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Morphometric comparison of ruptured and non-ruptured intracranial aneurysms

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ABSTRACT

Aims: Morphologic features of cerebral aneurysms that may be related to the rupture of a cerebral aneurysm. We used precise measurements and software to create a comprehensive data set and determine the parameters that may affect cerebral aneurysm rupture risk.

Methods: After excluding patients with vasospasm, late admission (later than 72 hours), and previous hemorrhage or treatment history, 95 consecutive patients with 112 cerebral aneurysms were included in the study. Ten morphological parameters of aneurysms were compared between ruptured and non-ruptured aneurysms. These parameters include the size, depth and neck size of the aneurysm, the diameter of the parent artery and their ratio to each other.

Results: There were 87 ruptured and 25 non-ruptured cerebral aneurysms. The mean size, d90, dmax, SR1, SR2, and AR1 parameters of the ruptured cerebral aneurysms were significantly higher than the non-ruptured aneurysms, and SR1 was the strongest parameter for determining aneurysm rupture risk, which is the ratio of the maximum depth of the aneurysm to the average size of the parent vessel. Nevertheless, there was no significant correlation between age, sex, and aneurysm location.

Conclusions*:* It is observed that the perpendicular (d90) and maximum depth (dmax) of the aneurysm and the ratios of including these elements are greater in ruptured aneurysms. These results suggest that the depth of an aneurysm is probably the most relevant factor to the risk of rupture.

Keywords*:* Aspect ratio; cerebral aneurysm; cerebral hemorrhage; ruptured aneurysms; rupture risk; size ratio

INTRODUCTION

Aneurysmal subarachnoid hemorrhage (a-SAH) has a high morbidity and mortality, whereas non-aneurysmal subarachnoid hemorrhage (n-SAH) has a better prognosis. Therefore, diagnosis and treatment of an aneurysm should be done before rupture.[1] There are some prognostic factors such as size, location, and multiplicity for the risk of rupture.[2] Certain risk factors have been associated with an aneurysm and its rupture. Many studies have reported that the risk of aneurysm rupture is 1-2% per year.[3] Some previous studies have shown that some factors increase the risk of aneurysm rupture, such as genetic predisposition, female gender, connective tissue disease, the growth rate of aneurysm and PHASES score, and the presence of multiple cerebral aneurysms.[4,5]

Some morphological parameters have been studied in relation to the risk of aneurysm rupture, and morphological studies have been associated with aneurysm shape, parent vessel size, and depth. Each method provides insight and important data on aneurysm growth, rupture, and potential regrowth. Some morphologic parameters have been reported in the literature, but measurements of these parameters have been calculated differently, and different parameters have been evaluated in various studies.[6-12] Appropriate parameters that characterize the geometry of the intracranial aneurysm can capture the characteristic hemodynamics and potentially predict the risk of rupture. Several previous studies have investigated such parameters.

The most used parameter is the size of the intracranial aneurysm. Although aneurysms larger than 10 mm are considered prone to bleeding, several studies have shown that a large percentage of ruptured aneurysms are smaller than ten millimeters.[13] The relationship between intracranial aneurysm rupture risk and intracranial aneurysm size has not been fully understood. The aneurysm's shape has also been studied, and certain shape parameters show a stronger correlation with rupture than intracranial aneurysm size. Aspect ratio (AR), defined as intracranial aneurysm height divided by neck diameter, is the most studied shape parameter. Although most results confirm the importance of AR, there is no common threshold in the literature. Other, more sophisticated shape parameters such as the undulation index, nonsphere index, and ellipticity index have been proposed to account for the three-dimensionality (3D) of the intracranial aneurysm.[13] 3D parameters promise better predictions than lower-dimensional parameters such as size or AR and are further investigated in the current study.

This study includes all parameters used in the various papers in the literature. Our aim was to find the strongest morphometric parameters for rupture risk by evaluating all parameters from the literature. We also investigated statistically significant associations between aneurysm rupture and other parameters such as age, sex, and location of the aneurysm.

METHODS

This is a retrospective observational single-center study. The study was carried out with the permission of Ethical Committe of Faculty of Başkent University Institutional Review Board (Date:26.06.2024, Decision No: KA24/238). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Patient Selection

Patients with vasospasm, late admission (later than 72 hours), and previous SAH or treatment history were excluded from the study. Except for these conditions, ninety-five consecutive patients who underwent cerebral digital subtraction angiography (DSA) (Artis Zee, Siemens, Germany) between 2012 and 2015 and had a cerebral aneurysm were included. The angiographic images and electronic medical records of the patients were scanned.

Imaging Technique

For cerebral DSA, a total of 10-12 ml of nonionic contrast agent (Optiray 300, Mallinckrodt Health, İstanbul, Türkiye) was injected from each internal carotid artery and vertebral arteries at a rate of 5 ml/second using an automated injection device (Liebel-Flarsheim, Angiomat Illumena, Cincinnati/USA). For 3D angiography, 35 ml of nonionic contrast agent was injected from the right or left carotid artery at a 5 ml/second rate with an automatic power injector. After the one-second delay and seven-second rotation duration, 3D images were obtained with Siemens DSA suit's version VB20/VB21 software.

Data Collection

Measurements were performed by two radiologists using the 3D angiography images. They reviewed the images together and reached consensus on the measurements. All angiographies in the SAH group were obtained within 12 hours of SAH. Ten morphological parameters were sought, all calculated by the 3D software of the DSA unit.

Morphometric Parameters

Size: If the aneurysms' shapes were regular (not lobulated), we used the maximum perpendicular height from the neck of the aneurysm or the axial diameter. For irregular and lobulated aneurysms, we used the arithmetic mean of the smallest and largest diameters of the aneurysm.

Depth (d_{90}, d_{max}): We used two different calculations for depth; d90 (Figure 1, black arrow): the maximum perpendicular distance from the center of the neck to any point on the aneurysm wall, dmax (Figure 1, white arrow): the maximum distance between the dome of the aneurysm and the center of the neck.

Figure 1. Volume rendering technique image of a ruptured right middle cerebral artery bifurcation aneurysm. * The lengths d90 and dmax are indicated by black and white arrows, respectively

Neck size (n): Neck size represents the largest axial diameter at the aneurysm orifice.

Size of the parent vessel (p): If the aneurysm was on the lateral side of the wall, we used only the size of the parent vessel from which the aneurysm originated. We used the arithmetic mean of the parent vessels' size if the aneurysm was located at a bifurcation (Figure 2).

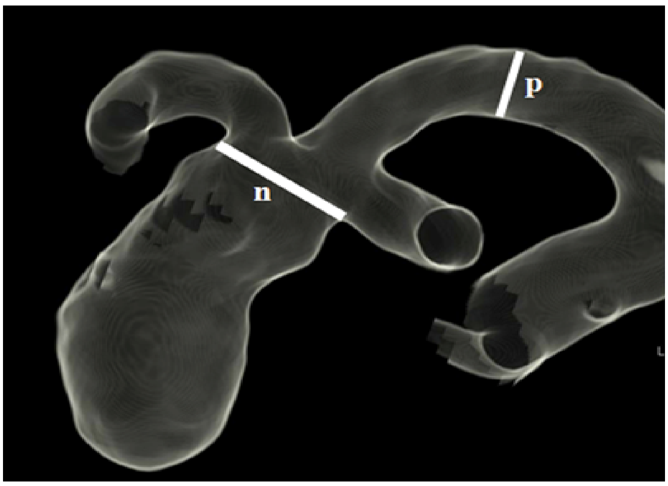

Figure 2. Volume Rendering Technique image of a ruptured right middle cerebral artery bifurcation aneurysm. *"Neck size" (n) and "size of the parent vessel" (p) are shewed

Aspect ratio (AR): AR1 was defined as the ratio of the maximum depth to the width of the aneurysm neck. AR2 was the perpendicular depth ratio to the aneurysm neck's width. AR1=dmax/n, AR2=d90/n.

Size ratio (SR): SR1 was calculated by dividing the maximum depth of the aneurysm by the average parent vessel size. SR2 was calculated by dividing the perpendicular depth of the aneurysm by the average parent vessel size. SR1=dmax/p, SR2=d90/p.

Ostium ratio (OR): OR was described as the ratio of the width of the aneurysm neck to the parent vessel size. OR=n/p.

Statistical Analysis

Two independent groups of ruptured and non-ruptured patients were compared using a T-test for normally distributed parameters. Mann-whitney U test was used for non-normally distributed parameters. Crosstab analysis with a chi-square test was used to determine the correlation between categorical parameters and the presence of rupture. Logistic regression models were sought and developed to predict rupture risk as a function of morphologic parameters. Logistic regression was used to evaluate the predictive value of rupture probability based on those independent parameters that differed significantly between ruptured and non-ruptured aneurysms. The logistic regression models were searched and developed in our study to predict the risk of rupture depending on the morphologic parameters.

RESULTS

Cerebral DSA was performed in 95 patients, with a total aneurysms of 112. Thirty-seven patients (40.2%) were male and had 35 ruptured cerebral aneurysms; 58 patients (59.8%) were female and had 52 ruptured cerebral aneurysms. There were 87 ruptured and 25 non-ruptured cerebral aneurysms. The mean age in the first group with a ruptured aneurysm was 56.6±11.04 years, and in the other group, 56.3±10.49 years. There was no statistically significant association between sex (Table 1), age, and rupture (Table 2).

Forty-two aneurysms (37.5%) were located at the anterior communicating artery (A-com), and 36 of them were ruptured (41.4%); 27 aneurysms (24.1%) were located at the middle cerebral artery (MCA) bifurcation, and 23 of them were ruptured (26.4%); 24 aneurysms (21.4%) were located at the internal carotid artery (ICA), and 14 of them were ruptured (16.1%); 11 aneurysms (9.8%) were located at the posterior communicating artery (P-com), and 8 of them were ruptured (9.2%); one aneurysm was located at the posterior cerebral artery (PCA), and it was unruptured (0.9%); five aneurysms (4.5%) were located at the basilar artery (BA), 4 of them were ruptured (4.6%); two aneurysms (1.8%) were located at the posterior inferior cerebellar artery (PICA), and both aneurysms were ruptured (1.8%). The most common aneurysm site was the A-com, followed by the MCA bifurcation. The most common non-ruptured aneurysm site was the ICA and then the A-com. The most common site of ruptured aneurysms was the A-com and then MCA.The morphological parameters of the ruptured aneurysms, such as size, d90, dmax, SR1, SR2, and AR1, were significantly different from those of the non-ruptured aneurysms. The mean size of the ruptured cerebral aneurysms was significantly larger (7.4±4.54 mm) compared with that of the non-ruptured aneurysms (4.92±3.06 mm) (p<0.001). Mean d90 was 6.55±3.81 mm in ruptured aneurysms and 3.81±1.6 mm in non-ruptured aneurysms (p<0.001).

The mean dmax value was 7.78±4.16 mm in ruptured aneurysms, and in non-ruptured aneurysms, 4,58±1.81 mm (p<0.001). Mean SR1 was 3.06±1.56 in ruptured aneurysms and 1.67±0.82 in non-ruptured aneurysms (p<0.001). Mean SR2 was 2.64±1.43 in ruptured aneurysms and 1.51±0.76 in non-ruptured aneurysms (p<0.001). In ruptured aneurysms, the mean AR1 value was 2.37±1.12; in non-ruptured aneurysms, 1.77±1.19 (p=0.001) (Table 2). Logistic regression was used to assess the independent predictive value of those parameters that differed significantly between ruptured and non-ruptured aneurysms (Table 3). In the final model, only SR1 remained, the most significant morphological predictive parameter for rupture (Table 3, Model 1.1). The risk of rupture of the aneurysm whose value of SR1 was known can be determined using a logistic regression model (Table 3, Model 1.2). Linear regression model 1.2 showed us the extent to which a change in SR1 value increases or decreases the probability of rupture of the intracranial aneurysm.

Table 1. Chi-Square analysis for rupture and sex

	RUPTURE					
	YES		NO		TOTAL	
SEX	Count	%Within rupture	Count	%Within Rupture	Count	%Within Rupture
MALE	35	40.2%	10	40%	45	40.2%
FEMALE	52	59.8%	15	60%	67	59.8%
TOTAL	87	100%	25	100%	112	100

Chi-square = 0.000, p=0.984

Table 2. Comparison of the parameters according to the groups.

	RUPTURE STATUS							
	YES			NO				
	N	Mean	Std. Deviation	N	Mean	Std. Deviation	TEST	Sig.
Age	87	56.6	11.04	25	56.3	10.49	t=-0.144	0.885
p	87	2.7138	0.8407	25	2.9	0.94296	t=0.95	0.344
n	87	3.323	1.24178	25	2.992	0.84504	t=-1.25	0.214
d90	87	6.5598	3.81312	25	3.8104	1.60573	t=-5.289	<0.001*
dmax	87	7.7885	4.16272	25	4.584	1.81675	t=-5.568	<0.001*
OR	87	1.3247	0.61757	25	1.124	0.47459	z=-1.654	0.098
SR2	87	2.6408	1.43862	25	1.51	0.76676	t=-5.199	<0.001*
AR2	87	2.0736	0.76272	25	1.748	0.66965	t=-1.93	0.056
SR1	87	3.0655	1.56293	25	1.676	0.82173	t=-5.92	<0.001*
AR1	87	2.377	1.12629	25	1.776	1.19906	z=-3.451	0.001*

p: size of the parent vessel (mm)
n: neck size (mm)
d90 and dmax: maximum and perpendicular depth of aneurysm (mm)
OR(n/p): ostium ratio (mm/mm)
AR1(dmax/n) and AR2(d90/n): aspect ratio (mm/mm)
SR1(dmax/p) and SR2(d90/p): size ratio (mm/mm)

Table 3: Logistic regression models of the aneurysms' morphologic parameters

MODEL 1. 1	B	S.E.	Wald	df	Sig.	Exp(B)	The correct classification ratio of the patient group (%)	The correct classification ratio of the control group (%)	General right classification ratio (%)
p	.545	.701	.605	1	.437	1.725	(83/87) = 95.4	(10/25) = 40.0	(93/112) = 83.0
n	-.353	.493	.514	1	.473	.702			
d90	.121	.575	.044	1	.833	1.129			
dmax	.396	.384	1.064	1	.302	1.486			
OR	-.788	1.068	.544	1	.461	.455			
SR_2	.716	1.341	.285	1	.594	2.046			
AR_2	-.731	.564	1.680	1	.195	.481			
SR_1	1.249	.890	1.967	1	.161	3.486			
AR_1	-.473	.460	1.057	1	.304	.623			
Size	-.271	.182	2.220	1	.136	.763			
Constant	-1.301	2.373	.300	1	.584	.272			
MODEL 1.2 FINAL MODEL									
SR_1	1.072	.276	15.108	1	.000	2.920	(83/87) = 95.4	(8/25) = 32.0	(91/112) = 81.3
Model 2									
d_{90}	.416	.125	11.111	1	.001	1.516	(83/87) = 95.4	(2/25) = 8.0	(85/112) = 75.9
Model 3									
d_{max}	.432	.122	12.490	1	.000	1.541	(83/87) = 95.4	(4/25) = 16.0	(87/112) = 77.7
Model 4									
SR_2	.984	.273	12.987	1	.000	2,674	(81/87) = 93,1	(3/25) = 12,0	(84/112) = 75.0
Model 5									
AR_1	.683	.302	5.120	1	.024	1.980	(87/87) = 100.0	(0/25) = 0.0	(87/112) = 77.7

p: size of the parent vessel (mm)
n: neck size (mm)
d90 and dmax: maximum and perpendicular depth of aneurysm (mm)
OR(n/p): ostium ratio (mm/mm)
AR1(dmax/n) and AR2(d90/n): aspect ratio (mm/mm)
SR1(dmax/p) and SR2(d90/p): size ratio (mm/mm)

DISCUSSION

Based on the results of two different recent meta-analyses on a population of 50 subjects, 33% male and 67% female, with a mean age of 50 years, without comorbidities, the incidence of cerebral aneurysms was reported to be 2%, and the annual probability of rupture 1.9%. From these results, we can infer that most cerebral aneurysms do not rupture.[14,15] The PHASES (population, hypertension, age, size of aneurysm, previous SAH from another aneurysm, location of aneurysm) score is a model that indicates the absolute risk of aneurysm rupture.[16] The aneurysm rupture risk increases when the PHASES score is high.[5]

We found that the mean size of ruptured cerebral aneurysms was significantly larger (7.4±4.54 mm) than that of non-ruptured aneurysms (4.92±3.06 mm). Indeed, many studies have reported that size is an important parameter for rupture, although the actual range for rupture risk is controversial.[17] However, most cases of a-SAH are due to small aneurysms in the anterior circulation,[18,19] so the size of aneurysm alone is not sufficient to assess rupture risk.

The aneurysm location is associated with the rupture status. Most clinical series reported that ruptured aneurysms were frequently located on the A-com, and the non-ruptured aneurysms were frequently located on the MCA, as found in the autopsy series. [17,20] Beck et al.[20] reported in their study of 155 aneurysms that ruptured aneurysms were more frequently located on the A-com than non-ruptured aneurysms. Similar to the literature, the most common aneurysm site and the most common rupture site in our study were A-com. In contrast to the autopsy series in the literature, the internal carotid artery is the most common site for non-ruptured aneurysms.

Several morphological parameters, including AR, SR, and OR, have been associated with cerebral aneurysm rupture.[6-8,11,12] SR is the most important calculation for predicting the rupture risk of these parameters. For example, in our serie, when the SR1 value is 1.3, the risk of rupture according to our model is 55.7%; when the SR1 value is 4, it increases to 95.7%, explaining that this increase in the SR1 value increases the risk of rupture by 40%. Dhar et al.[8] reported that AR and SR were significantly correlated with rupture. Their study included 45 aneurysms (25 non-ruptured, 20 ruptured). Ma D et al.[12] reported that SR and AR were associated with rupture. SR showed a more significant association with ruptured aneurysms than AR. Cai W et al.[7] studied AR and SR and reported that only SR could be a decisive factor correlating with aneurysm rupture. Nikolic I et al.[10] reported that OR and AR were statistically significant parameters for predisposition to rupture of intracranial aneurysms. However, they did not calculate SR in their study.

The values of SR1, SR2, and AR1 were significantly different between ruptured and non-ruptured aneurysms. These parameters were higher in ruptured aneurysms. Logistic regression was used to evaluate the independent predictive value of the parameters that differed significantly between ruptured and non-ruptured aneurysms, and only SR1 remained in the final model, which was the most significant morphological predictive parameter for rupture. OR, size, parent artery size, AR2, and neck size were not associated with rupture.The major limitation of this study is that the measurement of the aneurysms was performed after rupture, and the morphology of an aneurysm changes after rupture.[21] It is generally accepted that vasospasm affects the geometry of the truncal artery of the cerebral aneurysm approximately five days after hemorrhage.[9] In particular, the logistic regression data are misleading because if we want to predict the probability of rupture, we need to assess a non-ruptured aneurysm, and the model cannot be generalized to non-ruptured aneurysms. The best study design is to conduct a prospective study in a group of patients with nonruptured aneurysms and follow them up, but this is not feasible and ethical because patients diagnosed with cerebral aneurysm should be treated to prevent rupture of an aneurysm. Most of our patients underwent angiography within 24 hours of the first hemorrhage. Therefore, vasospasm is not expected in our patients, but some who had a quiet clinic may have contacted emergency services later. Apart from these, another study limitation is the small number of patients in the control group.

CONCLUSION

Increased size, d90, dmax, SR1, SR2, and AR1 were significantly associated with ruptured aneurysms. We can say that they are all predictive parameters for aneurysm behavior, and among them, SR1 is the strongest parameter for determining aneurysm rupture risk. These results show that the perpendicular and especially the maximum depth of an aneurysm is probably the factor that most influences the risk of aneurysm rupture. Compared to the maximum depth of the aneurysm, the perpendicular depth or its neck size seems less associated with the risk of rupture.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Ethical Committe of Faculty of Başkent University Institutional Review Board (Date:26.06.2024, Decision No: KA24/238).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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