Size is the Most Important Predictor of Aneurysm Rupture Among Multiple Cerebral Aneurysms: Post Hoc Subgroup Analysis of Unruptured Cerebral Aneurysm Study Japan

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BACKGROUND: Multiple cerebral aneurysms are encountered in approximately 15% to 35% of patients harboring unruptured cerebral aneurysms. It would be of clinical value to determine which of them is most likely to rupture.

OBJECTIVE: To characterize features of the ruptured aneurysm relative to other concomitant fellow aneurysms in patients with multiple cerebral aneurysms.

METHODS: From a total of 5720 patients who were prospectively registered in the Unruptured Cerebral Aneurysm Study in Japan, a subgroup of patients with multiple cerebral aneurysms who developed subarachnoid hemorrhage was extracted for this post hoc analysis. Intrapatient comparisons of each aneurysm were carried out using aneurysm-specific factors such as size, location, and shape to identify predictors of rupture among the fellow aneurysms in a patient with multiple cerebral aneurysms.

RESULTS: Twenty-five patients with 62 aneurysms were identified from the total cohort of 5720 patients. With the distinctiveness in size, which means the aneurysm was the single largest among the multiple aneurysms, the ruptured aneurysm in each case was discriminated from the other coexisting aneurysms with a sensitivity of 0.76 and specificity of 0.86.

CONCLUSION: Our results suggest that the largest aneurysm is likely to rupture among coexisting aneurysms in a patient with multiple cerebral aneurysms.

KEYWORDS: Cerebral aneurysm, Intracranial aneurysm, Multiple, Natural history, Post hoc, Rupture

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Multiple cerebral aneurysms are encountered in approximately 15% to 35% of patients harboring unruptured cerebral aneurysms.[1,2] It would be of clinical value to determine which of the multiple aneurysms is most likely to rupture. Potential predictors include diameter, shape, and location within the vasculature.[1-6] Identification of the aneurysm at highest risk of rupture would help target surgical management.

The Unruptured Cerebral Aneurysm Study (UCAS) is a large prospective cohort study of unruptured cerebral aneurysms in the Japanese population designed to clarify the natural history of unruptured cerebral aneurysms and to identify predictors of rupture.[7] From January 2001 to March 2004, 6697 aneurysms in 5720 patients were registered and followed for 3to 8 yr. The annual rupture risk of unruptured cerebral aneurysm was 0.95%. Aneurysms with large diameter, those located at the anterior communicating artery (Acom) or posterior communicating artery(Pcom), and those with a daughter sac were at increased risk of rupture.[1]

In this study, a subgroup of the patients with multiple aneurysms who developed subarachnoid hemorrhage was analyzed to characterize features of the ruptured aneurysm relative to other concomitant fellow aneurysms. This was done to help characterize predictors of rupture among multiple cerebral aneurysms.

ABBREVIATIONS: Acom, anterior communicating artery; **BA,** basilar artery; **ICA,** internal carotid artery; **MCA,** middle cerebral artery; **Pcom,** posterior communicating artery; **UCAS,** Unruptured Cerebral Aneurysm Study

METHODS

UCAS Japan

The UCAS Japan is a project of the Japan Neurosurgical Society designed to clarify the natural course of unruptured cerebral aneurysms. In this study, patients of age $\geq$ 20 yr were eligible for enrollment if they had an aneurysm larger than 3 mm. Patients with a past history of intracranial hemorrhage with an unknown or untreated cause, patients with decreased ability to engage in activities of daily life (modified Rankin score more than 2) and patients with an aneurysm located at the cavernous portion of the internal carotid artery (ICA) were excluded from the study. Detailed inclusion and exclusion criteria are available in the protocol described on the UCAS Japan website[7] and in a previously published report.[1] Investigators at each institution obtained the approval of the local institutional review board to conduct this study. Each patient was fully informed about this study and provided written consent to participate.

From January 2001 to March 2004, a total of 6697 aneurysms among 5720 patients were registered from any one of 283 institutions. Most aneurysms (91%) were detected incidentally.

At the time of registration, patient information, such as age, sex, smoking habits, reason for imaging, and family and past history of subarachnoid hemorrhage and other diseases were recorded. Aneurysm information was also collected, including largest diameter, presence of thrombosed or calcified component on the aneurysm wall, and presence of a daughter sac. A daughter sac was defined as an irregular protrusion of the aneurysm wall on 2-dimensional or 3-dimensional imaging.

In the total cohort, 111 ruptures were observed during a follow-up period of 3to 8 yr. Subarachnoid hemorrhage was identified by means of computed tomography, lumbar puncture, or autopsy. The culprit aneurysm that ruptured and caused subarachnoid hemorrhage in a multiple aneurysm case was determined by local investigators based on autopsy, microsurgical findings, or radiographic findings. When the site of aneurysm rupture was determined radiologically, the images at the registration and the images at the subarachnoid hemorrhage were compared and the aneurysms with any changes in the size or the shape with a focal clot accumulation were determined as the culprit aneurysms.

The primary results of the UCAS Japan were published previously.[1] The annual rupture risk of unruptured aneurysm was 0.95%, and independent risk factors for rupture were size (more than 7 mm), location (Acom or Pcom), and shape (the presence of a daughter sac) of the aneurysm.

Extracting the Subgroup for the Analysis

In the total cohort of the 5720 patients registered in the UCAS Japan, there were 793 patients who had multiple aneurysms at the time of registration (13.9%). Among them, aneurysm rupture was observed in 25 patients. These 25 patients harbored a total of 62 aneurysms, which were subjected to post hoc subgroup analysis.

Intrapatient Comparison of the Aneurysms

Multiple cerebral aneurysms coexisting in a patient share patient-specific characteristics, such as genetic background, hypertension, cigarette smoking habits, and so on. In order to characterize the aneurysm with eventual rupture among the coexisting aneurysms, intrapatient comparisons were carried out using aneurysm-specific factors, such as size, location, and shape.

Distinctiveness of Each Aneurysm when Compared with the Coexisting Aneurysms

For each aneurysm, the distinctiveness was evaluated and determined by comparing it to the other coexisting aneurysms in each patient in terms of size, location, and shape.

Distinctiveness in size. When an aneurysm was the single largest aneurysm in each patient, the aneurysm was considered "distinctive" in size, and the other aneurysm in that patient were "not distinctive." When the same largest diameter was found, none of the aneurysms were considered distinctive in size.

Distinctiveness in location. When an aneurysm was the only aneurysm located at the Acom or Pcom in a patient, the aneurysm was considered "distinctive" in location, and the other aneurysms in that patient were "not distinctive." When more than one aneurysm was located at the Acom or Pcom, none of the aneurysms were considered distinctive in location.

Distinctiveness in shape. A daughter sac was defined as an irregular protrusion of the aneurysmal wall on 2-dimensional or 3-dimensional imaging. When an aneurysm was the only aneurysm with a daughter sac in a patient, the aneurysm was considered "distinctive" in shape, and the other aneurysms in that patient were "not distinctive." When more than one aneurysms with a daughter sac was found, none of the aneurysms were considered distinctive in shape.

Aneurysm Scoring Based on UCAS Score (UCAS Aneurysm Score)

The UCAS score[6] is a recently published model for estimating the 3-yr rupture probability of unruptured cerebral aneurysms based on 6 parameters (ie, age, sex, hypertension, and aneurysm size, location, and daughter sac). In this study, the UCAS score was modified and computed for each aneurysm using only the size (0 for <7 mm, 2 for 7-10 mm, 5 for 10-20 mm, 8 for $\geq$20 mm), the location (0 for ICA, 1 for anterior cerebral artery and vertebral artery, 2 for middle cerebral artery (MCA) and basilar artery(BA), 3 for Acom and Pcom) and the daughter sac (0 for no, 1 for yes). Patient-specific factors, such as age, sex, and hypertension, were shared by all the coexisting aneurysms within a patient. Each aneurysm was labeled as to whether it had the highest score among the coexisting fellow aneurysms in each patient.

Aneurysm Scoring Based on PHASES Score (PHASES Aneurysm Score)

The PHASES score[3] is a model for predicting the 5-yr rupture probability of unruptured cerebral aneurysms and takes into account age, hypertension, history of subarachnoid hemorrhage, geographical region, aneurysm size, and aneurysm location. The PHASES score was modified and computed for each aneurysm using only the aneurysm-specific parameter, size (0 for <7.0 mm, 3 for 7.0-9.9 mm, 6 for 1.0-19.9 mm, 10 for $\geq$20 mm) and the aneurysm location (0 for ICA, 2 for MCA, 4 for anterior cerebral arteries, Pcom, and posterior circulation). Each aneurysm was labeled as to whether it had the highest score among the coexisting fellow aneurysms in each patient.

Statistical Analysis

For the statistical analysis, JMP Pro 11 software (SAS, Cary, North Carolina) was used in this study.

Characteristics of patients and aneurysms in this subgroup were compared to those of the total cohort using the z test for mean values and the chi-square test for proportional values.

Two-by-two contingency tables were created using the rupture state as the outcome variable and using the distinctiveness in size, location, and shape as the predictor variables; the sensitivity and the specificity were calculated for each predictor variable.

Pearson's chi-square tests for univariate analysis and conditional logistic regression model for multivariate analysis were done using the rupture status as the outcome variable and using the distinctiveness in size, location and shape as the predictor variables in order to calculate the odds ratio for rupture and their 95% confidential intervals. *P* values less than .05 were considered to indicate statistical significance.

RESULTS

Characteristics of Patients and Aneurysms

Details of patient and aneurysm characteristics can be found in Table 1. The mean age in this subgroup was 69.1 ± 11.8 (mean ± standard deviation), and it was significantly higher than that in the total cohort. Eighty per cent of the patients were female. Approximately 80% of the cases were discovered incidentally. There was one case (4%) with a past history of subarachnoid hemorrhage and which had more than one aneurysm after the ruptured aneurysm was treated. There were 3 cases (12%) with symptomatic aneurysms and there was 1 (4%) aneurysm in which the reason for diagnosis was not specified. The cases with symptomatic aneurysms were more frequent in this subgroup than in the total cohort. Former and current cigarette smokers were significantly lower in this subgroup.

There were 62 aneurysms in 25 patients, and the mean number of aneurysms per patient was 2.48 ± 0.82. Two, 3, 4, and 5 aneurysms were present in 17, 5, 2, and 1 patient(s), respectively. The aneurysm size was significantly larger in this subgroup (6.9 ± 4.1 mm) than in the total cohort (5.7 ± 3.7 mm). Twenty-one aneurysms were located at the MCA, 5 at the Acom, 3 at the ICA excluding the Pcom, 23 at the Pcom, 4 at the BA, 1 at the vertebral artery, and 55 at other locations. Twenty-six of 62 aneurysms (45.2%) were located at the Acom and Pcom. The Acom aneurysms were less frequent in this subgroup (8.1%) than in the total cohort (15.5%), but the frequency of Pcom aneurysm was higher in this subgroup (37.1%) than in the total cohort (15.5%). Eleven aneurysms had a daughter sac (17.7%). One aneurysm had a calcified wall. No aneurysm had a thrombosed wall.

TABLE 1. Patient and Aneurysm Characteristics

	Subcohort in this study	Total cohort	*P* value*
Number of cases	25	5720	
Age (years)	69.2 ± 11.8	62.5 ± 1.3	.0011
Female sex	80%	66.5%	.1527
Reason for diagnosis			
Incidental	80%	91.2%	
SAH	4%	3.8%	.0408
Other	16%	5.0%	
Fx. of SAH	16%	12.9%	.6438
Former and current smoking	4%	16.8%	.0869
Medical history			
Hypertension	60%	43.4%	.094
Diabetes mellitus	4%	6.3%	.636
Hyperlipidemia	4%	14.1%	.1468
Ischemic stroke	0%	7.0%	<.0001
PCKD	0%	.3%	<.0001
Number of aneurysms	62	6697	
Size	6.9 ± 4.1mm	5.7 ± 3.7mm	.0095
Location			
MCA	33.9%	36.2%	
Acom	8.1%	15.5%	
ICA	4.8%	18.6%	
Pcom	37.1%	15.5%	<.001
BA	6.5%	6.6%	
VA	1.6%	1.8%	
Other	8.1%	5.7%	
Shape			
Thrombosed	0%	1.8%	<.0001
Calcified	1.6%	1.7%	.9577
Daughter sac	17.7%	18.9%	.8158

Acom, anterior communicating artery; BA, basilar artery; ICA, internal carotid artery; Fx., family history; MCA, middle cerebral artery; PCKD, polycystic kidney disease; Pcom, posterior communicating artery; SAH, subarachnoid hemorrhage; VA, vertebral artery.
**P* values for mean values were calculated with the use of z test, and *P* values for proportions were calculated with the use of Spearman's chi-square test.

Distinctiveness in Size

In 19 of 25 patients (76%), the ruptured aneurysm was exclusively the largest among the coexisting aneurysms and was distinctive in size. In 5 patients, smaller aneurysms ruptured. There was 1 patient in whom all the aneurysms were of the same size. When 1 patient in whom all the aneurysms had the same size was excluded, the distinctiveness in size discriminated the ruptured aneurysm in 19 of 24 patients (79%). The sensitivity and the specificity of "distinctiveness in size" in discriminating the ruptured aneurysms in each patient were 0.76 and 0.86, respectively.

Distinctiveness in Location

In 8 of 25 patients (32%), the ruptured aneurysm was distinctive in location. Six patients had no aneurysms located at the Acom or Pcom. In 4 patients, more than 1 aneurysms was located at the Acom or Pcom. When these 10 patients were excluded, the distinctiveness in location discriminated the ruptured aneurysms in 8 of 15 patients (53%). The sensitivity and the specificity of "distinctiveness in location" were 0.32 and 0.73, respectively.

Distinctiveness in Shape

In 7 of 25 patients (28%), the ruptured aneurysm was distinctive in shape. Fifteen patients had no aneurysms with a

TABLE 2. Cases in Which the Ruptured Aneurysms Were Not Distinctive in Size

	Ruptured aneurysm			Fellow aneurysms		
Case	Location	Size (mm)	Daughter sac	Location	Size (mm)	Daughter sac
1	Pcom	7	no	Pcom	7	no
2	Pcom	4	no	MCA	10	no
				ICA	11	no
3	ACA	3	no	Pcom	3	no
4	Pcom	3	no	Pcom	8	no
5	ICA	4	no	Pcom	7	no
				Pcom	4	no
6	Pcom	5	no	BA	10	yes

ACA, anterior cerebral artery other than anterior communicating artery; BA, basilar artery; ICA, internal carotid artery; MCA, middle cerebral artery; Pcom, posterior communicating artery.

daughter sac. When these 15 patients were excluded, the distinctiveness in shape discriminated the ruptured aneurysms in 7 of 10 patients (70%). The sensitivity and the specificity of "distinctiveness in location" were 0.28 and 0.89, respectively.

UCAS Aneurysm Score

In 16 of 25 patients (64%), the UCAS aneurysm score of the ruptured aneurysm was exclusively the largest among the fellow aneurysms. In 6 patients, the aneurysm with the smaller scores ruptured. In 3 cases, the ruptured aneurysm had the largest score, but there were other aneurysms with the same score, and the UCAS aneurysm score did not discriminate the ruptured aneurysm. The sensitivity and the specificity of "the highest UCAS aneurysm score in each patient" in discriminating the ruptured aneurysm in each patient were 0.64 and 0.92, respectively.

PHASES Aneurysm Score

In 16 of 25 patients (64%), the PHASES aneurysm score of the ruptured aneurysm was exclusively the largest among the fellow aneurysms. In 6 cases, the aneurysm with smaller scores ruptured. In 3 cases, the ruptured aneurysm had the largest score, but there were other aneurysms with the same score, and the PHASES aneurysm score did not discriminate the ruptured aneurysm. The sensitivity and the specificity of "the highest PHASES aneurysm score in each patient" were 0.64 and 0.92, respectively.

Summary of the Results

Among the 6 patients in whom the ruptured aneurysms were not distinctive in size (Table 2), 1 patient had 2 aneurysms with the same largest diameter. In 5 patients, the smaller aneurysm ruptured. In 2 of these 6 patients, the ruptured aneurysms were located at the Acom or Pcom and could be discriminated with the distinctiveness in location. In 1 of the 6 patients, the PHASES aneurysm score discriminated the ruptured aneurysm. The distinctiveness in shape and the UCAS aneurysm score discriminated the rupture site in none of these 6 cases.

TABLE 3. Sensitivities and Specificities for Each Method to Discriminate the Ruptured Aneurysm Among the Coexisting Aneurysms

	Sensitivity	Specificity
Distinctiveness in size	0.76	0.86
Distinctiveness in location	0.32	0.73
Distinctiveness in shape	0.28	0.89
UCAS aneurysm score	0.64	0.92
PHASES aneurysm score	0.64	0.92

UCAS, Unruptured Cerebral Aneurysm Study.

TABLE 4. Contribution of Distinctiveness of the Aneurysms to Rupture Status

	Distinctiveness	Odds ratio (95% CI)	*P* value
	Size	5.4 (2.0-14.7)	.001
Univariate	Location	1.4 (0.5-3.9)	.533
	Shape	2.5 (0.6-9.8)	.183
	Size	5.7 (1.8-17.3)	.002
Multivariate	Location	1.6 (0.4-6.2)	.483
	Shape	1.2 (0.1-5.1)	.937

CI, confidential interval.

The sensitivity and the specificity for discriminating the ruptured aneurysms among the coexisting aneurysms are summarized in Table 3. The sensitivity of "distinctiveness in size" was 0.76, and it was higher than that for the other factors.

The results of univariate and multivariate analysis of 62 aneurysms are summarized in Table 4. Only the *P* value for the distinctiveness in size reached to the level of statistical significance in both univariate and multivariate analyses.

DISCUSSION

From a total of 5720 patients registered in UCAS Japan, 25 patients with multiple cerebral aneurysms with eventual rupture were identified, and the aneurysms of these patients were compared within each patient to identify predictors of rupture among the fellow aneurysms in a patient with multiple cerebral aneurysms.

For distinctiveness in size, the ruptured aneurysm in each case was discriminated from the other coexisting aneurysms with a sensitivity of 0.76 and specificity of 0.86. Our results suggest that the biggest aneurysm is likely to rupture among coexisting aneurysms in a patient with multiple cerebral aneurysms.

Distinctiveness in Size, Location, and Shape

We characterized each aneurysm according to distinctiveness in size, location, and shape. Only the distinctiveness in size was a significant predictor of ruptured aneurysm among multiple coexisting aneurysms.

Previous studies suggest that the location [1,2,4,5] and the shape[1,5] of aneurysms are strong predictors of rupture, and some clinicians expect that the smaller Acom aneurysms will rupture before larger MCA aneurysms in the patient with multiple cerebral aneurysms. To avoid underestimating the significance of location and shape, we recalculated the accuracy of distinctiveness in location and shape excluding the cases in which there were no aneurysms that were distinctive in location or shape. However, the recalculated accuracy of distinctiveness in location and shape for aneurysm rupture was 53% and 70%, respectively, which were less than that of the distinctiveness in size.

In the univariate and multivariate analyses, only distinctiveness in size reached the level of statistical significance (odds ratio ∼5.5). However, the sensitivity and specificity of the discrimination in size were not sufficiently high to be used as a diagnostic factor. Our results also emphasize the importance of the size of the aneurysm as a predictor of rupture, as described previously.[1,2,4,5]

Our results are not indicating that only the largest aneurysm should be treated leaving the others untreated since the SUAVe study[8] suggests that even small aneurysms might rupture with an annual risk of .94% in multiple aneurysm cases.

PHASES Aneurysm Score and UCAS Aneurysm Score

The PHASES score[3] and the UCAS score[6] are the prevailing scoring systems to estimate the probability of rupture among unruptured cerebral aneurysms for a certain period and are based on data from prospectively accumulated databases. Both scoring systems include a total of 6 factors with weighting coefficients based on cutting-edge statistics. Patient-specific factors, such as age and history of hypertension, were shared by the aneurysms within a patient. Only the aneurysm-related factors were incorporated as the aneurysm scores in this study.

It should be mentioned that neither scoring system is intended to predict which aneurysm is most likely to rupture among the multiple coexisting aneurysms in a certain patient. As to the PHASES score, when a patient had multiple aneurysms, the largest of these aneurysms served to categorize the patient. Thus, the PHASES aneurysm score might have been unsuitable for comparing the co-existing aneurysms in a patient. The UCAS score is designed to predict the rupture risk of an individual aneurysm, but it is still not intended for comparing multiple aneurysms in one patient.

Both scoring systems discriminated the ruptured aneurysm among the coexisting aneurysms with a sensitivity of 0.64. This value was lower than that of the distinctiveness in size, but this finding does not negate the effectiveness of these scoring systems; rather, it suggests that size is the strongest predictor (among the other aneurysm-specific factors) of the risk of aneurysm rupture in a patient with multiple aneurysms.

Limitations

The determination of rupture based on autopsy or microsurgery is more reliable than that based only on radiographic findings. We were not able to know how many radiographic findings were combined to determine the site of rupture by the local investigators from our database. However, the combinations of several radiographic findings are reported to identify the site of aneurysm rupture with the accuracy of 97.5%.[9] Our method to determine the site of aneurysm rupture may limit the accuracy of our results potentially.

Only 3 factors (ie, size, location, and shape) were included in this analysis as potential predictors of rupture, and there might be other potential factors that predict which aneurysm would rupture in a patient with multiple cerebral aneurysms.

The distinctiveness, the UCAS aneurysm score and the PHASES aneurysm score were relative criteria determined by intrapatient comparison of the aneurysm characteristics. The calculated sensitivity and the specificity for these criteria might have lost their original validity and should be treated only as a guide.

There were only 25 patients included in this post hoc analysis of multiple aneurysms with eventual rupture, despite the fact that the UCAS Japan is one of the largest cohorts that prospectively tracks cerebral aneurysms. The small sample size and the post hoc analysis design may limit the generalizability of our results.

This study was a post hoc analysis based on the cohort of UCAS Japan. As the number of post-hoc analyses increases, the reliability of the results would decrease according to the basic principles of statistical analysis.

This study is also limited by possible case selection bias in UCAS Japan, as described in a previous report. Although we aim to register all cases of unruptured cerebral aneurysms encountered at each institution, not all the eligible patients were enrolled.

CONCLUSION

Our results suggest that the largest aneurysm is likely to rupture among coexisting aneurysms in a patient with multiple cerebral aneurysms. This finding might help guide management of patients with multiple cerebral aneurysm cases.

Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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COMMENTS

In this paper, the authors perform a post-hoc analysis of the Japanese UCAS study to better understand the natural history of patients with multiple cerebral aneurysms. The authors are to be commended for their eloquent and practical study on this important topic, which presents frequently in the clinic and hospital.

The authors conclude that size, as opposed to location and morphology, is the most important feature when evaluating the rupture risk of patients with multiple aneurysms. It is important to note that the sensitivity and specificity of this finding were .76 and .86 respectively, which is an important reminder that there are no hard and fast rules regarding aneurysms. Although larger aneurysms are more likely to rupture, there is a lower yet very real rupture risk from small aneurysms as well. Particular consideration should be given to treatments such as clip ligation and flow diversion, which treat multiple aneurysms with one procedure to maximize patient benefit. Accordingly, despite scoring systems such as PHASES and retrospective papers such as this, each individual patient needs to be evaluated by a cerebrovascular team for the best approach to their aneurysms.

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This manuscript examines aneurysm-specific features - namely size, location, and shape - that may be used to predict rupture among multiple cerebral aneurysms. Using a post-hoc subgroup analysis of the Unruptured Cerebral Aneurysm Study in Japan (UCAS Japan), the authors report a sensitivity and specificity of 'distinctiveness in size' in determining the rupture source as .76 and .86, respectively, and conclude that the largest aneurysm has the highest risk of rupture in a patient with multiple cerebral aneurysms. Few studies have addressed the conundrum of how to predict or determine the source of rupture when multiple aneurysms are present, and so this manuscript attempts to add to the literature.

Based on our experience at the University of Illinois at Chicago, we have observed a less indolent natural history of small aneurysms than published in the ISUIA study. Additionally, we have found that aneurysm characteristics cannot reliably be used to determine rupture site in cases with non-definitive subarachnoid hemorrhage patterns. A sensitivity of only .76 as reported in this study in fact reflects that size should not be the primary factor in deciding to treat an aneurysm. Moreover, very small aneurysms should and can be safely treated with surgical clipping when indicated.[1]

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1. Bruneau M, Amin-Hanjani S, Koroknay-Pal P, et al. Surgical clipping of very small unruptured intracranial aneurysms: a multicenter international study. *Neurosurgery*. 2016;78(1):47-52.

This study evaluates the characteristics of aneurysms in patients with multiple lesions presenting with a subarachnoid hemorrhage from a large prospective cohort of unruptured aneurysms (UCAS Japan).[1] Twenty-five patients were identified and the aneurysm characteristics of size, shape, and location were analyzed to try and predict which lesion is the most likely aneurysm to rupture in patients with multiple aneurysms. They conclude that in patients with multiple aneurysms, the largest is the most likely to rupture.

The authors of this study have gone to great statistical lengths to mathematically prove what has been a long-held dogma in the cerebrovascular ethos. Although the UCAS dataset is large, they are left with relatively few patients from whom to draw conclusions regarding such esoteric questions. The authors themselves note this limitation, however, it bears repeating before concluding that the issue is settled beyond all doubt. Having said that, it seems unlikely that a more conclusive perspective on the subject will arise from a database of higher quality.

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