Morphometric Features of Ruptured and Unruptured Aneurysms in Surgically Treated Patients with Multiple Intracranial Aneurysms

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Abstract: OBJECTIVE: The purpose of the present research was to evaluate the morphometric characteristics of ruptured and unruptured aneurysms in series of surgically treated patients with multiple intracranial aneurysms. According to the findings the differences between ruptured and unruptured aneurysms were analyzed in patients with subarachnoid hemorrhage and multiple intracranial aneurysms. METHODS: Sixty eight patients with 174 multiple aneurysms and clinical presentation of aneurysmal subarachnoid hemorrhage were treated in two hospitals in Sofia, Bulgaria between 1991 and 2010. The ruptured aneurysm was identified from preoperative studies (head computed tomography, digital subtraction angiography, computed tomography angiography) and it was proved during the surgical procedure. The preoperative angiograms were used to perform measurements of morphometric characteristics of ruptured and unruptured cerebral aneurysms. We used univariable logistic regression analysis to obtain odds ratios. Cochran–Mantel–Haenszel test for dependence was performed to obtain adjusted odds ratio and *P* value for dependence. RESULTS: In 16 (23.53%) patients, the ruptured aneurysm was not the largest one. The calculated odds ratios with 95% confidence intervals revealed strong association with rupture for the aneurysm size ≥ 7.5 mm, aneurysm location at anterior communicating—anterior cerebral artery complex, irregular aneurysm shape and angle of inclination. The average value of the angle of inclination was $153.06^\circ \pm 21.16$ for the ruptured aneurysms and $106.78^\circ \pm 29.50$. After performing a test for dependence and adjustment for aneurysm size and location, size ratio, irregular shape, terminal aneurysm type and aneurysm inclination angle were strongly associated with aneurysm rupture. CONCLUSION: The only independent significant determinant for aneurysm rupture besides aneurysm size and location was aneurysm inclination angle ($P < 0.05$).

Key words: Intracranial aneurysms, rupture risk factors, morphometric characteristics.

1. Introduction

Improvements in cerebrovascular imaging methods identify incidental unruptured intracranial aneurysms more frequently [1]. The recent studies estimate a significantly low annual aneurysm rupture risk of 0.1% to 0.2% for the asymptomatic unruptured intracranial aneurysms [2, 3]. Although aneurysmal subarachnoid hemorrhage carries a mortality rate of 40% to 50% and a morbidity rate of 10% to 20% [4, 5], preventive

surgical or endovascular treatment carries a real risk of complications. Thus, the decision to treat incidental unruptured aneurysms depends on the risk of rupture. The studies designed to assess aneurysm morphology could be helpful in identifying discriminants of aneurysm rupture status. Morphologic and geometric characteristics of the aneurysms may be useful for predicting unfavorable course.

Multiple intracranial aneurysms are diagnosed in 15% to 35% of the patients after aneurysmal SAH [6]. The morbidity and mortality associated with aneurysmal SAH remain high despite advances in

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microneurosurgery, interventional neuroradiology, neuroanaesthesia and critical care. In addition to that, the prognosis after aneurysmal SAH in patients with multiple intracranial aneurysms is less favorable than in patients with single aneurysm. On the other hand, comparison of ruptured and unruptured aneurysms within the same patient, which is the case in multiple intracranial aneurysms, eliminates the patient specific characteristics. Aneurysmal morphology used to evaluate the aneurysm characteristics (aneurysm height, aneurysm width, aspect ratio, bottleneck ratio, size ratio, aneurysm inclination angle, parent vessel diameter etc.), is frequently studied in the cases of single cerebral aneurysms and far less in the cases with multiple intracranial aneurysms [7]. We provide valuable information comparing morphometric data of ruptured and unruptured aneurysms in patients with multiple intracranial aneurysms in order to complement and enrich the existing literature.

2. Materials and Methods

The patients' data from two hospitals "Queen Yoanna" (1991-1999) and "N. I. Pirogov" (2000-2010) were used to obtain information for aneurysms morphological features. The study included 68 patients with proven spontaneous aneurysmal subarachnoid hemorrhage on head computed tomography and/or lumbar puncture and multiple intracranial aneurysms diagnosed on digital subtraction angiography or computed tomography angiography (Siemens Somatom Definition AS). The analysis was made based on angiography findings of the aneurysm morphology and aneurysm relationships with parent vessel. The aneurysm measurement was made by radiologist (D. A.) and neurosurgeons (E. K., V. G.). Manual measurements on key dimensions of the sac from the biplane angiograms were made for all digital subtraction angiograms and/or computed tomography angiograms. Patients for whom the ruptured aneurysm (based on CT scanning and DSA) could not be determined were excluded from our study (e.g.,

patients with two anatomically adjacent aneurysms or if the neurosurgeon could not point out the ruptured aneurysm according to the surgical findings). Only patients with saccular aneurysms were included in the present study.

We used the following aneurysms features: aneurysm location on the main cerebral arteries, aneurysm size and shape, presence of daughter blebs. Measurements of maximal aneurysm height (from the neck to the dome of the aneurysm), aneurysm width (maximum horizontal aneurysm length), maximal neck width and parent artery diameter, were performed. The following ratios data was calculated: size ratio (maximum height of the aneurysm and average parent vessel size), aspect ratio (maximum height of the aneurysm and width of the neck), bottleneck ratio (maximum width of the aneurysm and width of the neck), height to width ratio (maximum height of the aneurysm and maximum width of the aneurysm) and ostium ratio (width of the aneurysm neck and diameter of the parent vessel). The angle between central parent artery axis and central aneurysm axis was measured (Fig. 1). Aneurysms were divided into two groups (Fig. 2): (1) Terminal aneurysms (neck and aneurysm lumen are direct continuation of the parent artery axis) and (2) Lateral (parent artery axis does not continue in aneurysm neck and lumen).

The results from aneurysm measurements and ratios were entered into a data sheets using Excel 2010 (XLSTAT). The form was specially created for the purpose of the research. The data was analyzed to identify the associations between the aneurysm characteristics, ratios and the rupture risk. The data analysis included statistics on descriptive and distribution facts. The odds ratios with 95% confidence intervals (CI) were calculated using univariable logistic regression to quantify how strongly the presence or absence of corresponding aneurysm features were associated with the presence of ruptured or unruptured aneurysms. Two-tailed Fisher exact test was used for statistical assessment. Statistical significance was defined

Fig. 1 Morphological aneurysm characteristics.

Legend: D—diameter.

Fig. 2 Types of aneurysms: (1) Terminal aneurysms (neck and aneurysm lumen are direct continuation of the parent artery axis) and (2) Lateral (parent artery axis does not continue in aneurysm neck and lumen).

as P -value < 0.05 . Confounding variables (aneurysm size and location) were adjusted using stratification

method (Cochran-Mantel-Haenszel test for dependence) and adjusted odds ratios were calculated.

3. Results and Analysis

During the study period, 68 patients with aneurismal subarachnoid hemorrhage and multiple intracranial aneurysms were investigated to determine the aneurysm characteristics. Patients with fusiform aneurysms as well as patients with insufficient quality of angiogram were excluded. From a total of 174 aneurysms, 68 were ruptured and 106 were unruptured. The observed group of patients included 44 women and 24 men, with an average age of 47.9 ± 8.01 . The aneurysms were divided into two groups: exposed group was the ruptured group and control group was the unruptured one. The baseline data of aneurysm characteristics and ratios for the exposed and control groups are summarized in Table 1.

The average value of the largest diameter for the ruptured aneurysms was 11.1 ± 6.06 mm and 7.48 ± 4.91 mm for the unruptured aneurysms. The calculated odds ratios with 95% confidence intervals revealed strong association with rupture for the aneurysm size $\geq$

7.5 mm, aneurysm location at anterior communicating—anterior cerebral artery complex, irregular aneurysm shape and angle of inclination. The average value of the angle of inclination was $153.06^\circ \pm 21.16$ for the ruptured aneurysms and $106.78^\circ \pm 29.50$. Univariate analysis identified that angle of inclination (central parent artery axis/ central aneurysm axis) is significantly more obtuse in the ruptured subset.

We found that in 16 (23.53%) patients the ruptured aneurysm was not the largest one. Size ratio, aspect ratio and ostium ratio as well as terminal aneurysm type were also associated with rupture propensity (Fig. 3). Aneurysm size and location are well known variables connected with aneurysm rupture. These confounding variables were adjusted using stratification method (Cochran-Mantel-Haenszel test). The adjusted odds ratios are summarized in Table 2.

After adjustment of odds ratios for the aneurysm size and location, size ratio, irregular shape and terminal aneurysm type show association with aneurysm rupture. This kind of association is not independent ($P > 0.05$)

Table 1 Comparison of morphology and ratio data for ruptured and unruptured aneurysms (patients with multiple intracranial aneurysms).

	Ruptured aneurysms <i>N</i> = 68	Unruptured aneurysms <i>N</i> = 106	OR (CI 95%)	<i>P</i> value
Aneurysm distribution				
Internal carotid artery	12 (17.7%)	44 (41.5%)	0.30 (0.14-0.63)	0.0014
Posterior communicating artery	9 (13.2%)	5 (4.7%)	3.08 (0.99-9.63)	0.0529
Anterior cerebral artery	26 (38.2%)	11 (10.4%)	5.35 (2.42-11.82)	< 0.0001
Middle cerebral artery	24 (35.3%)	46 (43.4%)	0.71 (0.38-1.33)	0.2883
Posterior circulation	6 (8.8%)	5 (4.7%)	1.96 (0.57-6.68)	0.2848
Aneurysm size				
larger than 7.5 mm; (≥ 7.5 mm)	52 (76.5%)	40 (37.7%)	5.36 (2.70-10.63)	< 0.0001
Aneurysm shape				
Irregular, daughter blebs	27 (39.7%)	16 (15.1%)	3.70 (1.80-7.61)	0.0004
Aneurysm ratios				
Size ratio $\geq$ median (1.71)	47 (69.1%)	36 (33.96%)	4.35 (2.27-8.36)	< 0.0001
Aspect ratio $\geq$ median (1.94)	42 (61.8%)	41 (38.7%)	2.56 (1.37-4.79)	0.0032
Bottleneck ratio $\geq$ median (1.52)	39 (57.4%)	47 (44.3%)	1.69 (0.91-3.12)	0.095
Height to width ratio $\geq$ median (1.16)	38 (55.9%)	47 (44.3%)	1.59 (0.86-2.94)	0.1382
Ostium ratio $\geq$ median (1.21)	41 (60.3%)	40 (37.7%)	2.51 (1.34-4.68)	0.004
Central parent artery axis/central aneurysm axis angle $\geq$ median (132.5°)	55 (80.9%)	37 (34.9%)	7.89 (3.82-16.28)	< 0.0001
Aneurysm Type I (terminal)	43 (63.2%)	26 (24.5%)	5.29 (2.73-10.26)	< 0.0001

Fig. 3 Forest plots comparing selective variable factors between ruptured and unruptured cerebral aneurysms.

Table 2 Adjusted Odds ratio for comparison of morphology and ratio data for ruptured and unruptured aneurysms (patients with multiple intracranial aneurysms).

Confounder Factors:	Adjusted Odds ratio (CI 95%)	Chi-square Mantel-Haenszel (χ^2_{MH})	P value*
Aneurysm location			
Aneurysm size (≥ 7.5 mm)			
Aneurysm shape			
Irregular, daughter blebs	3.62 (0.948-13.808)	1.81	0.142
Aneurysm ratios			
Size ratio $\geq$ median (1.71)	5.58 (2.113-14.712)	1.23	0.176
Aspect ratio $\geq$ median (1.94)	2.413 (0.759-7.663)	0.30	0.676
Bottleneck ratio $\geq$ median (1.52)	2.29 (0.920-5.697)	0.17	0.655
Height to width ratio $\geq$ median (1.16)	1.646 (0.615-4.403)	0.009	1
Ostium ratio $\geq$ median (1.21)	3.66 (1.308-10.251)	0.90	0.252
Central parent artery axis/central aneurysm axis angle $\geq$ median (132.5°)	10.29 (2.261-46.796)	6.49	0.015
Aneurysm Type I (terminal)	9.88(2.581-37.827)	2.67	0.08

* P value for dependence from confounding factors—aneurysm location and aneurysms size.

from the two confounding factors—aneurysm location and aneurysm size, which have already proved to be a

rupture risk factors. The other discriminants—aspect ratio, bottleneck ratio, height to width ratio and ostium

ratio show even more significant dependence from the confounding factors ($P > 0.05$). Only aneurysm inclination angle is an independent significant discriminant of rupture aneurysm status ($\chi^2_{MH} = 6.49$; $P = 0.15$; $P < 0.05$).

4. Discussion

According to International Study of Unruptured Intracranial Aneurysms (ISUIA), small anterior circulation aneurysms (7 mm) demonstrate a 0% risk of subarachnoid hemorrhage in 5 year period [2]. In other studies, a significant part of ruptured IAs are small [8, 9]. Intracranial aneurysm size is a widely used measurement for rupture risk assessment, but it may miss smaller aneurysms that have a higher rupture risk based on some other characteristics like location or relationship with the parent blood vessel [10]. There are many studies proposing better aneurysm parameters for rupture aneurysm status (aneurysm height, aneurysm width, aspect ratio, bottleneck ratio, size ratio, aneurysm inclination angle, parent vessel diameter etc.). Irregular shape is found more often in ruptured aneurysms [11-13]. Previous studies on aneurysm inclination angle showed different results from insignificant to strongly significant odds ratios [7, 14-16].

Our study proves some observations on ruptured and unruptured aneurysms. In 23% of the patients with aneurysmal SAH and multiple intracranial aneurysms, the ruptured aneurysm was not the largest one. Some of the measurements from the earlier periods were made on 2-dimensinal digital subtraction angiography, but for the recent measurements were used 3-dimensional computed tomography angiography and 3-dimensional rotational digital subtraction angiography images. Strongly proved risk factors for aneurysms rupture are aneurysm size and aneurysm location. These two risk factors can influence and confound the significance from the other determinants of rupture status. Ignoring the strongly proved aneurysm rupture risk factors, when assessing the association between other

determinants and rupture propensity, can lead to an overestimate or underestimate of the true association. This can change the direction of the observed associations. Comparison of ruptured and unruptured aneurysms within the same patient eliminates the risks from disturbance due to patient specific factors (blood pressure, smoking, arterial hypertension). After performing a test for dependence and adjusting for aneurysm size and location, size ratio, irregular shape, terminal aneurysm type and aneurysm inclination angle were strongly associated with aneurysm rupture. But the only independent significant determinant for aneurysm rupture was the aneurysm inclination angle ($P < 0.05$).

Our study examines two aneurysm types, which we believe are the proper way to classify aneurysms. (1) Terminal aneurysms (neck and aneurysm lumen are direct continuation of the parent artery axis) and (2) Lateral (parent artery axis does not continue in aneurysm neck and lumen). The difference between types is the continuation of the parent artery axis into aneurysm neck and lumen. Both terminal and lateral aneurysm types according our classification could be localized at bifurcation or on side wall. Similar kind of classification is used in experimental hemodynamic studies on cerebral aneurysm models in order to investigate the role of fluid dynamics in the etiology of aneurysms [17].

5. Conclusion

The current study has identified that the only independent significant determinant for aneurysm rupture besides the aneurysm size and location was the aneurysm inclination angle. Although size ratio, irregular shape and terminal aneurysm type were separately significantly higher in the ruptured group, they show dependence from confounding factors, which have already proved to be a strong rupture risk factors (aneurysm size and location).

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