¿Porque la SVD puede evolucionar a infarto lacunar o a HIC profunda?

¿Antitrombóticos o no, si tengo microhemorragias e infartos lacunares?

Pol Camps Renom

IV Congreso de la RICORS-ICTUS
12 de junio de 2025

MINISTERIO DE CIENCIA E INNOVACIÓN

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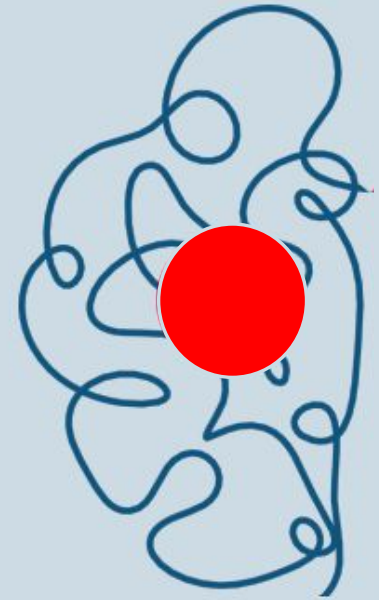

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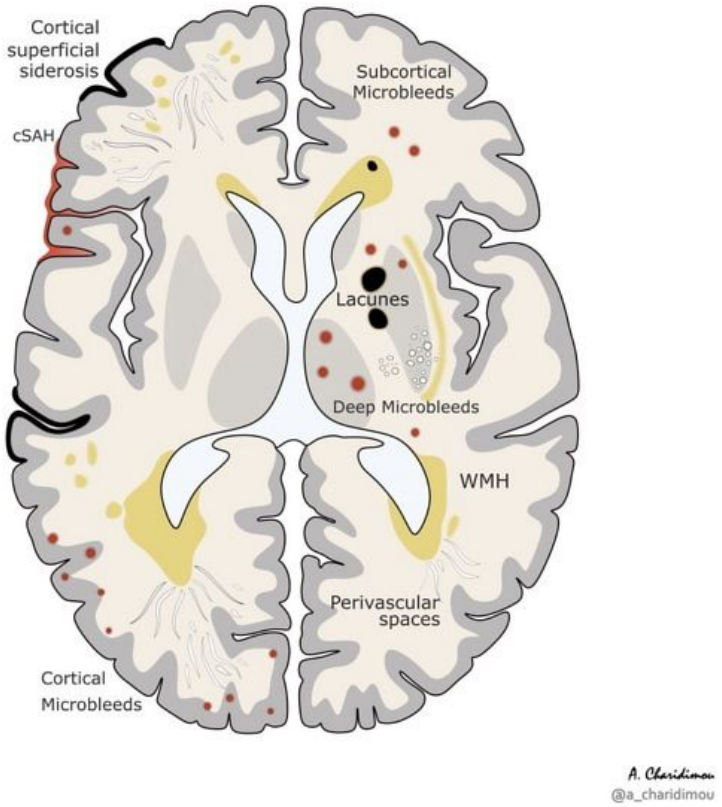
Tipos de SVD

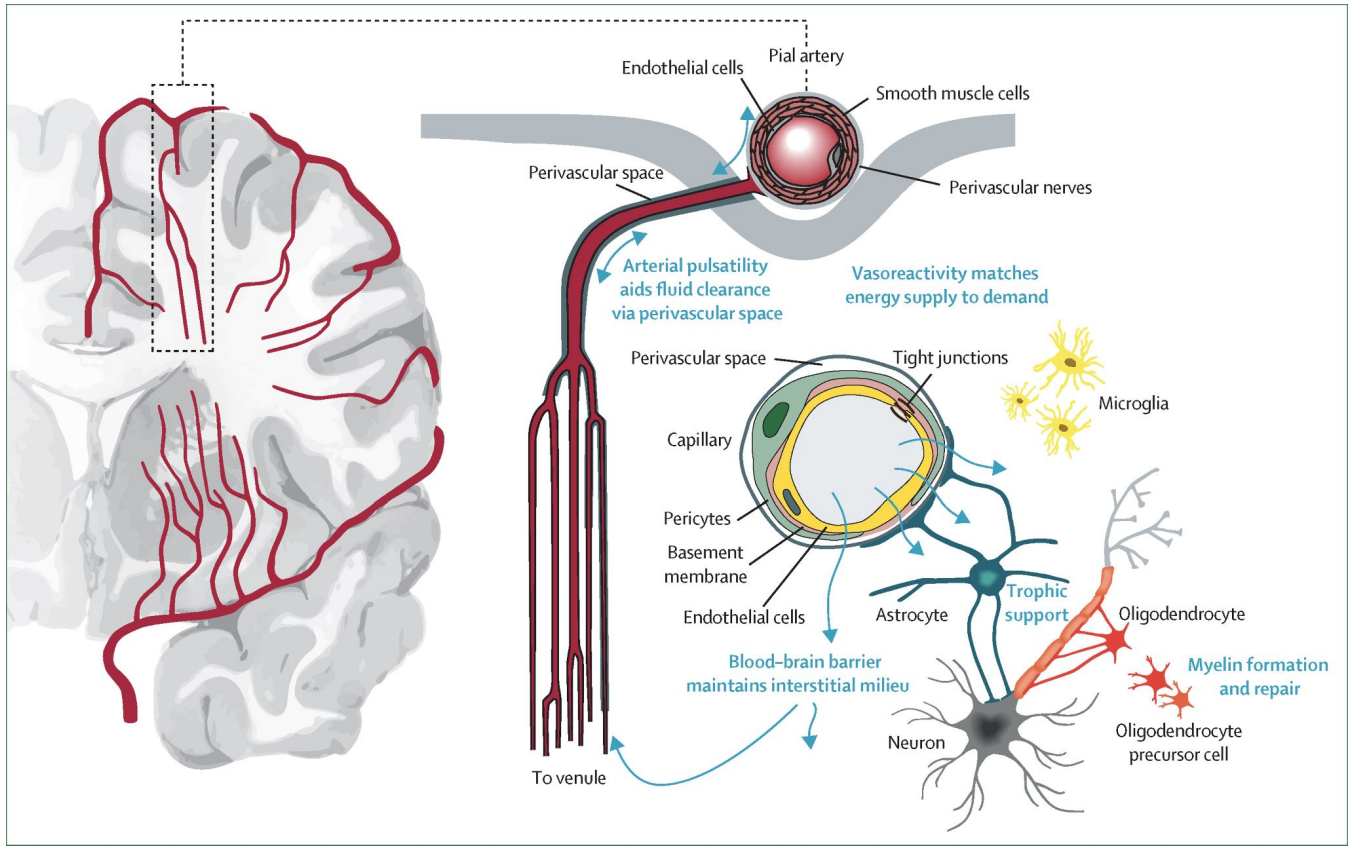


Existen 6 tipos diferentes de SVD

Los infartos lacunares son más frecuentemente causados por lipohialinosis y microateromatosis

La lipohialinosis se asocia a la vez a infartos lacunares y a hemorragias profundas

Lipohialinosis



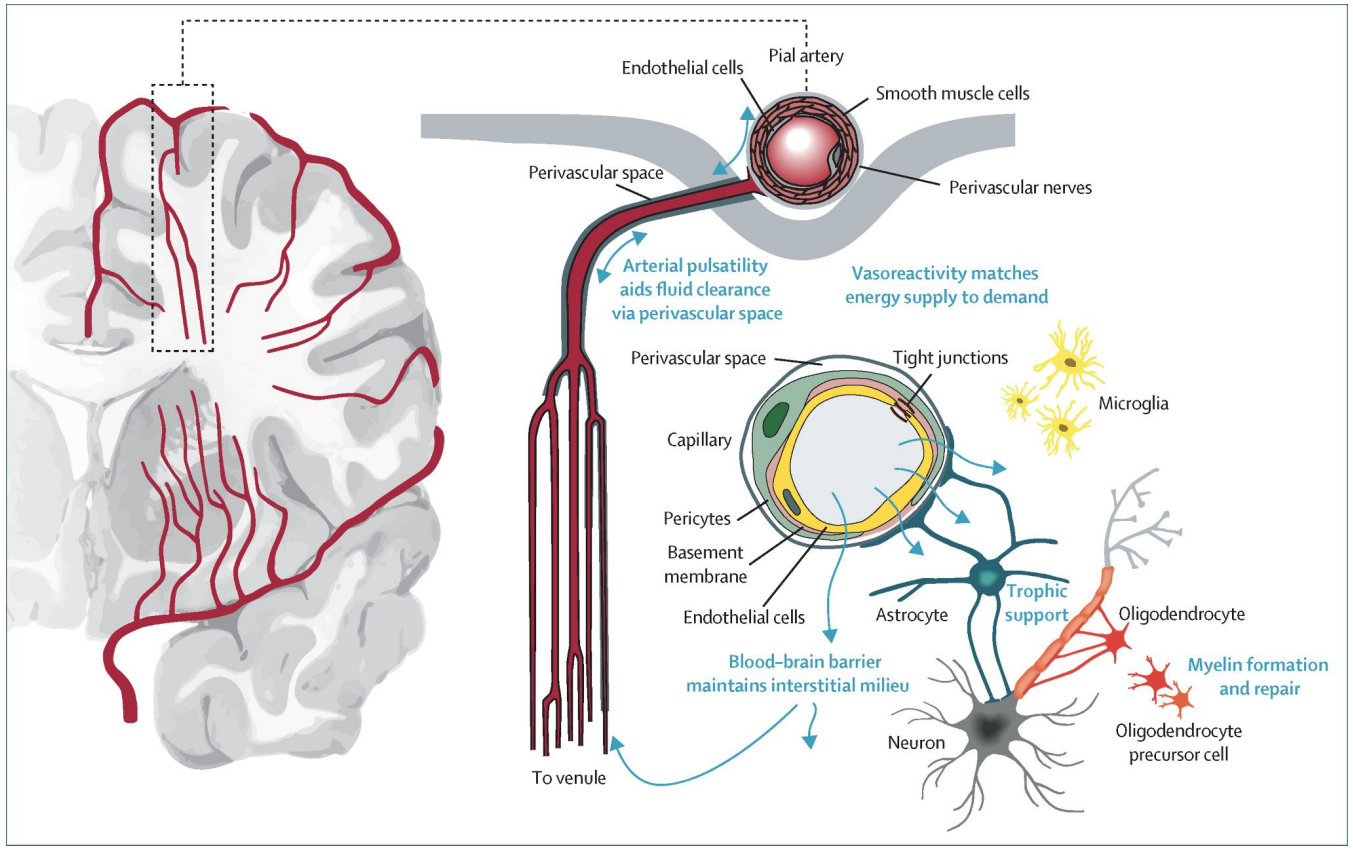
¿En qué consiste la lipohialinosis?

La lipohialinosis es una **degeneración de las paredes de las arteriolas pequeñas**, caracterizada por:

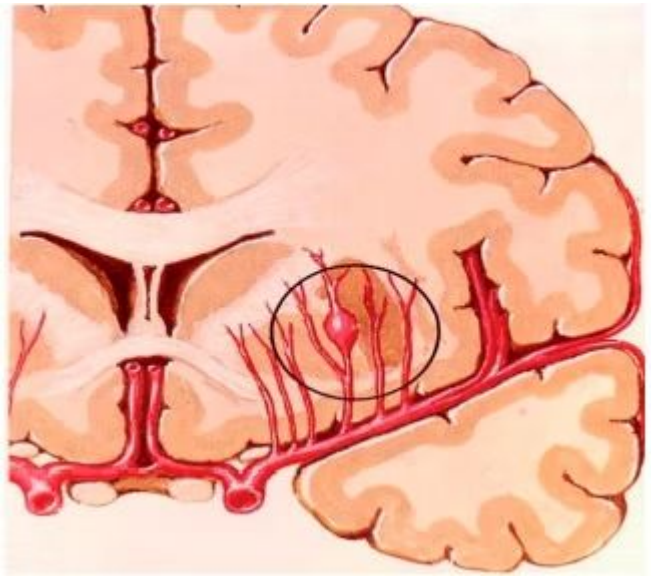
1. **Depósito de lípidos** (grasas) y material hialino (sustancia eosinofílica).
2. **Engrosamiento de la pared vascular**, lo que reduce el diámetro del vaso.
3. **Pérdida de células musculares lisas** de la pared del vaso.
4. **Fragilidad del vaso**, lo que aumenta el riesgo de ruptura o de oclusión (bloqueo).

Wardlaw JM et al. Lancet Neurol. 2019

Lipohialinosis

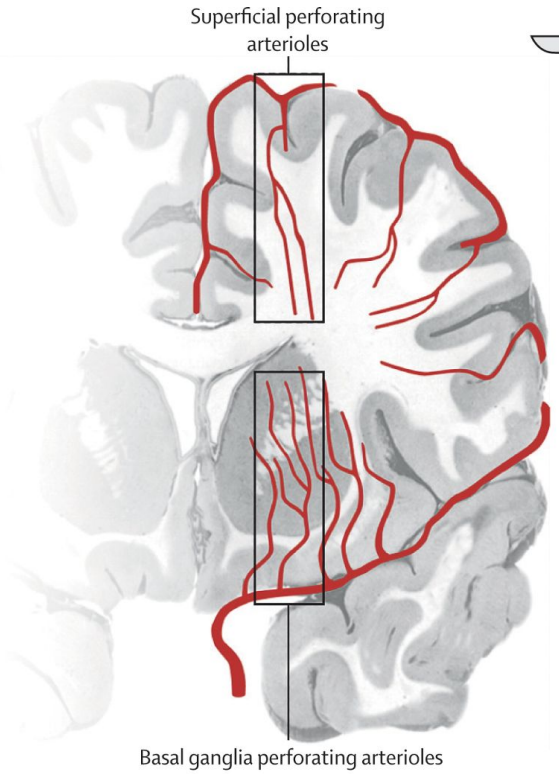


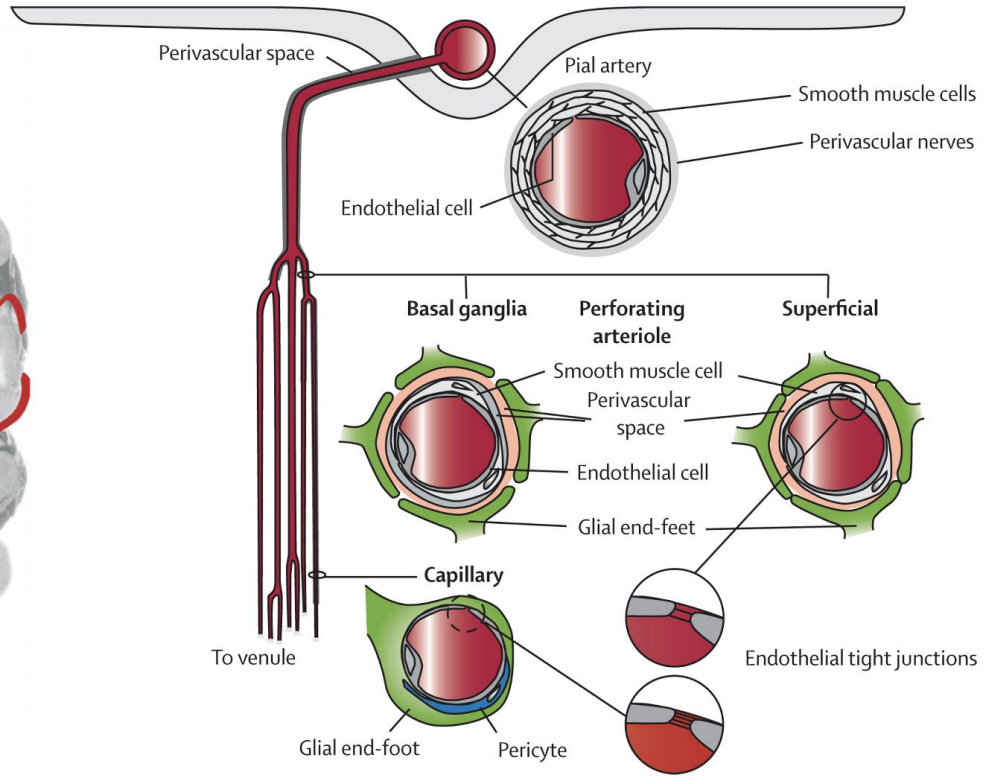
Microaneurismas de Charcot y Bouchard



Wardlaw JM et al. Lancet Neurol. 2019

Manifestaciones clínicas de la lipohialinosis

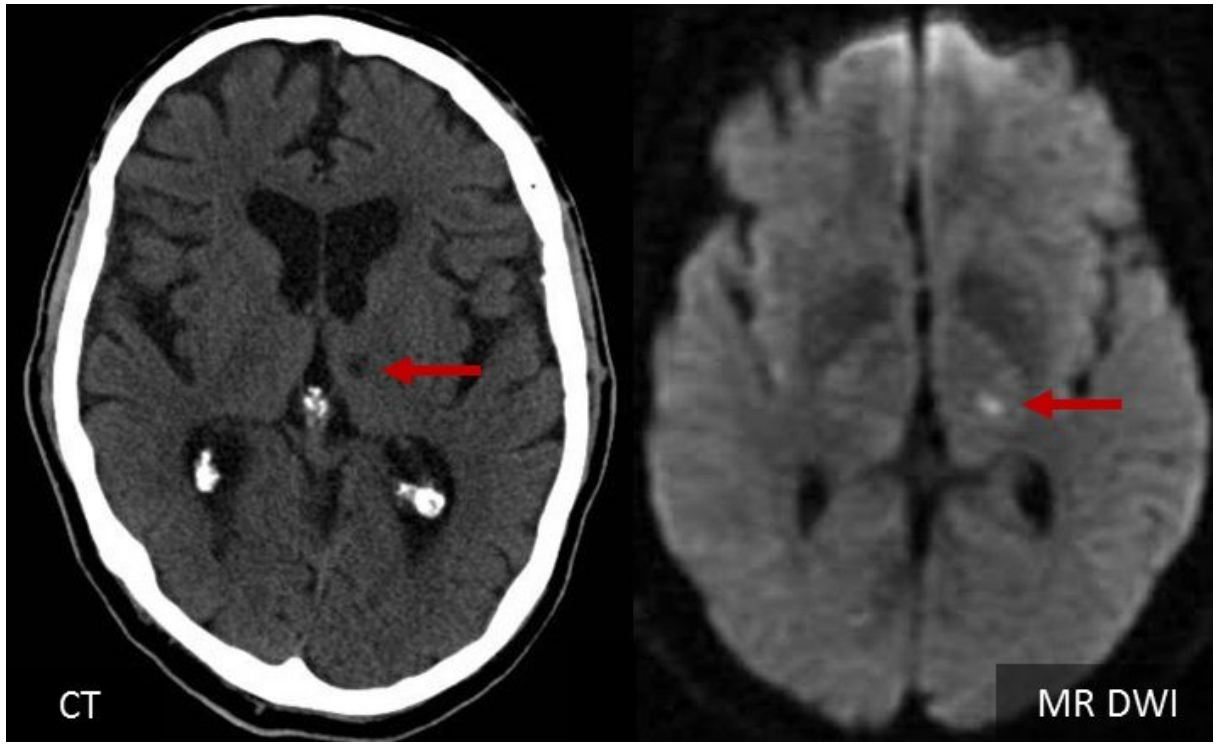




Existen formas ictales de presentación pero también formas progresivas (deterioro cognitivo y síndrome rígido-acinético)

Wardlaw JM et al. Lancet Neurol. 2013

Manifestaciones clínicas de la lipohialinosis



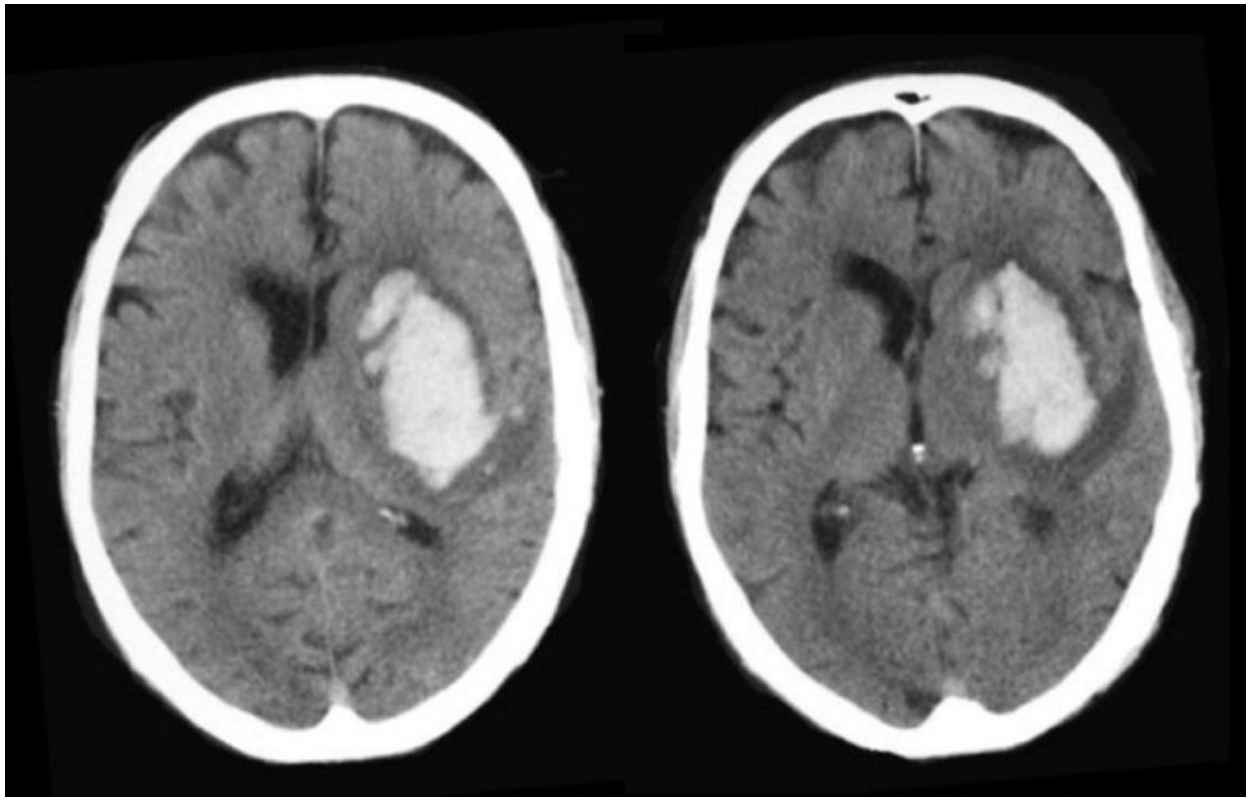
La incidencia anual de infartos lacunares podría oscilar entre 22 y 50 casos por cada 100.000 habitantes

Estos infartos suelen afectar a las pequeñas arterias perforantes que irrigan las estructuras profundas del cerebro, como los ganglios basales, el tálamo y la cápsula interna.

La mayoría de lacunares son formas esporádicas de SVD

Pantoni L et al. Lancet Neurol. 2010

Manifestaciones clínicas de la lipohialinosis

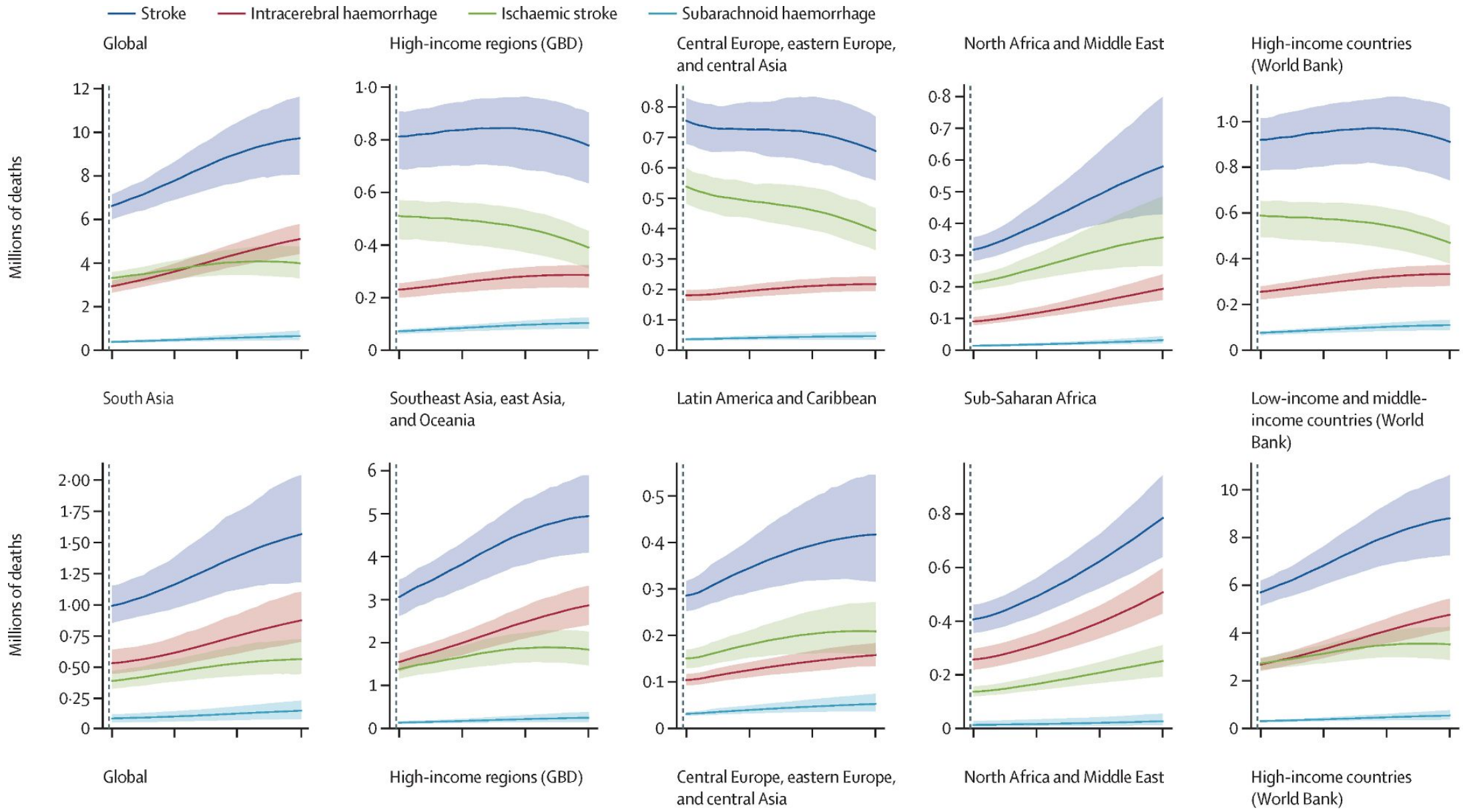


En España, la **hemorragia intracerebral (HIC)** representa aproximadamente el **10-15% de todos los ictus,** con una incidencia anual estimada de **15 casos por cada 100.000 habitantes.**

Se ven afectadas las mismas estructuras que en el infarto lacunar

El factor de riesgo más frecuente es la hipertensión arterial

Pantoni L et al. Lancet Neurol. 2010



Feigin VL et al. Lancet Neurol. 2024

Algunas diferencias

Infarto lacunar:

- **Mejor pronóstico funcional** en comparación con otros tipos de ictus.
- **Baja mortalidad** (generalmente <5%).

Hemorragia intracerebral profunda:

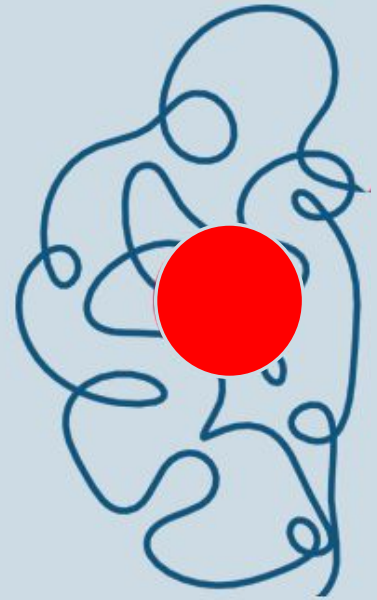
- **Mucho más grave** que los infartos lacunares.
- **Alta mortalidad**: entre **30-50% a 30 días,** especialmente si afecta a estructuras profundas como el tálamo o el tronco encefálico.
- Solo un **20% de los sobrevivientes recupera independencia funcional** al cabo de 6 meses.

Algunas diferencias

	Infarto lacunar	**Hemorragia profunda**
Edad media	>65 años	55–75 años
Sexo	Leve predominio masculino	Claro predominio masculino
Principal causa	Lipohialinosis por HTA	Ruptura por microaneurismas (Charcot-Bouchard)
Relación con edad	Más frecuente en >65	También en adultos más jóvenes con HTA severa

Martí-Vilalta JL, Arboix A, Mohr JP. Microangiopathies (Lacunes). In: Mohr JP, Wolf PhA, Grotta JC, Moskowitz MA, Mayberg MR, von Kummer R, eds. Stroke. Pathophysiology, diagnosis, and management (fifth edition). Elsevier Saunders. Philadelphia, 2011:485-515.

¿Antitrombóticos o no, si tengo microhemorragias e infartos lacunares?



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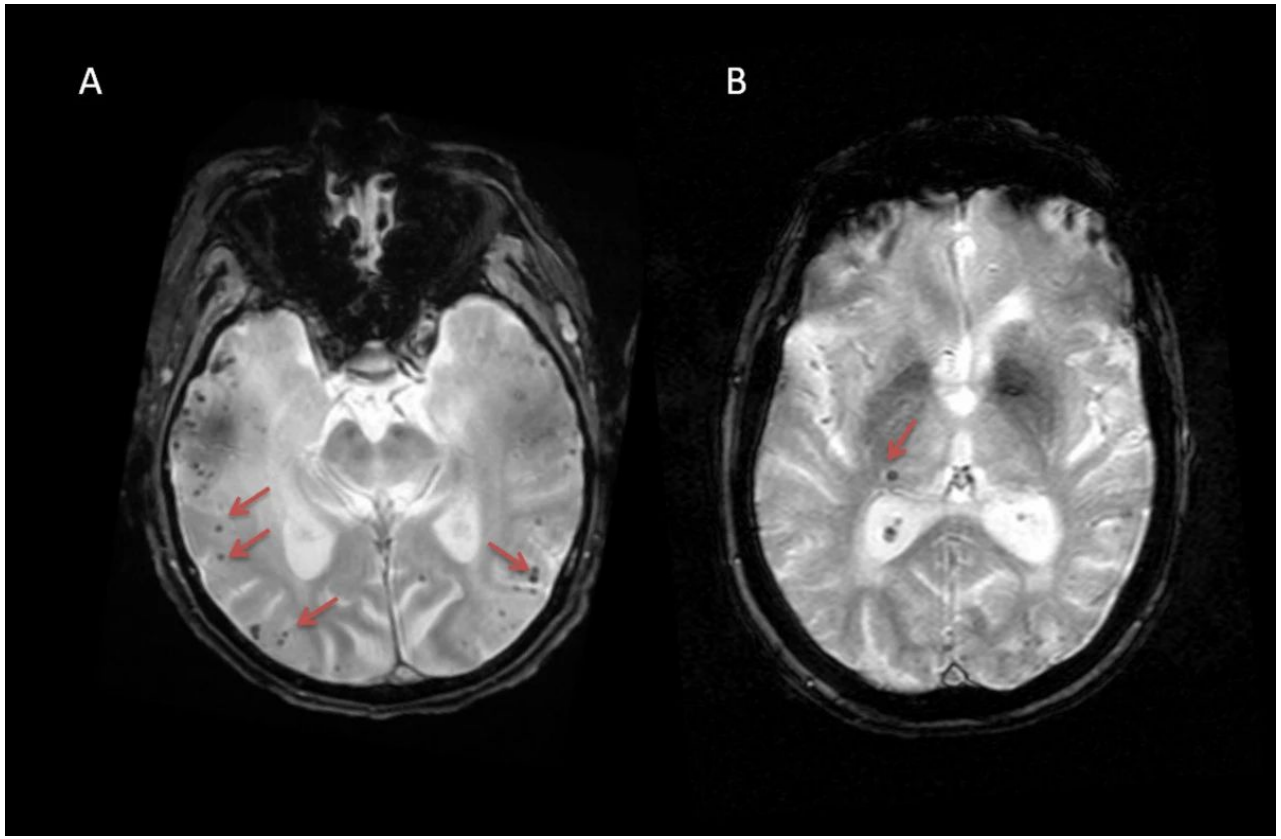
CMB y riesgo de ictus



Los CMB se asocian a mayor riesgo de hemorragia y de ictus isquémicos durante el seguimiento

Martínez-Ramírez S. et al. Alzhemier Res and Therapy. 2014.

CMB y riesgo de ictus

	n/N	All Strokes	*P* Value	n/N	Ischemic Stroke	*P* Value	n/N	Intracerebral Hemorrhage	*P* Value
Model 1*									
No microbleeds	59/3867	1.00 (Reference)		49/3867	1.00 (Reference)		5/3867	1.00 (Reference)	
Any microbleeds	34/892	1.93 (1.25–2.99)	0.004	23/892	1.52 (0.91–2.53)	0.124	6/892	5.64 (1.66–19.13)	0.006
Non–CAA-related microbleeds	18/259	3.35 (1.94–5.78)	<0.001	14/259	3.05 (1.65–5.63)	<0.001	2/259	5.92 (1.07–32.86)	0.046
CAA-related microbleeds	16/633	1.30 (0.74–2.28)	0.383	9/633	0.84 (0.41–1.74)	0.629	4/633	5.27 (1.38–20.23)	0.017
Model 2†									

Akoudad Saloua et al. Circulation. 2015.

Cerebral microbleeds and stroke risk after ischaemic stroke or transient ischaemic attack: a pooled analysis of individual patient data from cohort studies

Duncan Wilson, Gareth Ambler, Keon-Joo Lee, Jae-Sung Lim, Masayuki Shiozawa, Masatoshi Koga, Linxin Li, Michael Hennerici, Yuen Kwun Wong, Henry Ka Fung Mak, Luis Prats-Sánchez, Alejandro Martínez-Domeño, Ethem Murat Arsava, Solveig Horstmann, Jan Purrucker, Bonnie Yin Ka Lam, Adrian Wong, Young Dae Kim, T Robin Lemmens, Sebastian Eppinger, Thomas Gattringer, Ender Uysal, Zeynep Tanriverdi, Natan M Bornstein Jun Tanaka, Hideo Hara, Shelagh B Coutts, Lisa Hert, Alexandros Polymeris, David J Seiffge, Philippe Lyrer, Ale Rustam Al-Shahi Salman, Hans R Jäger, Gregory Y H Lip, Heinrich P Mattle, Leonidas D Panos, Jean-Louis Ma Christopher Karayiannis, Thanh Phan, Sarah Gunkel, Nicolas Christ, Jill Abrigo, Thomas Leung, Winnie Chu, F Derek Hayden, David J Williams, M Eline Kooi, Dianne H K van Dam-Nolen, Carmen Barbato, Simone Brownir Noortje Maaijwee, Christine Guevarra, Chathuri Yatawara, Anne-Marie Mendyk, Christine Delmaire, Sebastia Ying Zhou, Chao Xu, Saima Hilal, Bibek Gyanwali, Christopher Chen, Min Lou, Julie Staals, Régis Bordet, Naga Frank-Erik de Leeuw, Robert Simister, Aad van der Lugt, Peter J Kelly, Joanna M Wardlaw, Yannie Soo, Felix Flu Simon Jung, Vincent I H Kwa, Stefan T Engelter, Nils Peters, Eric E Smith, Yusuke Yakushiji, Dilek Necioglu Ork Ji Hoe Heo, Vincent Mok, Roland Veltkamp, Hakan Ay, Toshio Imaizumi, Beatriz Gomez-Anson, Kui Kai Lau, E Kazunori Toyoda, Hee-Joon Bae, Joan Marti-Fabregas, David J Werring, on behalf of the Microbleeds Internati

Irrespective of cerebral microbleed anatomical distribution or burden, the rate of ischaemic stroke exceeded that of intracranial haemorrhage 64 ischaemic strokes [95% CI 48–84] per 1000 patient-years vs 27 intracranial haemorrhages [17–41] per 1000 patient-years.

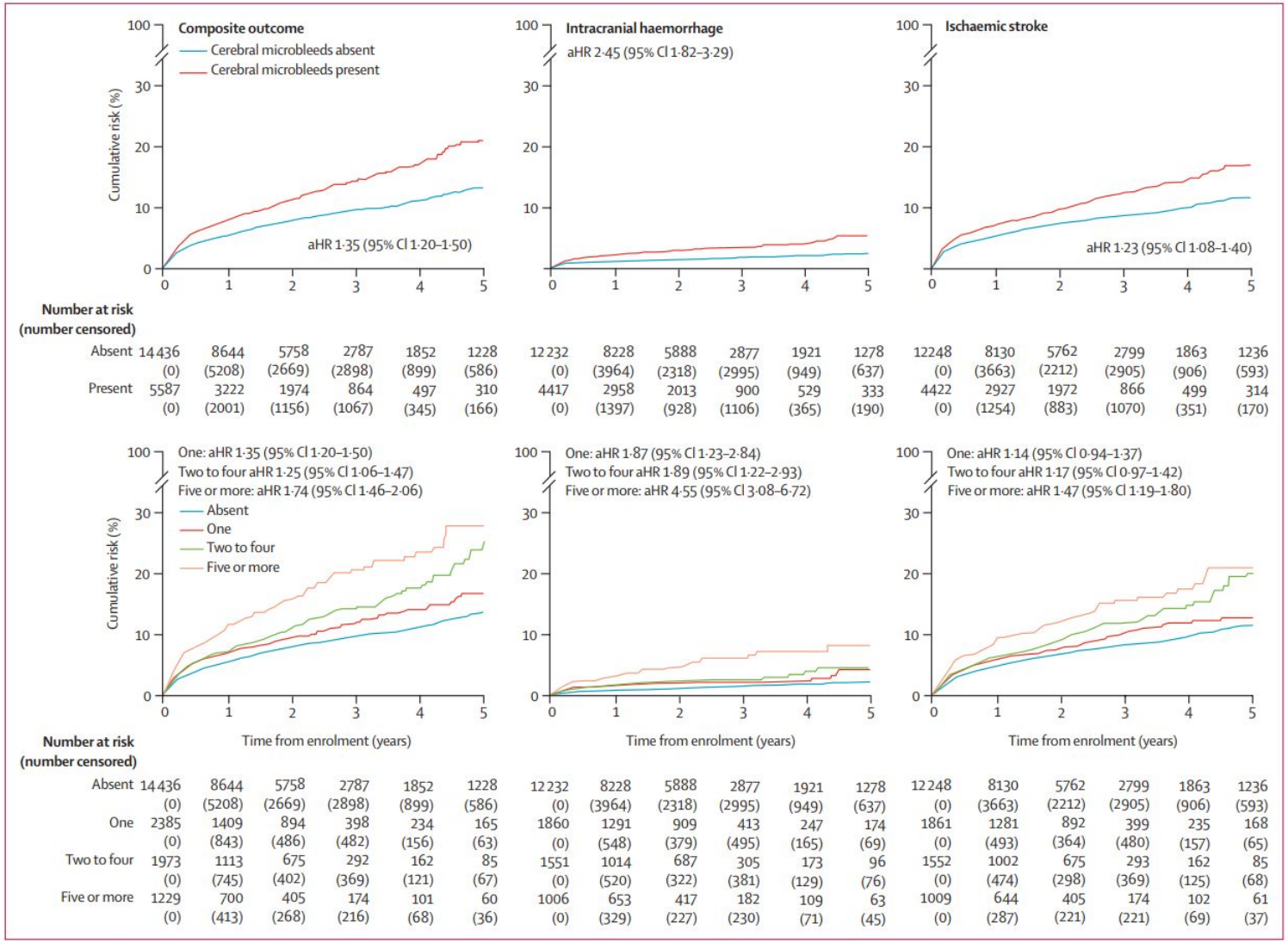


Figure 2: **Kaplan-Meier estimates for the primary outcomes in all patients (n=20 322)**

Cerebral microbleeds and intracranial haemorrhage risk in patients anticoagulated for atrial fibrillation after acute ischaemic stroke or transient ischaemic attack (CROMIS-2): a multicentre observational cohort study

*Duncan Wilson, Gareth Ambler, Clare Shakeshaft, Martin M Brown, Andreas Charidimou, Rustam Al-Shahi Salman, Gregory Y H Lip, Hannah Cohen, Gargi Banerjee, Henry Houlden, Mark J White, Tarek A Yousry, Kirsty Harkness, Enrico Flossmann, Nigel Smyth, Louise J Shaw, Elizabeth Warburton, Keith W Muir, Hans Rolf Jäger, David J Werring, on behalf of the CROMIS-2 collaborators**

	Absolute event rate*	Rate per 1000 patient-years (95% CI)	Absolute rate increase per 1000 patient-years (95% CI)	Univariable hazard ratio (95% CI)	Adjusted hazard ratio (95% CI)†
Symptomatic intracranial haemorrhage					
No cerebral microbleeds	7/2654	2·6 (1·1 to 5·4)	1 (ref)	1 (ref)	1 (ref)
Cerebral microbleeds present	7/712	9·8 (4·0 to 20·3)	7·2 (2·9 to 14·9)	3·73 (1·31 to 10·64)	3·67 (1·27 to 10·60)
1 cerebral microbleed	2/367	5·4 (0·7 to 19·7)	2·8 (−0·4 to 14·3)	2·04 (0·42 to 9·84)	2·03 (0·42 to 9·83)
≥2 cerebral microbleeds	5/345	14·4 (4·7 to 33·8)	11·8 (3·6 to 28·4)	5·58 (1·77 to 17·58)	5·46 (1·70 to 17·51)
Recurrent ischaemic stroke					
No cerebral microbleeds	39/2608	15·0 (10·6 to 20·4)	1 (ref)	1 (ref)	1 (ref)
Cerebral microbleeds present	17/704	24·1 (14·1 to 38·7)	9·1 (3·5 to 18·3)	1·62 (0·92 to 2·87)	1·53 (0·85 to 2·76)
1 cerebral microbleed	9/362	24·9 (11·4 to 47·2)	9·9 (0·8 to 32·2)	1·68 (0·82 to 3·47)	1·75 (0·84 to 3·65)
≥2 cerebral microbleeds	8/341	23·4 (10·1 to 46·2)	8·4 (−0·5 to 25·8)	1·56 (0·73 to 3·35)	1·32 (0·60 to 2·93)

Data are calculated on the 1447 participants with follow-up data available. *Calculated as number of events/patient-years. †Adjusted for age and hypertension for symptomatic intracranial haemorrhage, and adjusted for age, sex, hypertension, diabetes, previous ischaemic stroke, and age-related white matter hyperintensities score for recurrent ischaemic stroke.

Table 3: **Absolute event rates, absolute risks, and univariable and multivariable hazard ratios for symptomatic intracranial haemorrhage and recurrent ischaemic stroke during follow-up, according to baseline presence and burden of cerebral microbleeds**

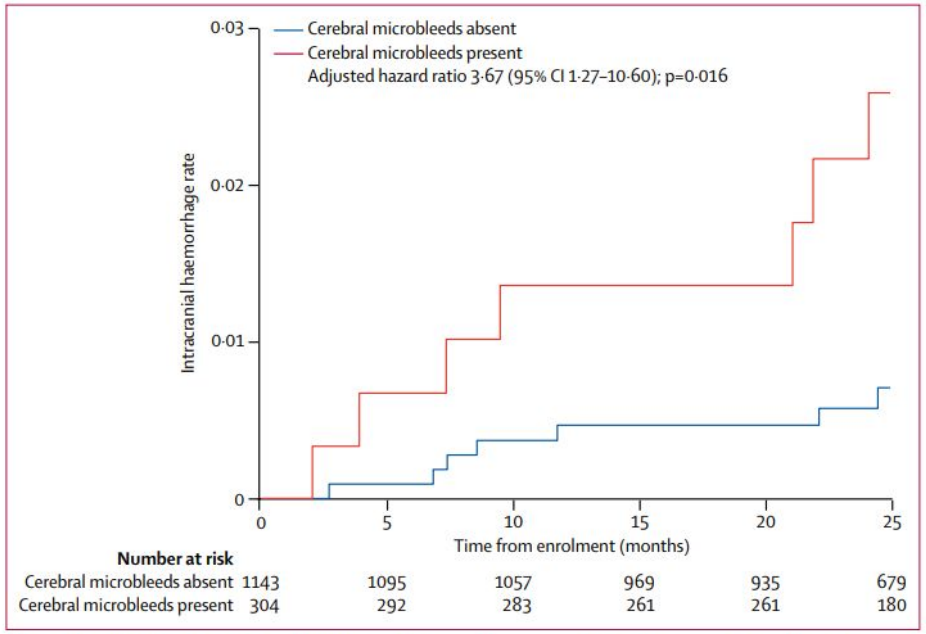


Figure 2: **Probability of symptomatic intracranial haemorrhage according to the presence or absence of cerebral microbleeds**
The hazard ratio (HR) and 95% CI are derived from the model adjusted for hypertension and age.

ARTICLE

MRI predicts intracranial hemorrhage in patients who receive long-term oral anticoagulation

Joan Martí-Fàbregas, MD, PhD, Santiago Medrano-Martorell, MD, Elisa Merino, MD, Luis Prats-Sánchez, MD, Rebeca Marín, RN, Raquel Delgado-Mederos, MD, PhD, Alejandro Martínez-Domeño, MD, Pol Camps-Renom, MD, Elena Jiménez-Xarrié, PhD, Mariluisa Zedde, MD, Manuel Gómez-Choco, MD, PhD, Lidia Lara, MD, Amèlia Boix, MD, Ana Calleja, MD, Ana María De Arce-Borda, MD, Yolanda Bravo, MD, PhD, Blanca Fuentes, MD, PhD, María Hernández-Pérez, MD, PhD, David Cánovas, MD, PhD, Laura Llull, MD, PhD, Beatriz Zandio, MD, Marimar Freijo, MD, Ignacio Casado-Naranjo, MD, Jordi Sanahuja, MD, Dolores Cocho, MD, PhD, Jerzy Krupinski, MD, PhD, Ana Rodríguez-Campello, MD, PhD, Ernest Palomeras, MD, PhD, Alicia De Felipe, MD, Marta Serrano, MD, Elena Zapata-Arriaza, MD, Josep Zaragoza-Brunet, MD, Inmaculada Díaz-Maroto, MD, Jessica Fernández-Domínguez, MD, PhD, Aida Lago, MD, José Maestre, MD, Manuel Rodríguez-Yáñez, MD, PhD, and Ignasi Gich, MD, PhD, for the HERO study investigators

Correspondence
Prof. Martí-Fàbregas
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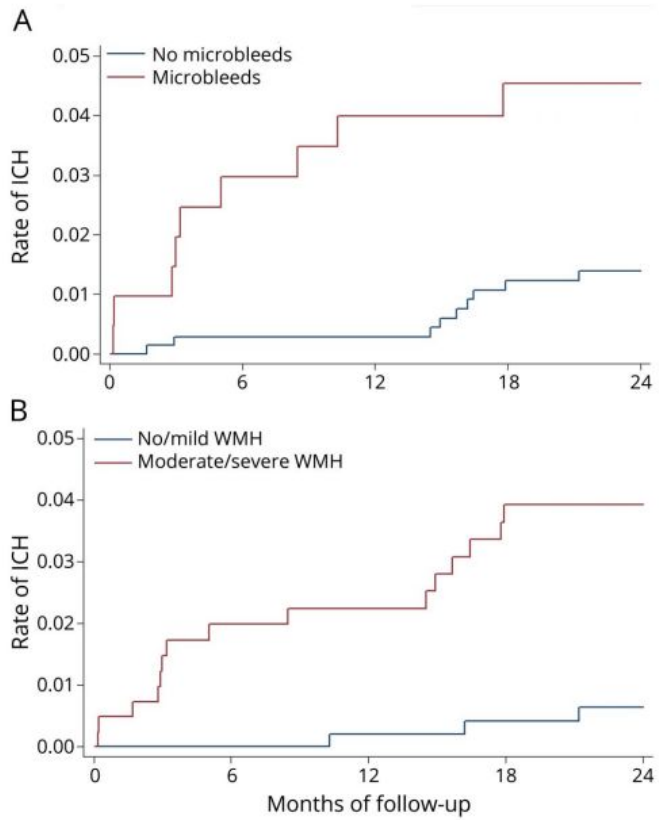
Neurology® 2019;92:e2432-e2443. doi:10.1212/WNL.0000000000007532

Table 3 Rate of intracranial hemorrhage per 100 patient-years (95% CI) according to MRI findings

	Rate	95% CI
All patients	1.01 per 100 patient-years	0.6–1.59
Patients without MB	0.66 per 100 patient-years	0.3–1.25
Patients with MB	2.33 per 100 patient-years	1.06–4.41
Patients with only 1 MB	2.19 per 100 patient-years	0.6–5.6
Patients with >1 MB	2.53 per 100 patient-years	0.82–5.89
Patients with no/mild WMH	0.3 per 100 patient-years	0.06–0.87
Patients with moderate/severe WMH	1.96 per 100 patient-years	1.1–3.23
Patients with MB and moderate/severe WMH	3.76 per 100 patient-years	1.62–7.4

Abbreviations: CI = confidence interval; MB = microbleed; WMH = white matter hyperintensity.

Figure 2 Probability of ICH according to the presence of MB and the degree of WMH



Kaplan-Meier cumulative incidence curves reflecting (A) the probability of ICH according to the presence/absence of MB; and (B) the probability of ICH according to the degree of WMH. ICH = intracranial hemorrhage; MB = microbleeds; WMH = white matter hyperintensities.

Effects of antiplatelet therapy after stroke due to intracerebral haemorrhage (RESTART): a randomised, open-label trial

*RESTART Collaboration**

	Start antiplatelet therapy (n=268)	Avoid antiplatelet therapy (n=268)	Log-rank test p value	Unadjusted analysis		Adjusted analysis	
				HR (95% CI)	p value	HR (95% CI)	p value
Primary outcome							
Recurrent symptomatic spontaneous intracerebral haemorrhage	12	23	0·057	0·51 (0·26–1·03)	0·062	0·51 (0·25–1·03)	0·060
Sensitivity analyses of the primary outcome							
Recurrent symptomatic spontaneous intracerebral haemorrhage or symptomatic stroke of uncertain subtype	12	24	0·041	0·49 (0·25–0·99)	0·046	0·49 (0·24–0·98)	0·044
Recurrent symptomatic spontaneous intracerebral haemorrhage or death of undetermined cause	13	25	0·047	0·51 (0·26–1·00)	0·051	0·51 (0·26–0·99)	0·048
Secondary outcomes							
All major haemorrhagic events (all types of symptomatic spontaneous or traumatic intracranial haemorrhage, or symptomatic major extracranial haemorrhage)	18	25	0·27	0·71 (0·39–1·30)	0·27	0·71 (0·39–1·30)	0·27
All major occlusive vascular events (ischaemic stroke; myocardial infarction; mesenteric ischaemia; peripheral arterial occlusion; deep vein thrombosis; pulmonary embolism; or carotid, coronary, or peripheral arterial revascularisation procedures)	39	38	0·97	1·01 (0·65–1·58)	0·97	1·02 (0·65–1·60)	0·92
All major haemorrhagic or occlusive vascular events	54	61	0·42	0·86 (0·60–1·24)	0·42	0·86 (0·60–1·24)	0·43
Major occlusive vascular events*	45	52	0·39	0·84 (0·56–1·25)	0·39	0·84 (0·56–1·25)	0·39
Major vascular events (as defined by the Antithrombotic Trialists' Collaboration)	45	65	0·026	0·65 (0·45–0·95)	0·027	0·65 (0·44–0·95)	0·025

HR=hazard ratio. *As defined in the trial protocol.

Table 3: **Risks of first occurrence of primary and secondary outcome events during follow-up**

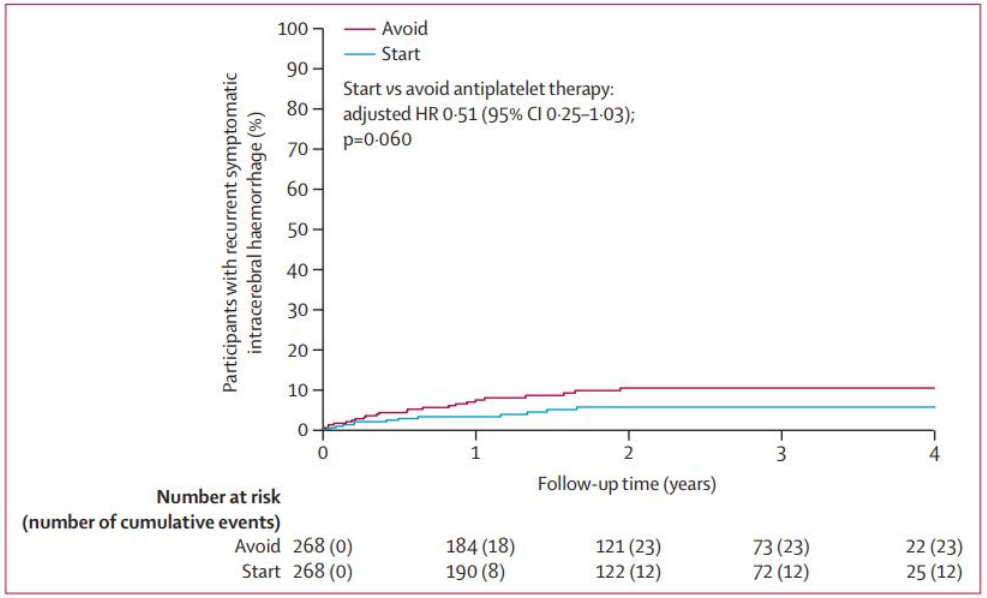


Figure 2: **Kaplan-Meier plot of the first occurrence of recurrent symptomatic intracerebral haemorrhage**
Numbers at risk refer to survivors under follow-up at the start of each year according to treatment allocation. Cumulative events indicate the participants in follow-up with a first event. HR=hazard ratio.

Rustam Al-Shahi Salman, et al. Lancet. 2019

Table 2 MRI findings in patients with and without new remote cerebral microbleeds (CMBs) following IV thrombolysis

	New CMBs (n = 16)	No new CMBs (n = 380)	*p* Value	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
CMB presence on pretreatment MRI, % (n)	50.0 (8)	28.2 (107)	0.059	2.55 (0.93–6.97)	2.41 (0.85–6.84)
No. of CMBs on pretreatment MRI, median (IQR)	0.5 (0–5.0)	0 (0–1.0)	0.026	1.15 (0.98–1.36)	1.13 (0.98–1.29)
No. of CMBs on pretreatment MRI, % (n)			<0.001		
0	50.0 (8)	71.8 (273)			
1	18.8 (3)	13.9 (53)		1.93 (0.50–7.52)	1.93 (0.48–7.67)
2–4	6.3 (1)	10.8 (41)		0.83 (0.10–6.83)	0.79 (0.09–6.62)
≥5	25.0 (4)	3.4 (13)		10.50 (2.80–39.42)	9.48 (2.36–38.10)
CMBs with a strictly lobar distribution on pretreatment MRI, % (n)	31.3 (5)	11.1 (42)	0.014	3.66 (1.21–11.04)	3.62 (1.15–11.38)
CMBs with a strictly deep or mixed distribution on pretreatment MRI, % (n)	12.5 (2)	14.7 (56)	0.804	0.83 (0.18–3.74)	0.77 (0.17–3.55)
PHr after IVT, % (n)	25.0 (4)	0.8 (3)	<0.001	41.89 (8.43–208.20)	67.43 (11.06–411.16)
sICH after IVT, % (n)	12.5 (2)	1.6 (6)	0.002	8.91 (1.65–48.11)	12.43 (2.07–74.60)
Time interval between pretreatment and follow-up MRI, hh:mm, median (IQR)	22:13 (20:24–25:31)	22:35 (20:19–24:19)	0.725	1.00 (1.00–1.00)	1.00 (1.00–1.00)

er del 24%

CI) Weight (%)

16.36

30.24

53.40

100.00

Braemswig TB, et al. Neurology. 2019

Charidimou A, et al. Neurology 2016

RESEARCH ARTICLE OPEN ACCESS

Cerebral Microbleeds and Treatment Effect of Intravenous Thrombolysis in Acute Stroke

An Analysis of the WAKE-UP Randomized Clinical Trial

Ludwig Schlemm, MD, MSc, Tim Bastian Braemswig, MD, Florent Boutitie, PhD, Jan Vynckier, MD, Märit Jensen, MD, Ivana Galinovic, MD, PhD, Claus Z. Simonsen, MD, PhD, Bastian Cheng, MD, Tae-Hee Cho, MD, PhD, Jens Fiehler, MD, Josep Puig, MD, Vincent Thijs, MD, Jochen Fiebach, MD, Keith Muir, MD, Norbert Nighoghossian, MD, Martin Ebinger, MD, PhD, Salvador Pedraza, MD, PhD, Götz Thomalla, MD, Christian Gerloff, MD, Matthias Endres, MD, Robin Lemmens, MD, PhD,* and Christian H. Nolte, MD*, on behalf of WAKE-UP Investigators

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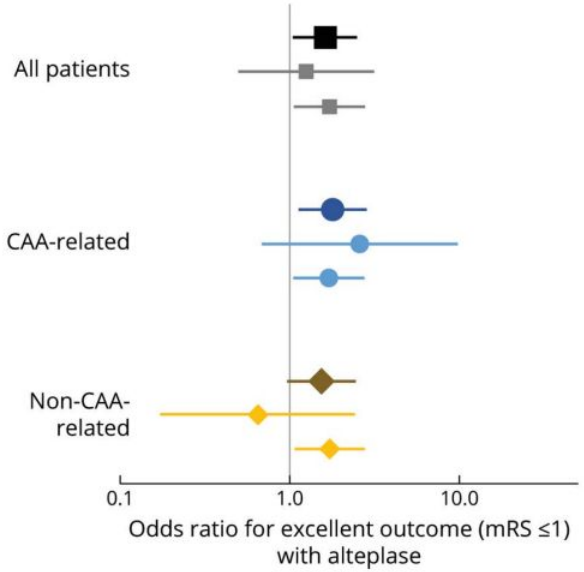
Neurology® 2022;98:e302-e314. doi:10.1212/WNL.0000000000013055

No evidence of reduced treatment effect of alteplase in patients with acute ischemic stroke with ≥1 CMBs

Figure 2 Association Between Alteplase Treatment and Functional Outcome at 90 Days According to Presence and Spatial Distribution of CMBs



Subgroup	Placebo	Alteplase	OR (95% CI)	p*
All	**99/222 (44.6%)**	**124/227 (54.6%)**	**1.61 (1.07–2.43)**	**0.022**
≥1 CMB	19/44 (43.2%)	25/52 (48.1%)	1.26 (0.51–3.09)	0.546
No CMB	80/178 (44.9%)	99/175 (56.6%)	1.72 (1.09–2.72)	
All	**86/200 (43.0%)**	**112/205 (54.6%)**	**1.79 (1.16–2.75)**	**0.008**
≥1 CMB	6/22 (27.3%)	13/30 (43.3%)	2.60 (0.70–9.60)	0.553
No CMB	80/178 (44.9%)	99/175 (56.6%)	1.71 (1.08–2.70)	
All	**93/200 (46.5%)**	**111/197 (56.3%)**	**1.54 (1.00–2.37)**	**0.048**
≥1 CMB	13/22 (59.1%)	12/22 (54.5%)	0.65 (0.18–2.39)	0.169
No CMB	80/178 (44.9%)	99/175 (56.6%)	1.72 (1.09–2.72)	

CONCLUSIONES

1. La SVD por lipohialinosis afecta las arteriolas perforantes y es causa de infartos lacunares y de hemorragias profundas
2. A pesar de tener un origen común y factores de riesgo en común ambas patologías presentan algunas diferencias epidemiológicas y pronósticas importantes
3. La presencia de CMB profundos incrementa el riesgo de HIC con los tratamientos antitrombóticos aunque el beneficio de estos en la prevención de recurrencias isquémicas parece mayor
4. La presencia de CMB profundos no contraindica el tratamiento con fibrinolisis endovenosa en fase aguda de un ictus isquémico

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Gracias por la atención!

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