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Review

Prevalence of Cerebral Amyloid Angiopathy Pathology and Strictly Lobar Microbleeds in East-Asian Versus Western Populations: A Systematic Review and Meta-Analysis

Anna M. De Kort,[1,2] Marcel M. Verbeek,[1,2,3] Floris H.B.M. Schreuder,[1] Catharina J.M. Klijn,[1] Lieke Jäkel[1,2]

[1]Department of Neurology, Radboud University Medical Center, Donders Institute for Brain, Cognition and Behaviour, Nijmegen, The Netherlands
[2]Radboud Alzheimer Centre, Radboud University Medical Center, Nijmegen, The Netherlands
[3]Department of Genetics, Radboud University Medical Center, Nijmegen, The Netherlands

Background and Purpose Possible differences in the prevalence of cerebral amyloid angiopathy (CAA) in East-Asian compared to Western populations have received little attention, and results so far have been ambiguous. Our aim is to compare the prevalence of CAA neuropathology and magnetic resonance imaging markers of CAA in East-Asian and Western cohorts reflecting the general population, cognitively normal elderly, patients with Alzheimer's disease (AD), and patients with (lobar) intracerebral hemorrhage (ICH).

Methods We performed a systematic literature search in PubMed and Embase for original research papers on the prevalence of CAA and imaging markers of CAA published up until February 17th 2022. Records were screened by two independent reviewers. Pooled estimates were determined using random-effects models. We compared studies from Japan, China, Taiwan, South Korea (East-Asian cohorts) to studies from Europe or North America (Western cohorts) by meta-regression models.

Results We identified 12,257 unique records, and we included 143 studies on Western study populations and 53 studies on East-Asian study populations. Prevalence of CAA neuropathology did not differ between East-Asian and Western cohorts in any of the investigated patient domains. The prevalence of strictly lobar microbleeds was lower in East-Asian cohorts of population-based individuals (5.6% vs. 11.4%, P=0.020), cognitively normal elderly (2.6% vs. 11.4%, P=0.001), and patients with ICH (10.2% vs. 24.6%, P<0.0001). However, age was in general lower in the East-Asian cohorts.

Conclusion The prevalence of CAA neuropathology in the general population, cognitively normal elderly, patients with AD, and patients with (lobar) ICH is similar in East-Asian and Western countries. In East-Asian cohorts reflecting the general population, cognitively normal elderly, and patients with ICH, strictly lobar microbleeds were less prevalent, likely due to their younger age. Consideration of potential presence of CAA is warranted in decisions regarding antithrombotic treatment and potential new anti-amyloid-β immunotherapy as treatment for AD in East-Asian and Western countries alike.

Keywords Cerebral amyloid angiopathy; Prevalence; Epidemiology; Asia; Europe; Microbleeds

Correspondence: Marcel M. Verbeek
Department of Neurology, 830 TML,
Radboud University Medical Center,
P.O. Box 9101, 6500 HB Nijmegen,
The Netherlands
Tel: +31-243614567
E-mail: marcel.verbeek@radboudumc.nl
https://orcid.org/0000-0002-5679-516X

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Introduction

Cerebral amyloid angiopathy (CAA) is a vasculopathy characterized by the accumulation of amyloid-β (Aβ) in cerebral vessel walls. CAA is associated with an increased risk of cognitive decline and intracerebral hemorrhage (ICH).[1,2] We have recently shown that approximately a quarter of the general elderly population has moderate-to-severe CAA pathology.[3] This underlines the importance of considering CAA in the differential diagnosis of patients presenting with cognitive decline or with transient neurological symptoms, which could indicate CAA-related transient focal neurological episodes (TFNEs). TFNEs are often mistakenly diagnosed as transient ischemic attacks, migraine aura, or focal seizures.[4] Interestingly, it has been suggested that superficial siderosis may induce seizure activity resulting in cortical spreading depression, which can cause focal seizures manifesting as TFNEs.[5] Avoiding misdiagnosis in patients with CAA is crucial, since the use of antithrombotic medication in CAA patients might be associated with an increased risk on ICH.[6]

Alzheimer's disease (AD) and CAA pathology frequently co-occur: moderate-to-severe CAA pathology is present in almost 50% of AD patients.[3] Recently, this has become increasingly important, as increased vascular Aβ deposition and subsequent local inflammation can occur as a frequent side-effect of anti-Aβ immunotherapy.[7] With the US Food and Drug Administration (FDA) approval of aducanumab[8] and lecanumab[9] as treatment for AD (The FDA approval of donanemab has been delayed to convene an advisory committee meeting to discuss the safety and efficacy data as of March 2024), proper awareness of the high prevalence of CAA has become even more important.

A definite diagnosis of CAA requires neuropathological post-mortem investigation of brain tissue. Clinically, probable or possible CAA can be diagnosed using the Boston Criteria 2.0, which are based on the presence of strictly lobar hemorrhagic lesions (ICH, cerebral microbleeds, cortical superficial siderosis [cSS], or convexity subarachnoidal hemorrhage) and associated white matter characteristics (severe perivascular spaces in the semi-oval center or white matter hyperintensities in a multispot pattern), in combination with clinical symptoms of ICH, TFNEs, or cognitive impairment.[10] These criteria are most accurate in patients presenting with ICH (sensitivity 90%, specificity 93%), and have a lower sensitivity (55%) and similar specificity (96%) to diagnose CAA in patients with presentations other than ICH.[10] Insight into the prevalence of CAA in different ethnicities may be helpful to estimate the a priori chance of CAA in individual patients. This is especially relevant in the light of risk assessment before treatment of AD patients with immunotherapy, as AD patients with more severe CAA are at increased risk of developing side effects.[11] Furthermore, more insight into the etiology of ICH or cognitive impairment in ethnic groups may inform tailored prevention measures such as intensified cardiovascular risk factor management.

Few studies have investigated the differences in CAA prevalence in East-Asian versus Western populations. It has been suggested that the proportion of CAA-related ICH is lower in East-Asian populations than in Western populations,[12] and that prevalence and severity of CAA pathology are lower in East-Asian populations.[13,14] A comparison of six East-Asian studies to four Western studies showed lower age-specific prevalence rates of CAA pathology in East-Asian versus Western populations; however, formal statistical assessment was not performed.[15] A more recent study on the prevalence of strictly lobar microbleeds in East-Asian versus Western populations did not show a difference in the prevalence and number of strictly lobar microbleeds, although a sensitivity analysis showed a trend towards higher prevalence of multiple strictly lobar microbleeds in Western populations.[16] This study also found a higher prevalence of strictly deep (a marker of deep perforator arteriopathy or arteriolosclerosis) and mixed microbleeds in East-Asian populations.

We set out to investigate the geographical differences of CAA prevalence in more detail, by performing a systematic review and meta-analysis to compare the prevalence of both CAA pathology and neuro-imaging markers associated with CAA in East-Asian versus Western populations.

Methods

For this systematic review and meta-analysis, we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Search strategy and selection criteria

We updated our previous comprehensive search strategy (performed in March 2018 and updated in June 2019) in Embase and PubMed[3] on February 17, 2022. The search syntax included the keywords "cerebral amyloid angiopathy," "cerebral hemorrhage," "neuroimaging," "neuropathology," "amyloid-beta," and "microbleeds." Controlled search terms (Medical Subject Headings [MeSH] term) were combined with free text words. The reference lists of eligible studies and relevant reviews were searched for additional potentially relevant studies. We applied neither date nor language restrictions; papers were translated when necessary. References were imported into Endnote 20, which was used to remove duplicates. The protocol for this review, to which we now added the geographical subgroup analyses, was registered in the International Prospective Register of System-

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atic Reviews (PROSPERO; registration number CRD42018093159).

Inclusion and exclusion criteria

Primary research papers were eligible for inclusion if they described one of the following study populations: (1) general population (community-dwelling elderly, or consecutive autopsy series in case of a subset of pathology studies), (2) cognitively healthy elderly (no mild cognitive impairment or dementia, no stroke), (3) patients with AD (either clinically or pathologically diagnosed), (4) patients with ICH (irrespective of location), or (5) patients with lobar ICH. If a study reported on more than one of these study populations and segregation of data was not possible, the study was excluded. We included papers that reported summary estimates on at least one of the following outcome parameters: (1) CAA prevalence according to neuropathological assessment, (2) CAA prevalence according to the (modified) Boston criteria (v1.0 or v1.5),[17,18] (3) the prevalence of strictly lobar cerebral microbleeds, or (4) the prevalence of cortical superficial siderosis. Other inclusion criteria were: (1) study population comprised at least 10 subjects, (2) mean age (or median age, if mean age was not reported) of the population of ≥55 years, and (3) clearly defined diagnostic criteria to detect CAA which included the use of either neuropathology or MRI (T2* or susceptibility-weighted imaging [SWI]). Studies were excluded if they were (1) reviews, conference abstracts, commentaries, editorials, policy reports; (2) primarily focused on other pathologies as a cause of hemorrhagic neuroimaging markers, such as central nervous system malignancy, vascular malformation, excessive warfarin use, antecedent head trauma or ischemic stroke, vasculitis, blood dyscrasia or coagulopathy; or (3) focused on patients with isolated convexity subarachnoid hemorrhage. If multiple papers reported on overlapping parts of the same cohort, the study reporting on the largest population was included. Finally, we selected the papers that reported on East-Asian study populations (China, Japan, South Korea, and Taiwan), and those reporting on Western study populations (from Europe and North America).

Data extraction and analysis

Data extraction was performed in Covidence systematic review software (Melbourne, Australia)[19] by two independent authors as previously described.[3] Quality of the studies was assessed using an adapted and combined version of the quality assessment tools by Hoy et al.[20] and the Newcastle-Ottawa scale[21] as previously described.[3] A lower score corresponds to higher quality and the maximum possible score was 18 points. The median quality assessment scores with interquartile ranges (IQR) for studies on neuropathology and microbleeds were calculated separately.

For the CAA pathology studies, moderate-to-severe CAA was considered the primary outcome, but also data on mild-to-severe CAA (including all CAA grades) was extracted. When the Boston criteria were used for CAA diagnosis, probable CAA was considered the primary outcome. In addition to the information on the prevalence of strictly lobar microbleeds and cortical superficial siderosis, we also collected information on prevalence of deep and mixed microbleeds. Not all outcomes were available for every domain. Statistical analyses were performed using the "meta" (version 7.0-0) and "metafor" (version 4.4-0) packages of R (version 4.1.3; R Foundation for Statistical Computing, Vienna, Austria). Pooled prevalence estimates of CAA were calculated as previously described,[3] using a DerSimonian-Laird random-effects model on Freeman-Tukey double arcsine-transformed data. In the same way, pooled prevalence estimates of hypertension were calculated. Heterogeneity was quantified using I^2 statistics[22] and tested using Cochran's Q. Potential geographical differences were assessed by univariable meta-regression analysis with geographical region as modifier and the prevalence in the two regions as outcome. In addition, a multivariable model with both geographical location and mean age (or median or midpoint of range, if mean was not reported) were included as modifiers. A *P*-value of less than 0.05 was considered statistically significant.

We have previously shown that CAA prevalence estimates are not influenced by the choice of random-effects model (as generalized linear mixed models did yield similar estimates), outliers (as assessed by influence analyses), low-quality studies (as sensitivity analysis including only high-quality studies yielded comparable estimates), and reporting bias (as assessed by inspection of funnel plots and Egger's tests).[3] Therefore sensitivity analyses were not performed for the geographical subgroups.

Data availability

Data used in this study are available to qualified investigators on request to the corresponding author.

Results

The combined searches resulted in 12,257 unique records. After full-text screening, a total of 196 studies were included that fulfilled the inclusion criteria (Figure 1, Table 1, and Supplementary Tables 1-19). Of these studies, 76 reported on European and 68 on North-American study populations (in total 56,788 participants, and one study pooled a European with a North-American population)[23] and 53 reported on East-Asian study populations (24,920 participants). Ten studies were conducted in other countries (including one study of which we could not find out where the participants came from despite contacting the au-

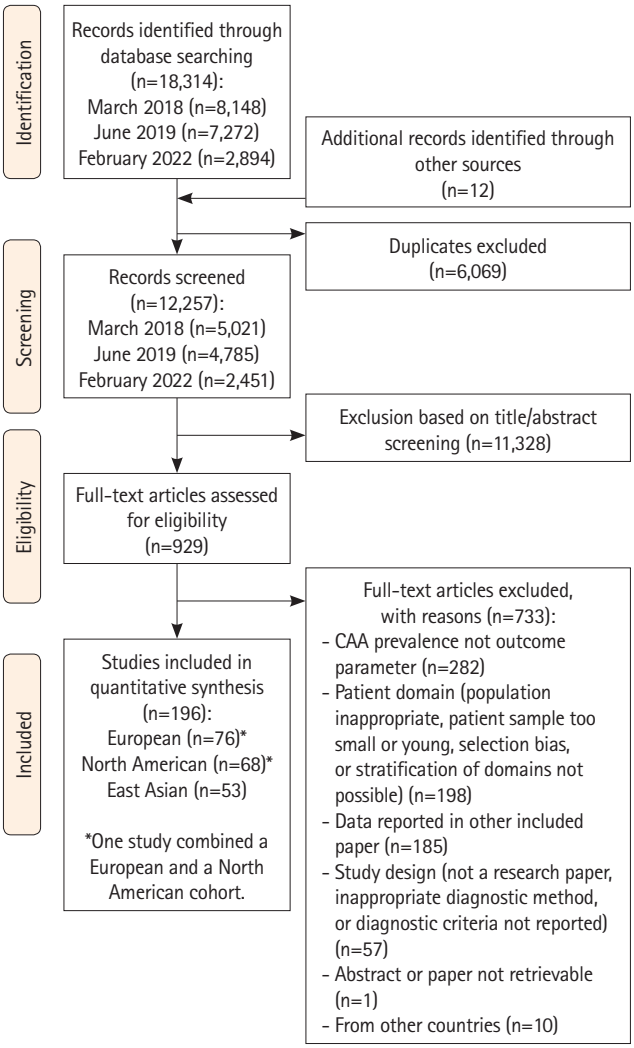

Figure 1. Flow diagram depicting the identification of records during three searches of PubMed and Embase as well the inclusion and exclusion of records during different screening stages. CAA, cerebral amyloid angiopathy.

thors), these were not included into the analyses (Figure 2). The median quality assessment score of East-Asian studies was 2.5 (IQR 1.0–4.5) and of Western studies 4.0 (IQR 2.25–6.0) (Table 2). The median quality assessment score of imaging studies was 2.0 (IQR 1.0–3.625) and of pathology studies 4.0 (IQR 2.5–6.0) (Table 2). Prevalence rates of hypertension were comparable in East-Asian and Western studies (Table 3). Details regarding MRI slice thickness, field strength, and use of SWI can be found in Table 4.

In the general population, prevalences of mild-to-severe CAA (East-Asian: 28.5% vs. Western: 46.0%) and moderate-to-severe CAA (East-Asian: 22.4% vs. Western: 23.5%) (Supplementary Figure 1) were similar in both geographical locations (Table 1). The prevalence of strictly lobar microbleeds was significantly lower in the East-Asian (5.6%) compared to the Western (11.4%, *P*=0.020) (Supplementary Figure 2) general population. However, East-Asian cohorts were on average 6 years younger compared to Western cohorts, and after inclusion of age into the regression model the geographical difference disappeared (*P*=0.17). East-Asian cohorts had a higher prevalence of deep microbleeds (5.7%) compared to Western cohorts (2.7%, *P*=0.008 [*P*<0.0001 in the multivariable model]) as well as a tendency towards a higher prevalence of mixed microbleeds (3.4% vs. 1.7%, *P*=0.092 [*P*=0.002 in the multivariable model]).

In cognitively normal elderly, prevalence of mild-to-severe CAA (33.2% vs. 30.7%) did not differ between East-Asian and Western cohorts. No East-Asian studies were included that specifically reported on moderate-to-severe CAA (Table 1 and Supplementary Figure 3). There was a significantly lower prevalence of strictly lobar microbleeds (2.6% vs. 11.4%, *P*=0.001) (Supplementary Figure 4) in East-Asian versus Western cohorts of cognitively normal elderly that on average were of comparable age. However, this difference was no longer present when age was taken into account (*P*=0.056). The prevalence of mixed microbleeds and strictly deep microbleeds did not differ between East-Asian and Western studies. The prevalence of cSS was similar in East-Asian (1.0%) and Western (0.6%) cohorts of cognitively normal elderly.

In patients with AD, the prevalence of mild-to-severe CAA (83.3% v.s 77.5%) and moderate-to-severe CAA (55.4% vs. 44.1%) (Supplementary Figure 5) was similar in East-Asian and Western cohorts (Table 1). The prevalence of strictly lobar microbleeds (22.2% vs. 23.8%) (Supplementary Figure 6), mixed microbleeds (5.7% vs. 6.3%), and strictly deep microbleeds (5.9% vs. 5.6%), and cSS (3.9% vs. 4.3%) was similar as well. Including age into the regression model did not alter the results.

In patients with ICH, the prevalence of mild-to-severe CAA (27.0% vs. 27.1%) and moderate-to-severe CAA (11.8% vs. 26.3%) (Supplementary Figure 7) did not differ between East-Asian and Western cohorts (Table 1). The prevalence of strictly lobar microbleeds was lower in East-Asian (10.2%) compared to Western (24.6%, *P*<0.0001 [*P*=0.008 in the multivariable model]) (Supplementary Figure 8) cohorts of ICH patients, with East-Asian cohorts being on average 7 years younger. In contrast, the prevalence of mixed microbleeds was higher in East-Asian cohorts (40.6%) compared to Western cohorts (20.6%, *P*=0.045), but not in the multivariable model (*P*=0.15). There was a tendency towards a lower prevalence of probable CAA according to the Boston criteria in East-Asian versus Western countries (9.5% vs. 27.4%, *P*=0.026), albeit not in the multivariable model (*P*=0.14). The prevalence of strictly deep microbleeds (21.8% vs. 16.7%, *P*=0.42) and of cSS (10.1% vs. 16.8%, *P*=0.13) was similar.

In patients with lobar ICH, the prevalence of mild-to-severe CAA (52.2% vs. 51.9%) and moderate-to-severe CAA (49.7%

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Table 1. A comparison of prevalence estimates of CAA pathology, microbleeds, cortical superficial siderosis, and probable CAA according to the Boston Criteria in East-Asian versus Western study populations

	East-Asian				Western				Meta-regression model (*P*)	
	Prevalence (%) [95% CI]	I^2 (%) [95% CI]	Studies (individuals)	Weighted mean age (yr)	Prevalence (%) [95% CI]	I^2 (%) [95% CI]	Studies (individuals)	Weighted mean age (yr)	Modifier: geographic location	Modifiers: geographic location+age*
Population-based cohorts										
Mild-severe CAA	28.5 [17.9–40.4]	95.4 [91.8–97.4]	5 (1,360)	78.4	46.0 [36.1–56.1]	98.3 [97.9–98.6]	17 (6,509)	84.0	0.074	0.20 (n=20)
Mod-severe CAA	22.4 [19.5–25.4]	0.0 [0.0–89.6]	3 (750)	80.6	23.5 [18.2–29.1]	93.5 [90.0–95.8]	10 (4,362)	86.5	0.85	0.49 (n=13)
SL CMBs	5.6 [3.2–8.6]	96.7 [95.1–97.8]	8 (8,807)	63.8	11.4 [7.4–16.1]	97.9 [96.9–98.6]	6 (12,783)	70.0	0.02	0.17 (n=14)
M CMBs	3.4 [2.1–5.0]	89.2 [77.6–94.8]	5 (5,997)	62.2	1.7 [1.1–2.4]	45.0 [0.0–83.7]	3 (3,562)	70.5	0.092	0.002 (n=8)
SD CMBs	5.7 [4.1–7.5]	83.7 [58.6–93.5]	4 (4,716)	58.8	2.7 [1.7–3.9]	64.3 [0.0–87.9]	4 (3,633)	71.0	0.008	<0.0001 (n=8)
cSS	NA	NA	0	NA	0.6 [0.2–1.2]	78.2 [5.1–95.0]	2 (7,461)	68.7	NA	NA
Probable CAA (BC)	NA	NA	0	NA	NA	NA	0	NA	NA	NA
Cognitively normal elderly										
Mild-severe CAA	33.2 [25.6–41.1]	0.00	2 (147)	81.9	30.7 [23.9–38.9]	93.1 [91.3–94.6]	33 (2,945)	80.9	0.98	0.80 (n=32)
Mod-severe CAA	NA	NA	0	NA	7.8 [3.9–12.6]	77.4 [62.4–86.4]	14 (906)	80.8	NA	NA
SL CMBs	2.6 [1.2–4.3]	91.8 [86.8–95.0]	9 (9,223)	60.6	11.4 [6.6–17.2]	97.0 [96.1–97.8]	13 (7,712)	61.9	0.001	0.056 (n=20)
M CMBs	0.8 [0.2–1.6]	40.4 [0.0–79.8]	4 (4,758)	61.8	1.5 [0.1–3.9]	79.0 [56.8–89.8]	7 (4,276)	56.2	0.72	0.94 (n=10)
SD CMBs	2.4 [1.2–4.0]	81.6 [57.3–92.0]	5 (6,209)	60.9	4.2 [1.4–8.1]	89.7 [82.2–94.1]	8 (4,604)	57.5	0.25	0.78 (n=12)
cSS	1.0 [0.0–4.5]	0.00	2 (110)	70.2	0.6 [0.3–1.0]	0.00	2 (1,994)	71.6	0.12	NA
Probable CAA (BC)	NA	NA	0	NA	5.1 [0.0–31.2]	79.1 [9.5–95.2]	2 (41)	74.4	NA	NA
Patients with AD										
Mild-severe CAA	83.3 [70.4–93.3]	82.7 [63.6–91.8]	6 (275)	85.3	77.5 [69.7–84.5]	97.5 [97.2–97.9]	50 (5,941)	80.9	0.58	0.43 (n=49)
Mod-severe CAA	55.4 [25.0–83.9]	90.4 [74.7–96.4]	3 (131)	85.7	44.1 [35.8–52.5]	93.0 [90.5–94.8]	20 (2,645)	81.3	0.35	0.11 (n=22)
SL CMBs	22.2 [14.9–30.3]	88.3 [80.0–93.2]	9 (1,257)	75.5	23.8 [16.0–32.6]	92.0 [87.4–94.9]	10 (1,542)	71.4	0.81	0.93 (n=17)
M CMBs	5.7 [0.4–15.5]	95.9 [93.2–97.5]	6 (1,117)	75.8	6.3 [3.0–10.5]	74.6 [42.3–88.8]	6 (902)	71.6	0.85	0.77 (n=11)
SD CMBs	5.9 [2.4–10.8]	85.8 [71.1–93.0]	6 (1,117)	75.8	5.6 [2.5–9.8]	83.8 [68.3–91.8]	7 (1,325)	70.4	0.98	0.72 (n=12)
cSS	3.9 [1.4–7.2]	30.5 [0.0–71.7]	6 (413)	75.8	4.3 [3.0–5.9]	0 [0.0–74.6]	6 (912)	69.9	0.75	0.70 (n=9)
Probable CAA (BC)	NA	NA	0	NA	14.3 [0.3–38.4]	NA	1 (14)	66.2	NA	NA
Patients with ICH										
Mild-severe CAA	27.0 [10.9–47.0]	91.7 [78.8–96.7]	3 (1,073)	57.2	27.1 [15.2–40.8]	94.4 [91.3–96.4]	9 (1,008)	70.6	0.97	0.51 (n=11)
Mod-severe CAA	11.8 [0.0–41.8]	95.8 [88.1–98.5]	2 (1,024)	56.8	26.3 [12.9–42.1]	82.5 [46.2–94.3]	3 (310)	82	0.27	NA
SL CMBs	10.2 [4.7–17.4]	84.5 [61.4–93.8]	4 (673)	61.0	24.6 [20.8–28.6]	32.9 [0.0–70.2]	8 (1,045)	67.7	<0.0001	0.008 (n=10)
M CMBs	40.6 [26.6–55.3]	74.9 [0.0–94.3]	2 (241)	62.1	20.6 [12.0–30.8]	85.5 [70.3–92.9]	6 (861)	67.8	0.045	0.15 (n=6)
SD CMBs	21.8 [18.4–25.4]	0.0 [0.0–89.6]	3 (547)	58.7	16.7 [9.6–25.0]	80.8 [58.7–91.1]	6 (861)	67.8	0.42	0.32 (n=7)
cSS	10.1 [4.7–17.3]	89.7 [78.7–95.0]	5 (895)	62.8	16.8 [10.9–23.5]	83.1 [64.5–92.0]	6 (1,188)	68.9	0.13	0.22 (n=10)
Probable CAA (BC)	9.5 [5.6–14.3]	65.6 [0.0–90.1]	3 (524)	65.1	27.4 [17.2–38.9]	95.6 [93.2–97.1]	8 (1,682)	69.7	0.026	0.14 (n=9)

Table 1. Continued

	East-Asian				Western				Meta-regression model (*P*)	
	Prevalence (%) [95% CI]	I^2 (%) [95% CI]	Studies (individuals)	Weighted mean age (yr)	Prevalence (%) [95% CI]	I^2 (%) [95% CI]	Studies (individuals)	Weighted mean age (yr)	Modifier: geographic location	Modifiers: geographic location+age*
Patients with lobar ICH										
Mild-severe CAA	52.2 [14.5–88.5]	92.8 [82.3–97.1]	3 (86)	73.2	51.9 [31.6–71.9]	79.9 [46.7–92.4]	4 (132)	77.3	0.97	NA
Mod-severe CAA	49.7 [27.9–71.6]	80.8 [39.7–93.9]	3 (106)	73.2	59.0 [30.9–76.1]	70.1 [0.0–91.2]	3 (117)	79.5	0.54	NA
SL CMBs	NA	NA	0	NA	27.1 [20.1–34.8]	NA	1 (140)	72.5	NA	NA
M CMBs	NA	NA	0	NA	NA	NA	0	NA	NA	NA
SD CMBs	NA	NA	0	NA	NA	NA	0	NA	NA	NA
cSS	NA	NA	0	NA	31.1 [23.1–40.0]	79.4 [45.2–92.3]	4 (627)	73.1	NA	NA
Probable CAA (BC)	NA	NA	0	NA	49.1 [31.9–66.4]	93.8 [89.2–96.5]	6 (547)	72.6	NA	NA

Two meta-regression models were applied to compare the prevalence between East-Asian and Western participants: univariable meta-regression including only geographic location (model 1) as well as multivariable meta-regression including geographic location and mean or median age (model 2). We only used model 2 in case more than 5 studies were available for analysis. Studies not reporting mean or median age were not included in model 2 (*); the number of studies included in the model is indicated in parentheses. The I^2 statistic describes the percentage of variation across studies that is due to heterogeneity rather than chance; there was substantial heterogeneity between studies.[22]

CAA, cerebral amyloid angiopathy; CI, confidence interval; CMBs, cerebral microbleeds; SL, strictly lobar; M, mixed; SD, strictly deep; cSS, cortical superficial siderosis; AD, Alzheimer's disease; ICH, intracerebral hemorrhage; BC, Boston Criteria; NA, not available.

vs. 59.0%) did not differ between East-Asian and Western cohorts (Table 1). No East-Asian imaging studies were included, and therefore, no comparison between the prevalence of imaging markers could be made.

Discussion

We demonstrate that the prevalence of CAA pathology does not differ between East-Asian and Western cohorts reflecting the general population, cognitively normal elderly, patients with AD, patients with ICH, and patients with lobar ICH. Furthermore, we found that in the East-Asian general population, cognitively normal elderly, and patients with ICH, the estimated prevalence of strictly lobar microbleeds was lower compared to Western cohorts, although this may be partly explained by a lower mean age in East-Asian cohorts.

Only a few studies to date have compared the prevalence of CAA pathology in East-Asian and Western countries.[13-15] We report comparable prevalence estimates of moderate-to-severe CAA in the East-Asian (22.4%) and Western (23.5%) general population. In addition, potential geographical differences regarding the prevalence of CAA imaging markers have received only limited attention. In an individual participant meta-analysis corrected for age, deep/infratentorial and mixed microbleeds were more commonly present in East-Asian (e.g., from Japan, South Korea, and China) versus Western (e.g., from Iceland, Australia, and the USA) stroke-free individuals aged 55–75 years (odds ratio [OR] 2.78, 95% confidence interval [CI] 1.77–4.35, $P<0.002$).[16] In contrast, the prevalence of strictly lobar microbleeds did not differ (OR 0.70, 95% CI 0.29–1.72, $P=0.44$) between East-Asian and Western individuals, although a trend was observed in a sensitivity analysis assessing only the prevalence of multiple strictly lobar microbleeds (OR 0.43, 95% CI 0.17–1.04, $P=0.062$). This individual participant data meta-analysis supports our study-level multivariable analysis in which East-Asian location was associated with a higher prevalence of mixed and strictly deep microbleeds in cohorts reflecting the general population. In our univariable, but not multivariable model, Western geographic location was associated with a higher prevalence of strictly lobar microbleeds in the general population, indicating at best a weak association between geographic location and the occurrence of strictly lobar microbleeds. Most likely, the lower prevalence of strictly lobar microbleeds in East-Asian study populations compared to Western study populations is due to a higher incidence of mixed microbleeds.

We show that the prevalence of CAA pathology and strictly lobar microbleeds does not differ between East-Asian and Western cohorts of patients with AD. This finding is relevant given

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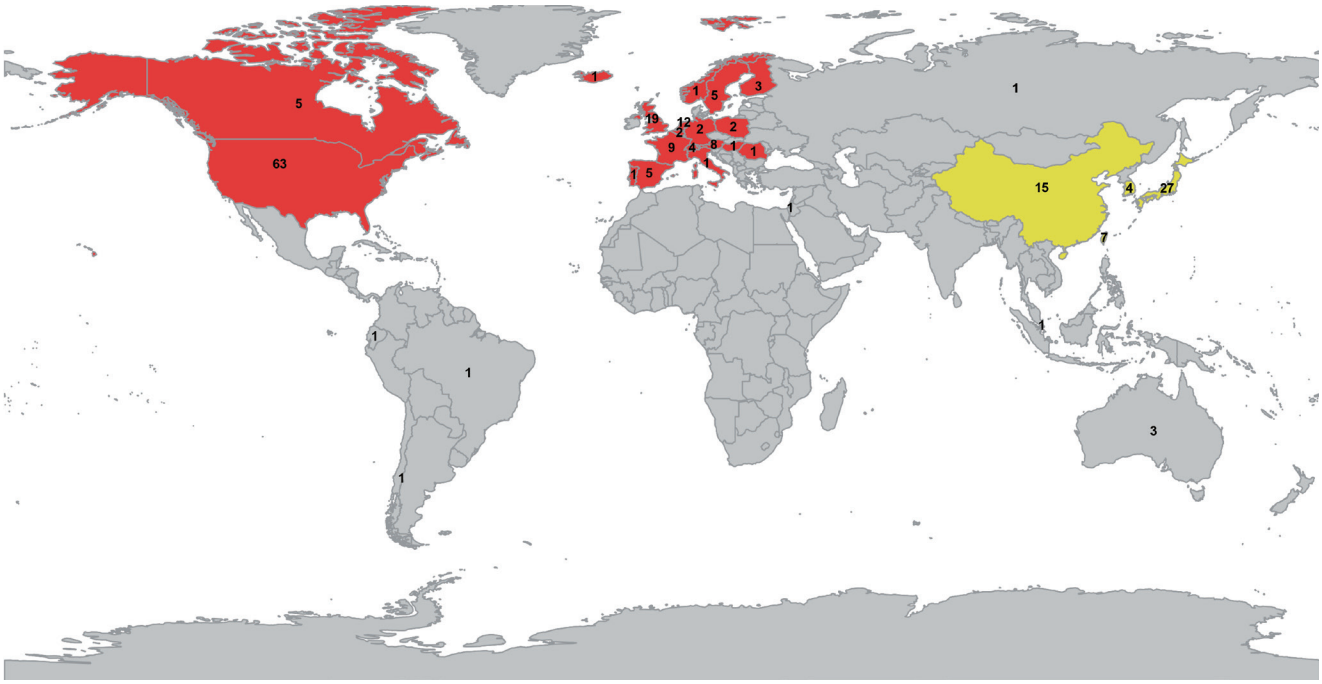

Figure 2. Of 196 included studies, 76 reported on European populations (one study pooled participants from Belgium and UK), 68 on North American study populations (one study pooled participants from The Netherlands and USA), and 53 reported on East-Asian study populations (in yellow). Included Western countries are indicated in red. In addition, 10 studies were conducted in other countries (of which in one study, the country was unclear).

Table 2. Assessment of quality of East-Asian and Western studies

	East-Asian	Western
General population		
Pathology	2.0 [0.0–3.0]	3.5 [1.4–6.0]
Strictly lobar CMBs	2.0 [0.8–2.3]	1.0 [1.0–1.4]
Cognitively normal elderly		
Pathology	3.5 [3.3–3.8]	4.5 [3.3–6.5]
Strictly lobar CMBs	2.0 [0.0–2.0]	2.5 [1.0–3.0]
Patients with AD		
Pathology	4.0 [2.3–6.9]	4.0 [3.0–7.0]
Strictly lobar CMBs	2.5 [1.0–5.0]	2.8 [1.0–3.0]
Patients with ICH		
Pathology	2.0 [2.0–5.0]	4.0 [1.0–5.5]
Strictly lobar CMBs	0.0 [0–0.6]	3.5 [2.1–5.3]
Patients with lobar ICH		
Pathology	5.5 [4.0–6.0]	5.0 [4.0–6.0]
Strictly lobar CMBs	NA	4.5

Values are presented as median [interquartile range].
CMBs, cerebral microbleeds; AD, Alzheimer's disease; ICH, intracerebral hemorrhage; NA, not available.

recent developments in the field of AD treatments. In 2021, aducanumab was approved by the FDA as a treatment for AD, and in January 2023, the FDA approved lecanemab.[8,9] In addition, lecanemab (but not aducanumab) was approved by the Ministry of Health, Labour and Welfare in Japan in September 2023,[24] and by the National Medical Products Administration in China in January 2024.[25] However, the safety and efficacy of aducanumab and lecanemab remain controversial.[26-28] Both immunotherapies come with frequent adverse effects in the form of amyloid-related imaging abnormalities (ARIA). ARIA is thought to reflect local inflammation associated with vascular deposition of Aβ that has been released as a result of antibody-mediated breakdown of neuritic plaques.[2] This leads to vasogenic edema (ARIA-E) and/or microbleeds, cortical superficial siderosis, and ICHs (ARIA-H). ARIA is asymptomatic in about 75% of patients, but may lead to headache, confusion, nausea, visual disturbances, and dizziness.[27,29] Immunotherapy may exacerbate pre-existing CAA, which is present in many patients with AD. Therefore, patients with AD and concomitant moderate-to-severe CAA are at higher risk of developing ARIA. It is therefore recommended to exert extreme caution when prescribing immunotherapy treatment in patients with AD with concomitant moderate-to-severe CAA, especially when they have other risk factors for ICH, such as anticoagulant use.[11] Furthermore, the apolipoprotein E (*APOE*) ε4 allele is a risk factor for severe CAA, since it has been found that *APOE ε4* carriers have more severe CAA, even when controlling for the extent of AD pathology.[30] In addition, it has been found that ARIA-E incidence is *APOE ε4*-dependent.[11] The FDA label lecanemab contains the recommendation to test for *APOE ε4* status prior to initiation of treatment, and discuss the accompanied risk of ARIA with patients. It remains a challenge to clinically

Table 3. The prevalence of hypertension in East-Asian versus Western cohorts

	East-Asian	Western	Meta-regression model (*P*)
	Prevalence of hypertension [95% CI]	Prevalence of hypertension [95% CI]	
General population			
Pathology	NA (0/5)	57.3 [50.7–63.8] (6/20)	NA
Strictly lobar CMBs	53.2 [41.8–64.4] (7/8)	59.3 [37.8–79.1] (5/6)	0.62
Cognitively normal elderly			
Pathology	NA (0/2)	44.2 [20.0–69.9] (4/35)	NA
Strictly lobar CMBs	42.6 [33.5–52.0] (8/9)	54.9 [38.0–71.2] (9/13)	0.22
Patients with AD			
Pathology	NA (0/6)	38.7 [28.6–49.2] (8/52)	NA
Strictly lobar CMBs	35.3 [29.6–41.1] (8/9)	40.6 [32.3–49.2] (5/10)	0.33
Patients with ICH			
Pathology	67.2 [64.2–70.1] (2/3)	79.7 [61.5–93.4] (6/9)	0.38
Strictly lobar CMBs	71.3 [66.6–75.8] (3/4)	65.2 [57.9–72.1] (6/8)	0.16
Patients with lobar ICH			
Pathology	48.3 [30.2–66.6] (1/5)	73.8 [46.7–94.0] (4/5)	0.41
Strictly lobar CMBs	NA (0/0)	58.6 [50.3–66.6] (1/1)	NA

In parenthesis, the number of studies reporting details on the used MRI acquisition in comparison to the total number of included studies is provided. A univariable meta-regression model was applied to compare the prevalence of hypertension between East-Asian and Western participants.
CI, confidence interval; CMBs, cerebral microbleeds; AD, Alzheimer's disease; ICH, intracerebral hemorrhage; MRI, magnetic resonance imaging; CI, confidence interval; NA, not available.

Table 4. MRI parameters used in East-Asian versus Western studies reporting the prevalence of strictly lobar microbleeds

	East-Asian			Western		
	Weighted mean slice thickness (mm)	Weighted mean field strength (tesla)	SWI use (%)	Weighted mean slice thickness (mm)	Weighted mean field strength (tesla)	SWI use (%)
General population	4.29 (7/8)	1.89 (7/8)	33.7 (8/8)	2.79 (5/6)	1.70 (6/6)	0.6 (6/6)
Cognitively normal elderly	5.68 (9/9)	1.82 (9/9)	16.2 (9/9)	3.58 (13/13)	1.94 (13/13)	0.8 (13/13)
Patients with AD	3.79 (8/9)	1.94 (7/9)	25.7 (9/9)	3.53 (8/10)	2.33 (10/10)	9.5 (9/10)
Patients with ICH	1.58 (2/4)	2.9 (4/4)	93.9 (3/4)	2.72 (3/9)	3.77 (3/8)	28.0 (5/8)

Weighted means (taking the number of individuals per study into account) were calculated for the used slice thickness and field strength in studies. In parenthesis, the number of studies reporting details on the used MRI acquisition in comparison to the total number of included studies is provided. No imaging studies were included regarding East-Asian patients with lobar ICH.
MRI, magnetic resonance imaging; SWI, susceptibility-weighted imaging; AD, Alzheimer's disease; ICH, intracerebral hemorrhage.

establish the severity of concomitant CAA, but it is important to note that in the phase III lecanemab trial, AD patients with four or more microbleeds, cortical superficial siderosis, and/or an ICH of >1 cm were excluded.[9] In addition, it was recently found that the presence of two to four microbleeds more than doubled the risk of ARIA-E in the phase II and III donanemab trials.[31] Our data indicates that CAA is equally prevalent in East-Asian compared to Western patients with AD. Therefore, screening for CAA and caution is warranted when prescribing immunotherapy to East-Asian as well as to Western patients with AD.

It has been suggested that the proportion of ICH caused by CAA is lower in Asian compared to Western countries.[15] This potential difference has been systematically assessed by studying consecutive patients with spontaneous ICH at two stroke centers during the same time period; one in the UK (279 patients) and one in Japan (214 patients).[12] Patients from the Japanese center had lower odds of CAA-related ICH (OR 0.55, 95% CI 0.31–0.98)[12] according to the Edinburgh criteria.[32] The authors observed proportions of CAA-related ICH of 10.2% in patients of East-Asian ethnicity and 23.8% in patients of white ethnicity. As the incidence of ICH is twice as high in East-Asian compared to white populations (51.8 vs. 24.2 per 100,000 person-years),[33] the authors estimated that the incidence for CAA-related ICH is comparable for East-Asian and white populations (5.3 vs. 5.8 per 100,000 person-years). In contrast, the incidence of other types of ICH (mainly associated with deep perforator vasculopathy) was 2.5-fold higher in those of East-Asian ethnicity compared to those of white ethnicity (46.5 vs. 18.4 per 100,000 per-

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son-years).[12] This indicates that the lower proportion of CAA-related ICH in East-Asian individuals with ICH is due to a higher incidence of ICH related to deep perforator vasculopathy rather than to a lower incidence of CAA-related ICH. This may also contribute to our finding that the prevalence of strictly lobar microbleeds was 2.5 times lower in East-Asian cohorts of ICH patients than in Western cohorts. Unfortunately, the East-Asian studies reporting on MRI markers of CAA that we included in our meta-analysis provided no details on ICH location.

Hypertension is considered a risk factor for deep microbleeds and deep ICH.[34,35] However, in previous studies demonstrating a higher prevalence of deep microbleeds[16] in East-Asian (compared to Western) stroke-free individuals and a higher proportion of deep ICH in East-Asian (compared to white) ICH patients,[12] the prevalence of hypertension did not differ between East-Asian participants and their Western counterparts. Similarly, we did not find evidence for a higher prevalence of hypertension in East-Asian cohorts, whereas deep and mixed microbleeds were more prevalent in the East-Asian general population and patients with ICH. It is possible that the increased prevalence of deep and mixed microbleeds might also be due to an increased susceptibility to develop hemorrhagic brain lesions in East-Asian individuals.[12,36] Whereas the exact underlying mechanisms of this increased susceptibility are yet unknown, East-Asians carrying an *APOE ε2* or *APOE ε4* allele have increased susceptibility to develop hemorrhagic lesions compared to Europeans with similar *APOE* polymorphisms.[37,38] Another explanation may be that epidermal growth factor-like repeat (EGFr) cysteine-altering *NOTCH3* mutations are more common in East-Asian populations than in Europe (9/1,000 vs. 3/1,000).[39] Such mutations may result in a mild CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy)-phenotype clinically indistinguishable from sporadic small vessel disease. In addition, a meta-analysis found that the occurrence rate of ICH in CADASIL is higher in CADASIL patients from Asia (17.7%) compared to CADASIL patients in Europe (2%).[40]

Strengths of this study include our comprehensive search and selection strategy, resulting in the largest dataset to date on available papers that report the prevalence of CAA. Additionally, we included papers both on CAA pathology as well as on radiological markers for CAA, enabling us to determine a reliable estimate of the prevalence of CAA in Western and East-Asian countries. Limitations of this study include the heterogeneity in methods that have been used to assess CAA pathology,[3] as well as potential differences between MRI acquisition protocols, of which we previously demonstrated this influenced the detection of microbleeds.[3] Also, included studies varied in quality, which may have introduced a bias. Another limitation is the large age differences (up to 15 years) between East-Asian and Western cohorts reflecting the general population and ICH patients. Microbleed prevalence has been reported to be associated with age.[3,36,41] We corrected for age in an additional statistical model but due to the small number of studies, and because we did not have individual patient data, no firm conclusions can be drawn from this model. However, the observation that the East-Asian populations were on average younger and that the prevalence of CAA pathology and of strictly lobar microbleeds were lower in East-Asians, may imply that the prevalence of these outcomes would be more similar to Western-based cohort when they would have been of similar age. Furthermore, our comprehensive search was designed to include all studies on strictly lobar microbleeds and we might not have included all available studies on deep or mixed microbleeds. Finally, we included studies based on the country they were conducted rather than ethnicity of the study populations. Therefore there may have been East-Asian participants in the Western cohorts and *vice versa*.

Conclusions

In this comprehensive meta-analysis, we show that the prevalence of pathologically established CAA is similar in East-Asian and Western countries, and radiological markers associated with CAA, i.e., strictly lobar microbleeds, are less prevalent in East-Asian cohorts of population-based individuals and cognitively normal elderly. The latter observation may be due to younger East-Asian cohorts, since after correction for age the difference was non-significant. In contrast, we show that the prevalence of strictly deep microbleeds and mixed microbleeds is higher in East-Asian population-based cohorts, even after correction for age. This indicates that deep perforating vasculopathy is more widely present in East-Asian populations and suggests that preventive measures are urgently warranted in these regions. Furthermore, caution should be employed when including East-Asian as well as Western patients with AD in immunotherapy trials considering similar prevalence estimates of pathological established CAA.

Supplementary materials

Supplementary materials related to this article can be found online at https://doi.org/10.5853/jos.2023.04287.

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Conflicts of interest

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Author contribution

Conceptualization: all authors. Study design: all authors. Methodology: all authors. Data collection: AMDK, MMV, LJ. Investigation: AMDK, LJ. Statistical analysis: LJ. Writing—original draft: AMDK, LJ. Writing—review & editing: all authors. Funding acquisition: MMV. Approval of final manuscript: all authors.

References

1. Attems J, Jellinger K, Thal DR, Van Nostrand W. Review: sporadic cerebral amyloid angiopathy. *Neuropathol Appl Neurobiol* 2011;37:75-93.
2. Greenberg SM, Bacskai BJ, Hernandez-Guillamon M, Pruzin J, Sperling R, van Veluw SJ. Cerebral amyloid angiopathy and Alzheimer disease - one peptide, two pathways. *Nat Rev Neurol* 2020;16:30-42.
3. Jäkel L, De Kort AM, Klijn CJM, Schreuder FHBM, Verbeek MM. Prevalence of cerebral amyloid angiopathy: a systematic review and meta-analysis. *Alzheimers Dement* 2022;18:10-28.
4. Smith EE, Charidimou A, Ayata C, Werring DJ, Greenberg SM. Cerebral amyloid angiopathy-related transient focal neurologic episodes. *Neurology* 2021;97:231-238.
5. Tanaka T, Fukuma K, Abe S, Matsubara S, Ikeda S, Kamogawa N, et al. Association of cortical superficial siderosis with post-stroke epilepsy. *Ann Neurol* 2023;93:357-370.
6. Wermer MJH, Greenberg SM. The growing clinical spectrum of cerebral amyloid angiopathy. *Curr Opin Neurol* 2018;31:28-35.
7. Boche D, Zotova E, Weller RO, Love S, Neal JW, Pickering RM, et al. Consequence of Aβ immunization on the vasculature of human Alzheimer's disease brain. *Brain* 2008;131(Pt 12):3299-3310.
8. Budd Haeberlein S, Aisen PS, Barkhof F, Chalkias S, Chen T, Cohen S, et al. Two randomized phase 3 studies of aducanumab in early Alzheimer's disease. *J Prev Alzheimers Dis* 2022;9:197-210.
9. van Dyck CH, Swanson CJ, Aisen P, Bateman RJ, Chen C, Gee M, et al. Lecanemab in early Alzheimer's disease. *N Engl J Med* 2023;388:9-21.
10. Charidimou A, Boulouis G, Frosch MP, Baron JC, Pasi M, Albucher JF, et al. The Boston criteria version 2.0 for cerebral amyloid angiopathy: a multicentre, retrospective, MRI-neuropathology diagnostic accuracy study. *Lancet Neurol* 2022;21:714-725.
11. Sveikata L, Charidimou A, Viswanathan A. Vessels sing their ARIAs: the role of vascular amyloid in the age of aducanumab. *Stroke* 2022;53:298-302.
12. Yakushiji Y, Tanaka J, Wilson D, Charidimou A, Noguchi T, Kawashima M, et al. Proportion of intracerebral haemorrhage due to cerebral amyloid angiopathy in the East and West: comparison between single hospital centres in Japan and the United Kingdom. *J Neurol Sci* 2020;416:117037.
13. Ng TH, Leung SY, Wong MP. Cerebral amyloid angiopathy in Chinese: incidence and significance. *Clin Neurol Neurosurg* 1991;93:19-23.
14. Masuda J, Tanaka K, Ueda K, Omae T. Autopsy study of incidence and distribution of cerebral amyloid angiopathy in Hisayama, Japan. *Stroke* 1988;19:205-210.
15. Chen YW, Lee MJ, Smith EE. Cerebral amyloid angiopathy in East and West. *Int J Stroke* 2010;5:403-411.
16. Yakushiji Y, Wilson D, Ambler G, Charidimou A, Beiser A, van Buchem MA, et al. Distribution of cerebral microbleeds in the East and West: individual participant meta-analysis. *Neurology* 2019;92:e1086-e1097.

 https://doi.org/10.5853/jos.2023.04287

17. Linn J, Halpin A, Demaerel P, Ruhland J, Giese AD, Dichgans M, et al. Prevalence of superficial siderosis in patients with cerebral amyloid angiopathy. *Neurology* 2010;74:1346-1350.
18. Knudsen KA, Rosand J, Karluk D, Greenberg SM. Clinical diagnosis of cerebral amyloid angiopathy: validation of the Boston criteria. *Neurology* 2001;56:537-539.
19. Veritas Health Innovation. Covidence systematic review software [Internet]. Melbourne: Veritas Health Innovation; 2022 [accessed February 1, 2022]. Available from: www.covidence.org.
20. Hoy D, Brooks P, Woolf A, Blyth F, March L, Bain C, et al. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. *J Clin Epidemiol* 2012;65:934-939.
21. Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis [Internet]. Ottawa: Ottawa Hospital Research Institute; 2017 [accessed May 26, 2023]. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm.
22. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;21:1539-1558.
23. Shoamanesh A, Akoudad S, Himali JJ, Beiser AS, DeCarli C, Seshadri S, et al. Cortical superficial siderosis in the general population: the Framingham heart and Rotterdam studies. *Int J Stroke* 2021;16:798-808.
24. Eisai. "LEQEMBI® intravenous infusion" (Lecanemab) approved for the treatment of Alzheimer's disease in Japan [Internet]. Eisai: Tokyo; 2023 [accessed March 1, 2024]. Available from: https://www.eisai.com/news/2023/news202359.html.
25. Biogen. "LEQEMBI®" (Lecanemab) approved for the treatment of Alzheimer's disease in China [Internet]. Cambridge: Biogen; 2024 [accessed March 1, 2024]. Available from: https://investors.biogen.com/news-releases/news-release-details/leqembir-lecanemab-approved-treatment-alzheimers-disease-china.
26. The Lancet. Lecanemab for Alzheimer's disease: tempering hype and hope. *Lancet* 2022;400:1899.
27. Reardon S. FDA approves Alzheimer's drug lecanemab amid safety concerns. *Nature* 2023;613:227-228.
28. Schneider LS. Aducanumab trials EMERGE but don't ENGAGE. *J Prev Alzheimers Dis* 2022;9:193-196.
29. Salloway S, Chalkias S, Barkhof F, Burkett P, Barakos J, Purcell D, et al. Amyloid-related imaging abnormalities in 2 phase 3 studies evaluating aducanumab in patients with early Alzheimer disease. *JAMA Neurol* 2022;79:13-21.
30. Yu L, Boyle PA, Nag S, Leurgans S, Buchman AS, Wilson RS, et al. APOE and cerebral amyloid angiopathy in community-dwelling older persons. *Neurobiol Aging* 2015;36:2946-2953.
31. Alzforum. Unlocking blood-brain barrier boosts immunotherapy efficacy, lowers ARIA [Internet]. Boston: Alzforum; 2023 [accessed March 1, 2024]. Available from: https://www.alzforum.org/news/conference-coverage/unlocking-blood-brain-barrier-boosts-immunotherapy-efficacy-lowers-aria#tying.
32. Rodrigues MA, Samarasekera N, Lerpiniere C, Humphreys C, McCarron MO, White PM, et al. The Edinburgh CT and genetic diagnostic criteria for lobar intracerebral haemorrhage associated with cerebral amyloid angiopathy: model development and diagnostic test accuracy study. *Lancet Neurol* 2018;17:232-240.
33. van Asch CJ, Luitse MJ, Rinkel GJ, van der Tweel I, Algra A, Klijn CJ. Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: a systematic review and meta-analysis. *Lancet Neurol* 2010;9:167-176.
34. Jolink WMT, Wiegertjes K, Rinkel GJE, Algra A, de Leeuw FE, Klijn CJM. Location-specific risk factors for intracerebral hemorrhage: systematic review and meta-analysis. *Neurology* 2020;95:e1807-e1818.
35. Poels MM, Vernooij MW, Ikram MA, Hofman A, Krestin GP, van der Lugt A, et al. Prevalence and risk factors of cerebral microbleeds: an update of the Rotterdam scan study. *Stroke* 2010;41(10 Suppl):S103-S106.
36. Young JH, Chang YP, Kim JD, Chretien JP, Klag MJ, Levine MA, et al. Differential susceptibility to hypertension is due to selection during the out-of-Africa expansion. *PLoS Genet* 2005;1:e82.
37. Tzourio C, Arima H, Harrap S, Anderson C, Godin O, Woodward M, et al. APOE genotype, ethnicity, and the risk of cerebral hemorrhage. *Neurology* 2008;70:1322-1328.
38. Zhao D, Zhang Z, Wu GB, Wang HY, Gao F, Duan XD, et al. Apolipoprotein E gene polymorphism and the risk of subarachnoid hemorrhage: a meta-analysis of case-control studies. *Acta Neurochir (Wien)* 2016;158:1515-1522.
39. Rutten JW, Dauwerse HG, Gravesteijn G, van Belzen MJ, van der Grond J, Polke JM, et al. Archetypal NOTCH3 mutations frequent in public exome: implications for CADASIL. *Ann Clin Transl Neurol* 2016;3:844-853.
40. Lai QL, Zhang YX, Wang JJ, Mo YJ, Zhuang LY, Cheng L, et al. Occurrence of intracranial hemorrhage and associated risk factors in cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy: a systematic review and meta-analysis. *J Clin Neurol* 2022;18:499-506.
41. Sveinbjornsdottir S, Sigurdsson S, Aspelund T, Kjartansson O, Eiriksdottir G, Valtysdottir B, et al. Cerebral microbleeds in the population based AGES-Reykjavik study: prevalence and location. *J Neurol Neurosurg Psychiatry* 2008;79:1002-1006.

Supplementary Table 1. Overview of the study characteristics and reported prevalence of CAA pathology in the general population

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	Prevalence CAA pathology: any (mild/moderate/ severe/moderate-to-severe; %)	QA
Alafuzoff[1]	2020	Sweden	West	Autopsy subjects aged 80–89 yrs	Uppsala University Hospital	119	84.1 (2.2)	NR	NR	27 (NR/NR/NR/NR)	6
Alafuzoff[2]	2009	Finland	West	Population that had been under continuous clinical follow-up because of a chronic disease	Kuopio University Hospital	701	NR	59.7	NR	25 (NR/NR/NR/NR)	2.5
Attems[3]	2008	Austria	West	Hospital population	3 hospitals in Vienna	2,060	78.5 (6.8)	54.0	NR	49 (NR/NR/NR/NR)	4
Cholerton[4]	2013	USA	West	Population, dementia-free at baseline	ACT	363	87.4 (6.7)	53.5	NR	31 (16/13/2/15)	5.5
Conner[5]	2019	USA	West	Community-based, longitudinal cohort study	Framingham Original, Offspring and Omni I cohorts	129	84.1	57.7	53.5	78 (52/19/7/26)	2
Erten-Lyons[6]	2013	USA	West	Population, initially free of dementia, chronic diseases, and depression at baseline, later, people with chronic disease and dementia (but not depression) were also included	Oregon Brain Aging Study	71	94.7 (5.5)	45.6	NR	37 (NR/NR/NR/NR)	5.5
Hamasaki[7]	2022	Japan	East Asia	Population ≥40 years, autopsied between 2009–2014	Hisayama	228	83	47.3	NR	36 (11/14/11/25)	0
Hamilton[8]	2021	UK	West	Recruited brain donors at six sites across the UK	Brains for Dementia Research	789	84.8	NR	52.0	NR (NR/NR/NR/30)	1.5
Itoh[9]	1993	Japan	East Asia	Hospital population	Yokufukai Geriatric Hospital	160	84.4 (7.7)	60.1	NR	48 (26/11/11/22)	3
Karanth[10]	2022	USA	West	Community-based cohort without dementia, stroke/TIA, major psychiatric/ neurologic illness, or chronic infectious disease at baseline.	UK-ADRC	785	83.8 (8.6)	NR	54.6	NR (NR/NR/NR/27)	9.5
Kovacs[11]	2013	Austria	West	Population, born between May 1925 and June 1926	VITA	223	82*	50.5	NR	51 (NR/NR/NR/NR)	3
Kövari[12]	2013	Switzerland	West	Hospital population	University Hospitals Geneva 2007	91	78.2 (11)	56.6	NR	54 (NR/NR/NR/NR)	0
Kövari[13]	2015	Switzerland	West	Hospital population	University Hospitals Geneva 2012–2014	113	81.1 (10.8)	45.5	NR	44 (NR/NR/NR/NR)	0
Masuda[14]	1988	Japan	East Asia	Population ≥40 years, autopsied between 1971–1983	Hisayama residents	400	NR	57.8	NR	23 (NR/NR/NR/NR)	0
Matthews[15]	2009	UK	West	Population ≥65 years	MRC CFAS (1989–2004)	446	81*†	38.0	NR	43 (20/19/4/23)	6
Moghekar[16]	2012	USA	West	Population ≥70 years, dementia-free at baseline	BLSA	50	88.6 (5.8)	40.0	68.0	46 (NR/NR/NR/NR)	3.5

Supplementary Table 1. Continued

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	Prevalence CAA pathology: any (mild/moderate/ severe/moderate-to-severe; %)	QA
Ng[17]	1991	China	East Asia	Hospital population	NR	210	70.5†	66.8	NR	10 (NR/NR/3/NR)	2
Oveisgharan[18]	2018	USA	West	ROS: older Catholic nuns, priests and brothers. MAP: population from Chicago area. Dementia-free at baseline	ROS & MAP	1,453	88.6	70.8	65.4	76 (41/22/13/35)	6
Robinson[19]	2018	USA	West	Population ≥90 years	90+ Study	185	97.7 (3.6)	68.0	NR	16 (9/7/0/7)	6
Robinson[20]	2018	UK	West	Population, dementia-free at baseline	UMLS CNHOA	97	89 (72–104)*	51.6	NR	NR (NR/NR/NR/27)	3.5
Tanprasertsuk[21]	2019	USA	West	Population ≥98 years	Georgia Centenarian study	49	102.2 (2.5)	82.7	51.0	59 (35/12/12/24)	10.5
Tanskanen[22]	2012	Finland	West	Population ≥85 years	Vantaa 85+ Study	306	92.3	42.9	NR	70 (NR/NR/NR/NR)	1
Vinters[23]	1983	Canada	West	Hospital population	Victoria Hospital	84	77.5	50.0	NR	36 (NR/NR/17/NR)	1
Vonsattel[24]	1991	USA	West	Hospital population ≥75 years, without ICH	MGH	66	82.3	47.8	NR	45 (20/24/2/26)	1
Xu[25]	2003	China	East Asia	Hospital population ≥60 years	Chinese PLA General Hospital	362	77.5	NR	NR	31 (10/14/7/21)	5.5

Prevalence of CAA pathology shows the overall prevalence (irrespective of CAA grade), and, if reported, the prevalence of different stages of CAA (mild, moderate, severe, or moderate-to-severe).

ACT, Adult Changes in Thought cohort; BLSA, Baltimore Longitudinal Study of Aging; MAP, Rush Memory and Aging Project; MGH, Massachusetts General Hospital; MRC CFAS, Medical Research Council Cognitive Function and Ageing Study; PLA, People Liberation Army; ROS, Religious Orders Study; UMLS CNHOA, University of Manchester Longitudinal Study of Cognition in Normal Healthy Old Age; UK-ARDC, Kentucky Alzheimer's Disease Research Center; VITA, Vienna Transdanube Aging; ADC, Alzheimer disease center; CAA, cerebral amyloid angiopathy; ICH, intracerebral hemorrhage; NR, not reported; QA, total score of quality assessment; UK, United Kingdom; USA, United States of America.

*Median age and/or age range were reported instead of mean age (SD); †The exact age was not provided, but an estimation could be made based on the available data.

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Supplementary Table 2. Overview of the study characteristics and reported prevalence of CAA pathology in cognitively normal elderly

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	Prevalence CAA pathology: overall (mild/moderate/ severe/moderate-to-severe) (%)	QA
Alakbarzade[26]	2021	UK	West	Cases without significant neurodegenerative pathology	Dementia Research network	25	82 (10.2)	40.0	NR	40 (NR/NR/NR/NR)	2.5
Bergeron[27]	1987	Canada	West	Clinically non-demented, age-matched	Toronto University Hospital	30	68 (9.8)	NR	NR	40 (17/13/10/23)	3.5
Bertrand[28]	2008	Poland	West	No neurodegenerative or psychiatric disease, no dementia, age-matched	Institute of Psychiatry and Neurology, Warsaw	14	74.96 (9.8)	50.0	NR	29 (14/14/0/14)	1.5
Brayne[29]	2009	UK	West	Clinically non-demented	CC75C	100	90.7 (4.5)	61.0	NR	30 (26/3/1/4)	2
Chalmers[30]	2003	UK	West	No AD pathological change	SWBB	53	75 (8.3)	45.3	NR	36 (26/6/4/9)	3
Cholerton[4]	2013	USA	West	CASI >86	ACT	196	86 (7.2)	52.0	NR	21 (12/8/1/9)	4.5
Cruz-Sánchez[31]	2000	Spain	West	No neurological disease	NR	38	67 (18)	34.2	NR	18 (NR/NR/NR/NR)	7
Daillaire-Théroux[32]	2022	Canada	West	Cognitively intact adults. n=9 for each of the following age groups: 50–59, 60–69, 70–79, 80–89	Centre Hospitalier Universitaire de Québec histological archives	36	69.2	47.2	NR	31 (NR/NR/NR/NR)	6.5
Davis[33]	1999	USA	West	Cognitively and neurologically normal	Kentucky University Hospital	59	83.9 (7.4)	52.5	25.4	76 (NR/NR/NR/NR)	1
De Reuck[34]	2013	France	West	Death not related to brain disease	NR	14	74*	64.3	NR	NR (NR/NR/7/NR)	4
De Reuck[35]	2019	France	West	No neurological disease/cognitive decline/stroke	Lille University Hospital	20	66 (12)	40.0	NR	0 (0/0/0/0)	4.5
Dickson[36]	1992	USA	West	Non-demented	Bronx Aging Study	14	89	71.4	NR	36 (NR/NR/NR/NR)	5.5
Dugger[37]	2014	USA	West	No clinico-neuropathological diagnosis	AZSAND, BSHRI, BBDP	166	83 (9.3)	44.0	NR	20 (NR/NR/NR/NR)	6.5
Erten-Lyons[6]	2013	USA	West	No cognitive impairment or dementia, CDR=0	Oregon Brain Aging Study	27	92.1 (5.1)	55.6	NR	41 (NR/NR/NR/NR)	5.5
Esiri[38]	2015	UK	West	No AD (CERAD criteria), Braak stage ≤2	OPTIMA	70	82.6 (7.7)	44.3	74.3	51 (NR/NR/0/NR)	4
Esiri[39]	1986	UK	West	No clinicopathological evidence for dementia/CNS disease	Radcliffe Infirmary, Oxford	26	81	NR	NR	27 (NR/NR/0/NR)	10.5
Guidoux[40]	2018	France	West	Non-neurologic patients, age- and sex matched	Hospices Civils de Strasbourg	59	76 (70–91)*	49.2	33.9	15 (NR/NR/NR/NR)	5.5
Haglund[41]	2002	Sweden	West	Non-demented, no AE/ neurodegenerative or vascular pathology	LLDS	10	79	NR	NR	20 (NR/NR/NR/NR)	4
Head[42]	2017	USA	West	Non-demented	UCI ADRC	37	80.3 (10.0)	40.5	NR	19 (11/8/0/8)	7
Honig[43]	2005	USA	West	Clinically non-demented	NACC (1985–2003)	225	82.9 (10)	56.4	NR	45 (NR/NR/NR/NR)	7.5
Jellinger[44]	2010	Austria	West	Pathologically and clinically non-demented, age-matched	Institute of Clinical Neurobiology, Vienna	486	79 (7.6)	54.9	NR	30 (NR/NR/20/NR)	3

Supplementary Table 2. Continued

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	Prevalence CAA pathology: overall (mild/moderate/ severe/moderate-to-severe) (%)	QA
Kawas[45]	2015	USA	West	90+ elderly without dementia	90+ study	85	97.5	63.5	NR	9 (NR/NR/NR/NR)	7.5
Kövari[12]	2013	Switzerland	West	Non-demented	University Hospitals Geneva 2007	59	75.6 (11.1)	49.2	NR	46 (NR/NR/NR/NR)	2
Love[46]	2003	UK	West	Neurologically normal, no pathological evidence of AD (CERAD)	Frenchay Hospital, Bristol	152	(60–102)*	48.7	NR	32 (NR/NR/NR/NR)	4
Magaki[47]	2014	USA	West	Non-demented	UCLA	124	70.7 (8.2)	41.1	NR	0 (0/0/0/0)	7
Malek-Ahmadi[48]	2019	USA	West	Elderly non-demented individuals	Rush Religious Order Study	98	NR	NR	NR	71 (NR/NR/NR/NR)	6
Matthews[15]	2009	UK	West	Clinically non-demented	MRC CFAS	178	NR	NR	NR	27 (17/10/0/10)	8
McAleese[49]	2019	UK	West	Non-cognitively impaired, with at least 1 deep WMH	Institute of Neuroscience, Newcastle	22	84.4 (8.6)	50.0	NR	36 (23/9/5/14)	3.5
McKee[50]	2006	USA	West	Cognitively intact, CDR=0	FHS	25	81.5 (15)	48.0	NR	60 (32/12/16/28)	3
Mountjoy[51]	1982	UK	West	Patients who died whilst under general medical/psychiatric care, no dementia	Newcastle General Hospital	30	76	50.0	NR	40 (NR/NR/NR/NR)	5
Premkumar[52]	1996	USA	West	No clinical or histopathological evidence of AD	CWRU	16	70	43.8	NR	0 (0/0/0/0)	6
Robinson[20]	2018	UK	West	Clinically cognitively unimpaired	UMLS CNHOA	57	89*	64.9	NR	NR (NR/NR/NR/16)	2.5
Shim[53]	2015	USA	West	Clinically healthy, cognitively normal	CCCVD	14	90.9 (6.0)	64.3	42.9	79 (NR/NR/NR/NR)	4
Sugarman[54]	2019	USA	West	Elderly with normal cognition	NACC-UDS and NACC-NDS	417	NR	NR	NR	17 (NR/NR/NR/NR)	10.5
Wu[55]	1992	USA	West	Clinically non-demented, age-matched	Albert Einstein College of Medicine, New York	34	79.1 (10.1)	70.6	NR	50 (44/3/3/6)	6.5
Xu[56]	2004	China	East Asia	No clinical or pathological involvement of CNS	PLA General Hospital, Beijing	28	65.8 (22.8)	17.9	NR	25 (NR/NR/NR/NR)	4
Yamada[57]	2002	Japan	East Asia	No AD/ neurodegenerative disease	Kanazawa University Hospital	119	85.7 (8)	NR	NR	35 (NR/NR/NR/NR)	3

Prevalence of CAA pathology shows the overall prevalence (irrespective of CAA grade), and, if reported, the prevalence of different stages of CAA (mild, moderate, severe, or moderate-to-severe).

ACT, Adult Changes in Thought cohort; AZSAND, Arizona Study of Aging and Neurodegenerative Disorders; BBDP, Brain and Body Donation Program; BSHRI, Banner Sun Health Research Institute; CCCVD, Cognitive Change in Cerebrovascular Disease; CC75C, Cambridge City over-75's Cohort; CWRU, Case Western Reserve University; FHS, Framingham Heart Study; HAAS, Honolulu-Asia Aging Study; LLDS, Lund Longitudinal Dementia Study; LPRI, Leningrad Psychoneurological Research Institute; MRC CFAS, Medical Research Council Cognitive Function and Ageing Study; NACC, National Alzheimer's Coordinating Center; OPTIMA, Oxford Project to Investigate Memory and Ageing; PLA, People Liberation Army; ROS, Religious Orders Study; SWBB, South Western Brain Bank; UCI ADRC, University of California at Irvine Alzheimer's Disease Research Center; UCLA, University of California Los Angeles; UMLS CNHOA, University of Manchester Longitudinal Study of Cognition in Normal Healthy Old Age; UMMC, University Malaya Medical Centre; AD, Alzheimer disease; CAA, cerebral amyloid angiopathy; CASI, cognitive abilities screening instrument; CDR, clinical dementia rating; CDR-SOB, clinical dementia rating–sum of boxes; CERAD, consortium to establish a registry for Alzheimer's disease; CNS, central nervous system; ICH, intracerebral hemorrhage; IHC, immunohistochemistry; MC, medical center; NR, not reported; QA, total score of quality assessment; UK, United Kingdom; USA, United States of America; WMH, white matter hyperintensity.

*Median age and/or age range were reported instead of mean age (SD).

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Supplementary Table 3. Overview of the study characteristics and reported prevalence of CAA pathology in patients with AD

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	Prevalence CAA pathology: overall (mild/moderate/ severe/moderate-to-severe) (%)	QA
Alakbarzade[26]	2021	UK	West	Neuropathologically confirmed AD	Brains for Dementia Research (UK)	15	82.9 (4.8)	53.3	NR	93 (NR/NR/NR/NR)	2.5
Attems[3]	2008	Austria	West	Pathologically diagnosed AD (CERAD, Braak, NIA-Reagan)	Three large hospitals in Vienna	760	NR	NR	NR	98 (NR/NR/NR/NR)	1
Bell[58]	1990	Canada	West	Clinically diagnosed AD, pathologically confirmed	NR	10	79.3 (9)	50.0	NR	60 (NR/NR/NR/NR)	4.5
Bergeron[27]	1987	Canada	West	Clinically and pathologically diagnosed AD	Toronto University Hospital	30	73 (8.1)	NR	NR	87 (3/30/53/83)	2
Boon[59]	2020	The Netherlands	West	Clinically and pathologically diagnosed late onset AD	Netherlands Brain Bank and Normal Aging Brain Collection	21	84.5 (5.9)	57.1	NR	90 (NR/NR/NR/NR)	12
Boyle[60]	2019	USA	West	Clinical probable AD	ROS & MAP	512	91 (5.9)	71.7	NR	46 (NR/NR/NR/NR)	4
Brayne[29]	2009	UK	West	Clinically diagnosed AD (DSM-IV)	CC75C	101	91.2	77.2	NR	60 (34/19/8/27)	3
Chalmers[30]	2003	UK	West	Pathologically confirmed AD	SWBB	125	78.6 (8.7)	56.0	NR	95 (63/18/14/32)	3
Chen[61]	2022	USA	West	Autopsy-confirmed AD	NACC	753	82.1 (8.6)	42.9	48.7	0 (NR/NR/NR/46)	8.5
Cruz-Sánchez[31]	2000	Spain	West	Clinically diagnosed AD (DSM-IV)	NR	28	77 (10)	50.0	NR	61 (NR/NR/NR/NR)	6
Del Ser[62]	2005	Canada	West	Clinically diagnosed AD (DSM-III), pathologically confirmed (Braak stage ≥4, CERAD). 22 cases also had IL	Dementia Study Project	57	79.3	66.7	29.8	46 (NR/NR/NR/NR)	1
De Reuck[35]	2019	France	West	Demented, pathologically diagnosed AD (Braak V or VI)	Lille University Hospital	92	76	48.9	NR	67 (20/15/33/48)	4.5
Dugger[63]	2014	USA	West	Demented, pathologically diagnosed with probable/definite AD (CERAD). Life expectancy <6 months at recruitment	Recruited participants from 22 centers in the USA	38	82 (11.2)	60.5	NR	92 (34/34/24/58)	1
Ellis[64]	1996	USA	West	Clinically and pathologically (CERAD) diagnosed (possible, probable, or definite) AD	CERAD study	117	76.4	35.9	21.4	83 (57/NR/NR/26)	7
Esiri[38]	2015	UK	West	Pathologically diagnosed AD (CERAD)	OPTIMA	154	78.3 (8)	56.5	61.0	94 (NR/NR/9/NR)	4
Esiri[39]	1986	UK	West	AD with or without CVD or other CNS disease	Radcliffe Infirmary, Oxford	45	82	66.7	NR	82 (NR/NR/24/NR)	10.5
Fallet-Bianco[65]	1990	France	West	Clinically demented, microscopically diagnosed AD or mixed dementia (AD and VaD)	Charles Richet Study	42	85.5	NR	NR	74 (NR/NR/NR/NR)	4

Supplementary Table 3. Continued

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	Prevalence CAA pathology: overall (mild/moderate/ severe/moderate-to-severe) (%)	QA
Glenner[66]	1981	USA	West	Clinically demented, pathologically diagnosed AD	AFIP	45	68.7	NR	NR	89 (NR/NR/NR/NR)	10
Haglund[41]	2002	Sweden	West	Clinically diagnosed AD, with pathological correlate of varying degrees of AE (15 had AD and VaD)	LLDS	52	78.6†	NR	NR	69 (NR/NR/NR/NR)	4
Hamasaki[7]	2022	Japan	East Asia	AD according to DSM III-R	Hisayama, Japan	77	89.6 (6.8)	62.3	NR	61 (21/22/18/40)	0
Head[42]	2017	USA	West	Pathologically diagnosed AD (Braak stage VI & amyloid plaque stage C, NACC)	UCI ADRC	79	76.1 (12.2)	50.6	NR	72 (41/14/18/32)	7
Helman[67]	2019	USA	West	Clinically demented, pathologically confirmed AD	NIH NeuroBioBank	12	80.6 (8.2)	33.3	NR	92 (33/8/50/58)	3
Honig[43]	2005	USA	West	Clinically demented, pathologically confirmed AD	NACC (1985–2003)	791	78.8 (8.8)†	49.6	NR	41 (NR/NR/NR/NR)	7.5
Itoh[9]	1993	Japan	East Asia	Pathologically diagnosed AD (Khachaturian)	Yokufukai Geriatric Hospital	33	86.5 (7.4)	NR	NR	76 (NR/NR/NR/NR)	3
Jellinger[68]	1977	Austria	West	Clinically diagnosed probable AD (NINCDS-ADRDA), pathologically confirmed definite AD (CERAD)	3 hospitals in Vienna	92	NR	NR	NR	78 (NR/NR/NR/NR)	12
Jellinger[69]	2003	Austria	West	Pathologically diagnosed AD	Neurological Institute, Vienna	730	82.4 (4.4)	65.5	NR	98 (NR/NR/NR/24)	1
Jicha[70]	2006	USA	West	Clinically demented, pathologically diagnosed AD	Mayo Alzheimer Disease Patient Registry	24	89.5	70.8	NR	33 (17/17/0/17)	1
Joachim[71]	1988	USA	West	Clinically and pathologically diagnosed AD	NR	131	77†	NR	NR	100 (NR/NR/NR/ NR)	9.5
Kovacs[11]	2013	Austria	West	Clinically diagnosed dementia (14 possible & 8 probable AD)	VITA	22	NR	NR	NR	45 (NR/NR/NR/NR)	4
Kövari[12]	2013	Switzerland	West	Pathologically diagnosed AD (Braak stage ≥4; 14 pure AD and 11 associated with vascular encephalopathy)	University Hospitals Geneva 2012–2014	10	84.4 (4.1)	50.0	NR	80 (NR/NR/NR/NR)	1
Kövari[13]	2015	Switzerland	West	Pathologically diagnosed AD (Braak stage ≥4)	University Hospitals Geneva 2007	25	85	NR	NR	68 (NR/NR/NR/NR)	1
Kurucz[72]	1981	USA	West	Clinically and pathologically diagnosed AD, infarction present in 11 cases	Warren State Hospital	41	NR	NR	NR	54 (37/NR/17/NR)	3

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Supplementary Table 3. Continued

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	Prevalence CAA pathology: overall (mild/moderate/ severe/moderate-to-severe) (%)	QA
Leech[73]	2001	USA	West	Clinically demented, pathologically confirmed AD (Khachaturian, or NIA-R, or CERAD)	Many hospitals in Oklahoma, Autopsy Assistance Network Oklahoma, Alzheimer's Research Texas Tech University	79	NR	NR	NR	32 (NR/NR/NR/NR)	16.5
Liu[74]	1999	China	East Asia	Clinically and pathologically diagnosed AD	Beijing Hospital	29	79.9 (7.2)	37.9	NR	86 (NR/NR/NR/NR)	7.5
Lopez[75]	1991	USA	West	Clinically and pathologically diagnosed AD	PUH & VAMC	40	71.6 (8.1)	47.5	NR	55 (NR/NR/NR/NR)	4
Magaki[47]	2014	USA	West	Clinically and pathologically diagnosed dementia (AD: 123 pure, AD+LBD, AD+IL: 24 AD+OL)	UCLA ADRC, ECBB	171	NR	NR	NR	73 (19/19/35/54)	7
Mandybur[76]	1975	UK	West	Clinically and pathologically diagnosed AD	Cincinnati General Hospital	15	69.3 (9.8)	60.0	73.3	87 (27/47/13/60)	7
Mann[77]	2018	UK	West	Clinically diagnosed late onset AD	MBB	34	80.8 (7.4)	47.1	NR	88 (NR/NR/NR/NR)	3
McAleese[49]	2019	UK	West	Clinico-pathologically diagnosed AD with >1 deep WML	Institute of Neuroscience, Newcastle	20	83.4 (6.3)	55.0	NR	80 (10/30/40/70)	3.5
McKee[50]	2006	USA	West	Clinically diagnosed probable AD, CDR 1–3	FHS	13	89 (6)	61.5	NR	100 (NR/NR/NR/ NR)	4
Mountjoy[51]	1982	UK	West	Clinically diagnosed senile dementia of Alzheimer type	Newcastle General Hospital	15	76.2	80.0	NR	60 (NR/NR/NR/NR)	4
Nation[78]	2012	USA	West	Clinically diagnosed possible (10) or probable (55) AD (NINDS-ARDRA), confirmed by NIA CERAD criteria for probable or definite AD. No VaD or mixed dementia	UCSD-ADRC	65	74.2 (7)	52.3	27.7	80 (NR/NR/NR/NR)	5
Olichney[79]	2000	USA	West	Clinically and pathologically diagnosed AD (DSM-III, NIH and CERAD)	SD ADRC	306	79.8	47.4	35.9	75 (NR/NR/19/NR)	3
Parker[80]	1985	USA	West	AD (not further specified)	Tennessee University Hospital	10	77 (70–86)*	40.0	NR	20 (NR/NR/NR/NR)	9
Pirttilä[81]	1996	Finland	West	Clinically diagnosed probable AD (NINCDS-ARDRA), pathologically confirmed definite AD (CERAD)	Kuopo University Hospital	18	84.4†	NR	NR	61 (22/NR/NR/39)	8
Pivtoraiko[82]	2021	USA	West	Clinical diagnosis of AD dementia (McKahn)	University of Pittsburgh ADRC	17	84 (10)	17.6	NR	82 (53/18/12/29)	5.5

Supplementary Table 3. Continued

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	Prevalence CAA pathology: overall (mild/moderate/ severe/moderate-to-severe) (%)	QA
Premkumar[52]	1996	USA	West	Clinically diagnosed probable AD confirmed by pathology (>95% definite AD)	CWRU	190	79	56.8	NR	96 (25/NR/NR/71)	6
Reimand[83]	2020	The Netherlands	West	Autopsy-confirmed AD	Amsterdam Dementia Cohort	11	64.3	27.3	NR	100 (NR/NR/NR/ NR)	14
Shim[53]	2015	USA	West	Clinically diagnosed AD (criteria comparable to NINCDS-ADRDA)	CCCVD	26	80.7 (9.2)	38.5	23.1	85 (NR/NR/NR/NR)	4
Shinohara[84]	2016	USA	West	Pathologically diagnosed AD	Mayo Clinic brain bank for neurodegenerative disorders at Jacksonville	428	81*†	57.5	NR	87 (NR/NR/NR/NR)	4
Spina[85]	2021	USA	West	Pathologically diagnosed AD	Memory and Aging Center, UCSF	48	83 (5.9)	29.2	NR	29 (54/17/8/25)	2
Tomimoto[86]	1999	Japan	East Asia	Pathologically diagnosed AD (CERAD)	NR	39	79 (9)	NR	NR	97 (15/33/49/82)	8
Vik-Mo[87]	2019	Norway	West	Clinically diagnosed AD (NINCDS-ARDRA), pathologically confirmed AD	Demvest	31	81.1	67.7	NR	NR (NR/NR/NR/58)	8
Wu[55]	1992	USA	West	Pathologically diagnosed AD	Albert Einstein College of Medicine, New York	34	80.8 (7.2)	70.6	NR	100 (56/15/29/44)	5
Yamada[88]	1988	Japan	East Asia	Clinically and pathologically diagnosed AD	Yokufukai Geriatric Hospital	15	83	NR	NR	87 (47/27/13/40)	5
Yamada[57]	2002	Japan	East Asia	Pathologically diagnosed AD (CERAD)	Kanazawa University Hospital	82	86.1 (7.9)	NR	NR	87 (NR/NR/NR/NR)	2
Yip[89]	2005	USA	West	Pathologically diagnosed AD (NIA-R criteria for intermediate/high likelihood of AD). 90% Braak stage ≥5	BU ADC Brain Bank	99	75.1 (7)	2.0	NR	91 (NR/NR/NR/NR)	5
Zarow[90]	1999	USA	West	Clinical-pathologic definite AD (CERAD, Khachaturian) definite AD	Rancho Los Amigos Medical Center	101	77.4 (8.8)	49.5	NR	81 (NR/NR/29/NR)	0

Prevalence of CAA pathology shows the overall prevalence (irrespective of CAA grade), and, if reported, the prevalence of different stages of CAA (mild, moderate, severe, or moderate-to-severe).

AFIP, Armed Forces Institute of Pathology; BU ADC, Boston University AD Center; CC75C, Cambridge City over-75's Cohort; CCCVD, Cognitive Change in Cerebrovascular Disease; CWRU, Case Western Reserve University; Demvest, Dementia study in Western Norway; ECBB, Easton Center Brain Bank; FHS, Framingham Heart Study; LLDS, Lund Longitudinal Dementia Study; MBB, Manchester Brain Bank; NACC, National Alzheimer's Coordinating Center; OPTIMA, Oxford Project to Investigate Memory and Ageing; PUH, Presbyterian University Hospital; ROS, Religious Orders Study; SD ARDC, San Diego Alzheimer's Disease Research Center; SWBB, South Western Brain Bank; UCI ADRC, University of California at Irvine Alzheimer's Disease Research Center; UCLA ADRC, University of California Los Angeles Alzheimer Disease Research Centre; UCSD ADRC, University of California San Diego Alzheimer's Disease research center; UCSF, University of San Francisco; VAMC, Veterans Administration Medical Center; VITA, Vienna Transdanube Aging; AD, Alzheimer disease; AE, Alzheimer's encephalopathy; CAA, cerebral amyloid angiopathy; CDR, clinical dementia rating; CDR-SOB, clinical dementia rating–sum of boxes; CERAD, consortium to establish a registry for Alzheimer's disease; CNS, central nervous system; CVD, cerebrovascular disease; DSM, diagnostic and statistical manual of mental disorders; IL, ischemic lesions; LBD, Lewy body dementia; NIA, national institute on aging; NIA-R, national institute on aging-Reagan; NINCDS-ADRDA, national institute of neurological and communicative disorders and stroke and the Alzheimer's disease and related disorders association; NR, not reported; OL, other lesions; QA, total score of quality assessment; UK, United Kingdom; USA, United States of America; VaD, vascular dementia; WML, white matter lesion.

*Median age and/or age range were reported instead of mean age (SD); †The exact age was not provided, but an estimation could be made based on the available data.

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Supplementary Table 4. Overview of the study characteristics and reported prevalence of CAA pathology in patients with intracerebral hemorrhage

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	Prevalence CAA pathology: overall (mild/moderate/ severe/moderate-to-severe) (%)	QA
Attems[3]	2008	Austria	West	Pathologically diagnosed ICH	3 Hospitals in Vienna	115	(62–96)*	NR	NR	49 (NR/NR/39/ NR)	1
Dye[91]	2014	USA	West	Evacuation of spontaneous ICH	UCLA	20	67	40.0	65.0	40 (NR/NR/NR/ NR)	5.5
Fazekas[92]	1999	Austria	West	Fatal ICH	Graz University Hospital	11	72	45.5	64.0		1
Guidoux[40]	2018	France	West	Fatal ICH	MASS	81	74 (25–91)*	45.7	69.0	25 (NR/NR/NR/ NR)	4
Holling[93]	2012	Germany	West	Surgically removed spontaneous ICH	Institute of Neuropathology, Münster	378	65 (0–91)*	46.8	NR	10 (NR/NR/NR/ NR)	5.5
Ishihara[94]	1991	Japan	East Asia	Spontaneous ICH	Yamaguchi University	50	72	NR	66.0	38 (12/NR/NR/26)	8
Lieber[95]	2019	USA	West	Patients undergoing minimally invasive ICH clot evacuation (15 out of 40 lobar)	Mount Sinai Hospital, New York	40	62.7	37.5	87.5	10 (NR/NR/NR/ NR)	9.5
Mendel[96]	2013	Poland	West	Fatal spontaneous ICH	IPN, Warsaw	189	NR	NR	NR		2
Ng[17]	1991	China	East Asia	Fatal spontaneous ICH	NR	49	66.6	38.8	NR	8 (NR/NR/NR/NR)	2
Ritter[97]	2005	Hungary	West	ICH & hypertension	Debrecen University Hospital	64	69.3 (12.9)	35.9	100.0	23 (NR/NR/NR/ NR)	6
Rodrigues[98]	2018	UK	West	First ever ICH, diagnosed by CT	LINCHPIN	110	83*	55.5	70.0	56 (18/NR/NR/38)	1
Tang[99]	2013	China	East Asia	Spontaneous ICH or multiple ICH that underwent surgery	71 Hospitals in Mainland China	974	56 (12)	29.2	67.0	38 (34/2/1/3)	2

Prevalence of CAA pathology shows the overall prevalence (irrespective of CAA grade), and, if reported, the prevalence of different stages of CAA (mild, moderate, severe, or moderate-to-severe).

IPN, Institute of Psychiatry and Neurology; LINCHPIN, Lothian IntraCerebral Haemorrhage, Pathology, Imaging and Neurological Outcome; MASS, Multiple Atherosclerosis Site in Stroke study; UCLA, University of California, Los Angeles; CAA, cerebral amyloid angiopathy, CT, computer tomography; ICH, intracerebral hemorrhage; NR, not reported; QA, total score of quality assessment; UK, United Kingdom; USA, United States of America.

*Median age and/or age range were reported instead of mean age (SD).

Supplementary Table 5. Overview of the study characteristics and reported prevalence of CAA pathology in patients with lobar intracerebral hemorrhage

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	Prevalence CAA pathology: overall (mild/moderate/ severe/moderate-to-severe) (%)	QA
Baron[100]	2022	France	West	ICH with autopsy (n=1) or hematoma evacuation (n=15) material	Pathology Department of GHU-Paris, Sainte-Anne site, University of Paris	16	65.8 (7.2)	62.5	56.3	44 (6/19/19/38)	6.5
Doden[101]	2016	Japan	East Asia	Cases with cortico-subcortical ICH who underwent hematoma evacuation	Aizawa Hospital	48	NR	NR	NR	NR (NR/NR/NR/46)	5.5
Guidoux[40]	2018	France	West	Fatal LICH	MASS	30	76 (53–91)*	60.0	53.3	50 (NR/NR/NR/NR)	4
Itoh[102]	1993	Japan	East Asia	Pathologically diagnosed LICH	Yokufukai Geriatric Hospital	29	NR	NR	NR	NR (NR/NR/NR/31)	3
Knudsen[103]	2001	USA	West	Spontaneous LICH, clinically & radiographically diagnosed with possible/ probable CAA	MGH or SRH	39	NR	NR	NR	NR (NR/NR/NR/74)	6
Lin[104]	2018	Japan	East Asia	Surgically removed LICH	Fukui University Hospital	29	73.2	51.7	48.3	83 (10/7/66/72)	4
Minakawa[105]	1995	Japan	East Asia	Surgically treated patients with LICH without an angiographic lesion	Kuwana Hospital	19	NR	NR	NR	53 (NR/NR/NR/NR)	6
Ritter[97]	2005	Hungary	West	LICH & hypertension	Debrecen University Hospital	24	72.1 (14.1)	41.7	100.0	33 (NR/NR/NR/NR)	5
Rodrigues[98]	2018	UK	West	First-ever LICH	LINCHPIN	62	83*	62.9	67.7	74 (16/NR/NR/58)	2
Yoshimura[106]	1992	Japan	East Asia	Autopsy-proven massive LICH	Tokyo Metropolitan Geriatric Medical Center	38	NR	NR	NR	21 (NR/NR/NR/NR)	6

Prevalence of CAA pathology shows the overall prevalence (irrespective of CAA grade), and, if reported, the prevalence of different stages of CAA (mild, moderate, severe, or moderate-to-severe).
LINCHPIN, Lothian IntraCerebral Haemorrhage, Pathology, Imaging and Neurological Outcome; MASS, Multiple Atherosclerosis Site in Stroke study; MGH, Massachusetts General Hospital; SRH, Spaulding Rehabilitation Hospital; CAA, cerebral amyloid angiopathy; ICH, intracerebral hemorrhage; LICH, lobar intracerebral hemorrhage; NR, not reported; QA, total score of quality assessment; UK, United Kingdom; USA, United States of America.
*Median age and/or age range were reported instead of mean age (SD).

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Supplementary Table 6. Overview of the study characteristics and reported prevalence of strictly lobar microbleeds in the general population

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	MRI parameters (field strength [T]/sequence/ slice thickness [mm])	Prevalence MBs strictly lobar/strictly deep/mixed (%)	QA
Aarts[107]	2014	The Netherlands	West	Population, dementia free	Rotterdam Scan Study	4,945	64 (11)	55.1	34.3	1.5/T2*/NR	13/NR/NR	1
Chung[108]	2016	Taiwan	East Asia	Population, free of neuropsychiatric diseases	ILAS	962	62.5 (8.6)	55.8	37.1	3/SWI/2	5/2/7	2
Elmståhl[109]	2019	Sweden	West	Population 70–87 years	Good Aging in Skåne (GÅS)	344	77	57.3	58.1	3/T2*/3	16/2/3	0
Graff-Radford[110]	2021	USA	West	Population, dementia at baseline excluded	MSCA	1,253	74	46.8	65.7	3/T2*/3.3	18/2/3	1
Han[111]	2018	China	East Asia	Population, stroke-free	Shunyi Study	1,211	55.6 (9.3)	62.6	49.1	3/SWI/1.5	5/2/4	1
Kim[112]	2012	South Korea	East Asia	Population, stroke- and TIA-free	Seoul National University Hospital	1,452	69.7 (4.4)	42.7	50.3	1.5/T2*/6	2/NR/NR	2
Miwa[113]	2014	Japan	East Asia	Population, free of recent (<3 months) symptomatic vascular event, >1 vascular risk factor, free of MCI and dementia	OSACA2	524	67.7 (8.3)	42.4	74.0	1.5/T2*/5	6/7/8	0
Paganini-Hill[114]	2019	USA	West	Population ≥90 years	90+ study	71	93	NR	NR	3/SWI/NR	14/NR/6	3
Qiu[115]	2012	Iceland	West	Population	AGES Reykjavik	4,205	76.2	57.8	80.3	1.5/T2*/NR	6/NR/NR	4
Romero[116]	2014	USA	West	Population	Framingham Original and Offspring cohort	1,965	67.2 (10.7)	54.0	56.0	1.5/T2*/5	6/1/2	1.5
Tsushima[117]	2003	Japan	East Asia	Hospital population	Gunma University Hospital	2,019	56.6 (15.9)	43.5	34.7	1/T2*/5	2/3/5	1
Wang[118]	2019	China	East Asia	Population, stroke- and cancer-free	Taizhou Imaging Study	562	59.3 (2.7)	53.9	55.2	3/T2*/5	9/NR/NR	2
Ying[119]	2021	China	East Asia	Population ≥50 years, stroke- and dementia-free	Shanghai elderly community-based cohort	796	68	56.0	NR	1.5 or 3/SWI/ NR	15/NR/NR	1
Yubi[120]	2018	Japan	East Asia	Population	Hisayama Study	1,281	75 (7)	56.6	70.7	1.5/T2*/5	5/4/NR	6

Prevalence of microbleeds shows the prevalence of (1) strictly lobar microbleeds, (2) strictly deep microbleeds, and (3) mixed microbleeds.
AGES, Age, Gene/Environment Susceptibility; ILAS, I-Lan Longitudinal Aging Study; MSCA, Mayo Clinic Study of Aging; OSACA2, Osaka Follow-Up Study for Carotid Atherosclerosis; MBs, microbleeds; MRI, magnetic resonance imaging; NR, not reported; QA, total score of quality assessment; SD, standard deviation; SWI, susceptibility-weighted imaging; T, tesla; USA, United States of America.

Supplementary Table 7. Overview of the study characteristics and reported prevalence of strictly lobar microbleeds in cognitively normal elderly

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	MRI parameters (field strength [T]/sequence/ slice thickness [mm])	Prevalence MBs strictly lobar/strictly deep/mixed (%)	QA
Atri[121]	2005	USA	West	Retired nurses, no stroke/dementia	CANHSMR	23	78	100	52.2	1.5/T2*/5	4/NR/NR	2
Barnaure[122]	2017	Switzerland	West	Cognitively normal	Geneva University Hospitals	328	74.2	62.2	NR	3/T2*/1.1	20/6/NR	2.5
Brundel[123]	2014	The Netherlands	West	Clinically healthy, non-diabetic	UDES	49	71.1 (4.5)	38.8	51.0	7/T2*/0.35	22/6/12	2.5
Chang[124]	2021	China	East Asia	No cognitive or subjective impairment, MMSE ≥28	Chinese PLA General Hospital	15	78	26.7	66.7	NR/SWI/1.2	27/NR/NR	5
Chiang[125]	2015	USA	West	Clinically normal	ADNI-2, ADNI-GO	151	NR	NR	NR	3/T2*/4	22/6/2	1
Donaghy[126]	2020	UK	West	Healthy controls, recruited through research case register or partners of participants	Secondary care services in the North of England	20	75.9 (7.3)	20.0	60.0	3/SWI/3	15/0/0	5
Graff-Radford[127]	2017	USA	West	Cognitively normal	ARIC	1,072	NR	NR	NR	3/T2*/3.3	14/NR/NR	0
Gregg[128]	2015	USA	West	32/55 CDR 0, 13/55 CDR 0.5	GEMS	55	86.8 (2.7)	40.0	NR	3/T2* or SWI/3 (gradient echo) and 1.5 or 1.2 for SWI	25/5/7	4
Ham[129]	2014	South Korea	East Asia	Cognitively normal	Yonsei University Hospital	49	70.4 (6.7)	61.2	42.9	3/T2*/5	10/0/2	2
Johansson[130]	2016	Sweden	West	Clinically healthy	University hospital, Umea	41	70.5 (5.4)	43.9	68.3	3/T2*/5	10/15/0	1.5
Kwon[131]	2016	South Korea	East Asia	Neurologically healthy; free of strokes/ TIA's/neurological symptoms	Seoul National University Hospital	1,737	55.9 (9.1)	45.4	25.9	1.5/T2*/5	2/NR/NR	0
Mendes[132]	2018	France	West	Clinically healthy	PHRC-CAPP	19	64 (55–76)*	73.7	47.4	3/T2* or SWI/2.5	5/NR/NR	5.5
Mitaki[133]	2017	Japan	East Asia	Neurologically normal	Shimane University, Izumo	4,024	61.6 (10.1)	45.5	31.5	1.5/T2*/7	1/2/1	1.5
Nakata-Kudo[134]	2006	Japan	East Asia	Normal neurological examination and MRI findings (age-matched to AD group in study)	Kyoto University Hospital	26	71.2 (6.4)	61.5	38.5	1.5/T2*/5	0/0/0	3.5
Ochi[135]	2009	Japan	East Asia	Free of CVD/ severe cognitive dysfunction/dementia	Ehime University Hospital	443	67.1 (8.1)	63.7	56.7	3/T2*/6	2/NR/NR	2
Romero[136]	2020	USA	West	Dementia-, stroke-, and other neurological disease-free Framingham Heart Study participants	Framingham Heart Study	3,680	55 (13)	53.6	39.4	1.5/T2*/5	4/1/1	2.5
Roob[137]	1999	Austria	West	No history of neuropsychiatric disease, normal neurological examination	ASPS	280	60	46.8	31.8	NR/T2*/5	3/3/0	0

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Supplementary Table 7. Continued

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	MRI parameters (field strength [T]/sequence/ slice thickness [mm])	Prevalence MBs strictly lobar/strictly deep/mixed (%)	QA
Wang[138]	2019	Taiwan	East Asia	Free of stroke/ dementia cognitive impairment	ILAS	659	62.1 (8.3)	56.0	37.2	3/SWI/2	5/6/2	0
Wollenweber[139]	2017	Austria	West	Stroke/dementia-free, normal neurologic examination	ASPFS	372	65 (10.7)	43.3	63.2	3/T2*/4	2/NR/NR	3
Yakushiji[140]	2015	Japan	East Asia	Population, free of neurological disorders, normal neurological examination	Kashima Scan Study	1,451	58 (22–84)*	53.5	NR	1.5/T2*/7	3/3/NR	0
Yilmaz[141]	2019	The Netherlands	West	Stroke- and dementia-free population	Rotterdam Study	1,622	73.1 (7.6)	54.3	78.7	1.5/T2*/0.8	18/NR/NR	0
Zhang[142]	2018	China	East Asia	Hypertensive elderly, free of stroke/ dementia/MCI	3 Centers in northern China	819	64.4 (8.3)	44.8	55.2	3/SWI/1.2	4/NR/NR	2

Prevalence of microbleeds shows the prevalence of (1) strictly lobar microbleeds, (2) strictly deep microbleeds, and (3) mixed microbleeds.
ADNI-2, Alzheimer's Neuro-imaging Initiative 2; ADNI-GO, Alzheimer's Neuro-imaging Initiative GO; ARIC, Atherosclerosis Risk in Communities; ASPFS, Austrian Stroke Prevention Family Study; ASPS, Austrian Stroke Prevention Study; CANHSMR, Cognitive Assessment in Nurses Health Study Massachusetts Residents' cohort; GEMS, Ginkgo Evaluation of Memory Study; ILAS, I-Lan Longitudinal Aging Study; PHRC-CAPP, French multicenter investigation on primary progressive aphasias; UDES, Utrecht Diabetic Encephalopathy Study; AD, Alzheimer's disease; CDR, clinical dementia rating; CVD, cerebrovascular disease; MBs, microbleeds; MCI, mild cognitive impairment; MRI, magnetic resonance imaging; NR, not reported; QA, total score of quality assessment; SD, standard deviation; SWI, susceptibility-weighted imaging; T, tesla; TIA, transient ischemic attack; USA, United States of America.
*Median age and/or age range was reported instead of mean age (SD).

Supplementary Table 8. Overview of the study characteristics and reported prevalence of strictly lobar microbleeds in patients with AD

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	MRI parameters (field strength [T]/sequence/ slice thickness)	Prevalence MBs strictly lobar/strictly deep/mixed (%)	QA
Benedictus[143]	2013	The Netherlands	West	Probable AD (NINCDS-ADRDA)	ADC	371	69 (9)	55.0	34.8	3/T2*/3	18/3/5	0
Boyano[144]	2018	Spain	West	AD (NINCDS-ADRDA)	ACRSF	152	81	NR	NR	3/T2*/2.4	15/13/16	1
Chang[124]	2021	China	East Asia	Probable AD (NINCDS-ADRDA)	Chinese PLA General Hospital	15	76	40.0	60.0	NR/SWI/1.2	53/NR/NR	5
Charidimou[145]	2016	USA	West	Clinically diagnosed AD	Memory clinic, MGH	86	NR	NR	NR	3/NR/5	29/NR/NR	3
Chiang[125]	2015	USA	West	Probable AD (NINCDS-ADRDA)	ADNI-2 and ADNI-GO	86	NR	NR	NR	3/T2*/4	35/3/3	1
Chiu[146]	2020	Taiwan	East Asia	Mild to moderate AD (DSM-IV) no comorbidities (such as obvious vascular insults, vitamin B12/ folate deficiency, and metabolic disorders)	Shuang Ho Hospital	112	76 (8)	70.5	32.1	1.5 or 3/ T2*/2.4 (1.5 T) or 2 (3 T)	6/5/17	6.5
De Kort[147]	2021	The Netherlands	West	Probable AD (NINCDS-ADRDA)	Radboud University Medical Center	17	74	NR	NR	1.5 or 3.0/ either T2* or SWI/NR	18/NR/NR	8.5
Donaghy[126]	2020	UK	West	Probable AD (NINCDS-ADRDA)	Secondary care services in the North of England	18	75.8 (7.1)	11.1	61.1	3/SWI/3	44/0/6	4
Ikeda[148]	2021	Japan	East Asia	Probable AD (NINCDS-ADRDA)	Gunma University Hospital, Geriatrics Research Institute and Hospital, Maebashi Red Cross Hospital	85	69.8 (8.4)	57.6	21.2	1.5 or 3/T2*/5 or 5.5	31/NR/NR	11.5
Inoue[149]	2016	Japan	East Asia	AD (NINCDS-ADRDA)	Kumamoto University Hospital	162	75 (9)	65.4	41.4	3/combined T2* and SWI/2	25/3/19	1
Kuroda[150]	2020	Japan	East Asia	Probable AD (NINCDS-ADRDA)	Showa University School of Medicine, Japan	40	78.9 (7.9)	55.0	NR	1.5/T2*/6	50/NR/NR	4.5
Mendes[151]	2020	Switzerland	West	Probable/Possible AD (NINCDS-ADRDA)	Geneva University Hospitals	114	82	67.5	57.0	3/T2*/NR	9/NR/NR	2.5
Nagasawa[152]	2014	Japan	East Asia	AD (NINCDS-ADRDA)	Toho University Hospital	559	78.4 (7.7)	57.4	36.0	1.5/T2*/5	13/11/0	0
Nakata-Kudo[134]	2006	Japan	East Asia	32 Probable AD, 10 Possible AD (NINCDS-ARDRA). 42 AD patients without CVD and 8 with CVD	Kyoto University Hospital	50	74.5	66.0	48.0	1.5/T2*/5	16/0/0	1
Noguchi-Shinohara[153]	2017	Japan	East Asia	Probable AD (NINCDS-ADRDA)	Kanazawa University Hospital	88	68 (8.3)	42.0	38.6	1.5/T2*/6	17/18/3	2.5
Shams[154]	2016	Sweden	West	AD (ICD-10 classification)	KIDS	423	68 (8)	45.2	35.7	1.5/NR/NR	16/4/NR	3
Sparacia[155]	2017	Italy	West	Probable AD (NINCDS-ADRDA)	University Hospital Palermo	54	76.8 (5.2)	63.0	NR	1.5/SWI/1.2	70/24/6	1
van der Vlies[156]	2012	Netherlands	West	Probable AD (NINCDS-ADRDA)	VUMC memory clinic	221	68 (9)	49.3	30.8	NR/T2*/5	10/3/5	3

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Supplementary Table 8. Continued

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	MRI parameters (field strength [T]/sequence/ slice thickness)	Prevalence MBs strictly lobar/strictly deep/mixed (%)	QA
Zhang[157]	2016	China	East Asia	Probable AD (NINCDS-ADRDA)	Weihai Municipal Hospital, China	146	72.1 (7.4)	56.8	26.7	3/SWI/1.2	20/4/8	0

Prevalence of microbleeds shows the prevalence of (1) strictly lobar microbleeds, (2) strictly deep microbleeds, and (3) mixed microbleeds.
ACRSF, Alzheimer's Center Reina Sofia Foundation-CIEN Foundation; ADC, Amsterdam Dementia Cohort; ADNI-2, Alzheimer's Disease Neuroimaging Initiative-2; ADNI-GO, Alzheimer's Disease Neuroimaging Initiative-GO; CMBs, cerebral microbleeds; KIDS, Karolinska Imaging Dementia Study; MGH, Massachusetts General Hospital; VUMC, Vrije Universiteit Medisch Centrum, Amsterdam, the Netherlands; AD, Alzheimer's disease; CAA, cerebral amyloid angiopathy; CDR, clinical dementia rating; CMBs, cerebral microbleeds; CVD, cerebrovascular disease; ICD-10, International Statistical Classification of Diseases and Related Health Problems-10; MBs, microbleeds; MRI, magnetic resonance imaging; NR, not reported; NINCDS-ARDRA, neurological and communicative disorders and stroke Alzheimer disease and related disorders association; QA, total score of quality assessment; SWI, susceptibility-weighted imaging; USA, United States of America.

Supplementary Table 9. Overview of the study characteristics and reported prevalence of strictly lobar microbleeds in patients with intracerebral hemorrhage

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	MRI parameters (field strength [T]/sequence/ slice thickness)	Prevalence MBs strictly lobar/strictly deep/mixed (%)	QA
Biffi[158]	2016	USA	West	Spontaneous ICH	MGH ICH LS	522	NR	NR	NR	NR/NR/NR	26/25/10	2.5
Fazekas[92]	1999	Austria	West	Fatal ICH	University Hospital Graz	11	72	45.5	63.6	1.5/T2*/5	18/9/36	1
Ghelmez[159]	2013	Romania	West	ICH, not further specified	NINND, Bucharest	24	NR	NR	NR	NR/combined T2* and SWI/ NR	17/13/21	10.5
Haussen[160]	2012	USA	West	Spontaneous ICH	BIDMC, Boston	163	68.4 (15.2)	40.5	66.3	NR/T2*/NR	24/13/15	0
Jolink[161]	2020	The Netherlands	West	Spontaneous ICH	FETCH	31	60 (12)	29.0	61.3	7/T2*/0.35	16/NR/NR	5
Laible[162]	2015	Germany	West	Spontaneous ICH	University Hospital Heidelberg	97	65.9 (13.9)	44.3	76.3	3/SWI/NR	19/9/30	3
Marti-Fabregas[163]	2013	Spain	West	Spontaneous supratentorial ICH	6 University hospitals in Spain	44	68.9 (11.1)	29.5	63.6	NR/T2*/NR	39/32/30	4
Schwarz[164]	2022	UK	West	Spontaneous non-cerebellar ICH	CROMIS-2 ICH	153	69	38.6	56.2	NR/either T2* or SWI/NR	30/NR/NR	6
Tsai[165]	2017	Taiwan	East Asia	Spontaneous ICH	National Taiwan University Hospital	57	65.7 (13.4)	43.9	NR	3/SWI/1.6	14/19/49	0
Wang[166]	2019	China	East Asia	Spontaneous ICH	Beijing Tiantan Hospital	306	56 (13.3)	28.4	73.2	3/SWI/1.6	4/21/NR	0
Xu[167]	2019	China	East Asia	Spontaneous ICH (first-ever [139] or recurrent [45])	West China Hospital	184	61 (12.5)	24.5	66.3	3/SWI/NR	15/24/34	2.5

Prevalence of microbleeds shows the prevalence of (1) strictly lobar microbleeds, (2) strictly deep microbleeds, and (3) mixed microbleeds.
ATACH-2, Antihypertensive Treatment of Acute Cerebral Haemorrhage 2; BIDMC, Beth Israel Deaconess Medical Center; CMBs, cerebral microbleeds; DECIPHER, DiffErenCes in the Imaging of Primary Haemorrhage based on Ethnicity or Race; MGH ICH LS, Massachusetts General Hospital Intracerebral Haemorrhage Longitudinal Study; NINND, National Institute of Neurology and Neurovascular Diseases; BOMBS, Brain Observer MicroBleed Scale; ICH, intracerebral hemorrhage; MBs, microbleeds; MRI, magnetic resonance imaging; NR, not reported; QA, total score of quality assessment; SWI, susceptibility-weighted imaging; SBP, Systolic Blood Pressure; T, tesla; USA, United States of America.

Supplementary Table 10. Overview of the study characteristics and reported prevalence of strictly lobar microbleeds in patients with lobar intracerebral hemorrhage

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	MRI parameters (field strength [T]/ sequence/ slice thickness (mm)	Prevalence MBs strictly lobar/ strictly deep/ mixed (%)	QA
Schwarz[168]	2022	UK	West	Spontaneous LICH	CROMIS-2 (ICH) and SIGNaL register	140	72.5	57.9	58.6	NR/either T2* or SWI/NR	27/NR/NR	4.5

Prevalence of microbleeds shows the prevalence of (1) strictly lobar microbleeds, (2) strictly deep microbleeds, and (3) mixed microbleeds.
CROMIS-2, Clinical Relevance of Microbleeds In Stroke; SIGnaL, Stroke InvestiGation in North and Central London; ICH, intracerebral hemorrhage; MBs, microbleeds; MRI, magnetic resonance imaging; NR, not reported; QA, total score of quality assessment; SWI, susceptibility-weighted imaging; T, tesla.

Supplementary Table 11. Overview of the study characteristics and reported prevalence of cortical superficial siderosis in the general population

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	MRI parameters (field strength [T]/sequence/ slice thickness [mm])	Prevalence any cSS/ fcSS/dcSS (%)	QA
Pichler[169]	2017	USA	West	Population aged 50–89	Mayo Clinic study of Aging	1,412	68*	47.2	NR	3/T2*/3.3	0.9 (0.5/0.4)	0
Shaomanesh[170]	2021	The Netherlands and USA	West	Framingham: Population, Rotterdam: dementia at baseline excluded	Framingham Original and Offspring Cohort and Rotterdam Study	6,049	68.9	54.7	64.8	1.5/T2*/ Framingham: 5; Rotterdam 0.8	0.4	2.5

Prevalence of cSS shows the prevalence of cSS (irrespective of type), and, if reported, the prevalence of focal cSS and disseminated cSS.
cSS, cortical superficial siderosis; dcSS, disseminated cortical superficial siderosis; fcSS, focal cortical superficial siderosis; MRI, magnetic resonance imaging; NR, not reported; QA, total score of quality assessment; SD, standard deviation; SWI, susceptibility-weighted imaging; T, tesla; USA, united states of America.
*Median age and/or age range are reported instead of mean age (SD).

Supplementary Table 12. Overview of the study characteristics and reported prevalence of cortical superficial siderosis in cognitively normal elderly

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	MRI parameters (field strength [T]/ sequence/slice thickness [mm])	Prevalence any cSS/ fcSS/dcSS (%)	QA
Chang[124]	2021	China	East Asia	No cognitive or subjective impairment, MMSE ≥28	Chinese PLA General Hospital	15	78	26.7	66.7	NR/SWI/1.2	0 (0/0)	5
Cheng[171]	2020	China	East Asia	Healthy controls (sex- and age-matched)	Shanghai Aging Study	95	69 (8.3)	33.7	40.0	3/SWI/2	2.1	4.5
Wollenweber[139]	2017	Austria	West	Stroke/ dementia-free, normal neurologic examination	ASPFS	372	65 (10.7)	43.3	63.2	3/T2*/4	0.5	3
Yilmaz[141]	2019	The Netherlands	West	Stroke- and dementia-free population	Rotterdam Study	1,622	73.1 (7.6)	54.3	78.7	1.5/T2*/0.8	0.6	0

Prevalence of cSS shows the prevalence of cSS (irrespective of type), and, if reported, the prevalence of focal cSS and disseminated cSS.
ASPFS, Austrian Stroke Prevention Family Study; PLA, People's Liberation Army; cSS, cortical superficial siderosis; dcSS, disseminated cortical superficial siderosis; fcSS, focal cortical superficial siderosis; MRI, magnetic resonance imaging; NR, not reported; QA, total score of quality assessment; ST, slice thickness; SWI, susceptibility-weighted imaging; T, tesla.

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Supplementary Table 13. Overview of the study characteristics and reported prevalence of cortical superficial siderosis in patients with AD

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	MRI parameters (field strength [T]/sequence/ slice thickness [mm])	Prevalence any cSS/ fcSS/dcSS (%)	QA
Carmona-Iragui[172]	2017	Spain	West	Probable dementia in EOAD (d-EOAD)	Barcelona SPIN cohort	23	61.8*	60.9	13.0	NR/NR/NR	8.7	9.5
Chang[124]	2021	China	East Asia	Probable AD (NINCDS-ADRDA)	Chinese PLA General Hospital	15	76	40.0	60.0	NR/SWI/1.2	6.7 (6.7/0)	5
Charidimou[145]	2016	USA	West	Clinically diagnosed AD	MGH	86	NR	NR	NR	3/NR/5	5.8	3
De Kort[147]	2021	The Netherlands	West	Probable AD (NINCDS-ADRDA)	Radboud University Medical Center	17	74	NR	NR	1.5 or 3.0/ either T2* or SWI/NR	0 (0/0)	8.5
Inoue[149]	2016	Japan	East Asia	AD (NINCDS-ADRDA)	Kumamoto University Hospital	162	75 (9)	65.4	67.0	3/combined T2* and SWI/2	4.9	1
Kuroda[150]	2020	Japan	East Asia	Probable AD (NINCDS-ADRDA)	Showa University School of Medicine, Japan	40	78.9 (7.9)	55.0	NR	1.5/T2*/6	0	4.5
Mendes[151]	2020	Switzerland	West	Probable/Possible AD (NINCDS-ADRDA)	Geneva University Hospitals	114	82	67.5	57.0	3/T2*/NR	5.3	2.5
Na[173]	2015	South Korea	East Asia	Probable AD (NINCDS-ADRDA)	Samsung Medical Center	62	NR	NR	NR	3/T2*/5	4.8 (1.6/3.2)	2
Shams[154]	2016	Sweden	West	AD (ICD-10 classification)	KIDS	423	68 (8)	45.2	35.7	1.5/NR/NR	5 (4.3/0.7)	3
Tsai[174]	2021	Taiwan	East Asia	Probable AD (NINCDS-ADRDA)	National Taiwan University Hospital (NTUH) and NTUH Bei-Hu Branch	10	75.6 (8.1)	70.0	90.0	3/SWI/2	0	4
Umino[175]	2021	Japan	East Asia	Probable AD (NINCDS-ADRDA)	Mie University School of Medicine	124	NR	NR	NR	3/SWI/0.5	8.9	4.5
Zonneveld[176]	2014	The Netherlands	West	Probable AD (NINCDS-ADRDA)	Amsterdam Dementia Cohort	249	68 (9)	52.6	NR	3/SWI/3	4.8 (3.6/1.2)	0

Prevalence of cSS shows the prevalence of cSS (irrespective of type), and, if reported, the prevalence of focal cSS and disseminated cSS.
Biomarkers and Lifestyle Study of Ageing; KIDS, Karolinska Imaging Dementia Study; MGH, Massachusetts General Hospital; SPIN, Barcelona Memory Unit of Hospital de Sant Pau from the Sant Pau Initiative on Neurodegeneration; PLA, people's liberation army; AD, Alzheimer's disease; cSS, cortical superficial siderosis; dcSS, disseminated cortical superficial siderosis; EOAD, Early onset Alzheimer's disease; fcSS, focal cortical superficial siderosis; ICD-10, International Statistical Classification of Diseases and Related Health Problems-10; MRI, magnetic resonance imaging; NINCDS-ADRDA, National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders; NR, not reported; QA, total score of quality assessment; SD, standard deviation; SWI, Susceptibility-weighted imaging; T, tesla; USA, United States of America.
*Median age and/or age range are reported instead of mean age (SD).

Supplementary Table 14. Overview of the study characteristics and reported prevalence of cortical superficial siderosis in patients with intracerebral hemorrhage

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	MRI parameters (field strength [T]/sequence/ slice thickness [mm])	Prevalence any cSS/fcSS/ dcSS (%)	QA
Castello[177]	2022	USA	West	Spontaneous ICH	MGH	612	70.5 (13)	47.1	74.8	1.5 or 3/ either T2* or SWI/5 for T2*; SWI was NR	13.7 (9/4.7)	5
Damien[178]	2021	Belgium	West	Spontaneous ICH	Brussels Erasme-ULB Hospital	30	66.7 (15.8)	40.0	NR	NR/T2*/NR	26.7	9
Jolink[161]	2020	The Netherlands	West	Spontaneous ICH	FETCH	31	60 (12)	29.0	61.3	7/T2*/0.35	9.7	5
Moulin[179]	2018	France	West	Spontaneous ICH	PITCH	258	68 (54–80)*	41.9	64.0	1.5/T2*/5	19 (11.2/7.8)	1
Pinho[180]	2021	Portugal	West	Non-traumatic ICH	Hospital de Braga	104	64.8 (13.5)	40.4	73.1	1.5/T2*/NR	30.8 (13.5/17.3)	4.5
Schwarz[164]	2022	UK	West	Spontaneous non-cerebellar ICH	CROMIS-2 ICH	153	69	38.6	56.2	NR/either T2* or SWI/NR	7.8 (5.2/2.6)	6
Suda[181]	2017	Japan	East Asia	ICH	Nippon Medical School	150	NR	NR	NR	1.5/T2*/5	4.7	1
Tsai[182]	2021	Taiwan	East Asia	Spontaneous ICH	National Taiwan University Hospital	300	63.4	35.3	89.3	1.5 or 3/ SWI/2	6	4.5
Xu[167]	2019	China	East Asia	ICH patients (first-ever [139] or recurrent [45])	West China Hospital	184	61 (12.5)	24.5	66.3	3/SWI/NR	23.9 (13/10.9)	2.5
Ye[183]	2021	China	East Asia	Spontaneous ICH	Tongji Hospital	135	56	NR	NR	3/SWI/NR	10.4 (6.7/3.7)	4.5

Prevalence of cSS shows the prevalence of cSS (irrespective of type), and, if reported, the prevalence of focal cSS and disseminated cSS.
CROMIS-2-I ICH, The Clinical Relevance of Microbleeds in Stroke study-2-Intracerebral Haemorrhage; FETCH, inding the Etiology in Spontaneous Cerebral Hemorrhage; MGH, Massachusetts General Hospital; PITCH, Prognosis of IntraCerebral Haemorrhage; cSS, cortical superficial siderosis; dcSS, disseminated cortical superficial siderosis; fcSS, focal cortical superficial siderosis; ICH, intracerebral hemorrhage; MRI, magnetic resonance imaging; QA, total score of quality assessment; SD, standard deviation; SWI, Susceptibility-weighted imaging; UK, United Kingdom; USA, United States of America.
*Median age and/or age range are reported instead of mean age (SD).

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Supplementary Table 15. Overview of the study characteristics and reported prevalence of cortical superficial siderosis in patients with lobar intracerebral hemorrhage

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	MRI parameters (field strength [T]/ sequence/slice thickness [mm])	Prevalence any cSS/fcSS/dcSS (%)	QA
Boulouis[184]	2016	USA	West	Spontaneous LICH	MGH	254	75 (11)	55.1	67.7	1.5/T2*/5	28.3	4
Renard[185]	2020	France	West	Spontaneous LICH	Nîmes University Hospital	68	74	48.5	NR	56×1.5 T and 12×3.0 T/T2*/NR	48.5 (8.8/39.7)	7.5
Schwarz[168]	2022	UK	West	Spontaneous LICH	CROMIS-2 (ICH) and SIGNaL register	140	72.5	57.9	58.6	NR/either T2* or SWI/ NR	22.1 (12.1/10)	4.5
Viguier[187]	2019	France	West	Spontaneous LICH	Toulouse Hospital	165	70.5 (13.9)	46.1	49.7	1.5/T2*/5	30.3	4

Prevalence of cSS shows the prevalence of cSS (irrespective of type), and, if reported, the prevalence of focal cSS and disseminated cSS.
CROMIS-2, Clinical Relevance of Microbleeds In Stroke; SIGnaL, Stroke InvestiGation in North and Central London; cSS, cortical superficial siderosis; dcSS, disseminated cortical superficial siderosis; fcSS, focal cortical superficial siderosis; ICH, intracerebral hemorrhage; LICH, lobar intracerebral hemorrhage; MRI, magnetic resonance imaging; NR, not reported; QA, total score of quality assessment; SD, standard deviation; SWI, Susceptibility-weighted imaging; UK, United Kingdom; USA, United States of America.

Supplementary Table 16. Overview of the study characteristics and reported prevalence of CAA according to the Boston criteria in cognitively normal elderly

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	MRI parameters (field strength [T]/ sequence/ slice thickness [mm])	Prevalence CAA (probable/ possible) (%)	QA
Atri[121]	2005	USA	West	Retired nurses, no stroke or dementia	CANHSMR	23	78	100.0	52.2	1.5/T2*/5	0/1	5.5
van Rooden[188]	2014	The Netherlands	West	MMSE>25, GDS≤4, no stroke or cognitive impairment, recruited	LUMC	18	69.7	33.0	NR	7/T2*/3	3/2	1.5

Prevalence of CAA according to Boston criteria shows the prevalence of probable and possible CAA.
CANHSMR, Cognitive Assessment in Nurses Health Study Massachusetts Residents; LUMC, Leiden University Medical Center; CAA, cerebral amyloid angiopathy; CROMIS-2, Clinical Relevance of Microbleeds In Stroke; ICH, intracerebral hemorrhage; MRI, magnetic resonance imaging; NR, not reported; SD, standard deviation; SWI, Susceptibility-weighted imaging; T, tesla; QA, quality assessment score; USA, United States of America.

Supplementary Table 17. Overview of the study characteristics and reported prevalence of CAA according to the Boston criteria in patients with AD

Author	Year	Country	Area	Definition domain	Study cohort	n	Age: mean (SD) or median (range)*	Female (%)	MRI parameters (field strength [T]/sequence/ slice thickness [mm])	Prevalence CAA (probable/ possible)	QA
van Rooden[188]	2014	The Netherlands	West	Probable AD (NINCDS-ARDRA criteria)	3 Memory clinics in the Netherlands	14	66	29	7/T2*/3	2/2	3

Prevalence of CAA according to Boston criteria shows the prevalence of probable and possible CAA.
AD, Alzheimer's Disease; MRI, magnetic resonance imaging; NINCDS-ARDRA, neurological and communicative disorders and stroke Alzheimer disease and related disorders association; SD, standard deviation; QA, quality assessment score.

Supplementary Table 18. Overview of the study characteristics and reported prevalence of CAA according to the Boston criteria in patients with intracerebral hemorrhage

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	MRI parameters (field strength [T]/sequence/ slice thickness [mm])	Prevalence CAA (probable/ possible)	QA
Charidimou[189]	2013	UK; Belgium	West	Spontaneous ICH	4 Stroke centers in UK and Belgium	121	69.4	43.0	71.1	1.5/T2*/5	53/23	3
Jolink[161]	2020	The Netherlands	West	Spontaneous ICH	FETCH	31	60 (12)	29.0	61.3	7/T2*/0.35	5/NR	6
Martí-Fàbregas[190]	2016	Spain	West	ICH	5 Hospitals in Spain	439	70.8 (14.5)	38.7	75.2	NR/T2*/NR	45/89	5
Pasi[191]	2019	USA	West	Spontaneous supratentorial ICH	MGH 2003–2012	307	70.2 (12.6)	56.7	77.5	1.5/either T2* or SWI/1.8 (SWI) or 3 (SWAN)	87/NR	6
Pasi[192]	2018	USA	West	Spontaneous non-cerebellar ICH	MGH 2010–2017	482	NR	NR	NR	1.5/T2* or SWI/5	191/91	4
Pinho[180]	2021	Portugal	West	Non-traumatic ICH	Hospital de Braga	104	64.8 (13.5)	40.4	73.1	1.5/T2*/NR	41/7	8.5
Schwarz[164]	2022	UK	West	Spontaneous non-cerebellar ICH	CROMIS-2 ICH	153	69	38.6	56.2	NR/either T2* or SWI/NR	23/43	1.5
Segal[193]	1999	USA	West	Spontaneous ICH	MGH 1995–1997	45	76.1 (8.9)	48.9	53.3	NR/T2*/NR	15/NR	1.5
Tsai[194]	2018	Taiwan	East Asia	Spontaneous ICH	National Taiwan University Hospital	214	NR	NR	NR	3/SWI/1.6	15/9	7.5
Xu[167]	2019	China	East Asia	Spontaneous ICH (139 first-ever, 45 recurrent)	West China Hospital	184	61 (12.5)	24.5	66.3	3/SWI/NR	26/NR	4.5
Yakushiji[186]	2020	Japan	East Asia	Spontaneous ICH	Saga University Faculty of Medicine	126	71 (60-78)*	47	93	3/SWI/3	10/NR	0

Prevalence of CAA according to Boston criteria shows the prevalence of probable and possible CAA.
FETCH, Finding the Etiology in Spontaneous Cerebral Hemorrhage; MGH, Massachusetts General Hospital; CAA, cerebral amyloid angiopathy; CROMIS-2, Clinical Relevance of Microbleeds In Stroke; ICH, intracerebral hemorrhage; MRI, magnetic resonance imaging; NR, not reported; SBP, Systolic Blood pressure; SD, standard deviation; SWI, Susceptibility-weighted imaging; T, tesla; UK, United Kingdom; USA, United States of America; QA, quality assessment score.
*Median age and interquartile range were reported instead of mean age (SD).

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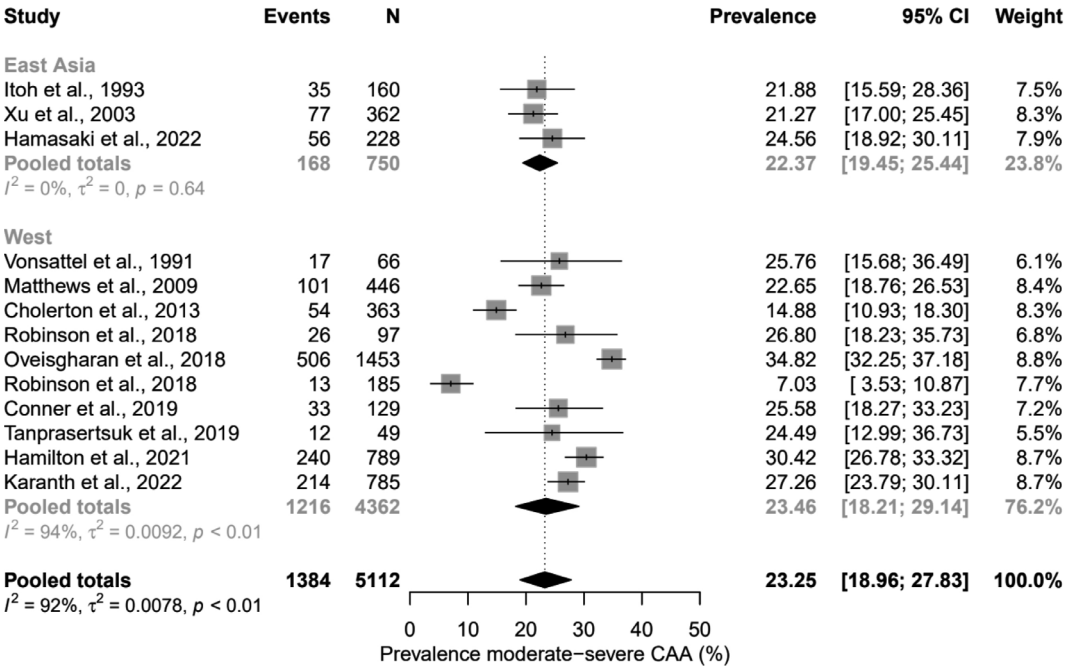
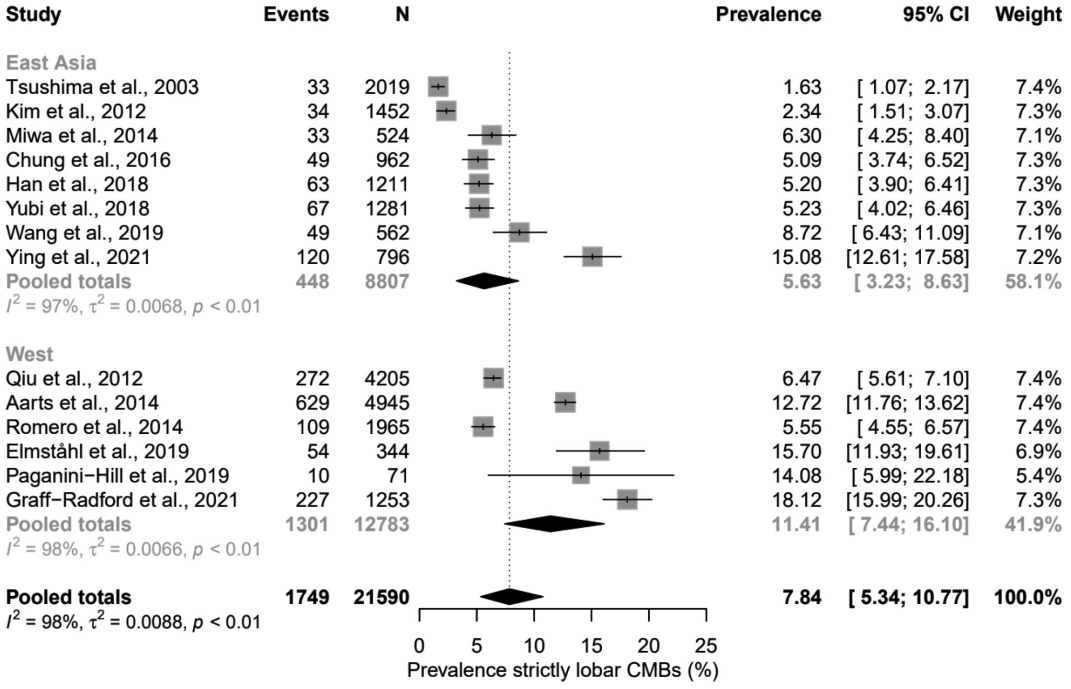
Supplementary Table 19. Overview of the study characteristics and reported prevalence of CAA according to the Boston criteria in patients with lobar intracerebral hemorrhage

Author	Year	Country	Area	Definition domain	Study acronym/ name of cohort	n	Age: mean (SD) or median (range)	Female (%)	Hypertension (%)	MRI parameters (field strength [T]/sequence/ slice thickness [mm])	Prevalence CAA (probable/ possible)	QA
Charidimou[189]	2013	UK; Belgium	West	Strictly lobar ICH	4 Stroke centers in UK and Belgium	76	71.1	46.1	64.5	1.5/T2*/5	53/23	6
Greenberg[195]	1996	USA	West	Spontaneous LICH	4 Hospitals in USA	45	75.3	51.1	64.4	1.5/T2*/NR	27/12	6.5
Jamieson[196]	2012	UK	West	Spontaneous LICH	European Basic Stroke Register	53	77 (8)	49.1	56.6	NR/NR/NR	6/47	2.5
Renard[185]	2020	France	West	Spontaneous LICH	Nîmes University Hospital	68	74	48.5	NR	1.5 T (n=56) and 3.0 T (n=13)/T2*/ NR	51/NR	2
Schwarz[168]	2022	UK	West	Spontaneous LICH	CROMIS-2 (ICH) and SIGNaL register	140	72.5	57.9	58.6	NR/either T2* or SWI/NR	54/NR	4.5
Viguier[187]	2019	France	West	Spontaneous LICH	University Hospital Toulouse	165	70.5 (13.9)	46.1	49.7	1.5/T2*/5	72/NR	3

Prevalence of CAA according to Boston criteria shows the prevalence of probable and possible CAA.
CAA, cerebral amyloid angiopathy; CROMIS-2, Clinical Relevance of Microbleeds In Stroke; SIGnaL, Stroke InvestiGation in North and Central London; LICH, lobar intracerebral hemorrhage; MRI, magnetic resonance imaging; NR, not reported; SD, standard deviation; ST, slice thickness; UK, United Kingdom; USA, United States of America.



Supplementary Figure 1. Forest plots showing the prevalence of moderate-to-severe CAA pathology in the East-Asian and Western general populations. CAA, cerebral amyloid angiopathy; CI, confidence interval.



Supplementary Figure 2. Forest plots showing the prevalence of strictly lobar CMBs in the East-Asian and Western general populations. CMBs, cerebral microbleeds; CI, confidence interval.

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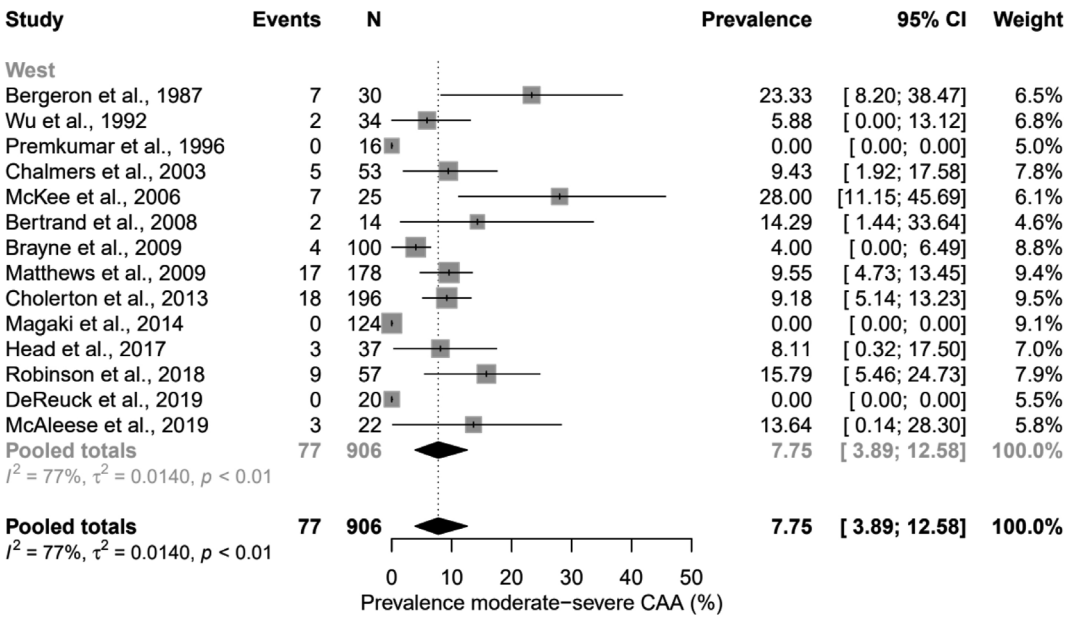
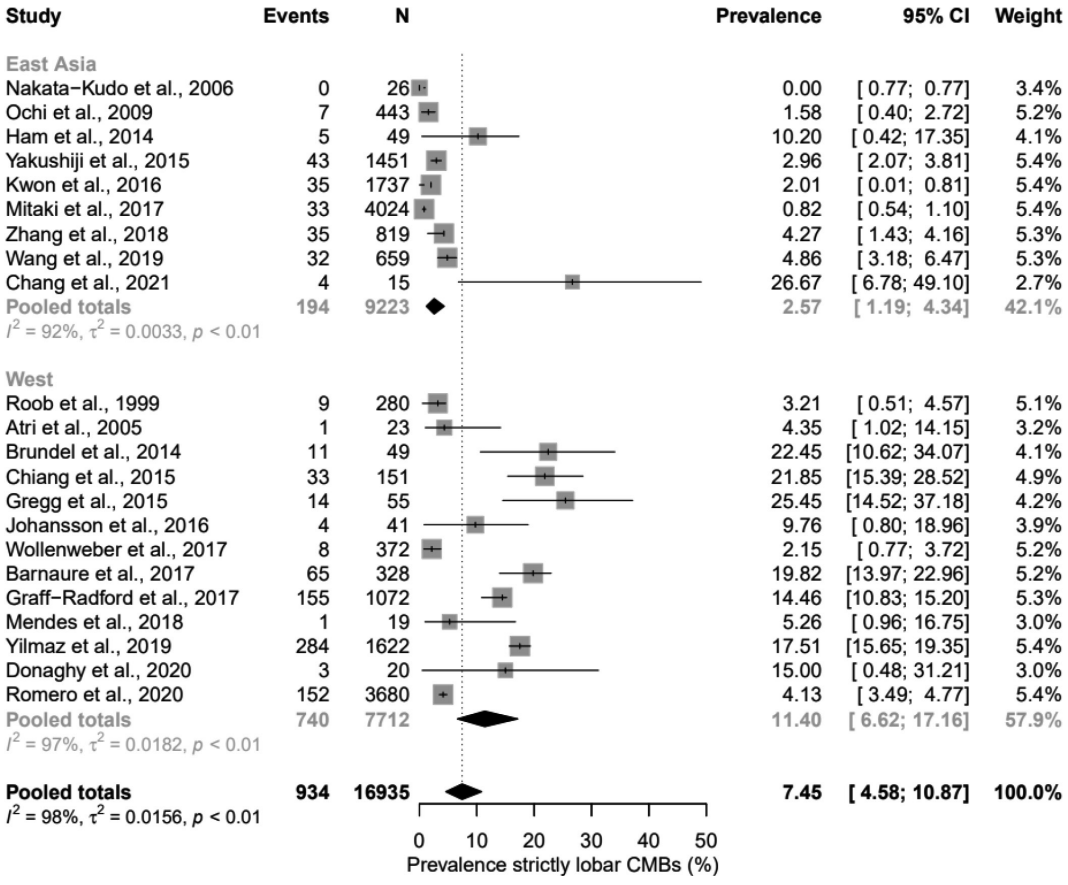
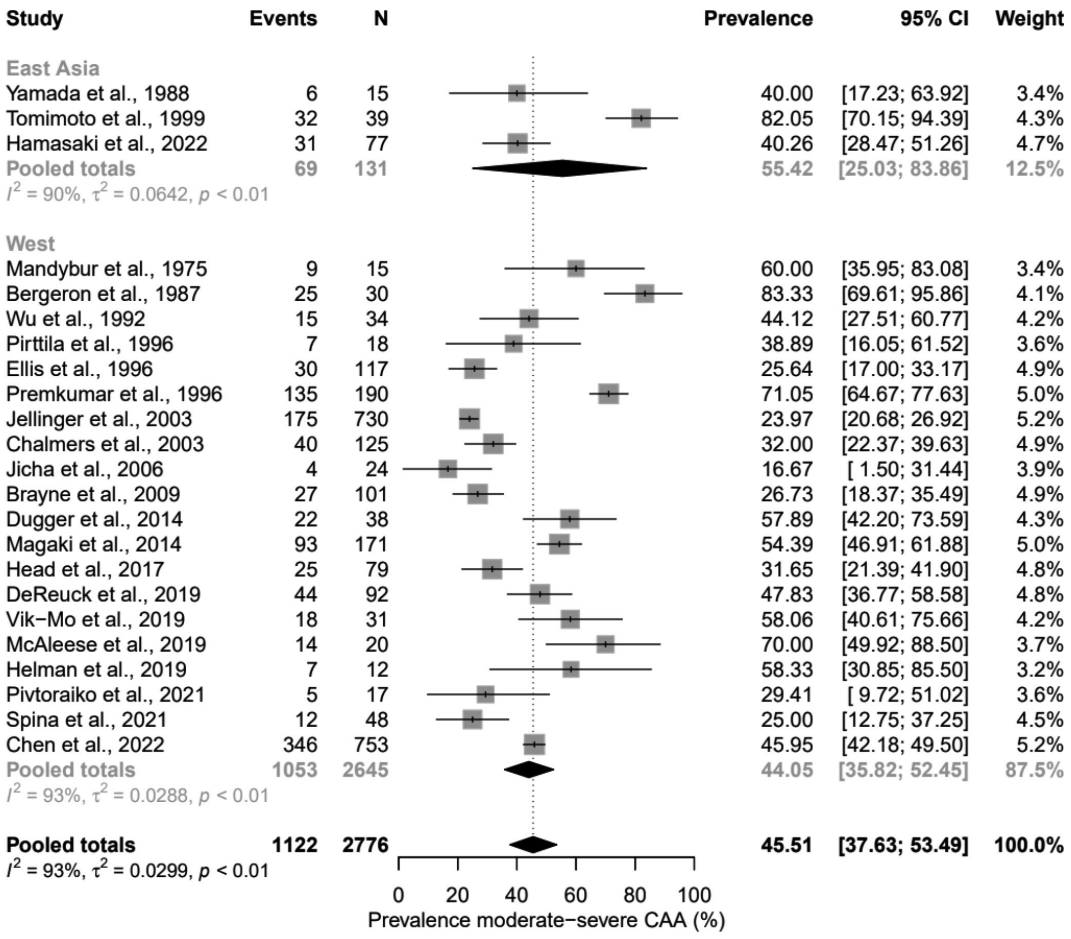


Supplementary Figure 3. Forest plots showing the prevalence of moderate-to-severe CAA pathology in Western cognitively normal elderly. No studies were included that reported on the prevalence of moderate-to-severe CAA pathology in East Asian cognitively normal elderly. CAA, cerebral amyloid angiopathy; CI, confidence interval.



Supplementary Figure 4. Forest plots showing the prevalence of strictly lobar CMBs in East-Asian and Western cognitively normal elderly. CMBs, cerebral microbleeds; CI, confidence interval.



Supplementary Figure 5. Forest plots showing the prevalence of moderate-to-severe CAA pathology in East-Asian and Western patients with Alzheimer's disease. CAA, cerebral amyloid angiopathy; CI, confidence interval.

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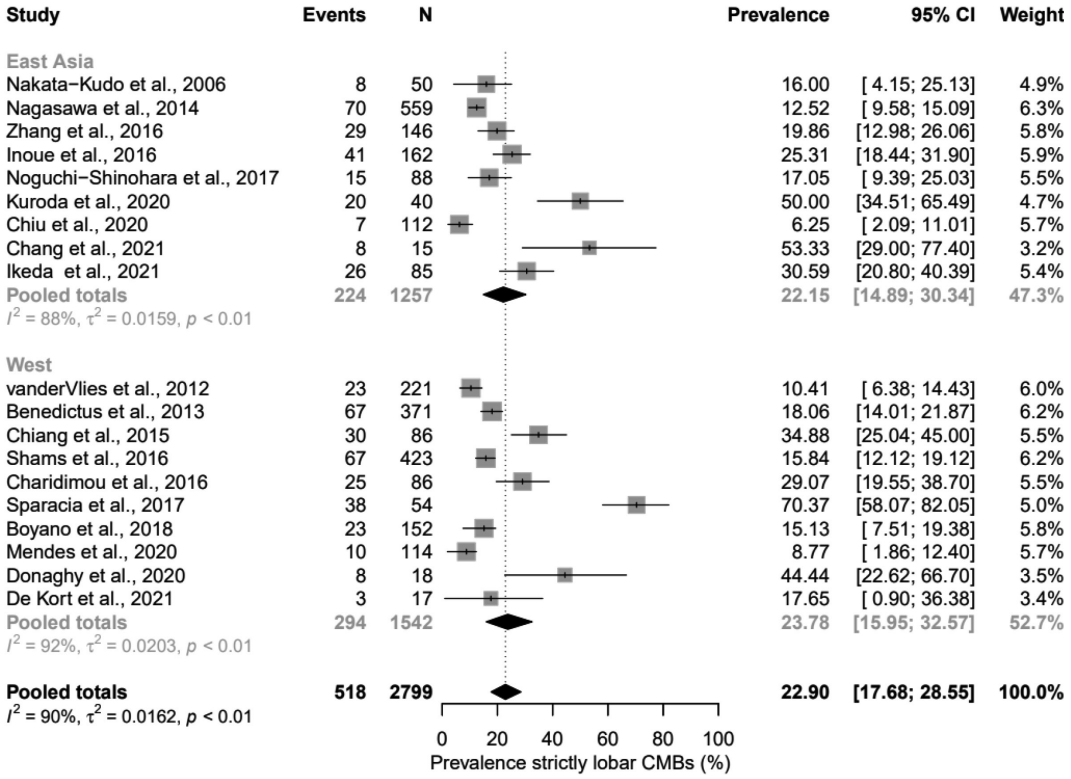
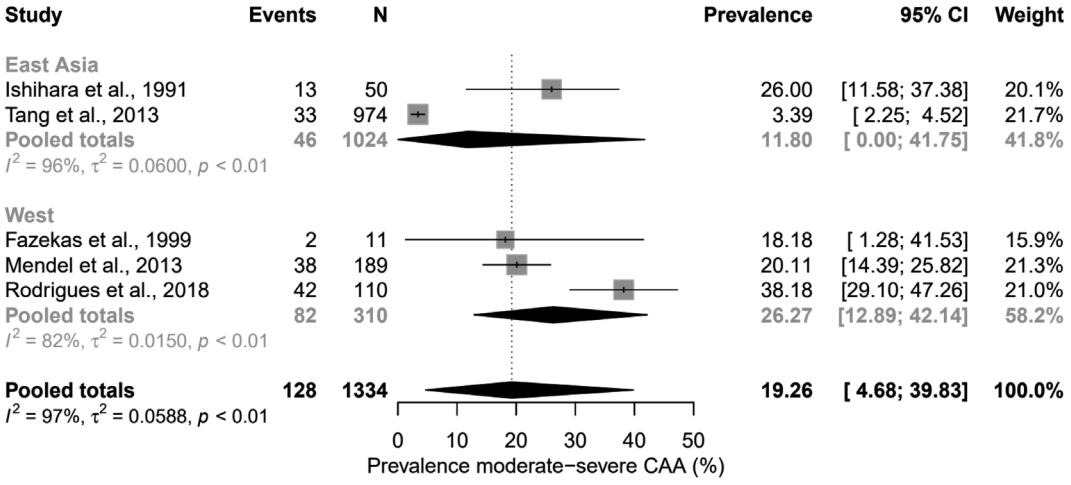
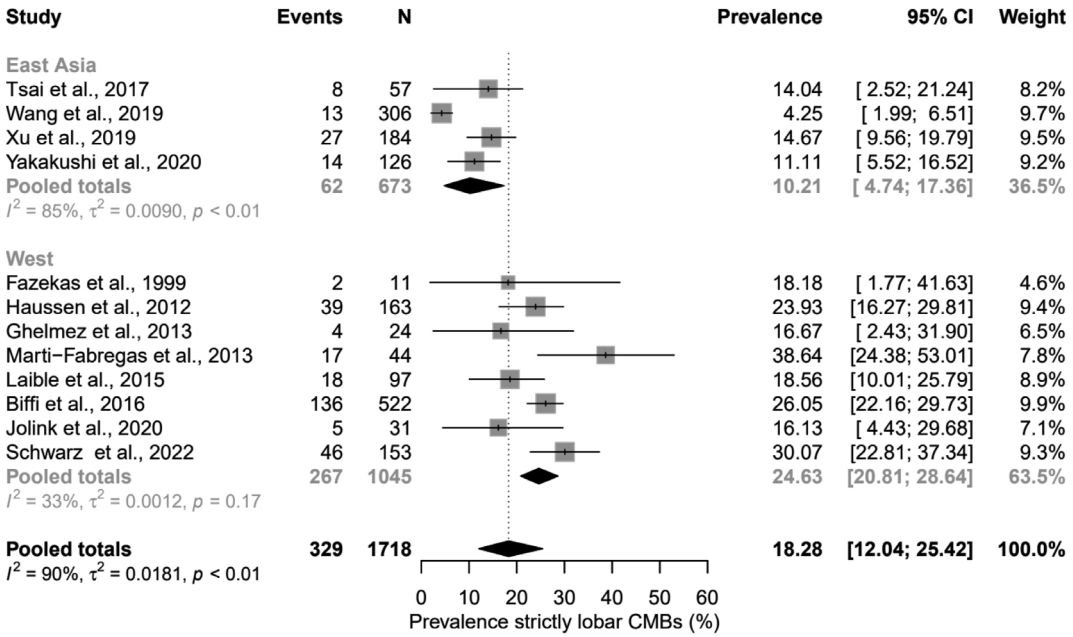


Supplementary Figure 6. Forest plots showing the prevalence of strictly lobar CMBs in East-Asian and Western patients with Alzheimer's disease. CMBs, cerebral microbleeds; CI, confidence interval.



Supplementary Figure 7. Forest plots showing the prevalence of moderate-to-severe CAA pathology in East-Asian and Western patients with ICH. CAA, cerebral amyloid angiopathy; ICH, intracerebral hemorrhage; CI, confidence interval.



Supplementary Figure 8. Forest plots showing the prevalence of strictly lobar CMBs in East-Asian and Western patients with ICH. CMBs, cerebral microbleeds; ICH, intracerebral hemorrhage; CI, confidence interval.

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Supplementary References

1. Alafuzoff I, Libard S. Mixed brain pathology is the most common cause of cognitive impairment in the elderly. *J Alzheimers Dis* 2020;78:453-465.
2. Alafuzoff I, Aho L, Helisalmi S, Mannermaa A, Soininen H. β-amyloid deposition in brains of subjects with diabetes. *Neuropathol Appl Neurobiol* 2009;35:60-68.
3. Attems J, Lauda F, Jellinger KA. Unexpectedly low prevalence of intracerebral hemorrhages in sporadic cerebral amyloid angiopathy: an autopsy study. *J Neurol* 2008;255:70-76.
4. Cholerton B, Larson EB, Baker LD, Craft S, Crane PK, Millard SP, et al. Neuropathologic correlates of cognition in a population-based sample. *J Alzheimers Dis* 2013;36:699-709.
5. Conner SC, Pase MP, Carneiro H, Raman MR, McKee AC, Alvarez VE, et al. Mid-life and late-life vascular risk factor burden and neuropathology in old age. *Ann Clin Transl Neurol* 2019;6:2403-2412.
6. Erten-Lyons D, Dodge HH, Woltjer R, Silbert LC, Howieson DB, Kramer P, et al. Neuropathologic basis of age-associated brain atrophy. *JAMA Neurol* 2013;70:616-622.
7. Hamasaki H, Shijo M, Nakamura A, Honda H, Yamada Y, Oda Y, et al. Concurrent cardiac transthyretin and brain β amyloid accumulation among the older adults: the Hisayama study. *Brain Pathol* 2022;32:e13014.
8. Hamilton CA, Matthews FE, Erskine D, Attems J, Thomas AJ. Neurodegenerative brain changes are associated with area deprivation in the United Kingdom: findings from the brains for dementia research study. *Acta Neuropathol Commun* 2021;9:198.
9. Itoh Y, Yamada M, Hayakawa M, Otomo E, Miyatake T. Subpial βA4 peptide deposits are closely associated with amyloid angiopathy in the elderly. *Neurosci Lett* 1993;155:144-147.
10. Karanth SD, Katsumata Y, Nelson PT, Fardo DW, McDowell JK, Schmitt FA, et al. Cancer diagnosis is associated with a lower burden of dementia and less Alzheimer's-type neuropathology. *Brain* 2022;145:2518-2527.
11. Kovacs GG, Milenkovic I, Wöhrer A, Höftberger R, Gelpi E, Haberler C, et al. Non-Alzheimer neurodegenerative pathologies and their combinations are more frequent than commonly believed in the elderly brain: a community-based autopsy series. *Acta Neuropathol* 2013;126:365-384.
12. Kövari E, Herrmann FR, Hof PR, Bouras C. The relationship between cerebral amyloid angiopathy and cortical microinfarcts in brain ageing and Alzheimer's disease. *Neuropathol Appl Neurobiol* 2013;39:498-509.
13. Kövari E, Charidimou A, Herrmann FR, Giannakopoulos P, Bouras C, Gold G. No neuropathological evidence for a direct topographical relation between microbleeds and cerebral amyloid angiopathy. *Acta Neuropathol Commun* 2015;3:49.
14. Masuda J, Tanaka K, Ueda K, Omae T. Autopsy study of incidence and distribution of cerebral amyloid angiopathy in Hisayama, Japan. *Stroke* 1988;19:205-210.
15. Matthews FE, Brayne C, Lowe J, McKeith I, Wharton SB, Ince P. Epidemiological pathology of dementia: attributable-risks at death in the Medical Research Council cognitive function and ageing study. *PLoS Med* 2009;6:e1000180.
16. Moghekar A, Kraut M, Elkins W, Troncoso J, Zonderman AB, Resnick SM, et al. Cerebral white matter disease is associated with Alzheimer pathology in a prospective cohort. *Alzheimers Dement* 2012;8(5 Suppl):S71-S77.
17. Ng TH, Leung SY, Wong MP. Cerebral amyloid angiopathy in Chinese: incidence and significance. *Clin Neurol Neurosurg* 1991;93:19-23.
18. Oveisgharan S, Arvanitakis Z, Yu L, Farfel J, Schneider JA, Bennett DA. Sex differences in Alzheimer's disease and common neuropathologies of aging. *Acta Neuropathol* 2018;136:887-900.
19. Robinson JL, Corrada MM, Kovacs GG, Dominique M, Caswell C, Xie SX, et al. Non-Alzheimer's contributions to dementia and cognitive resilience in the 90+ study. *Acta Neuropathol* 2018;136:377-388.
20. Robinson AC, Davidson YS, Horan MA, Pendleton N, Mann DMA. Pathological correlates of cognitive impairment in the University of Manchester longitudinal study of cognition in normal healthy old age. *J Alzheimers Dis* 2018;64:483-496.
21. Tanprasertsuk J, Johnson EJ, Johnson MA, Poon LW, Nelson PT, Davey A, et al. Clinico-neuropathological findings in the oldest old from the Georgia centenarian study. *J Alzheimers Dis* 2019;70:35-49.
22. Tanskanen M, Mäkelä M, Myllykangas L, Notkola IL, Polvikoski T, Sulkava R, et al. Prevalence and severity of cerebral amyloid angiopathy: a population-based study on very elderly Finns (Vantaa 85+). *Neuropathol Appl Neurobiol* 2012;38:329-336.
23. Vinters HV, Gilbert JJ. Cerebral amyloid angiopathy: incidence and complications in the aging brain. II. The distribution of amyloid vascular changes. *Stroke* 1983;14:924-928.
24. Vonsattel JP, Myers RH, Hedley-Whyte ET, Ropper AH, Bird ED, Richardson EP Jr. Cerebral amyloid angiopathy without and with cerebral hemorrhages: a comparative histological study. *Ann Neurol* 1991;30:637-649.
25. Xu D, Yang C, Wang L. Cerebral amyloid angiopathy in aged Chinese: a clinico-neuropathological study. *Acta Neuropathol* 2003;106:89-91.
26. Alakbarzade V, French JM, Howlett DR, Attems J, Francis PT,

Stratton S, et al. Cerebral amyloid angiopathy distribution in older people: a cautionary note. *Alzheimers Dement (N Y)* 2021;7:e12145.
27. Bergeron C, Ranalli PJ, Miceli PN. Amyloid angiopathy in Alzheimer's disease. *Can J Neurol Sci* 1987;14:564-569.
28. Bertrand E, Lewandowska E, Stepień T, Szpak GM, Pasennik E, Modzelewska J. Amyloid angiopathy in idiopathic Parkinson's disease. Immunohistochemical and ultrastructural study. *Folia Neuropathol* 2008;46:255-270.
29. Brayne C, Richardson K, Matthews FE, Fleming J, Hunter S, Xuereb JH, et al. Neuropathological correlates of dementia in over-80-year-old brain donors from the population-based Cambridge city over-75s cohort (CC75C) study. *J Alzheimers Dis* 2009;18:645-658.
30. Chalmers K, Wilcock GK, Love S. APOEε4 influences the pathological phenotype of Alzheimer's disease by favouring cerebrovascular over parenchymal accumulation of Aβ protein. *Neuropathol Appl Neurobiol* 2003;29:231-238.
31. Cruz-Sánchez FF, Durany N, Thome J, Riederer P, Zambón D. Correlation between Apolipoprotein-E polymorphism and Alzheimer's disease pathology. *J Alzheimers Dis* 2000;2:223-229.
32. Dallaire-Théroux C, Saikali S, Richer M, Potvin O, Duchesne S. Histopathological analysis of cerebrovascular lesions associated with aging. *J Neuropathol Exp Neurol* 2022;81:97-105.
33. Davis DG, Schmitt FA, Wekstein DR, Markesbery WR. Alzheimer neuropathologic alterations in aged cognitively normal subjects. *J Neuropathol Exp Neurol* 1999;58:376-388.
34. De Reuck J, Deramecourt V, Cordonnier C, Leys D, Pasquier F, Maurage CA. Prevalence of cerebrovascular lesions in patients with Lewy body dementia: a neuropathological study. *Clin Neurol Neurosurg* 2013;115:1094-1097.
35. De Reuck J. The impact of cerebral amyloid angiopathy in various neurodegenerative dementia syndromes: a neuropathological study. *Neurol Res Int* 2019;2019:7247325.
36. Dickson DW, Crystal HA, Mattiace LA, Masur DM, Blau AD, Davies P, et al. Identification of normal and pathological aging in prospectively studied nondemented elderly humans. *Neurobiol Aging* 1992;13:179-189.
37. Dugger BN, Adler CH, Shill HA, Caviness J, Jacobson S, Driver-Dunckley E, et al. Concomitant pathologies among a spectrum of parkinsonian disorders. *Parkinsonism Relat Disord* 2014;20:525-529.
38. Esiri M, Chance S, Joachim C, Warden D, Smallwood A, Sloan C, et al. Cerebral amyloid angiopathy, subcortical white matter disease and dementia: literature review and study in OPTIMA. *Brain Pathol* 2015;25:51-62.
39. Esiri MM, Wilcock GK. Cerebral amyloid angiopathy in dementia and old age. *J Neurol Neurosurg Psychiatry* 1986;49:1221-1226.
40. Guidoux C, Hauw JJ, Klein IF, Labreuche J, Berr C, Duyckaerts C, et al. Amyloid angiopathy in brain hemorrhage: a postmortem neuropathological-magnetic resonance imaging study. *Cerebrovasc Dis* 2018;45:124-131.
41. Haglund M, Englund E. Cerebral amyloid angiopathy, white matter lesions and Alzheimer encephalopathy - a histopathological assessment. *Dement Geriatr Cogn Disord* 2002;14:161-166.
42. Head E, Phelan MJ, Doran E, Kim RC, Poon WW, Schmitt FA, et al. Cerebrovascular pathology in Down syndrome and Alzheimer disease. *Acta Neuropathol Commun* 2017;5:93.
43. Honig LS, Kukull W, Mayeux R. Atherosclerosis and AD: analysis of data from the US National Alzheimer's Coordinating Center. *Neurology* 2005;64:494-500.
44. Jellinger KA. Prevalence and impact of cerebrovascular lesions in Alzheimer and Lewy body diseases. *Neurodegener Dis* 2010;7:112-115.
45. Kawas CH, Kim RC, Sonnen JA, Bullain SS, Trieu T, Corrada MM. Multiple pathologies are common and related to dementia in the oldest-old: the 90+ study. *Neurology* 2015;85:535-542.
46. Love S, Nicoll JA, Hughes A, Wilcock GK. APOE and cerebral amyloid angiopathy in the elderly. *Neuroreport* 2003;14:1535-1536.
47. Magaki S, Yong WH, Khanlou N, Tung S, Vinters HV. Comorbidity in dementia: update of an ongoing autopsy study. *J Am Geriatr Soc* 2014;62:1722-1728.
48. Malek-Ahmadi M, Chen K, Perez SE, Mufson EJ. Cerebral amyloid angiopathy and neuritic plaque pathology correlate with cognitive decline in elderly non-demented individuals. *J Alzheimers Dis* 2019;67:411-422.
49. McAleese KE, Graham S, Dey M, Walker L, Erskine D, Johnson M, et al. Extravascular fibrinogen in the white matter of Alzheimer's disease and normal aged brains: implications for fibrinogen as a biomarker for Alzheimer's disease. *Brain Pathol* 2019;29:414-424.
50. McKee AC, Au R, Cabral HJ, Kowall NW, Seshadri S, Kubilus CA, et al. Visual association pathology in preclinical Alzheimer disease. *J Neuropathol Exp Neurol* 2006;65:621-630.
51. Mountjoy CQ, Tomlinson BE, Gibson PH. Amyloid and senile plaques and cerebral blood vessels. A semi-quantitative investigation of a possible relationship. *J Neurol Sci* 1982;57:89-103.
52. Premkumar DR, Cohen DL, Hedera P, Friedland RP, Kalaria RN. Apolipoprotein E-epsilon4 alleles in cerebral amyloid angiopathy and cerebrovascular pathology associated with Alzheimer's disease. *Am J Pathol* 1996;148:2083-2095.
53. Shim YS, Yang DW, Roe CM, Coats MA, Benzinger TL, Xiong C,

 https://doi.org/10.5853/jos.2023.04287

et al. Pathological correlates of white matter hyperintensities on magnetic resonance imaging. *Dement Geriatr Cogn Disord* 2015;39:92-104.
54. Sugarman MA, McKee AC, Stein TD, Tripodis Y, Besser LM, Martin B, et al. Failure to detect an association between self-reported traumatic brain injury and Alzheimer's disease neuropathology and dementia. *Alzheimers Dement* 2019;15:686-698.
55. Wu E, Lipton RB, Dickson DW. Amyloid angiopathy in diffuse Lewy body disease. *Neurology* 1992;42:2131-2135.
56. Xu Dan, Hu Yazhuo, Gui Qiuping, Zhu Mingwei, Zhang Honghong, Wang Luning. [Histomorphological features of brain aging: different types of cerebral amyloid angiopathy and beta-amyloid protein disposition in brain parenchyma]. *Chinese J Clin Rehabil* 2004;8:6885-6887. Chinese
57. Yamada M. Risk factors for cerebral amyloid angiopathy in the elderly. *Ann N Y Acad Sci* 2002;977:37-44.
58. Bell MA, Ball MJ. Neuritic plaques and vessels of visual cortex in aging and Alzheimer's dementia. *Neurobiol Aging* 1990;11:359-370.
59. Boon BDC, Bulk M, Jonker AJ, Morrema THJ, van den Berg E, Popovic M, et al. The coarse-grained plaque: a divergent Aβ plaque-type in early-onset Alzheimer's disease. *Acta Neuropathol* 2020;140:811-830.
60. Boyle PA, Yu L, Leurgans SE, Wilson RS, Brookmeyer R, Schneider JA, et al. Attributable risk of Alzheimer's dementia attributed to age-related neuropathologies. *Ann Neurol* 2019;85:114-124.
61. Chen ZC, Gan J, Yang Y, Meng Q, Han J, Ji Y. The vascular risk factors and vascular neuropathology in subjects with autopsy-confirmed dementia with Lewy bodies. *Int J Geriatr Psychiatry* 2022;37:gps.5683.
62. Del Ser T, Hachinski V, Merskey H, Munoz DG. Alzheimer's disease with and without cerebral infarcts. *J Neurol Sci* 2005;231:3-11.
63. Dugger BN, Clark CM, Serrano G, Mariner M, Bedell BJ, Coleman RE, et al. Neuropathologic heterogeneity does not impair florbetapir-positron emission tomography postmortem correlates. *J Neuropathol Exp Neurol* 2014;73:72-80.
64. Ellis RJ, Olichney JM, Thal LJ, Mirra SS, Morris JC, Beekly D, et al. Cerebral amyloid angiopathy in the brains of patients with Alzheimer's disease: the CERAD experience, part XV. *Neurology* 1996;46:1592-1596.
65. Fallet-Bianco C, Roudier M, Lamour Y, Davous P. [Neuropathologic study of 50 cases of senile dementia]. *Rev Neurol (Paris)* 1990;146:687-696. French
66. Glenner GG, Henry JH, Fujihara S. Congophilic angiopathy in the pathogenesis of Alzheimer's degeneration. *Ann Pathol* 1981;1:120-129.
67. Helman AM, Siever M, McCarty KL, Lott IT, Doran E, Abner EL, et al. Microbleeds and cerebral amyloid angiopathy in the brains of people with Down syndrome with Alzheimer's disease. *J Alzheimers Dis* 2019;67:103-112.
68. Jellinger K. Cerebrovascular amyloidosis with cerebral hemorrhage. *J Neurol* 1977;214:195-206.
69. Jellinger KA, Mitter-Ferstl E. The impact of cerebrovascular lesions in Alzheimer disease--a comparative autopsy study. *J Neurol* 2003;250:1050-1055.
70. Jicha GA, Parisi JE, Dickson DW, Johnson K, Cha R, Ivnik RJ, et al. Neuropathologic outcome of mild cognitive impairment following progression to clinical dementia. *Arch Neurol* 2006;63:674-681.
71. Joachim CL, Morris JH, Selkoe DJ. Clinically diagnosed Alzheimer's disease: autopsy results in 150 cases. *Ann Neurol* 1988;24:50-56.
72. Kurucz J, Charbonneau R, Kurucz A, Ramsey P. Quantitative clinicopathologic study of cerebral amyloid angiopathy. *J Am Geriatr Soc* 1981;29:61-69.
73. Leech RW, Brumback RA, Poduslo SE, Schiffer R, Adesina A. Dementia: the University of Oklahoma autopsy experience. *J Okla State Med Assoc* 2001;94:507-511.
74. Liu D, Hk N, Man K, Luo X, Yang L, Sun Z. [Pathomorphological and amyloid beta-protein immunohistochemical findings in autopsied brains of Alzheimer's disease]. *Zhonghua Bing Li Xue Za Zhi* 1999;28:405-408. Chinese
75. Lopez OL, Claassen D. Cerebral amyloid angiopathy in Alzheimer's disease: clinicopathological correlations. *Dementia* 1991;2:285-290.
76. Mandybur TI. The incidence of cerebral amyloid angiopathy in Alzheimer's disease. *Neurology* 1975;25:120-126.
77. Mann DMA, Davidson YS, Robinson AC, Allen N, Hashimoto T, Richardson A, et al. Patterns and severity of vascular amyloid in Alzheimer's disease associated with duplications and missense mutations in APP gene, Down syndrome and sporadic Alzheimer's disease. *Acta Neuropathol* 2018;136:569-587.
78. Nation DA, Delano-Wood L, Bangen KJ, Wierenga CE, Jak AJ, Hansen LA, et al. Antemortem pulse pressure elevation predicts cerebrovascular disease in autopsy-confirmed Alzheimer's disease. *J Alzheimers Dis* 2012;30:595-603.
79. Olichney JM, Hansen LA, Hofstetter CR, Lee JH, Katzman R, Thal LJ. Association between severe cerebral amyloid angiopathy and cerebrovascular lesions in Alzheimer disease is not a spurious one attributable to apolipoprotein E4. *Arch Neurol* 2000;57:869-874.
80. Parker JC Jr, Philpot J. Postmortem evaluation of Alzheimer's disease. *South Med J* 1985;78:1411-1413.

81. Pirttilä T, Mehta PD, Soininen H, Kim KS, Heinonen O, Paljärvi L, et al. Cerebrospinal fluid concentrations of soluble amyloid beta-protein and apolipoprotein E in patients with Alzheimer's disease: correlations with amyloid load in the brain. *Arch Neurol* 1996;53:189-193.
82. Pivtoraiko VN, Racic T, Abrahamson EE, Villemagne VL, Handen BL, Lott IT, et al. Postmortem neocortical 3H-PiB binding and levels of unmodified and pyroglutamate Aβ in Down syndrome and sporadic Alzheimer's disease. *Front Aging Neurosci* 2021;13:728739.
83. Reimand J, Boon BDC, Collij LE, Teunissen CE, Rozemuller AJM, van Berckel BNM, et al. Amyloid-β PET and CSF in an autopsy-confirmed cohort. *Ann Clin Transl Neurol* 2020;7:2150-2160.
84. Shinohara M, Murray ME, Frank RD, Shinohara M, DeTure M, Yamazaki Y, et al. Impact of sex and APOE4 on cerebral amyloid angiopathy in Alzheimer's disease. *Acta Neuropathol* 2016;132:225-234.
85. Spina S, La Joie R, Petersen C, Nolan AL, Cuevas D, Cosme C, et al. Comorbid neuropathological diagnoses in early versus late-onset Alzheimer's disease. *Brain* 2021;144:2186-2198.
86. Tomimoto H, Akiguchi I, Akiyama H, Ikeda K, Wakita H, Lin JX, et al. Vascular changes in white matter lesions of Alzheimer's disease. *Acta Neuropathol* 1999;97:629-634.
87. Vik-Mo AO, Bencze J, Ballard C, Hortobágyi T, Aarsland D. Advanced cerebral amyloid angiopathy and small vessel disease are associated with psychosis in Alzheimer's disease. *J Neurol Neurosurg Psychiatry* 2019;90:728-730.
88. Yamada M, Tsukagoshi H, Otomo E, Hayakawa M. Systemic amyloid deposition in old age and dementia of Alzheimer type: the relationship of brain amyloid to other amyloid. *Acta Neuropathol* 1988;77:136-141.
89. Yip AG, McKee AC, Green RC, Wells J, Young H, Cupples LA, et al. APOE, vascular pathology, and the AD brain. *Neurology* 2005;65:259-265.
90. Zarow C, Zaias B, Lyness SA, Chui H. Cerebral amyloid angiopathy in Alzheimer disease is associated with apolipoprotein E4 and cortical neuron loss. *Alzheimer Dis Assoc Disord* 1999;13:1-8.
91. Dye JA, Rees G, Yang I, Vespa PM, Martin NA, Vinters HV. Neuropathologic analysis of hematomas evacuated from patients with spontaneous intracerebral hemorrhage. *Neuropathology* 2014;34:253-260.
92. Fazekas F, Kleinert R, Roob G, Kleinert G, Kapeller P, Schmidt R, et al. Histopathologic analysis of foci of signal loss on gradient-echo T2*-weighted MR images in patients with spontaneous intracerebral hemorrhage: evidence of microangiopathy-related microbleeds. *AJNR Am J Neuroradiol* 1999;20:637-642.
93. Holling M, Jeibmann A, Fischer BR, Albert FK, Ebel H, Paulus W, et al. Histopathological analysis of intracerebral hemorrhage: implications for clinical management. *Acta Neurochir (Wien)* 2012;154:439-443.
94. Ishihara T, Takahashi M, Yokota T, Yamashita Y, Gondo T, Uchino F, et al. The significance of cerebrovascular amyloid in the aetiology of superficial (lobar) cerebral haemorrhage and its incidence in the elderly population. *J Pathol* 1991;165:229-234.
95. Lieber AC, McNeill IT, Scaggiante J, Nistal DA, Fowkes M, Umphlett M, et al. Biopsy during minimally invasive intracerebral hemorrhage clot evacuation. *World Neurosurg* 2019;124:e169-e175.
96. Mendel TA, Wierzba-Bobrowicz T, Stępień T, Szpak GM. The association between cerebral amyloid angiopathy and atherosclerosis in patients with intracerebral hemorrhages. *Folia Neuropathol* 2013;51:243-249.
97. Ritter MA, Droste DW, Hegedüs K, Szepesi R, Nabavi DG, Csiba L, et al. Role of cerebral amyloid angiopathy in intracerebral hemorrhage in hypertensive patients. *Neurology* 2005;64:1233-1237.
98. Rodrigues MA, Samarasekera N, Lerpiniere C, Humphreys C, McCarron MO, White PM, et al. The Edinburgh CT and genetic diagnostic criteria for lobar intracerebral haemorrhage associated with cerebral amyloid angiopathy: model development and diagnostic test accuracy study. *Lancet Neurol* 2018;17:232-240.
99. Tang YJ, Li Y, Wang S, Zhu MW, Sun YL, Zhao JZ. The incidence of cerebral amyloid angiopathy in surgically treated intracranial hemorrhage in the Chinese population. *Neurosurg Rev* 2013;36:533-539.
100. Baron JC, Boulouis G, Benzakoun J, Schwall C, Oppenheim C, Turc G, et al. Cerebral amyloid angiopathy-related acute lobar intra-cerebral hemorrhage: diagnostic value of plain CT. *J Neurol* 2022;269:2126-2132.
101. Doden T, Sato H, Sasahara E, Murata T, Yako T, Kitazawa K, et al. Clinico-radiological characteristics and pathological diagnosis of cerebral amyloid angiopathy-related intracerebral hemorrhage. *J Stroke Cerebrovasc Dis* 2016;25:1736-1745.
102. Itoh Y, Yamada M, Hayakawa M, Otomo E, Miyatake T. Cerebral amyloid angiopathy: a significant cause of cerebellar as well as lobar cerebral hemorrhage in the elderly. *J Neurol Sci* 1993;116:135-141.
103. Knudsen KA, Rosand J, Karluk D, Greenberg SM. Clinical diagnosis of cerebral amyloid angiopathy: validation of the Boston criteria. *Neurology* 2001;56:537-539.
104. Lin CM, Arishima H, Kikuta KI, Naiki H, Kitai R, Kodera T, et al. Pathological examination of cerebral amyloid angiopathy

https://doi.org/10.5853/jos.2023.04287

in patients who underwent removal of lobar hemorrhages. *J Neurol* 2018;265:567-577.
105. Minakawa T, Takeuchi S, Sasaki O, Koizumi T, Honad Y, Fujii Y, et al. Surgical experience with massive lobar haemorrhage caused by cerebral amyloid angiopathy. *Acta Neurochir (Wien)* 1995;132:48-52.
106. Yoshimura M, Yamanouchi H, Kuzuhara S, Mori H, Sugiura S, Mizutani T, et al. Dementia in cerebral amyloid angiopathy: a clinicopathological study. *J Neurol* 1992;239:441-450.
107. Aarts N, Akoudad S, Noordam R, Hofman A, Ikram MA, Stricker BH, et al. Inhibition of serotonin reuptake by antidepressants and cerebral microbleeds in the general population. *Stroke* 2014;45:1951-1957.
108. Chung CP, Chou KH, Chen WT, Liu LK, Lee WJ, Chen LK, et al. Cerebral microbleeds are associated with physical frailty: a community-based study. *Neurobiol Aging* 2016;44:143-150.
109. Elmståhl S, Ellström K, Siennicki-Lantz A, Abul-Kasim K. Association between cerebral microbleeds and hypertension in the Swedish general population "Good Aging in Skåne" study. *J Clin Hypertens (Greenwich)* 2019;21:1099-1107.
110. Graff-Radford J, Lesnick T, Rabinstein AA, Gunter JL, Przybelski SA, Noseworthy PA, et al. Cerebral microbleeds: relationship to antithrombotic medications. *Stroke* 2021;52:2347-2355.
111. Han F, Zhai FF, Wang Q, Zhou LX, Ni J, Yao M, et al. Prevalence and risk factors of cerebral small vessel disease in a Chinese population-based sample. *J Stroke* 2018;20:239-246.
112. Kim CK, Kwon HT, Kwon HM. No significant association of aspirin use with cerebral microbleeds in the asymptomatic elderly. *J Neurol Sci* 2012;319:56-58.
113. Miwa K, Tanaka M, Okazaki S, Yagita Y, Sakaguchi M, Mochizuki H, et al. Multiple or mixed cerebral microbleeds and dementia in patients with vascular risk factors. *Neurology* 2014;83:646-653.
114. Paganini-Hill A, Bryant N, Corrada MM, Greenia DE, Fletcher E, Singh B, et al. Blood pressure circadian variation, cognition and brain imaging in 90+ year-olds. *Front Aging Neurosci* 2019;11:54.
115. Qiu C, Cotch MF, Sigurdsson S, Eiriksdottir G, Jonasson F, Klein R, et al. Cerebral microbleeds and age-related macular degeneration: the AGES-Reykjavik study. *Neurobiol Aging* 2012;33:2935-2937.
116. Romero JR, Preis SR, Beiser A, DeCarli C, Viswanathan A, Martinez-Ramirez S, et al. Risk factors, stroke prevention treatments, and prevalence of cerebral microbleeds in the Framingham heart study. *Stroke* 2014;45:1492-1494.
117. Tsushima Y, Aoki J, Endo K. Brain microhemorrhages detected on T2*-weighted gradient-echo MR images. *AJNR Am J Neuroradiol* 2003;24:88-96.
118. Wang Y, Jiang Y, Suo C, Yuan Z, Xu K, Yang Q, et al. Deep/mixed cerebral microbleeds are associated with cognitive dysfunction through thalamocortical connectivity disruption: the Taizhou imaging study. *Neuroimage Clin* 2019;22:101749.
119. Ying YQ, Wang YQ, Xia YW, Wu DH, Wu WW, Cheng X, et al. [The analysis of association between imaging biomarkers of cerebral small vessel disease and cognitive impairment: a Shanghai elderly community-based cohort]. *Chinese J Contemp Neurol Neurosurg* 2021;21:843-852. Chinese
120. Yubi T, Hata J, Ohara T, Mukai N, Hirakawa Y, Yoshida D, et al. Prevalence of and risk factors for cerebral microbleeds in a general Japanese elderly community. *Neurol Clin Pract* 2018;8:223-231.
121. Atri A, Locascio JJ, Lin JM, Yap L, Dickerson BC, Grodstein F, et al. Prevalence and effects of lobar microhemorrhages in early-stage dementia. *Neurodegener Dis* 2005;2:305-312.
122. Barnaure I, Montandon ML, Rodriguez C, Herrmann F, Lövblad KO, Giannakopoulos P, et al. Clinicoradiologic correlations of cerebral microbleeds in advanced age. *AJNR Am J Neuroradiol* 2017;38:39-45.
123. Brundel M, Reijmer YD, van Veluw SJ, Kuijf HJ, Luijten PR, Kappelle LJ, et al. Cerebral microvascular lesions on high-resolution 7-Tesla MRI in patients with type 2 diabetes. *Diabetes* 2014;63:3523-3529.
124. Chang Y, Liu J, Wang L, Li X, Wang Z, Lin M, et al. Diagnostic utility of integrated 11C-Pittsburgh compound B positron emission tomography/magnetic resonance for cerebral amyloid angiopathy: a pilot study. *Front Aging Neurosci* 2021;13:721780.
125. Chiang GC, Cruz Hernandez JC, Kantarci K, Jack CR Jr, Weiner MW; Alzheimer's Disease Neuroimaging Initiative. Cerebral microbleeds, CSF p-Tau, and cognitive decline: significance of anatomic distribution. *AJNR Am J Neuroradiol* 2015;36:1635-1641.
126. Donaghy PC, Firbank M, Mitra D, Petrides G, Lloyd J, Barnett N, et al. Microbleeds in dementia with Lewy bodies. *J Neurol* 2020;267:1491-1498.
127. Graff-Radford J, Simino J, Kantarci K, Mosley TH Jr, Griswold ME, Windham BG, et al. Neuroimaging correlates of cerebral microbleeds: the ARIC study (Atherosclerosis Risk in Communities). *Stroke* 2017;48:2964-2972.
128. Gregg NM, Kim AE, Gurol ME, Lopez OL, Aizenstein HJ, Price JC, et al. Incidental cerebral microbleeds and cerebral blood flow in elderly individuals. *JAMA Neurol* 2015;72:1021-1028.
129. Ham JH, Yi H, Sunwoo MK, Hong JY, Sohn YH, Lee PH. Cerebral microbleeds in patients with Parkinson's disease. *J Neurol* 2014;261:1628-1635.
130. Johansson E, Ambarki K, Birgander R, Bahrami N, Eklund A,

Malm J. Cerebral microbleeds in idiopathic normal pressure hydrocephalus. *Fluids Barriers CNS* 2016;13:4.
131. Kwon HM, Park JH, Park JH, Jeong HY, Lim JS, Jeong HG, et al. Visceral fat is an independent predictor of cerebral microbleeds in neurologically healthy people. *Cerebrovasc Dis* 2016;42:90-96.
132. Mendes A, Bertrand A, Lamari F, Colliot O, Routier A, Godefroy O, et al. Cerebral microbleeds and CSF Alzheimer biomarkers in primary progressive aphasias. *Neurology* 2018;90:e1057-e1065.
133. Mitaki S, Nagai A, Oguro H, Yamaguchi S. Serum lipid fractions and cerebral microbleeds in a healthy Japanese population. *Cerebrovasc Dis* 2017;43:186-191.
134. Nakata-Kudo Y, Mizuno T, Yamada K, Shiga K, Yoshikawa K, Mori S, et al. Microbleeds in Alzheimer disease are more related to cerebral amyloid angiopathy than cerebrovascular disease. *Dement Geriatr Cogn Disord* 2006;22:8-14.
135. Ochi N, Tabara Y, Igase M, Nagai T, Kido T, Miki T, et al. Silent cerebral microbleeds associated with arterial stiffness in an apparently healthy subject. *Hypertens Res* 2009;32:255-260.
136. Romero JR, Demissie S, Beiser A, Himali JJ, DeCarli C, Levy D, et al. Relation of plasma β-amyloid, clusterin, and tau with cerebral microbleeds: Framingham heart study. *Ann Clin Transl Neurol* 2020;7:1083-1091.
137. Roob G, Schmidt R, Kapeller P, Lechner A, Hartung HP, Fazekas F. MRI evidence of past cerebral microbleeds in a healthy elderly population. *Neurology* 1999;52:991-994.
138. Wang PN, Chou KH, Peng LN, Liu LK, Lee WJ, Chen LK, et al. Strictly lobar cerebral microbleeds are associated with increased white matter volume. *Transl Stroke Res* 2020;11:29-38.
139. Wollenweber FA, Baykara E, Zedde M, Gesierich B, Achmüller M, Jouvent E, et al. Cortical superficial siderosis in different types of cerebral small vessel disease. *Stroke* 2017;48:1404-1407.
140. Yakushiji Y, Noguchi T, Charidimou A, Eriguchi M, Nishihara M, Hara M, et al. Basal ganglia cerebral microbleeds and global cognitive function: the Kashima scan study. *J Stroke Cerebrovasc Dis* 2015;24:431-439.
141. Yilmaz P, Ikram MA, Ikram MK, Niessen WJ, Viswanathan A, Charidimou A, et al. Application of an imaging-based sum score for cerebral amyloid angiopathy to the general population: risk of major neurological diseases and mortality. *Front Neurol* 2019;10:1276.
142. Zhang J, Liu L, Sun H, Li M, Li Y, Zhao J, et al. Cerebral microbleeds are associated with mild cognitive impairment in patients with hypertension. *J Am Heart Assoc* 2018;7:e008453.
143. Benedictus MR, Goos JD, Binnewijzend MA, Muller M, Barkhof F, Scheltens P, et al. Specific risk factors for microbleeds and white matter hyperintensities in Alzheimer's disease. *Neurobiol Aging* 2013;34:2488-2494.
144. Boyano I, Ramos A, López-Alvarez J, Mendoza-Rebolledo C, Osa-Ruiz E, Rodríguez I, et al. Cerebral microbleeds in advanced dementia: clinical and pathological correlates. *Am J Alzheimers Dis Other Demen* 2018;33:362-372.
145. Charidimou A, Ni J, Martinez-Ramirez S, Vashkevich A, Ayres A, Rosand J, et al. Cortical superficial siderosis in memory clinic patients: further evidence for underlying cerebral amyloid angiopathy. *Cerebrovasc Dis* 2016;41:156-162.
146. Chiu WT, Lee TY, Chan L, Wu D, Huang LK, Chen DY, et al. Deep cerebral microbleeds are associated with poor cholinesterase inhibitor treatment response in people with Alzheimer disease. *Clin Neurol Neurosurg* 2020;195:105959.
147. De Kort AM, Kuiperij HB, Kersten I, Versleijen AAM, Schreuder FHBM, Van Nostrand WE, et al. Normal cerebrospinal fluid concentrations of PDGFRβ in patients with cerebral amyloid angiopathy and Alzheimer's disease. *Alzheimers Dement* 2022;18:1788-1796.
148. Ikeda M, Kodaira S, Kasahara H, Takai E, Nagashima K, Fujita Y, et al. Cerebral microbleeds, cerebrospinal fluid, and neuroimaging markers in clinical subtypes of Alzheimer's disease. *Front Neurol* 2021;12:543866.
149. Inoue Y, Nakajima M, Uetani H, Hirai T, Ueda M, Kitajima M, et al. Diagnostic significance of cortical superficial siderosis for Alzheimer disease in patients with cognitive impairment. *AJNR Am J Neuroradiol* 2016;37:223-227.
150. Kuroda T, Honma M, Mori Y, Futamura A, Sugimoto A, Yano S, et al. Increased presence of cerebral microbleeds correlates with ventricular enlargement and increased white matter hyperintensities in Alzheimer's disease. *Front Aging Neurosci* 2020;12:13.
151. Mendes A, Herrmann FR, Scheffler M, Gabriel G, Sveikata L, Rakotomiaramanana B, et al. Cortical superficial siderosis: a descriptive analysis in a memory clinic population. *J Alzheimers Dis* 2020;73:1467-1479.
152. Nagasawa J, Kiyozaka T, Ikeda K. Prevalence and clinicoradiological analyses of patients with Alzheimer disease coexisting multiple microbleeds. *J Stroke Cerebrovasc Dis* 2014;23:2444-2449.
153. Noguchi-Shinohara M, Komatsu J, Samuraki M, Matsunari I, Ikeda T, Sakai K, et al. Cerebral amyloid angiopathy-related microbleeds and cerebrospinal fluid biomarkers in Alzheimer's disease. *J Alzheimers Dis* 2017;55:905-913.
154. Shams S, Martola J, Charidimou A, Cavallin L, Granberg T, Shams M, et al. Cortical superficial siderosis: prevalence and biomarker profile in a memory clinic population. *Neurology*

 https://doi.org/10.5853/jos.2023.04287

2016;87:1110-1117.

155. Sparacia G, Agnello F, La Tona G, Iaia A, Midiri F, Sparacia B. Assessment of cerebral microbleeds by susceptibility-weighted imaging in Alzheimer's disease patients: a neuroimaging biomarker of the disease. *Neuroradiol J* 2017;30:330-335.
156. van der Vlies AE, Goos JD, Barkhof F, Scheltens P, van der Flier WM. Microbleeds do not affect rate of cognitive decline in Alzheimer disease. *Neurology* 2012;79:763-769.
157. Zhang JB, Li MF, Zhang HX, Li ZG, Sun HR, Zhang JS, et al. Association of serum vascular endothelial growth factor levels and cerebral microbleeds in patients with Alzheimer's disease. *Eur J Neurol* 2016;23:1337-1342.
158. Biffi A, Rattani A, Anderson CD, Ayres AM, Gurol EM, Greenberg SM, et al. Delayed seizures after intracerebral haemorrhage. *Brain* 2016;139(Pt 10):2694-2705.
159. Ghelmez D, Sorin Tuţă S, Popa C. Cerebral microbleeds (CMBs) - relevance for mechanisms of cerebral hemorrhage--analysis of 24 MRI evaluated patients. *J Med Life* 2013;6:437-439.
160. Haussen DC, Henninger N, Kumar S, Selim M. Statin use and microbleeds in patients with spontaneous intracerebral hemorrhage. *Stroke* 2012;43:2677-2681.
161. Jolink WM, Lindenholz A, van Etten ES, van Nieuwenhuizen KM, Schreuder FH, Kuijf HJ, et al. Contrast leakage distant from the hematoma in patients with spontaneous ICH: a 7 T MRI study. *J Cereb Blood Flow Metab* 2020;40:1002-1011.
162. Laible M, Horstmann S, Möhlenbruch M, Wegele C, Rizos T, Schüler S, et al. Renal dysfunction is associated with deep cerebral microbleeds but not white matter hyperintensities in patients with acute intracerebral hemorrhage. *J Neurol* 2015;262:2312-2322.
163. Martí-Fàbregas J, Delgado-Mederos R, Granell E, Morenas Rodríguez E, Marín Lahoz J, Dinia L, et al. Microbleed burden and hematoma expansion in acute intracerebral hemorrhage. *Eur Neurol* 2013;70:175-178.
164. Schwarz G, Banerjee G, Hostettler IC, Ambler G, Seiffge DJ, Brookes TS, et al. Magnetic resonance imaging-based scores of small vessel diseases: associations with intracerebral haemorrhage location. *J Neurol Sci* 2022;434:120165.
165. Tsai HH, Tsai LK, Chen YF, Tang SC, Lee BC, Yen RF, et al. Correlation of cerebral microbleed distribution to amyloid burden in patients with primary intracerebral hemorrhage. *Sci Rep* 2017;7:44715.
166. Wang X, Feng H, Wang Y, Zhou J, Zhao X. Enlarged perivascular spaces and cerebral small vessel disease in spontaneous intracerebral hemorrhage patients. *Front Neurol* 2019;10:881.
167. Xu M, Cheng Y, Song Q, Yuan R, Zhang S, Hao Z, et al. Total burden of cerebral small vessel disease in recurrent ICH versus first-ever ICH. *Aging Dis* 2019;10:570-577.
168. Schwarz G, Banerjee G, Hostettler IC, Ambler G, Seiffge DJ, Ozkan H, et al. MRI and CT imaging biomarkers of cerebral amyloid angiopathy in lobar intracerebral hemorrhage. *Int J Stroke* 2023;18:85-94.
169. Pichler M, Vemuri P, Rabinstein AA, Aakre J, Flemming KD, Brown RD Jr, et al. Prevalence and natural history of superficial siderosis: a population-based study. *Stroke* 2017;48:3210-3214.
170. Shoamanesh A, Morotti A, Romero JM, Oliveira-Filho J, Schlunk F, Jessel MJ, et al. Cerebral microbleeds and the effect of intensive blood pressure reduction on hematoma expansion and functional outcomes: a secondary analysis of the ATACH-2 randomized clinical trial. *JAMA Neurol* 2018;75:850-859.
171. Cheng X, Su Y, Wang Q, Gao F, Ye X, Wang Y, et al. Neurofilament light chain predicts risk of recurrence in cerebral amyloid angiopathy-related intracerebral hemorrhage. *Aging (Albany NY)* 2020;12:23727-23738.
172. Carmona-Iragui M, Balasa M, Benejam B, Alcolea D, Fernández S, Videla L, et al. Cerebral amyloid angiopathy in Down syndrome and sporadic and autosomal-dominant Alzheimer's disease. *Alzheimers Dement* 2017;13:1251-1260.
173. Na HK, Park JH, Kim JH, Kim HJ, Kim ST, Werring DJ, et al. Cortical superficial siderosis: a marker of vascular amyloid in patients with cognitive impairment. *Neurology* 2015;84:849-855.
174. Tsai HH, Chen YF, Yen RF, Lo YL, Yang KC, Jeng JS, et al. Plasma soluble TREM2 is associated with white matter lesions independent of amyloid and tau. *Brain* 2021;144:3371-3380.
175. Umino M, Maeda M, Kogue R, Nakamura S, Ii Y, Tomimoto H, et al. Evaluation of cortical superficial siderosis in patients with cognitive dysfunction using 3D FLAIR and 3D DIR. *Eur Radiol* 2021;31:6411-6418.
176. Zonneveld HI, Goos JD, Wattjes MP, Prins ND, Scheltens P, van der Flier WM, et al. Prevalence of cortical superficial siderosis in a memory clinic population. *Neurology* 2014;82:698-704.
177. Castello JP, Pasi M, Kubiszewski P, Abramson JR, Charidimou A, Kourkoulis C, et al. Cerebral small vessel disease and depression among intracerebral hemorrhage survivors. *Stroke* 2022;53:523-531.
178. Damien C, Cisse F, Ligot N, Toure ML, Konaté M, Barry SD, et al. Insights in the pathophysiology of haemorrhagic strokes in a sub-Sahara African country, an epidemiological and MRI study. *Trop Med Int Health* 2021;26:166-172.
179. Moulin S, Casolla B, Kuchcinski G, Boulouis G, Rossi C, Hénon H, et al. Cortical superficial siderosis: a prospective observa-

tional cohort study. *Neurology* 2018;91:e132-e138.
180. Pinho J, Araújo JM, Costa AS, Silva F, Francisco A, Quintas-Neves M, et al. Intracerebral hemorrhage recurrence in patients with and without cerebral amyloid angiopathy. *Cerebrovasc Dis Extra* 2021;11:15-21.
181. Suda S, Shimoyama T, Suzuki S, Ouchi T, Arakawa M, Aoki J, et al. Prevalence and clinical characteristics of cortical superficial siderosis in patients with acute stroke. *J Neurol* 2017;264:2413-2419.
182. Tsai HH, Chen SJ, Tsai LK, Pasi M, Lo YL, Chen YF, et al. Long-term vascular outcomes in patients with mixed location intracerebral hemorrhage and microbleeds. *Neurology* 2021;96:e995-e1004.
183. Ye X, Li G, Liu X, Song G, Jia Y, Wu C, et al. Apolipoprotein E genotype predicts subarachnoid extension in spontaneous intracerebral haemorrhage. *Eur J Neurol* 2021;28:1992-1999.
184. Boulouis G, van Etten ES, Charidimou A, Auriel E, Morotti A, Pasi M, et al. Association of key magnetic resonance imaging markers of cerebral small vessel disease with hematoma volume and expansion in patients with lobar and deep intracerebral hemorrhage. *JAMA Neurol* 2016;73:1440-1447.
185. Renard D, Parvu T, Tatu L, Thouvenot E. Subarachnoid extension of lobar hemorrhage on acute/subacute MRI is associated with cerebral amyloid angiopathy criteria. *Acta Neurol Belg* 2020;120:863-866.
186. Yakushiji Y, Tanaka J, Wilson D, Charidimou A, Noguchi T, Kawashima M, et al. Proportion of intracerebral haemorrhage due to cerebral amyloid angiopathy in the East and West: comparison between single hospital centres in Japan and the United Kingdom. *J Neurol Sci* 2020;416:117037.
187. Viguier A, Raposo N, Patsoura S, Calviere L, Albucher JF, Ruidavets JB, et al. Subarachnoid and subdural hemorrhages in lobar intracerebral hemorrhage associated with cerebral amyloid angiopathy. *Stroke* 2019;50:1567-1569.
188. van Rooden S, Goos JD, van Opstal AM, Versluis MJ, Webb AG, Blauw GJ, et al. Increased number of microinfarcts in Alzheimer disease at 7-T MR imaging. *Radiology* 2014;270:205-211.
189. Charidimou A, Meegahage R, Fox Z, Peeters A, Vandermeeren Y, Laloux P, et al. Enlarged perivascular spaces as a marker of underlying arteriopathy in intracerebral haemorrhage: a multicentre MRI cohort study. *J Neurol Neurosurg Psychiatry* 2013;84:624-629.
190. Martí-Fàbregas J, Prats-Sánchez L, Martínez-Domeño A, Camps-Renom P, Marín R, Jiménez-Xarrié E, et al. The H-ATOMIC criteria for the etiologic classification of patients with intracerebral hemorrhage. *PLoS One* 2016;11:e0156992.
191. Pasi M, Pongpitakmetha T, Charidimou A, Singh SD, Tsai HH, Xiong L, et al. Cerebellar microbleed distribution patterns and cerebral amyloid angiopathy. *Stroke* 2019;50:1727-1733.
192. Pasi M, Charidimou A, Boulouis G, Auriel E, Ayres A, Schwab KM, et al. Mixed-location cerebral hemorrhage/microbleeds: underlying microangiopathy and recurrence risk. *Neurology* 2018;90:e119-e126.
193. Segal AZ, Chiu RI, Eggleston-Sexton PM, Beiser A, Greenberg SM. Low cholesterol as a risk factor for primary intracerebral hemorrhage: a case-control study. *Neuroepidemiology* 1999;18:185-193.
194. Tsai HH, Pasi M, Tsai LK, Chen YF, Lee BC, Tang SC, et al. Distribution of lacunar infarcts in Asians with intracerebral hemorrhage: a magnetic resonance imaging and amyloid positron emission tomography study. *Stroke* 2018;49:1515-1517.
195. Greenberg SM, Briggs ME, Hyman BT, Kokoris GJ, Takis C, Kanter DS, et al. Apolipoprotein E epsilon 4 is associated with the presence and earlier onset of hemorrhage in cerebral amyloid angiopathy. *Stroke* 1996;27:1333-1337.
196. Jamieson EI, Newman D, Metcalf AK, Naguib MF, Saada J, Potter JF, et al. Dementia is strongly associated with 90-day mortality in lobar cerebral amyloid angiopathy related intracerebral haemorrhage. *J Neurol Sci* 2012;322:161-165.

https://doi.org/10.5853/jos.2023.04287