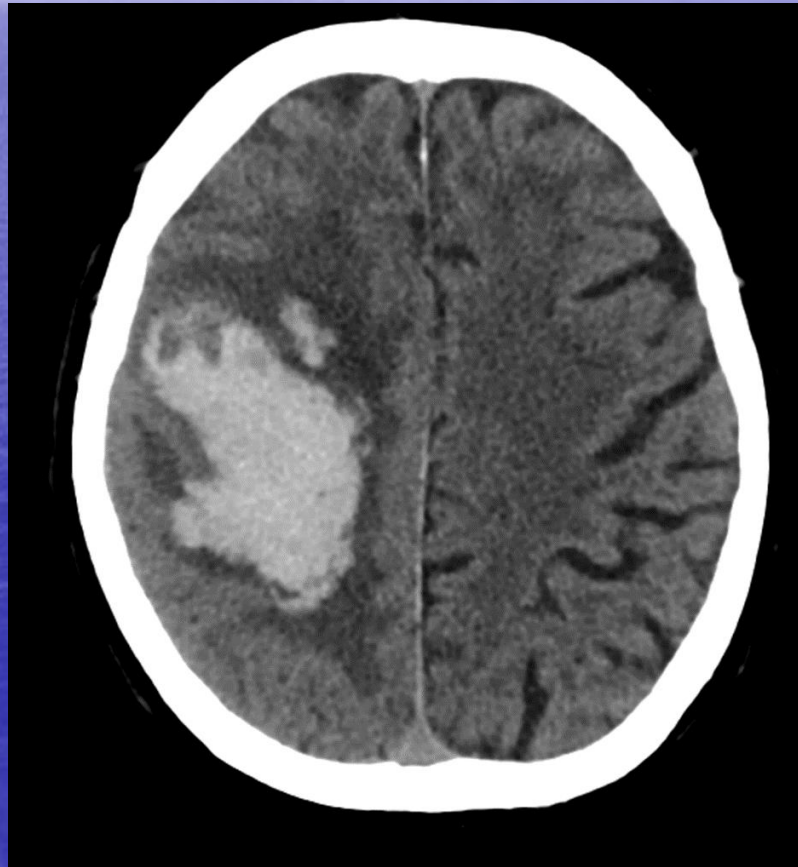


CONTROINDICAZIONI ALLA TERAPIA ANTICOAGULANTE ORALE: IL PUNTO DI VISTA DEL NEUROLOGO

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CONTROINDICAZIONE !!!!!!!



EMORRAGIA CEREBRALE

- 20% degli stroke è emorragico
- Evento ad elevata mortalità
 - Fino al 50% nel primo mese
 - > 50% ad 1 anno
- Il rischio di emorragia aumenta con età
- Maggiore incidenza tra gli uomini
- Maggiore incidenza negli asiatici

Evento ad elevata mortalità

	Mid-year of study	Patients with intracerebral haemorrhage (n)	Case fatality					
			Men	Women	<65 years	65–74 years	75–84 years	>85 years
Oxford, UK ¹⁵	1983	66	..	..	42.0 (20.3–66.5)	44.4 (21.5–69.2)	58.0 (36.6–77.9)	80.0 (28.4–99.5)
Okinawa, Japan ⁵⁵	1989	1412	18.8 (16.1–21.5)	16.2 (13.3–19.1)	17.3 (14.6–19.9)	14.5 (10.4–18.7)	18.8 (13.8–23.7)	24.8 (17.1–32.5)
Arcadia, Greece ^{16*}	1994	77	44.0 (30.0–58.7)	51.8 (32.0–71.3)	33.3 (14.6–57.0)	31.8 (13.9–54.9)	63.2 (38.4–83.7)	60.0 (32.3–83.7)
Malmö, Sweden ¹⁸	1995	699	23.9 (19.4–28.3)	22.7 (18.2–27.1)	14.3 (8.9–19.6)	18.9 (13.4–24.5)	29.8 (24.0–35.5)	31.3 (22.4–41.4)
China ^{59†}	1998	2275	48.4 (45.7–51.1)	50.7 (47.5–53.9)	..	..	..	..
Melbourne, Australia ²⁷	1998	151	29.2 (19.0–41.1)	50.6 (39.1–62.1)	..	..	..	..
Örebro, Sweden ²⁹	1999	44	..	..	25.0 (3.2–65.1)	21.4 (4.7–50.8)	12.5 (1.6–38.3)	33.3 (4.3–77.7)
Overall	..	..	35.4 (33.6–37.1)	35.3 (33.2–37.4)	17.6 (15.3–20.0)	18.1 (14.8–21.4)	26.8 (23.1–30.5)	30.9 (25.1–36.7)

Data are % (95% CI). *Patients older than age 18 years. †Patients older than age 25 years.

Table 4: Intracerebral haemorrhage case fatality at 1 month according to sex and age

rischio di emorragia aumenta con età

	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	7 256 660	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	8 651 73	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	8 120 77	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	5 318 45	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	1 705 80	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

Incidenza aumenta con età: perché?

The higher incidence of intracerebral haemorrhage in elderly patients has been attributed to high prevalences of amyloid angiopathy and hypertension, and to the use of antithrombotic drugs in this age group.⁴ In a subset of

Ma sono proprio gli anziani che spesso il neurologo deve scoagulare

- Incidenza dello stroke ischemico aumenta con l'età
- Incidenza della fibrillazione atriale aumenta con l'età (1,5% nella fascia di età 50-59 anni → >20% nella fascia di età tra 80-89 anni)
- Lo stroke ischemico cardioembolico per FA è associato a maggiore mortalità e morbidità

Patients presenting with ICH carry a different prognosis...according to the cause of the bleeding

JAMA Intern Med 2017;177:563

E' importante trovare la causa
dell'emorragia cerebrale

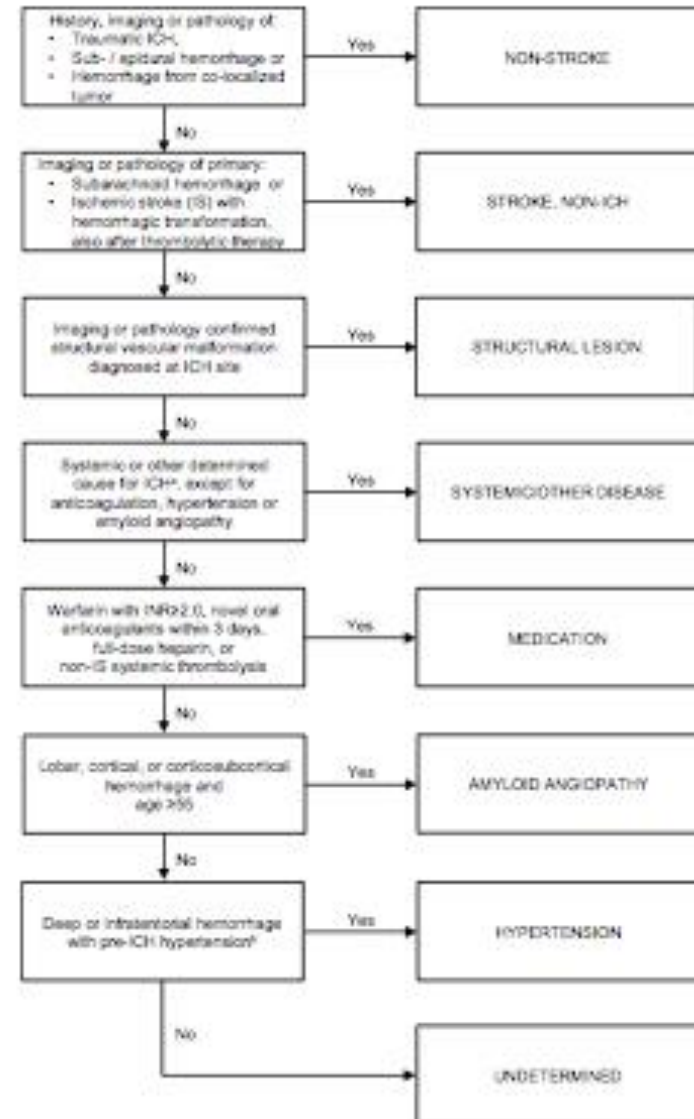
The H-ATOMIC Criteria for the Etiologic Classification of Patients with Intracerebral Hemorrhage

- Hypertension
- cerebral Amyloid angiopathy
- Tumour
- Oral anticoagulants
- vascular Malformation
- Infrequent causes
- Cryptogenetic

SMASH-U

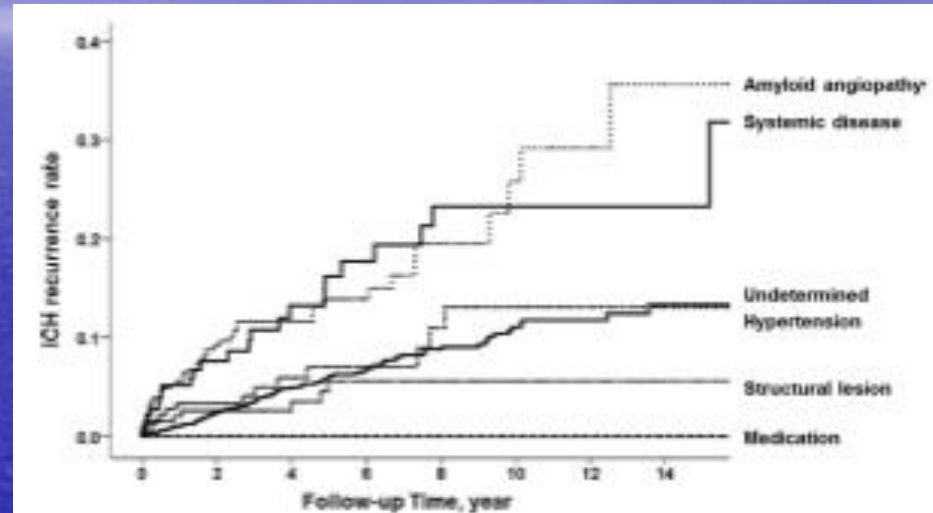
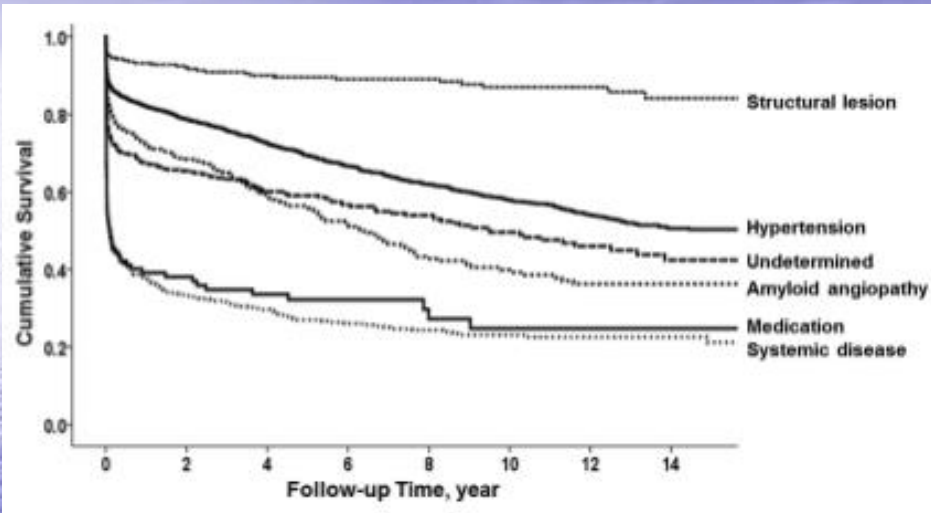
A Proposal for Etiologic Classification of Intracerebral Hemorrhage

- Structural vascular lesions
- Medication
- cerebral Amyloid angiopathy
- Systemic disease
- Hypertension
- Undetermined



SMASH-U

A Proposal for Etiologic Classification of Intracerebral Hemorrhage



Prognosi e rischio recidiva
dipendono dalla eziologia

Quali le cause più frequenti di emorragia cerebrale?

- Angiopatia ipertensiva (35-50%)
- Angiopatia amiloidea cerebrale (12-20%)
- Malattie sistemiche (5-10%)
- Indeterminata (10-20%)
- Malformazioni vascolari (5-8%)
- Farmaci (3-14%)

Le percentuali dipendono dalle popolazioni

Fattori influenzanti la prognosi e la frequenza di recidive

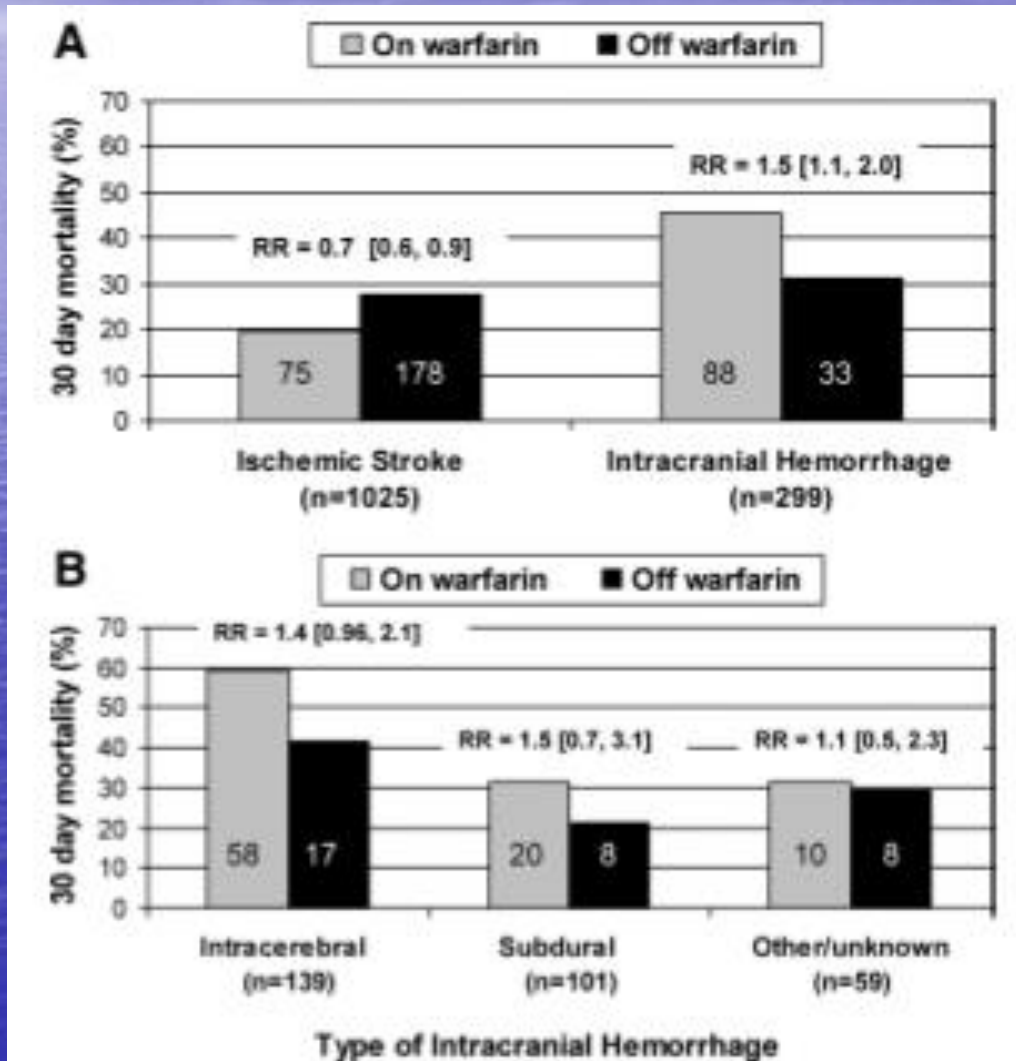
- Localizzazione
- Farmaci anticoagulanti
- Età

Localizzazione

Table 2 Multivariable logistic regression analyses for associations between ICH sites of involvement and outcome

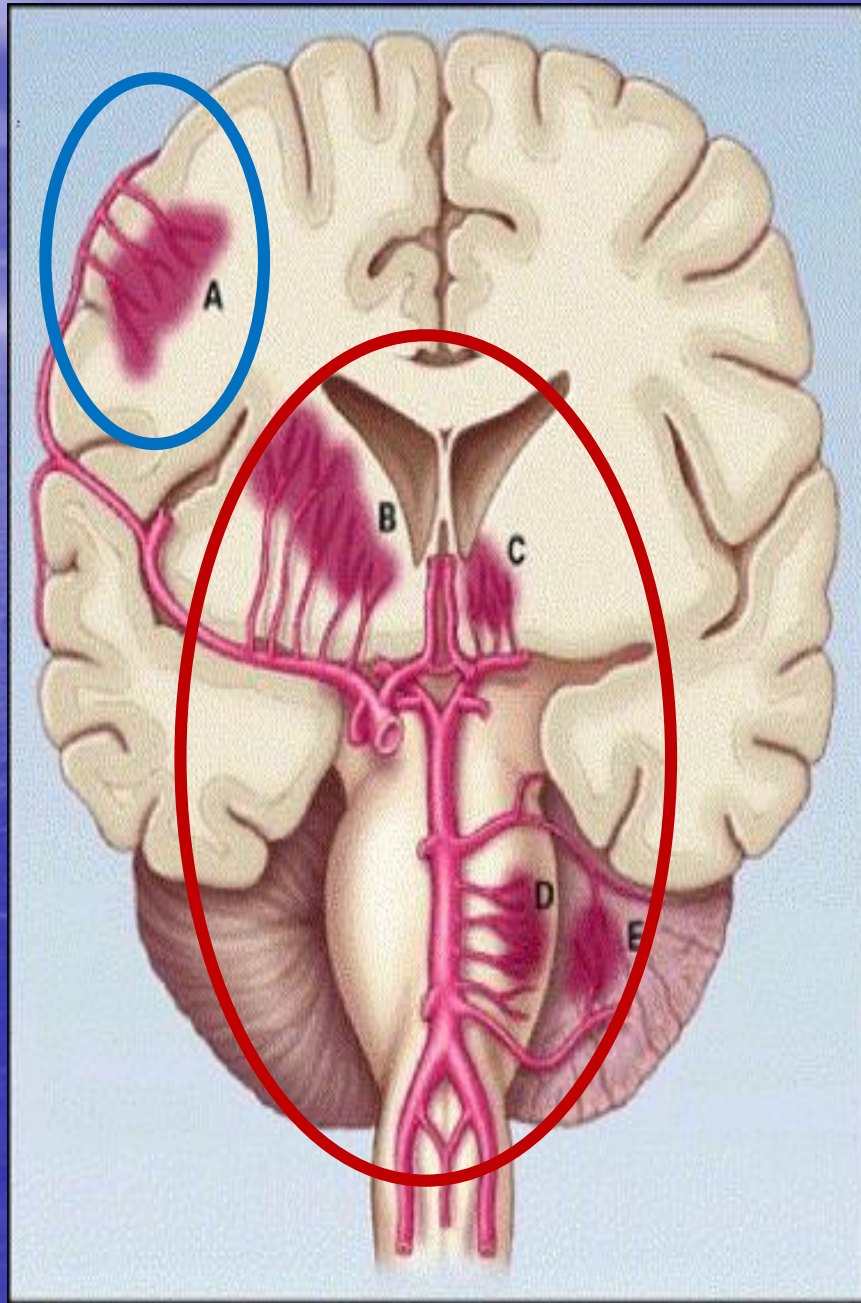
	No.	Death or major disability		Major disability		Death	
		OR	95% CI	OR	95% CI	OR	95% CI
Caudate head	42	0.42	0.16-1.14	0.24	0.09-0.62 ^a	2.19	0.77-6.26
Thalamus	640	2.24	1.40-3.57 ^b	1.18	0.82-1.71	1.97	1.18-3.29 ^a
Putamen/globus pallidus	1,161	1.36	0.87-2.14	0.86	0.60-1.22	1.11	0.68-1.82
External capsule	553	1.05	0.78-1.40	0.96	0.74-1.25	1.23	0.81-1.87
Anterior limb of internal capsule	102	1.03	0.56-1.91	1.00	0.59-1.71	0.94	0.45-1.97
Posterior limb of internal capsule	957	2.10	1.65-2.68 ^b	1.81	1.45-2.26 ^b	1.04	0.72-1.51
Lobar	297	1.34	0.86-2.08	0.61	0.43-0.88 ^a	1.95	1.21-3.15 ^a
Infratentorial	141	3.04	1.68-5.50 ^b	1.27	0.77-2.11	2.45	1.09-5.50 ^c

I pazienti con emorragia cerebrale in warfarin hanno una mortalità a 30 giorni significativamente maggiore rispetto a quelli con stroke ischemico in warfarin (45,6% vs 19,6% $p<0,001$)



EMORRAGIA LOBARE

- Rischio di recidiva a 1 anno: ~ 15% (*)
- Spesso associata ad angiopatia amiloide



EMORRAGIA PROFONDA

- Rischio di recidiva a 1 anno: ~ 2% (*)
- Spesso associata ad ipertensione

Alto rischio di recidiva di emorragia cerebrale (9-15% rischio annuale)

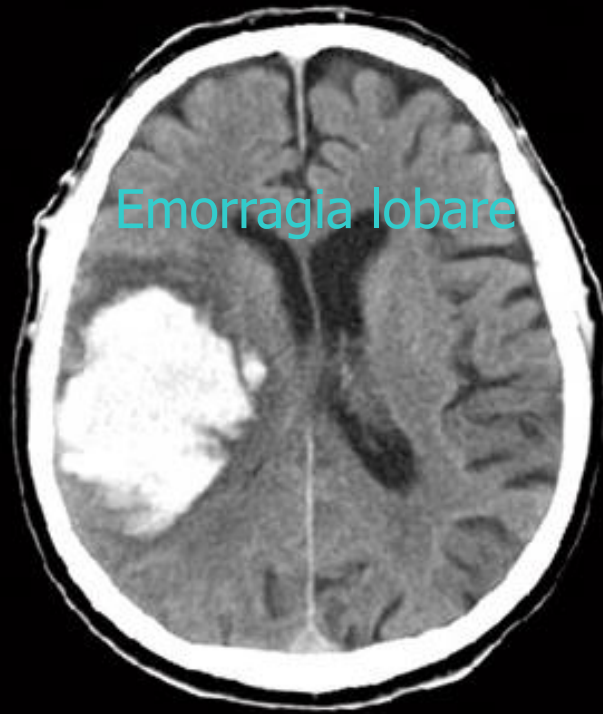
- Età avanzata
- Emorragia lobare
- Microsanguinamenti cerebrali lobar
- Emosiderosi corticale superficiale
 - Focale
 - Multifocale
- Microinfarti corticali
- Allargamento spazi perivascolari centro semiovale

Amiloidosi cerebrale

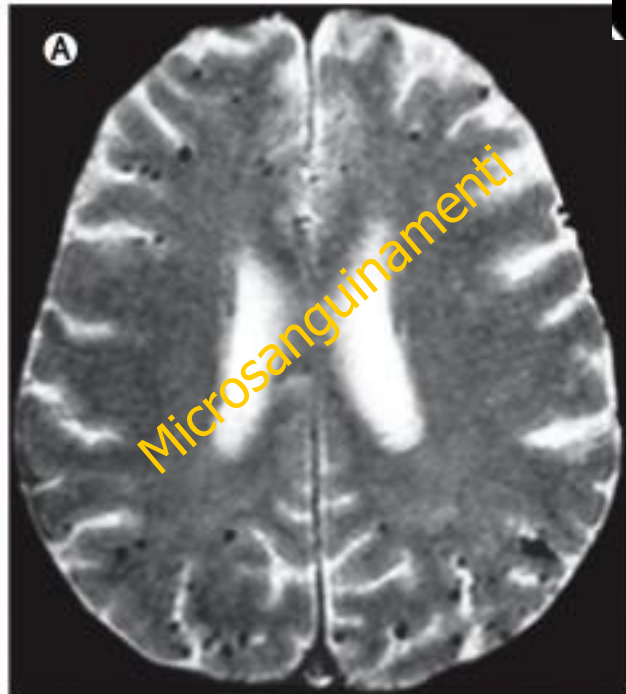
Table 1 Classic and modified Boston criteria for CAA-related hemorrhage

	Classic Boston criteria ²	Modified Boston criteria
Definite CAA	Full postmortem examination demonstrating: • Lobar, cortical, or corticosubcortical hemorrhage • Severe CAA with vasculopathy • Absence of other diagnostic lesion	No modification ^a
Probable CAA with supporting pathology	Clinical data and pathologic tissue (evacuated hematoma or cortical biopsy) demonstrating: • Lobar, cortical, or corticosubcortical hemorrhage • Some degree of CAA in specimen • Absence of other diagnostic lesion	No modification ^a
Probable CAA	Clinical data and MRI or CT demonstrating: • Multiple hemorrhages restricted to lobar, cortical, or corticosubcortical regions (cerebellar hemorrhage allowed) • Age ≥ 55 y • Absence of other cause of hemorrhage	Clinical data and MRI or CT demonstrating: • Multiple hemorrhages restricted to lobar, cortical, or corticosubcortical regions (cerebellar hemorrhage allowed) or • Single lobar, cortical, or corticosubcortical hemorrhage and focal^b or disseminated^c superficial siderosis • Age ≥ 55 y • Absence of other cause of hemorrhage or superficial siderosis
Possible CAA	Clinical data and MRI or CT demonstrating: • Single lobar, cortical, or corticosubcortical hemorrhage • Age ≥ 55 y • Absence of other cause of hemorrhage	Clinical data and MRI or CT demonstrating: • Single lobar, cortical, or corticosubcortical hemorrhage or • Focal^b or disseminated^c superficial siderosis • Age ≥ 55 y • Absence of other cause of hemorrhage or superficial siderosis

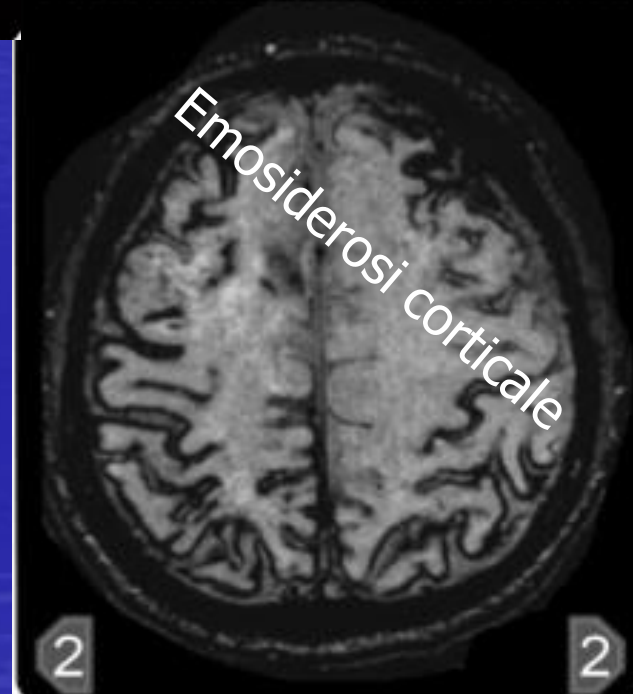
Emorragia lobare



Microsanguinamenti



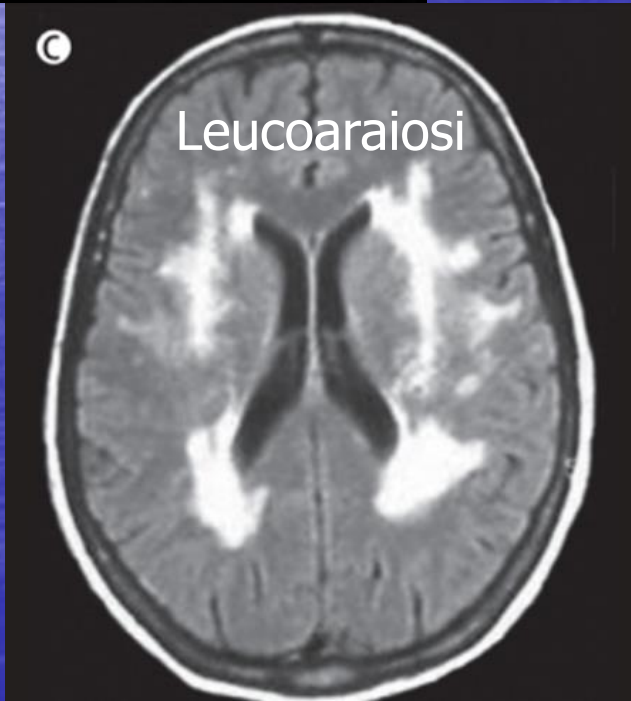
Emosiderosi corticale



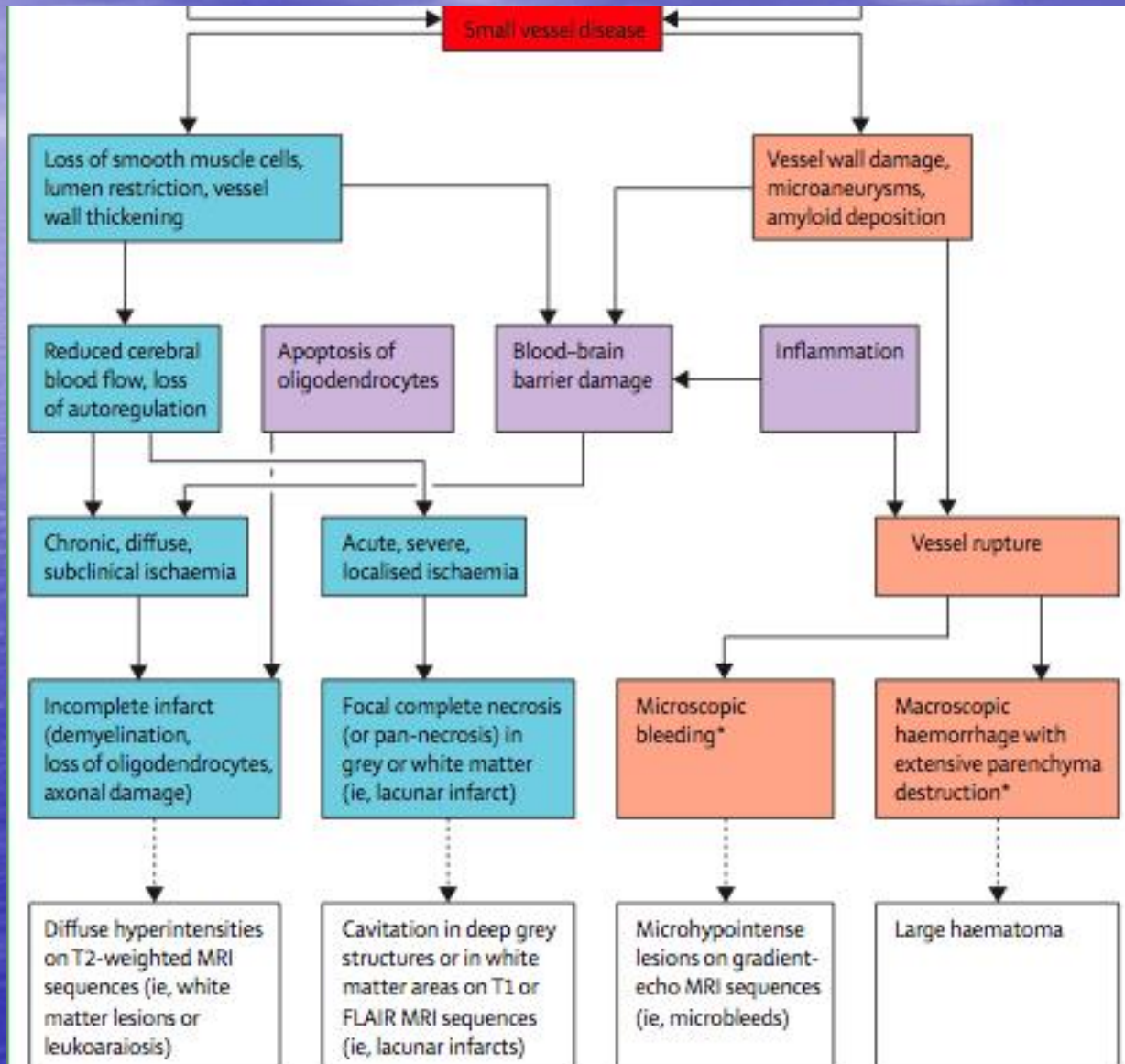
Basso rischio recidiva di emorragia cerebrale (2% rischio annuale)

- Emorragia profonda
 - Talamo
 - Gangli della base
 - Tronco cerebrale
- Microsanguinamenti cerebrali profondi
- Infarti lacunari profondi
- Leucoaraiosi
- Ipertensione arteriosa

Malattia dei piccoli vasi ipertensiva



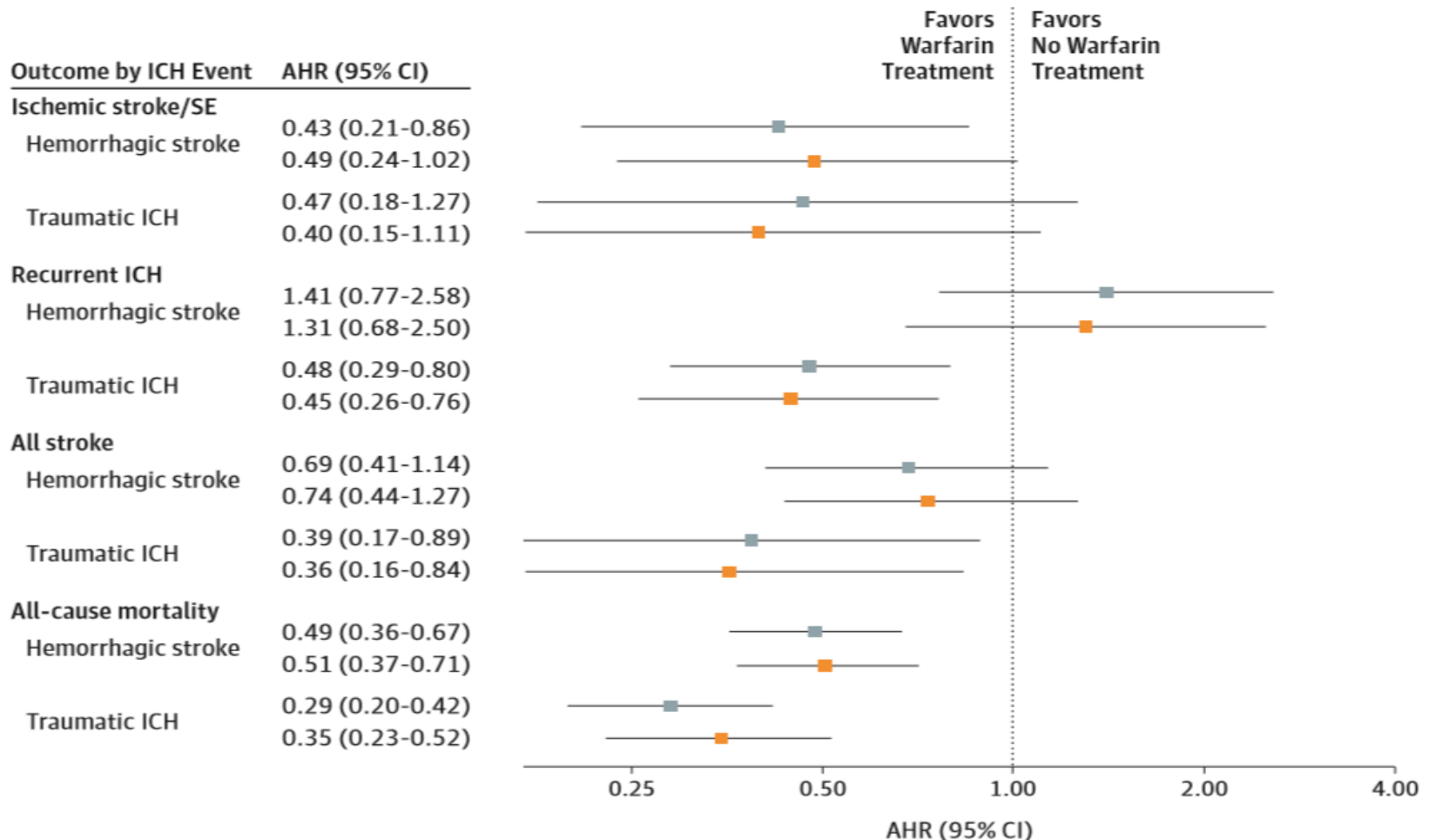
Small vessel disease: patogenesi del danno cerebrale



DSB marker	Characteristics in CMA	Characteristics in Hypertensive DSD
Microbleeds 	Lobar location [1]	Predominantly deep location [2]
Cortical microinfarcts 	Lobar location [33,37]	Not yet characterized. Hypertension is a possible risk factor for cortical microinfarcts in the elderly [38]
Cortical subarachnoid hemorrhage or superficial siderosis 	Common [9]	Not present
Cortical atrophy 	Present [27]	Not yet characterized
White matter lesions 	Severe, often sub-cortical spots [38]	Severe, often in basal ganglia [36]
Lacunar infarcts 	Upper-deep [39]	Deep-rostral [39]
Visible perivascular spaces 	Predominantly lacunar territory [40]	Predominantly basal ganglia [40]

Quali pazienti possono riprendere warfarin?

Figure 2. Forest Plots of Studied Outcomes and Associations With Resumption or No Resumption of Warfarin Treatment



Sintesi 11.5.d

- Ripresa della TAO dopo tre settimane: nel paziente a rischio tromboembolico elevato per: $CHA_2DS_2-VASc \geq 5$ o $CHADS_2 \geq 4$, protesi valvolare meccanica mitralica, trombosi delle camere cardiache, tromboembolismo venoso e arterioso < 30 giorni
- Ripresa della TAO dopo la trentesima settimana: pazienti ad alto rischio emorragico per: microbleeds multiple alla RM-gradient ECHO, leucoaraiosi, emorragie lobari non correlabili ad angiopatia amiloidea **Basso rischio di recidiva**
- Controindicazioni assolute alla ripresa della TAO: emorragia lobare correlabile ad angiopatia amiloidea **Alto rischio di recidiva**

forward 20
1997/2017



SPREAD

Stroke Prevention And Educational Awareness Diffusion

Raccomandazione 11.5.I

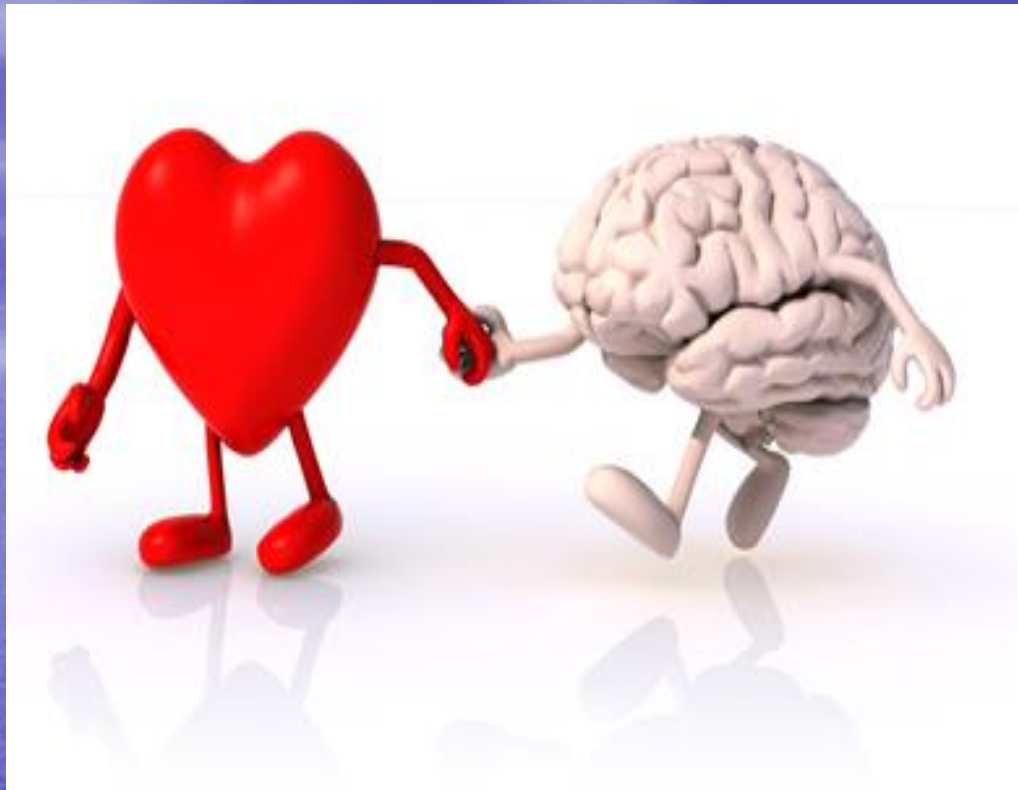
Forte a favore

Grado A

In caso di ictus emorragico in pazienti trattati con AVK o antiaggreganti per FANV, dopo aver valutato con attenzione la necessità della ripresa del trattamento anticoagulante mediante CHA₂DS₂-VASc, è raccomandato scegliere un NAO per il netto guadagno, in complicità emorragiche intracraniche, rispetto alla terapia con AVK*.

***GPP**

Nei casi con rischio tromboembolico ed emorragico elevati, il gruppo ISO-SPREAD ritiene opportuno considerare la chiusura percutanea dell'auricola sinistra.



GRAZIE PER L'ATTENZIONE... E
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