

Middle cerebral artery aneurysms: aneurysm angiographic morphology and its relation to pre-operative and intra-operative rupture

Aneurismas da artéria cerebral média: morfologia angiográfica dos aneurismas e sua relação com ruptura pré-operatória e intra-operatória

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ABSTRACT

Objective: Correlate the middle cerebral artery bifurcation aneurysm morphology with the pre-operative and intra-operative risk of rupture. **Methods:** Forty patients with 46 middle cerebral artery bifurcation aneurysms were treated microsurgically by the same surgeon. Aneurysms were classified according to shape and the Fisher test was applied to analyze the effect of morphology on the pre-operative and intra-operative rupture. **Results:** Pre-operative and intra-operative ruptures were observed in 8/46 patients (17.4%) and 14/46 patients (30.4%) respectively. Thirty-two cases (69.6%) had no symptoms postoperatively, modified Rankin score (MRS) of 0; 6.5% had MRS of 1 (no significant disability); 13% had MRS of 2 (slight disability); 4.3% had moderately severe disability (MRS of 4); and there were 3 deaths (6.5%) post-operatively. The morphology was not directly related to the rupture rate. **Conclusion:** In general, ruptures are not affected by the morphology or the studied variables. Larger series are needed to validate these outcomes.

Keywords: aneurysm; subarachnoid hemorrhage; middle cerebral artery.

RESUMO

Objetivo: Correlacionar a morfologia do aneurisma da bifurcação da artéria cerebral média com o risco de ruptura pré-operatória e intra-operatória. **Métodos:** 40 pacientes com 46 aneurismas de bifurcação da artéria cerebral média receberam tratamento microcirúrgico pelo mesmo cirurgião. Os aneurismas foram classificados de acordo com a morfologia e o teste de Fisher foi aplicado para analisar o efeito da morfologia sobre a ruptura pré-operatória e intra-operatória. **Resultados:** As rupturas pré e intra-operatória foram observadas em 8/46 pacientes (17,4%) e 14/46 (30,4%) respectivamente. Trinta e dois casos (69,6%) não apresentaram sintomas pós-operatórios, pontuação de Rankin modificada (MRS) de 0, 6,5% tinham MRS de 1 (sem incapacidade significativa), 13% tinham MRS de 2 (leve incapacidade), 4,3% moderadamente grave (MRS de 4) e houve 3 óbitos (6,5%) durante o pós-operatório. A morfologia não estava diretamente relacionada à taxa de ruptura pré-operatória ou intra-operatória. **Conclusão:** Em geral, as rupturas não são afetadas pela morfologia ou pelas variáveis estudadas. São necessárias séries maiores para validar esses resultados.

Palavras-chave: aneurisma; hemorragia subaracnoidea; artéria cerebral média.

Middle cerebral artery aneurysms are some of the most common vasculopathies in the anterior cerebral circulation, with an overall incidence of 18% to 20% of all aneurysms encountered¹. Aneurysms in this location are typically complex, multi-lobed, and incorporate eloquent vascular branches;

and therefore pose critical surgical management strategic points, particularly when they are ruptured. Aspects to be considered are shape, vascular variations (trifurcation, bifurcation, or anatomical variations such as middle cerebral artery duplication or “fenestration”), M1 segment length, size, branch

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incorporation, and whether they are ruptured or not. The aneurysm neck is an important aspect when considering the endovascular treatment of the aneurysm. As opposed to endovascular therapies, neck-dome proportion is not as important when microsurgery is considered, since adequate neck dissection and sometimes aneurysm dome dissection are pivotal in determining complete aneurysm obliteration and avoidance of eloquent incorporated cortical branches. In order to obtain complete comprehension of the relationship between the nearby vascular branches and perforating arteries, surgical dissection of the neck and dome are sometimes needed when microsurgical clipping is considered; this is especially true when we are dealing with middle cerebral artery bifurcation aneurysm. The authors propose a simple morphological classification of middle cerebral artery bifurcation aneurysms in order to study the relationship of the aneurysm's morphology and its tendency to rupture pre-operatively or intra-operatively. The afore-mentioned morphological characteristics are particularly addressed by the authors, especially regarding the current technical repertoire and the surgeons' expertise.

METHODS

From January 1998 to July 2015, 40 patients with 46 bifurcation aneurysms of the middle cerebral artery were surgically clipped by the senior author. Pre-operative historical and radiological records were reviewed in detail and morphological aspects charted. Middle cerebral artery bifurcation aneurysms were classified according to shape into globoid, pear-shaped, bilobar, beak-shaped, multilobar, and fusiform (see classification model in Figure 1).

There were 27 females and 13 male patients. Average age was 50.20 years old (min = 15 years old, max = 75 years old).

The same surgeon and surgical team operated all the aneurysms. Categorical and scalar variables were described for each patient and Fisher's test was applied to analyze the effect of the morphology on the pre-operative and intra-operative rupture rate. Fisher's test was also applied to verify the degree of association between the interest categorical variables (right side, left side, gender, presence of associated aneurysms other than middle cerebral artery bifurcation aneurysms, anatomical features such as an M1 segment of the middle cerebral artery larger than 3 cm, presence of trifurcated middle cerebral artery and aspect ratio higher than 1.5) and the rupture variables. The Mann-Whitney test was applied to verify the degree of association between the scalar variables (age and size of the aneurysm) and the rupture variables.

Classification

We classified middle cerebral artery aneurysms based on their shapes into globoid, pear-shaped, beak-shaped, bilobar, multilobar and associated with fibromuscular dysplasia (fusiform), as shown in Figure 1.

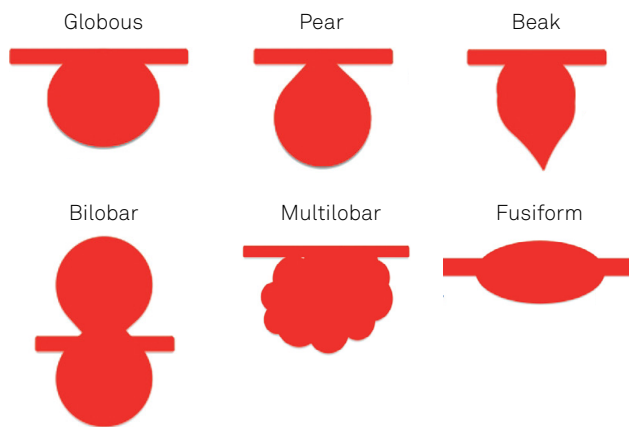


Figure 1. Classification model of aneurysms according to shape into globoid, pear-shaped, bilobar, beak-shaped, multilobar and fusiform.

There were 16 beak-shaped aneurysms (34.8% of all aneurysms) with one pre-operative rupture in this category. Pear-shaped aneurysms were also seen in 14 of the aneurysms (30.4%), with one ruptured aneurysm at presentation. A globoid shape was encountered in nine cases (19.60% of the aneurysms), with one ruptured aneurysm at presentation (11.1%). A bilobar shape was seen in two cases (4.3%) with one ruptured aneurysm at presentation (50%). A multilobar shape was seen in three cases (6.5%) with two ruptured aneurysms at presentation (66.6%). A fusiform aneurysm was seen in two cases (4.3%) and none of those were ruptured at presentation. All the categorical variables evaluated during data collection are described in Table 1. Examples of the morphology can be seen in Figures 2 and 3 (A to E).

Middle cerebral artery segment anatomic variations

A long M1 segment was observed in 26%, M1 trifurcation was observed in approximately 11%, and M1 bifurcation was observed in 89% of the angiographies.

Associated aneurysms

Seven cases had one associated aneurysm other than the bifurcation of the middle cerebral artery on the right side and two patients had two associated aneurysms on the right side of the head. Four patients had one associated aneurysm on the left side other than the bifurcation of the middle cerebral artery (Table 1). Only one aneurysm was distal to the bifurcation of the middle cerebral artery. All the ruptures were related to the aneurysm of the bifurcation of the middle cerebral artery. Spearman's analysis was done to verify the degree of relationship between the variables of interest (Table 2). The relationship between the presence of associated aneurysms and middle cerebral artery bifurcation aneurysms, as well as the relationship between left side and right side of the associated aneurysms are weak; that is, nothing makes us believe that there is a higher probability of finding an associated rupture due to previously-ruptured aneurysms in our series (Table 2).

Table 1. Description of all the categorical variables evaluated during data collection.

Variable	Category	Frequency	Percentage
Pre-operative rupture	absent	38	82.6
	present	8	17.4
Right sided middle cerebral artery bifurcation aneurysm	absent	23	50
	present	23	50
Left sided middle cerebral artery bifurcation aneurysm	absent	23	50
	present	23	50
Year of surgery	1998	4	8.7
	1999	1	2.2
	2005	1	2.2
	2006	3	6.5
	2007	2	4.3
	2008	8	17.4
	2009	6	13
	2010	2	4.3
	2011	2	4.3
	2012	5	10.9
	2013	5	10.9
Sex	female	32	69.6
	male	14	30.4
Intra-operative rupture	absent	32	69.6
	Present	14	30.4
Modified rankin score	0	32	69.6
	1	3	6.5
	2	6	13
	4	2	4.3
	6	3	6.5
Presence of associated right side aneurysms other than the bifurcation of the MCA	0	37	80.4
	1	7	15.2
	2	2	4.3
	> 2	0	0.0
Presence of associated Left Side Aneurysms other than the bifurcation of the MCA	0	42	91.3
	1	4	8.7
	2	0	0.0
	> 2	0	0.0
Pear-shaped middle cerebral artery aneurysm	Absent	32	69.6
	Present	14	30.4
Beak-shaped middle cerebral artery aneurysm	Absent	30	65.2
	Present	16	34.8
Globous-shaped middle cerebral artery aneurysm	Absent	37	80.4
	Present	9	19.6
Bilobar-shaped middle cerebral artery aneurysm	Absent	44	95.7
	Present	2	4.3
Multilobar-shaped middle cerebral artery aneurysm	Absent	43	93.5
	Present	3	6.5
Fusiform-shaped middle cerebral artery aneurysm	Absent	44	95.7
	Present	2	4.3
M1 segment longer than 3 cm	Absent	34	73.9
	Present	12	26.1
Trifurcated middle cerebral artery	Absent	41	89.1
	Present	5	10.9
Aspect ratio > 1.5	Absent	18	39.1
	Present	28	60.9

MCA: Middle Cerebral Artery; M1: Segment M1 of Middle Cerebral Artery.

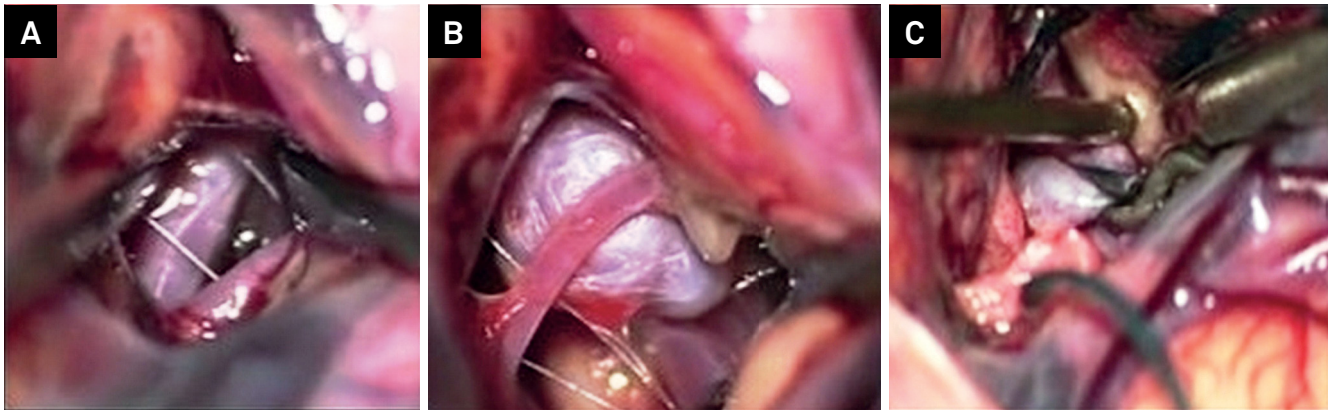


Figure 2. Intra-operative vision and clipping of middle cerebral artery aneurysms.

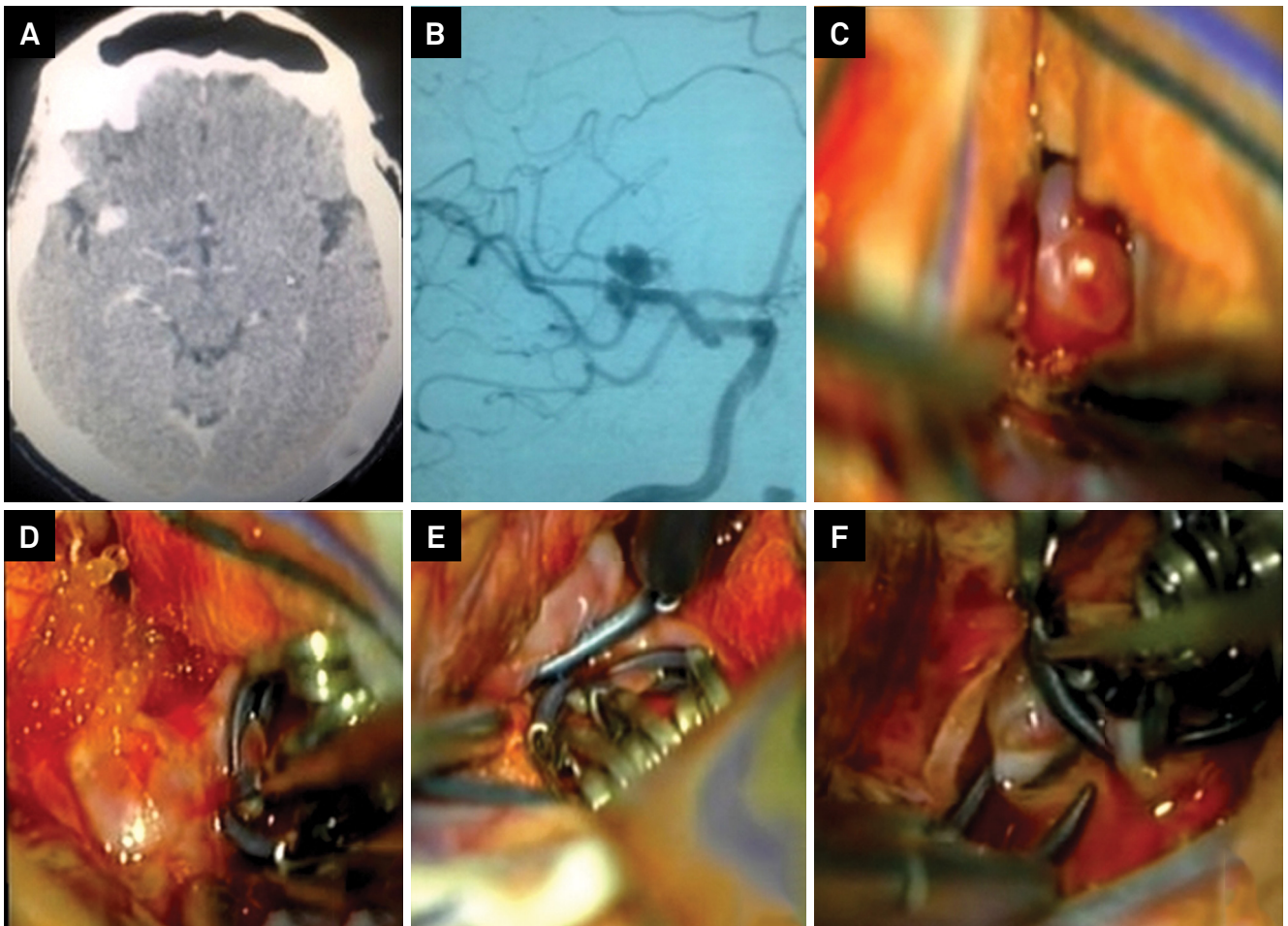


Figure 3. A. CT scan axial section of a patient with middle cerebral artery aneurysm. B. Angiogram of a patient with MCA aneurysm in M2 portion. C. Identification of the aneurysm. D. E. F. Intra-operative vision of clipping a middle cerebral artery aneurysm.

RESULTS

The average aneurysm size was 6.59 mm. Pre-operative and intra-operative ruptures were observed in 8/46 patients (17.4%) and 14/46 patients (30.4%) respectively. The average age was 50.2 years old (15–75), with a median age of 51.5 years of age (Table 3). Thirty-two cases (69.6%) had no symptoms postoperatively (modified Rankin score (MRS) of 0, 6.5% had an MRS

of 1 (no significant disability), 13% had MRS of 2 (slight disability), 4.30% had moderately severe disability (MRS of 4) and there were 3 deaths (6.5%) post-operatively. Fourteen aneurysms were classified as pear shaped (30.4%), 16 aneurysms were classified as beak shaped (34.8%), 9 were considered to be globous shaped (19.6%), 2 patients (4.3%) had bilobar shaped aneurysms, 3 patients (6.5%) had multilobar shaped aneurysms and 2 (4.3%) had fusiform aneurysms (Table 1).

Fisher's test was applied to analyze the effect of morphology on the pre-operative and intra-operative rupture (Tables 4 and 5, respectively). Statistical analysis showed that the morphology of the aneurysm does not affect the rate of pre-operative or intra-operative rupture. Fisher's test was also applied to verify the degree of association between the categorical variables of interest (right side, left side, gender, presence of associated aneurysms other than middle cerebral artery bifurcation aneurysms, anatomical features such as an M1 segment of the middle cerebral artery larger than 3 cm, the presence of a trifurcated middle cerebral artery and aspect ratio higher than 1.5) and the rupture variables

(Tables 6 and 7). The Mann-Whitney test was applied to verify the degree of association between the scalar variables (age and size of the aneurysm) and the rupture variables (Tables 8 and 9). According to the analyses, none of the variables seemed to affect the rate of pre-operative or intra-operative rupture. Spearman's correlation analysis was applied to verify the degree of relationship between the morphology variables and the above-mentioned categorical variables of interest (Table 10). According to this analysis the relationship between those variables seemed to be weak, showing that they do not represent bias when correlating the morphology of the aneurysms and the risk of rupture.

Table 2. Spearman analysis was done to verify the degree of relationship between the variables of interest.

Variable	Statistics	Right sided bifurcation middle cerebral artery aneurysm	Left sided bifurcation middle cerebral artery aneurysm	Presence of associated left side aneurysms other than the bifurcation of the MCA
Left sided middle cerebral artery bifurcation aneurysm	Coef. Correl. (r)	-1.000	—	—
	Sig. (p)	< 0.001	—	—
	n	46	—	—
Right sided middle cerebral artery bifurcation aneurysm	Coef. Correl. (r)	+0.031	-0.031	—
	Sig. (p)	0.839	0.839	—
	n	46	46	—
Presence of associated left sided aneurysms other than the bifurcation of the MCA	Coef. Correl. (r)	0.000	0.000	-0.152
	Sig. (p)	> 0.999	> 0.999	0.315
	n	46	46	46

MCA: Middle Cerebral Artery ;Coef. Correl.: Correlation Coefficient ; Sig: statistical significance.

Table 3. Scalar variables (age and size of the operated aneurysms).

Variable	n	Min	Max	Average	Standard deviation	Percentile 25	Percentile 50 (Median)	Percentile 75
Age	46	15	75	50.2	12.9	42	51.5	59.75
Size of the aneurysm	46	3	15	6.59	2.65	5	6	7.25

Table 4. Fisher's test to verify the association between the morphology of the aneurysms and the pre-operative rate of rupture.

Middle cerebral artery aneurysm	Category	Pre-operative Rupture				Sig. (p)
		Absent		Present		
		Frequency	Percentage	Frequency	Percentage	
Pear-shaped	Absent	25	65.8	7	87.5	0.225
	Present	13	34.2	1	12.5	
Beak-shaped	Absent	24	63.2	6	75	0.523
	Present	14	36.8	2	25	
Globous-shaped	Absent	31	81.6	6	75	0.670
	Present	7	18.4	2	25	
Bilobar-shaped	Absent	37	97.4	7	87.5	0.213
	Present	1	2.6	1	12.5	
Multilobar-shaped	Absent	37	97.4	6	75	0.020
	Present	1	2.6	2	25	
Fusiform-shaped	Absent	36	94.7	8	100	0.507
	Present	2	5.3	0	0.0	

Table 5. Fisher's test to verify the association between the morphology of the aneurysms and the intra-operative rate of rupture.

Middle cerebral artery aneurysm	Category	Intra-operative rupture				Sig. (p)
		Absent		Present		
		Frequency	Percentage	Frequency	Percentage	
Pear-shaped	Absent	24	75	8	57.1	0.226
	Present	8	25	6	42.9	
Beak-shaped	Absent	19	59.4	11	78.6	0.208
	Present	13	40.6	3	21.4	
Globous-shaped	Absent	27	84.4	10	71.4	0.308
	Present	5	15.6	4	28.6	
Bilobar-shaped	Absent	30	93.8	14	100	0.339
	Present	2	6.3	0	0.0	
Multilobar-shaped	Absent	30	93.8	13	92.9	0.910
	Present	2	6.3	1	7.1	
Fusifor-shaped	Absent	30	93.8	14	100	0.339
	Present	2	6.3	0	0.0	

Table 6. Fisher's test to verify the association between the variables of interest and pre-operative rupture.

Variable	Category	Pre-operative Rupture				Sig. (p)
		Absent		Present		
		Frequency	Percentage	Frequency	Percentage	
Right sided middle cerebral artery bifurcation aneurysm	Absent	19	50	4	50	> 0.999
	Present	19	50	4	50	
Left sided middle cerebral artery bifurcation aneurysm	Absent	19	50	4	50	> 0.999
	Present	19	50	4	50	
Sex	Female	26	68.4	6	75	0.713
	Male	12	31.6	2	25	
Presence of associated right side aneurysms other than the bifurcation of the MCA	0	29	76.3	8	100	0.308
	1	7	18.4	0	0.0	
	2	2	5.3	0	0.0	
	> 2	0	0.0	0	0.0	
Presence of associated left side aneurysms other than the bifurcation of the MCA	0	34	89.5	8	100	0.337
	1	4	10.5	0	0.0	
	2	0	0.0	0	0.0	
	> 2	0	0.0	0	0.0	
M1 segment > 3 cm	Absent	29	76.3	5	62.5	0.419
	Present	9	23.7	3	37.5	
Trifurcated middle cerebral artery	Absent	34	89.5	7	87.5	0.871
	Present	4	10.5	1	12.5	
Aspect ratio > 1.5	Absent	15	39.5	3	37.5	0.917
	Present	23	60.5	5	62.5	

MCA: Middle Cerebral Artery ;M1: Segment M1 of Middle Cerebral Artery.

Table 7. Fisher test to verify the association between the variables of interest and intra-operative rupture.

Variable	Category	Pre-operative Rupture				Sig. (p)
		Absent		Present		
		Frequency	Percentage	Frequency	Percentage	
Right sided middle cerebral artery bifurcation aneurysm	Absent	19	50	4	50	> 0.999
	Present	19	50	4	50	
Left sided middle cerebral artery bifurcation aneurysm	Absent	19	50	4	50	> 0.999
	Present	19	50	4	50	
Sex	Female	26	68.4	6	75	0.713
	Male	12	31.6	2	25	
Presence of associated right side aneurysms other than the bifurcation of the MCA	0	29	76.3	8	100	0.308
	1	7	18.4	0	0.0	
	2	2	5.3	0	0.0	
	> 2	0	0.0	0	0.0	
Presence of associated left side aneurysms other than the bifurcation of the MCA	0	34	89.5	8	100	0.337
	1	4	10.5	0	0.0	
	2	0	0.0	0	0.0	
	> 2	0	0.0	0	0.0	
M1 segment > 3 cm	Absent	29	76.3	5	62.5	0.419
	Present	9	23.7	3	37.5	
Trifurcated middle cerebral artery	Absent	34	89.5	7	87.5	0.871
	Present	4	10.5	1	12.5	
Aspect ratio > 1.5	Absent	15	39.5	3	37.5	0.917
	Present	23	60.5	5	62.5	

MCA: Middle Cerebral Artery ;M1: Segment M1 of Middle Cerebral Artery.

Table 8. Mann-Whitney's test was applied to verify the degree of association between the scalar variables (age and size of the aneurysm) and pre-operative rupture.

Variable	Pre-operative rupture	n	Mean	SD	Min	Max	Percentile 25	Percentile 50 (Median)	Percentile 75	Sig. (p)
Age	Absent	38	50.76	13.46	15	75	42.75	52.00	62.00	0.303
	Present	8	47.50	10.09	32	65	39.5	49.50	52.50	
	Total	46	50.20	12.90	15	75	42	51.50	59.75	
Size of the aneurysm	Absent	38	6.37	2.57	3	15	5	6.00	7.00	0.209
	Present	8	7.63	2.93	5	12	5	7.00	11.00	
	Total	46	6.59	2.65	3	15	5	6.00	7.25	

SD: standard deviation.

Table 9. Mann-Whitney's test applied to verify the degree of association between the scalar variables (age and size of the aneurysm) and intra-operative rupture.

Variable	Intra-operative Rupture	n	Mean	SD	Min	Max	Percentile 25	Percentile 50 (Median)	Percentile 75	Sig. (p)
Age	Absent	32	51.34	12.55	15	75	44.5	52	58.75	0.2624
	Present	14	47.57	13.78	21	67	38.75	46.5	62.75	
	Total	46	50.2	12.9	15	75	42	51.5	59.75	
Size of the aneurysm	Absent	32	6.63	2.94	3	15	5	6	8	0.618
	Present	14	6.5	1.91	5	12	5	6.5	7	
	Total	46	6.59	2.65	3	15	5	6	7.25	

SD: standard deviation.

Table 10. Spearman correlation analysis to verify the degree of relationship between the morphology variables (first line above) and the categorical variables of interest (left column).

Variable	Statistics	Pear*	Beak*	Globous*	Bilobar*	Multilobar*	Fusiform*
Right sided middle cerebral artery bifurcation aneurysm	Coef. Correl. (r)	0.000	0.365	-0.164	0.000	-0.264	-0.213
	Sig. (p)	> 0.999	0,013	0.275	> 0.999	0.076	0.155
	n	46	46	46	46	46	46
Left sided middle cerebral artery bifurcation aneurysm	Coef. Correl. (r)	0.000	-0.365	0.164	0.000	0.264	0.213
	Sig. (p)	> 0.999	0.013	0.275	> 0.999	0.076	0.155
	n	46	46	46	46	46	46
Age	Coef. Correl. (r)	0.153	0.002	-0.008	0.088	-0.100	-0.301
	Sig. (p)	0.310	0.991	0.957	0.559	0.510	0.042
	n	46	46	46	46	46	46
Sex	Coef. Correl. (r)	0.076	-0.086	-0.088	0.091	0.017	0.091
	Sig. (p)	0.616	0.569	0.561	0.549	0.913	0.549
	n	46	46	46	46	46	46
Modified rankin score	Coef. Correl. (r)	0.042	-0.027	-0.043	-0.138	0.273	-0.138
	Sig. (p)	0.784	0.856	0.776	0.359	0.066	0.359
	n	46	46	46	46	46	46
Presence of associated right side aneurysms other than the bifurcation of the MCA	Coef. Correl. (r)	0.289	0.080	-0.242	-0.105	-0.130	-0.105
	Sig. (p)	0.052	0.598	0.105	0.489	0.390	0.489
	n	46	46	46	46	46	46
Presence of associated left side aneurysms other than the bifurcation of the MCA	Coef. Correl. (r)	-0.036	0.099	0.042	-0.066	-0.082	-0.066
	Sig. (p)	0.810	0.514	0.780	0.664	0.590	0.664
	n	46	46	46	46	46	46
Size of the aneurysm	Coef. Correl. (r)	-0.112	-0.505	0.448	0.057	0.128	0.348
	Sig. (p)	0.457	< 0.001	0.002	0.705	0.395	0.018
	n	46	46	46	46	46	46
M1 segment > 3 cm	Coef. Correl. (r)	-0.178	-0.018	0.206	-0.127	-0.157	0.359
	Sig. (p)	0.237	0.905	0.169	0.402	0.298	0.014
	n	46	46	46	46	46	46
Trifurcated middle cerebral artery	Coef. Correl. (r)	-0.079	0.038	0.004	0.268	-0.092	-0.074
	Sig. (p)	0.601	0.801	0.980	0.072	0.542	0.623
	n	46	46	46	46	46	46
Aspect ratio > 1,5	Coef. Correl. (r)	-0.051	-0.163	0.283	-0.047	-0.149	0.171
	Sig. (p)	0.739	0.280	0.057	0.754	0.323	0.256
	n	46	46	46	46	46	46

*Shaped middle cerebral artery aneurysm. MCA: Middle Cerebral Artery; M1: Segment M1 of Middle Cerebral Artery.

DISCUSSION

Intracranial aneurysms occur in diverse shapes and forms. However, shape is an independent factor since the final conformation will depend on the aneurysm wall's outer molecular composition and the influence of external factors such as underlying systemic hypertension, history of tobacco abuse, as well as local environmental changes such as shear stress forces and hemodynamic characteristics of such². In reality, according to classic studies by Pierre Lasjaunias and others, molecular wall weakening was likely the most important factor linked to aneurysm formation, explaining multiple aneurysms, and mirror aneurysmal formation in humans. Several inheritable connective tissue disorders have been associated with intracranial aneurysms, such as autosomal-dominant polycystic kidney disease, Ehlers Danlos type 4 syndrome and neurofibromatosis type 1^{3,4,5}. Despite the knowledge of several syndromic features related to aneurysm formation, the true incidence of these alterations in the population is still unknown. One feasible hypothesis is that the genetic disorders related to aneurysm formation remain undiagnosed, because there is a high index of phenotypical expression, and a complete genetic evaluation is lacking in most cases. The understanding of the true pathobiology of the aneurysm formation is essential in developing strategies for the prevention, diagnosis and treatment of such a treacherous disease.

It is also well known that hemodynamic alterations within the internal cerebral artery, from either anatomic/pathologic hypoplastic segments or iatrogenic occlusion, can directly influence the development of intracranial aneurysms^{6,7}. There is also evidence that *de novo* aneurysms can arise in the anterior communicating artery or contralateral internal cerebral artery after coiling or clipping of intracranial aneurysms^{8,9}. This imbalance between local hemodynamic stress and arterial wall strength makes the arterial wall prone to aneurysm formation, and factors such as the above-mentioned make them prone to rupture. There is some evidence showing that biologic changes at the cellular and molecular levels are related to a higher risk of aneurysm formation^{10,11,12,13}. Human samples and animal models show a common pathway for the intracranial birth, progression and subsequent rupture, initiating with the endothelial dysfunction and progressing with inflammation and degenerative changes that culminate with aneurysm rupture^{11,12}.

Aneurysm rupture risk is related to the aneurysm morphology, in association with the aneurysm location and local hemodynamic factors rather than size, as initially suggested^{14,15,16,17}. There are significant controversial points in the management of intracranial aneurysms and, in most circumstances, small aneurysms will rupture in a not-insignificant proportion in clinical practice and accurate answers on their treatment indications are lacking.

Since the middle cerebral artery is embryological and phylogenetically diverse and has different developmental ages, anatomical variations and genetic compositions, aneurysm

formation processes in this topography are typically complex, frequently involving multiple branches and sometimes having an unfavorable neck for unassisted endovascular embolization, which can make microsurgical clipping hazardous. The challenge of a perfect arterial dissection and identification of crucial branches that cannot be sacrificed during clipping makes the microsurgical procedure even more difficult. In some instances, utilization of the STA-MCA bypass techniques¹⁸, ultrasound flow probe measurement of branch flow patency^{19,20,21}, and adequate neurosurgical technique with proper temporary clipping application, will decrease morbidity and mortality associated with microsurgical approaches for middle cerebral artery aneurysms. The improvement in imaging technology permits adequate study of the vascular anatomy of the patients, directions of the vessels and detailed assessment of the three-dimensional morphology expected intra-operatively²².

As presented in our study, middle cerebral artery aneurysms can present with diverse morphological features. Our study showed that neither pre-operative rupture nor intra-operative rupture are associated with a specific morphology in aneurysms of the bifurcation of the middle cerebral artery, but further studies with larger series are needed to reach a firm conclusion on this topic. Ruptured aneurysms are associated with higher morbidity and mortality and treatment after rupture will significantly affect outcome, since the chances of clinical cerebral vasospasm becomes higher, increasing the long-term morbidity and mortality associated with those^{23,24,25,26,27,28}. In addition, aneurysm dissection after a rupture can be challenging, and correct neck identification may not be optimal. Survival and outcomes will be directly linked to the postoperative neurological critical care.

In conclusion, we noticed that morphology does not seem to be directly related to an increased rate of pre-operative or intra-operative rupture when dealing with middle cerebral artery bifurcation aneurysms. Pre- or intra-operative ruptures were more likely to be related to higher morbidity and mortality, albeit directly dependent on how aggressive the neurological critical care was carried out after surgery. Larger multi-center case series and uniform treatment paradigms will likely correlate with safety of microsurgical treatments, particularly when endovascular treatment is not indicated or with ruptured aneurysms that cannot be coiled unassisted, i.e., without stent or balloon utilization. Medical treatments that inhibit the inflammatory cascade are likely to prevent progression and rupture of aneurysms¹². Statins and anti-inflammatory therapies using aspirin will permit, in the longer term, one more step in the comprehension of aneurysm wall formation and rupture. Further studies are needed to correlate the shape of the aneurysms and the risk of rupture and the feasibility of microsurgical clipping without raising the morbidity/mortality of the microsurgical procedure. All effort should be made to stabilize the progression of the disease and diminish the risks of rupture and the morbidity and mortality related to the surgical procedures of intracranial aneurysms.

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