

## Review Article

# Morphological Differences between Single and Multiple Unruptured Aneurysms

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The natural history and risk of rupture in multiple unruptured aneurysms is not clearly known. Various Morphometric indices have been proposed to correlate with risk of rupture of intracranial aneurysms. The present study aims to characterize and compare the morphology of patients with unruptured single and multiple aneurysms and correlate the results with rupture risk reported in previous studies. All patients with unruptured single and multiple aneurysms who presented to the hospital from 2009 to 2012 and who had complete 3D digital subtraction angiographic studies were included in the study. Their angiograms were analyzed for aneurysm height, width, and neck width and parent artery diameter. Aspect ratio, bottleneck ratio, height to width ratio and size ratio (SR) of single and multiple aneurysms were compared. 30 patients with single aneurysms and 18 patients with multiple (38) aneurysms were included in the study. Multiple aneurysms had a significantly smaller height and size ratios when compared to single aneurysms. There was no difference in age, gender, history of smoking and hypertension, aneurysm width, neck width, parent artery diameter, aspect ratio, bottle neck ratio and height to width ratio in both the groups. Multiple aneurysms have a lower size ratio than single aneurysms which may translate to a lower rupture risk per aneurysm. However, when patients with multiple aneurysms are considered, the cumulative risk of rupture should be taken into consideration.

**Keywords:** Unruptured aneurysm; Size ratio; Aspect ratio; Bottleneck ratio**Introduction**

Intracranial aneurysms are reported in 0.2 to 9.9 percent of autopsy studies in general population [1,2]. Patients with unruptured intracranial aneurysms (UIA) constitute a unique cohort when compared to those with previous aneurysmal subarachnoid hemorrhage (SAH). The prevalence of unruptured aneurysms in general population varies with studies reporting a prevalence of up to 6.5% [3]. The decision whether to actively treat unruptured aneurysms remains a matter of debate due to the small risk of rupture in these aneurysms and the risk of morbidity and mortality due to treatment. On the other hand, treatment of UIAs with high risk of rupture can potentially reduce the morbidity and mortality associated with aneurysmal SAH. With rapid advances in intracranial imaging and greater availability of advanced imaging modalities, more and more patients are being diagnosed with UIAs. Multiple intracranial aneurysms are reported in 15-33.5% of patients with intracranial aneurysms [4]. The risk of SAH in patients with multiple intracranial aneurysms remains a matter of debate with some studies reporting an increased risk whereas others reporting similar risk of rupture as in single aneurysms [5,6]. Hence, it is unclear whether multiple unruptured aneurysms behave differently than single unruptured aneurysms.

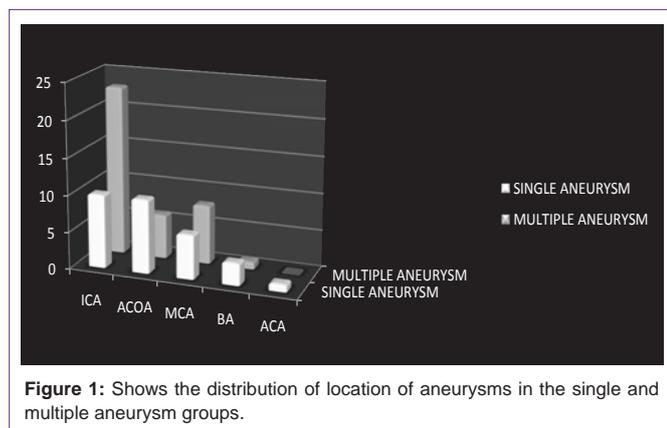
The major ethical issue in evaluating the natural history of unruptured aneurysms is that, patients with high risk aneurysms cannot be left untreated. Recently, literature has focused on anatomical and morphological characteristics of these lesions with an

aim of identifying characteristics associated with high risk of rupture [7-9]. Apart from aneurysm location and size, various parameters have been proposed to identify risk of rupture. Of these, aspect ratio, bottleneck factor and size ratio have been widely studied between ruptured and unruptured aneurysms. However, to date, no study has evaluated the difference in aneurysm morphology between single and multiple unruptured aneurysms. The present study is an attempt to fulfill this lacuna.

**Patients and Methods**

This is a retrospective study conducted at our institution. Patients who presented to the hospital between 2009 and 2012 were included in the study. Fifty-six patients with unruptured aneurysms presented to the hospital during the study period. Of these, thirty five patients had single unruptured aneurysm and twenty one patients had multiple unruptured aneurysms. Due to incomplete 3D study or unavailable images, eight patients were excluded from the study, leaving thirty patients with single unruptured aneurysms and eighteen patients with multiple unruptured aneurysms. Patients with multiple aneurysms with a history of SAH were excluded from the study. Demographic details, smoking and hypertension were recorded from the case records and aneurysm characteristics recorded from the 3D angiograms of these patients. Aneurysm height, maximum width, neck width and parent artery diameter at the site of aneurysm were measured. In cases where the aneurysm originated at branching point, the mean of all the vessels in relation to the aneurysm was calculated.

Aspect ratio was calculated by dividing height by neck width,



**Figure 1:** Shows the distribution of location of aneurysms in the single and multiple aneurysm groups.

bottleneck factor was calculated by dividing maximum width by neck width, height-width ratio was calculated by dividing maximum height by width and size ratio was calculated by dividing maximum height by parent artery diameter.

### Statistical Analysis

Age, gender, smoking and hypertension were compared between the two groups using Fisher’s extract test and Chi square test. Aspect ratio, bottleneck ratio, height-width ratio and size ratio were compared between the two groups using Mann-Whitney U test. Statistical analysis was performed using SPSS 20 (SPSS Inc.). A statistical difference of  $P < 0.05$  was considered significant.

### Results

Forty eight patients were included in the study. Thirty patients had single unruptured aneurysms and eighteen patients had thirty-eight unruptured aneurysms. Two patients had three unruptured aneurysms and the rest had two unruptured aneurysms. Majority of the aneurysms in both the groups were located on the internal carotid artery followed by anterior communicating artery, middle cerebral artery and basilar artery in that order. There was one aneurysm on the anterior cerebral artery in the single aneurysm group. Figure 1 depicts the distribution of aneurysms on arteries in both the groups. There were 23 (61%) aneurysms on ICA in the multiple aneurysms group as against 10 (33.3%) in the single aneurysm group.

The mean age of patients with single and multiple aneurysms was 59.3 years and 56.7 years. There were 21 (70%) females with single aneurysms and 16 (89%) with multiple aneurysms. There was no significant difference between age and gender between the two groups ( $P = 0.37$  and  $P = 0.17$  respectively).

There was no significant difference in prevalence of smoking and hypertension between both the groups ( $P = 0.76$  and  $P = 0.70$  respectively). Table 1 lists the age and gender distribution and prevalence of patients along with prevalence of smoking and hypertension in both the groups.

Table 2 lists the maximum height, width, and neck width and parent artery diameter of patients in both the groups. It was noted that patients with multiple unruptured aneurysms had smaller height, width and neck width whereas the parent artery diameter was almost similar. On performing Mann Whitney U test, only the maximum height of the aneurysm was significantly smaller in the

multiple aneurysms group ( $P = 0.010$ ). The mean height of patients with single aneurysms was  $6.38 \pm 3.6$  mm 2SD and that of patients with multiple aneurysms was  $4.22 \pm 2.9$  mm 2SD. There was no significant difference in maximum width and neck width between the two groups.

Table 3 lists the aspect ratio, bottleneck ratio, height to width ratio and size ratio of aneurysms in both the groups. Mann Whitney U test shows no significant difference in the aspect ratio, bottleneck ratio and height-width ratio between the two groups. However, the size ratio of patients with multiple aneurysms was significantly smaller ( $1.84 \pm 1.3$  2SD) when compared to the size ratio of single aneurysms ( $2.43 \pm 1.5$  2SD).

### Discussion

It is a very well known fact that the patients with a history of SAH are at a higher risk of another SAH than those without. Patients with multiple unruptured aneurysms form a subset of the all the patients with unruptured aneurysms. The natural history and rupture rate in patients harboring multiple unruptured intracranial aneurysms remains to be elucidated.

Juvela et al. [10] reported a follow-up study of 142 patients with unruptured aneurysms. During the follow-up period, rupture occurred in 24% of patients with single unruptured aneurysm and 21% of patients with multiple unruptured aneurysms. The difference was not significant. The authors concluded that unruptured aneurysms should be treated irrespective of their size. In the SUAV e study, Sonobe et al. [6] reported a cumulative rupture rate of 3.14% and 3.44% for single and multiple unruptured aneurysms. The annual risk of rupture of single unruptured aneurysms  $< 5$  mm was 0.34% and 0.95% respectively. The difference in rupture rate in both the groups was significant. It is very important to recognize patients with

**Table 1:** Age and gender distribution of patients with unruptured aneurysms.

	Single aneurysm n=30	Multiple aneurysms n=18	P
Age in years (Mean)	59.53	56.67	0.34
Male n (%)	09 (30)	02 (11.1)	0.12
Female n (%)	21 (70)	16 (88.9)	
Smoking n (%)	19 (63.3)	12 (66.6)	0.41
Hypertension n (%)	20 (66.7)	11 (61.1)	0.46

**Table 2:** Morphological characteristics of aneurysms.

	Single aneurysm (n=30) Mean $\pm$ 2SD	Multiple aneurysms (n=38) Mean $\pm$ 2SD	P
Maximum height (mm)	6.38 $\pm$ 3.6	4.22 $\pm$ 2.9	0.01
Maximum width (mm)	5.06 $\pm$ 2.6	3.6 $\pm$ 2.7	0.6
Neck width (mm)	2.9 $\pm$ 0.4	2.4 $\pm$ 0.6	0.1
Parent artery diameter (mm)	2.3 $\pm$ 0.4	2.4 $\pm$ 0.4	0.68

**Table 3:** Morphometric characteristics of aneurysms.

	Single aneurysm n=30 mean $\pm$ 2SD	Multiple aneurysms n=38 mean $\pm$ 2SD	P
Aspect ratio	1.76 $\pm$ 0.6	1.8 $\pm$ 1.0	0.52
Bottleneck ratio	1.3 $\pm$ 0.4	1.6 $\pm$ 1.2	0.75
Height/width ratio	1.2 $\pm$ 0.3	1.2 $\pm$ 0.5	0.48
Size ratio	2.43 $\pm$ 1.5	1.84 $\pm$ 1.2	0.01

multiple aneurysms as a separate group because the rupture risk is greater than in patients with single unruptured aneurysm. Whether the morphology of aneurysm differs between both the groups remains unknown.

A number of morphometric indices have been studied in ruptured and unruptured aneurysms to predict the risk of rupture in unruptured aneurysms [7-9]. Two of the most basic factors are aneurysm size and location. In the ISUIA study [11], the risk of rupture of aneurysms <10mm was 0.05% per year for patients without a history of SAH when compared to 0.5% for those with a history of SAH. When aneurysms >10mm were considered, the annual risk of rupture was 1% in both the groups. In a follow-up paper [12], the 5-year cumulative rupture rates for patients without prior SAH, with anterior circulation aneurysms excluding cavernous carotid or posterior communicating artery aneurysms were 0, 2.6, and 14.5% for aneurysms < 7, 7-12, and 13-24 mm, respectively, compared with rates of 2.5, 14.5, and 18.4%, respectively, for the same size aneurysm in the posterior circulation excluding posterior communicating artery aneurysms. Patients with a history of previous SAH with aneurysms < 7 mm in size had a 0.1% yearly rupture rate. In contrast, Juvela et al. [5] reported a rupture rate of 1.3% per year with majority of aneurysms being less than 7mm in size. In a study of 30 patients with multiple aneurysms, Hoh et al [7] reported significant difference in aneurysm height, diameter, aspect ratio, and bottle neck factor and aneurysm/parent artery ratio between ruptured and unruptured aneurysms. Studies have reported aspect ratios varying from 1.6 to 3.47 to be associated with ruptured aneurysms [9,13,14]. It has been proposed that aspect ratios greater than 3 are associated with very high risk of rupture whereas ratios less than 1.4 are associated with a lower risk. Ryu et al. [15] analyzed the height-width ratio, aspect ratio, bottleneck factor, volume and volume-neck ratio in 195 patients with 214 aneurysms. They observed significantly higher values in all the indices except the volume. They concluded that aspect ratio is a good indicator of rupture risk of an aneurysm.

In our study, although the height, width and neck width of aneurysms is smaller in multiple aneurysms than in single aneurysms, only the difference in height was significant. The mean aspect ratios for single and multiple unruptured aneurysms were 1.76+/-0.6 2SD and 1.8+/-1.0 2SD and there was no significant difference between them. We did not observe any significant difference in bottleneck ratio and height-width ratio between both the groups. This indicates that the morphological characteristics of unruptured multiple aneurysms are the same as that in single aneurysms and hence, the rupture rates would be expected to be similar.

Dhar et al. [16], in a study of 45 patients, analyzed various parameters between ruptured and unruptured aneurysms. They observed that size ratio and aneurysm angle with respect to parent artery had the strongest correlation to rupture potential, although significant differences were found in aspect ratio, undulation, non sphericity and ellipticity index. In another study, Tremmel et al. [17] reported that a higher size ratio, irrespective of aneurysm type and absolute aneurysm or vessel size gives rise to flow patterns consistent with those in ruptured aneurysms. Rahman et al. [8], in a prospective study, reported that a size ratio of >3 was significantly associated with ruptured aneurysms. In our study, the size ratio of patients with single aneurysms was significantly greater than the size ratio of

multiple aneurysms. This indicates that the rupture risk of individual aneurysm in patients with multiple aneurysms is smaller than that in patients with multiple aneurysms. One possible explanation for the observed similar or higher rupture risk in multiple aneurysms despite having smaller size ratios is that the cumulative risk of rupture of all the aneurysms in a patient when taken together may be higher than the cumulative rupture risk in patients with single aneurysm.

This study has certain limitations because it is a retrospective analysis with a small sample. Patients with multiple aneurysms may more often present with SAH than patients with single aneurysms due to the cumulative risk of each aneurysm. Nevertheless, this study provides an insight into the morphological characteristics of unruptured aneurysms. Further studies with larger sample size could help understand the relative risk of rupture in patients with single and multiple aneurysms.

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