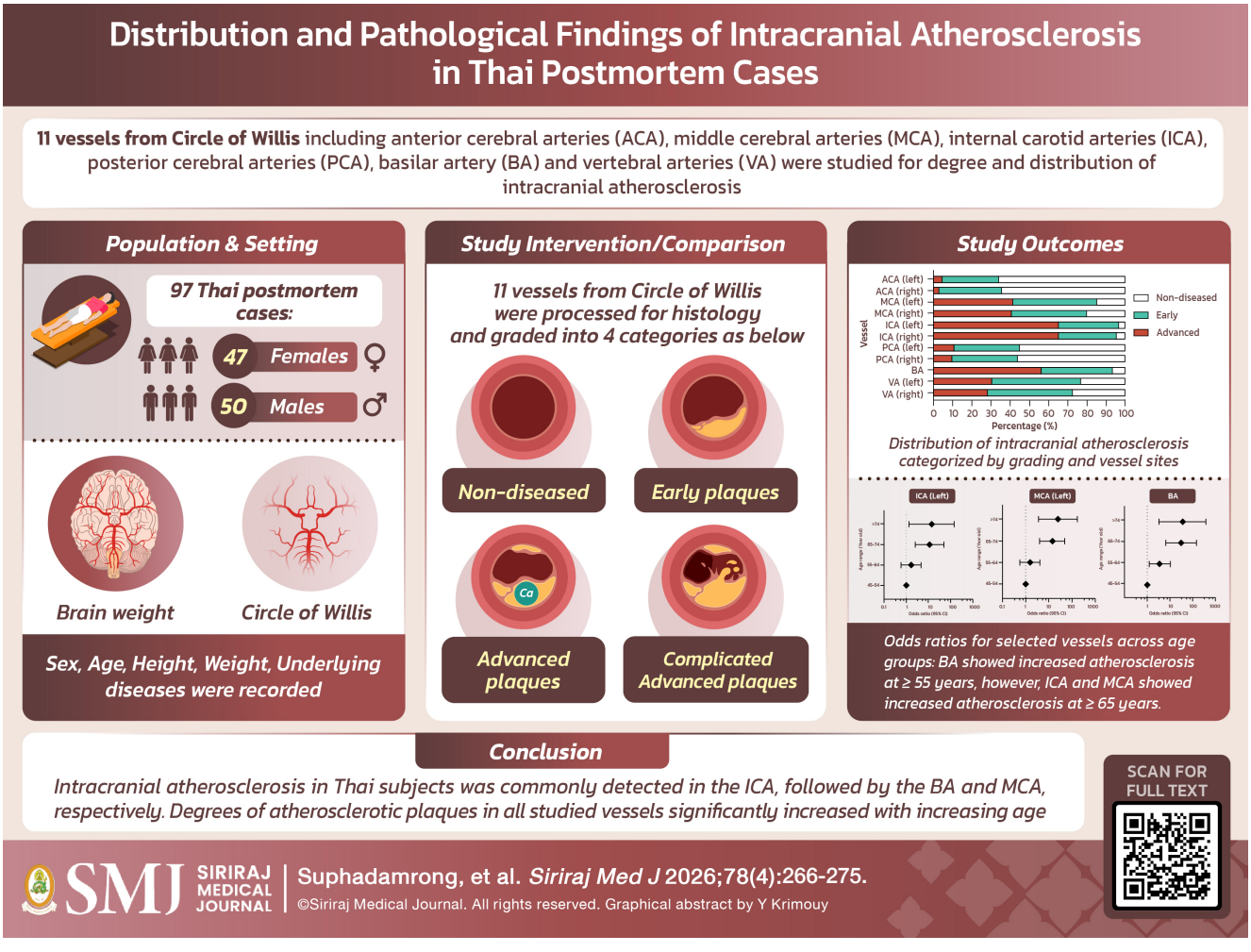
Distribution and Pathological Findings of Intracranial Atherosclerosis in Thai Postmortem Cases

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ABSTRACT

Objective: To determine the distribution and pathological findings of intracranial atherosclerosis in Thai postmortem cases.

Materials and Methods: The prospective cross-sectional study was conducted on Thai postmortem cases aged 45 years or older. Sex, age, weight, height, and brain weight were recorded for each case. Intracranial atherosclerosis was assessed in 11 vessels of the Circle of Willis (CoW), including the anterior cerebral arteries (ACA), middle cerebral arteries (MCA), internal carotid arteries (ICA), posterior cerebral arteries (PCA), basilar artery (BA) and vertebral arteries (VA), using histological examination. Grading of atherosclerotic plaques in each vessel was recorded. Descriptive statistics, bivariate correlation, and ordinal logistic regression were performed where appropriate.

Results: A total of 97 Thai subjects were recruited, consisting of 47 female and 50 male subjects, with a mean age of 61.41 years. Brain weights in male subjects were significantly higher than those in female subjects ($p < 0.001$). Brain weights in both female and male subjects were negatively correlated with increasing age ($p < 0.001$). Early and advanced atherosclerotic plaques were most frequently detected in the ICA, followed by the BA and MCA, respectively. Using ordinal logistic regression, it was found that degrees of intracranial atherosclerosis in all vessels of the CoW significantly increased with increasing age ($p < 0.05$).

Conclusion: Intracranial atherosclerosis in Thai subjects was commonly detected in the ICA, followed by the BA and MCA, respectively. The degrees of atherosclerotic plaques in all studied vessels significantly increased with increasing age.

Keywords: Intracranial atherosclerosis; brain; Thai; autopsy (Siriraj Med J 2026;78(4):266-275)

INTRODUCTION

Stroke, or cerebrovascular disease (CVD), is one of the leading causes of death worldwide, including in Thailand.[1] Suwanwela NC reported that the prevalence of stroke in Thai people over 45 years old between 2004 and 2006 was 1.88%.[2] However, Chantkran W et al. indicated that the prevalence of stroke in 2018 was 3.9%, and the prevalence rates between 2014 and 2018 were relatively stable.[1] According to these two figures, it was suggested that the prevalence of stroke in Thai people was gradually increasing. In addition, both studies stated that the prevalence of stroke in Thai people was higher in males than in females and was more prevalent with increasing age.[1,2] Increased prevalence of stroke in Thai people also affects strategic plans to enhance quality of life in stroke patients. A previous study stated that high modified Barthel Index score at discharge time had an effect on good quality of life in Thai stroke patients.[3] Intracranial atherosclerosis is considered one of the main causes of ischemic stroke, and it is more prevalent in Asian populations than in Caucasian populations.[4,5] A previous study indicated that intracranial atherosclerosis was present in approximately 45–62% of patients with ischemic stroke[4], whereas the prevalence of intracranial atherosclerosis in asymptomatic Chinese and Japanese people was 20.6% and 15%, respectively.[5] In addition, the prevalence of the posterior circulation ischemic stroke in Korean people was 39.8% of all ischemic stroke[6] whereas overall prevalence of the posterior circulation stroke ranged from 5% to 19%.[7] These figures may indicate that Asian populations may have different patterns of intracranial atherosclerosis from Caucasian populations.

Data on the distribution of intracranial atherosclerosis are relatively limited. Denswil NP et al. stated that intracranial atherosclerosis was most commonly found in the basilar artery (BA), followed by the internal carotid arteries (ICA), vertebral arteries (VA), and middle cerebral arteries (MCA), respectively.[8] In addition, advanced stages of atherosclerosis were most commonly detected in the ICA followed by the BA and VA, respectively.[8] However, Llopis G et al. suggested that intracranial atherosclerosis was most commonly detected in the posterior cerebral arteries (PCA) and BA, followed by the MCA, ICA, and VA, respectively.[9] Moreover, people aged 40 years or older had a significantly higher prevalence of intracranial atherosclerosis than those aged 30–39 years or younger.[9] Furthermore, classification of intracranial atherosclerosis was potentially associated with ischemic stroke, because the degree of intracranial stenosis was not directly associated with occurrence of ischemic stroke, in contrast to coronary artery disease.[8,10] According to previous studies, plaque calcification and some types of complicated plaques, such as intraplaque hemorrhage, were potentially related to the occurrence of ischemic

stroke.[8,10] Therefore, the pathological characteristics and distribution of intracranial atherosclerosis are likely to be important data for further studies of stroke in the Thai population.

Currently, there is still scarce information about the distribution and characteristics of intracranial atherosclerosis in Thai people. Moreover, Thai people that are located in South East Asia may present with more prominent intracranial atherosclerosis in the posterior circulation. Thus, the authors aim to study its distribution and pathological findings in Thai postmortem cases. In addition, the authors will also consider the association between anthropological parameters and intracranial atherosclerosis in the Thai population. Age classification and severity of intracranial atherosclerosis in each vessel will be studied to demonstrate the difference patterns of vessels in the anterior and posterior circulation. This study will provide data on intracranial atherosclerosis in Thai people to expand regional analysis of intracranial atherosclerosis in Asian populations. Thai-specific age thresholds in developing intracranial atherosclerosis will be analyzed in this study to deliver fundamental findings in Thai population. This information will be important data for further studies of the occurrence of CVD and the relationship between sites of stroke and intracranial atherosclerosis in the Thai population.

MATERIALS AND METHODS

Study design and data collection

A prospective cross-sectional study was conducted on subjects sent for autopsy at the Department of Forensic Medicine, Siriraj Hospital, Mahidol University. The inclusion criteria were Thai individuals aged 45 years or older who were sent for autopsy at the Department of Forensic Medicine, Siriraj Hospital, Mahidol University between 16 December 2024 and 30 September 2025. The exclusion criteria included decomposed bodies, bodies with head injury, and bodies with any gross pathologies in the white matter of the brain. This study was approved by the Siriraj Institutional Review Board, Faculty of Medicine Siriraj Hospital, Mahidol University (COA No. Si 967/2024; SIRB protocol No. 888/2567 (IRB2)).

Sex, age, weight, height, brain weight, underlying diseases, and cause of death were recorded for each case. Body weights were quantified in kilograms (kg) on an Empire® digital balance. Body heights were measured in centimeters (cm) from the vertex to the heel using a stainless-steel tape measure. Brain weights were assessed by using a Sunford® digital balance, model FEH5000. Body mass index (BMI) was calculated by dividing weight (kg) by the square of height in meters. The Du Bois and Du Bois formula was employed for the calculation of body surface area (BSA), expressed in square meters, as described in Equation 1.[11,12]

$$BSA\ [m^2] = 0.007184 \times height\ [cm]^{0.725} \times weight\ [kg]^{0.425}$$

Equation 1

Evaluation of intracranial atherosclerosis

When the routine autopsy procedure was performed, the skull cap was removed and the brain was exposed. Then, the brain was removed from the base of the skull by severing the attachment sites of brain structures to the base of the skull, including the olfactory bulb, optic chiasma, both sides of the ICA, all cranial nerves, and both sides of the VA.[13] Next, each brain was placed for photography and was weighed on a digital balance to assess brain weight. Next, the collected brains were fixed in 10% formalin solution for one week. Then, the Circle of Willis (CoW) was carefully dissected from the base of the brain and preserved as completely as possible, as shown in Fig 1. After complete dissection, both ACA, both MCA, both ICA, both PCA, the BA, and both VA were identified. Thus, a total of 11 arteries were dissected from the CoW and prepared for the next step. Then, they



Fig 1. Dissection of the Circle of Willis.

were serially cut into multiple sections and prepared for histological study. The sampling strategy included all segments of both ICA, both VA and the BA whereas the other vessels were taken for 5 segments from the origins (around 2 cm from the origins of vessels) as the representative samples for histology. After histological slides of all vessels were prepared, the first author identified all slides and blinded them to send for the corresponding author and the consultant pathologist in the department for grading the atherosclerotic plaques. Pathological findings at each site of the Circle of Willis from both the left and right sides were identified according to the classification stated below.

Classification of atherosclerotic plaques

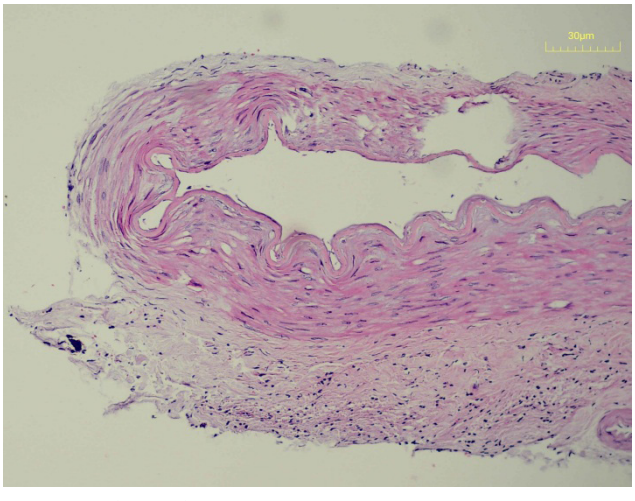
All CoW sections were stained with haematoxylin–eosin (H&E). Grading of intracranial atherosclerosis was categorized according to a revised American Heart Association classification[14] and the description from the study of Denswil NP et al.[8] Atherosclerotic plaques were classified into four groups, as described below and shown in Fig 2:

1. Non-diseased group: no intimal thickening or inflammatory infiltration
2. Early plaques: intimal thickening (accumulation of smooth muscle cells and/or proteoglycans) and fatty streaks (foamy macrophages)
3. Advanced plaques: fibrous, lipid-rich, and/or calcified tissue with a fibrous cap in which >40% of the area was lipid core or calcified tissue
4. Complicated advanced plaques: fibrous cap rupture, intraplaque hemorrhage (IPH), or chronic total occlusion of the lumen

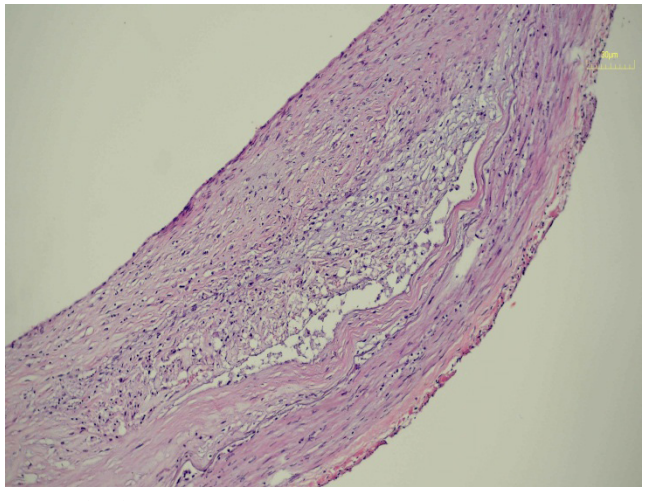
Histological findings were reviewed by two raters including the corresponding author and the consultant pathologist in the department. Raters were blinded and the information after review was collected by the first author to analyze for inter-rater reliability.

Statistical analysis

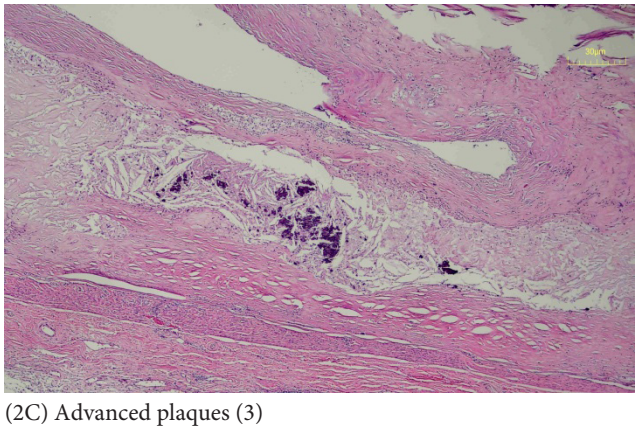
Statistical analysis was performed using IBM SPSS® Statistics for Windows, version 29. Descriptive statistics, including the mean, median, and standard deviation (SD), were analyzed. Comparisons of continuous data



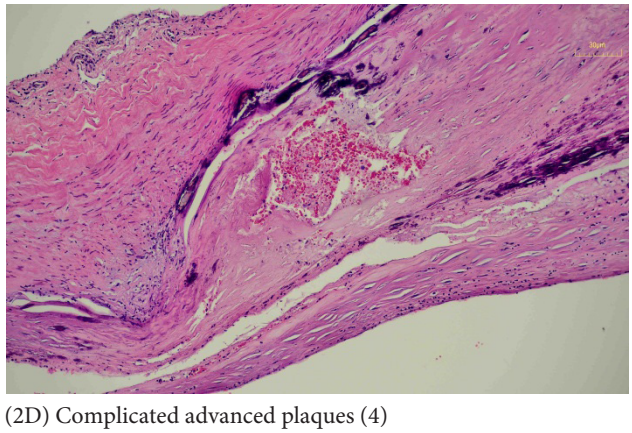
(2A) Non-diseased group (1)



(2B) Early plaques (2)



(2C) Advanced plaques (3)



(2D) Complicated advanced plaques (4)

Fig 2. Classification of pathological findings of intracranial atherosclerosis.

between female and male subjects were performed using the Mann–Whitney U test. Correlations between anthropometric parameters and brain weight were assessed using Spearman's correlation. Ordinal logistic regression with Bonferroni's correction was performed to evaluate associations between age and intracranial atherosclerosis. Cohen's Kappa coefficient score was analyzed for inter-rater reliability and a Kappa coefficient score in this study was 0.91 reflecting good agreement between the corresponding author and the consultant pathologist in the department.

RESULTS

There were 97 Thai subjects recruited in this study, consisting of 47 females (48.45%) and 50 males (51.55%). The mean age among the 97 subjects was 61.41 years. The mean BMI and BSA were 25.31 ± 4.83 kg/m^2 and 1.72 ± 0.17 m^2, respectively. A comparison of descriptive statistics between female and male subjects is shown in Table 1. BSA and brain weight in male subjects were significantly higher than those in female subjects ($p < 0.001$).

Table 2 shows correlations between brain weight and anthropometric parameters. The data showed significant negative correlations between brain weight and age in both female and male subjects ($p = 0.001$ and $p < 0.001$, respectively), whereas BMI and BSA did not show significant correlations with brain weight. Linear regression analysis between age and brain weight for both female and male subjects is shown in Fig 3. According to the linear regression curves, brain weight in male subjects decreased at a more rapid rate than in female subjects.

When subjects were divided into two groups based on underlying diseases related to metabolic syndrome, including diabetes mellitus, hypertension, dyslipidemia, coronary artery disease, gout, and chronic kidney disease, there were 42 subjects who did not have histories of these underlying diseases (35 subjects with no history of any underlying diseases and seven subjects with other underlying diseases, including asthma/chronic obstructive pulmonary disease and psychiatric disorders), whereas there were 55 subjects who had at least one of these underlying diseases. Comparison of brain weights between these two groups was performed using the Mann–Whitney U test.

TABLE 1. Comparison of descriptive statistics between female and male subjects.

Parameters	Female (mean ± SD, range)	Male (mean ± SD, range)	p-value
Age (years)	61.15 ± 10.62 (45–85)	61.66 ± 10.32 (45–85)	0.795
BMI (kg/m^2)	26.33 ± 5.78 (16.81–41.20)	24.34 ± 3.54 (17.64–35.45)	0.161
BSA (m^2)	1.66 ± 0.20 (1.35–2.12)	1.78 ± 0.13 (1.54–2.27)	<0.001
Brain weight (g)	1,163.66 ± 83.31 (1,032–1,317)	1,295.64 ± 102.59 (1,060–1,454)	<0.001

TABLE 2. Correlation between brain weight and anthropometric parameters.

Subjects	Correlation between brain weight and anthropometric parameters		Spearman's correlation	p-value
Female (N = 47)	Brain weight vs	Age (years)	−0.457	0.001
		BMI (kg/m^2)	0.238	0.108
		BSA(m^2)	0.201	0.175
Male (N = 50)	Brain weight vs	Age (years)	−0.747	<0.001
		BMI (kg/m^2)	0.118	0.414
		BSA(m^2)	0.120	0.408

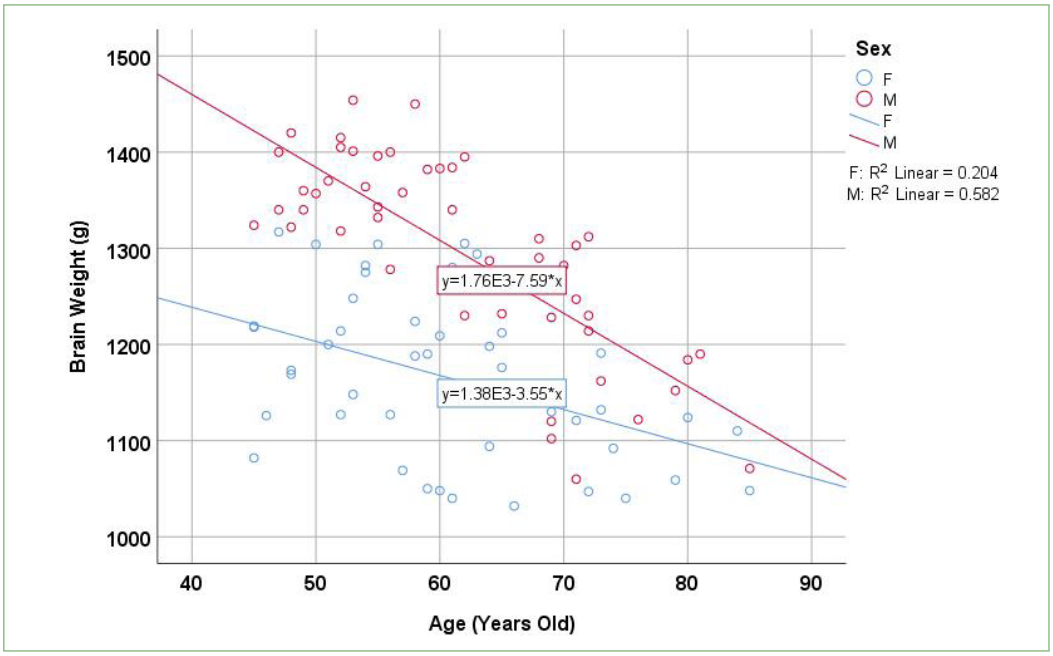


Fig 3. Relationship between age and brain weight (g) in both female (blue dots and line) and male (red dots and line) subjects.

Median (mean ± SD) brain weights in subjects without underlying diseases and in subjects with underlying diseases related to metabolic syndrome were 1,247.50 g (1,238.33 ± 112.87 g) and 1,212.00 g (1226.62 ± 116.38 g), respectively. Although brain weights in subjects without underlying diseases were relatively higher than those in subjects with underlying diseases related to metabolic syndrome, statistical analysis did not show a significant difference between these two groups (p = 0.526).

The distribution of intracranial atherosclerosis across six vessel types of the Circle of Willis is shown in Fig 4. It was found that advanced stages of atherosclerosis were more common in the ICA, followed by the BA and MCA, respectively, whereas the ACA was least likely to have advanced stages of atherosclerosis.

The subjects were divided into four groups according to age: 45–54, 55–64, 65–74 and ≥75 years. As the number of cases in group 4 (degree of intracranial atherosclerosis) was small, further statistical analysis was performed by combining groups 3 and 4. Thus, the degree of intracranial atherosclerosis was classified into three groups for statistical analysis in this study. Ordinal logistic regression with Bonferroni's correction was performed on the three severity groups of intracranial atherosclerosis in each vessel and the four age groups to demonstrate the degree of risk associated with age. The results are shown with forest plots in Fig 5A and 5B. These findings showed that the degrees of intracranial atherosclerosis in all vessels increased with increasing age, with the highest odds ratio (OR) observed in the BA. In addition, the BA and left VA (posterior circulation) showed a significantly increased degree of intracranial atherosclerosis from age ≥55 years, whereas the other vessels showed this increase from age ≥65 years.

DISCUSSION

This study showed that brain weights in Thai male subjects were significantly higher than those in Thai

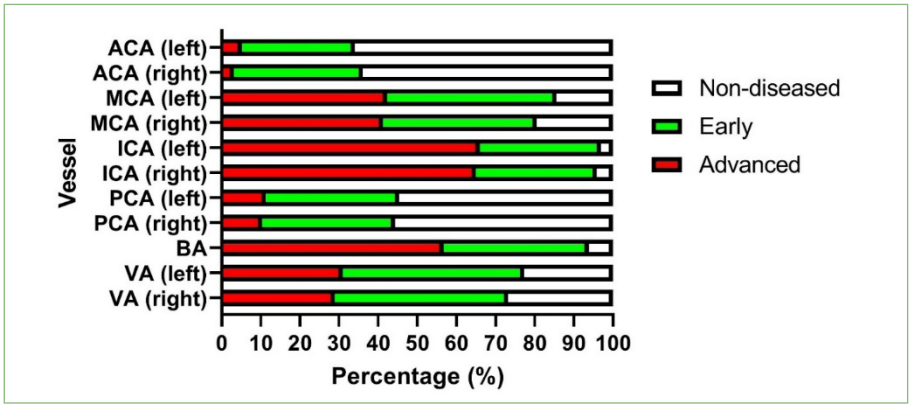


Fig 4. Distribution of intracranial atherosclerosis across six vessel types of the CoW (11 vessels).

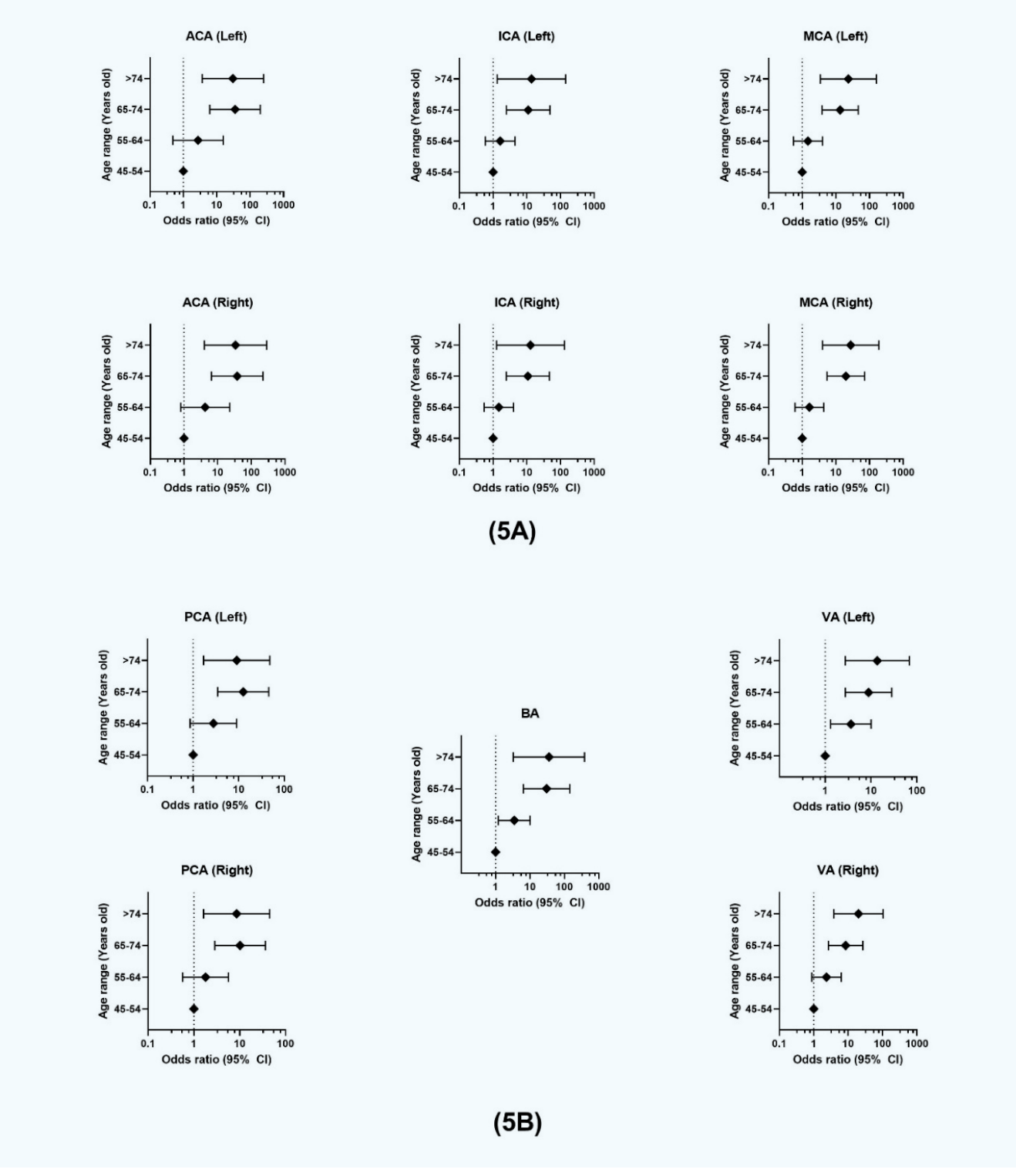


Fig 5. Odds ratios and 95% confidence interval (95% CI) for six vessel types of the CoW (11 vessels) across four age groups: (5A): ACA (left and right), ICA (left and right) and MCA (left and right) and (5B): PCA (left and right), BA and VA (left and right).

female subjects. In addition, brain weights in both Thai male and female subjects significantly decreased with increasing age. These findings were consistent with previous studies.[15,16] When focusing on brain weight after 45 years of age, it was suggested that brain weights in Thai male and female subjects were smaller than those reported in a previous study.[16] That study indicated that rate of brain weight reduction in both male and female subjects occurred to a similar degree, resulting in brain weights that were 10-15% higher in males than in females.[16] However, this study showed that the rate of brain weight reduction in Thai male subjects was

more rapid than that in Thai female subjects, as shown in Fig 3. This study also showed that brain weights in subjects who had underlying diseases related to metabolic syndrome were not significantly different from those in subjects who had no underlying diseases. However, this finding was in contrast to a previous study that showed a significant difference in brain weights between subjects who had underlying diseases and those who had no underlying diseases.[15] Brain weights in subjects who had hypertension, coronary artery disease, dyslipidemia, and a history of smoking were significantly lower than those in subjects who had no underlying diseases.[15] As this study consisted of a relatively small number of subjects, a larger sample size should be recruited in further studies to elucidate this finding.

This study showed that intracranial atherosclerosis was most commonly detected in the ICA, followed by the BA, MCA, and VA, respectively (as shown in Fig 4). In addition, early and advanced atherosclerotic plaques were present in a similar sequence (Fig 4). Our results were comparable to a previous study that showed the most common areas of intracranial atherosclerosis occurring in the BA, followed by the ICA, VA, and MCA, respectively.[8] However, the previous study also reported that advanced stages of intracranial atherosclerosis were most commonly found in the ICA, followed by the BA, VA, and MCA, respectively.[8] When considering the ACA and PCA, it was found that atherosclerosis in the ACA and PCA was present in approximately 30–40%, whereas advanced atherosclerotic plaques were present in <10% for the ACA and around 10% for the PCA, respectively. This finding contrasts with the previous study, which reported atherosclerosis in the ACA and PCA at 75–80%[8], while advanced atherosclerotic plaques were present in 10–20%. This may result from the difference in age range between these two studies, because our study had an overall mean age of 61.41 years, with a similar mean age between male and female subjects. However, the previous study had an overall median age of 68 years, with the mean ages for male and female subjects being 62.4 and 72.9 years, respectively.[8] The higher age group in the previous study may have resulted in a higher prevalence of intracranial atherosclerosis in the ACA and PCA.

After atherosclerotic involvement of each vessel in CoW was examined, age group and all six vessel types in CoW were analyzed for potential difference between the anterior and posterior circulation. When ordinal logistic regression was performed, it was found that the degree of intracranial atherosclerosis in all of vessels of the CoW significantly increased with increasing age groups both in the anterior and posterior circulation. For the anterior circulation, including the ICA, MCA, and ACA, the risk of intracranial atherosclerosis increased significantly at the age group ≥65 years. Interestingly, for the posterior circulation, including the BA and left VA, the risk of intracranial atherosclerosis increased significantly at the age group ≥55 years, with the BA showing a higher OR than the other common vessels, including the ICA and MCA. This finding suggests that the BA (posterior circulation) in Thai subjects in this study presents an earlier and higher risk of atherosclerosis than the ICA and MCA. Because intracranial atherosclerotic stenosis is more prevalent in Asian and African-American populations compared to Caucasian populations[4,5,10], this finding may serve as a foundational basis for future research, particularly in Thai patients ≥55 years old, who are more prone to have intracranial atherosclerosis. Moreover, this result was consistent with the finding in the previous research that showed the higher rate of infarction location at the middle territory supplied by the BA than other territories in the posterior circulation and this study suggested that developed atheromatous plaque in the BA may play an important role in the posterior circulation stroke.[6] The study in Spanish people in Madrid showed that the BA as well as MCA and PCA presented with the highest frequency in atheromatous plaques among overall vessels in CoW.[9] This previous study hypothesized that this may be related to high turbulent flow in these vessels and this may explain earlier atherosclerotic development of the BA in this study.[9] In addition, a previous study suggested that subjects with posterior circulation strokes had higher plaque thickness and luminal area at the plaque than subjects with anterior circulation strokes, even though they had similar degrees of atherosclerosis.[17] Because plaque characterization in this study was limited to histological grading without further identification of plaque composition and the supporting study in molecular staining and hemodynamic findings, the association between plaque development and other biological characteristics could not be performed. Thus, further research should concentrate on comparing the characteristics of atherosclerotic plaques between anterior and posterior circulation.

This study had several limitations. First, the validity of the histories of underlying diseases in autopsy cases may be questionable, because subjects might not have informed their relatives about their underlying conditions. In addition, some subjects might have experienced symptoms related to underlying diseases but did not seek medical attention or treatment for these symptoms. This may lead to categorical bias for negative information in underlying diseases related to metabolic syndromes.

Second, the number of subjects who were ≥75 years old was relatively small compared with other age groups. This may have affected the prevalence of intracranial atherosclerosis, especially in the ACA and PCA, where the incidence of advanced atherosclerotic plaques was low. Third, this study did not include brains that had any gross pathological findings such as infarction or hemorrhage. Thus, this study did not provide the correlation between pathological findings and gross stroke patterns. Functional implication of atheromatous plaque characteristics for gross stroke patterns should be carefully interpreted. Lastly, our study had a relatively small sample size. Therefore, the ordinal logistic regression analysis could not be performed separately between male and female subjects to assess the effect of sex in the Thai population, although a previous study showed no significant difference in the degree of atherosclerosis between male and female subjects.[8] Thus, further research with a larger sample size should be conducted to elucidate this finding in the Thai population.

CONCLUSIONS

Brain weight was significantly negatively associated with increasing age. In addition, brain weight in Thai male subjects was significantly higher than in female subjects. Intracranial atherosclerosis in Thai subjects was most prevalent in the ICA, followed by the BA, MCA, and VA, respectively. The degree of atherosclerotic plaques in all 11 vessels of the CoW significantly increased with age, particularly in the BA.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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DECLARATIONS

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The authors did not receive grants or funding for this research.

Conflict of Interest

The authors declare no potential conflict of interest.

Registration Number of Clinical Trial

Not applicable.

Authors' Contributions

Conceptualization and Methodology, P.S., P.P.; Investigation, P.S.; Formal analysis, P.S.; Data Curation, P.S., P.P.; Visualization and Writing – Original Draft, P.S.; Writing – Review & Editing, P.S., P.P.; Supervision, P.P. All authors read and approved the final version of this manuscript submitted for publication.

Use of Artificial Intelligence

The authors did not employ any artificial intelligence tools in the analysis, writing or any steps of development of this research.

Ethical Approval

This study was approved by the Siriraj Institutional Review Board, Faculty of Medicine Siriraj Hospital, Mahidol University (COA No. Si 967/2024; SIRB protocol No. 888/2567 (IRB2)).

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