Bifurcation Location and Growth of Aneurysm Size Are Significantly Associated with an Irregular Shape of Unruptured Intracranial Aneurysms

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■ BACKGROUND AND OBJECTIVE: **Previous studies firmly proved that an irregular aneurysmal shape was associated strongly with intracranial aneurysm (IA) rupture, but it is unclear how irregularly shaped IAs form. We aimed to identify the factors related to irregular shape of IAs.**

■ METHODS: **We retrospectively analyzed of consecutive patients evaluated or treated for IA at our institution from June 2015 to July 2016. According to the imaging morphology of aneurysm, the enrolled patients were divided into irregular and regular group. Demographic data and imaging data of the 2 groups were compared to identify the factors related to aneurismal irregular shape.**

■ RESULTS: **There were 429 aneurysms (180 irregular and 249 regular aneurysms), including 315 unruptured aneurysms and 114 ruptured aneurysms. Most unruptured aneurysms occurred in the internal carotid arteries (53.3%), anterior communicating artery (10.8%), and posterior communicating artery (10.8%), anterior cerebral artery (5.4%), middle cerebral artery (9.8%), and posterior circulation (9.8%). In univariate analysis, for unruptured aneurysm, irregular aneurysmal shape was significantly related to aneurysm size ($P = 0.009$), aspect ratio ($P = 0.003$), size ratio ($P = 0.002$), and location at the bifurcation ($P = 0.009$) but not with smoking status, hypertension, hyperlipidemia, or diabetes mellitus. In multivariate logistic analysis, irregular aneurysms occurred mainly in unruptured aneurysms with a larger size (diameter ≥5 mm; odds ratio [OR] 2.106; 95% confidence interval [CI] 1.183–3.749; $P = 0.011$); location at a bifurcation (OR 2.017; 95% CI 1.191–3.413; $P = 0.006$), and aspect ratio (≥0.8; OR 4.992; 95% CI 1.318–18.915; $P = 0.018$).**

■ CONCLUSIONS: **Location at a bifurcation, an increased aneurysm size, and greater aspect ratio are significant independent factors associated with an irregular shape in unruptured IAs but not with smoking status, hypertension, hyperlipidemia, or diabetes mellitus.**

INTRODUCTION

Intracranial aneurysm (IA) is a common cerebrovascular disease with a prevalence of approximately 5%,[1] is the most common cause of subarachnoid hemorrhage (SAH),[2] and is associated with high mortality and morbidity rates.[3] Recent studies have indicated that 17%–76% of IAs are irregularly shaped aneurysms.[4,5]

Furthermore, an irregular aneurysmal shape was associated strongly with IA rupture in large observational series and also was an independent predictor of rupture risk in a Japanese natural history study.[6] Abboud et al.[5] reported that the rate of aneurysm rupture is increased for irregular aneurysms and an irregular shape accounts for 76%in all IAs.

Key words
- Irregular shape
- Related factors
- Unruptured intracranial aneurysms

Abbreviations and Acronyms
AR: Aspect ratio
BMI: Body mass index
CI: Confidence interval
DM: Diabetes mellitus
IA: Intracranial aneurysm
OR: Odds ratio
SAH: Subarachnoid hemorrhage
SR: Size ratio
WSS: Wall shear stress

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Citation: World Neurosurg. (2017) 107:255-262.
http://dx.doi.org/10.1016/j.wneu.2017.07.063

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

Many reports have hypothesized that an irregular aneurysmal shape may be related to degeneration and weakness of the lesion wall.[7] Moreover, Cebral et al.[8] have reported that irregular aneurysms with blebs form at or adjacent to regions with high wall shear stress (WSS) and are aligned to major intra-aneurysmal flow structures. However, few studies have investigated the factors related to irregular shape in IAs. Here, we performed a retrospective review of patients with IAs to identify the factors related to irregular shape in IAs.

METHODS

Patient Population and Exclusion Criteria

Our study was approved by the review committee of Beijing Tiantan Hospital and conformed to the tenets of the Declaration of Helsinki, and informed consent was obtained from all participants when they were enrolled. We performed a single-center study of patients evaluated or treated for IAs at our institution, from June 2015 to July 2016. All patients received conventional digital subtraction angiography of the internal and external carotid artery and vertebral artery. Thereafter, 3-dimensional rotational angiography was performed to identify aneurysmal morphologic features. Patients were divided into a regular group and an irregular group according the shape of their aneurysm on 3-dimensional rotational angiography. The regular group was defined as patients with IAs that appeared smooth and regular on 3-dimensional rotational angiography, whereas the irregular group was defined patients with IAs with small blebs or secondary aneurysms protruding from the IA fundus on 3-dimensional rotational angiography, or where the aneurysm fundus was clearly bi- or multilobular.[4,9-11]

Our exclusion criteria were the following: (1) multiple aneurysms; (2) dissecting, fusiform, traumatic, or mycotic aneurysms; (3) aneurysms without 3-dimensional rotational angiography that was sufficiently clear and readable to allow evaluation of lesion geometry and morphology; (4) aneurysms associated with Moyamoya disease, arteriovenous malformation, or arteriovenous fistula; (5) aneurysms with a maximum diameter <2 mm, which was too small to allow accurate measurements; (6) aneurysms with a maximum diameter ≥25 mm; and (7) aneurysms with a thrombus present in the lumen.

Data Collection and Definitions

Information on smoking was obtained from the medical history recorded by the treating physicians during interviews of patients or family members, and for some information we couldn't collect in the medical record system, we obtained information using a telephone survey. These data included sex, age, hypertension (yes/no), hyperlipidemia (yes/no), diabetes mellitus (DM; yes/no), history of stroke (yes/no), previous SAH (yes/no), smoking status (nonsmoker/current smoker/former smoker), alcohol use (yes/no), and body mass index (BMI). Nonsmokers affirmed they had never smoked or smoked <100 cigarettes (lifetime). Patients who smoked at the time of treatment or smoked ≥100 cigarettes during the past year were considered current smokers. Patients who had smoked ≥100 cigarettes but had not smoked during the past year were considered former smokers.[12] Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, and/or self-reported treatment of hypertension (medical records checked) with antihypertensive medication within 2 weeks before the interview.[13] DM was defined as random blood glucose ≥11.1 mmol/L, fasting plasma glucose ≥7.0 mmol/L, or 2-hour value of 75-g oral glucose tolerance test ≥11.1 mmol/L and/or self-reported treatment of DM (medical records checked).[14] Hyperlipidemia was defined as dyslipidemia in the plasma, Diagnostic criteria included total cholesterol ≥6.22 mmol/L, triglycerides ≥2.26 mmol/L, low-density lipoprotein cholesterol ≥4.14 mmol/L; one of the aforementioned conditions mentioned can be used to diagnose hyperlipidemia.[15] History of stroke mainly meant patients with history of cerebral infarction or hemorrhages, which were diagnosed by the clinical symptoms, signs, and brain imaging data, etc.[16] Previous SAH was defined as the patient suddenly found persistent severe headache, vomiting, the meningeal stimulation were positive, some patients with disturbance of consciousness, and computed tomography found a high-density sign in the cisterna or subarachnoid space in the past.[17]

Definition of Imaging Variables

Aneurysmal neck width was defined as a virtual line separating the aneurysm from the parental artery.[18] Maximum height was defined as the largest length from the neck to the tip of the aneurysmal dome tip.[19] Maximum width was defined as the largest length of the dome perpendicular to its height.[20] Aneurysm size was defined as the largest of these measurements.[21] The aspect ratio (AR) was the ratio of the maximal perpendicular height of the aneurysm to the average neck diameter of the aneurysm.[22] The size ratio (SR) was the ratio between the maximal aneurysm height and the mean artery diameter.[23] The mean artery diameter was determined by averaging the diameter of the cross-section of the vessel at the neck of the aneurysm (D1) with the diameter of the cross section at a distance of $1.5 \times D1$ from the neck of the aneurysm. This mean vessel diameter was calculated for all vessels involved with the aneurysm and was then averaged to generate the composite mean artery diameter used to calculate the SR.[20] Bifurcation aneurysms were defined as aneurysms located at the parent artery bifurcations, including the internal carotid artery, anterior cerebral artery, middle cerebral artery, anterior communicating artery, posterior communicating artery, and apex of the basilar artery.[20,24] All morphologic parameters were based on 3-dimensional rotational angiography and were evaluated by 2 experienced neurosurgeons.

Statistical Analysis

Demographic and clinical characteristics were analyzed for differences according to the shape of the aneurysm. Data relating to categorical variables were analyzed by the Fisher exact test or Pearson χ^2 test. Data relating to continuous variables were analyzed by 2-tailed t-tests or the Kruskal—Wallis H test. Univariate analysis was performed to compare the value of each index between the regular and irregular groups. Variables with a $P < 0.20$ between each pair of groups were entered into the multivariate analysis. Multivariate logistic regression also was used to calculate the odds ratios (ORs) and 95% confidence intervals (CIs). A P value less than 0.05 (2-sided) was considered statistically significant. SPSS (version 23.0; IBM Corp., Armonk, New York, USA) was used to perform the statistical analyses.