ORIGINAL ARTICLE

MORPHOLOGICAL PARAMETERS FOR RUPTURE RISK ASSESSMENT OF MCA (MIDDLE CEREBRAL ARTERIES) ANEURYSMS BY CTA (COMPUTED TOMOGRAPHY ANGIOGRAPHY)

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PJR April - June 2020; 30(2): 75-81

Introduction

Intracranial aneurysms are present in 2% - 5% of the general population with the rupture risk of 0.7% - 1.9% per annum, causing subarachnoid haemorrhage (SAH).[1] The incidence of multiple intracranial aneurysms presenting with SAH varies from 15% to 35%.[2-6]
It is vital to determine an aneurysm causing SAH in patients with multiple intracranial aneurysms if all of them cannot be treated at a time either by endovascular coiling or surgical clipping or due to its high risk of rebleeding if left untreated. Identifying preoperatively aneurysm with the high risk of rupture in cases without SAH is also valuable for preventive treatment.[9,10] The rupture risk assessments for multiple intracranial aneurysms are mainly based on morphology.[4,5,7,8,11,12]
This study aimed to define the most reliable morphological parameter for evaluation of rupture risk of an intracranial aneurysm considering there is no significant morphological change after the aneurysm ruptures.

Materials and Methods

The retrospective study was approved by The first hospital of Jilin's ethics committee and written informed consents were obtained from patients or their family members. During a 5-year period (June 2011 to May 2016), 115 patients, suffering SAH with 126 MCA saccular aneurysms (72 ruptured, 54 unruptured) were diagnosed and treated by either coiling or clipping in our institute. Based on the different rupture status, all aneurysms were divided into two groups, ruptured and unruptured and performed a retrospective analysis.

The inclusion criteria:
1) Multiple intracranial saccular aneurysms with MCA aneurysm(s) with different rupture status in the same patient;
2) Single and/or bilateral MCA aneurysm(s) with different rupture status in the same patient.
3) Ruptured aneurysms identified by intraoperative findings or head CT scan imaging or 3D-DSA images.

The exclusion criteria:
1) Intracranial aneurysms without MCA aneurysm.
2) Fusiform or dissecting aneurysms;
3) Ruptured aneurysms that could not be identified;
4) Incomplete 3D-DSA images or inadequate data.

Criteria for Ruptured and Unruptured aneurysm
1. Cases of bilateral MCA aneurysms with SAH and/or ICH confined to one side of the MCA territory as shown by NCCT were included. The site which was cleared of any radiological evidence of bleeding was taken as the unruptured and the site with bleeding manifestation was taken as the ruptured aneurysm.

2. A patient with multiple aneurysms along with MCA aneurysm(s) in whom aneurysm other than MCA

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Submitted 26 March 2020, Accepted 26 April 2020

aneurysm was ruptured, as indicated by radiological signs of bleeding in the sites other than MCA territory and/or postsurgical image where an aneurysm other than MCA aneurysm was operated was taken as unruptured MCA aneurysm.

3. Patient with radiological evidence of SAH and /or ICH at the area of MCA distribution with MCA aneurysm was taken as the ruptured aneurysm.

4. A patient who had undergone surgery for MCA aneurysm for conditions like SAH and/or ICH as demonstrated by pre-operative and postoperative CT and/or CTA was taken as the ruptured aneurysm.

Data Collection and Analysis

Morphological parameters of an aneurysm included

Five size indices-

1. Neck width: the average orifice diameter of an aneurysm
2. Depth (H_{pr}): maximal perpendicular distance between the top of the aneurysm dome and the plane of the surface of the neck
3. Maximum height (H_{max}): maximum distance from the centroid of the neck plane to any point on the dome of an aneurysm
4. Maximum width (W_{max}): maximum diameter of an aneurysm taken at its maximum bulge if present or taken at the half the distance of aneurysm depth if the bulge is not present
5. Volume (V): volume of an aneurysm as calculated by the CTA software on 3D reconstruction image.

Four shape indices–

6. Aspect ratio (AR): the ratio of the maximum perpendicular height (H_{pr}) to the neck width. AR= depth/ neck width
7. Size ratio (SR): the ratio of maximum aneurysm height to the average parent vessel diameter). Thus SR= H_{max} / D_{av}, where H_{max} is the maximum height defined as above. Dav is the average vessel diameter of the parent artery taken as the mean of two diameters D1 and D2. D1 is the diameter of the vessel at just proximal to the neck of an aneurysm and D2 is the diameter of the same vessel at a distance of 1.5 D1 upstream).

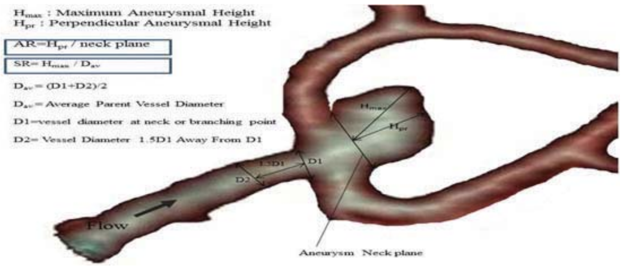

Figure 1: Size Ratio (SR) and Aspect ratio (AR)

8. Neck vessel ratio (NVR): the ratio of the diameter of an aneurysmal neck (NP), defined as the maximum distance of the point of origin of an aneurysm, to the average diameter of the parent vessel (D).
9. Height width ratio (HWR): the ratio of the maximum height of an aneurysm / maximum width of the aneurysm.

Isolation of the model:

The criterion for isolation was defined by using a cutting plane at a distance of approximately one diameter of the parent vessel from the aneurysm neck. The geometrical variable e.g. volume is only measured for the dome. All other measurements were done in the dome with a portion of the adjacent vessels. All further geometric measurements were performed on the isolated aneurysm model including complete 3D morphological descriptors using custom algorithms.

Imaging of MCA Aneurysm and CTA:

Even though DSA has been the gold standard of aneurysm imaging in the past, during the last decade CTA has become the primary imaging method in many centers as it is non-invasive, fast, and offers a similar resolution in aneurysms larger than 2 mm. Most of the radiological analyses of an intracranial aneurysm in the past were done in DSA data. In this work, however, the study is solely based on CTA data analysis. CTA seems to solve certain problems compared to planar DSA images: it gives more accurate information on the aneurysm location with respect to the surrounding vessels, bony structure, Sylvian fissure and with the possible ICH.
Statistical analysis was performed with an SPSS 20.0 package. $P<0.05$ was regarded as statistically significant. Ruptured and unruptured aneurysm groups were analysed separately. Results were expressed

CTA protocol for intracranial vessels for 64 slice dual source MDCT image acquisition	
Scan range	C3 to vertex
Rotation time	0.5sec
Pitch	0.85
Speed	0.51mm/rotation
Helical slice thickness	0.6mm
Effective mA	230mA
Scan time	5.22 sec
Kilo voltage	120 kv
Field of view (FOV)	208mm
Contrast administration	
Bolus-triggering software	Aortic arch
ROI	100 HU above baseline
Triggering threshold	
Contrast volume	1.5-2mL/kg
50 kg	70 mL
50 kg	
Injection rate	2.0-3.0 mL/sec
50 kg	4.0 mL/sec
50 kg	370mgl/mL
contrast concentration	350mgl/mL
saline chaser	
Volume	20mL
Rate	4mL/sec

Table 1: Computed tomography angiography (CTA) protocol for intracranial aneurysms.

as the mean value and standard deviation of all variables. Crosstabulation table and the Pearson Chi-square test were used for the qualitative variables. For quantitative data, the one sample Kolmogorov-Smirnov test was performed to test the normal distribution. Durbin Watson test and Levene s robust test were used to testing for the presence of auto-correlation and to test for equality of variance respectively. The major part of variables did not pass assumptions. Hence, the Man-Whitney independent nonparametric test was used to identifying differences between two groups. ROC (receiver operating characteristics) curve analysis and Multivariate logistic regression with the Backward LR method was performed between the statistically significant parameters in Man-Whitney test to identify those parameters retaining significance when all significant parameters are taken into account. The area under the curve (AUC) values from ROC curve analysis for each parameter were calculated and compared which gave the idea of a parameter's ability to discriminate between the two subgroups namely ruptured and unruptured aneurysms. The odds ratio (OR), 95% confidence interval (CI) and p values of the results were obtained. Finally, the parameter(s) which remain through all the regression steps is the strongest parameter which predicts the rupture risk of an aneurysm independent of other factors.

Results

A total of 115 patients (84 female -73.04% and 31 male- 26.95%) with 126 MCA aneurysms (54 unruptured and 72 ruptured) were selected for the study. Of the entire population, 22 patients had bilateral MCA aneurysms and rest other patient had single or multiple intracranial aneurysms. The patient-related variables are presented in (Tab. 2). Regarding the age, the most common age range for unruptured and ruptured groups was the 51-60-year-old category (Fig: 2). The mean age for an unruptured aneurysm is greater than the ruptured group. We found more cases of both ruptured and unruptured aneurysm on the right side of the brain vasculature than on the left side.

		Unruptured (%), (mean±SD)	Ruptured (%), (mean±SD)
Sex	Male	9 (29.03%)	22 (70.96%)
	Female	40 (47.6%)	44 (52.38%)
Side	Right	30 (38.5%)	48 (61.5%)
	Left	24 (50%)	24 (50%)
Age		55.59±5.12	52.56±7.38

Table 2: Patient-related variables for unruptured and ruptured aneurysms

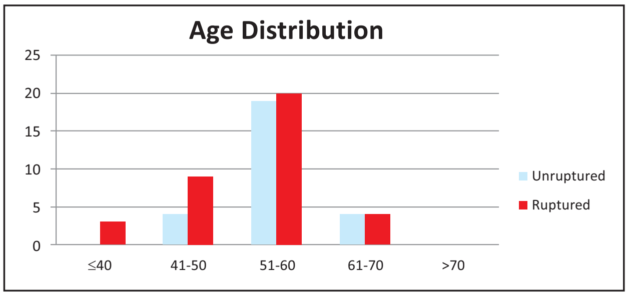

Figure 2: Bar graphs showing patient s age distribution of the population.

Morphologic Factors

As present in (Tab. 3) the ruptured aneurysms had significantly larger value of the maximum height of an aneurysm ($p \leq 0.001$), aneurysm depth ($p \leq 0.001$), aneurysm neck width ($p<0.05$), aneurysm width ($p<0.05$), size ratio ($p \leq 0.001$), neck-vessel ratio ($p<0.05$), height-width ratio ($p<0.05$) and aspect ratio index ($p<0.05$) than the unruptured aneurysm.

	Unruptured (mean±SD)	Ruptured (mean±SD)	p value	AUC
Maximum height (H_{max})	2.76±1.22	5.21±3.32	0.001	0.78
Aneurysm depth (H_{pr})	2.49±1.10	4.50±3.14	0.001	0.77
Neck width (NP)	3.76±1.15	4.57±1.50	0.031	0.66
Aneurysm width (W_{max})	3.43±0.97	4.83±2.11	0.01	0.69
Aneurysm volume	205.9±180.74	510.7±518.13	0.001	0.75
Aspect Ratio (AR)	0.66±0.21	0.99±0.55	0.002	0.73
Neck Vessel ratio (NVR)	1.50±0.48	2.58±4.24	0.014	
Size ratio (SR)	1.11±0.54	4.60±15.20	0.68	
Height WidthRatio (HWR)	0.81±0.28	1.08±0.43	0.68	
			0.001	0.78
			0.011	0.69

(Significant level <0.05)

Table 3: Size and shape indices for Ruptured and Unruptured aneurysms

ROC analysis and Binary Logistic Regression Analysis

The ROC-AUC values associated with rupture are displayed in (Fig. 3). Maximum height (H_{max}) and SR had the highest AUC values (AUC > 0.7) whereas the neck width (NP) and the neck-vessel ratio (NVR) both showed small AUC values (AUC< 0.7). To find the odds of aneurysm rupture that only includes independently significant markers, multivariate logistic regression was performed. At the end of the regression, only SR remained as the significant and independent parameters among all other parameters. In total 9 parameters which were found to be significant were analysed with backward LR method.

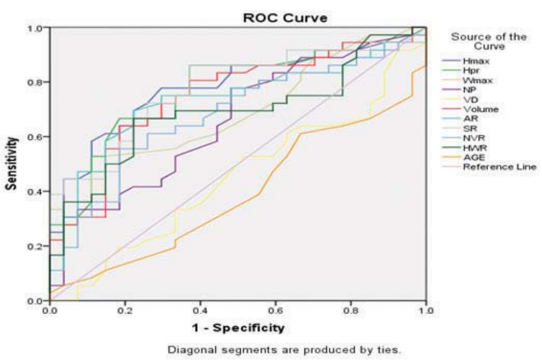

Figure 3: ROC curve of statistically significant morphological parameters

Discussion

Many studies have explored the risk factors of aneurysm rupture by comparing the difference between ruptured and unruptured solitary aneurysms, mainly based on clinical and/or morphologic data. With the technological advancements in vascular imaging, we have attempted to explore the potential rupture risk of multiple aneurysms in the same patient through the aneurysmal geometry and identify which parameters can be reliable indexes as one aneurysm ruptured, and the others did not. In terms of morphology, many parameters were significantly associated with the ruptured aneurysms by univariate analysis. However, after multivariate logistic regression analysis, only size ratio was an independently significant parameter for rupture.

Size ratio (SR):

Among the statistically significant parameters, SR was found to be an important and significant ($p \leq 0.001$) parameter for aneurysm rupture risk when logistic regression was performed. When 1.05 was defined as the optimal threshold for distinguishing the two subgroups - the ruptured and the unruptured aneurysms, 83% of all ruptured aneurysms were found to have SRs greater than 1.05, whereas 63% of all unruptured aneurysms had SRs of less than 1.05. SR not only takes into account about the aneurysm size but also considers the local vessel caliber and incorporates it into a quantifiable parameter. By doing so, it indirectly accounts for the effect of aneurysm location on its rupture. Different individual has a different diameter of the parent vessel as it varies greatly from individual to individual with different geometry. Thus to resolve this we incorporate aneurysm geometry to parent vessel geometry by taking size ratio (SR). However, the question arises that whether the vessel diameter itself, rather than the SR, influences the correlation with aneurysm rupture. In fact when the vessel diameter was individually tested for this hypothesis and it was found that vessel diameter was indeed insignificant (p=0. 491). Thus we can say that SR is a strong independent predictor for correlating rupture risk of an aneurysm.

Aspect ratio (AR), Height width ratio (HWR), Neck vessel ratio (NVR), Volume:

Most but not all previous studies showed that mean aspect ratio was higher in ruptured aneurysms than unruptured.[7,8,16-18] Ujiie et al reviewed the two-dimensional angiogram from 129 ruptured and 78 unruptured aneurysms and found that almost 80% of the ruptured aneurysms showed a higher aspect ratio (>1.6), whereas almost 90% of the unruptured aneurysms showed a small aspect ratio (<1.6).[16] In our study, the aspect ratio for ruptured aneurysms was found to present a smaller threshold than reported in the literature (0.99 instead of 1.6, Ujiie et al. 1999).

A possible explanation for this behaviour is that in our study aspect ratio was measured from the 3D reconstructed model, while in the literature it was measured from the 2D projection views. The reason may be that the measurements of 2D angiogram can be more exaggerated due to an overlay effect than 3D reconstructed images.[7,8,18]

Geometric variables such as AR, volume, HWR, and NVR are correlated to the aneurysm rupture event for their higher values. The group of ruptured aneurysms has larger mean values than the group of unruptured.

H_{max}, H_{pr}, W_{max}, and Neck plane:

These all one-dimensional parameters show higher mean value for the ruptured aneurysm as compared to unruptured one. After Man-Whitney test and ROC curve analysis, H_{max} and H_{pr} found to be statistically significant ($p \leq 0.001$) with AUC value 78 for H_{max} and 77 for H_{pr}. Thus it proved to be a good predictor for risk of rupture but however, when they are subjected to logistic regression analysis they could not regain their property till the last step thus indicating that though significant they could not be taken as a sole independent factor for predicting rupture risk. However, it can be used as a useful parameter for predicting the risk of rupture when taken along with other para-meters.

Our study has few limitations as this methodology does not account for the possible morphological changes and other factors such as the hemodynamic effect that unruptured aneurysms may experience over time. Examining a population over time without treatment is desirable but due to the unacceptable ethical dilemma present with regard to patient safety, such a study will never be completed. For that reason, studies like the one proposed, are important because they use image-based modeling to elucidate possible factors involved in the risk. On the other hand, in this work, a single aneurysm location was selected (MCA) which presents an aneurysm incidence of 20%. Nevertheless, in the literature, it has been reported that other aneurysm's location presents higher frequencies of rupture. It is not unreasonable to think that the risk of aneurysm rupture will be determined by a multitude of factors that also include genetics, other diseases present, familial history and patient s age. Definitely, the parameters proposed in this work do not suffice on their own to explain the natural history of an aneurysm leading to rupture. Naturally, future research will need to carefully weigh all these factors.

Conclusion

Morphology has been considered as a potential surrogate of rupture. Here the morphological variables characterizing cerebral aneurysms have been studied. We have proved the feasibility of using a complete and efficient image-based pipeline producing patient-specific models from medical images of patients with a cerebral aneurysm. We have used these geometric models of the aneurysm sac including the parent vessel to obtain a set of representative indices.

Conflict of Interest: None

ACKNOWLEDGMENTS:

Foremost, I would like to express my sincere gratitude to my advisor Prof. Dr. Tong Dan, Ph.D. Neuroradiologist for the continuous support of my research, for her patience, motivation, enthusiasm, and immense knowledge. Her guidance helped me in all the time of research and writing of this article.

Besides my advisor, I would like to thank my senior colleague Dr. Ting Ting Yuan for her invaluable suggestion, comments, ideas and help she has provided in the completion of my original article.

My sincere thanks also go to Dr. Cao Dian Bo, Dr.

Qiu Xiang, and Dr. Lan Wen Jing, for offering me the opportunities to study in their groups and sharing me with their experience and immense knowledge of their field.

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