVD	2	13	.	SVD	1	4	11
No SVD	17	55	76	No SVD	6	27	50

Patient characteristics, NCCT and CTA (DIAGRAM+ score)							
CTA Negative							
Age 18-50 years			Age 51-70 years				
	Deep	Lobar	Posterior Fossa		Deep	Lobar	Posterior Fossa
SVD	1	5	.	SVD	1	2	4
No SVD	9	29	51	No SVD	3	11	24
CTA Positive							
Age 18-50 years			Age 51-70 years				
	Deep	Lobar	Posterior Fossa		Deep	Lobar	Posterior Fossa
SVD	14	.	.	SVD	.	17	34
No SVD	56	84	93	No SVD	28	61	79

Low	1-5%
Intermediate	6-25%
High	>25%

CLINICAL

- Young age
- No history of hypertension
- Thunderclap headache

IMAGING

- Lobar – Infratentorial location
- No CT signs of SVD
- Extensive IVH
- CT calcifications

NEGATIVE CTA

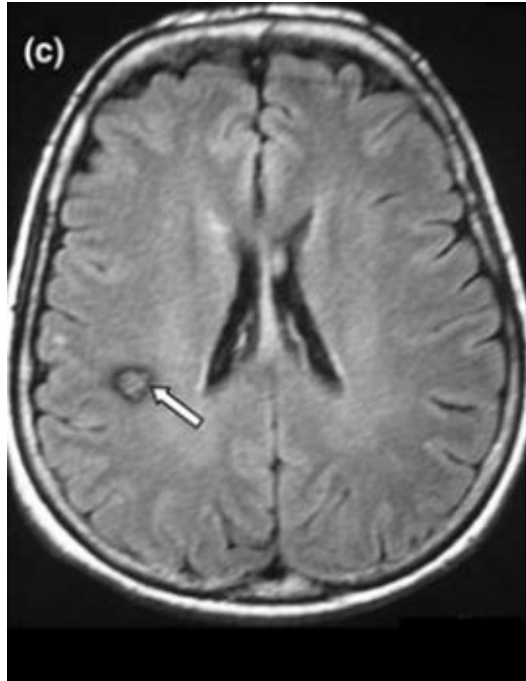
Table 3. Yield of intracranial macrovascular causes from the optimised model compared to the actual yield.

Predictors			Observed proportion of patients with a macrovascular cause for each combination of predictors in our dataset, % (95% CI) [raw numbers]	Model predicted proportion of patients with a macrovascular cause for each combination of predictors, %
CTA result	SVD on CT	HTN		
Positive	No	No	95.3% (84.2–99.4) [41/43]	95.8%
Positive	No	Yes	85.7% (57.2–98.2) [12/14]	86.4%
Positive	Yes	No	80.0% (44.4–97.4) [8/10]	83.7%
Positive	Yes	Yes	75.0% (19.4–99.4) [3/4]	59.0%
Negative	No	No	23.1% (12.5–36.8) [12/52]	22.1%
Negative	No	Yes	5.9% (0.1–28.7) [1/17]	7.3%
Negative	Yes	No	6.3% (0.2–30.2) [1/16]	6.1%
Negative	Yes	Yes	0% [0/17]	1.8%

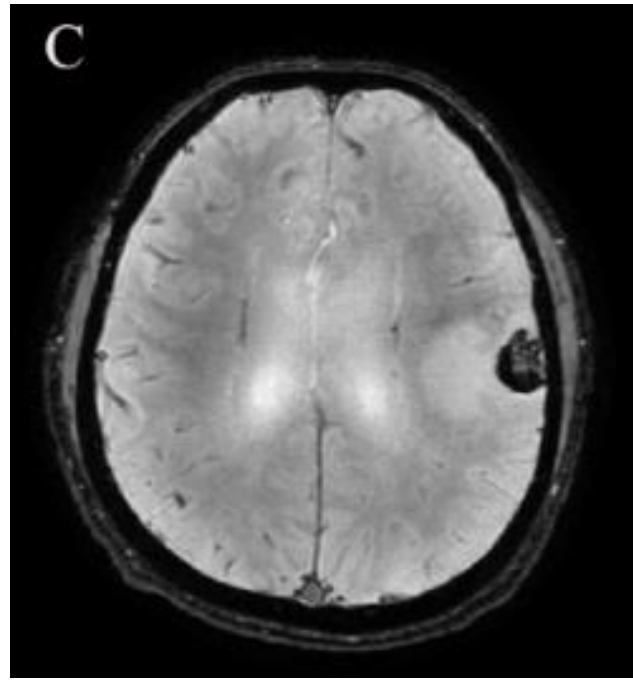
CTA: computed tomography angiography; HTN: hypertension; SVD: small vessel disease.

'Positive' includes CTA showing a 'definite' or 'possible' macrovascular cause; 'negative' denotes CTA showing no suspicion of a vascular malformation.

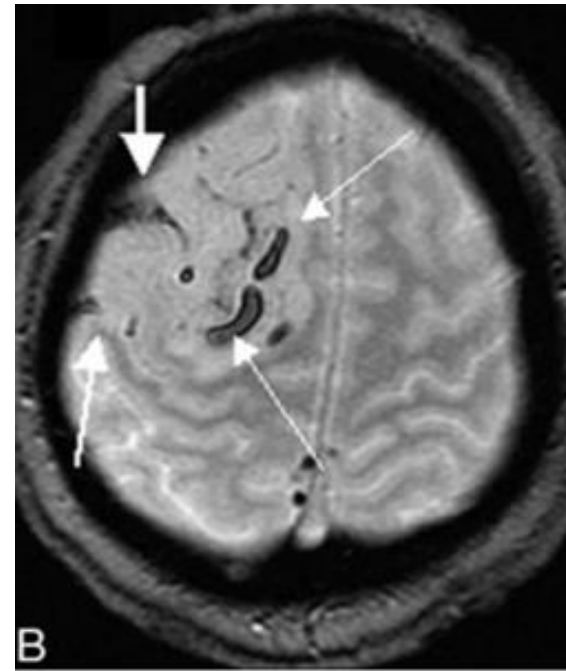
MRI – ADDED VALUE



CAVERNOMA



TUMOR

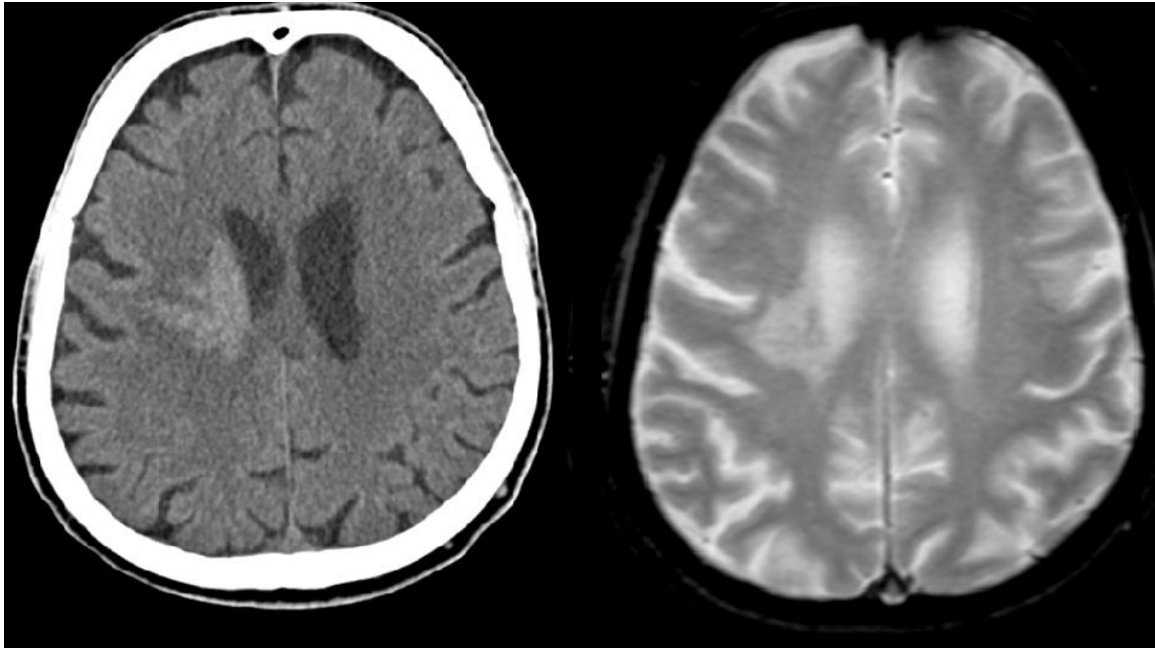


CORTICAL CVT

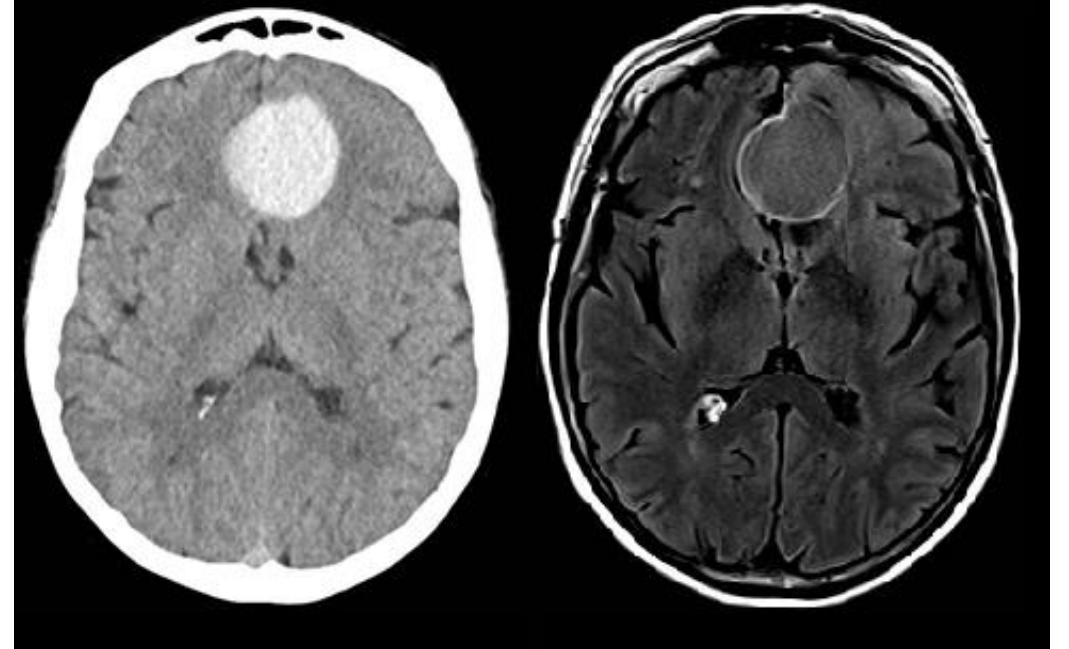


Small Vessel

MRI – ADDED VALUE

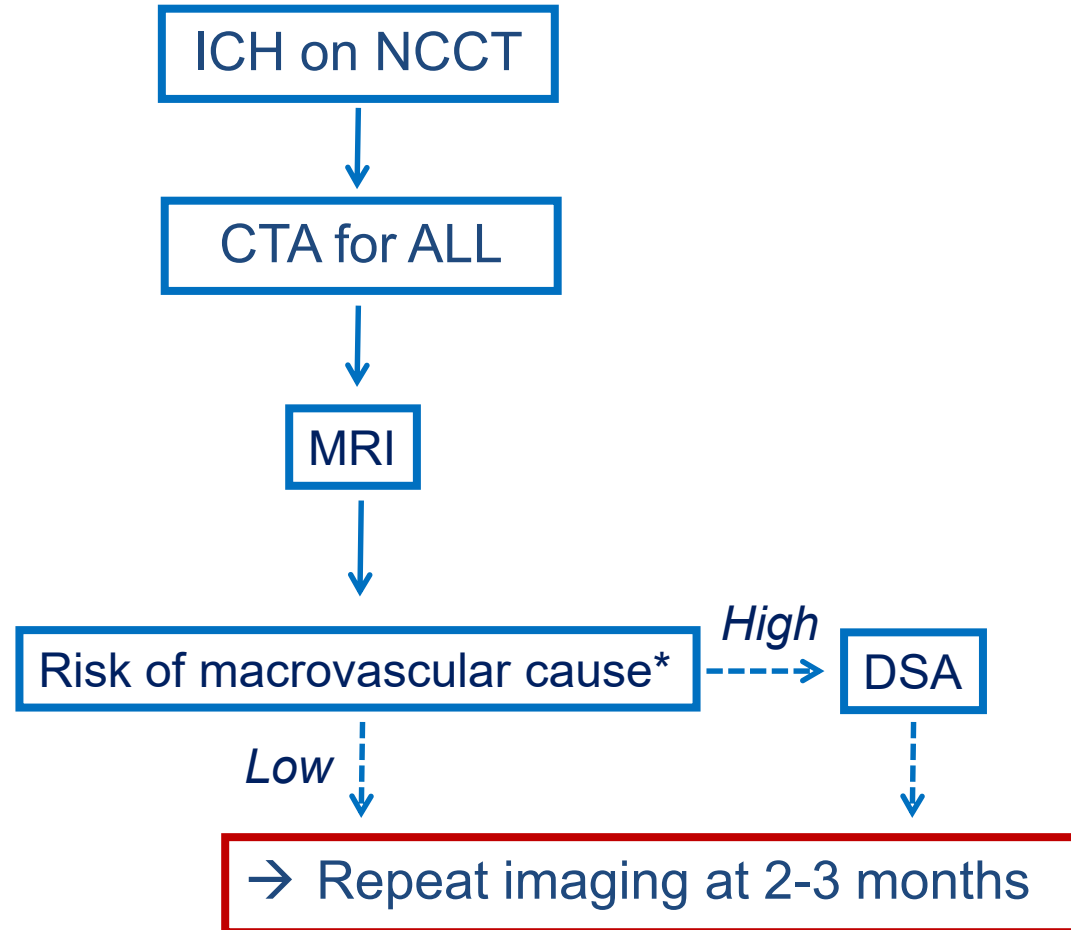


CNS Lymphoma



Epidermoid Cyst

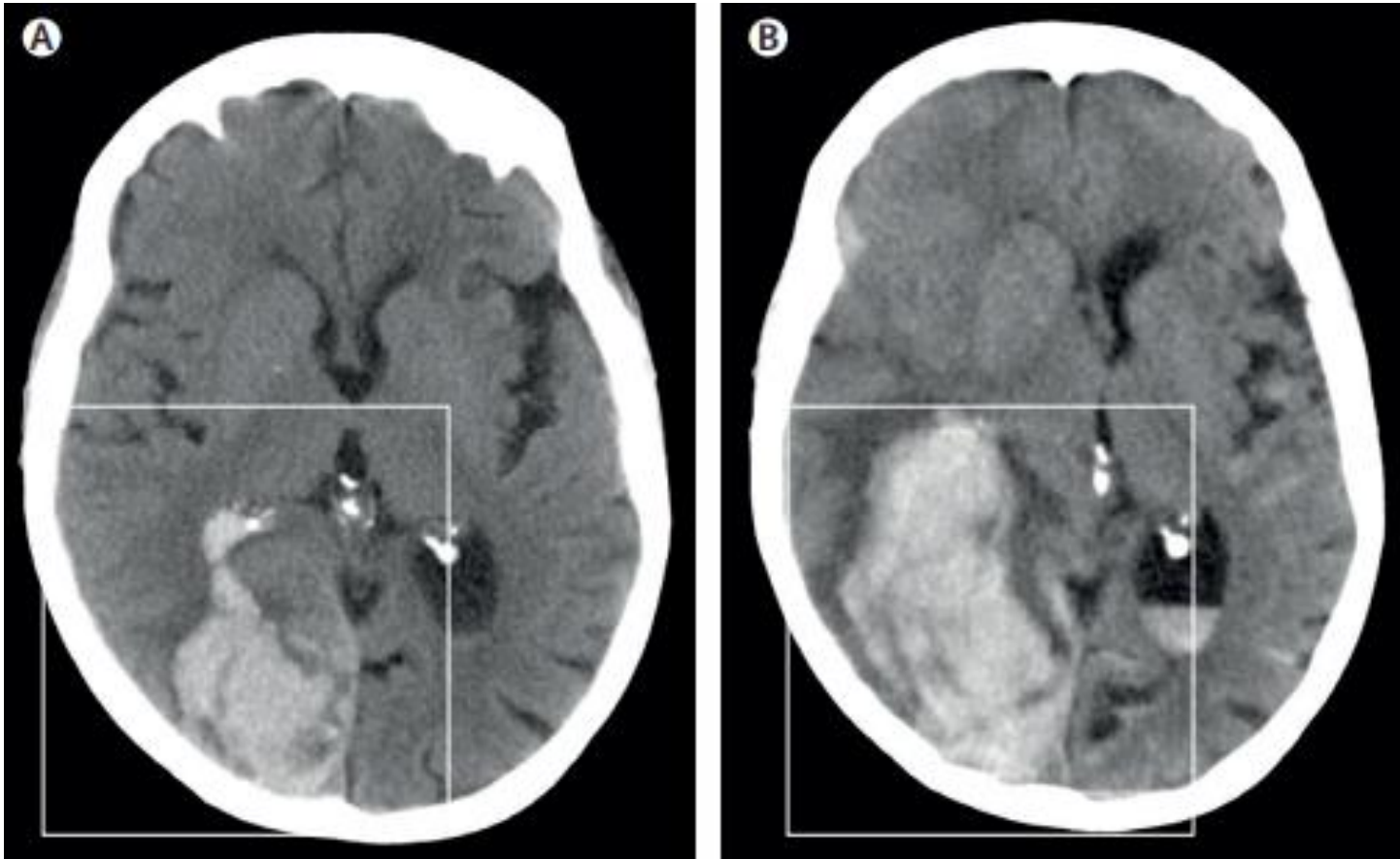
CLINICAL PRACTICE



***High Risk of Macrovascular Cause**

- Young Age
 - Lobar location
 - Infratentorial location
 - No history of hypertension
 - No signs of small vessel disease
-

HEMATOMA EXPANSION



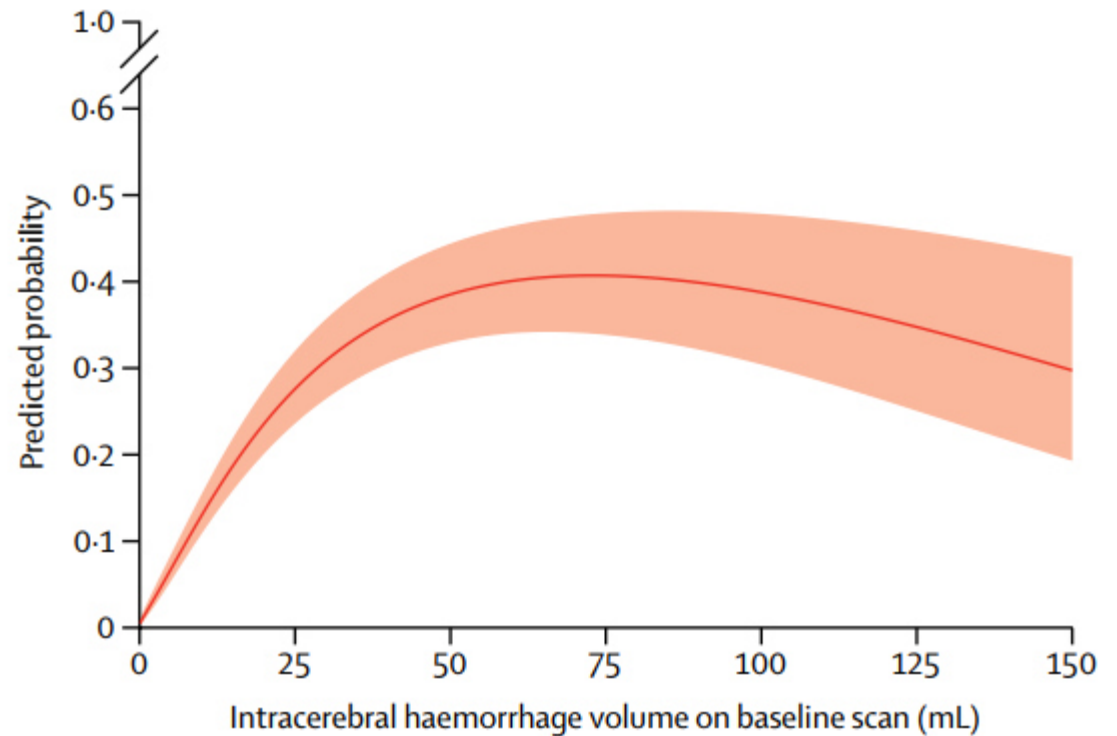
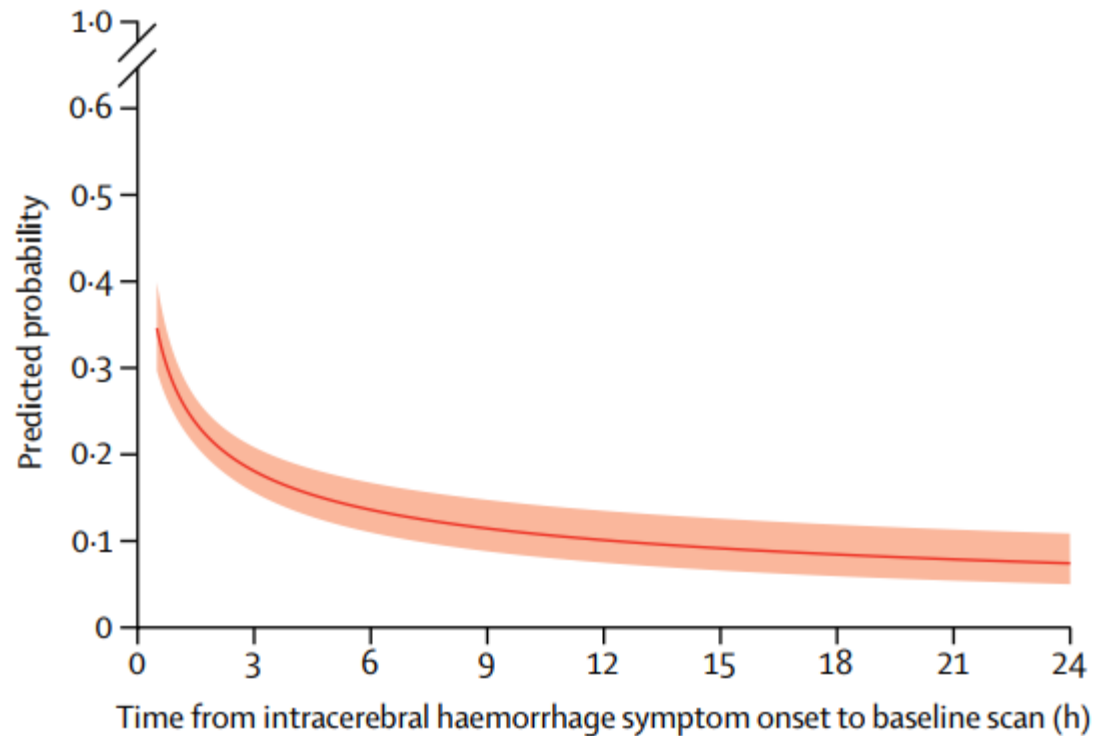
ICH is a dynamic Disease

HE frequency:

- Overall: 20%
- Early presenters (< 6h): 33%
- Anticoagulation: > 50%

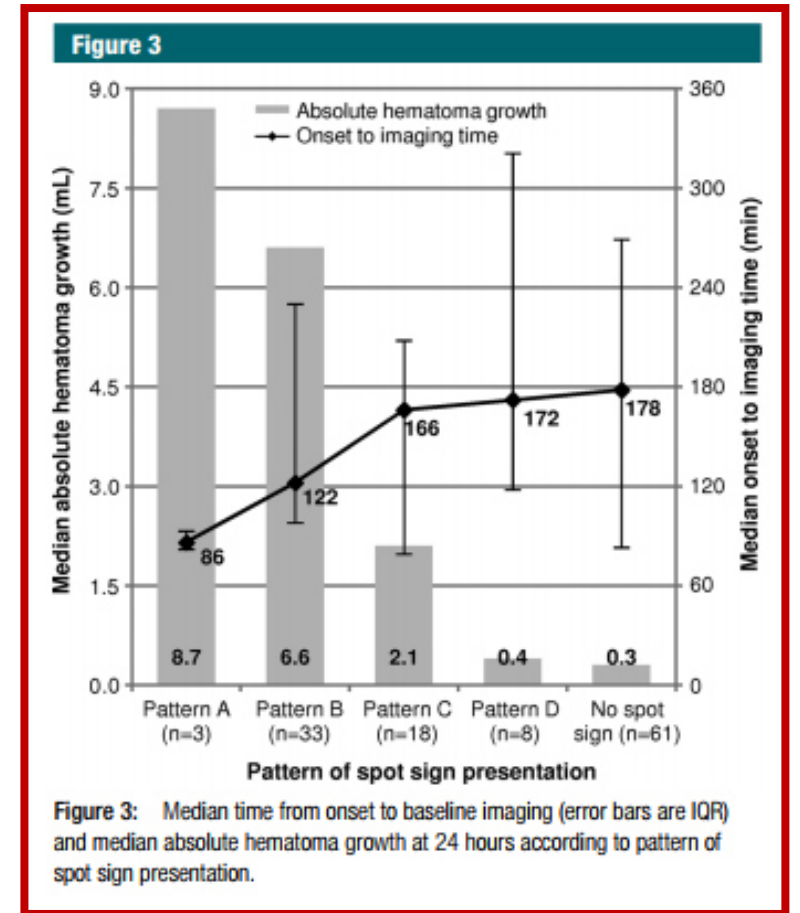
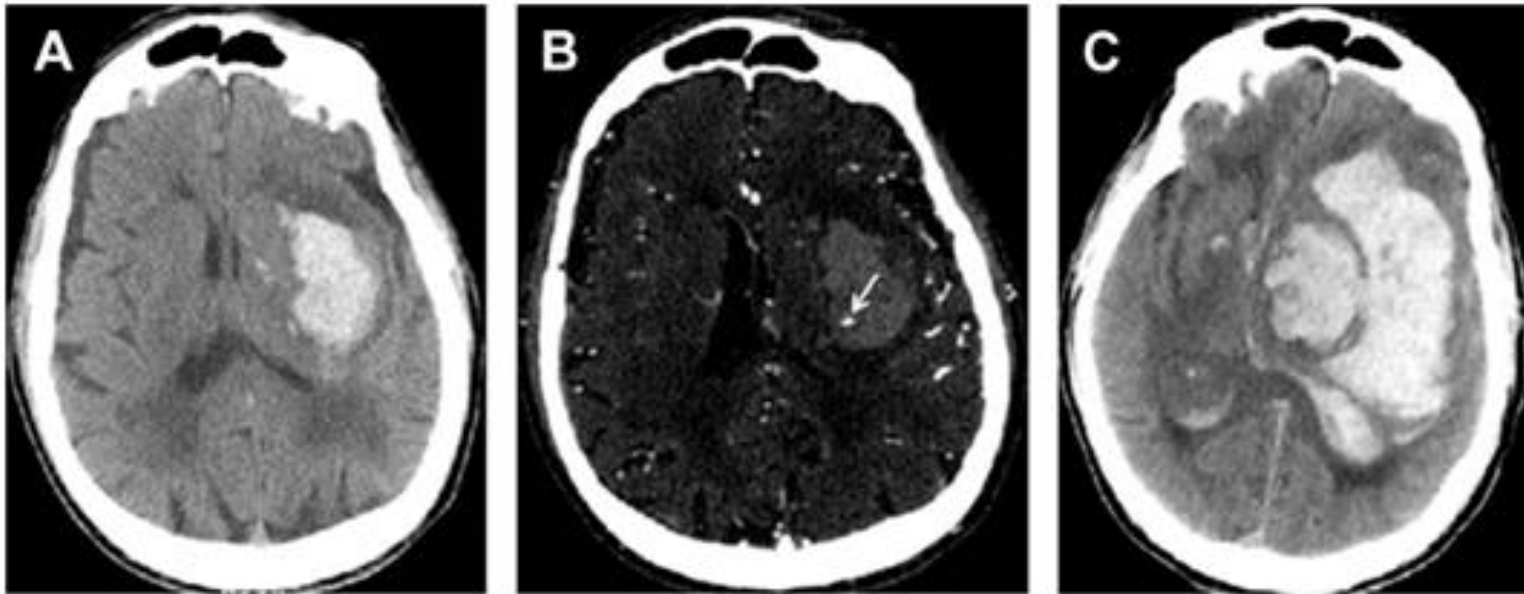
Definition

- $\geq 33\%$ and / or $\geq 6\text{ mL}$

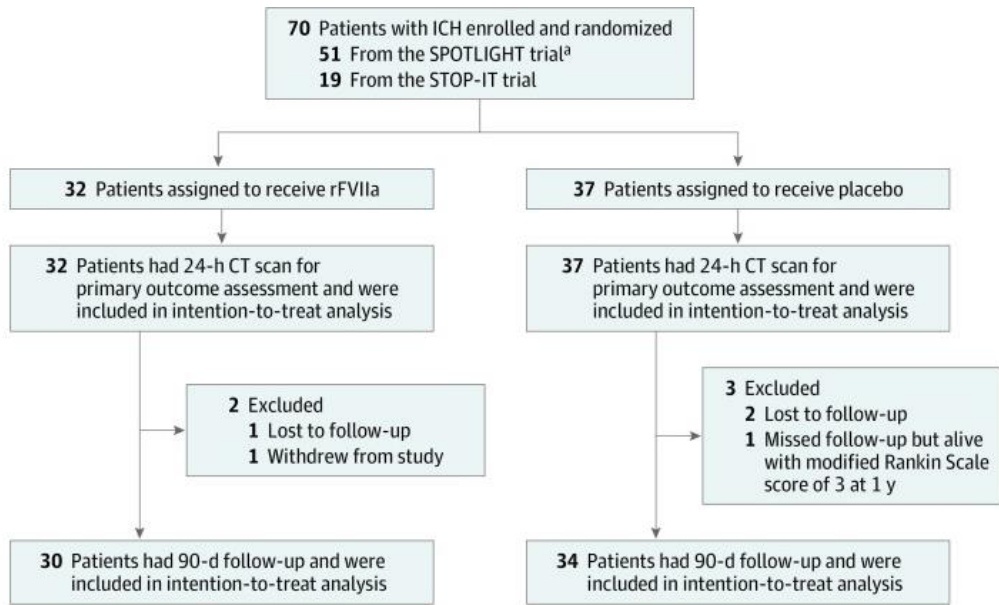


Ultra-Early Hematoma Growth: ICH volume/imaging time \rightarrow mL/h

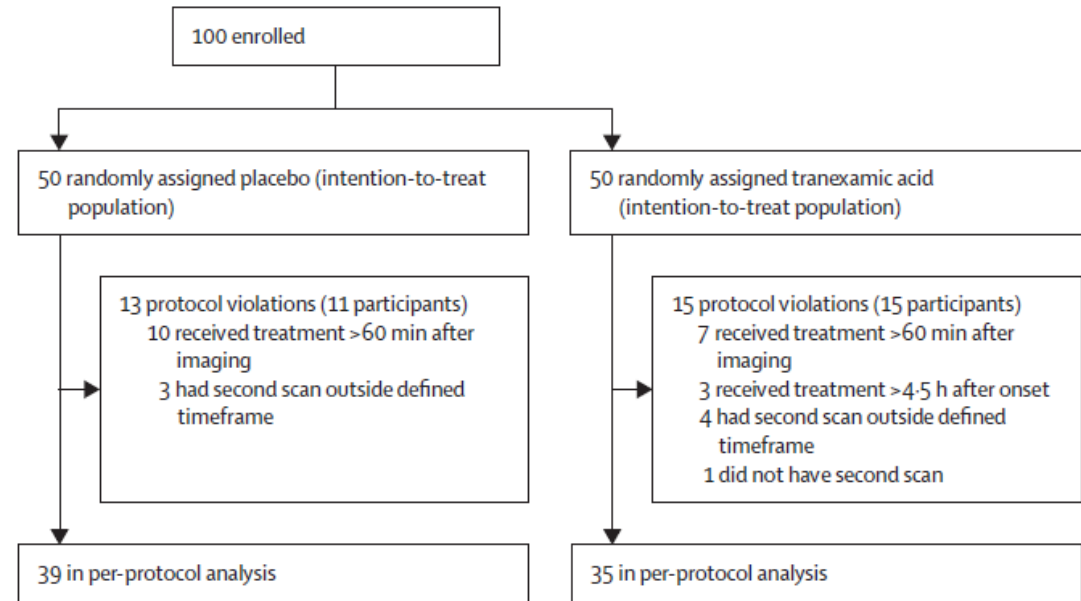
CTA SPOT SIGN



CTA SPOT SIGN IN CLINICAL TRIALS

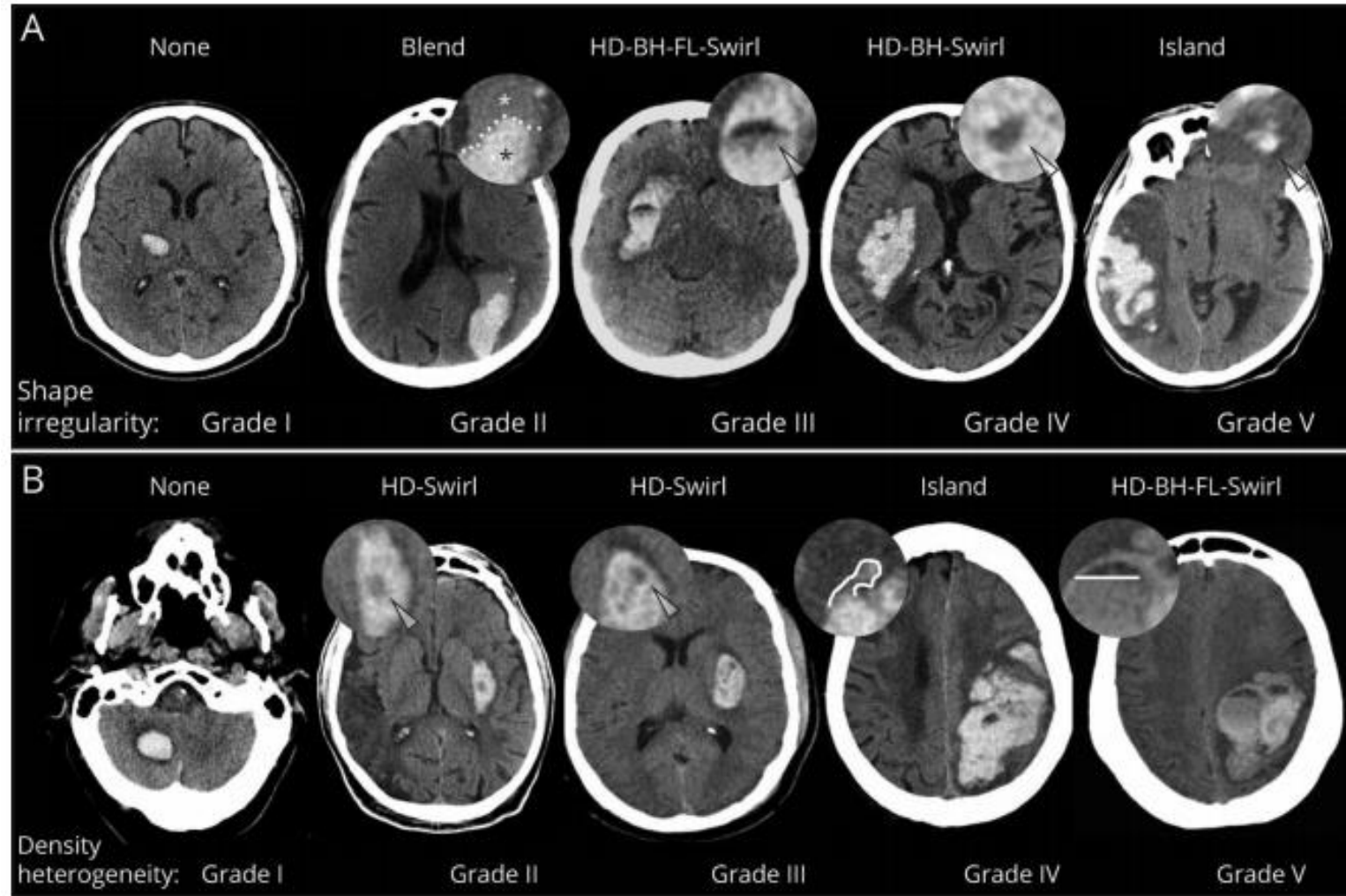


26 sites
US and Canada
5+ years
→ 70 patients

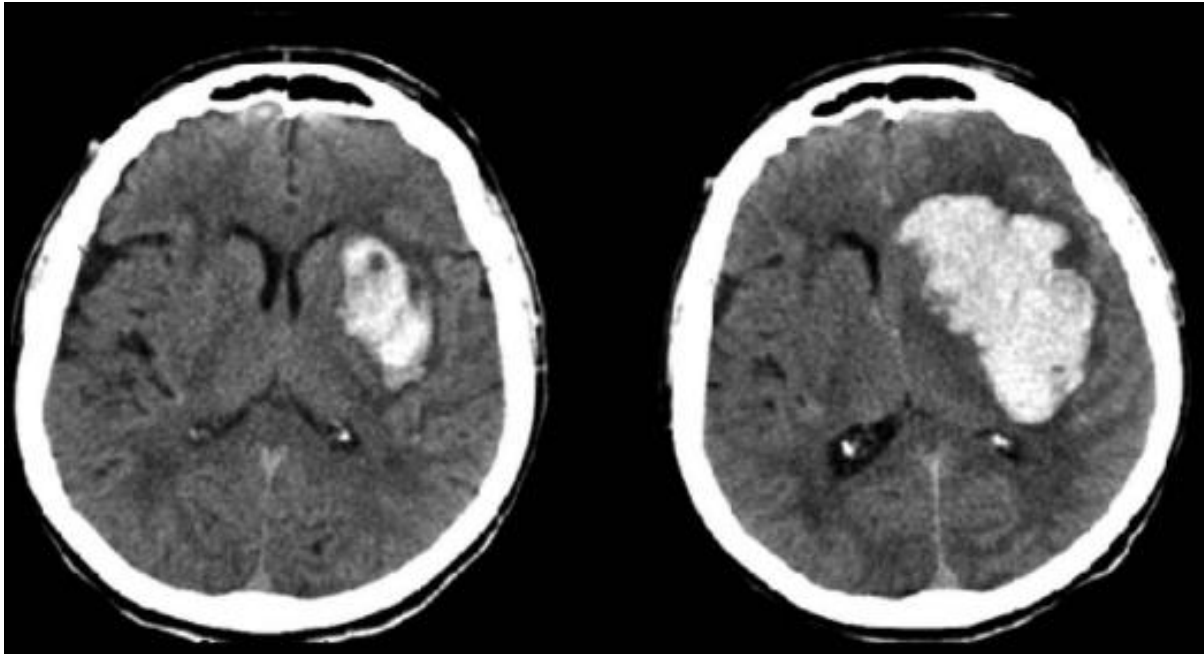


13 sites
Australia
6+ years
→ 100 patients

NCCT MARKERS



NCCT MARKERS



Standards for Detecting, Interpreting, and Reporting Noncontrast Computed Tomographic Markers of Intracerebral Hemorrhage Expansion

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Significant hematoma expansion (HE) affects one-fifth of people within 24 hours after acute intracerebral hemorrhage (ICH), and its prevention is an appealing treatment target. Although the computed tomography (CT)-angiography spot sign predicts HE, only a minority of ICH patients receive contrast injection. Conversely, noncontrast CT (NCCT) is used to diagnose nearly all ICH, so NCCT markers represent a widely available alternative for prediction of HE. However, different NCCT signs describe similar features, with lack of consensus on the optimal image acquisition protocol, assessment, terminology, and diagnostic criteria. In this review, we propose practical guidelines for detecting, interpreting, and reporting NCCT predictors of HE.

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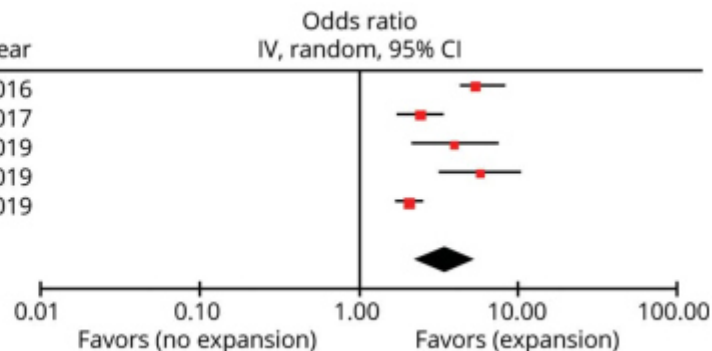
D. Hypodensity

Study or subgroup	Log (odds ratio)	SE	Weight (%)	Odds ratio IV, random, 95% CI	Year
Ref #20	1.6771	0.1652	21.7	5.35 (3.87, 7.40)	2016
Ref #26	0.8796	0.1751	21.4	2.41 (1.71, 3.40)	2017
Ref #36	1.3788	0.3231	16.7	3.97 (2.11, 7.48)	2019
Ref #33	1.7299	0.3058	17.2	5.64 (3.10, 10.27)	2019
Ref #35	0.7129	0.1052	23.1	2.04 (1.66, 2.51)	2019

Total (95% CI)

Heterogeneity: Tau² = 0.23; Chi² = 31.57, df = 4 (p < 0.00001); I² = 87%

Test for overall effect: z = 5.27 (p < 0.00001)



NCCT ACCURACY

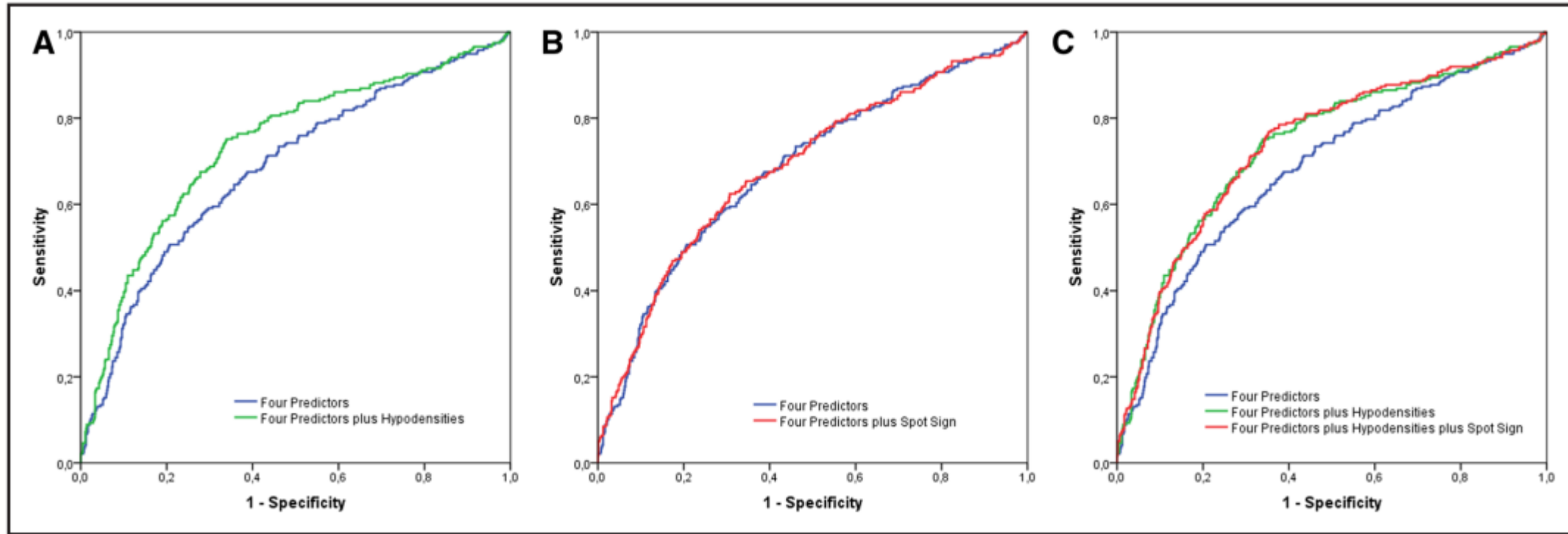


Figure 4. ROC curves for the predicted probability of hematoma expansion in patients with CTA (n=895).

A, 4 predictors: AUC, 0.68; 95% CI, 0.64 to 0.73; 4 predictors plus hypodensities: AUC, 0.74; 95% CI, 0.70 to 0.78. **B**, 4 predictors: AUC, 0.68; 95% CI, 0.64 to 0.73; 4 predictors plus spot sign: AUC, 0.69; 95% CI, 0.65 to 0.73. **C**, 4 predictors: AUC, 0.68; 95% CI, 0.64 to 0.73; 4 predictors plus hypodensities: AUC, 0.74; 95% CI, 0.70 to 0.78; 4 predictors plus hypodensities plus spot sign: AUC, 0.74; 95% CI, 0.70 to 0.78. AUC indicates area under the curve; CTA, computed tomography angiography; and ROC, receiver operating characteristic curves.

IS THE SPOR SIGN DEAD?

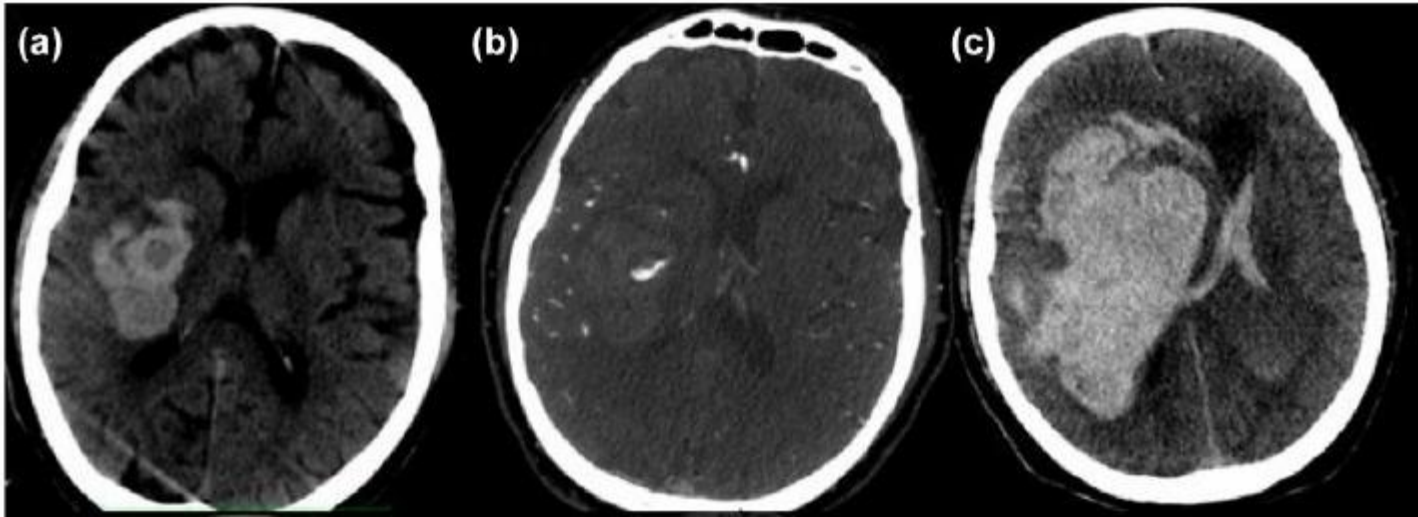
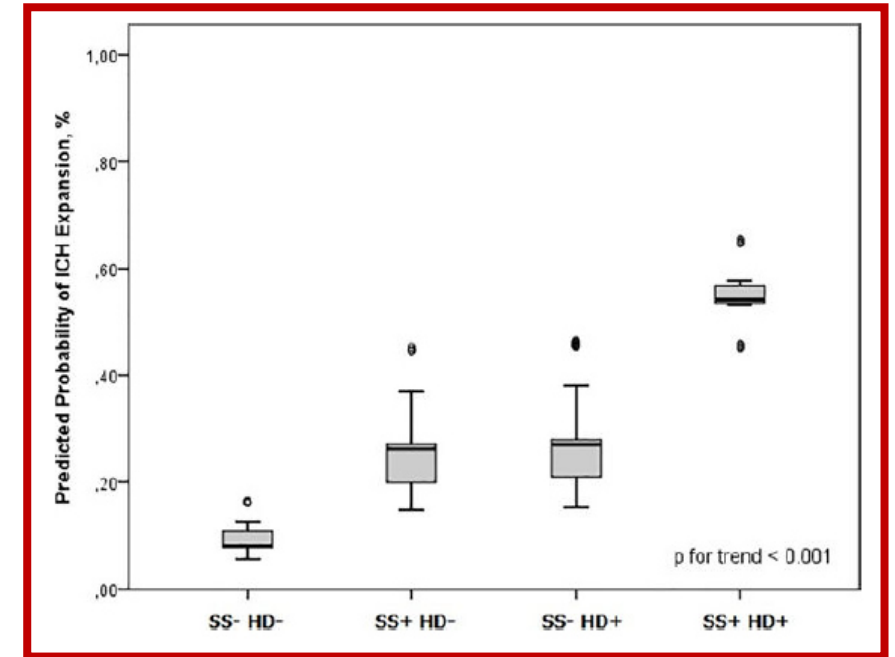


Table 3. Accuracy of spot sign and hypodensity sign at various combinations in predicting hematoma expansion (≥ 6 mL or $\geq 33\%$).

CT markers	Spot sign - hypodensity sign -	Spot sign - hypodensity sign +	Spot sign + hypodensity sign -	Spot sign + hypodensity sign + (no-colocalized)	Black-&-White sign +
Prevalence	112 (56%)	44 (22%)	18 (9%)	12 (6%)	14 (7%)
Sensitivity (95%CI)	26% (14.6%–40.3%)	18% (8.6%–31.4%)	14% (5.8%–26.7%)	12% (4.5%–24.3%)	28% (16.2%–42.5%)
Specificity (95%CI)	34% (24.5%–42.2%)	76.7% (69.1%–83.2%)	92.7% (87.3%–96.3%)	96% (91.5%–98.5%)	100% (97.6%–100%)
Positive predictive value (95%CI)	11.6% (7.5%–17.5%)	20.5% (11.7%–33.2%)	38.9% (20.7%–60.8%)	50% (25.3%–74.8%)	100% (76.8%–100%)



HE Shift Analysis

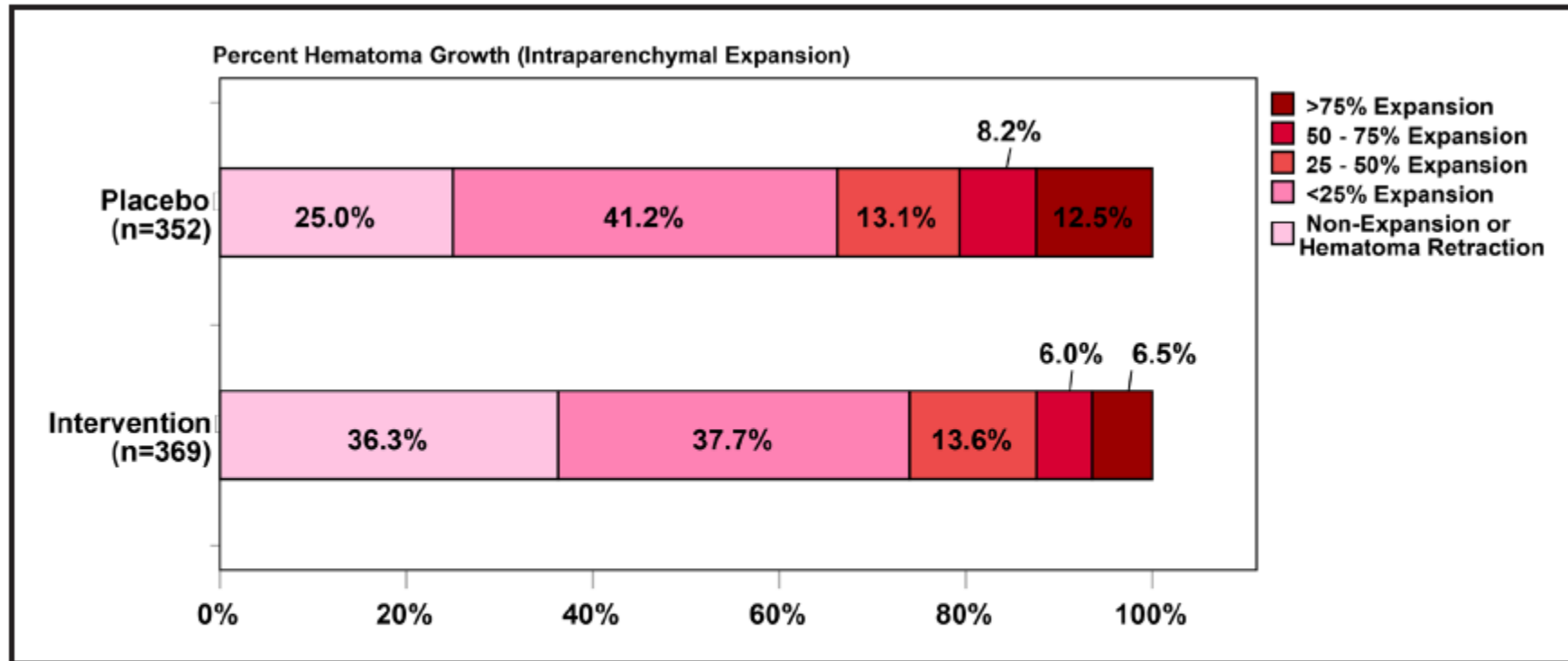
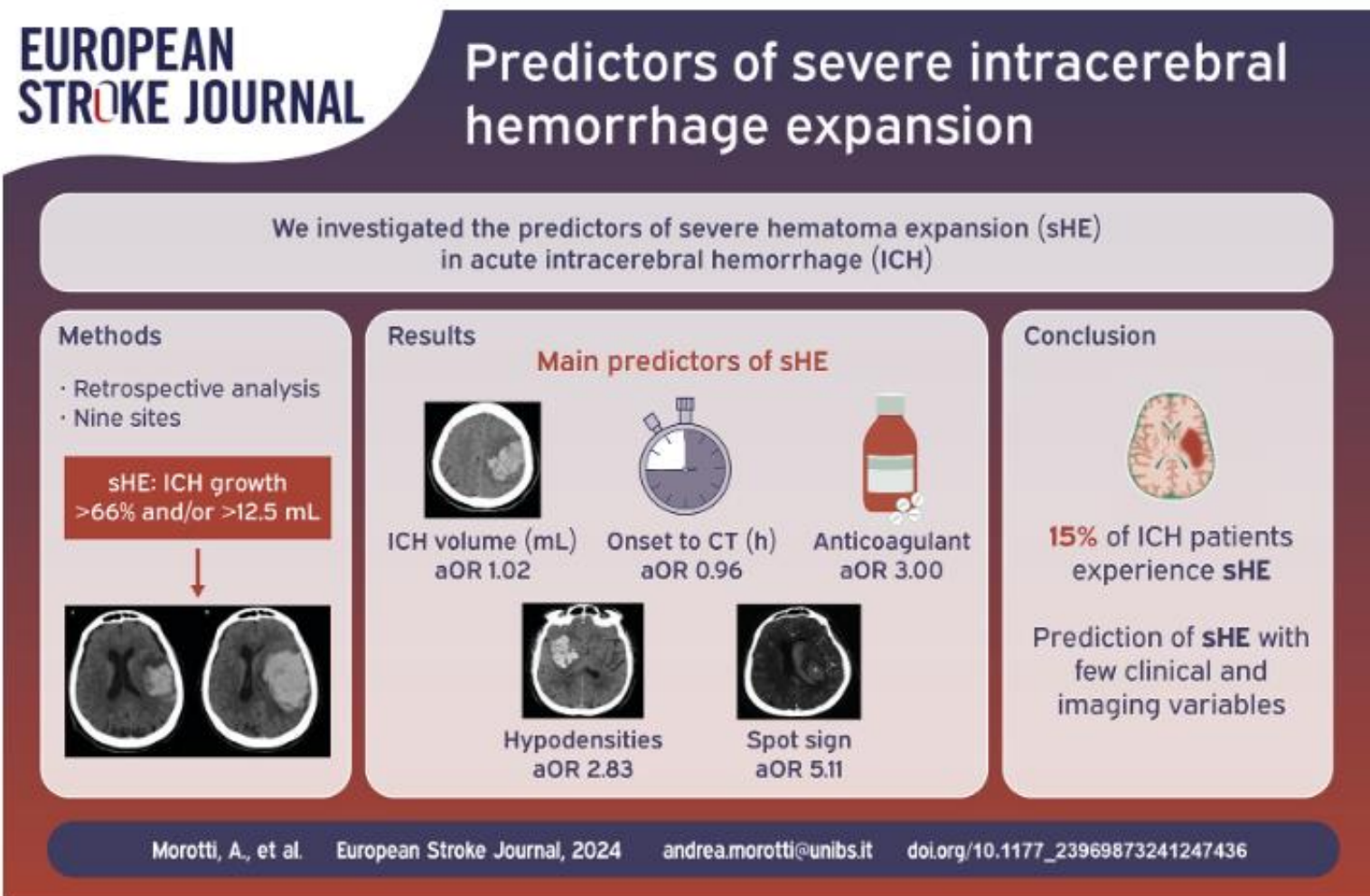


Figure 3. Polychotomous percent hematoma volume change (intraparenchymal) quintiles stratified by treatment status.

Adjusting for onset to treatment time, baseline intraparenchymal hemorrhage volume, and study (as a random effect), an ordinal analysis of percent hematoma volume change showed a significant between-group difference favoring treatment recombinant activated factor VIIa (rFVIIa) (adjusted common odds ratio; and rFVIIa [acOR], 0.61 [95% CI, 0.47–0.80]), proportional odds assumption met.

Severe HE (>66% and/or >12.5 mL)



IMAGING PREDICTORS OF OUTCOME

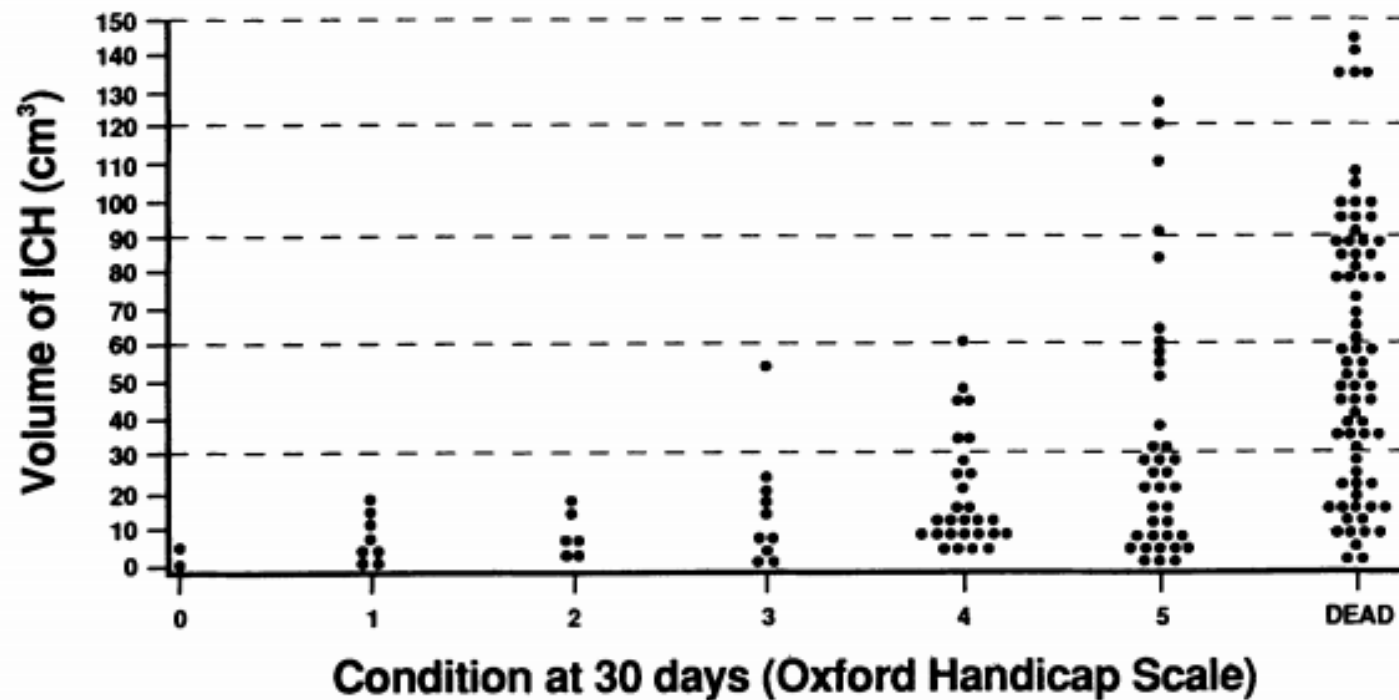
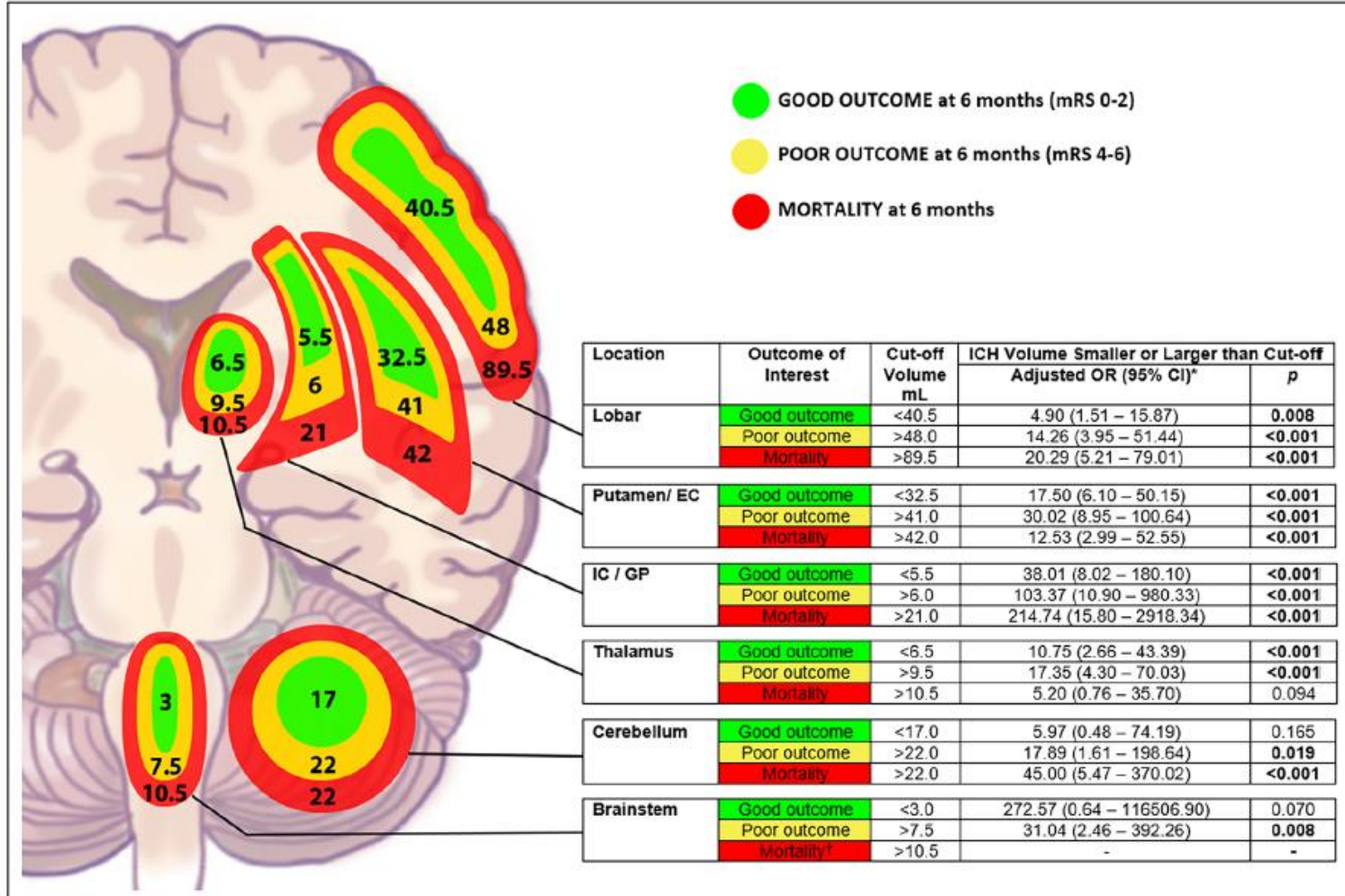
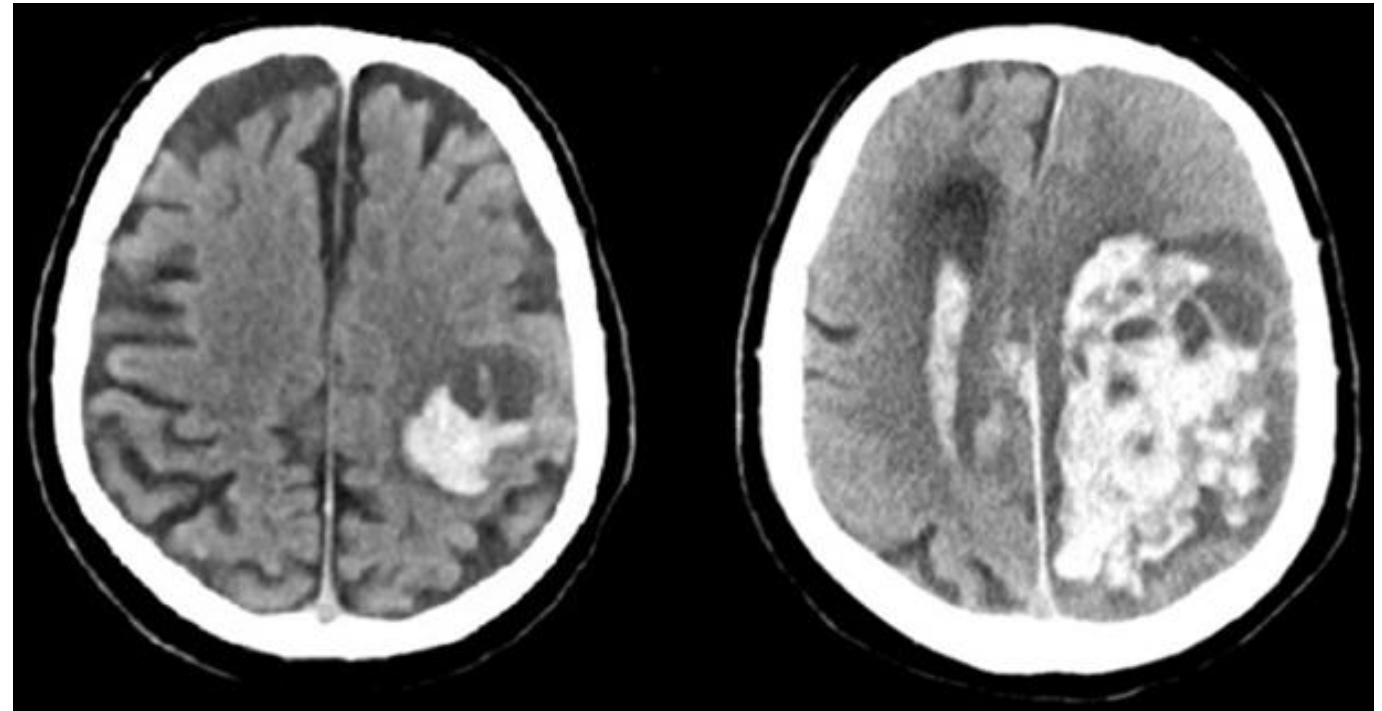
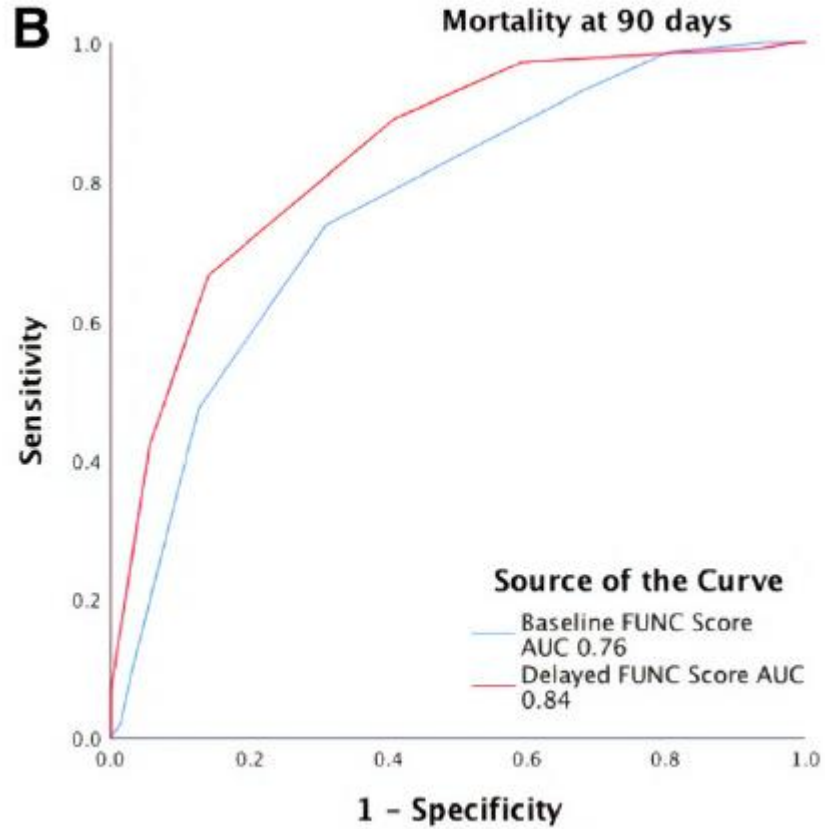


FIG 7. Plot shows 30-day outcomes for 162 patients with intracerebral hemorrhages (ICH) as measured by modified Oxford Handicap Scale according to volume of parenchymal hemorrhage. According to the modified Oxford Handicap Scale,²⁰ 0=no symptoms; 1=minor symptoms that do not interfere with life-style; 2=minor handicap; 3=moderate handicap; 4=moderately severe handicap; 5=severe handicap; 6=dead.

HIGHER VOLUME TOLERANCE IN LOBAR BLEEDINGS



ADMISSION vs DELAYED PROGNOSTICATION



TAKE HOME MESSAGES

ETIOLOGY

- Vascular imaging (**arteries** + veins)
- MRI → SVD and non macrovascular causes
- DSA → macrovascular causes
- Keep searching → repeat imaging

HEMATOMA EXPANSION

- ICH volume – Anticoagulation – NCCT time
- NCCT markers \pm CTA spot sign
- Severity Spectrum

OUTCOME

- Delayed prognostication
-

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