Funded by the European Union NextGenerationEU
RICORS - ICTUS

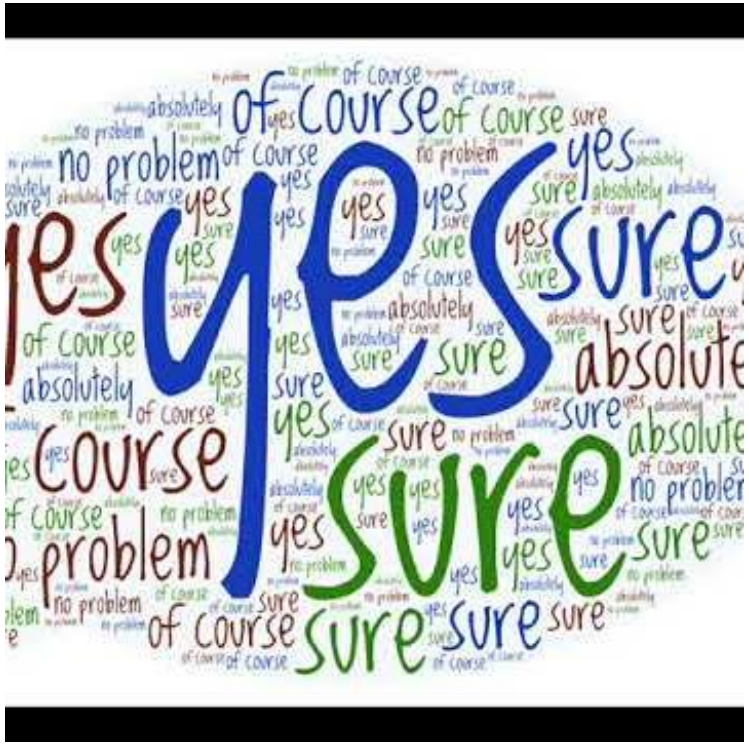
Is it important to correctly classify ICH?

[Characteristics and classification of the different etiologies of intracerebral hemorrhage in humans]

Joan Martí Fàbregas

Hospital de Sant Pau, Barcelona (Spain)

Is it important to correctly classify ICH?



Is it important to correctly classify ICH?

Relevance of ICH classification

Etiology and outcome

ICH associated with oral anticoagulants have the worst prognosis

Cardiovascular events after ICH

CAA more hemorrhagic recurrences

Microbleed burden and location predict recurrences

Risk factors may be location-specific

Etiology and location may influence treatment

SWITCH, ENRICH, ENRICH-AF, idarucizumab, andexanet

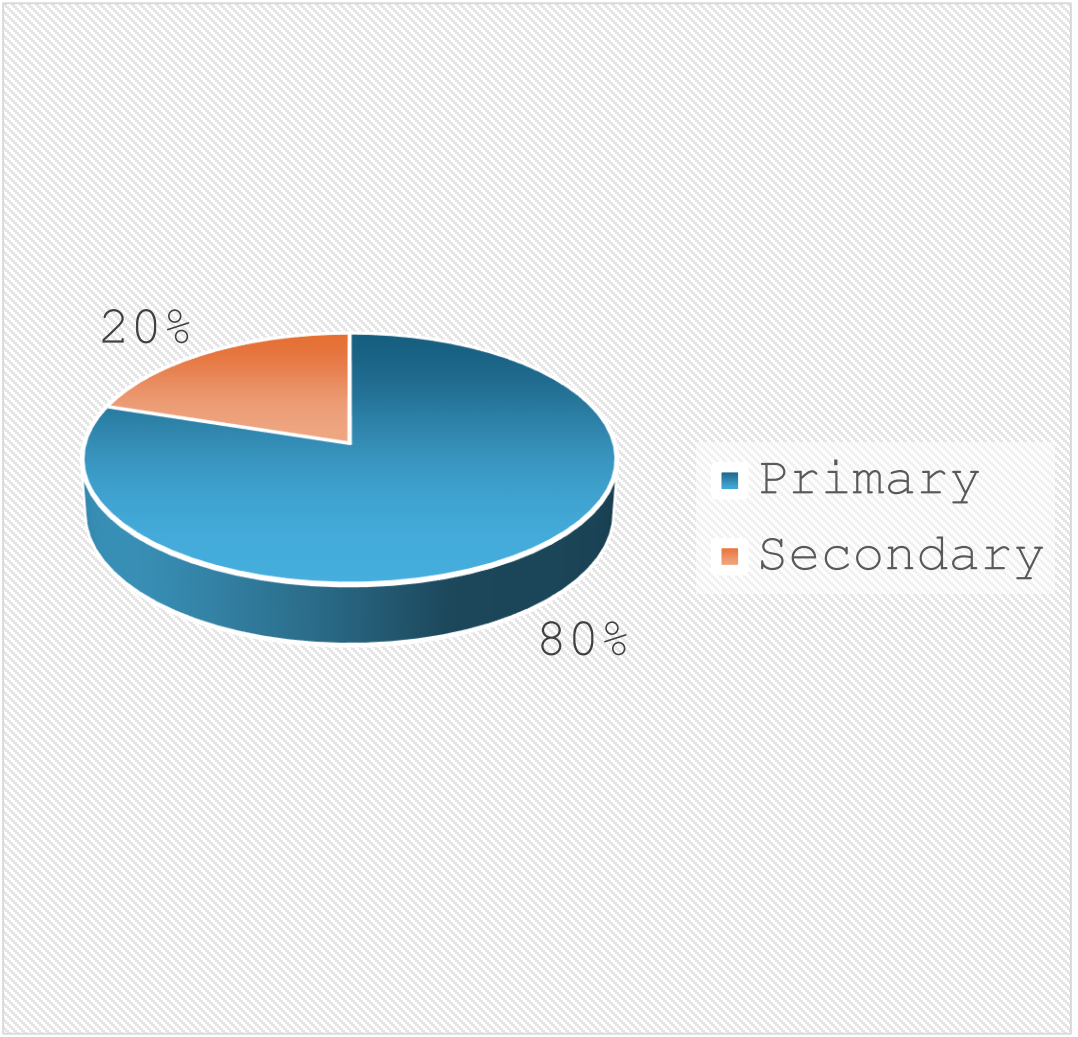
Planning of secondary prevention measures

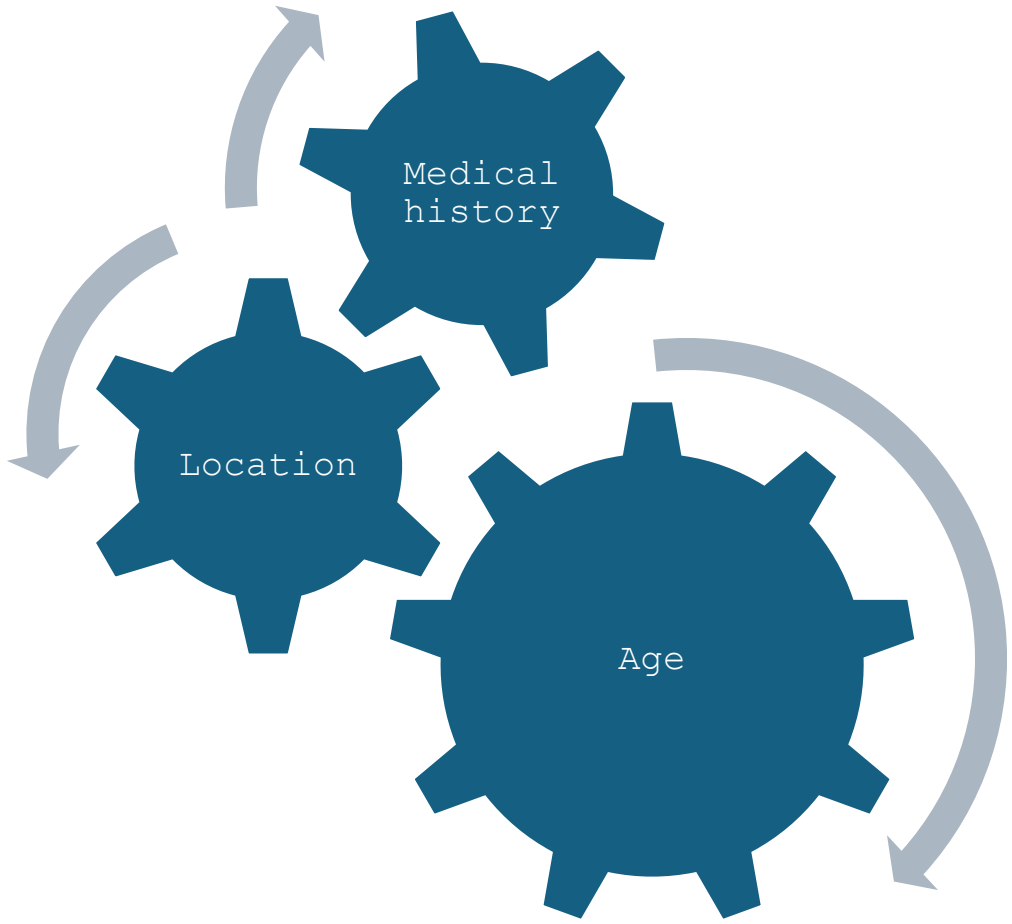
BP control, statins, anti-amyloid immunotherapies, vascular malformations

Etiology varies over the years

Is it important to correctly classify ICH? Yes

>30 potential etio





Diagnostic Work up

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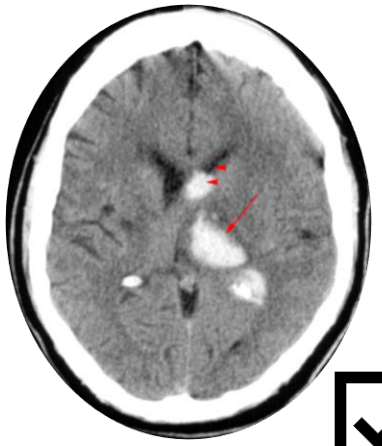
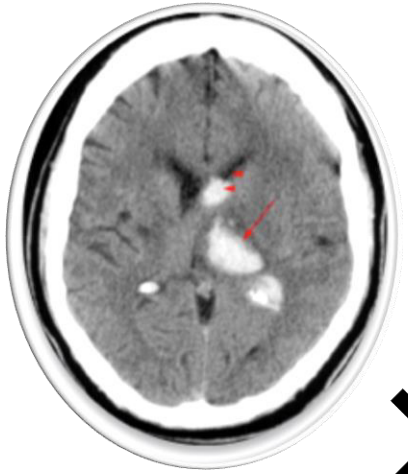
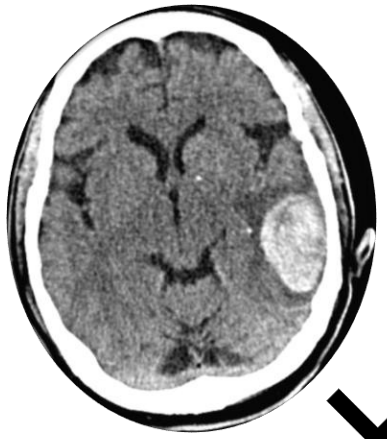
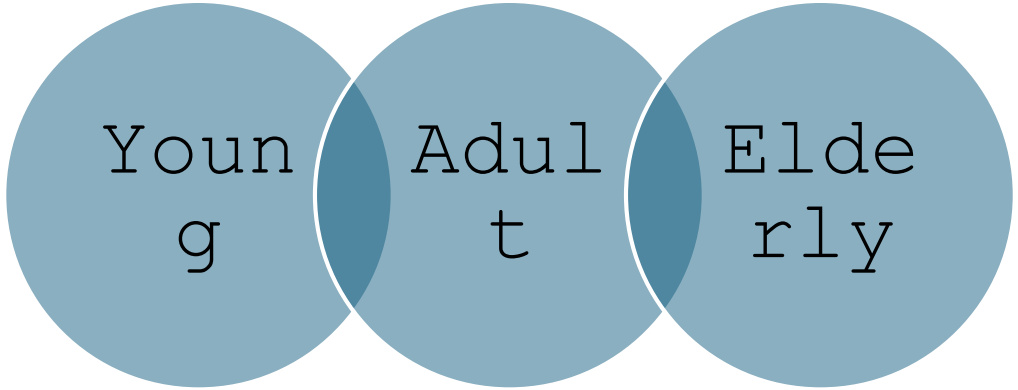
Classification system

	Hypertensive	Normotensive
	1  ☑	2  ✕
	3  ✕	4  ☑



Risk factor vs etiology

Hypertension

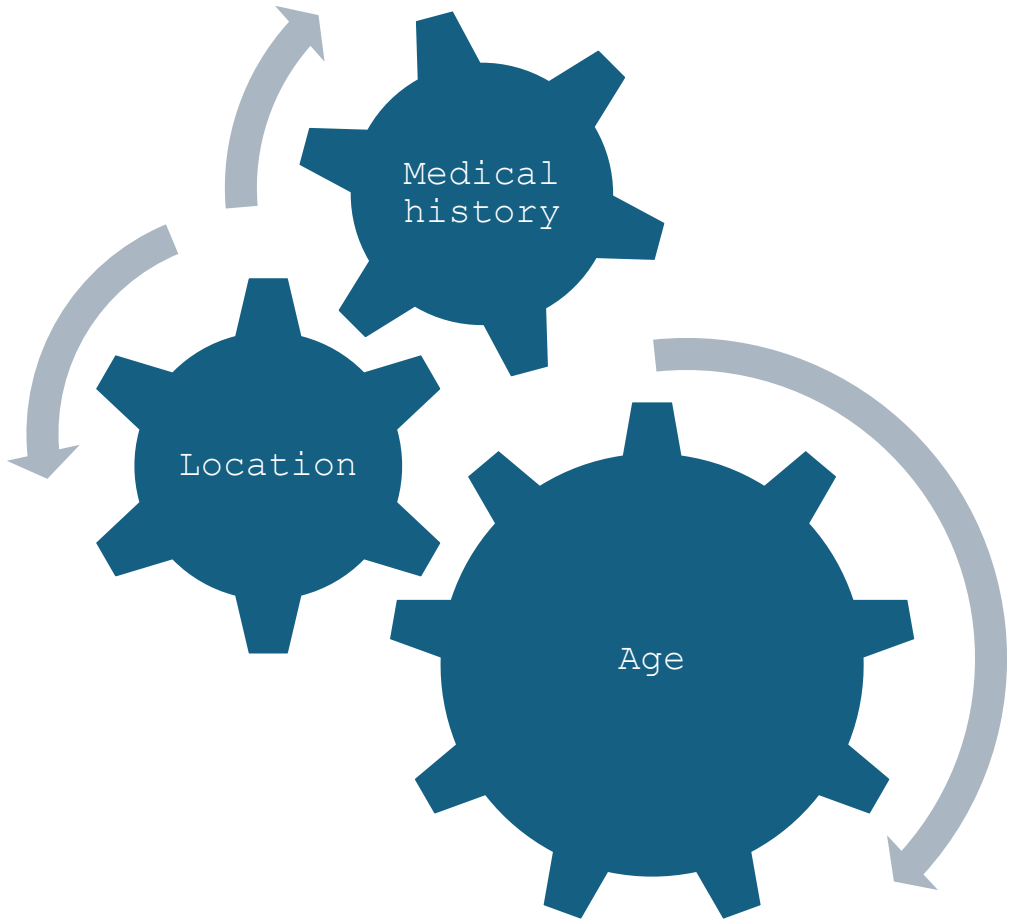
A risk factor or a etiology?

Oral anticoagulants

Is a risk factor?

Only if INR>2? >3? In the case of VKA?

Only amplifies the effects of an underlying hemorrhagic-prone angiopathy?



Diagnostic Work up

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Classification system

Table 1. Prevalence and 95% CIs of AVMs and Aneurysms Based on 9 Studies in Which 726 Patients With ICH Were Investigated With Catheter Angiography[3–5,14,17,18,21,25,28]

	AVMs		Aneurysms	
	Percent	95% CI	Percent	95% CI
Overall	20	17 to 23	13	11 to 16
Age*				
Young (<50 y)	27	19 to 37	30	21 to 40
Old (≥50 y)	18	13 to 24	20	14 to 27
Blood pressure†				
Hypertensive	6	3 to 10	8	5 to 13
Normotensive	28	24 to 33	13	10 to 17
Location‡				
Lobar	31	25 to 37	20	16 to 26
Deep	11	6 to 18	3	1 to 8
Posterior fossa	37	23 to 54	0	0 to 10

Radiological Investigation of Spontaneous Intracerebral Hemorrhage

Systematic Review and Trinational Survey

Charlotte Cordonnier, MD, PhD; Catharina J.M. Klijn, MD, PhD; Janneke van Beijnum, MD; Rustam Al-Shahi Salman, MA, PhD, FRCP Edin

(*Stroke*. 2010;41:685-690.)

Predicting the presence of macrovascular causes in non-traumatic intracerebral haemorrhage: the DIAGRAM prediction score

Hilkens NA, et al. J Neurol Neurosurg Psychiatry 2018

- 298 patients aged 18–70 years
- Multicenter (Netherlands)
- Prospective
- Excluded
  - >70 y
  - > 45 with hypertension and deep ICH
  - Oral anticoagulants
  - Known macrovascular etiology
  - Tumour

CTA within 7 days followed by MRI/MRA within 4-8 weeks if CTA was negative

IADSA if CTA/MR inconclusive or negative

DIAGRAM score

- Patient characteristics and NCCT

DIAGRAM score +

- Patients characterístics and NCCT and CTA

External validation

DIAGRAM score

- 69/298 (**23%**) had an underlying macrovascular cause
  - 45% in the validation cohort
- c-statistic **0.83** (without CTA), **0.91** (with CTA)

Table 2 Macrovascular causes underlying ICH in development and validation cohort

	Development cohort n (%)	Validation cohort n (%)
Arteriovenous malformation	34 (49)	68 (87)
Dural arteriovenous fistula	13 (19)	7 (9)
Cavernoma	10 (14)	–
Cerebral venous sinus thrombosis	4 (6)	–
Aneurysm	7 (10)	2 (3)
Developmental venous anomaly*	1 (1)	–
Carotid cavernous fistula	–	1 (1)
Total	69	78

*This patient had a large developmental venous anomaly with partial thrombosis, which was clearly the cause of the ICH.
ICH, intracerebral haemorrhage.

Table 3 Odds ratios for presence of a macrovascular cause from multivariable models in the development cohort

	Patient characteristics and NCCT OR (95% CI)	Patient characteristics, NCCT and CTA OR (95% CI)
Age	0.95 (0.93 to 0.98)	0.97 (0.94 to 1.00)
Location		
Deep	1 (ref)	1 (ref)
Lobar	7.2 (2.8 to 22.4)	4.0 (1.3 to 14.2)
Posterior fossa	19.3 (5.8 to 75.4)	9.9 (2.5 to 44.9)
Absence of SVD	11.8 (4.4 to 41.2)	11.8 (3.7 to 48.6)
Positive or inconclusive CTA	–	15.9 (7.5 to 35.5)

CTA, CT angiography; NCCT, non-contrast CT; ref, reference; SVD, small vessel disease.

DIAGRAM score

Patient characteristics and NCCT (DIAGRAM score)

Age 18-50 years	Deep	Lobar	Posterior Fossa
SVD	2	13	.
No SVD	17	55	76

Age 51-70 years	Deep	Lobar	Posterior Fossa
SVD	1	4	11
No SVD	6	27	50

Patient characteristics, NCCT and CTA (DIAGRAM+ score)

CTA Negative

Age 18-50 years	Deep	Lobar	Posterior Fossa
SVD	1	5	.
No SVD	9	29	51

Age 51-70 years	Deep	Lobar	Posterior Fossa
SVD	1	2	4
No SVD	3	11	24

CTA Positive

Age 18-50 years	Deep	Lobar	Posterior Fossa
SVD	14	.	.
No SVD	56	84	93

Age 51-70 years	Deep	Lobar	Posterior Fossa
SVD	.	17	34
No SVD	28	61	79

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

Figure 1 Calibration plots of DIAGRAM prediction models in the development and validation cohort. Model based on patient characteristics and NCCT (A), model based on patient characteristics, NCCT and CTA (B). The triangles indicate the observed frequencies with 95% CI by quintiles of predicted probability. CTA, CT angiography; DIAGRAM, DIagnostic AngioGRAphy to find vascular Malformations; NCCT, non-contrast CT.

ORIGINAL RESEARCH

J.E. Delgado Almandoz
P.W. Schaefer
N.P. Forero
J.R. Falla
R.G. Gonzalez
J.M. Romero

Diagnostic Accuracy and Yield of Multidetector CT Angiography in the Evaluation of Spontaneous Intraparenchymal Cerebral Hemorrhage

BACKGROUND AND PURPOSE: Multidetector CT angiography (MDCTA) is emerging as the favored initial diagnostic examination in the evaluation of patients presenting with spontaneous intraparenchymal hemorrhage (IPH). This study aims to evaluate the diagnostic accuracy and yield of MDCTA for the detection of vascular etiologies in adult patients presenting to the emergency department with IPH.

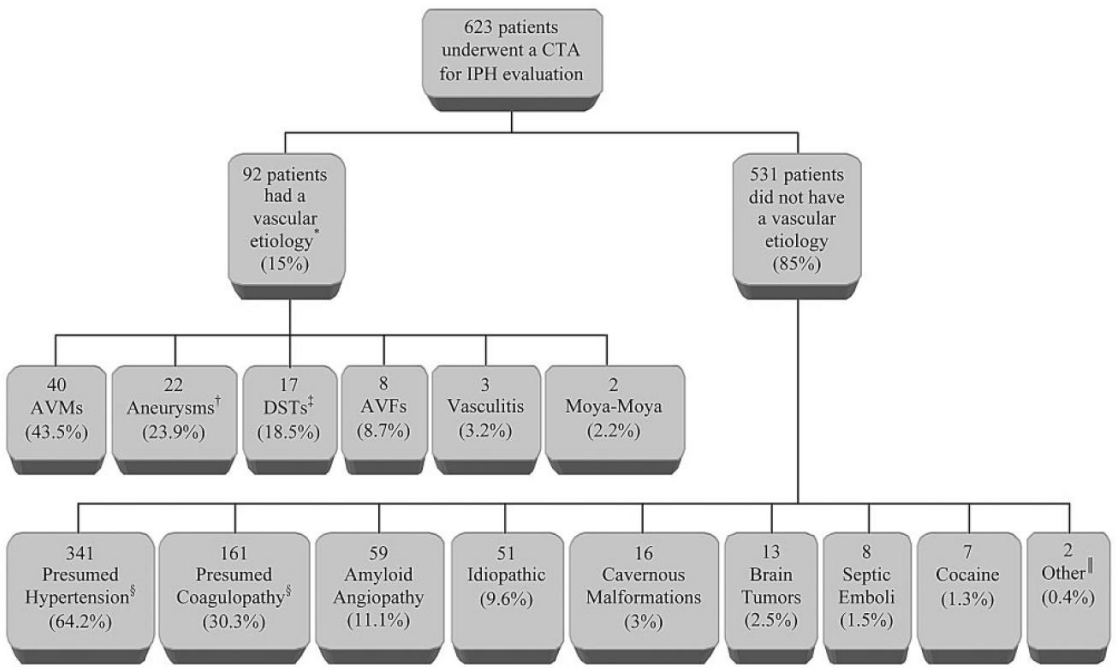
MATERIALS AND METHODS: We conducted a retrospective study of 623 consecutive adult patients presenting to the emergency department with IPH, who were evaluated with MDCTA during a 9-year period. CT angiograms were reviewed by 2 neuroradiologists to determine the IPH site and the presence of a vascular etiology. Patients with associated subarachnoid hemorrhage in the basal cisterns were excluded from the study. Medical records were reviewed for risk factors and correlation with final diagnosis. The diagnostic accuracy of MDCTA compared with conventional angiography, intraoperative evaluation, and pathologic findings was determined, when available. Multiple-variable logistic regression analysis was performed to determine clinical and radiologic factors that predict a higher yield of MDCTA.

RESULTS: MDCTA demonstrated a vascular etiology in 91 patients (14.6%), with a sensitivity of 96%, specificity of 99%, and diagnostic accuracy of 98%. We found independent, statistically significant higher yields of MDCTA in patients with the following characteristics: 1) age younger than 46 years (47%); 2) lobar (20%) or infratentorial (16%) IPH, especially lobar IPH with associated intraventricular hemorrhage (25%); 3) female sex (18%); or 4) neither known hypertension nor impaired coagulation at presentation (33%).

CONCLUSIONS: MDCTA is an accurate diagnostic examination in the evaluation of adult patients presenting with spontaneous IPH and should be performed in all patients with the aforementioned clinical and radiologic characteristics.

Table 1: Diagnostic accuracy of multidetector CT angiography in IPH

Findings	Confirmed Vascular Lesion*	Confirmed No Vascular Lesion	Total
Positive CTA	73	2	75
Negative CTA	3	132	135
Total	76	134	210
Sensitivity		96.1% (88.1%–99.0%)†	
Specificity		98.5% (94.2%–99.7%)†	
Accuracy		97.6%	
PPV		97.3% (89.8%–99.5%)†	
NPV		97.8% (93.2%–99.4%)†	



ORIGINAL RESEARCH

Practical Scoring System for the Identification of Patients with Intracerebral Hemorrhage at Highest Risk of Harboring an Underlying Vascular Etiology: The Secondary Intracerebral Hemorrhage Score

J.E. Delgado Almandoz
P.W. Schaefer
J.N. Goldstein
J. Rosand
M.H. Lev
R.G. González
J.M. Romero

BACKGROUND AND PURPOSE: An ICH patient's risk of harboring an underlying vascular etiology varies according to baseline clinical and NCCT characteristics. Our aim was to develop a practical scoring system to stratify patients with ICH according to their risk of harboring a vascular etiology.

MATERIALS AND METHODS: Using a data base of 623 patients with ICH evaluated with MDCTA during a 9-year period, we developed a scoring system based on baseline clinical characteristics (age group [0–2 points], sex [0–1 point], neither known HTN nor impaired coagulation [0–1 point]), and NCCT categorization (0–2 points) to predict the risk of harboring a vascular lesion as the ICH etiology (SICH score). We subsequently applied the SICH score to a prospective cohort of 222 patients with ICH who presented to our emergency department during a 13-month period. Using ROC analysis, we calculated the AUC and MOP for the SICH score in both the retrospective and prospective patient cohorts separately and the entire patient population. Patients with SAH in the basal cisterns were excluded.

RESULTS: A vascular etiology was found in 120 of 845 patients with ICH evaluated with MDCTA (14.2%), most commonly AVMs (45.8%), aneurysms with purely intraparenchymal rupture (21.7%), and DVSTs (16.7%). The MOP was reached at a SICH score of >2, with the highest incidence of vascular ICH etiologies in patients with SICH scores of 3 (18.5%), 4 (39%), 5 (84.2%), and 6 (100%). There was no significant difference in the AUC between both patient cohorts (0.86–0.87).

CONCLUSIONS: The SICH score successfully predicts a given ICH patient's risk of harboring an underlying vascular etiology and could be used as a guide to select patients with ICH for neurovascular evaluation to exclude the presence of a vascular abnormality.

Table 2: Calculation of the SICH score

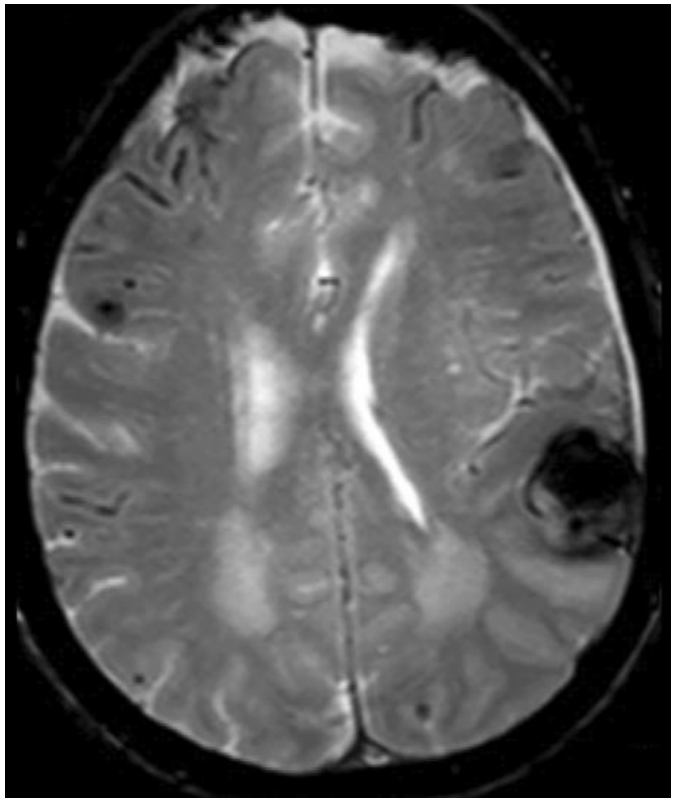
Parameter	Points
NCCT categorization[a]	
High probability	2
Indeterminate	1
Low probability	0
Age group	
18–45 years	2
46–70 years	1
≥71 years	0
Sex	
Female	1
Male	0
Neither known HTN nor impaired coagulation[b]	
Yes	1
No	0

Note:—The SICH score is calculated by adding the total number of points for a given patient.
[a] High-probability NCCT: an examination with either 1) enlarged vessels or calcifications along the margins of the ICH or 2) hyperattenuation within a dural venous sinus or cortical vein along the presumed venous drainage path of the ICH. Low-probability NCCT: an examination in which neither 1) nor 2) is present and the ICH is located in the basal ganglia, thalamus, or brain stem. Indeterminate NCCT: an examination that does not meet criteria for a high- or low-probability NCCT.
[b] Impaired coagulation defined as admission INR >3, aPTT >80 seconds, platelet count <50,000, or daily antiplatelet therapy.

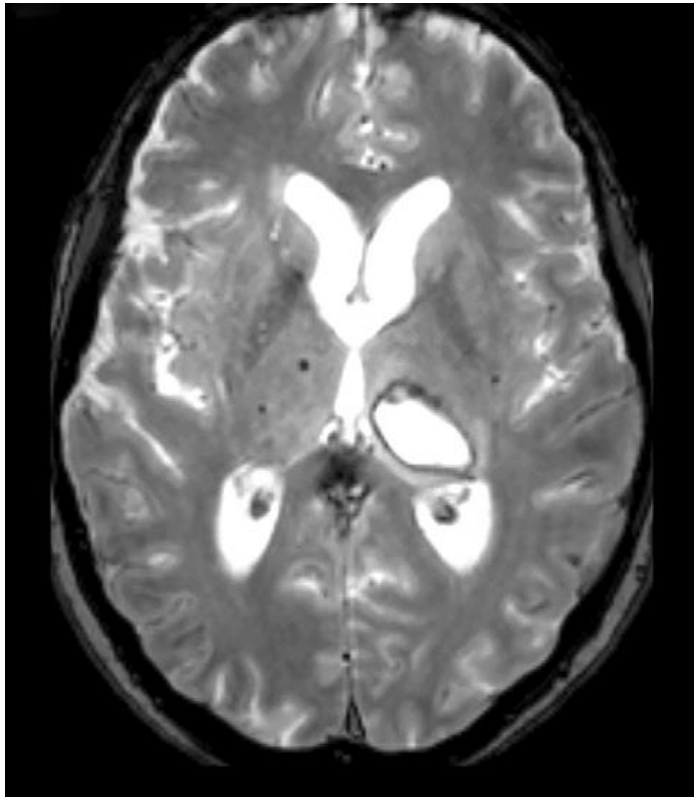
	Retrospective-Derivation Cohort (n = 623)		Prospective-Validation Cohort (n = 222)		All Patients (n = 845)	
Score	No. (%)	% Positive CTAs	No. (%)	% Positive CTAs	No. (%)	% Positive CTAs
0	37 (5.9)	0	15 (6.8)	0	52 (6.1)	0
1	145 (23.3)	1.4	67 (30.2)	1.5	212 (25.1)	1.4
2	209 (33.5)	5.3	68 (30.6)	4.4	277 (32.8)	5.1
3	138 (22.2)	18.1	40 (18.0)	20	178 (21.1)	18.5
4	61 (9.8)	39.3	21 (9.5)	38.1	82 (9.7)	39
5	28 (4.5)	85.7	10 (4.5)	80	38 (4.5)	84.2
6	5 (0.8)	100	1 (0.4)	100	6 (0.7)	100
AUC (95% CI)		0.86 (0.83–0.89)		0.87 (0.82–0.91)		0.87 (0.84–0.89)
MOP		>2		>2		>2
Sensitivity		85.7		86.2		85.8
Specificity		71.1		75.6		72.3
P value		<.0001		<.0001		<.0001

MR-markers of intracranial hemorrhagic-prone angiopathies

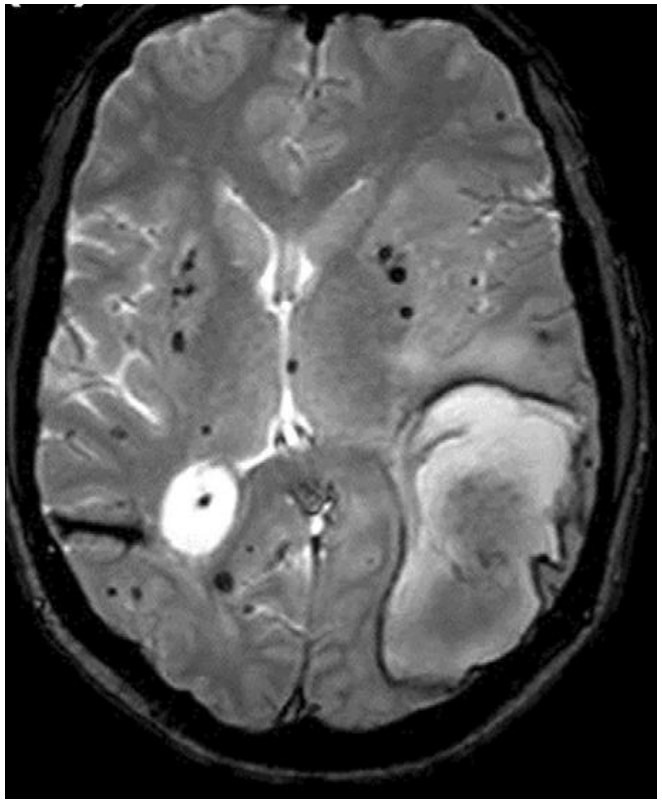
Raposo et al, Ann Neurol 20



Amyloid angiopathy



Arteriolosclerosis/Deep perforator arteriopathy

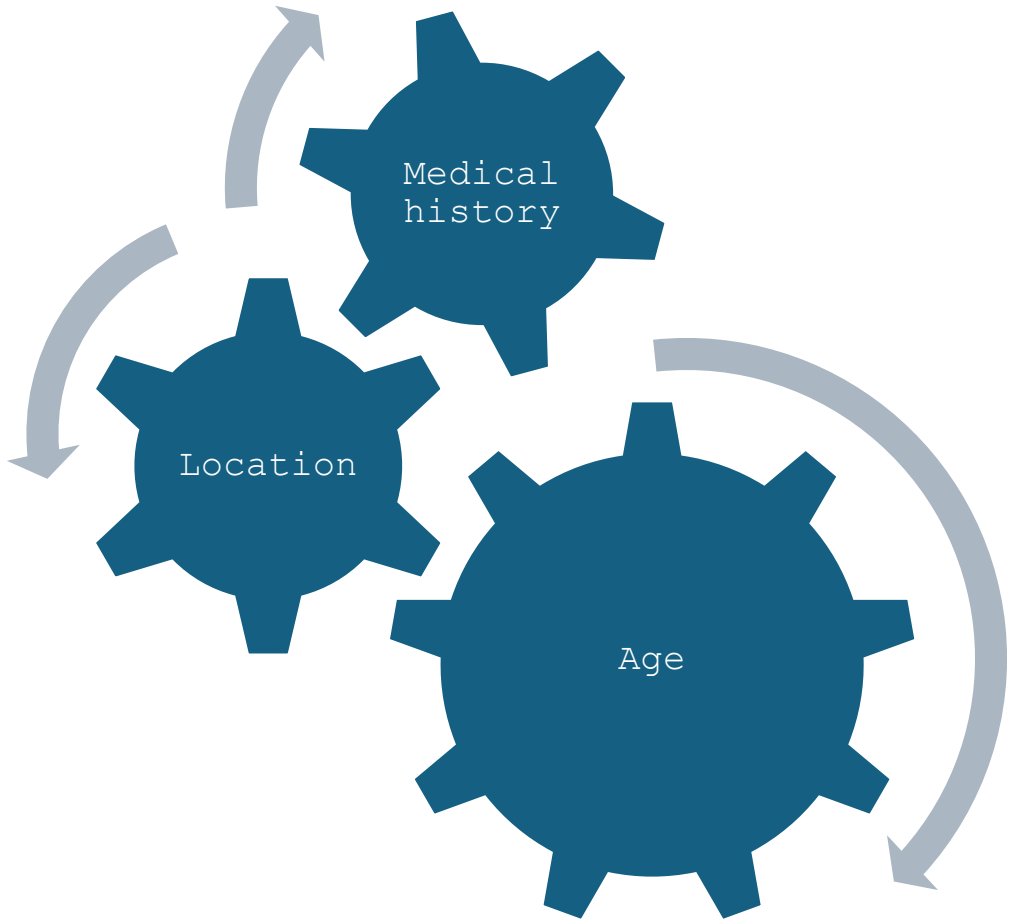


Mixed

Uncommon Causes of Nontraumatic Intracerebral Hemorrhage

Hugo Tartarin, MD; Andrea Morotti, MD; Ellis S. Van Etten, MD, PhD; Moran Hausman-Kedem, MD; Andreas Charidimou, MD, PhD; Eric Jouvent, MD, PhD; Sophie Susen, MD, PhD; Charlotte Cordonnier, MD, PhD; Marco Pasi, MD, PhD; Grégoire Boulouis, MD, PhD

Stroke. 2024;55:00–00. DOI: 10.1161/STROKEAHA.123.043917



Diagnostic Work up

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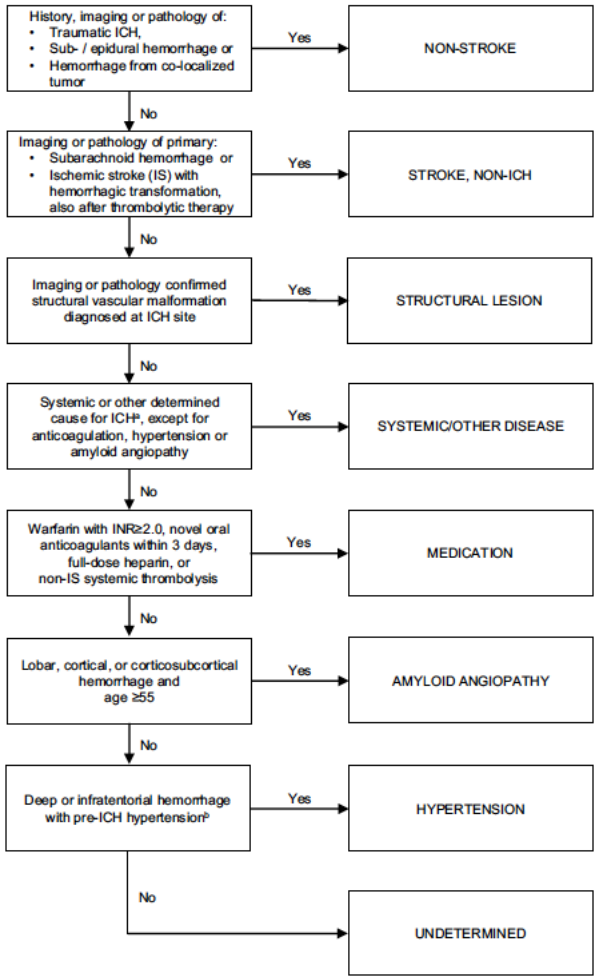
Classification system

SMASH-U

A Proposal for Etiologic Classification of Intracerebral Hemorrhage

Atte Meretoja, MD, PhD, MSc(Stroke Med); Daniel Strbian, MD, PhD; Jukka Putaala, MD, PhD; Sami Curtze, MD, PhD; Elena Haapaniemi, MD, PhD; Satu Mustanoja, MD, PhD, MSc(Stroke Med); Tiina Sairanen, MD, PhD, MSc(Stroke Med); Jarno Satopää, MD; Heli Silvennoinen, MD, PhD; Mika Niemelä, MD, PhD; Markku Kaste, MD, PhD; Turgut Tatlisumak, MD, PhD

(*Stroke*. 2012;43:2592-2597.)



A retrospective analysis of consecutive patients from the Helsinki ICH registry

1013 patients, 25% with angiography (any type)

S 5%
M 14%
A 20%
S 5%
H 35%
U 21%

Interrater reliability k, 0.89

RESEARCH ARTICLE

The H-ATOMIC Criteria for the Etiologic Classification of Patients with Intracerebral Hemorrhage

PLOS ONE | DOI:10.1371/journal.pone.0156992 June 8, 2016

Joan Martí-Fàbregas[1]*, Luis Prats-Sánchez[1], Alejandro Martínez-Domeño[1], Pol Camps-Renom[1], Rebeca Marín[1], Elena Jiménez-Xarrié[1], Blanca Fuentes[2], Laura Dorado[3], Francisco Purroy[4], Susana Arias-Rivas[5], Raquel Delgado-Mederos[1]

7 categories, not mutually exclusive

H Hypertension
A Amyloid angiopathy
T Tumour
O Oral anticoagulants
M Vascular Malformation
I Infrequent
C Cryptogenic

Degree of certainty (definite, proba

Prefefined etiologic work-up

Prospective, multicenter

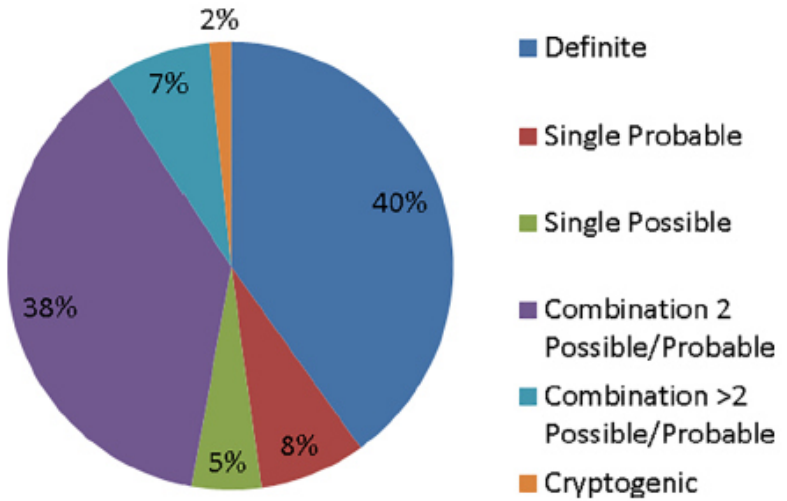


Fig 1. Distribution of etiologic categories in 439 patients (percentages are rounded).

N=439 consecutive patients with ICH

A Causal Classification System for Intracerebral Hemorrhage Subtypes

Nicolas Raposo, MD, PhD,[1,2] Maria Clara Zanon Zotin, MD,[3,4] David J. Seiffge, MD,[5] Qi Li, MD, PhD,[6] Martina B. Goeldlin, MD,[5,7] Andreas Charidimou, MD, PhD,[3] Ashkan Shoamanesh, MD,[8] Hans Rolf Jäger, MD, FRCP,[9] Charlotte Cordonnier, MD, PhD,[10] Catharina JM Klijn, MD, PhD,[11] Eric E. Smith, MD, MPH,[12] Steven M. Greenberg, MD, PhD,[3] David J. Werring, MD, PhD,[9] and Anand Viswanathan, MD, PhD[3]

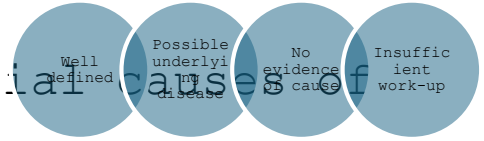
ANN NEUROL 2023;93:16–28

Imaging-based classification using validated
neuroimaging biomarkers

Comprehensive classification system

ICH subgroups include the main known causes of ICH, and recognize that SVD and structural macrovascular lesions are predominant causes

Can have multiple potential causes of ICH



Level of diagnostic certainty

A arteriolosclerosis

C CAA

M Mixed SVD

O Other well defined subtype

S secondary causes

CADMUS

A Novel MRI-Based Classification of Spontaneous Intracerebral Hemorrhage Associated With Cerebral Small Vessel Disease

Martina B. Goeldlin, MD, Madlaine Mueller, MD, Bernhard M. Siepen, MD, Wenpeng Zhang, MSc, Hatice Ozkan, MPhil, Martina Locatelli, MD, Yang Du, Waldo Valenzuela, PhD, Piotr Radojewski, MD, Arsany Hakim, MD, Johannes Kaesmacher, MD, PhD, Thomas R. Meinel, MD, PhD, Leander Clénin, MMed, Mattia Branca, PhD, Davide Strambo, MD, Tim Fischer, MD, Friedrich Medlin, MD, Nils Peters, MD, Emmanuel Carrera, MD, Karl-Olof Lovblad, MD, Grzegorz M. Karwacki, MD, Carlo W. Cereda, MD, Julien Niederhauser, MD, Marie-Luise Mono, MD, Achim Mueller, MD, Susanne Wegener, MD, Sabine Sartoretti, MD, Alexandros A. Polymeris, MD, PhD, Valerian Altersberger, MD, Mira Katan, MD, Marios Psychogios, MD, Rolf Sturzenegger, MD, Claude Nauer, MD, Michael Schaerer, MD, Carlos Buitrago Tellez, MD, Susanne Renaud, Katharina Minkner Klahre, Werner J. Z'Graggen, MD, David Bervini, Leo H. Bonati, MD, Roland Wiest, MD, Marcel Arnold, MD, Robert J. Simister, PhD, Duncan Wilson, MD, PhD, Hans Rolf Jäger, MD, Urs Fischer, MD,* David J. Werring, MD, PhD,* and David J. Seiffge, MD,* for Swiss Stroke Registry Investigators and SIGNAL Investigators

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Neurology® 2024;102:e207977. doi:10.1212/WNL.0000000000207977

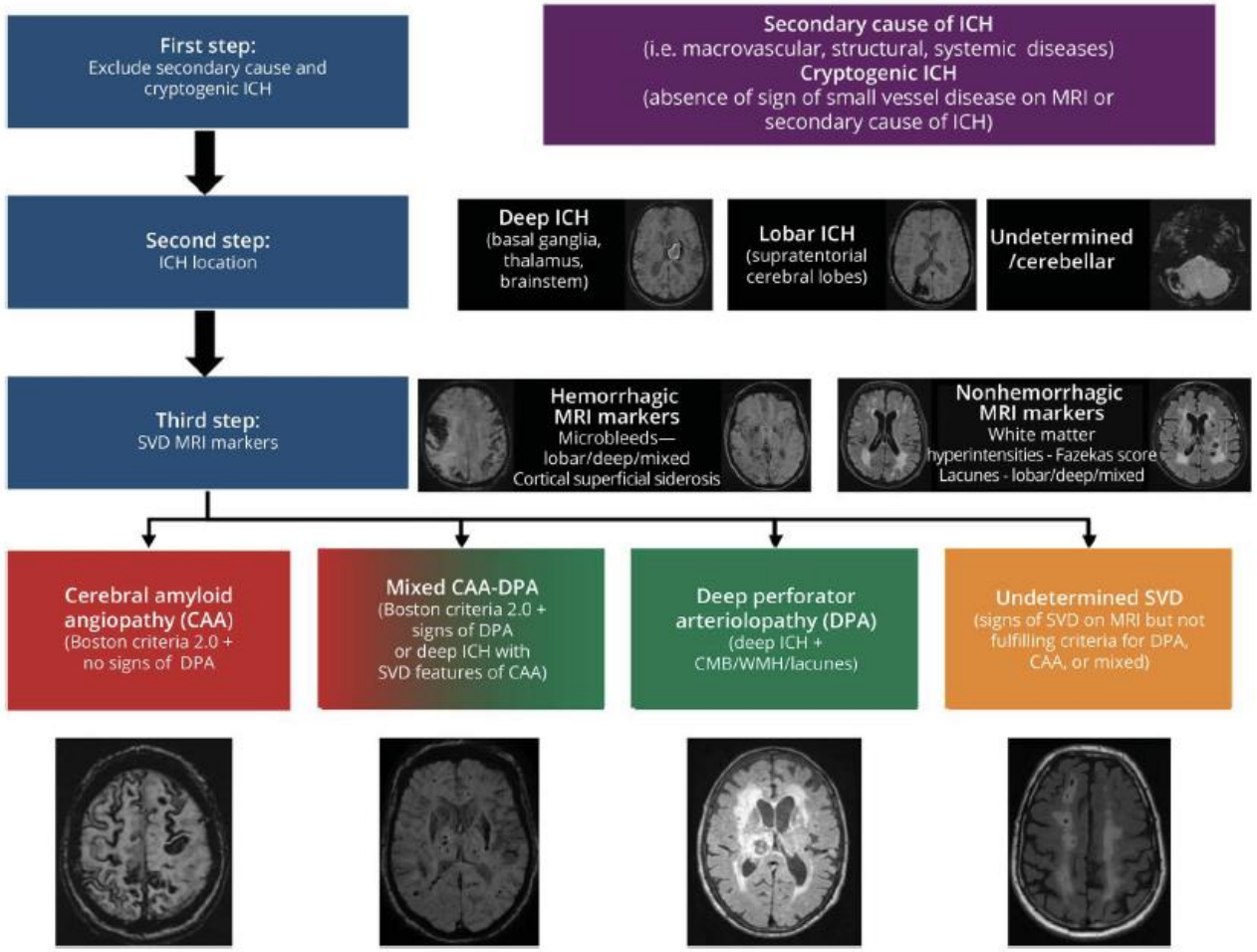
Prospective Swiss stroke registry and prospective Stroke InvestiGation in North And central London (SIGNAL)
Retrospective analysis

3 steps classification system

4 mutually exclusive SVD phenotypes

3,572 patients with ICH, MRI available in 1,439 patients (40.3%). In 212 patients (14.7%), ICH was due to a secondary cause, resulting in 1,180 patients (**33%**) eligible for this study (**36%** in

Figure 1 CADMUS SVD Classification



CADMUS

A Novel MRI-Based Classification of Spontaneous Intracerebral Hemorrhage Associated With Cerebral Small Vessel Disease

Martina B. Goeldlin, MD, Madlaine Mueller, MD, Bernhard M. Siepen, MD, Wenpeng Zhang, MSc, Hatice Ozkan, MPhil, Martina Locatelli, MD, Yang Du, Waldo Valenzuela, PhD, Piotr Radojewski, MD, Arsany Hakim, MD, Johannes Kaesmacher, MD, PhD, Thomas R. Meinel, MD, PhD, Leander Clénin, MMed, Mattia Branca, PhD, Davide Strambo, MD, Tim Fischer, MD, Friedrich Medlin, MD, Nils Peters, MD, Emmanuel Carrera, MD, Karl-Olof Lovblad, MD, Grzegorz M. Karwacki, MD, Carlo W. Cereda, MD, Julien Niederhauser, MD, Marie-Luise Mono, MD, Achim Mueller, MD, Susanne Wegener, MD, Sabine Sartoretti, MD, Alexandros A. Polymeris, MD, PhD, Valerian Altersberger, MD, Mira Katan, MD, Marios Psychogios, MD, Rolf Sturzenegger, MD, Claude Nauer, MD, Michael Schaerer, MD, Carlos Buitrago Tellez, MD, Susanne Renaud, Katharina Minkner Klahre, Werner J. Z'Graggen, MD, David Bervini, Leo H. Bonati, MD, Roland Wiest, MD, Marcel Arnold, MD, Robert J. Simister, PhD, Duncan Wilson, MD, PhD, Hans Rolf Jäger, MD, Urs Fischer, MD,* David J. Werring, MD, PhD,* and David J. Seiffge, MD,* for Swiss Stroke Registry Investigators and SIGNAL Investigators

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- Agreement 12.2%

Figure 2 Sankey Diagram Comparing SMASH-U and CADMUS Classification in the Swiss Stroke Registry

CAA = cerebral amyloid angiopathy; DPA = deep perforator arteriopathy; SVD = small vessel disease.

Knowns and unknowns

ICH is a **heterogeneous** entity	• Prognosis, risk of recurrence, distribution of risk factors and treatment may depend on etiology
Age, location and a good clinical history are essential to determine the etiology	
It is necessary to define the best **work-up strategy**	• CT-angio is recommended for all patients • MRI recommended for all patients where possible • Conventional angiography: individualize case by case, use DIAGRAM score
There are several **etiological classification systems** available, with advantages and disadvantages for each. There is no consensus on the use of these systems.	