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Risk Factors and Morphological Differences of Ruptured Saccular Aneurysm in Different Sites of Anterior Circulation in Patients Presenting with Subarachnoid Haemorrhage

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Abstract

Background: All sites of intracranial aneurysms have always been considered together in most of the studies of risk factors of aneurysm rupture. Therefore, it is not known whether some risk factors predispose to aneurysm rupture at a particular location. Morphologies also vary in accordance to different sites of the aneurysm. Objective: The purpose of the present study was to observe the differences in the risk factors, the size, aspect ratio and size ratio among the anterior circulation aneurysms. **Methodology:** This hospital based cross-sectional study carried out in the Department of Neurology at Dhaka Medical College Hospital (DMCH), Dhaka during July 2013 to June 2015 for a period of two (02) years. Patients with subarachnoid haemorrhage caused by ruptured anterior circulation saccular aneurysms admitted in the Departments of Neurology, Internal Medicine and Neurosurgery Departments at Dhaka Medical College Hospital (DMCH), Dhaka and the Department of Neurointervention at National Institute of Neurosciences and Hospital, Dhaka were enrolled in this study. Patients' ≥18 years of age with subarachnoid haemorrhage caused by anterior circulation aneurysm which was confirmed by computed tomogram (CT-scan) and/or CSF study and digital subtraction angiography were included in this study. The risk factors were identified by interviewing the patients and the morphology were measured from the digital subtraction angiogram. Results: A total number of 85 patients with ruptured saccular anterior circulation aneurysm were enrolled in this study. In this study anterior communicating artery aneurysm (ACom) was the most frequent site of aneurysm (42%). The mean age of the patients with ACom aneurysm (51.72 ± 9.26 years) was significantly higher than posterior communicating artery (47.5 \pm 8.2 years) aneurysm and middle cerebral artery (MCA) (43.41 \pm 8.0 years) aneurysm. Above the age of 50 ACom aneurysm was the most frequent aneurysm (OR 5.5, p<0.05). Among the female Posterior communicating artery (PCom) aneurysm (46.7%) was the most frequent aneurysm and among the male ACom aneurysm (37.5%) was the most frequent aneurysm. Family history was exclusive in MCA aneurysm (3.5%). The mean size of MCA (7.79 \pm 0.71 cm) was higher than ACom (6.12 \pm 2.7cm) aneurysm and PCom (6.5 ± 2.4 cm) aneurysm and proportion of aneurysm >10 mm was also higher among the middle cerebral artery (35.6%) aneurysms. The size ratio was significantly higher in ACom (3.08±1.23) and MCA (3.04±0.97) aneurysm. ACom (76.4%) and MCA (83.3%) had also more frequent high risk size ratio. Conclusion: In conclusion anterior circulation aneurysms differ in respects of risk factors and morphology. [Journal of National Institute of Neurosciences Bangladesh, 2017;3(1): 21-28]

Keywords: Subarachnoid haemorrhage; anterior circulator aneurysm; anterior communicating artery aneurysm; ruptured saccular aneurysm

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Introduction

Subarachnoid haemorrhage accounts for only 5% of strokes1. Aneurysms are the cause of subarachnoid haemorrhage in 85% of cases¹. Saccular aneurysms arise at sites of arterial branching, usually at the base of the brain². Approximately 80% of intracranial aneurysms (IA) arise from anterior circulation³. The most common locations for anterior circulation aneurysms are the anterior communicating artery (ACom) followed by the posterior communicating artery (PCom), the middle cerebral artery (MCA)⁴.

Modifiable risk factors for subarachnoid haemorrhage are hypertension, smoking, and excessive alcohol intake and non-modifiable factors are age, female gender and positive family history⁵. In most of the studies about risk factors, all sites of intracranial aneurysms have always been considered together. Therefore, it is not known whether some risk factors predispose to aneurysm rupture at a particular location or whether some sites of aneurysms are linked to a specific risk factor. In some studies it has been found that Family history is the risk factor for MCA aneurysm⁶ and male gender is the risk factor for ACom aneurysm⁷.

Pathogenesis of intracranial aneurysms is still under study. Intracranial aneurysms are not congenital but develop in the course of life⁸. According to the current view, cerebral aneurysms are acquired degenerative lesions resulting from hemodynamic stress9. Animal studies conducted by Hashimoto et al¹⁰ and Hazama et al¹¹ clearly showed that hemodynamic stress leads to degenerative changes of internal elastic lamina and muscularis media of arterial wall immediately adjacent to the apex of bifurcation. However, it is still not clear why aneurysms occur in some preferential site, like ACom complex, PCom complex and MCA bifarcation¹². This issue was partially addressed in glass model studies, showing that the magnitude and distribution of hemodynamic stress on the vessel bifurcation depend not only on blood flow but also on the bifurcation angle and flow pulsatility¹³⁻¹⁴.

Using computational fluid dynamics, Hassan¹⁵ suggested high wall shear stress (WSS) may be responsible for rupture of high-flow aneurysms, whereas the predominant factors causing rupture in low-flow aneurysms are high intra-aneurysmal pressure and flow stasis. Findings of other researchers^{16, 17} also support this view. Hemodynamics is strongly dependent on the geometry of the aneurysmal sac and its feeding vessel^{15, 16}. Therefore, suitable parameters characterizing intracranial aneurysm geometry can capture the characteristic hemodynamics and potentially predict rupture risk. The most ubiquitous parameter is

intracranial aneurysm size. Aneurysms exceeding 10 mm in size are considered to be dangerous, though it may rupture in smaller size as well¹⁸⁻²⁰. Therefore, it has been postulated that other factor like shape and caliber of the vessel wall might have some contribution. Most commonly studied shape parameter is Aspect ratio¹⁹⁻²¹. Size ratio is an important parameter which takes into account not only the aneurysm size itself but also the local vessel caliber²². By doing so, it indirectly accounts for the effect of aneurysm location on rupture²². In this context this present study was undertaken to observe the differences in risk factors as well as morphology among the anterior circulation aneurysm.

Methodology

This was a hospital-based cross sectional study done in the Department of Neurology at Dhaka Medical College Hospital, Dhaka from July 2013 to June 2015 for a period of two (02) years. Patients with subarachnoid haemorrhage caused by ruptured anterior circulation saccular aneurysms admitted in the Departments of Neurology, Internal Medicine and Neurosurgery Departments at Dhaka Medical College Hospital (DMCH), Dhaka and the Department of Neurointervention at National Institute Neurosciences and Hospital, Dhaka were enrolled in this study. Patients' ≥18 years of age with subarachnoid haemorrhage caused by anterior circulation aneurysm which was confirmed by computed tomogram (CT-scan) and/or CSF study and digital subtraction angiography was included in this study. Aneurysms at multiple sites, aneurysms other than saccular aneurysm and patient with Ehler's Danlos syndrome or other collagen tissue disorders were excluded from this study. Subarachnoid haemorrhage was defined as the haemorrhage in the subarachnoid space confirmed by CT scan of head and / or CSF examination. Anterior circulation Aneurysm was defined as aneurysm from the internal carotid artery and its branches. In this study ACom, PCom and MCA aneurysms were considered. Aneurysm size was defined as the maximum perpendicular height of the aneurysm; it is the maximum perpendicular distance of the dome from the neck plane 19. Aspect ratio was defined as the ratio of the height and the neck of the aneurysm23. The aneurysm-to-vessel size ratio (SR) incorporates the geometries of the aneurysm and its parent vessel and defined as SR - (maximum aneurysm height)/(average vessel diameter). Here, the average vessel diameter (DV) was obtained by measuring two representative vessel cross sections upstream of the aneurysm like D1 at the proximal neck and D2 at 1.5 X

D1 upstream²². High risk morphology of aneurysms was defined as size >10 mm²² with the aspect ratio of more than 1.6²³ and size ratio of more than 2.05²². Data were collected by a pre-designed Data sheet. Patients' information were obtained using information sheet which included questionnaire, clinical findings and digital subtraction angiography (DSA) findings. Statistical analysis was carried out by using the Statistical Package for Social Sciences (SPSS) version 16.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean, standard deviation, and categorical variables as frequencies and percentages. The differences among the groups were analyzed by unpaired t-test (continuous variable) and Z test of proportion (discrete variable). A p-value <0.05 was considered as significant.

Results

A total number of 85 patients with ruptured saccular anterior circulation aneurysm were enrolled in this study. The mean age of the study subjects was $48.24 \pm$

Table 1: General Demographic Characteristics of the Total Study Subjects (n=85)

Variables	Frequency	Percentage	
Age	48.24±9.26 years		
Sex			
• Male	33	38.8	
• Female	52	61.2	
Tobacco users	34	40.0	
Alcoholism	6	7.0	
Hypertension	24	28.2	
Diabetes	11	12.9	
Family History	3	3.5	

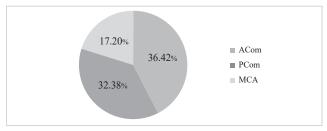


Figure I: Distribution of the site of the Aneurysm

Table 2: Difference of the Non-modifiable Risk Factors of Anterior Circulation Aneurysm (n=85)

Risk Factors	ACom	PCom	MCA	P value
Age	51.72 ± 9.26	47.5 ± 8.2	43.41 ± 8.0	Acom vs MCA p < 0.05
				MCA vs PCom p < 0.05
				ACom vs PCom p < 0.05
				ACom vs Average p < 0.05
				PCom vs Average p >0.05
Sex				MCA vs Average p < 0.05
• Male	19 (57.5%)	8(24.2%)	6(18%)	Male ACom-2.79
• Female	17 (32.7%)	24(46.1%)	11(21.2%)	Female PCom-2.67
Family history	0	0	3 (17.60%)	Female- MCA-1.2

Table 3: Difference of the Modifiable Risk Factors of Anterior Circulation Aneurysm (n=85)

Risk Factors	ACom	PCom	MCA	P value
Tobacco user	16(44.4%)	11(34.3%)	07(41.2%)	ACom (OR 1.2; p-0.73)
				PCom (OR 0.6, p -0.411)
				MCA (OR 1.14, p-0.80)
Alcohol	4 (11.10%)	1(3.10%)	1 (5.90%)	ACom (OR 2.9 p-0.22)
				PCom (OR 0.29, p -0.0.29)
				MCA (OR 0.83, p-0.83)
Hypertension	11(30.6%)	9 (28.1%)	4(23.5%)	ACom (OR 1.2 p-0.68)
				PCom (OR 0.99, p 0.99)
				MCA (OR 0.73, p0.63)

Table 4: Location of Anterior Circulation Aneurysms According to Age (n=85)

Age Group Location of the aneutron ACom A PCom A	Location of the aneurysm			Odd Ratio	P value
	PCom A	MCA A			
>50	20	6	2	>50 Acom 5.5	0.0006
≤ 50	16	26	15	≤50PCom 3.07	0.034
				≤50 MCA 4.9	0.043

9.26 years. Most of the study subjects were within the age group of 41-59 years. Female to male ratio was 1.6. The frequency of tobacco users and alcoholics were 40% and 7%, respectively. Total 28.2% had hypertension, 12.9% had diabetes and 3.5% had positive family history of subarachnoid haemorrhage (Table 1).

ACom was the most frequent site of aneurysm (42.0%) among the anterior circulation aneurysms (Figure I).

The mean age (51.72 ± 9.26) of the patients with ACom aneurysm was significantly higher than others (Table-2). Among the female PCom was the most frequent aneurysm and among the male ACom was the most frequent aneurysm. Family history was exclusive in MCA aneurysm (3.5%) (Table 2).

Regarding tobacco use, alcoholism and hypertension there were no significant differences among the anterior circulation aneurysm (Table 3).

Above the age of 50 ACom was the most frequent aneurysm (OR-5.5, p<0.5). Below the age of 50 PCom and MCA was the most frequent aneurysm (Table 4). The mean size, aspect ratio and size ratio of the aneurysm in the whole study subjects were 6.6 ± 2.7

mm, 1.81 ± 0.35 and 2.7 ± 1.08 , respectively. The proportion of the high risk size, aspect ratio and size ratio were 18.8%, 77.6% and 85.9%, respectively among the whole study subjects (Table 5).

The mean size of MCA was higher than other aneurysm and proportion of aneurysm >10 mm was also higher among the MCA aneurysms. There was no significant difference in mean Aspect ratio among the ACom, PCom and MCA aneurysms. The mean size ratio of ACom, PCom and MCA aneurysm was 3.08 ± 1.23 , 2.1 ± 0.70 and 3.04 ± 0.97 . The size ratio was significantly higher in ACom and MCA aneurysm. (Table 6)

Table 5: Morphologic Features of the Aneurysms of the Whole Study Subjects (n=85)

Character	Parameter
Size (mm)	6.6±2.7 mm
Aspect ratio	1.81 ± 0.35
Size ratio	2.7 ± 1.08
High risk size (n/%)	16(18.8%)
High risk aspect ratio (n/%)	66(77.6%)
High risk size ratio (n/%)	73(85.9%)

Table 6: Difference of Morphologic Parameters of Anterior Circulation Aneurysm (n=85)

Parameter	ACom	PCom	MCA	P value
Size	6.12 ± 2.7	6.5 ± 2.4	7.79 ± 0.71	ACom vs MCA p < 0.05
				MCA vs PCom p >0.05
				ACom vs PCom p >0.05
Neck diameter	3.3 ± 1.06	3.2 ± 1.08	4.1 ± 1.4	ACom vs MCA p < 0.05
				MCA vs PCom p < 0.05
				ACom vs PCom p >0.05
Aspect ratio	1.82 ± 0.30	1.89 ± 0.28	1.97 ± 0.32	ACom vs MCA p >0.05
				MCA vs PCom p >0.05
				ACom vs PCom p >0.05
Mean diameter of feeding Vessels	1.98 ± 0.25	3.2 ± 0.41	3.2 ± 0.41	ACom vs MCA p < 0.05
				MCA vs PCom p >0.05
				ACom vs PCom p < 0.05
Mean size ratio	3.08 ± 1.23	2.1 ± 0.70	3.04 ± 0.97	ACom vs MCA p >0.05
				MCA vs PCom p < 0.05
				ACom vs PCom p < 0.05

Table 7: Difference of high risk Morphology among the Anterior Circulation Aneurysm (n=85)

Parameter	ACom	PCom	MCA	P value	
High risk size	5,13.8	5.15.6	6,35.6	ACom (OR 0.34, p0.060)	
				PCom (OR 0.42, p 0.138)	
High risk aspect ratio	26(72.2%)	26(81.3%)	14(82.2%)	MCA (OR 10, p 0.0001)	
				ACom (OR 0.5 p 0.3)	
High risk size ratio	30(83.3%)	17(53.1%)	13(76.4%)	PCom (OR 1.4, p 0.5)	
				MCA (OR 1.4, p 0.6)	
				ACom vs MCA p > 0.05	
				MCA vs PCom p < 0.05	
				ACom vs PCom p < 0.05	

Regarding proportion of the high risk aspect ratio there was no significant differences observed among the anterior circulation aneurysm. ACom and MCA also had more frequent high risk size ratio. Thus in this study difference in age, sex and positive family history among the anterior circulation aneurysm had been observed. The anterior circulation aneurysms were also different regarding size and size ratio (Table 7).

Discussion

This study was conducted to assess the differences in the risk factors and morphology among ruptured anterior circulation saccular aneurysm in patients with subarachnoid haemorrhage. Total 85 cases of anterior circulation aneurysm were enrolled in this study. Among the anterior circulation aneurysm ACom was the most frequent aneurysm (42.4%) which is consistent with the findings of Bryce et al²³ and Howng et al²⁴. Another study done in Bangladesh by Shamsul et al²⁵ also found ACom as most prevalent aneurysm (ACom 42.30%, PCom 26.9%, MCA 9.6%). Their percentage was slightly different as in that study all anterior and posterior circulation aneurysms were considered. Here only ACom, PCom and MCA aneurysm among the anterior circulation aneurysm were considered.

The mean age of the study population was $48.24\pm9.^{26}$ years and most of the study populations were within the age group of 38-57. This is consistent with Shamsul et al²⁵ where the average age was 45.9 years. Age of the patients with ACom aneurysm was significantly higher than that of PCom and MCA aneurysm (p <0.05). This was consistent with findings of Lindner et al²⁶. After the age of 50 ACom aneurysms were significantly the most frequent aneurysm (OR 5.5, p<0.05) than the other two. At and the below 50 PCom (OR 3.07, p<0.5) and MCA aneurysms (OR 4.9, p<0.05) were significantly most frequent aneurysm. These findings were consistent with Zhao et al²⁷.

In this study 61.2% were female. Female to male ratio was 1.6.which was similar to the study done by Ashay et al²⁸ and Linn et al²⁹ also reported that subarachnoid hemorrhage due to ruptured aneurysm is \approx 1.6 times higher in women than in men. Among the male ACom (57.5%) was the most frequent Aneurysm (OR 2.79, p<0.05) and among the female PCom was the most frequent aneurysm (OR 2.67, p<0.05). Ali et al³⁰ also found the similar distribution in accordance to gender. Total 28.2% patients were found to be hypertensive in this study population. This is much higher than the prevalence of hypertension (13.5%) in community³². This was consistent with an Indian study Ashay et al²⁸

and Japanese study³¹. Here, 12.9% were found to be diabetic, which is near to the prevalence of diabetes (10%) in the community³³. Hiroki et al³¹ and Ashay et al²⁸ also found similar prevalence of diabetes in their studies. There were no significant differences in the prevalence of tobacco taking, alcoholism and hypertension among the anterior circulation aneurysms, which was consistent with the findings of Linder et al²⁶.

Positive family history of subarachnoid haemorrhage in this study subjects was 3.5%. Positive family history was found exclusively in MCA aneurysms (OR 33, p=0.023) in this study. Ruigork et al⁶ stated positive family history as a recognized risk factor for MCA aneurysm in younger patients. In this study the mean age of the patients with positive family history was $38.3\pm2.^8$ years. It was significantly lower than that of patients without positive family history (p <0.05). This may explain why in the current study, patients with MCA aneurysms were more often younger than patients with ACom aneurysm.

Thus it can be assumed that an elderly male with SAH has a high probability to have ACom and a female of 41 to 50 with subarachnoid haemorrhage has high probability of having PCom aneurysm. Accordingly a young patient with positive family history has high probability of having MCA aneurysm. In this study the mean size of the Aneurysms was 6.6±2.7 mm. This size is far below the IUSA recommended critical diameter of 10 mm. Dhar et al³⁴ in their study found average size of the aneurysm 5.5±1.9. A Korean study also found the average size of aneurysm 6.15±1.3. Average Size of aneurysm found in other study was 7.20±4.30³⁵, 5.59±2.79³⁶.

The size of ACom aneurysm was 6.12±2.7, PCom aneurysm was 6.5±2.4 and MCA aneurysm was 7.79±.71. In this study MCA aneurysm is larger than other aneurysm which is significant in case of Acom (p value <0.05). These findings were similar to Luciana et al³⁶. Jeon et al³⁵ in their study found size of Acom, PCom and MCA aneurysm 6.67, 6.35 and 7.09 respectively. In this study only 18.8% had size >10 mm. It is consistent with findings of Thomas and Bogusław³⁷ which were 14.4%. In a study by Nahed et al³⁸ it was found that 65.7% of ruptured aneurysms were smaller than 7 mm.

Wiebers et al³⁹ state that the aneurysms shrink after being ruptured; therefore, the reported size of a ruptured aneurysm is likely to be smaller than its pre rupture size. But recently, Kataoka et al⁴⁰ undertook a study to answer this question. They performed histological evaluations of both unruptured and ruptured aneurysms and found no histological

evidence to support the notion that aneurysms shrink after rupturing. Furthermore, Yasui et al⁴¹ analyzed 25 patients with known untreated aneurysms that went on to rupture and recorded the size before and after rupture. In almost every case, the aneurysm increased in size. Thus it is to be argued that the risk of small aneurysms rupturing is not insignificant and the findings of this also support this.

In this study significantly lower proportion (13.8%) of the patients with ACom aneurysm (OR 0.34, p <0.05) had high risk size. In MCA aneurysm significantly higher proportion (35.6%) of the patient had high risk size (0R 10, p<0.05). These findings were similar to Yaseer and Mahmoud⁴². Joo et al⁴³ in their study concluded that the majority of aneurysm ruptured before reaching 7 mm (71.8%) and 10 mm (87.9%) in diameter, and the most frequent site of ruptured aneurysms was the Acom aneurysm.

The underlying Mechanism for larger size of aneurysm in MCA than ACom might be due to intra-aneurysmal hemodynamic stress, which is more in the AComA than MCA⁴⁴⁻⁴⁵. This indicates that the ACom aneurysm is the most dangerous site for rupture of small aneurysm. Therefore, aneurysms located in the ACom may bleed before they reach a large size⁴⁶. It is recommended that ACom aneurysm of any size should be considered for surgical or endovascular treatment when discovered⁴².

In this study the mean aspect ratio (AR) was 1.81±0.35, which is consistent with findings of Luciana et al³⁶ which was 1.86. Total 77.6% possess AR >1.6. This is consistent with findings of Ujiie et al⁴⁷ where they found 80.18% of ruptured aneurysms with an AR>1.6.A Korean study done by Jeong et al³⁵ also found the same result. (70% rupture aneurysm had AR>1.8). There was no significant difference of aspect ratio among the anterior circulation aneurysm, although the size of MCA aneurysm was significantly higher than ACom aneurysm. This could be explained by large neck size of the MCA aneurysm. In this study neck size of ACom, PCom and MCA aneurysms were 3.3 ± 1.06 , 3.2 ± 1.08 and 4.1 ± 1.4 , respectively. The neck size of the MCA aneurysm was significantly higher than ACom (p <0.05). This findings was consistent with it is consistent with Luciana et al³⁶.

Mean size ratio in this study was 2.7±1.08. The size ratio of Qit et al⁴⁸, Tomasz et al³⁷ and Dhar et al³⁴ were 2.67, 2.22, and 2.8 respectively. So the findings of this study were similar to others. The size ratio of ACom, PCom and MCA aneurysm was 3.08±1.23, 2.1±0.70 and 3.04±0.97 respectively. The size ratio was significantly higher in ACom and MCA aneurysm than PCom aneurysm. This finding is consistent with

Kashiwazaki et al49.

Among the anterior circulation aneurysms 71.8% possesses the high risk size ratio. It was consistent with Dhar et al³⁴ and Rahman et al⁵⁰ where they found patients with high risk size ratio in 77.0% and 69.0% respectively. In this study ACom, PCom and MCA aneurysm possess high risk size ratio in 83.3%, 53.1% and 76.4% of the population respectively. Thus ACom and MCA possess significantly high percentage of patients with high risk size ratio (p<0.05). This could be explained by higher diameter of the feeding vessel of PCom.

Size ratio (SR) takes into account not only the aneurysm size itself but also the local vessel caliber and incorporates it into a quantifiable parameter. By doing so, it indirectly accounts for the effect of intracranial aneurysm (IA) location on rupture. In this study critical size of the aneurysm was present in very small proportion of the patients whereas high risk aspect ratio and size ratio were present in large proportion of the study subjects. In dealing with the patients of aneurysm size should not be the only deciding factor, aspect ratio and size ratio should also be considered. Size and the size ratio of the anterior circulation aneurysm were different. In recommending about the critical parameter aneurysm should be individualized according to location.

The present study had some limitations. Its cross sectional design and small sample size were the incipient limitations. Prospective observational study was beyond the logistical and economic resources of this study. This study was not designed to assess the influence of the established risk factors on the development of aneurysms. The conclusion that could be drawn from the results is that risk factors like age, gender and positive family history influence the site of aneurysm. More over the prevalence of familial preponderance is low in this study. Therefore no clear conclusion can be made about the influence of positive family history on the specific location preponderance. For the measurement 2D angiogram was used. Three dimensional angiogram would give more accurate measurement of the parameter. This was not a blinded study so scope of observer bias could not be ruled out. Another significant limitation of this study was the fact that aneurysm measurement was done after intracranial aneurysm rupture. There was scope of alteration of the morphology. It must be stressed that the current study does not, in any way, correlate size, aspect ratio and size ratio with future risk of rupture. A prospective study is necessary to validate the findings of this study.

In this study differences in risk factor and morphology

were observed among the different anterior circulation aneurysm. So recommendation should be individualized rather than generalized. A comprehensive scoring system for the assessment of rupture risk might be proposed considering the presence of risk factors and different dimension of morphology like location, size, aspect ratio and size ratio.

Conclusion

In this study difference in the risk factors among the different site of anterior circulation aneurysm was observed. This implies that some risk factors predispose for aneurysm rupture at a particular location, or some sites of aneurysms are linked to a specific risk factor. There were also differences in morphology among the different location of anterior circulation aneurysm. This implies heterogeneous haemodynamics and different risk of rupture in anterior circulation aneurysm.

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