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Original Scientific Paper

CLINICAL CHARACTERISTICS AND MORPHOLOGICAL PARAMETERS ASSOCIATED WITH RUPTURE OF ANTERIOR COMMUNICATING ARTERY ANEURYSMS

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SUMMARY – We analyzed aneurysm morphology, demographic and clinical characteristics in patients with anterior communicating artery (ACoA) aneurysms to investigate the risk factors contributing to aneurysm rupture. A total of 219 patients with ACoA aneurysms were admitted to our hospital between January 2016 and December 2020, and morphological and clinical characteristics were analyzed retrospectively in 153 patients (112 ruptured and 41 unruptured). Medical records were reviewed to obtain demographic and clinical data on age, gender, presence of hemorrhage, history of hypertension, diabetes, heart disease, and kidney disease. Morphological parameters examined on 3-dimensional digital subtraction angiography included aneurysm size, neck diameter, aspect ratio, size ratio, bottleneck ratio, height/width ratio, aneurysm angle, (in)flow angle, branching angle, number of aneurysms *per* patient, shape of the aneurysm, aneurysm wall morphology, variation of the A1 segment, and direction of the aneurysm. Male gender, aspect ratio, height/width ratio, non-spherical and irregular shape were associated with higher odds of rupture, whilst controlled hypertension was associated with lower odds of rupture, when tested using univariate logistic regression model. In multivariate model, controlled hypertension, presence of multiple aneurysms, and larger neck diameter reduced the odds of rupture, while irregular wall morphology increased the risk of rupture. Regulated hypertension represented a significant protective factor from ACoA aneurysm rupture. We found that ACoA aneurysms in male patients and those with greater aspect ratios and height/width ratios, larger aneurysm angles, presence of daughter sacs and irregular and non-spherical shapes were at a higher risk of rupture.

Key words: *Anterior communicating artery; Intracranial aneurysm; Aneurysm rupture; Aneurysm morphology; Clinical risk factors; Subarachnoid hemorrhage*

Introduction

With continuous advancements in medical imaging technology, a growing number of unruptured intracranial aneurysms, which may affect 2% to 10% of the general population, are being discovered[1,2]. Anterior communicating artery (ACoA) aneurysms

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account for approximately 30%-37% of intracranial aneurysms and are commonly related to intracranial aneurysm rupture[3,4]. Patients with ruptured ACoA aneurysms have historically been observed to have poor neuropsychological outcomes and higher incidence of vasospasm and permanent neurological deficits[5,6]. Thus, knowing the risk factors for rupture is crucial for counseling and managing patients with ACoA aneurysms[5].

Analyzing morphological characteristics of an aneurysm has been more frequently used to evaluate its rupture risk. Several parameters, including aspect ratio, size ratio and aneurysm inflow angle, have been shown to have greater association with aneurysm rupture status than the size alone[7-12]. However, such studies grouped together all aneurysm types, which may alter characteristics that are indicative to the vascular anatomy of a specific location. Vascular anatomy and hemodynamics of ACoA is more complex than other areas of the intracranial circulation because of the relative dominance of the A1 arteries, configuration of the A2 arteries, and different locations along the anterior communicating artery complex where an aneurysm could arise[1,5,13]. Our approach in examining morphological parameters, in a location specific manner, may yield results that would otherwise have been confounded by the heterogeneity of the samples. Therefore, we analyzed aneurysm morphology, as well as socio-demographic and clinical characteristics in patients with ACoA aneurysms to investigate the risk factors contributing to aneurysm rupture at this specific location.

Patients and Methods

Patient selection

Between January 2016 and December 2020 (5-year period), a total of 219 patients with ACoA aneurysm were admitted to our hospital. Ruptured aneurysms were defined as ones associated with subarachnoid hemorrhage (SAH), alone or combined with intracerebral hemorrhage. In patients with SAH and multiple aneurysms, the ruptured aneurysm was identified based on the pattern and location of hemorrhage. We excluded the cases with fusiform, traumatic, or mycotic aneurysms, reoperated/re-embolized aneurysms, cases associated with arteriovenous malformations, cases in which 3-dimensional digital subtraction angiograms (3D DSA) were not available or were of poor quality, and cases associated with severe vasospasm that precluded measurements. Finally, 153 patients (112 ruptured and 41 unruptured) were enrolled in the study. Medical records were reviewed to obtain demographic and clinical data on patient age, gender, presence of hemorrhage, history of hypertension, diabetes, heart disease, and kidney disease. Hypertension was defined as taking antihypertensive agents, systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg before the onset of SAH[1]. Diabetes was defined as taking oral antidiabetic agents or treatment with insulin injections.

Three-dimensional digital subtraction angiograms

Three-dimensional digital subtraction angiograms of ACoA aneurysms and the adjacent vasculature were performed on a monoplane DSA unit with rotational capabilities (Axiom Artis; Siemens Healthcare, Erlangen, Germany). The 3D DSA acquisition typically involved a 1-3 second delay, followed by a 2.5 mL/s injection of the contrast medium (iopromide, 300 mg/mL, Ultravist 300; Bayer Schering Pharma AG, Berlin, Germany) to a total of 12-15 mL. The rotational angiographic data were then transferred to an independent workstation (Leonardo Workplace; Siemens Healthcare, Erlangen, Germany) for generation of 3-dimensional reformatted images and precise measurements. Measurements were made on a metric scale (mm) to 0.01 decimal point.

Definition of morphological parameters

Morphological parameters examined on 3D DSAs included 13 variables: aneurysm size, width, neck diameter, maximum height, perpendicular height, parent vessel diameter, aspect ratio, size ratio, bottleneck ratio, height/width ratio, aneurysm angle, (in)flow angle, and branching angle (parent/daughter angle). These parameters have already been defined and depicted in the literature[1,4,5,14-16], and in Figure 1. The 5 categorical variables included the number of aneurysms in patient (single or multiple), shape of the aneurysm (spherical, non-spherical or irregular; in spherical aneurysms, width is 80% to 100% of its length, whereas aneurysms with multiple lobules, daughter sacs, or other types of wall protrusions were defined as irregular ones), aneurysm wall morphology (smooth or irregular), variation of the A1 segment, and direction of the aneurysm dome. We defined A1 dominance as more than 50% difference in diameter between the two A1 segments, which includes aplastic and hypoplastic unilateral

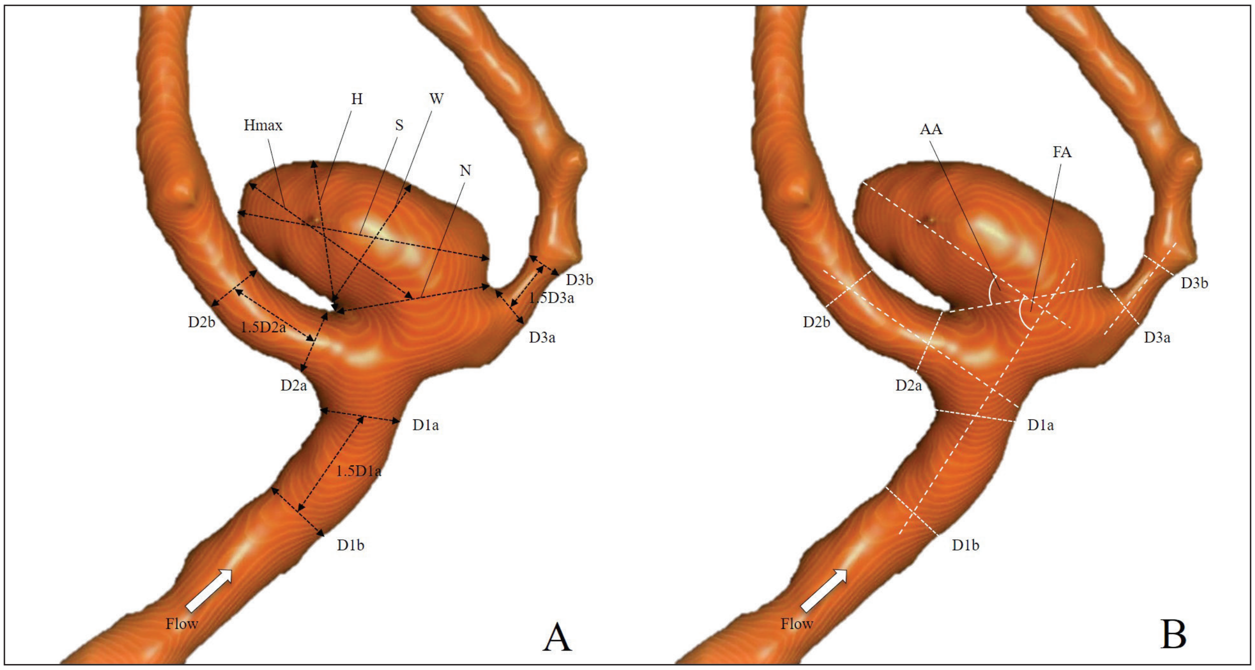

Fig. 1. Definition of morphological parameters of ACoA aneurysms on 3D DSA: (A) aneurysm size (S) is defined as maximum diameter of aneurysm dome. Aneurysm neck diameter (N) is the largest cross-sectional diameter of the aneurysm neck. The maximum aneurysm height (Hmax) is measured between the center of the aneurysm neck and the greatest distance to the aneurysm dome. Maximal perpendicular height (H) is the largest perpendicular distance from the neck of the aneurysm to the dome of the aneurysm. Aneurysm width (W) is the maximum dome diameter perpendicular to Hmax. The aspect ratio (AR) is calculated as the ratio between the maximum perpendicular height divided by the neck size (H/N). The size ratio (SR) is the ratio between Hmax and the mean vessel diameter of all branches associated with the aneurysm (D1-D3); for example, the mean vessel diameter of a proximal branch, which is determined by averaging the cross-sectional diameter of the vessel just proximal to the neck of the aneurysm (D1a) and the cross-sectional diameter at 1.5D1a from the neck of the aneurysm (D1b), and the mean vessel diameter of a distal branch which is determined by averaging the cross-sectional diameter of the vessel just distal to the neck of the aneurysm (D2a) and the cross-sectional diameter at 1.5D2a from the neck of the aneurysm (D2b). The bottleneck ratio (BNR) was defined as the ratio of dome width to neck width (W/N). The height/width ratio (H/W) was measured as the ratio of the maximal perpendicular height to the maximum diameter of the width of the aneurysm; (B) aneurysm angle (AA) is the angle between the plane formed by the neck of the aneurysm and the plane formed by the maximum height of the aneurysm. (In)Flow angle (FA) is the angle between the main vector of flow (centerline through the D1a and D1b) and the plane formed by the maximum height of the aneurysm. Branching angle (BA) is the angle between the main vector of flow (centerline through the D1a and D1b) and the vector of flow of branching vessel(s).

A1 segment aneurysms. The orientation of aneurysm dome was classified according to 6 directions: anterior, superior, posterior, inferior, medial, and lateral (Fig. 2).

Statistical analysis

The outcome variable was defined as the aneurysm rupture. The χ^2-test and Fisher exact test (in case the number of patients in a group was lower than 5) were used to verify the association between various characteristics of patients and outcomes. Numerical data were first analyzed graphically, and the normality of their distribution was verified using the Shapiro-Wilk test. In case the Shapiro-Wilk test confirmed normal distribution, numerical data were presented as means and standard deviations, and Student's t-test or ANOVA was used to compare between two or more groups, respectively. Oth-

Fig. 2. Classifying the direction of aneurysm dome. After positioning the patient, with the head fixed in a dedicated mold, the machine arm was calibrated so that the patient`s anterior skull base was parallel to the horizontal line on the anterior and profile planes of the DSA. Then, 3D DSA acquisition was performed, and data were transferred to an independent workstation. The direction of the aneurysm was determined according to projection cube on 3D DSA images in dedicated software (Leonardo Workplace; Siemens Healthcare, Erlangen, Germany).

erwise, numerical data were presented as median values with minimum and maximum values, and the Kruskal-Wallis test was used to compare numerical variables between different groups. Logistic regression was used to calculate the odds ratios and 95% confidence intervals (95% CI) for the likelihood of aneurysm rupture and each individual morphological and clinical characteristic. A 2-sided $p<0.05$ was considered as statistically significant. Significant predictors were then used in a multiple logistic regression model. The false discovery rate was controlled using the Tukey (for parametric) and Benjamini-Hochberg (nonparametric) procedure for multiple testing. Statistical analyses and visualizations were done using the R language and environment for statistical computing, including the following additional packages: Hmisc, dplyr, compareGroups, finalfit[17-21].

Results

This study included 78 female and 75 male patients, median age 57. Table 1 summarizes demographic and clinical characteristics of study patients according to the aneurysm rupture status. Gender, hypertension under control, and heart disease were significantly associated with aneurysm rupture. Among ruptured aneurysms, there was a higher proportion of male patients, and among unruptured aneurysms there was a higher proportion of patients with hypertension under control and those with heart disease.

Table 1. Socio-demographic and clinical characteristics of patients with ruptured and unruptured ACoA aneurysms

	All N=153	Ruptured N=112	Unruptured N=41	p value
Age (years)	57.0 (21.0-80.0)	56.0 (21.0-80.0)	57.0 (41.0-74.0)	0.426
Gender:				0.016
Female	78 (51.0%)	50 (44.6%)	28 (68.3%)	
Male	75 (49.0%)	62 (55.4%)	13 (31.7%)	
Hypertension:				0.867
No	52 (34.0%)	39 (34.8%)	13 (31.7%)	
Yes	101 (66.0%)	73 (65.2%)	28 (68.3%)	
Hypertension under control:				<0.001
No	58 (57.4%)	52 (71.2%)	6 (21.4%)	
Yes	43 (42.6%)	21 (28.8%)	22 (78.6%)	
Diabetes mellitus:				0.661
No	146 (96.1%)	107 (96.4%)	39 (95.1%)	
Yes	6 (3.9%)	4 (3.6%)	2 (4.9%)	
Heart disease:				0.005
No	133 (86.9%)	103 (92.0%)	30 (73.2%)	
Yes	20 (13.1%)	9 (8.0%)	11 (26.8%)	
Kidney disease:				1.000
No	151 (98.7%)	110 (98.2%)	41 (100.0%)	
Yes	2 (1.3%)	2 (1.8%)	0 (0.0%)	

Table 2 summarizes morphological parameters of the aneurysms divided by the aneurysm rupture status. Aneurysms with smaller neck diameters, greater aspect ratios and height/width ratios, larger aneurysm angles, presence of daughter sacs, irregular wall morphology, irregular and non-spherical shapes were significantly associated with aneurysm rupture. A lower rate of ACoA aneurysm rupture was shown in patients with multiple aneurysms.

Table 2. Differences in morphological parameters measured by 3D DSA between ruptured and unruptured ACoA aneurysms

	All patients N=153	Ruptured N=112	Unruptured N=41	p value
Aneurysm size	6.5 (1.2-15.0)	6.5 (1.2-15.0)	6.6 (1.8-13.7)	0.499
Aneurysm size groups:*				0.180
Very small	5 (3.3%)	2 (1.8%)	3 (7.3%)	
Small	40 (26.1%)	27 (24.1%)	13 (31.7%)	
Medium	89 (58.2%)	67 (59.8%)	22 (53.7%)	
Large	19 (12.4%)	16 (14.3%)	3 (7.3%)	
Neck diameter	2.8 (1.4-7.5)	2.7 (1.5-7.5)	3.3 (1.4-6.4)	0.047
Maximum height	5.9 (1.2-13.0)	5.9 (1.2-13.0)	5.8 (1.6-10.0)	0.301
Perpendicular height	5.1 (1.0-12.0)	5.0 (1.0-12.0)	5.5 (1.5-10.0)	0.858
Maximum width	4.7 (1.7-10.0)	4.6 (1.9-10.0)	5.0 (1.7-9.6)	0.223
Number of aneurysms:				0.002
Single	112 (73.2%)	90 (80.4%)	22 (53.7%)	
Multiple	41 (26.8%)	22 (19.6%)	19 (46.3%)	
Aspect ratio	1.7 (0.3-4.0)	1.8 (0.3-4.0)	1.5 (0.7-2.7)	0.002
Size ratio	2.7 (0.7-6.1)	2.7 (0.7-6.1)	2.7 (0.7-4.9)	0.124
Height/width ratio	1.1 (0.1-2.2)	1.1 (0.1-2.2)	0.9 (0.6-1.9)	0.010
Bottleneck ratio	1.6 (0.8-3.5)	1.6 (0.9-3.5)	1.5 (0.8-2.9)	0.400
Inflow angle	142.0 (94.0-177.0)	144.0 (94.0-177.0)	135.0 (103.0-173.0)	0.107
Aneurysm angle	72.0 (21.0-90.0)	70.0 (21.0-90.0)	80.0 (35.0-90.0)	0.007
Branching angle	116.9 (17.4)	116.8 (16.7)	116.9 (19.6)	0.982
Dominance:				0.206
Co-dominant	53 (34.6%)	35 (31.2%)	18 (43.9%)	
A1 one side dominant	100 (65.4%)	77 (68.8%)	23 (56.1%)	
Direction:				0.748
Anterior	62 (40.5%)	48 (42.9%)	14 (34.1%)	
Superior	20 (13.1%)	15 (13.4%)	5 (12.2%)	
Inferior	10 (6.5%)	7 (6.2%)	3 (7.3%)	
Medial	61 (39.9%)	42 (37.5%)	19 (46.3%)	
Shape:				<0.001
Spherical	28 (18.3%)	10 (8.9%)	18 (43.9%)	
Non-spherical	29 (19.0%)	20 (17.9%)	9 (22.0%)	
Irregular	96 (62.7%)	82 (73.2%)	14 (34.1%)	
Daughter sac (bleb):				<0.001
No	79 (51.6%)	43 (38.4%)	36 (87.8%)	
Yes	74 (48.4%)	69 (61.6%)	5 (12.2%)	
Wall morphology:				<0.001
Smooth	50 (32.7%)	21 (18.8%)	29 (70.7%)	
Irregular	103 (67.3%)	91 (81.2%)	12 (29.3%)	

*very small (0.0-2.9 mm), small (3.0-4.9 mm), medium (5.0-9.9 mm), large (10.0-24.9 mm), giant (≥25.0 mm)

Table 3. Univariable and multivariable logistic regression analysis

Dependent: Ruptured aneurysm		Unruptured	Ruptured	OR (univariable)	OR (multivariable)
Gender	Female	28 (35.9)	50 (64.1)	-	-
	Male	13 (17.3)	62 (82.7)	2.67 (1.27-5.83, p=0.011)	1.08 (0.19-6.15, p=0.928)
Hypertension under control	No	6 (10.3)	52 (89.7)	-	-
	Yes	22 (51.2)	21 (48.8)	0.11 (0.04-0.29, p<0.001)	0.01 (0.00-0.09, p=0.001)
Aneurysm size groups:*	Very small	3 (60.0)	2 (40.0)	-	-
	Small	13 (32.5)	27 (67.5)	3.12 (0.46-25.94, p=0.243)	-
	Medium	22 (24.7)	67 (75.3)	4.57 (0.71-36.41, p=0.108)	-
	Large	3 (15.8)	16 (84.2)	8.00 (0.96-86.72, p=0.061)	-
	Giant	0 (-)	0 (-)	-	-
Neck diameter	Mean (SD)	3.4 (1.3)	2.9 (0.9)	0.66 (0.47-0.92, p=0.016)	0.33 (0.13-0.71, p=0.009)
Maximum height	Mean (SD)	5.6 (2.3)	6.2 (2.4)	1.11 (0.95-1.32, p=0.187)	-
Perpendicular height	Mean (SD)	5.2 (2.2)	5.3 (2.1)	1.02 (0.87-1.22, p=0.792)	-
Maximum width	Mean (SD)	5.4 (2.3)	4.9 (1.9)	0.89 (0.74-1.06, p=0.195)	-
Number of aneurysms	Single	22 (19.6)	90 (80.4)	-	-
	Multiple	19 (46.3)	22 (53.7)	0.28 (0.13-0.61, p=0.001)	0.01 (0.00-0.11, p=0.001)
Aspect ratio	Mean (SD)	1.6 (0.5)	1.9 (0.6)	2.78 (1.41-5.96, p=0.005)	3.74 (0.52-38.77, p=0.217)
Size ratio	Mean (SD)	2.7 (1.1)	3.0 (1.2)	1.33 (0.96-1.87, p=0.094)	-
Height/width ratio	Mean (SD)	1.0 (0.2)	1.1 (0.3)	3.97 (1.24-14.25, p=0.026)	2.25 (0.05-123.23, p=0.681)
Bottleneck ratio	Mean (SD)	1.6 (0.5)	1.7 (0.6)	1.59 (0.79-3.39, p=0.210)	-
Inflow angle	Mean (SD)	138.3 (17.5)	143.5 (19.4)	1.01 (1.00-1.03, p=0.130)	-
Aneurysm angle	Mean (SD)	73.6 (15.5)	64.9 (19.0)	0.97 (0.95-0.99, p=0.012)	0.96 (0.90-1.02, p=0.260)
Branching angle	Mean (SD)	116.9 (19.6)	116.8 (16.7)	1.00 (0.98-1.02, p=0.980)	-
Dominance	Co-dominant	18 (34.0)	35 (66.0)	-	-
	A1 one side dominant	23 (23.0)	77 (77.0)	1.72 (0.82-3.59, p=0.147)	-
Shape	Spherical	18 (64.3)	10 (35.7)	-	-
	Non-spherical	9 (31.0)	20 (69.0)	4.00 (1.36-12.56, p=0.014)	0.45 (0.01-10.62, p=0.629)
	Irregular	14 (14.6)	82 (85.4)	10.54 (4.15-28.56, p<0.001)	0.61 (0.05-7.16, p=0.685)
Daughter sac (bleb)	No	36 (45.6)	43 (54.4)	-	-
	Yes	5 (6.8)	69 (93.2)	11.55 (4.55-35.66, p<0.001)	6.81 (1.06-60.84, p=0.056)
Wall morphology	Smooth	29 (58.0)	21 (42.0)	-	-
	Irregular	12 (11.7)	91 (88.3)	10.47 (4.71-24.66, p<0.001)	11.43 (1.37-166.90, p=0.041)

*very small (0.0-2.9 mm), small (3.0-4.9 mm), medium (5.0-9.9 mm), large (10.0-24.9 mm), giant (≥25.0 mm)

Demographic and clinical characteristics of patients that were significantly associated with aneurysm rupture, as well as all morphological characteristics of the aneurysms were tested using univariable logistic regression. Then, the variables significantly associated with rupture were included in the multivariable logistic regression model. Results of these analyses are presented in Table 3. Male gender was associated with 2.67 times higher odds of rupture (95% CI: 1.27-5.83). Hypertension under control was associated with almost 10 times lower odds of rupture (odds ratio (OR): 0.11, 95% CI: 0.04-0.29). Higher aspect ratio was associated with 2.78 (95% CI: 1.41-5.96) and higher height/width ratio with 3.97 (95% CI: 1.24-14.25) times higher odds of rupture. Non-spherical shape was associated with 4 times higher odds of rupture (95% CI: 1.36-12.56), while irregular shape was associated with more than 10 times higher odds of rupture (OR: 10.54, 95% CI: 4.15-28.56). In the multivariable model, hypertension under control, neck diameter, number of aneurysms, and wall morphology remained significant predictors of aneurysm rupture. Controlled hypertension, presence of multiple aneurysms and larger neck diameter reduced the odds of rupture, while irregular wall morphology increased the risk of rupture. Figure 3 shows the odds ratios and 95% CI of the predictors in the multivariable model graphically.

Discussion

In our study, several socio-demographic and clinical characteristics were significantly associated with aneurysm rupture. Male gender was statistically associated with a higher risk of rupture of ACoA aneurysms based on the univariate logistic regression model, but this parameter was no longer statistically significant in the multivariate logistic regression model. Regulated hypertension was associated with lower odds of ACoA aneurysm rupture and represented a significant protective factor. Considering morphological characteristics, ACoA aneurysms with smaller neck diameters, greater aspect ratios and height/width ratios, larger aneurysm angles, presence of daughter sacs, irregular wall morphology, irregular and non-spherical shapes were statistically significantly associated with aneurysm rupture.

The socio-demographic part of most studies on intracranial aneurysms emphasizes female predominance in both patients with intracranial aneurysms and patients with ruptured intracranial aneurysms[4,22,23]. However, Krzyzewski *et al.* observed a less common occurrence of ACoA aneurysms in female compared to male patients[24]. Our study, which had an almost even gender distribution, showed that ACoA aneurysms more often ruptured in male patients, and to our knowledge, this is the first study to report such results.

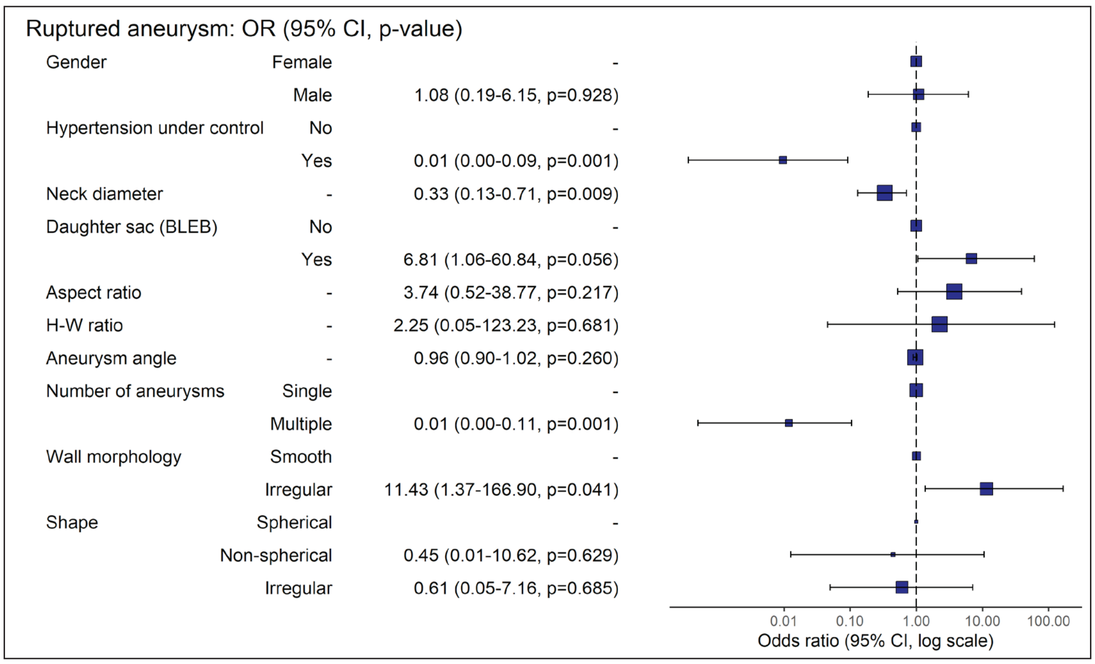

Fig. 3. Odds ratios and 95% confidence intervals of the predictors of rupture in the multivariable logistic regression plot.

This finding could be related to the fact that male gender is more commonly associated with hypertension[25].

Hypertension may impact the formation of aneurysms, as well as aneurysm rupture, but this relationship remains controversial[23]. In our study, there was no significant difference in the incidence of hypertension between ruptured and unruptured groups. Few studies have investigated the relationship of aneurysm rupture and unstable blood pressure rather than high blood pressure only, and found that unstable blood pressure with fluctuations was a risk factor for aneurysm rupture[23,26-28]. In our study, in the group of patients with hypertension, those with unstable hypertension were more likely to have ruptured aneurysm. This supports the relationship between erratic blood pressure levels and rupture of cerebral aneurysms[23]. Thus, patients with hypertension and ACoA aneurysm, who do not take antihypertensive therapy on a regular basis, are at a greater risk of aneurysm rupture.

Heart disease showed negative association with rupture of ACoA aneurysms (Table 1). This paradox could be explained by the fact that patients with diagnosed heart disease often regularly comply with scheduled physician checkups, already have prescribed medication therapy (antihypertensives) and avoid physical activity, thus also avoiding sudden fluctuations in blood pressure. This relationship has also been presented in the study of Inagawa[29], which provided evidence that, although heart disease is associated with atherosclerosis and may contribute to aneurysm formation, may also reduce the risk of aneurysm rupture.

Although the size of the aneurysm is one of the strongest related factors for its rupture and the risk of rupture increases as the size of the aneurysm increases, controversy remains regarding the critical size for rupture[1,5,30-32]. Like other authors, we found a higher proportion of ruptured ACoA aneurysms to be ≥5 mm compared to unruptured ones, but this difference and the overall difference in size was not statistically significant, even after the aneurysms were divided into size specific subgroups.

Similar to the study by Lin *et al.*[15], the presence of multiple intracranial aneurysms, along with ACoA aneurysm, reduced the odds of ACoA aneurysm rupture in our study. The possible explanation is that aneurysms at other locations could present with neurological symptoms or even rupture before the ACoA aneurysm, so that ACoA aneurysm is diagnosed incidentally.

Although many studies asserted the importance of aspect ratio (AR) in intracranial aneurysm rupture, this was not found statistically significant in most of them, and there has been no consensus regarding a common threshold AR value[1,7,33,34]. Nevertheless, Raghavan *et al.*[7] and Dhar *et al.*[9] report that ruptured aneurysms were associated with a significantly greater AR, and Beck *et al.*[35] and Choi *et al.*[36] report that aneurysms with an AR value of more than 1.6 exhibited a high probability of rupture. Our results showed that ruptured ACoA aneurysms had significantly higher AR values and that higher AR was associated with almost 3 times higher odds of ACoA aneurysm rupture.

Along with AR, higher size ratio (SR) values were associated with aneurysm rupture in many studies[1,4,15,37]. Furthermore, Dhar *et al.*[9] report that the SR was the most significant correlative factor for aneurysm rupture. We did not confirm correlation of SR values and rupture of ACoA aneurysms.

Additional morphological parameters such as bottleneck ratio (BNR) and height/width ratio (H/W) have been developed in an effort to predict the rupture status of intracranial aneurysms more accurately. We found that H/W ratio values were significantly higher in ruptured ACoA aneurysms compared to unruptured ones and that aneurysms with higher H/W ratio values were associated with 4 times higher odds of rupture. The plausible cause could be that in our experience, ruptured ACoA aneurysms had a more elongated shape. Hoh *et al.*[38] also found that patients with ruptured aneurysms had higher H/W values, and even stated that with an increase in H/W ratio of 0.1, the likelihood of rupture increased by 23%.

Dhar *et al.*[9] report that the aneurysm angle (AA) was correlated with ruptured intracranial aneurysms, with an optimal threshold value of 112 degrees above which an intracranial aneurysm may be considered dangerous. Our results showed significant association between a lower AA and rupture of ACoA aneurysms. Analyzing the results reported by Dhar *et al.*[9], we presume that ours are comparable since our measuring scale was from 0 to 90 degrees, meaning that their value of 112 was our value of 78 degrees. Therefore, their dangerous AA being above 112 degrees could be our lower AA.

A neuroanatomical study by Wang *et al.*[39] showed dense fibrous trabeculae to differ by location around an ACoA; the distribution anterior to the ACoA may be sparse and an anterior direction of the aneurysm dome may indicate a tendency to rupture more easily[5]. Our study demonstrated that anterior and medial direction of the ACoAs aneurysm dome was considerably more frequent in patients with ruptured aneurysms (48 of 112; 43% and 42 of 112; 38%), but without statistical significance.

The irregular shape of the aneurysm on 3D DSA may reflect focal weakness with subsequent protrusions of the aneurysm wall and thrombosis on the luminal surface, which are related to degeneration and rupture of the wall[4,40]. Our results showed that ACoA aneurysms with irregularities in shape and wall morphology were strongly associated with aneurysm rupture (Table 3). Lindgren *et al*. report that irregular shape was the only factor consistently associated with high odds ratio of the incidence of ruptured intracranial aneurysms at diagnosis in every location independently of patient background or aneurysm size[4,41]. Raghavan *et al*. found that non-sphericity index was the best predictor of rupture, meaning that the more an aneurysm shape deviates from that of a sphere, the greater is the risk of rupture[7].

Study limitations

The main limitation of our study was related to the case-control study design. All conclusions made on the examined parameters can be associated with ruptured aneurysms only and are not necessarily predictors of rupture risk. On the other hand, true natural history series are impossible to carry out nowadays because high-risk lesions will always be treated before rupture. We compared morphological characteristics between ruptured and unruptured ACoA aneurysms, with an assumption that these parameters do not change significantly before and after the aneurysm rupture. It is possible that the rupture causes the aneurysm to shrink, at least with respect to its appearance on angiograms. However, there are studies that demonstrated that the rupture did not significantly change the aneurysm morphology[42,43]. This study was focused on aneurysms located at the ACoA, where multiple anatomic configurations and variants are observed. Therefore, the factors identified can currently be applied only to this localization, whereas factors associated with aneurysm rupture at other intracranial locations will be the subject of our future research.

Conclusion

Controlled hypertension represented a significant protective factor from ACoA aneurysm rupture. It is the risk factor that can be contained by medication therapy. ACoA aneurysms in male patients, and those with smaller neck diameters, greater aspect ratios and height/width ratios, larger aneurysm angles and irregularities in shape and wall morphology are associated with a higher risk of rupture. These socio-demographic, clinical, and morphological characteristics are easy to evaluate in every-day clinical practice and should be used in risk assessment of patients with ACoA aneurysms.

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Sažetak

POVEZANOST KLINIČKIH KARAKTERISTIKA I MORFOLOŠKIH PARAMETARA S RUPTUROM ANEURIZME PREDNJE KOMUNIKACIJSKE ARTERIJE

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Analizirali smo morfologiju aneurizme, demografske i kliničke karakteristike u bolesnika s aneurizmom prednje komunikacijske arterije (ACoA) kako bismo istražili čimbenike rizika koji doprinose rupturi aneurizme. Ukupno je 219 bolesnika s aneurizmom ACoA primljeno u našu bolnicu u razdoblju od siječnja 2016. do prosinca 2020. godine, a morfološke i kliničke karakteristike analizirane su retrospektivno u 153 bolesnika (112 puknutih i 41 neprekinuta). Pregledani su medicinski zapisi kako bi se dobili demografski i klinički podaci za dob, spol, prisutnost krvarenja, povijest hipertenzije, dijabetes, srčane bolesti i bolesti bubrega. Morfološki parametri ispitani na trodimenzionalnoj digitalnoj subtrakcijskoj angiografiji uključivali su veličinu aneurizme, promjer vrata, odnos između normalne visine aneurizme i širine vrata aneurizme (*aspect ratio*), odnos između visine aneurizme i prosječnog promjera svih krvnih žila povezanih s aneurizmom (*size ratio*), odnos između širine fundusa aneurizme i širine vrata aneurizme (*bottleneck ratio*), odnos između najveće normalne visine aneurizme i širine aneurizme *(height/width ratio)*, kut aneurizme, ugao ulaska tijeka krvne struje u fundus aneurizme (*inflow angle*), kut grananja, broj aneurizma po bolesniku, oblik aneurizme, morfologiju stijenke aneurizme, varijaciju segmenta A1 i smjer aneurizme. Muški spol, odnos između normalne visine aneurizme i širine vrata aneurizme, odnos između najveće normalne visine aneurizme i širine aneurizme, nesferičan i nepravilan oblik bili su povezani s većim izgledima za puknuće, dok je kontrolirana hipertenzija bila povezana s manjom vjerojatnosti puknuća kada je testirano primjenom modela s univarijatnom logističkom regresijom. U multivarijatnom modelu su kontrolirana hipertenzija, prisutnost više aneurizma i veći promjer vrata smanjili izglede za puknuće, dok je nepravilna morfologija stijenke povećala rizik od puknuća. Regulirana hipertenzija predstavlja značajan zaštitni čimbenik od pucanja aneurizme ACoA. Utvrdili smo da su aneurizme ACoA u muških bolesnika i one s većim odnosom između normalne visine aneurizme i širine vrata aneurizme te one s većim odnosom između najveće normalne visine aneurizme i širine aneurizme, većim kutovima aneurizme, prisutnošću kćeri vrećica te nepravilnim i nesferičnim oblicima u većem riziku od puknuća.

Ključne riječi: *Prednja komunikacijska arterija; Intrakranijska aneurizma; Ruptura aneurizme; Morfologija aneurizme; Klinički čimbenici rizika; Subarahnoidno krvarenje*