

Impact of Risk Factors on the Size of Ruptured Intracranial Saccular Aneurysms

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Abstract:

Background: Un-ruptured intracranial aneurysms (UIAs) are common and prevalence is about 2 to 8%. Several studies have shown that the decision to treat un-ruptured aneurysms should not be based on aneurysm size alone. A study suggest that treatment of UIAs smaller than 7 mm in hypertensive patients and smokers may be beneficial.

Aim and objective: The goal of this study is analysis of correlation of age, gender, location of the aneurysm, history of hypertension and cigarette smoking, previous history of SAH with the size of ruptured aneurysms. **Materials and Methods:** This hospital based observational cross-sectional study was conducted in the Department of Neurology & Neurosurgery, Dhaka Medical College Hospital (DMCH), Dhaka. Total 44 patients with SAH were taken by inclusion & exclusion criteria. The aneurysms size, site of location and aneurysm multiplicity was assessed by three-dimensional rotational digital subtraction angiography (DSA). **Results:** The mean age of the study population was 49.24 ± 11.5. About half of the population were within 51-60 years. The male female ratio was 1:1.2. Out of 44 population, 93.2% were presented with headache, 90.9% with vomiting. In this study aneurysms mean size was 5.72 ± 4.010 mm. 93.2% of aneurysms were below 10 mm, 75.0% were below 7 mm and 50.0% below 5 mm. Size of ruptured aneurysm is small in hypertensive population and is significant (p-value 0.037). Aneurysm size was significantly (p-value 0.013) smaller in case of smoker. Mean aneurysm size in hypertensive smoker population was significantly (p-value-0.004) smaller than hypertensive non-smoker. Population with one risk factor had mean aneurysm size was 8.32 ± 6.84 mm, two risk factors had 5.26 ± 1.86 mm, three risk factors had 4.79 ± 2.05 mm and more than three risk factors had 2.85 ± 1.43. **Conclusion:** This study shows that more the risk factors, smaller the size of aneurysms. Therefore, history of hypertension, cigarette smoking, female sex, age and positive family history should be considered in the assessment of treatment of un-ruptured intracranial aneurysms.

Key words: SAH, risk factors, intracranial Aneurysms, aneurysms size

Introduction

Subarachnoid haemorrhage (SAH) is one kind of stroke, measuring 1 to 7% of stroke patients. SAH is responsible for 5% of stroke death¹. Incidence

of SAH is approximately 6-15 per 100,000 people per year². Up to 50% of all cases of SAH are fatal and 10-15% die before reaching hospital³. After hospital admission one-third will die, about one-

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third will recover with severe disability and about one-third will have excellent recovery⁴. Those who survive often have neurological and cognitive impairment³. The economic impact of SAH is severe because it mostly affect the patients in 40s and 50s during their most productive years⁵. Though incidence of SAH in Bangladesh is unknown. In Kashmir, India the incidence of SAH is 13/100000⁶. Bangladesh is culturally, religiously almost same as Kashmir.

Cerebral aneurysms are the most common cause of non-traumatic subarachnoid hemorrhage and is responsible for 70 to 75% of spontaneous SAH⁷. Ruptured "Berry" aneurysm is the most common among the aneurysmal SAH and is responsible for 85% of cases⁸.

In a univariate analysis, family history of SAH, systemic hypertension, cigarette smoking and regular alcohol consumption were significant risk factors for aneurysmal SAH. In a multivariate analysis, after adjustment for other risk factors, family history of SAH, cigarette smoking and hypertension remained significant⁹.

Size of intracranial aneurysm is a key prognostic factor for rupture¹⁰. In general large aneurysms are more likely to rupture¹¹⁻¹⁵. One large, multicenter trial suggested that aneurysms 10 mm or larger had a 1% annual risk of rupture, with smaller aneurysms having a much smaller risk of rupture. There seems to be a general agreement that the unruptured aneurysm e" 10mm in diameter should be treated surgically¹⁶. Recent studies, including the prospective arm of the International Study of Unruptured Intracranial Aneurysms (ISUIA) suggest that aneurysms smaller than 10 mm have higher rates of rupture than previously predicted¹⁷.

Age and sex also influences on size of aneurysms^{18,19}. Site of aneurysm also impact on size of ruptured intracranial aneurysms (RIAs)^{20,21}. The size at which aneurysms rupture appears to be smaller in those patients with the combination of hypertension and smoking than in those with either risk factor alone²².

Recently, unruptured intracranial aneurysms (UIAs) are increasingly detected due to the increased availability and improved sensitivity of noninvasive

imaging technique²³. Unruptured intracranial aneurysms (UIAs) are common, with autopsy studies placing their prevalence at approximately 2 to 8%^{24,25}.

The ISUIA 2 study concluded that aneurysms < 7 mm in size in the anterior circulation have an annual rupture risk of 0-0.1% per year¹⁶. But there are many studies that contradict with this study. The natural history of small un-ruptured aneurysms (<5 mm in diameter) without surgical treatment and found that the annual rupture rate was 0.8% for 380 aneurysms followed up for a mean of 13.8 months²⁶. The annual bleeding rate was 1.92%²⁷, 1.3%²⁸, 1.5²⁹ and 2.3%³⁰.

Several studies have shown that the decision to treat un-ruptured aneurysms should not be based on aneurysm size alone³¹⁻³⁴. A study suggest that treatment of UIAs smaller than 7 mm in hypertensive patients and smokers may be beneficial²².

The aim of this study is to find out the effect of risk factors on size of ruptured aneurysms, to assess the critical size at which most of aneurysms ruptured. So that we can able to draw a conclusion that a critical sized un-ruptured aneurysms with risk factors should consider either microsurgery or coiling.

Materials and Methods:

This was an observational, cross-sectional study. Forty four patients with aneurysmal subarachnoid haemorrhage admitted in Department of Neurology and Neurosurgery, Dhaka medical college hospital (DMCH) were included for the study following proposed inclusion and exclusion criteria.

Following admission, patients with SAH was diagnosed clinically and was confirmed by CT scan of head or by lumbar puncture (LP) in CT scan negative cases. Non-Aneurysmal SAH, Other than saccular aneurysms (Fusiform, traumatic and mycotic aneurysm) and arterio-venous malformation associated aneurysm were excluded.

A written informed consent was taken from each patient or their guardians. History regarding demographic profile (age, sex, marital status, education, socioeconomic level, family details); risk

factors (hypertension, prior history of SAH, smoking habit & alcohol, drug abuse) and clinical presentation was noted on the questionnaire.

The aneurysm size, site of location and aneurysm multiplicity was assessed by three-dimensional rotational digital subtraction angiography (DSA).

The location of the aneurysm was classified as follows: A) anterior circulation and B) posterior circulation. Multiplicity of aneurysm is defined in this study as the occurrence of two or more than two aneurysms.

Smokers were divided into smoker and never smokers; current and past smokers were included as smoker. Patients who consumed alcohol were classified as heavy (30ml /day or more) or light drinkers (less than 30ml /day).

Hypertension was defined if it had been diagnosed before admission. If systolic BP \geq 140 mm Hg and Diastolic BP \geq 90 mmHg was diagnosed as hypertensive. Hypertensive patients were divided into 2 groups, those who took antihypertensive medication regularly (medicated group) and those who either took it irregularly or not at all (poorly controlled group). Blood pressure readings at admission or during subsequent hospitalization was taken into account because it is considered to be reflective of initial or subsequent clinical conditions. A history of SAH was recorded separately from other cerebrovascular diseases (CVD) in both the patient's and his or her family medical history.

Hunt and Hess grading was recorded from patient history and examination. Subjects with incomplete data was excluded. The data was analysed using standard statistical procedures.

The statistical analysis was performed using SPSS software v. 26.0. Continuous parameters were expressed as mean \pm SD and categorical parameters as percentage. Differences between groups were analysed using Student t-test for metric variables and Chi-square test for ordinal or nominal scaled variables. The correlation between aneurysm size and risk factors were evaluated by one-way analysis of variance (ANOVA). Analysis of variance (univariate ANOVA) was among three groups. Statistical significance was defined as $p < 0.05$ (CI% 0.95).

Results:

The study was conducted to assess the impact of risk factors on the size of ruptured intracranial aneurysms. Total 44 cases of subarachnoid hemorrhage were enrolled in this study. The mean age of the study population was 49.24 ± 11.5 . About half of the population were within 51-60 years.

Out of 44 population, 54.5% were female. The male female ratio was 1:1.2. Presentation of subarachnoid hemorrhage in this study was, 93.2% population were presented with headache, 90.9% with vomiting, 81.8% had neck stiffness, 52.3% were unconscious, 15.9% had seizure, and 15.9% hemiplegia. In this study 59.1% were hypertensive, 47.73% were smoker, 15.9% were alcoholic and were light drinker, 6.8% were substances abuser and 11.4% had positive family history of SAH. 43.2% of population were in Hunt and Hess scale 2. In this study, aneurysms mean size was 5.72 ± 4.010 mm. According to International Study on Un-ruptured Intracranial Aneurysms (ISUIA), 65.9% aneurysm size were 3-7mm, 20.5% were 8-12 mm, 9.1% were below 3 mm.

Table-I
Distribution of the study patients by aneurysms size (n=44)

| | Frequency | Percentage |
|--------|-----------|------------|
| <10 mm | 41 | 93.2 |
| >10 mm | 3 | 6.8 |
| <7 mm | 33 | 75.0 |
| >7 mm | 11 | 25.0 |
| <5 mm | 22 | 50.0 |
| >5 mm | 22 | 50.0 |

In table-I, 93.2% of aneurysms were below 10 mm, 75.0% were below 7 mm and 50.0% below 5 mm.

Table-II
Aneurysm size relation with hypertension (n=44)

| | Hypertension | | p-value |
|--------------------|---------------------|---------------------|---------|
| | Hypertensive (n=26) | Normotensive (n=18) | |
| Mean \pm SD | Mean \pm SD | | |
| Aneurysm size (mm) | 4.68 ± 2.69 | 7.23 ± 5.10 | 0.037 |

Table-II shows, size of ruptured aneurysm is small in hypertensive population and is significant (P value 0.037)

Table-III
Aneurysm size relation with smoking (n=44)

| | Smoking status | | p-value |
|--------------------|----------------|---------------------|---------|
| | Smoker (n=21) | Never smoker (n=23) | |
| | Mean±SD | Mean±SD | |
| Aneurysm size (mm) | 4.18±1.74 | 7.13±4.93 | 0.013 |

Table-III shows aneurysm size were 4.18±1.74 mm in smoker which is significantly (P value – 0.013) smaller than never smoker.

Table-IV
Aneurysm size relation with hypertension and smoking (n=26)

| Hypertension | N | Mean±SD | p-value | |
|--------------|--------------|---------|-----------|-------|
| Yes | Smoker | 14 | 3.36±1.35 | 0.004 |
| | Never smoker | 12 | 6.22±3.07 | |

Table-IV shows mean aneurysm size in hypertensive smoker population was 3.36±1.35 mm which is significantly (p-value-0.004) smaller than hypertensive non-smoker.

Table-V
Aneurysm size relation with presence of risk factors (n=44)

| Risk factors | N | Mean±SD | p-value |
|----------------------|----|-----------|---------|
| One risk factor | 11 | 8.32±6.84 | 0.063 |
| Two risk factors | 17 | 5.26±1.86 | |
| Three risk factors | 13 | 4.79±2.05 | |
| > Three risk factors | 3 | 2.85±1.43 | |

Table-V shows aneurysm size was dependent to presence of number of risk factors. More risk factors had small aneurysm.

Discussion:

The study was conducted to assess the impact of risk factors on the size of ruptured intracranial aneurysms. Total 44 cases of subarachnoid hemorrhage were enrolled in this study. The mean age of the study sample was 49.24 ±11.5 years. About half of the population were within 51-60 years. This is consistent with Reaz Mahmud et al where the average age was 48.24±9.26³⁵. Another two studies conducted in Bangladesh the mean age was 45.00±9.4 and 45.9 years^{36,37}. In an epidemiological study done in India had shown average age of subarachnoid hemorrhage in their population was 49.63 years³⁸. Worldwide the mean

age of aneurysmal rupture is in the range of 50 to 55 years. The mean age of this study coincides with the both worldwide and sub-continent.

Subarachnoid hemorrhage (SAH) is a disease with definite female preponderance. In this study 54.5% were female. The male female ratio was 1:1.2. The ratios of men to women were constant at approximately 1.2:1³⁹, 1: 1.5⁴⁰ and 1:1.3⁴¹. A Bangladeshi study shows the male female ratio was 1:1.6³⁵.

93.2% population were presented with headache, 90.9% with vomiting, 81.8% had neck stiffness, 52.3% were unconscious, 15.9% had seizure, and 15.9% hemiplegia. According to a Bangladeshi study, headache, neck rigidity and vomiting was invariably (100%) complained by the patients at the onset. Two-thirds (66.7%) of the patients were unconscious at presentation and 10% exhibited cranial nerve palsy³⁶.

In this study 59.1% were hypertensive, 47.73% were smoker, 15.9% were alcoholic and were light drinker, 6.8% were substances abuser and 11.4% had positive family history of SAH. In Bangladesh a study of thirty SAH population revealed 44% of the patients had smoking habit and nearly half (46.7%) had hypertension³⁷. Another study was

conducted at Dhaka medical college and Hospital showed hypertension, smoking, diabetes mellitus and family history of SAH were found in 46.6%, 43.3%, 10.0% and 6.7% respectively⁴². Presence of risk factors in study population were more or less same with Bangladeshi research. An international study showed hypertension was identified in 52%²⁴.

In this study, mean size of ruptured aneurysms was 5.72 ± 4.010 mm. According to International Study on Un-ruptured Intracranial Aneurysms (ISUIA) classification, 65.9% aneurysm size were 3-7mm, 20.5% were 8-12 mm, 9.1% were below 3 mm. Many studies showed the mean size of aneurysms were 5.59 ± 29 mm²⁷, 6.6 ± 2.7 mm³⁵, 5.8 mm⁴³, 5 ± 1.9 mm⁴⁴ and 5.0 mm⁴⁵. A total of 64 studies with 10873 intracranial aneurysms mean ruptured intracranial aneurysm size was 6.99 ± 4.14 mm⁴⁶. The mean aneurysm size of this study is similar to findings in the national and international literature.

In this study shows 93.2% of aneurysms were below 10 mm, 75.0% were below 7 mm and 50.0% below 5 mm. About 91%²¹, 80%³⁶, 85.6%⁴⁷ and 93.2%⁴⁸ were <10 mm in size. A study showed 75% of ruptured aneurysms <7 mm⁴⁸. A study found 13% of the ruptured aneurysms they studied were less than 5 mm in diameter and 57% were between 5 and 10 mm in diameter⁴⁰. More than half of the ruptured aneurysms measured less than 7 mm⁴⁸. In this study most of the aneurysms size were below 10 mm diameter which is similar to that of many literatures.

A study believes aneurysms shrink after rupture, so the calculated size of ruptured aneurysm does not reflect their size before rupture¹⁷. But there are lots of studies that established size of ruptured aneurysms do not change rather size increase^{29, 49- 51}.

In this study, 35.4% were ACom aneurysms, 29.2% were PCom aneurysms, 16.7% were MCA bifurcation. 87.5% aneurysms were in anterior circulation and 12.5% were in posterior circulation which is consistent with findings of both national and international publications^{42, 52}.

In this study aneurysms size was smaller in older female patient which is consistent with Young-

GyunJeong et al¹⁸. It is due to effect of estrogen hormone.

In this study mean aneurysm size in male was 5.67 ± 3.09 mm and in female was 5.77 ± 4.71 mm. Aneurysms size was 6.17 mm for males, and 5.91 mm for females⁵³. A study showed gender-specific risk factor distribution did not differ significantly among males and females²².

In this study mean aneurysm size were more in case of positive family history population. It is different from other literatures¹⁸. This difference may be due to poor number of positive family history population in this study.

In this study mean aneurysm size was 4.68 ± 2.69 mm in hypertensive patients and in normotensive population it was 7.23 ± 5.10 mm. Size of ruptured aneurysm is small in hypertensive population and is significant (p-value 0.037). There was a significant correlation between hypertension and the rupture of aneurysms smaller than 5 mm⁵⁴. Hypertensive patients (6.27 ± 3.28 mm) had significantly smaller ruptured intracranial aneurysms than normotensive (8.08 ± 4.73 mm)²².

In this study aneurysms mean size was 4.18 ± 1.74 mm in case of smoker and 7.13 ± 4.93 mm in never smoker. Aneurysm size was significantly (p-value 0.013) smaller in case of smoker. A study showed, patients with a history of cigarette smoking had only slightly smaller ruptured aneurysms (7.61 ± 4.29 mm) compared to patients with no risk factors (8.08 ± 4.73 mm)²².

In this study mean size of aneurysm in male hypertensive population 5.04 ± 3.57 mm which is smaller than male normotensive patient. In case of female hypertensive population mean size is 4.41 ± 1.90 mm which is smaller than female normotensive patient and also from male hypertensive patient. In this study, male smoker had mean aneurysm size 4.65 ± 1.79 mm which was significantly smaller than male never smoker (p-value 0.040) and in female smoker mean aneurysm size was 3.42 ± 1.44 mm which was also smaller than female non-smoker and male smoker.

In this study mean aneurysm size in hypertensive smoker population was significantly (p-value-0.004)

smaller than hypertensive non-smoker. A study of 373 ruptured intracranial aneurysms and showed that the sizes of the ruptured IAs were significantly smaller in patients with a combined history of hypertension and cigarette smoking than those with hypertension alone, smoking alone or non-hypertension and non-smoking²².

In this study population with one risk factor had mean aneurysm size of 8.32±6.84 mm, two risk factors had 5.26±1.86mm, three risk factors had 4.79±2.05 mm and more than three risk factors had 2.85±1.43. So, aneurysm size was dependent to presence of number of risk factors. More risk factors had smaller aneurysm which is consistent with Nima Etminan et al in which presence of one risk factor had smaller size than no risk factors and two risk factors had smaller size than one risk factor²².

Conclusion:

The present analysis demonstrates that hypertension, smoking have a significant influence on the size of ruptured aneurysms in patients suffering from SAH. Other risk factors female sex, age, positive family history have also impact on aneurysm size but lesser extent. But when one risk factor is associated with other factors it decreases the size of ruptured aneurysm. In case of more the risk factors, the size become smaller. As a consequence, data strongly suggest that patients with these risk factors have a lower threshold of aneurysm rupture than patients without risk factors. Therefore, Size cannot be considered the only factor to determine treatment recommendations rather the history of hypertension, cigarette smoking, female sex, age and positive family history should be considered in the assessment of treatment of un-ruptured intracranial aneurysms.

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