

Asymptomatic Basilar Artery Plaque Distribution and Vascular Geometry

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Aim: Development of atherosclerotic plaques is affected by vascular geometry and hemodynamics. Hemodynamics in the basilar artery (BA) is unique as the flow converges from vertebral arteries (VAs). Here, we investigated the characteristics of BA plaque based on VA and BA geometry.

Methods: Consecutive patients evaluated using high-resolution magnetic resonance imaging (MRI) at a general health center were screened. Geometric characteristics of VA (VA dominance and VA-BA angles) and BA (BA convexity and BA angles) were assessed. The burden of BA plaques was investigated in each wall (anterior, posterior, left, and right lateral). The characteristics of BA plaques were compared according to VA dominance (right vs. left), BA angle of lateral view (lateral mid-BA angle; dichotomized), and total plaque burden (divided by tertiles).

Results: Of the 1029 subjects, BA plaques were observed in 98 (9.5%) patients, and were more frequently located at the anterior wall (32.4%) and posterior wall (35.0%) than the right wall (15.3%) and left lateral wall (17.6%). Right and left lateral plaques were more frequent in the left and right convex BA, respectively ($p=0.009$ and $p=0.024$, respectively). Anterior plaques were more frequently observed in low lateral mid-BA angle ($p=0.043$). BA plaques were predominant in anterior and posterior walls in patients with lower plaque burden, whereas they were predominant in right and left lateral walls in patients with higher plaque burden ($p=0.001$ and $p=0.025$, respectively).

Conclusions: Asymptomatic BA plaque location was associated with BA convexity and lateral mid-BA angle. The anteriorly and posteriorly located BA plaques may extend to the lateral walls as the plaque burden increases.

Key words: Basilar artery, Plaque geometry, HR-MRI

Introduction

Atherosclerosis is a progressive disease¹, the initiation and progression of which is associated with local hemodynamic stress, typically altered by the geometry of vasculature². Of note, areas where the artery bifurcates, bends, or merges are susceptible to atherosclerotic development³. The vertebrobasilar system demonstrates a high variation in anatomy. Although two vertebral arteries (VAs) join to form a common basilar artery (BA) trunk, the dominance of one VA is often

observed⁴. At the vertebrobasilar junction (VBJ), various angles between VAs and BA are measurable. These angles may influence the hemodynamics and blood flow which merge from each VA to the BA. The shear stress inside the vertebrobasilar arterial system can be affected by these geometrical parameters, leading to early atherosclerotic changes or progression of pre-existing atherosclerotic plaques.

High-resolution magnetic resonance imaging (HR-MRI) is useful to detect early atherosclerotic changes, before they are discernible on routine angiog-

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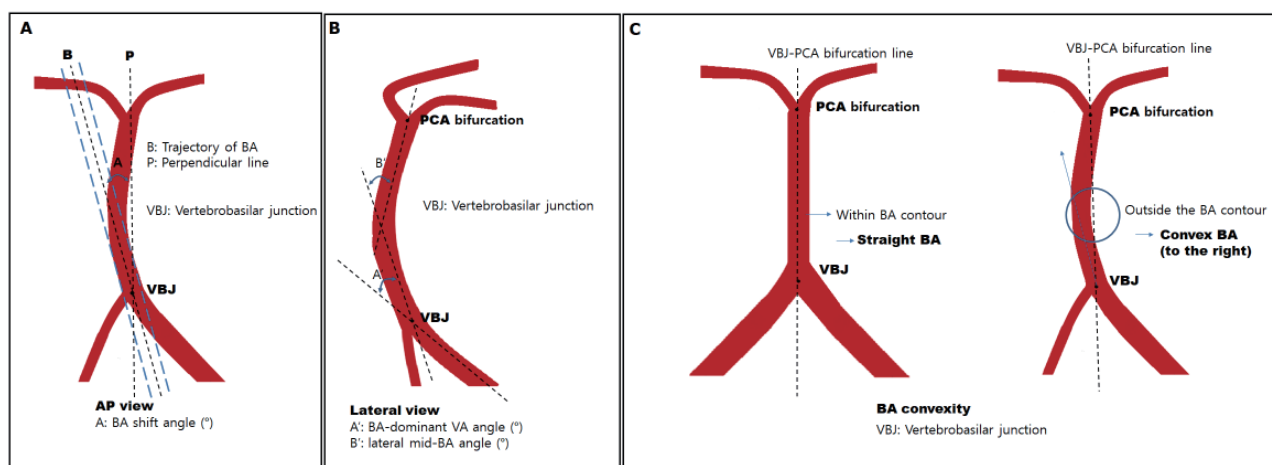


Fig. 1. Illustration of the measurement of vascular geometry in vertebrobasilar arterial system
A, anteroposterior view. B, lateral view. C, convexity of the basilar artery.

raphy (i.e., magnetic resonance angiography [MRA] or computed tomography angiography [CTA])^{5, 6}. The association between atherosclerosis and vascular geometry has been investigated in patients with pontine infarction⁷ or BA stenosis⁸. BA plaques were observed in a high proportion of patients with pontine infarction, although they were not visible on MRA⁹. Therefore, individuals without a previous history of stroke need to be investigated for early BA atherosclerotic changes and the progression associated with vascular geometry, leveraging the use of HR-MRI.

Aim

In this study, we investigated the incidence of BA atherosclerotic plaques in individuals who received HR-MRI during a routine health check-up. In addition, the association between various geometrical parameters of the vertebrobasilar arteries and BA plaque location, as well as the change in the plaque distribution according to the plaque burden, was quantitatively analyzed.

Methods

Study Population

All individuals older than 20 years visiting a non-advertised health promotion center of a university hospital to receive MRA between September 2009 and June 2010 were consecutively enrolled in the study. An additional HR-MRI, focusing on the BA, was performed in these individuals. Those with a previous history of stroke, poor imaging quality, none visualized or unmeasurable BA or VA at any side, asymptomatic pontine ischemic lesions, and without HR-

MRI data were excluded. This study was approved by the local institutional review board for retrospective analysis and consent waiver was granted.

Image Acquisition

All MRIs were performed using 3-Tesla MR machines (Achieva; Philips, Best, the Netherlands) with an 8-channel SENSE head coil. HR-MRI, proton density image (PDI) was obtained along the axis of BA using the following parameters: relaxation time/echo time=2500/30 ms, matrix=320×220, field of view=120×110 mm, and slice thickness/gap=2/0 mm. The black-blood technique with a prerogional saturation pulse of 80-mm thickness was used to saturate the incoming arterial flow.

Measurement of Vascular Geometry

The geometry of the vertebrobasilar arterial system was evaluated using the following aspects: 1) the dominance of VA, 2) the direction of BA convexity, 3) various angles measured from the anteroposterior (AP) view, 4) various angles measured from the lateral view, and 5) BA angle from the lateral view (lateral mid-BA angle; **Fig. 1A**).

From the AP view, three imaginary lines were drawn from the VBJ, maximally including each vessel in the midline (BA, left VA, and right VA). For BA, the trajectory of BA from the VBJ (blue broken line) was drawn, and the midline of the trajectory (B line in **Fig. 1A**) was used. The BA shift angle was defined as the angle between the trajectory of BA from VBJ (B line) and the perpendicular line (P line; **Fig. 1A**). From the lateral view, the angle between BA and dominant VA (BA-VA angle), and the lateral mid-BA angle were measured. An imaginary line between the VBJ

and posterior cerebral artery (PCA) bifurcation point was drawn, maximally including BA in the midline. The point where the two lines conjoined was regarded as the mid-BA point, and the angle between the two lines was regarded as lateral mid-BA angle (Fig. 1B).

The dominant VA was defined as having a larger diameter or as the VA connected to the BA in a more straight fashion^{4, 10}. The diameter of each VA was measured at the point 3-mm apart from the VBJ⁴. The direction of BA convex curvature was defined according to the BA course from the VBJ (right convex, left convex, and straight BA)⁴. A line between VBJ and PCA bifurcation point was drawn. If the VBJ-PCA bifurcation line was within the contour of BA, it was considered as having a straight BA. If the VBJ-PCA bifurcation line was outside the BA contour, it was regarded as convex, and the convexity (right or left) was determined by the trajectory from the VBJ (Fig. 1C). The vascular geometry was measured by an experienced neuroradiologist (Y. L.), blinded to all clinical data and the plaque location.

Measurement of Basilar Plaque

BA plaques were defined as a focal, eccentric wall thickening on PDI cross section, indicating an atheromatous plaque. The presence, length, volume, and the vertical and horizontal location of BA plaque were investigated using the PDI.

As the slice thickness of our protocol was 2 mm, the plaque length was $2 \times$ the sum of the number of axial slices with visible BA plaque. Similarly, the plaque proximity to VBJ was calculated as $2 \times$ the number of slices where the plaque was first observed from the VBJ¹¹. The plaque volume was calculated based on the sum of the plaque area measured from each slice. The plaque area on each slice was traced manually and quantified using an image analyzer (MIPAV; Medical Image Processing Analysis and Visualization: National Institutes of Health, Bethesda, MD, USA)⁶.

To define the horizontal location, we refer a previous report showing the plaque distribution on middle cerebral artery for reference¹². All cross sections of the BA were divided into four quadrants: anterior, right lateral, posterior, or left lateral. If the plaque was distributed in more than two quadrants, the quadrant with the maximal plaque thickness was chosen. The distribution of plaque in each quadrant was presented as the percentage of cross sections classified into one of the four quadrants, on each slices demonstrating a BA plaque (Fig. 2) The average of percentages throughout the slices including BA plaque was used as the plaque burden in each quadrant. The degree of BA stenosis was also measured on HR-MRI by dividing

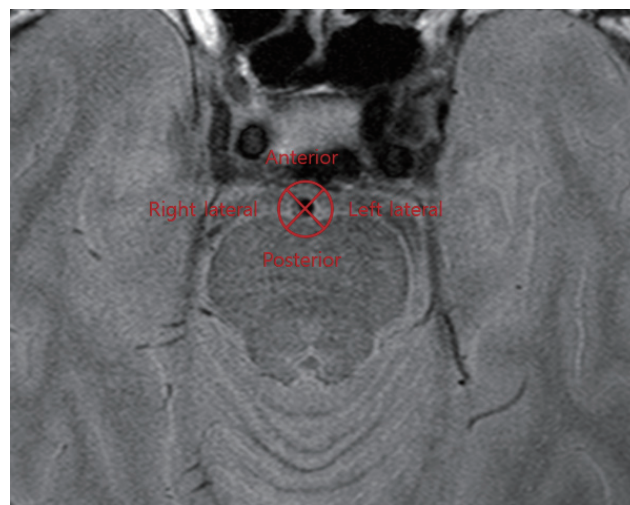


Fig. 2. Distribution of the plaque burden at basilar artery

“blood lumen area” excluding the plaque by “vessel inner wall area” and multiplying by 100¹³). The location of BA plaque was measured by a stroke neurologist (H. Y. K.), blinded to all clinical and MRA data.

Statistical Analysis

The differences in the plaque distribution were measured using Kruskal–Wallis test of the mean percentages of the distribution based on Tukey’s test using ranks for multiple comparisons. After defining the dominant VA type, we compared the clinical factors, BA curvature, and the distribution and characters of BA plaque according to VA dominance. The distribution was also analyzed according to the BA curvature direction. To evaluate the influence of lateral mid-BA angle on plaque distribution, we dichotomized the participants according to the lateral mid-BA angle. The degree of plaque burden was divided into three tertiles, and clinical factors and distribution and characteristics of BA plaque were compared among the three groups. Chi-square test, Student *t*-test, and Mann–Whitney *u* test were used as appropriate¹⁴. Multivariate analysis was performed to investigate the independent factors related to the plaque burden in each location. Demographics, risk factors, dominance of VA, BA angle (lateral mid-BA view; high vs. low), and the plaque burden (low, middle, and high) were entered for each model. A probability value of <0.05 was considered significant. All statistical analyses were performed using the SPSS software for Windows (version 17.0; SPSS Inc.).

Results

Of the 1245 individuals who were screened dur-

Table 1. The distribution and characteristics of patients with BA plaque

Characteristic	No. of patients (%) or mean [SD]
Age in years	68.2 [9.0]
Men	48 (49.0)
Hypertension	74 (75.5)
Diabetes	33 (33.7)
Hyperlipidemia	10 (10.2)
Smoking	19 (19.4)
Alcohol users	29 (29.6)
Plaque distribution	
Anterior	32.4 [40.0]
Right lateral	15.3 [29.0]
Left lateral	17.4 [30.3]
Posterior	35.0 [41.8]
Plaque characters	
Plaque proximity to VA confluence, mm	5.2 [4.5]
Plaque length, mm	8.4 [5.7]
Degree of BA stenosis on HR-MRI	36.6 [14.6]
Plaque burden, mm ³	37.6 [32.4]

Results expressed in number of patients (%) or mean [SD].

VA, vertebral artery; BA, basilar artery; MRA, magnetic resonance angiography; HR-MRI, high-resolution MRI.

ing the study period, 216 patients were excluded (absence of HR-MRI data: 201; poor image quality: 8; and none visualized or unmeasurable BA or vertebral artery: $n=7$), thereby enrolling 1029 patients into the study. Of the 1029 enrolled participants, BA plaques were present in 98 (9.5%) patients. The mean age of patients with BA plaques was 68.2 (SD=9.0) years, and 48 of these patients (49.0%) were men. The baseline demographics of these patients are presented in **Table 1**.

BA plaques were more frequently located at the posterior wall (35.0%) and anterior wall (32.4%), followed by the right lateral wall (15.3%) and left lateral wall (17.4%). The mean plaque length and volume (SD) were 8.4 mm (5.7) and 37.6 mm³ (32.4), respectively.

Geometric Characteristics and The Distribution of BA Plaques

From the AP view, the diameter of VA was significantly different between right and left VA (2.4 ± 0.6 vs. 2.6 ± 0.7 mm, respectively), and the dominant VA was more frequent on the left side than the right side (61 vs. 37 patients, respectively). There was no difference in terms of demographics and risk factors between patients with right and left dominant VA. In addition, the dominant pattern of VA could not be attributed to plaque distribution or BA plaques characteristics (**Table 2**). However, the dominant VA of

one side was associated with the convex curvature of the BA to the contralateral side ($p=0.030$).

Right convexity was demonstrated in 45 (46%) patients, left convexity in 30 (31%) patients, and straight BA in 23 (23%) patients. There was no difference in the burden of plaques located at anterior or posterior BA walls according to the direction of BA convexity from the AP view. However, BA plaque distribution on the right lateral wall was higher in patients with left convex BA than in those with right convex or straight BA (27.8% vs. 7.1% or 15.0%, respectively; $p=0.009$). Moreover, the BA plaque distribution on the left lateral wall was more frequent in patients with right convex BA than those with left convex or straight BA (26.1% vs. 7.9% or 12.6%, respectively; $p=0.024$). The plaque distribution on the right lateral wall ($r=0.268$, $p=0.008$) and left lateral wall ($r=0.230$, $p=0.023$) demonstrated a weak but significant correlation with the degree of BA shift angle toward the opposite direction.

From the lateral view, the mean angle (SD) of lateral mid-BA was 21.4° (15.3), and the mean BA-VA angle (SD) was 14.00° (28.1). There was no difference in terms of demographics and risk factors between patients with high and low lateral mid-BA angle (**Table 3**). The presence of anterior BA plaques was higher in patients with low lateral mid-BA angle than in those with high lateral mid-BA angle (41.0% vs. 23.8%; $p=0.043$), whereas the posterior distribu-

Table 2. Characteristics and distribution of plaques according to the dominant vertebral artery

	Right dominant VA (<i>n</i> = 37)	Left dominant VA (<i>n</i> = 61)	<i>p</i>
Age, year	70.2 [9.7]	67.0 [8.4]	0.079
Men	19 (51.4)	29 (47.5)	0.715
Hypertension	25 (67.6)	49 (80.3)	0.154
Diabetes	12 (32.4)	21 (34.4)	0.840
Hyperlipidemia	3 (8.1)	7 (11.7)	0.576
Smoking	5 (13.5)	14 (23.0)	0.252
Alcohol users	13 (35.1)	16 (26.2)	0.349
Plaque distribution			
Anterior	29.4 [38.4]	34.2 [40.9]	0.565
Right lateral	18.6 [32.8]	16.6 [28.4]	0.399
Left lateral	18.7 [33.5]	16.6 [28.4]	0.737
Posterior	33.2 [40.9]	36.0 [42.6]	0.755
Plaque burden			
BA stenosis on HRMRI	38.6 [13.9]	35.5 [15.1]	0.331
Plaque burden, mm ³	43.0 [34.1]	34.29 [31.2]	0.200
VBJ to plaque, mm	4.59 [4.83]	5.44 [4.37]	0.373
Basilar artery axis			
BA shift angle (°), AP view	-0.5 [23.9]	-7.8 [24.8]	0.158
Direction of BA convex curvature			
Right convex	12 (32.4)	33 (54.1)	
Left convex	17 (45.9)	13 (21.3)	0.030
Straight	8 (21.6)	15 (24.6)	

Results expressed in number of patients (%) or mean [SD].

BA, basilar artery; VA, vertebral artery; AP, anteroposterior; MRA, magnetic resonance angiography; HR-MRI, high-resolution MRI.

Table 3. Characteristics and distribution of plaques according to lateral mid-BA angle

	BA curvature angle of lateral view		<i>p</i>
	Low (<i>n</i> = 49)	High (<i>n</i> = 49)	
Age, year	67.9 [10.3]	68.5 [7.6]	0.764
Men	26 (53.1)	22 (44.9)	0.419
Hypertension	34 (69.4)	40 (81.6)	0.159
Diabetes	15 (30.6)	18 (36.7)	0.521
Hyperlipidemia	4 (8.3)	6 (12.2)	0.526
Smoking	10 (20.4)	9 (18.4)	0.798
Alcohol consumption	17 (34.7)	12 (24.5)	0.269
Plaque distribution			
Anterior	41.0 [43.5]	23.8 [34.2]	0.043
Right lateral	15.8 [30.4]	14.8 [27.8]	0.887
Left lateral	15.9 [30.7]	18.9 [30.1]	0.789
Posterior	27.4 [40.0]	42.5 [42.5]	0.052
Plaque burden			
BA stenosis on HRMRI	34.8 [13.3]	38.5 [15.8]	0.211
Plaque burden, mm ³	33.9 [31.4]	41.2 [33.3]	0.267
VBJ to plaque, mm	5.8 [4.8]	4.4 [4.2]	0.120
Basilar artery axis			
BA shift angle (°), AP view	-3.8 [24.5]	-6.3 [24.9]	0.617
Direction of BA convex curvature			
Right convex	18 (36.7)	27 (55.1)	0.181
Left convex	17 (34.7)	13 (26.5)	
Straight	14 (28.6)	9 (18.4)	

Results expressed in number of patients (%) or mean [SD].

BA, basilar artery; VA, vertebral artery; AP, anteroposterior; MRA, magnetic resonance angiography; HR-MRI, high-resolution MRI.

Table 4. Characteristics and distribution of plaques according to plaque burden

	Plaque burden			<i>p</i>
	Low (<i>n</i> = 33)	Middle (<i>n</i> = 33)	High (<i>n</i> = 32)	
Age, year	68.5 [8.1]	67.5 [11.1]	68.6 [9.0]	0.871
Male patients	14 (42.4)	20 (60.6)	14 (43.8)	0.259
Hypertension	23 (71.9)	24 (72.7)	27 (84.4)	0.420
Diabetes	7 (21.2)	14 (42.4)	12 (37.5)	0.162
Hyperlipidemia	6 (18.2)	2 (6.1)	2 (6.2)	0.178
Smoking	5 (15.2)	6 (18.2)	8 (25.0)	0.590
Alcohol consumption	7 (21.2)	15 (45.5)	7 (21.9)	0.049
Plaque distribution				
Anterior	35.9 [47.2]	33.3 [40.8]	28.0 [30.4]	0.953
Right lateral	8.1 [26.4]	16.6 [32.3]	21.5 [27.2]	0.001
Left lateral	12.1 [30.7]	20.1 [36.3]	20.0 [22.1]	0.025
Posterior	43.9 [48.0]	30.0 [43.8]	30.7 [31.1]	0.421
Plaque burden				
BA stenosis on HRMRI	4.2 [7.0]	8.1 [12.6]	15.6 [13.4]	< 0.001
Plaque burden, mm ³	10.2 [4.0]	27.7 [10.3]	76.0 [27.0]	< 0.001
VBJ to plaque, mm	6.6 [3.4]	6.1 [4.3]	2.6 [4.7]	< 0.001
Basilar artery axis				
BA shift angle (°), AP view	-3.2 [25.7]	-9.8 [29.1]	-3.2 [16.6]	0.454
Direction of BA convex curvature				
Right convex	15 (45.5)	17 (51.5)	13 (40.6)	0.938
Left convex	10 (30.3)	9 (27.2)	11 (34.4)	
Straight	8 (24.2)	7 (21.2)	8 (25.0)	

Results expressed in number of patients (%) or mean [SD].

BA, basilar artery; VA, vertebral artery; AP, anteroposterior; MRA, magnetic resonance angiography; HR-MRI, high-resolution MRI.

tion of BA plaques was marginally higher in patients with high lateral mid-BA angle than those with low lateral mid-BA angle (42.5% vs. 27.4%; $p=0.052$). However, there was no significant correlation between the lateral mid-BA angle and the burden of BA plaques in each wall.

Plaque Burden and The Distribution of BA Plaques

The total plaque volume was associated with the plaque distribution, as shown in **Table 4**. At the early stage of atherosclerosis with low plaque volume, the plaques were predominantly located at the posterior wall (43.9%) and anterior wall (35.9%). However, at the advanced stage of atherosclerosis with high plaque volume, the plaques were more evenly distributed, than those at the early stage atherosclerosis with low plaque volume, as the distribution of plaque increased in the lateral wall (**Table 4**).

According to the multivariate analysis, only the presence of hypertension was independently associated with posterior plaque burden (standardized beta = 0.264, $p=0.020$) and anterior plaque burden (standardized beta = -0.328, $p=0.001$), whereas the BA

shift angle was independently associated with higher plaque burden in the right lateral wall (standardized beta = 0.268, $p=0.008$) and left lateral wall (standardized beta = 0.220, $p=0.028$).

Discussion

In our study, asymptomatic BA plaques were demonstrated in 9.5% individuals who received HR-MRI during a routine health check-up. The asymptomatic BA plaques were most frequently located at the anterior and posterior walls of the BA. The convexity of BA was associated with the location of plaque, and the plaque burden in the contralateral BA wall correlated with the degree of BA shift angle. On the contrary, the presence of anterior plaques was associated with low lateral mid-BA angle, whereas posterior plaques were marginally associated with high lateral mid-BA angle. With an increase in the plaque burden across patients, there was a significant increase in the percentage of lateral plaques.

From the lateral view, BA runs on the anterior surface of pons that is anteriorly convex. The flow

along the inner curvature (posterior wall) of BA forms a centrifugal effect, and reduces the shear stress at the posterior wall of BA²⁾. A computational flow dynamic study based on MRA also demonstrated an area with low shear stress at the posterior wall of BA¹⁵⁾. This may cause endothelial dysfunction, formation of early atherosclerosis, and finally lead to the predominant location of plaques in the posterior BA wall¹⁶⁾. Furthermore, the predominant distribution of posterior wall plaque was slightly greater in those with higher lateral mid-BA angle. For the same reason, the presence of plaque at the right and left lateral walls was associated with the direction of BA (left or right convex BA, respectively).

The BA curvature observed from the AP view is affected by the unequal blood flow from the VAs⁴⁾. The congenital asymmetric flow of VA progressively curves and elongates the BA in an asymmetric manner and results in a convexity of BA to the opposite side of dominant VA¹⁷⁾. In addition, pontine infarctions were predominantly located at the inner side of BA curvature, which was explained by the traction of pontine perforators or the higher thrombogenicity in the inner curvature⁴⁾. In the present study, early BA plaques were more frequently observed in the inner curvature (left lateral plaque in the right BA convexity, and right lateral plaque in the left BA convexity), and the plaque distribution on the lateral wall was independently associated with the BA shift angle. These findings may help explaining the pathophysiologic mechanism of higher incidence of pontine infarction in the opposite side to BA convexity⁴⁾.

According to our results, patients with lower BA plaque burden showed more plaque burden in the anterior and posterior walls. On the contrary, at more advanced stages, plaque burden in the lateral wall increased and the plaques were distributed evenly. These findings may also be explained by the fact that the lateral mid-BA curvature is congenital, whereas the BA curvature observed from the AP view progressively increases. The development of BA plaque may begin from the posterior and anterior walls and progressively extend to the lateral wall, because the lateral BA curvature increases progressively due to alteration in hemodynamics caused by dominance in the VA flow⁴⁾.

There are several limitations in our study. First, the sample size was small, implying caution while interpreting the results, especially those of the multi-variable analysis. Second, the association among BA plaque distribution, BA and VA geometry, and burden of plaque progression was analyzed only in patients diagnosed with a BA plaque, excluding those without. Third, the demographics, risk factors, and the geome-

try of BA or VA were not obtained from individuals without a BA plaque who received a health check-up. However, the aim of this study was not to compare the characteristics between those with and without BA plaque. Instead, we intended to evaluate the association between VA and BA geometry and BA plaque location and characteristics. Fourth, the reason for the higher burden of plaque in the anterior wall cannot be explained by BA geometry. Anterior plaques were also predominant in symptomatic BA plaques¹⁸⁾. A hemodynamic study measuring hemodynamic parameters on each wall may help in exploring the reason for anterior plaque dominance¹⁹⁾.

Conclusion

The presence of asymptomatic BA plaques is not uncommon. The location of BA plaque is affected by the geometry of VA and BA. Early atherosclerotic plaques are located at the anterior and posterior wall, which was determined by the lateral BA angle, and the plaques progressively extend to the lateral wall. The direction of extension is associated with the convexity of BA from AP view.

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Conflict of Interest

None.

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