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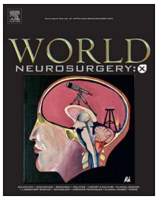

A novel predictor of ischemic complications in the treatment of ruptured middle cerebral artery aneurysms: Neck-branching angle

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ABSTRACT

Objective: The risk factors of procedural cerebral ischemia (CI) in ruptured middle cerebral artery (MCA) aneurysms are unclear. This study proposed the neck-branching angle (NBA), a simple quantitative indicator of the aneurysm neck and branch vessels, and analyzed its usefulness as a predictor of procedural CI in ruptured MCA aneurysms.
Methods: We retrospectively analyzed 128 patients with ruptured saccular MCA aneurysms who underwent surgical or endovascular treatment between January 2014 and June 2021. We defined the NBA as the angle formed by the MCA aneurysm neck and M2 superior or inferior branch vessel line. The superior and inferior NBA were measured on admission via three-dimensional computed tomography angiography on admission. We divided the patients into clipping (106 patients) and coiling (22 patients) groups according to the treatment. Risk factors associated with procedural CI were analyzed in each group.
Results: Both groups showed that an enlarged superior NBA was a significant risk factor for procedural CI (clipping, $P < 0.0005$; coiling group, $P = 0.007$). The receiver operating characteristic curve showed the closed thresholds of the superior NBA with procedural CI in both groups (clipping group, 128.5°, sensitivity and specificity of 0.667 and 0.848, respectively; coiling group, 130.9°, sensitivity and specificity of 1 and 0.889, respectively).
Conclusion: The NBA can estimate the procedural risk of ruptured MCA aneurysms. In addition, an enlarged superior NBA is a risk factor for procedural CI in both clipping and coiling techniques.

1. Introduction

Ruptured middle cerebral artery (MCA) aneurysms represent 20–30% of total ruptured aneurysms worldwide.[1] Surgical clipping is the chosen treatment technique for ruptured MCA aneurysms owing to their anatomical configuration[2]; however, endovascular coiling is gaining popularity.[3] To date, only few studies have compared these two treatments in ruptured MCA aneurysms, with no difference between the techniques regarding complication rates and neurological outcomes.[4–6]

Previous studies have reported several factors that should be considered during the surgical treatment of MCA aneurysms, including a large or complex aneurysm,[2,7,8] an irregular and wide neck,[2,7,9] incorporated branch vessels arising from the aneurysm neck,[3,10,11] narrow parent artery space,[12] and shorter parent artery.[13] These characteristics make it challenging to quantify the degree of procedural surgical risk. Therefore, the development of a simple quantitative indicator is required to precisely ascertain the perioperative risk of procedural complications in ruptured MCA aneurysms.

Herein, we propose the neck-branching angle (NBA) as a simple quantitative indicator that reflects the width of the aneurysm neck, degree of branch vessels incorporated into the aneurysm, and space of the parent artery, all of which have been identified as critical structures for preserving blood flow during both clipping and coiling.[3,7,10–12] We hypothesized that a high NBA would correlate with an increased risk of

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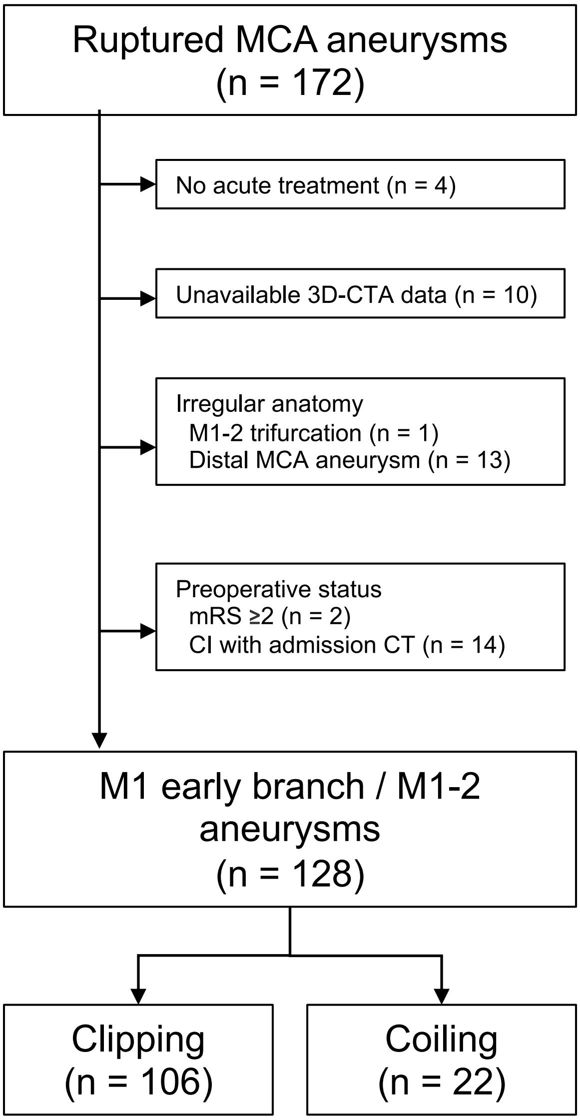

Fig. 1. Patient selection flow. In total, 172 patients with ruptured MCA aneurysms were enrolled during the study period. Patients who did not undergo surgical treatment (n = 4), had unavailable 3D-CTA data (n = 10), irregular anatomy (n = 14), or an undesirable preoperative status were excluded. A total of 128 patients were enrolled in this study. 3D-CTA, three-dimensional computed tomography angiography; CI, cerebral ischemia; MCA, middle cerebral artery; mRS, modified Rankin Scale.

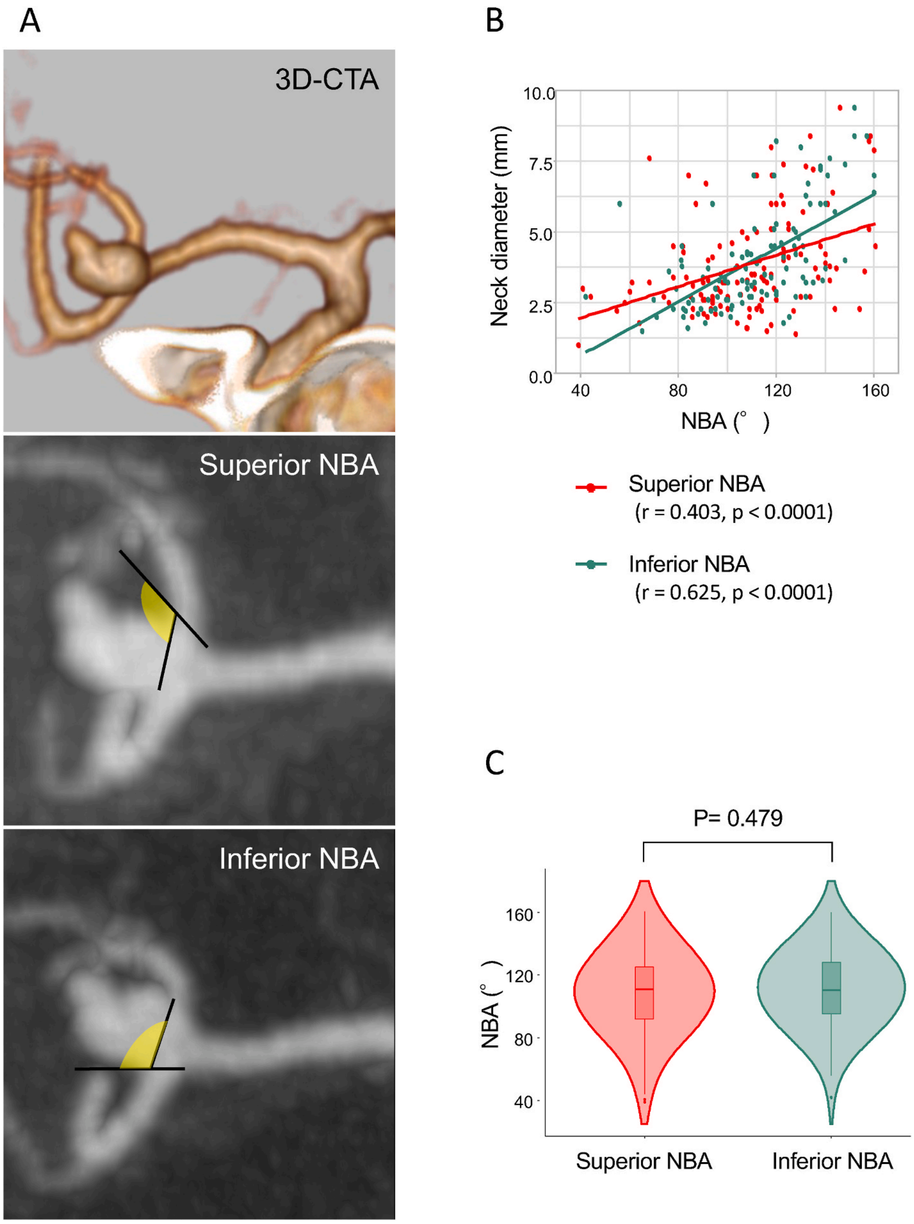

Fig. 2. Measurement of superior/inferior NBA (A) The concept and definition of NBA, with a representative case of superior and inferior NBA measurement. Volume-rendered 3D-CTA image of the right M1-2 bifurcation aneurysm archived from DICOM data upon admission. The 3D-CTA image was reconstructed into a 10-mm slab MIP image using the Aquarious NET® viewer. Two images showed the best separation of the aneurysm neck and each M2 branch. The aneurysm neck and M2 branch line were drawn on each separate image, and the angle between the aneurysm neck and M2 branch line was defined as the NBA (middle, superior NBA; lower, inferior NBA). (B) Scatter plot, Spearman's rank correlation coefficient, and P values between neck diameter and NBA. (C) Violin plot of the superior and inferior NBA. No significant differences were observed between the two angles. 3D-CTA, three-dimensional computed tomography angiography; DICOM, digital imaging and communications in medicine; MIP, maximum intensity projection; NBA, neck-branching angle.

Table 1
Patient characteristics and outcomes of the clipping and coiling groups.

Variable N (%)/median (IQR)	Clipping N = 106 (82.8%)	Coiling N = 22 (17.2%)	P-value
Patient characteristics			
Age (y)	66.5 (55.0–73.5)	58.0 (52.3–68.3)	0.177
Male sex	28 (26.4)	13 (59.1)	0.005
Right side	61 (57.5)	13 (59.1)	1
HT	43 (40.6)	12 (54.5)	0.246
DM	7 (6.6)	3 (13.6)	0.374
DL	12 (11.3)	4 (18.2)	0.476
Smoking	4 (3.8)	5 (22.7)	0.008
History of SAH	0 (0.0)	1 (4.5)	0.172
Multiple Aneurysms	13 (12.3)	3 (13.6)	1
WFNS Grade			0.641
I–III	46 (43.4)	11 (50.0)	
IV–V	60 (56.6)	11 (50.0)	
Fisher Group			0.543
1	4 (3.8)	0 (0.0)	
2	9 (8.5)	0 (0.0)	
3	64 (60.4)	16 (72.7)	
4	29 (27.4)	6 (27.3)	
Radiological findings			
ICH	34 (32.1)	7 (31.8)	1
ISH	24 (22.6)	2 (9.1)	0.243
Location			0.528
M1-2	91 (85.8)	17 (77.3)	
M1 early frontal branch	13 (12.3)	5 (22.7)	
M1 early temporal branch	2 (1.9)	0 (0.0)	
Aneurysm projection			1
Anterior - Inferior	40 (37.7)	8 (36.4)	
Anterior - Superior	28 (26.4)	6 (27.3)	
Posterior - Inferior	9 (8.5)	2 (9.1)	
Posterior - Superior	18 (17.0)	4 (18.2)	
Lateral	11 (10.4)	2 (9.1)	
Aneurysm shape			0.685
Regular margin Single-sac	30 (28.3)	7 (31.8)	
Irregular margin Single-sac	38 (35.8)	7 (31.8)	
Secondary sac	20 (18.9)	6 (27.3)	
Lobulated	18 (17.0)	2 (9.1)	
Aneurysm diameter (mm)	6.5 (4.9–8.5)	4.5 (3.4–7.2)	0.021
D/N ratio	1.4 (1.1–1.8)	1.4 (1.0–1.6)	0.449
Neck diameter (mm)	3.5 (2.7–4.8)	2.7 (2.2–3.3)	0.006
Aspect ratio	1.5 (1.1–1.8)	1.4 (1.1–1. 8)	0.687
Length of the parent artery (mm)	19.3 (17.1–22.2)	17.0 (11.8–19.1)	0.003
Superior NBA (°)	111.6 (91.7–123.5)	107.9 (93.4–132.5)	0.977
Inferior NBA (°)	115.3 (95.0–129.0)	100.0 (96.6–109.0)	0.108
Intraoperative findings			
Intraoperative rupture	13 (12.3)	0 (0.0)	0.123
ICH evacuation	40 (37.8)	4 (18.2)	0.090
Operation time (min)	307.0 (253.5–367.8)	153.5 (120.0–185.5)	<0.001
Outcome			
Procedural CI	12 (11.3)	4 (18.2)	0.476
DCI	15 (14.2)	3 (13.6)	1
mRS at discharge			0.817
0–2	47 (44.3)	9 (40.9)	
3–6	59 (55.7)	13 (59.1)	

CI, cerebral ischemia; DCI, delayed cerebral ischemia; DL, dyslipidemia; DM, diabetes mellitus; D/N ratio, Dome-to-neck ratio; HT, hypertension; ICH, Intracerebral Hematoma; IQR, interquartile range; ISH, Intrasylvian Hematoma; mRS, modified Rankin Scale; NBA, Neck-Branching Angle; SAH, subarachnoid hemorrhage; WFNS, World Federation of Neurosurgical Societies.

procedural cerebral ischemia (CI). Thus, this study aimed to identify the association between the NBA and procedural CI in patients with ruptured MCA aneurysms.

2. Materials and methods

2.1. Study design and patient selection

This retrospective multicenter analysis included 128 patients with ruptured saccular MCA aneurysms who underwent acute surgical treatment between January 2014 and June 2021 and admitted to one of four stroke centers: Osaka University Hospital, Osaka Neurological Institute, Osaka National Hospital, and Kansai Rosai Hospital. The patient selection method is illustrated in Fig. 1.

During the study period, 172 patients with ruptured MCA aneurysms were initially admitted to these centers. To measure the NBA, we excluded patients with low quality or missing three-dimensional computed tomography angiography (3D-CTA) data on admission. We also excluded patients with M1-2 trifurcation, distal MCA (M2 or beyond segment) aneurysms, no acute surgical treatment within 24 h of onset, prehospital modified Rankin Scale (mRS) ≥2, and procedural CI from admission computed tomography (CT).

Postoperative symptomatic procedural CI was set as the primary outcome. This retrospective multicenter study was approved by the Osaka University Clinical Research Review Committee (approval number 19486-3). All the procedures adhered to the ethical guidelines of the Declaration of Helsinki. Informed consent was not required because of the retrospective nature of the study.

2.2. Data collection

All data were retrospectively collected from medical charts and radiological data. We collected information on patient characteristics, including age, sex, side, previous history, presence of multiple aneurysms, World Federation of Neurosurgical Societies (WFNS) grade (I–III: good, IV–V: poor),[14] and the Fisher group. We also collected data on intraoperative findings and outcomes, including surgical treatment (clipping or coiling), intraoperative rupture,[15] intracerebral hematoma (ICH) evacuation, operation time, procedural CI, delayed cerebral ischemia (DCI),[16] and mRS at discharge (0–2: good, 3–6: poor). Among the surgical treatments, clipping was adopted as the first-line treatment, whereas coiling was performed in cases of a narrow neck, preferring endovascular treatment. Aneurysm occlusion and preservation of branch vessels were verified using indocyanine green fluorescence angiography and micro-doppler analysis for clipping, and digital subtraction angiography for coiling.

Procedural CI was defined as acute cerebral infarction identified by diffusion-weighted imaging (DWI) of magnetic resonance imaging (MRI) or CT within 24 h after surgical treatment. An infarct lesion was defined as symptoms in awake patients or an infarct size >3 cm in patients under intubation and general anesthesia.[11,17] We divided the surgical treatment into two groups (clipping and coiling) and collected information on the following intraoperative findings: for the clipping group, application of the temporary clip to the parent artery (M1), maximum temporary clipping time,[2,18] number of clips, and reconstruction techniques such as bypass surgery[2,7,19]; for the coiling group, adjunctive techniques such as balloon-assisted, stent-assisted, or double catheter technique, induction of antiplatelets, volume embolization ratio (VER), and ICH evacuation. Antiplatelet induction was defined as drug administration until the end of coiling.

We also collected data on radiological findings from CT or 3D-CTA, including ICH, intrasylvian hematoma (ISH), aneurysm location,[20] projection,[21] shape,[9] aneurysm and neck diameter, dome-to-neck (D/N) ratio, aspect ratio, length of the MCA parent artery,[22] and NBA. We defined hematoma as ICH and ISH, in case of 10 mL or more as calculated using the ABC/2 Formula.[23,24]

2.3. NBA measurement in MCA aneurysms

We measured the NBA by reconstructing the Digital Imaging and

Table 2
Characteristics of the 16 patients with procedural CI.

Operation	Age	Sex	WFNS Grade	ICH	ISH	Aneurysm diameter (mm)	Superior NBA (°)	Inferior NBA (°)	Ischemic lesion
Clipping	46	F	IV–V	Yes	Yes	4.6	138	118	Frontal + Temporal
Clipping	56	M	IV–V	Yes	No	16	160	NA	Frontal + Temporal
Clipping	62	M	IV–V	Yes	Yes	20.4	158	120	Frontal + Temporal
Clipping	70	F	IV–V	No	Yes	8	96	108	Frontal + Temporal
Clipping	77	F	IV–V	No	Yes	4.8	130	110	Frontal + Temporal
Clipping	54	F	I–III	No	No	11.5	140	128	Frontal
Clipping	64	M	I–III	No	Yes	5.2	156	76	Frontal
Clipping	69	F	IV–V	Yes	No	16	159	157	Frontal
Clipping	51	M	IV–V	Yes	No	4.8	118	NA	Basal ganglia
Clipping	63	F	I–III	No	No	2.6	120	NA	Basal ganglia
Clipping	64	F	I–III	No	Yes	5.2	137	131	Basal ganglia
Clipping	78	F	I–III	No	Yes	12.8	111	141	Basal ganglia
Coiling	56	M	IV–V	Yes	No	17.5	146	152	Frontal + Temporal
Coiling	59	M	I–III	No	No	2.7	134	109	Frontal + Temporal
Coiling	59	Me	IV–V	Yes	Yes	7.1	145	103	Frontal
Coiling	70	M	IV–V	Yes	No	7.9	140	107	Frontal

CI, cerebral ischemia; ICH, intracerebral Hematoma; ISH, intrasylvian hematoma; NBA, neck-branching angle; WFNS, World Federation of Neurosurgical Societies.

Communications in Medicine (DICOM) data of 3D-CTA on admission, using the image viewer Aquarious NET® (version 4.4.8.85, TeraRecon Inc, Foster City, CA, USA).[25] Although previous studies have used standalone software for angle measurement,[26] we used network-connected software for simple and practical use in acute surgical treatment. First, we reconstructed the 3D-CTA data (Fig. 2A, upper). Second, we reconstructed a 10-mm slab maximum intensity projection (MIP) image and set the cross-section with the best separation of the aneurysm neck and each M2 branch (Fig. 2A–C). Finally, we drew the aneurysm neck and M2 branch line for each cross-section and measured the NBA as the angle between the aneurysm neck and M2 branch line (superior NBA, angle for the superior M2; inferior NBA, angle for the inferior M2). Among the M1 early cortical branch aneurysms, we measured one NBA (superior NBA, angle for the M1 early frontal branch aneurysm; inferior NBA, angle for the M1 early temporal branch aneurysm). For the composition of the NBA, we measured the neck diameter; however, we did not measure the parent arterial space owing to its small diameter and the possibility of erroneous estimation.

2.4. *Statistical analysis*

Categorical variables are presented as frequencies (percentages), and continuous variables as medians and interquartile ranges (IQR). Fisher's exact test was used to compare categorical variables. Spearman's rho correlation coefficient and the Spearman test, Mann–Whitney *U* test, or Kruskal–Wallis test, followed by the Tukey post-test, were used to compare continuous variables. Receiver operating characteristic (ROC) curve analysis was used to determine the best NBA cut-off value of NBA causing procedural CI. Statistical significance was set at $P < 0.05$. We used R 3.5.2 for Windows (www.R-project.org; R Foundation for Statistical Computing, Vienna, Austria) for all statistical analyses.

3. Results

3.1. *Patients population*

Among the 128 patients with ruptured MCA aneurysms, 106 (82.8%) were in the clipping group and 22 (17.2%) were in the coiling group. The mean age of the patients was 65 years, and 41 (32.0%) patients were male. A poor grade (WFNS: IV–V) was evident in 71 (55.5%) patients, ICH and ISH were recorded in 41 (32.0%) and 26 (20.3%) patients respectively, and the mean aneurysm diameter was 6.4 mm. A comparison of the four stroke centers is shown in Supplementary Table 1.

3.2. *Characteristics and outcome of the clipping and coiling groups*

Patient characteristics, radiological and intraoperative findings, and outcomes of the two groups are shown in Table 1. The percentages of males ($P = 0.005$) and current smokers ($P = 0.008$) were significantly higher in the coiling group. The median aneurysm diameter ($P = 0.021$) and parent artery length ($P = 0.003$) were longer in the clipping group. No other characteristics significantly differed between the two groups.

The median superior or inferior NBA in the two groups were as follows: superior NBA was 111.6° and 107.9 in the clipping and coiling group, respectively ($P = 0.977$); inferior NBA was 115.3° and 100.0° in the clipping and coiling group, respectively ($P = 0.108$). There was a moderately positive correlation between superior NBA ($r = 0.403$), inferior NBA ($r = 0.625$), and neck diameter (Fig. 2B). Violin plots showed no significant differences in the values between the superior and inferior NBA (Fig. 2C).

The median operative time was longer in the clipping group ($P < 0.001$). In the coiling group, four patients (18.2%) underwent ICH evacuation, followed by endovascular coiling. The overall procedural CI rate was 12.5%, with no significant difference between the two groups ($P = 0.476$). A summary of the patients presenting with procedural CI is shown in Table 2. In the clipping group, the infarct lesions were in the frontotemporal lobe in five cases, frontal lobe in three cases, and basal ganglia in four cases. In the coiling group, the frontotemporal lobe was present in two cases, and the frontal lobe in two cases.

3.3. *Procedural CI*

3.3.1. *Clipping group*

The factors associated with procedural CI in the clipping group are shown in Table 3. Twelve (11.3%) of the 106 patients presented with procedural CI. None of the patient characteristics were associated with procedural CI. Radiological findings showed that the incidence of ISH was higher ($P = 0.005$), and the superior NBA was larger with the occurrence of procedural CI ($P < 0.0005$). The ROC curve showed a threshold of 128.5° for superior NBA as procedural CI, with a sensitivity and specificity of 0.667 and 0.848, respectively (Fig. 3). No other radiological findings, including the inferior NBA, were associated with procedural CI. The maximum duration of temporary clipping ($P = 0.004$) and intraoperative rupture ($P = 0.039$) significantly increased with the occurrence of procedural CI. The prevalence of good outcomes was also lower in the procedural CI group ($P = 0.001$).

3.3.2. *Coiling group*

Factors associated with procedural CI in the coiling group are shown in Table 4. Four (18.2%) of the 22 patients presented with procedural CI.

Table 3

Patient characteristics and outcomes in the clipping group with and without procedural CI.

Variable n (%)/median (IQR)	Procedural CI		P-value
	No N = 94 (88.7%)	Yes N = 12 (11.3%)	
Patient characteristics			
Age (y)	67.0 (55.0–74.0)	63.5 (55.5–69.3)	0.491
Male sex	24 (25.5)	4 (33.3)	0.729
Right side	55 (58.5)	6 (50.0)	0.758
HT	38 (40.4)	5 (41.7)	1
DM	5 (5.3)	2 (16.7)	0.179
DL	12 (12.8)	0 (0.0)	0.352
Smoking	4 (4.3)	0 (0.0)	1
History of SAH	0 (0.0)	0 (0.0)	NA
Multiple Aneurysms	12 (12.8)	1 (8.3)	1
WFNS Grade			1
I–III	41 (43.6)	5 (41.7)	
IV–V	53 (56.4)	7 (58.3)	
Fisher Group			0.874
1	4 (4.3)	0 (0.0)	
2	9 (9.6)	0 (0.0)	
3	56 (59.6)	8 (66.7)	
4	25 (26.6)	4 (33.3)	
Radiological findings			
ICH	29 (30.9)	5 (41.7)	0.516
ISH	17 (18.1)	7 (58.3)	0.005
Aneurysm location			0.349
M1-2	82 (87.2)	9 (75.0)	
M1 early frontal branch	10 (10.6)	3 (25.0)	
M1 early temporal branch	2 (2.1)	0 (0.0)	
Aneurysm projection			0.832
Anterior-Inferior	36 (38.3)	4 (33.3)	
Anterior-Superior	24 (25.5)	4 (33.3)	
Posterior-Inferior	9 (9.6)	0 (0.0)	
Posterior-Superior	15 (16.0)	3 (25.0)	
Lateral	10 (10.6)	1 (8.3)	
Aneurysm Shape			0.451
Regular margin Single-sac	27 (28.7)	3 (25.0)	
Irregular margin Single-sac	34 (36.2)	4 (33.3)	
Secondary sac	19 (20.2)	1 (8.3)	
Lobulated	14 (14.9)	4 (33.3)	
Aneurysm diameter (mm)	6.5 (5.0–8.4)	6.6 (4.8–13.6)	0.359
D/N ratio	1.4 (1.1–1.8)	1.4 (1.2–1.8)	0.916
Neck diameter (mm)	3.4 (2.6–4.6)	3.9 (3.3–7.2)	0.109
Aspect ratio	1.5 (1.1–1.8)	1.5 (1.1–1.7)	0.599
Length of the parent artery (mm)	19.3 (17.1–21.9)	20.1 (17.2–22.5)	0.889
Superior NBA (°)	108.5 (90.0–122.3)	137.5 (119.5–156.5)	<0.0005
Inferior NBA (°)	113.0 (94.8–128.3)	120.0 (110.0–131.0)	0.287
Intraoperative findings			
Application of the temporary clip	69 (73.4)	11 (91.7)	0.286
Maximum temporary Clipping time (min)	5.0 (0–7.0)	11.0 (5.8–16.3)	0.004
Number of clips	1.0 (1.0–2.0)	1.0 (1.0–2.0)	0.691
Reconstruction technique	0 (0.0)	0 (0.0)	NA
Intraoperative rupture	9 (9.6)	4 (33.3)	0.039
intracerebral hematoma evacuation	28 (29.7)	5 (41.7)	0.509
Operation time (min)	304.0 (250.5–362.5)	346.5 (302.3–445.3)	0.056
Outcome			
DCI	12 (12.8)	3 (25.0)	0.371
mRS at discharge			0.001
0–2	47 (50.0)	0 (0.0)	
3–6	47 (50.0)	12 (100.0)	

CI, cerebral ischemia; DCI, delayed cerebral ischemia DL, dyslipidemia; DM, diabetes mellitus; D/N ratio, dome-to-neck ratio; HT, hypertension; ICH, Intracerebral Hematoma; IQR, interquartile range; ISH, intrasylvian hematoma; mRS, modified Rankin Scale; NBA, neck-branching angle; SAH, subarachnoid hemorrhage; WFNS, World Federation of Neurosurgical Societies.

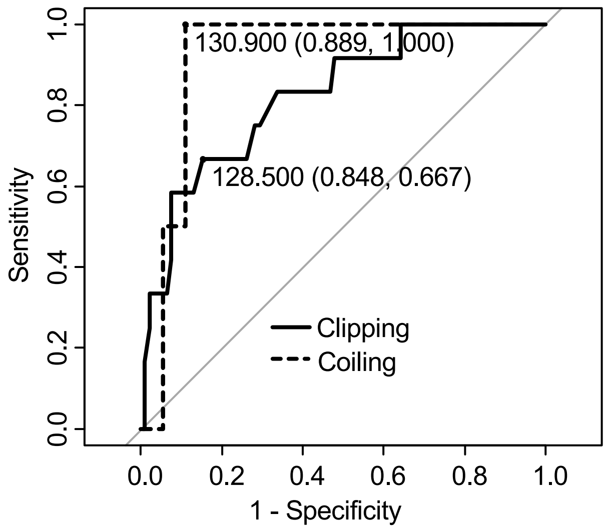

Fig. 3. The ROC curve in the clipping/coiling group The ROC curve in the clipping (solid line) and coiling group (dashed line) for prediction of procedural CI based on superior NBA. The thresholds, sensitivity, and specificity of each group are also shown. The AUC was 0.823 (95% confidence interval: 0.698–0.947) for the clipping group, while the coiling group was 0.917 (95% confidence interval: 0.794–1.000) AUC, area under the curve; CI; cerebral ischemia; NBA neck-branching angle; ROC, receiver operating characteristic.

None of the patient characteristics were associated with procedural CI. From the radiological findings, only the superior NBA was significantly larger in the procedural CI group (P = 0.007). The ROC curve showed a threshold of 130.9° in the superior NBA as a procedural CI, with a sensitivity and specificity of 1 and 0.889, respectively; comparable to the clipping group (Fig. 3). None of the other radiological findings were associated with procedural CI. Although the differences were not statistically significant, all four patients had procedural CI that resulted in poor outcomes.

4. Discussion

In this study, we proposed the NBA as a quantitative indicator of the aneurysm neck and branch vessels and analyzed the association with procedural CI on ruptured MCA aneurysms. An enlarged superior NBA was observed as a risk factor for procedural CI in both the clipping and coiling groups, with similar respective thresholds. Therefore, a superior NBA is suggested as a practical indicator to measure the risk of procedural CI for acute surgical treatment of subarachnoid hemorrhage (SAH).

4.1. Morphological significance of the NBA

This NBA quantitatively and comprehensively demonstrated the vascular structures near the aneurysm neck, which strongly correlated with the development and growth of MCA aneurysms. The development of MCA aneurysms is associated with a larger M1-2 bifurcation angle,[27] which tends to be asymmetrical.[28] The inclined side of M2 results in wall shear stress on the vessel itself, which contributes to aneurysm growth.[29] Consequently, we speculate that MCA aneurysms grow on one side of the inclined M2 branch.

The NBA represents these developmental processes; an enlarged NBA indicates a wider neck, more incorporated M2 on the aneurysm, and a narrower parent artery space (Fig. 4A). Thus, these structures can be seen as warning characteristics of MCA aneurysms during surgical

Table 4
Patient characteristics and outcomes in the coiling group with and without procedural CI.

Variable n (%)/median (IQR)	Procedural CI		P-value
	No N = 18 (81.8%)	Yes N = 4 (18.2%)	
Patient characteristics			
Age (y)	57.5 (50.3–68.3)	59.0 (58.3–61.8)	0.550
Male sex	9 (50.0)	4 (100.0)	0.115
Right side	11 (61.1)	2 (50.0)	1
HT	9 (50.0)	3 (75.0)	0.594
DM	2 (11.1)	1 (25.0)	0.47
DL	4 (22.2)	0 (0.0)	0.554
Smoking	4 (22.2)	1 (25.0)	1
History of SAH	1 (5.6)	0 (0.0)	1
Multiple Aneurysms	3 (16.7)	0 (0.0)	1
WFNS Grade			0.586
I–III	10 (55.6)	1 (25.0)	
IV–V	8 (44.4)	3 (75.0)	
Fisher Group			0.292
1	0 (0.0)	0 (0.0)	
2	0 (0.0)	0 (0.0)	
3	0 (0.0)	0 (0.0)	
4	4 (22.2)	2 (50.0)	
Radiological findings			
ICH	4 (22.2)	3 (75.0)	0.077
ISH	1 (5.6)	1 (25.0)	0.338
Aneurysm location			0.535
M1-2	13 (82.2)	4 (100.0)	
M1 early frontal branch	5 (27.8)	0 (0.0)	
M1 early temporal branch	0 (0.0)	0 (0.0)	
Aneurysm projection			0.680
Anterior-Inferior	6 (33.3)	2 (50.0)	
Anterior-Superior	5 (27.8)	1 (25.0)	
Posterior-Inferior	2 (11.1)	0 (0.0)	
Posterior-Superior	4 (22.2)	0 (0.0)	
Lateral	1 (5.6)	1 (25.0)	
Aneurysm shape			0.351
Regular margin Single-sac	7 (38.9)	0 (0.0)	
Irregular margin Single-sac	5 (27.8)	2 (50.0)	
Secondary sac	5 (27.8)	1 (25.0)	
Lobulated	1 (5.6)	1 (25.0)	
Aneurysm diameter (mm)	4.2 (3.4–6.4)	7.5 (6.0–10.3)	0.217
D/N ratio	1.4 (1.0–1.6)	1.4 (1.2–1.6)	0.898
Neck diameter (mm)	2.4 (2.1–3.2)	3.7 (3.5–5.1)	0.033
Aspect ratio	1.3 (1.1–2.0)	1.6 (1.4–1.7)	0.494
Length of the parent artery (mm)	17.8 (13.3–19.3)	12.6 (10.5–13.7)	0.061
Superior NBA (°)	102.0 (91.2–114.3)	142.4 (138.7–144.9)	0.007
Inferior NBA (°)	99.0 (93.2–101.7)	108.2 (106.4–119.8)	0.060
Intraoperative findings			
Adjunctive Techniques			0.087
Simple	10 (55.6)	2 (50.0)	
Balloon Assist	7 (38.9)	0 (0.0)	
Stent assist	1 (5.6)	0 (0.0)	
Double catheter	1 (5.6)	2 (50.0)	
Antiplatelet Induction	8 (44.4)	1 (25.0)	0.616
VER (%)	47.0 (33.0–64.5)	23.8 (20.5–34.0)	0.060
Intraoperative Rupture	18 (100.0)	4 (100.0)	NA
Operation time (min)	160.0 (120.3–185.5)	122.0 (116.3–160.5)	0.639
intracerebral hematoma evacuation	2 (11.1)	2 (50.0)	0.135
Outcome			
DCI	3 (16.7)	0 (0.0)	1
mRS at discharge			0.115
0–2	9 (50.0)	0 (0.0)	
3–6	9 (50.0)	4 (100.0)	

CI, cerebral ischemia; DCI, delayed cerebral ischemia DL, dyslipidemia; DM, diabetes mellitus; D/N ratio, dome-to-neck ratio; HT, hypertension; ICH, intracerebral hematoma; IQR, interquartile range; ISH, intrasylvian hematoma; mRS, modified Rankin Scale; NBA, neck-branching angle; SAH, subarachnoid hemorrhage; VER, volume embolization ratio; WFNS, World Federation of Neurosurgical Societies.

treatment.[2,3,7,10,21] Although previous studies on MCA aneurysms analyzed the angle between the parent artery and neck,[30,31] tip of the aneurysmal dome,[30,31] or M2 branch,[27] we proposed a novel angle between the neck and branch vessels.

4.2. The superior NBA is a simple quantitative predictor for procedural CI

We hypothesized that the state of hypercoagulability, mechanical damage caused by SAH,[32,33] and complex morphology of MCA aneurysms induce procedural CI. Consequently, we demonstrated that an enlarged superior NBA was associated with procedural CI regardless of the treatment procedure. In both clipping and coiling techniques, enlargement of the NBA complicates the ability to separate the neck and branch vessels and operative manipulation is more complex.[3,9,10,12] Interestingly, only the superior NBA was identified as a risk factor. Considering the lack of difference in the median angle between the superior and inferior NBA (Fig. 2B and C), the occurrence of procedural CI is, therefore, likely linked to a particular anatomical element of the superior M2 in combination with an enlarged NBA.

4.3. The impact of the superior NBA on surgical clipping

The enlarged superior NBA contributes to procedural CI during surgical clipping due to the disturbance of its manipulation. The essential steps in clipping involve identifying the parent artery, aneurysm neck, and branch vessel.[34] Nevertheless, SAH, particularly ISH, impairs manipulation of the subarachnoid structures during clipping,[34,35] resulting in damage to the cerebral vessels.[24]

Our study also showed that ISH was associated with procedural CI in the clipping group. Furthermore, the enlarged superior NBA represents the higher branched position of the superior M2 and the closer lenticulostriate artery (LSA),[36] both of which are associated with impaired flow in the superior M2 due to the difficulty of neck clipping[9,12] and LSA injury due to prolonged temporary clipping (Fig. 4B).[9,18,37–39] In this study, patients with procedural CI presented with infarct lesions in the frontal lobe, frontotemporal lobe, or basal ganglia, a longer temporary clipping time, and higher rate of intraoperative rupture. Together, the enlarged superior NBA impairs the essential steps for surgical clipping of ruptured MCA aneurysms, leading to poor surgical performance and procedural CI.

4.4. Impact of the superior NBA on endovascular coiling

The enlarged superior NBA also contributes to the occurrence of procedural CI during endovascular coiling, owing to the disturbance of the appropriate adjunctive technique. In the acute stage of SAH, the lack of dual antiplatelet agent induction impedes the preferred stent-assisted coil embolization of wide-neck aneurysms.[40,41] Only one patient underwent the stent-assisted technique in this study. If the stent-assisted technique is not a viable option for MCA aneurysms with a wide neck and incorporated superior M2, the balloon-assisted technique is considered to preserve superior M2 flow.[3,10,21] However, guiding a microcatheter to the superior M2 is more complex than guiding it to the inferior branch owing to the usual passage through the large curvature of the vessel.[42] In this study, none of the patients with procedural CI who underwent the balloon-assisted technique showed infarction in the perfusion area of the superior M2. These findings suggest that an enlarged superior NBA in ruptured MCA aneurysms impairs the proper adjunctive technique, leading to coil migration to the superior M2 branch and possible thromboembolism (Fig. 4C).

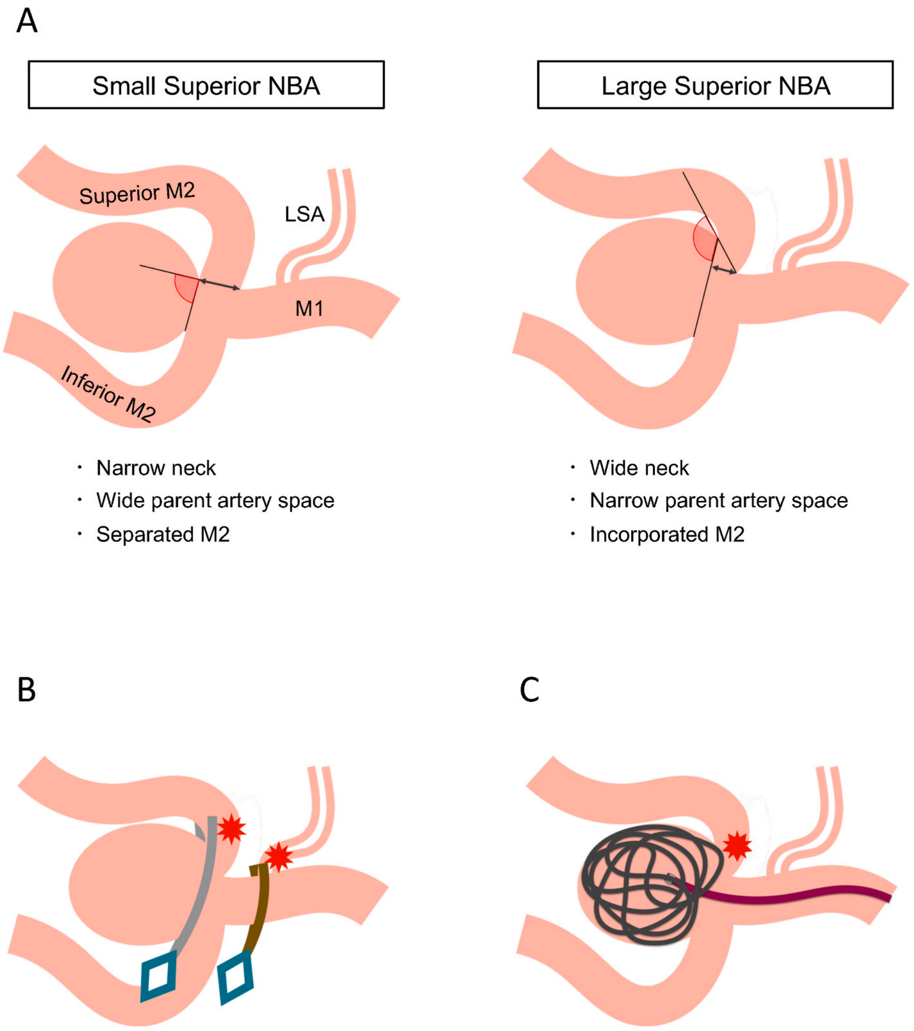

Fig. 4. Morphological characteristics of enlarged superior NBA (A) A wider neck, more incorporated M2 superior branch on aneurysm, and a narrower parent artery space (double arrow) are typical of enlarged superior NBAs in comparison to small superior NBAs. (B) The association of an enlarged superior NBA and procedural CI in surgical clipping. The wider neck, incorporated M2 superior branch on aneurysm, and a higher branched position closed to LSA cause unintended clip involvement in the M2 superior branch, or LSA injury due to prolonged temporary clipping. (C) The association of enlarged superior NBA and procedural CI in endovascular coiling. The difficulty of guiding the microcatheter to the M2 superior branch disables preservation of the M2 superior branch flow. Therefore, the inserted coil would migrate to the superior M2 branch. CI, cerebral ischemia; LSA, lenticulostriate artery; NBA, neck-branching angle.

4.5. Technical solutions in clipping and coiling against the superior NBA

In the surgical management of MCA aneurysms displaying characteristics of an enlarged NBA, various strategies have been reported to avoid procedural CI. For surgical clipping, multiple clipping or clipping to intentionally leave residuals of the neck[43] prevent kinking or constriction of the M2 branch.[44] These techniques may be a solution for ruptured MCA aneurysms in cases of an enlarged superior NBA. However, for endovascular coiling, adjunctive techniques with stenting or balloons are impaired owing to apprehensions regarding the capacity to access tortuous vessels.[45] Further development of device technology is required to solve these problems.

5. Limitations

Our study has some limitations. First, the NBA could not fully quantify the complex 3D morphological characteristics of MCA aneurysms. Morphological features, other than the NBA components, were evaluated separately. Regarding the NBA components, we evaluated only the neck diameter, which was deemed to have the lowest measurement inaccuracy. For the simple measurement of the NBA itself, a 10 mm slab MIP image was used, which might introduce inaccuracies compared to utilizing software capable of three-dimensional measurements.[46] Second, the 49 excluded patients (28.3%) and different proportions of surgical versus endovascular treatment among the four stroke centers ($P < 0.001$) could have resulted in selection bias. Third, owing to the limited sample size, we did not adjust for other warning structures and risk factors associated with procedural complications in MCA aneurysms to demonstrate that the superior NBA was an independent predictor.[2,7,8,11,13] Fourth, the procedural CI may have been over-or underestimated because of the high proportion (55.5%) of poor-grade SAH cases, which were evaluated based on CT findings alone. Fifth, although superior NBA was a predictor of ischemic complications for both clipping and coiling, it unfortunately did not contribute to treatment choice, as the cutoff values for each treatment were nearly equal. Sixth, ischemic complications might also be related to other factors unrelated to the surgical procedure, such as early brain injury or vasospasm. However, NBA may serve as an indicator of procedural CI exacerbated by the distinctive pathophysiology of SAH.[4,32,33] Further validated research is warranted to explore the utility of NBA. Seventh, we have not presented the particular anatomical element of superior M2 that only superior NBA relates to procedural CI. Further research is requisite to substantiate our theories regarding the superior NBA as a risk factor for Procedural CI. Finally, MCA aneurysms that required bypass surgery during acute treatment were not included in this study.[19]

6. Conclusions

Our results showed that the NBA can be used as a quantitative predictor of ischemic complications during the treatment of ruptured MCA aneurysms. We also revealed that a larger superior NBA was associated with procedural ischemic complications for both clipping and coiling procedures. NBA represents the morphological characteristics of MCA aneurysms and helps predict the difficulty of aneurysm treatment.

CRediT authorship contribution statement

Tomofumi Takenaka: Writing – original draft, Visualization, Resources, Methodology, Investigation, Conceptualization. **Hajime Nakamura:** Writing – review & editing, Methodology, Conceptualization. **Shuhei Yamada:** Resources, Methodology, Investigation. **Tomoki Kidani:** Resources, Investigation. **Akihiro Tateishi:** Resources, Investigation. **Shingo Toyota:** Supervision, Resources, Investigation. **Toshiyuki Fujinaka:** Supervision, Resources, Investigation. **Takuyu Taki:** Supervision, Resources, Investigation. **Akatsuki Wakayama:** Supervision, Resources, Investigation. **Haruhiko Kishima:** Writing – review & editing, Supervision.

Declaration of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.wnsx.2024.100370.

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Abbreviation List

3D-CTA: three-dimensional computed tomography angiography
CI: cerebral ischemia
DCI: Delayed cerebral ischemia
D/N ratio: dome-to-neck ratio
DICOM: digital imaging and communications in medicine
DL: dyslipidemia
DM: diabetes mellitus
HT: hypertension
ICH: intracerebral hematoma
IQR: interquartile range
ISH: intrasylvian hematoma
LSA: lenticulostriate artery
MCA: middle cerebral artery
MIP: maximum intensity projection
mRS: modified Rankin Scale
NBA: neck-branching angle
ROC: receiver operating characteristic
SAH: subarachnoid hemorrhage
VER: volume embolization ratio
WFNS: World Federation of Neurosurgical Societies