Original article

Diagnostic accuracy of cerebral amyloid angiopathy criteria in the first pathologically confirmed Thai cohort: a pilot study

Thanapoom Taweephol[a, b], Thachamai Smitasiri[c, d], Thanakit Pongpitakmetha[e, f, g, *], Sekh Thanprasertsuk[c, d, f, g], Anand Viswanathan[h]

[a]*Department of Microbiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*
[b]*Neurological Institute, University Hospitals Cleveland Medical Center, Case Western Reserve University, Cleveland, Ohio, USA*
[c]*Department of Physiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*
[d]*Cognitive, Clinical and Computational Neuroscience (CCCN) Center of Excellence, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*
[e]*Department of Pharmacology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*
[f]*Chula Neuroscience Center, King Chulalongkorn Memorial Hospital, the Thai Red Cross Society, Bangkok, Thailand*
[g]*Comprehensive Headache and Orofacial Pain (CHOP) research group and service, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*
[h]*J. Philip Kistler Stroke Research Center, Department of Neurology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA*

Abstract

Background: The gold standard for diagnosing cerebral amyloid angiopathy (CAA) is full brain postmortem examination, which is rarely performed. Current diagnostic criteria are primarily based on clinical-radiological features and were developed from Western populations and thus may have limited applicability to Asian populations.

Objectives: We aimed to evaluate the accuracy of current diagnostic criteria and examine the clinical-radiological characteristics of Thai patients with CAA.

Methods: Brain histopathological specimens were reviewed from patients with clinical symptoms of CAA who underwent neurosurgical procedures, including intracerebral hemorrhage (ICH) evacuation, between 2011 and 2021 at King Chulalongkorn Memorial Hospital, Thai Red Cross Society. Patient characteristics and clinical events were collected retrospectively. Trained investigators systematically rated the radiological biomarkers from brain imaging performed closest to the date of pathological confirmation. The diagnostic accuracies of the Modified Boston Criteria v1.5, Boston Criteria v2.0, and Simplified Edinburgh Criteria were compared.

Results: Thirty-five pathological reports were reviewed. Eight patients (median age of 76.7 years) with confirmed CAA had 11 clinical events, including weakness, altered consciousness, headache, seizures, and aphasia. Receiver operating characteristic curve analysis revealed that the Boston Criteria v2.0 had higher sensitivity compared to the Modified Boston Criteria v1.5. Moreover, the Simplified Edinburgh Criteria demonstrated lower sensitivity compared to both of the Boston Criteria. The area under the curve for probable CAA using the Modified Boston Criteria v1.5 was 0.9 (95% confidence interval 0.8–1.0).

Conclusion: This pilot study reveals the diagnostic performance of CAA criteria and demonstrates its applicability among the Asian population. In resource-limited settings, the simplified Edinburgh criteria, which are computerized tomography-based criteria, are valuable for diagnosing patients with CAA-ICH. This is a pilot study with a relatively small sample size; larger studies with Asian cohorts are warranted to further validate these findings.

Keywords: Cerebral amyloid angiopathy, diagnostic criteria, neuroimaging, neuropathology.

***Correspondence to Thanakit Pongpitakmetha,** Department of Pharmacology, Faculty of Medicine, Chulalongkorn University, Bangkok, 10330, Thailand.
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Sporadic cerebral amyloid angiopathy (CAA) is a common small vessel disease that affects the elderly. Imaging biomarkers of CAA include hemorrhagic biomarkers such as lobar cerebral microbleed (CMB), convexity subarachnoid hemorrhage (cSAH), and cortical superficial siderosis (cSS), as well as non-hemorrhagic biomarkers such as subcortical white matter hyperintensities (WMH) and enlarged perivascular spaces (EPVS) in the centrum semiovale.[1] The clinical presentations of CAA vary from focal neurological deficit caused by intracerebral hemorrhage (ICH), cognitive impairment, and transient focal neurological events (TFNEs), previously referred to as amyloid spells.[1-5]

The gold standard for CAA diagnosis requires a full postmortem brain autopsy, which is rarely performed in clinical practice. However, the current diagnostic criteria of CAA are often used in clinical practice to diagnose probable and possible CAA and are primarily based on clinical and neuroimaging characteristics. According to the original Boston Criteria v1.0,[6, 7] diagnosing probable CAA requires at least two hemorrhagic lesions, either ICH and/or CMB, that are restricted to the lobar brain regions. Furthermore, according to the modified Boston Criteria v1.5,[8] cSS was included as an additional hemorrhagic lesion. This increased the diagnostic sensitivity (v1.0 with 89.5% *vs.* v1.5 with 94.7%) without a decrease in the specificity (81.2%) in patients with CAA who already had ICH (CAA-ICH). However, studies found that the diagnostic accuracy for patients with CAA but without ICH (CAA–non-ICH), who typically presented with cognitive impairment, remained relatively poor.

In addition, according to the recent Boston Criteria v2.0,[1] non-hemorrhagic biomarkers, including severe EPVS in centrum semiovale with more than 20 lesions per cerebral hemisphere and the presence of at least 10 subcortical WMH spots, were employed. This resulted in an improved diagnostic accuracy of probable CAA (overall sensitivity 74.5% and specificity 95.0%) in patients with CAA-ICH (sensitivity 90.2% and specificity 92.9%) and CAA–non-ICH (sensitivity 55.1% and specificity 96.2%).

Although the magnetic resonance imaging (MRI)-based Boston Criteria exhibits high sensitivity and specificity, many resource-limited countries cannot consistently implement MRI studies for patients with ICH or those presenting with cognitive decline. Therefore, the simplified [9] and full [10] Edinburgh Criteria, which are computerized tomography (CT)-based, have been proposed. In the full Edinburgh Criteria,[10] based on brain computed tomography (CT) and apolipoprotein E (*APOE)* status, the presence of at least one of the three core features in patients with ICH, including SAH extension from ICH, finger-like projections (FLP) of ICH, and at least one *APOE* ε4 allele, can lead to a medium–high probability of CAA. The simplified Edinburgh Criteria,[9] demonstrated that the presence of SAH and FLP in patients with ICH, regardless of *APOE* status, has a sensitivity of 29.6% and a specificity of 87.2%, using the modified Boston Criteria v1.5 as the reference standard.[11] Therefore, both versions of the Edinburgh Criteria are suitable for selecting patients to subsequently undergo brain MRI. However, the confidence level for applying these criteria in the Asian population, especially in Southeast Asia, remains limited and has not been well validated.

The primary objective of this study was to explore the accuracy of current diagnostic criteria in the first pathologically confirmed cohort of Thai patients with CAA. The secondary objective was to describe the clinical and neuroimaging characteristics of these patients.

Materials and methods

This study was reviewed and approved by our institutional review board at the Faculty of Medicine, Chulalongkorn University (IRB no.: 702/63), and conducted in accordance with the relevant guidelines. Patient information was obtained from electronic medical records (EMRs) following the IRB-approved study protocol. Informed consent was waived due to the retrospective nature of the study.

Case selection and study population

We reviewed pathological reports that included Congo Red-stained brain histopathological specimens at King Chulalongkorn Memorial Hospital, Thai Red Cross Society, from January 2011 to December 2021. These reports pertained exclusively to patients who presented clinically with symptomatic CAA and who subsequently underwent neurosurgical operations. The certified pathologists diagnosed CAA based on distinctive vascular morphological changes that were identified from hematoxylin and eosin staining, accompanied by the presence of green birefringence that was observed under polarized light microscopy in Congo Red-stained specimens.[12] For further

confirmation of CAA diagnosis, the modified Vonsattel grading system was systematically applied.[13, 14] Criteria for patient inclusion included the following prerequisites: 1) pathologically confirmed diagnosis of CAA,[1] 2) age equal to or exceeding 50 years,[2] and 3) at least one available neuroimaging modality,[3] either brain CT or MRI, at the time of the relevant clinical event. Patients exhibiting active inflammatory features related to CAA, as discerned via MRI scans, were excluded.

Clinical data

The patients' baseline characteristics, including demographic data, full medical history, and clinical presentation, were obtained from EMRs. For patients with multiple clinical events of symptomatic CAA, each event was independently collected and analyzed.

Neuroimaging data acquisition and analysis

Imaging biomarkers from the brain CT and MRI performed closest to the date of pathological confirmation of CAA were systematically rated by trained investigators (T.P. and S.T.), who were blinded to the clinical information. The raters adhered to the Standards for Reporting Vascular Changes on Neuroimaging (STRIVE)-2 [15] when applicable, as well as a predefined standard visual rating method.[16] Detailed descriptions of the scales used for the MRI [1] and CT [9, 10] ratings have been previously described. The interrater agreement level between the two trained raters using a representative sample of 20 scans was excellent (K = 0.9). Discrepancies in radiological ratings were resolved by consensus (T.P. and S.T.).

The best-quality neuroimaging studies closest to the clinical event were used to determine the diagnosis level of CAA based on the modified Boston Criteria v1.5,[8] Boston Criteria v2.0,[1] and simplified Edinburgh Criteria.[9] The full Edinburgh Criteria were not applied because of the absence of *APOE* status. Within the Boston Criteria, the diagnostic levels included possible and probable CAA, whereas the simplified Edinburgh Criteria incorporated low, intermediate, and high probabilities of CAA. CT scans were used to rate ICH and were applied in accordance with the Boston Criteria.

The simplified diagnostic framework of the Boston Criteria v2.0, Edinburgh Criteria, and simplified Edinburgh Criteria for sporadic CAA is summarized in **Figure 1.**

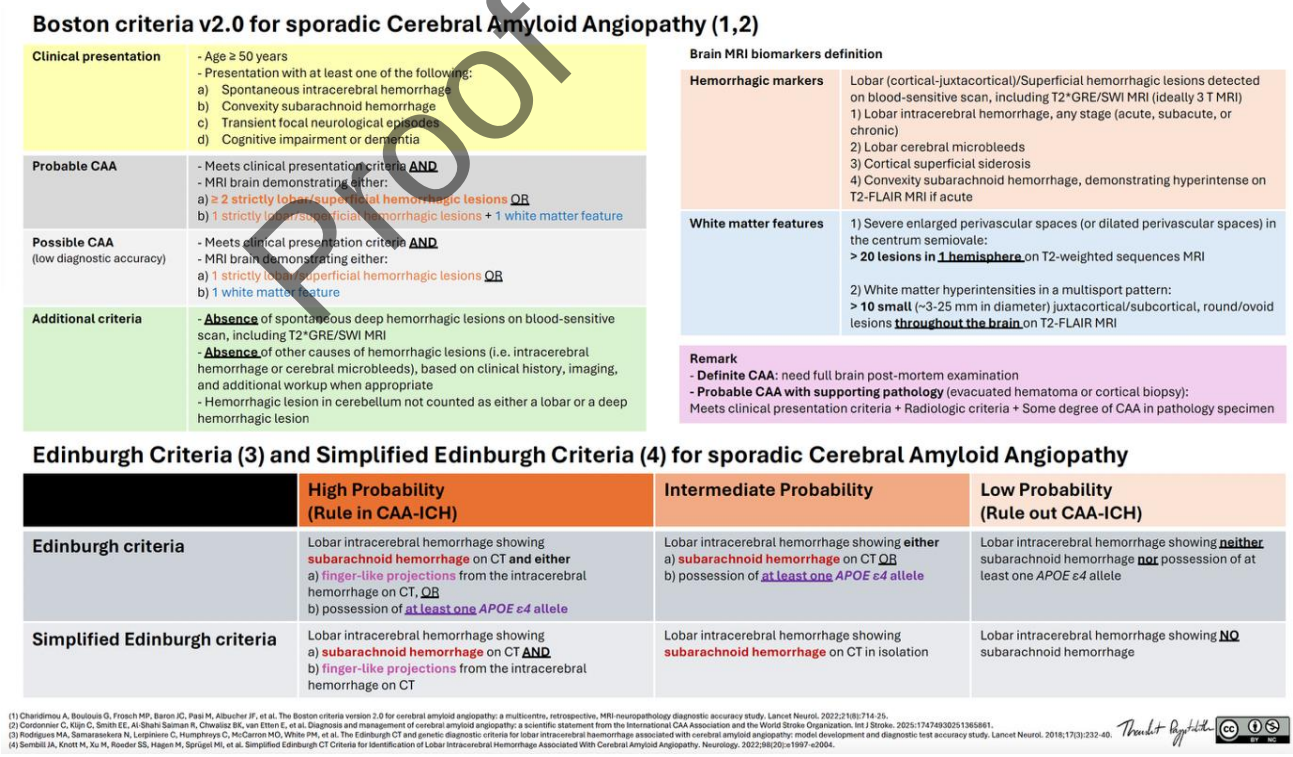

Figure 1. Simplified diagnostic framework of the Boston criteria v2.0, Edinburgh criteria, and simplified Edinburgh criteria for diagnosis of sporadic cerebral amyloid angiopathy. ApoE, apolipoprotein; CAA, cerebral amyloid angiopathy; CT, computerized tomography; FLAIR, fluid attenuated inversion recovery; GRE, gradient echo sequences; ICH, intracerbreal hemorrhage; MRI, magnetic resonance imaging; SWI, susceptibility weighted imaging; T, Tesla. Simplified diagnostic framework of the Boston criteria v2.0, Edinburgh criteria, and simplified Edinburgh criteria for diagnosis of sporadic cerebral amyloid angiopathy

Statistical analysis

Categorical variables were analyzed using the chi-square test, Fisher's exact test, odds ratio, or logistic regression as appropriate. Continuous variables were analyzed using an unpaired *t*-test for normally distributed data and a Wilcoxon rank-sum test for non-normally distributed data. Linear regression was applied when appropriate. Visualized histograms and the Shapiro-Wilk test were used to test the normal distribution of variables. For normally distributed data, the mean and standard deviation were reported, whereas the median and interquartile range (IQR) were used for non-normally distributed data. Diagnostic accuracy, sensitivity, specificity, and area under the curve (AUC) of each diagnostic criterion were assessed using receiver operating characteristic curve analysis and compared between criteria.

IBM SPSS Statistics version 29.0 (IBM Corporation, Armonk, NY, USA) was used for all analyses. Statistical tests were two-tailed, and significance was defined as $P < 0.05$. The manuscript was prepared according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[18]

Results

Eight participants meeting the inclusion criteria were identified from 35 patients who had pathological reports confirming CAA. A comprehensive analysis of 11 notable clinical events, including weakness, altered consciousness, headache, seizure, and aphasia, pertaining to these individuals was conducted, where each event was treated as an independent case. However, only nine of these events allowed for a detailed evaluation of clinical information through recent EMRs, as some data was unavailable because of the transition from conventional to EMR systems.

The median age of the participants was 76.7 years, with an IQR of 17.63 years, and the majority were female (81.8%). The most common underlying diseases were hypertension (44.4%) and dyslipidemia (44.4%), and none of the patients had atrial fibrillation. Notably, one patient had a history of hemorrhagic stroke, another had a history of ischemic stroke, and one patient experienced both events. Of the nine patients, three (33.3%) were using statins prior to the event, whereas only one patient had a history of antiplatelet (aspirin) use. The two most common clinical presentations of the events of interest were weakness (77.8%) and altered consciousness (77.8%). Less frequent clinical presentations were headache (55.6%), seizure (22.2%), and aphasia (11.1%). None of the patients exhibited CAA-related TFNEs or cognitive impairment, and two patients died within 90 days following the events. A comprehensive presentation of the clinical characteristics is provided in **Table 1**.

The brain CT scans allowed for the evaluation of all 11 events. In 10 events (90.9%), the CT scans revealed strictly lobar ICH. In another event, the CT scan revealed lobar ICH and cerebellar hemorrhage. Single acute ICHs were identified in seven events (63.6%), whereas multiple acute ICHs were identified in four events (36.4%). SAH adjacent to ICH was evident in nine events (81.8%), whereas SAH remote from ICH occurred in two events (18.8%). The feature of FLP was present in four events (36.4%), and intraventricular hemorrhage was observed in three events (27.3%).

Brain MRIs were only available in five events for assessment. Among these, three patients exhibited lobar CMBs (60.0%), and three patients had cSS (50.0%). Notably, the unique feature of severe EPVS at the centrum semiovale (more than 20 EPVS per hemisphere) was not identified in this cohort. However, the pattern of more than 10 subcortical WMH spots was observed in all patients.

According to the best available data from the CT and MRI biomarkers, the patients were evaluated for each criterion. In the simplified Edinburgh Criteria, the patients with high, intermediate, and low probabilities of CAA were 4, 4, and 3, respectively. The number of probable CAA cases was six (54.5%) using the modified Boston Criteria v1.5 and seven (63.6%) with the Boston Criteria v2.0, primarily because of the inclusion of the patterns featuring more than 10 subcortical WMH spots. Detailed radiological characteristics and the number of patients diagnosed by each criterion are presented in **Table 1**.

The comparisons of the diagnosis levels between the criteria are outlined in **Table 2.** A significant difference was only observed between the modified Boston Criteria v1.5 and Boston Criteria v2.0, as demonstrated by Fisher's exact test. However, no significant difference was found in the comparison of diagnoses between the simplified Edinburgh Criteria and both versions of the Boston Criteria.

Table 1. Clinical and radiological characteristics in Thai pathological-based (CAA) cohort.

Total (n = 11)	Frequency (%)
Demographic data (n = 11)	
Age (years)	76.7 (17.6)*
Gender (female)	9.0 (81.8%)
Death within 90 days after event	2.0 (18.2%)
Underlying disease (n = 9)	
Previous ischemic stroke	2 (22.2%)
Previous hemorrhagic stroke	2 (22.2%)
Previous cognitive impairment/dementia	2 (22.2%)
Hypertension	4 (44.4%)
Dyslipidemia	4 (44.4%)
Diabetes mellitus type 2	0 (0.0%)
Atrial fibrillation	0 (0.0%)
Previous myocardial infarction	0 (0.0%)
Chronic kidney disease	0 (0.0%)
Chronic liver disease	0 (0.0%)
Smoking	0 (0.0%)
Alcohol drinking	0 (0.0%)
Previous medication use (n = 9)	
Antiplatelet	1 (11.1%)
Anticoagulants	0 (0.0%)
Antihypertensive	1 (11.1%)
Statin	3 (33.3%)
Clinical presentation of interested events (n = 9)	
Weakness	7 (77.8%)
Alteration of consciousness	7 (77.8%)
Headache	5 (55.6%)
Seizure	2 (22.2%)
Aphasia	1 (11.1%)
Transient focal neurological events (or amyloid spells)	0 (0.0%)
Cognitive impairment/dementia	0 (0.0%)
CT radiologic biomarkers (n = 11)	
ICH location	
Strictly lobar	10 (90.9%)
Strictly deep	0 (0.0%)
Mixed – lobar + cerebellum	1 (9.1%)
Number of ICH	
Single	7 (63.6%)
Multiple	4 (36.4%)
Subarachnoid hemorrhage	
Adjacent to ICH	9 (81.8%)
Remote from ICH	2 (18.2%)
Finger-like projection presence	4 (36.4%)
Intraventricular hemorrhage	3 (27.3%)
MRI radiologic biomarkers (n = 5)	
Cerebral microbleeds (presence)	
Lobar	3 (60.0%)
0 - 5 CMBs	1 (20.0%)
> 5 CMBs	2 (40.0%)
Deep	0 (0.0%)
Cerebellum	0 (0.0%)

Table 1. (Cont.) Clinical and radiological characteristics in Thai pathological-based (CAA) cohort.

Total (n = 11)	Frequency (%)
Cortical superficial siderosis	
Focal	2 (40.0%)
Disseminated	1 (20.0%)
EPVS or DPVS (per hemisphere)	
Centrum semi-ovale	5 (100.0%)
0 EPVS/hemisphere (absence)	0 (0.0%)
1 - 10 EPVS/hemisphere (mild)	3 (60.0%)
11 - 20 EPVS/hemisphere (moderate)	2 (40.0%)
21 - 40 EPVS/hemisphere (frequent)	0 (0.0%)
> 40 EPVS/hemisphere (severe)	5 (100.0%)
Basal ganglia	0 (0.0%)
0 EPVS/hemisphere (absence)	5 (100.0%)
1 - 10 EPVS/hemisphere (mild)	0 (0.0%)
11 - 20 EPVS/hemisphere (moderate)	0 (0.0%)
21 - 40 EPVS/hemisphere (frequent)	5 (100.0%)
> 40 EPVS/hemisphere (severe)	0 (0.0%)
WMH	
Periventricular WMH	5 (100.0%)
Fazekas 1	0 (0.0%)
Fazekas 2	1 (20.0%)
Fazekas 3	4 (80.0%)
Subcortical WMH	5 (100%)
Fazekas 1	1 (20.0%)
Fazekas 2	2 (40.0%)
Fazekas 3	2 (40.0%)
WMH Fazekas overall score, combined from periventricular and subcortical WMH	5 (2)*
WMH dominant pattern	
Multiple subcortical spots	2 (40.0%)
Peri-basal ganglia	0 (0.0%)
Posterior subcortical patches	1 (20.0%)
Anterior subcortical patches	2 (40.0%)
Multiple spots WMH	5 (100.0%)
1 - 10 subcortical WMH spots	0 (0.0%)
> 10 subcortical WMH spots	5 (100.0%)
Diagnostic criteria	
Simplified Edinburgh criteria (n = 11)	
High probability CAA	4 (36.4%)
Intermediate probability CAA	4 (36.4%)
Low probability CAA	3 (27.3%)
Modified Boston criteria v1.5† (n = 11)	
Probable CAA	6 (54.5%)
Possible CAA	5 (45.5%)
Boston criteria v2.0† (n = 11)	
Probable CAA	7 (63.6%)
Possible CAA	4 (36.4%)

*Median (IQR); †Boston criteria was assessed based on the best available imaging. CT scan was allowed for rating ICH.
CAA, cerebral amyloid angiopathy; CMBs, cerebral microbleeds; CT, computerized tomography; DPVS, dilated perivascular space; EPVS, enlarged perivascular space; ICH, intracerebral hemorrhage; MRI, magnetic resonance imaging; WMH, white matter hyperintensities.

Table 2. Comparisons of the level of diagnosis between modified Boston criteria v1.5, Boston criteria v2.0, and simplified Edinburgh criteria in Thai pathological-confirmed (CAA) cohort.

N (frequency)		Simplified Edinburgh criteria			Total
		High probability	Intermediate probability	Low probability	
Modified Boston criteria v1.5	**Probable CAA**	2 (18.2%)	3 (27.3%)	1 (9.1%)	6 (54.5%)
	Possible CAA	2 (18.2%)	1 (9.1%)	2 (18.2%)	5 (45.5%)
Total		4 (36.4%)	4 (36.4%)	3 (27.3%)	11 (100.0%)
				Fisher exact test 1.358 (*P*-value 0.766)	
Boston criteria v2.0	**Probable CAA**	2 (18.2%)	4 (36.4%)	1 (9.1%)	7 (63.6%)
	Possible CAA	2 (18.2%)	0 (0%)	2 (18.2%)	4 (36.4%)
Total		4 (36.4%)	4 (36.4%)	3 (27.3%)	11 (100.0%)
				Fisher's exact test 3.596 (*P*-value 0.309)	
N (frequency)		**Modified Boston criteria v1.5**			**Total**
		Probable CAA		**Possible CAA**	
Boston criteria v2.0	**Probable CAA**	6 (54.5%)		1 (9.1%)	7 (63.6%)
	Possible CAA	0 (0.0%)		4 (36.4%)	4 (36.4%)
Total		6 (54.5%)		5 (45.5%)	11 (100.0%)
				Fisher's exact test - (*P*-value 0.015)*	

*$P < 0.05$; CAA, cerebral amyloid angiopathy.

Table 3. The diagnostic accuracy of the cerebral amyloid angiopathy criteria using modified Boston criteria v1.5 and Boston criteria v2.0 as reference standards.

	AUC (95% CI)	Standard error	*P*-value	sensitivity	specificity
Reference standard: probable CAA in modified Boston criteria v1.5					
Simplified Edinburgh criteria (high *vs.* intermediate-low probability)	0.5 (0.1–0.8)	0.18	0.855	33.3%	60.0%
Simplified Edinburgh criteria (high-intermediate *vs*. low probability)	0.6 (0.3–1.0)	0.18	0.523	83.3%	40.0%
Reference standard: probable CAA in Boston criteria v2.0					
Simplified Edinburgh criteria (high *vs.* intermediate-low probability)	0.4 (0.0–1.0)	0.19	0.571	28.6%	50.0%
Simplified Edinburgh criteria (high-intermediate *vs.* low probability)	0.7 (0.3–1.0)	0.19	0.345	85.7%	50.0%
Modified Boston criteria v1.5 (probable *vs*. possible CAA)	0.9 (0.8–1.0)	0.09	**0.023***	85.7%	100.0%

*$P < 0.05$; CAA, cerebral amyloid angiopathy.

The diagnostic accuracy of the criteria, using the Boston Criteria v1.5 and v2.0 as reference standards, is summarized in **Table 3**. Boston Criteria v2.0 exhibited higher sensitivity compared with that of v1.5 (probable CAA, 63.6% *vs.* 54.4%, respectively), which is likely attributable to the inclusion of non-hemorrhagic biomarkers. In contrast, the simplified Edinburgh Criteria revealed a lower sensitivity compared with the Boston Criteria. Grouping the high–intermediate vs. low probability group compared to the high vs. intermediate–low probability group in the simplified Edinburgh Criteria resulted in better diagnosis sensitivity (83.3% *vs.* 33.3%, respectively) without losing much specificity (40.0% *vs.* 60.0%, respectively) when using probable CAA in the modified Boston Criteria v1.5 as the reference standard. Similar results were observed when comparing the simplified Edinburgh Criteria with probable CAA in the Boston Criteria v2.0 as a reference standard, resulting in a sensitivity of 85.7% *vs.* 28.6% and specificity of 50.0% *vs.* 50.0%, respectively. The AUC of probable CAA in Boston Criteria v1.5, using v2.0 as a reference standard, was 0.93 (95% confidence interval 0.8–1.0, $P = 0.023$, sensitivity 85.7%, and specificity 100.0%). The primary results of this study are visualized and summarized in **Figure 2.**

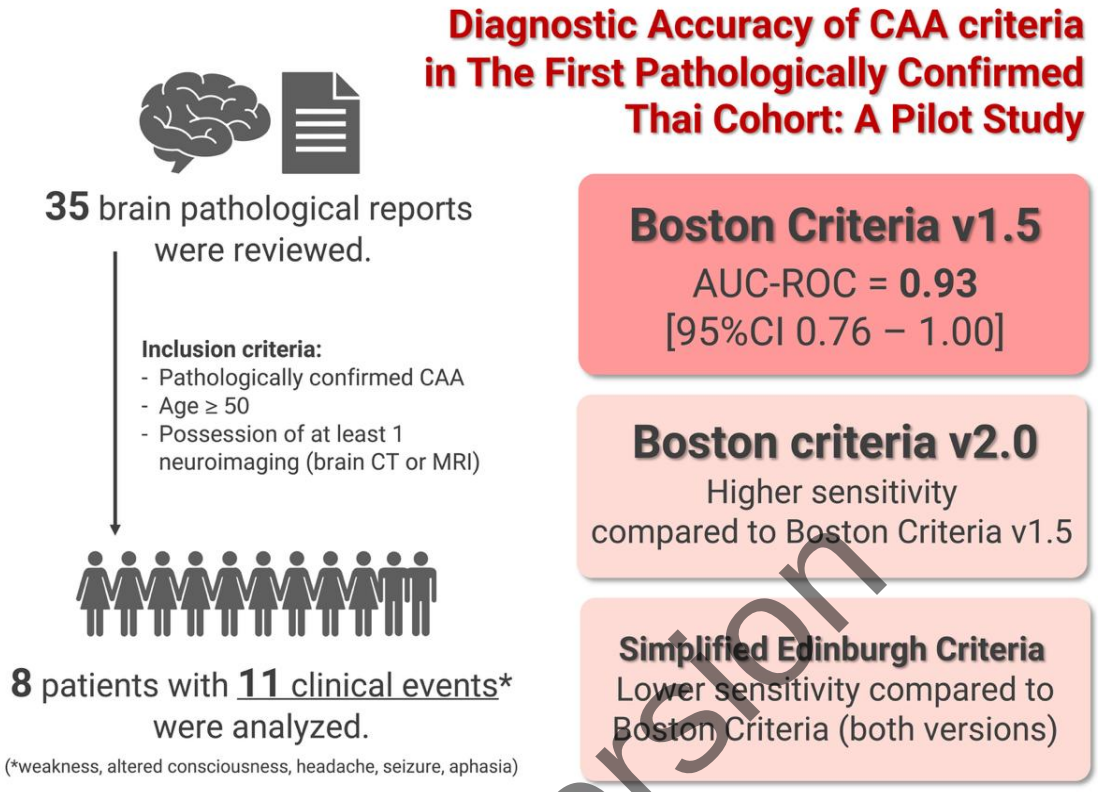

Figure 2. Graphical abstract and summary of key findings.

Discussion

This study presents the first established cohort of Thai patients with CAA based on pathological data. The clinical characteristics did not substantially differ from those of previously established larger cohorts.[1, 9] Radiological biomarkers in CT scans in this cohort revealed large amounts of SAH and FLP. These differences may arise from the severe ICH that required surgical intervention in our cohort, whereas not all patients in the simplified Edinburgh Criteria cohort might have undergone surgery. The number of positive hemorrhagic biomarkers, including ICH, CMBs, and cSS in MRI scans in our cohort, was similar to those published for the Boston Criteria v2.0 cohort. However, the non-hemorrhagic biomarkers exhibited substantial differences. The multi-spot WMH pattern was higher in our cohort, whereas severe EPVS in the centrum semiovale was absent. These differences may result from the obscuring of severe and large ICH that require surgical evacuation to detect EPVS in MRI scans.

In this cohort, the overall applicability of the current criteria revealed promising results with high sensitivity and specificity despite the small sample size. The AUC of the simplified Edinburgh Criteria when separating patients into high–intermediate and low probability groups both exhibited fair accuracy, which aligns with previous studies.[9] However, only applying the simplified Edinburgh Criteria using this cut-off (rule-out criteria) could misdiagnose some pathologically confirmed patients as having a low probability of CAA (approximately 27.0%). If clinical information still raises suspicion of CAA with low probability based on the simplified Edinburgh Criteria, an MRI scan is suggested to increase the diagnostic accuracy. The MRI scan, especially at a higher magnetic strength, could achieve a higher detection rate of hemorrhagic (CMBs, cSS, and small ICH) and non-hemorrhagic (EPVS and multi-spot pattern of WMHs) biomarkers than a CT scan.[1, 19, 20] However, for patients with a lobar ICH and only a CT scan, where MRI is not feasible, the simplified Edinburgh Criteria are a reasonable alternative for diagnosis, according to the International CAA Association (iCAAA) and the World Stroke Organization (WSO) statement in 2025.[21]

In our cohort, the Boston Criteria v2.0 exhibited higher sensitivity to diagnose probable CAA compared with the modified Boston Criteria v1.5 without compromising specificity. The primary reason for increasing sensitivity is the inclusion of non-hemorrhagic biomarkers in the diagnostic criteria. The AUC of the modified Boston Criteria v1.5 in our cohort demonstrated good accuracy and high sensitivity and specificity when using probable CAA in the Boston Criteria v2.0 as the reference standard. However, the Boston Criteria v2.0 appears to be more complex in real-world clinical practice because clinicians need to review multiple MRI sequences. The visual rating scales of non-hemorrhagic biomarkers, including EPVS and multiple subcortical WMH spots, are more challenging than counting the hemorrhagic biomarkers and require training before application. Therefore, the modified Boston Criteria v1.5 is still an acceptable diagnostic criterion in clinical practice and widely used in many clinical settings, especially for CAA-ICH or CAA-TFNE presentations.[5, 9, 22] The use of CT scans in the case of the CAA-ICH presentation remains valuable in the simplified Edinburgh Criteria as well as in the modified Boston Criteria v1.5, particularly in resource-limited settings, such as low-to-middle-income countries, where MRI access is restricted.

The recently updated scientific statement on diagnosis and management of CAA proposed by iCAAA and WSO in 2025 has highlighted the primary topics for clinicians, ranging from 1) diagnosis, testing, and prediction of ICH risk; 2) the use of antithrombotic agents and vascular interventions; 3) vascular risk factors and concomitant medications; 4) treatment of CAA manifestations; and 5) inflammatory CAA, including CAA-related inflammation and amyloid-beta-related angiitis.[21] In line with our study, the diagnostic Edinburgh Criteria and simplified version for CAA-associated lobar ICH could predict moderate or severe CAA pathology in patients with a considerable amount of lobar ICH.[9, 10, 23] Patients with CAA and multiple prior ICHs and multifocal or disseminated cSS have a higher risk of future CAA-related ICH.[24 - 27] Moreover, cSS progression over time could predict a higher risk of future CAA-related ICH.[28, 29] Apart from recurrent ICH, CAA-related ICH could result in further cognitive decline or dementia.[30, 31] In a patient with CAA presenting with acute ICH, blood pressure management should be controlled and maintained to reduce the risk of ICH recurrence and promote a good outcome similar to other causes of ICH, according to the 2022 Guideline from the American Heart Association/American Stroke Association.[32] Antithrombotic agents, including antiplatelet and anticoagulant medications, should be personalized based on major ischemic vascular events, potential bleeding risk, compliance, and patient preference.[21] Patients with CAA have been shown to have an increased risk for adverse events from anti-amyloid therapy for Alzheimer's disease. Therefore, these treatments should not be used for CAA treatment outside the context of a research trial.[33, 34]

The primary limitation of this study is the small sample size despite retrieving data over more than 10 years from a single-center pathological dataset. The major obstacles were the lack of routine sending of surgical pathological tissue from hematoma evacuation in patients with hemorrhagic stroke, which occurred throughout the clinical practice of the limited-resource country; the lack of postmortem or autopsy study; and the lack of infrastructure for a brain bank. Further multi-center collaboration and raising awareness of CAA can improve future studies in our country. Moreover, brain histopathology from normal controls and/or hypertensive arteriopathy from hematoma evacuation will enhance the diagnostic accuracy of current criteria under different settings. To bridge the gap, further collaboration between neurologists, neurosurgeons, and neuropathologists is required to encourage further surgical-pathological study of patients with hemorrhagic strokes at our center. Second, some data were unavailable because of the retrospective cohort design; therefore, a future prospective cohort will fill this gap. Third, the clinical presentation of patients from this study primarily resulted from severe ICH leading to surgery. This cohort primarily reflects the CAA-ICH population that required surgical intervention, and none of the patients had CAA-related TFNEs or cognitive impairment/dementia. Therefore, the further application and generalizability of CAA-ICH with conservative management, CAA–non-ICH, CAA in memory clinic settings, and CAA-related TFNEs, usually presented with cSAH, within the Asian population should be interpreted with caution.

For future directions, further analysis of the current clinic-radiological cohort in our institution, accompanied by the available pathological correlation, will reveal the true burden of CAA in the Thai population, especially in patients with CAA-non-ICH.

Furthermore, clinical trials of iron-chelating agents, such as deferoxamine, to reduce iron toxicity and improve the recovery outcomes in patients with acute hemorrhagic stroke and CAA or non-CAA should be studied in Thailand because of the high prevalence of thalassemia disease, which induces a relatively high iron overload.[35-37]

Conclusion

The use of the latest diagnostic criteria for CAA in the Thai population demonstrates its applicability within the broader Asian context, despite the limitations of the small sample size of the pathological cohort study. Even in resource-limited settings, expedited MRI studies are imperative to confirm the diagnosis when the CAA-ICH is suspected based on clinical presentations and/or CT findings. Timely and accurate CAA diagnosis is crucial for effective management, particularly in secondary prevention, to address bleeding concerns. Further, larger and well-designed confirmatory studies within an Asian cohort are essential to enhance our understanding of CAA in this population.

Author contributions

All authors designed and conceptualized the study, data interpretation, and revised the manuscript for intellectual content. T.P. and S.T. performed imaging analysis, data analysis, and statistical analysis. T.P., S.T., and T.T. drafted the first draft of the manuscript. S.T., A.V. supervised the project.

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Conflict of interest statement

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Data availability statement

All data are deposited locally (T.P.) and are not publicly available due to patient privacy. Deidentified data may be shared by the corresponding author upon reasonable request.

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