Bifurcation Location Is Significantly Associated with Rupture of Small Intracranial Aneurysms (<5 mm)

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■ BACKGROUND AND OBJECTIVE: **Patients with small (<5 mm) unruptured intracranial aneurysms (UIAs) are at risk of subarachnoid hemorrhage, but risk assessment of these patients remains controversial in daily clinical practice. We aimed to identify the risk factors of aneurysmal rupture in these patients.**

■ METHODS: **We retrospectively analyzed consecutive patients with small UIAs who were admitted to our center between February 2009 and December 2014. The enrolled patients were divided into ruptured and unruptured groups. The risk factors for aneurysmal rupture were determined using multivariate logistic regression analysis.**

■ RESULTS: **A total of 548 patients with 618 small intracranial aneurysms (267 ruptured and 351 unruptured) were included. Univariate analysis showed that rupture of small aneurysms was related to sex, age, smoking, hypertension, aspect ratio, size ratio, irregular shape, aneurysm width, height, and neck diameter, and location at bifurcation or posterior circulation. Multivariate logistic regression showed that rupture was associated with bifurcation location (odds ratio [OR], 5.409; 95% confidence interval [CI], 3.656–8.001; *P* < 0.001), size ratio (OR, 3.092; 95% CI, 2.002–4.774; *P* < 0.001), location (OR, 2.624; 95% CI, 1.428–4.824; *P* = 0.002), hypertension (OR, 1.698; 95% CI, 1.1140–2.527; *P* = 0.009), and age at diagnosis of UIA (OR, 1.826; 95% CI, 1.225–2.723; *P* = 0.003).**

■ CONCLUSIONS: **This study showed that 70.4% of small ruptured intracranial aneurysms (<5 mm) were located at parent artery bifurcations and that bifurcation location was a significant independent factor for the risk of rupture of small UIAs (<5 mm). Prophylactic treatment should be recommended for small UIAs in this location.**

INTRODUCTION

The prevalence of unruptured intracranial aneurysms (UIAs) is 1%–7%.[1] The most serious damage caused by UIAs is a result of subarachnoid hemorrhage (SAH), which has a 30-day mortality of 40%.[2] The rupture risk is known to increase with increasing aneurysm size.[1,3,4] Thus, most small UIAs (<5 mm) are believed to be associated with a low risk of rupture. However, several studies[5,6] have reported the rupture of small aneurysms. Kassell et al.[7] assessed 1092 cases to analyze the size distribution of ruptured aneurysms and found that 13% of ruptured aneurysms were <5 mm in diameter. A study by Kashiwazaki et al.[8] clearly showed that approximately 30% of ruptured intracranial aneurysms (RIAs) were small (<5 mm) and that some small UIAs also had a risk of rupture.[9-12]

Several previous studies have investigated the risk factors of rupture in patients with small UIAs. In the Japanese Small Unruptured Intracranial Aneurysm Verification study,[9] the rupture of small UIAs was found to be related to age, hypertension, and the presence of multiple aneurysms. However, those prospectively studied groups did not include small aneurysms that had been previously treated, and many patients with small UIAs that may have been at high risk of rupture were treated and were not enrolled into the studies. Kashiwazaki et al.[8]

Key words
- Risk factors
- Small
- Unruptured intracranial aneurysms

Abbreviations and Acronyms
AR: Aspect ratio
CI: Confidence interval
IA: Intracranial aneurysm
OR: Odds ratio
RIA: Ruptured intracranial aneurysm
SAH: Subarachnoid hemorrhage
SR: Size ratio
UIA: Unruptured intracranial aneurysm

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found that size ratio (SR) might predict the risk of rupture in small UIAs, but the potential risk factors of rupture included in that multivariate analysis may be insufficient, and no systematic analyses of the risk factors for rupture of small UIAs are available.

We tried to analyze as many factors associated with the rupture of small IAs as possible to investigate the predictors of rupture in a large cohort of patients with small UIAs and RIAs.

METHODS

Study Design and Ethics

This was a retrospective study. The design was approved by the review committee of Beijing Tiantan Hospital, and informed consent was obtained from all participants.

Patient Selection

We retrospectively reviewed consecutive patients who attended our institution with small intracranial aneurysms (IAs) (<5 mm) from February 2009 to December 2014. All patients in this study were examined using three-dimensional rotational angiography. All patients with SAH were examined using computed tomography. All patients presented with SAH caused by a ruptured aneurysm. The exclusion criteria were as follows: 1) fusiform, traumatic, mycotic, or partially thrombosed aneurysms; 2) aneurysm diameter ≥5 mm; 3) intracranial hemorrhage for unknown reasons, or inability to identify the location of the ruptured aneurysm by computed tomography or neurosurgical findings; 4) inability to evaluate aneurysm geometry and morphology based on three-dimensional rotational angiography; and 5) aneurysms that were related to cerebral arteriovenous malformation, arteriovenous fistula, or moyamoya disease.

Definition of Variables and Data Collection

Bifurcation aneurysms were defined as aneurysms located at parent artery bifurcations in the circle of Willis and therefore originating from more than 1 parent vessel (internal carotid artery terminus, middle cerebral artery bifurcation, anterior communicating artery, and apex of the basilar artery).[13] The maximum aneurysm height was the maximum perpendicular distance between the neck and any point on the dome of the aneurysm. The maximum aneurysm width was the maximum horizontal length of the aneurysm. In terminal aneurysms, the average diameter of the parent artery and the other branching vessels was used to determine the average vessel diameter.[8,14] All morphologic parameters were based on three-dimensional rotational angiography and evaluated by 2 experienced neurosurgeons.

SR was defined as the maximum aneurysm height/average of the parent diameter.

The aspect ratio (AR) was defined as the ratio of the maximum perpendicular height to the average neck diameter.[15]

The following variables were potential risk factors for aneurysmal rupture in patients with small IAs (all data were collected prospectively). Patient-specific characteristics included age (year), sex (female/male), hypertension (yes/no), heart comorbidities (coronary heart disease, heart valve disease, arrhythmias, and heart dysfunction; yes/no), hypercholesterolemia (yes/no), diabetes mellitus (yes/no), cerebral ischemic comorbidities (cerebral infarction, transient ischemic attack, and cerebral vascular stenosis, coronary artery bypass grafting, and percutaneous transluminal coronary arterioplasty; yes/no), previous SAH (yes/no), family history of SAH (yes/no), smoking (current or previous smoking; yes/no), and alcohol use (current or previous intake >5 drinks per day; yes/no).[16] Aneurysm-specific characteristics included multiple IAs (yes/no), irregular shape (yes/no), location (internal carotid artery rather than the posterior communicating artery/posterior communicating artery/anterior communicating artery/middle cerebral artery/posterior circulation), bifurcation aneurysm (yes/no), aneurysm neck diameter (mm), parent artery diameter (mm), maximum aneurysm width (mm), AR, and SR.

Statistical Analysis

The data used in this study were analyzed using SPSS software (version 19.0 [IBM Corp., Armonk, New York, USA]). Data were described using frequencies (percentages) for categorical variables and means ± standard deviation or medians (interquartile ranges) for continuous variables. Data relating to categorical variables were analyzed by Fisher exact test or the Pearson χ^2 test. Data relating to continuous variables were analyzed using the Mann-Whitney U test or Student t test. Unconditional logistic regression analysis was used to calculate univariate and multivariate odds ratios (ORs) with 95% confidence intervals (CIs). A P value <0.05 was regarded as statistically significant.

RESULTS

Study Population

A total of 548 consecutive patients with 618 small aneurysms, including 267 RIAs and 351 UIAs, were included in this study. Seventy-six patients were excluded for the following reasons: the location of the ruptured aneurysm could not be identified ($n = 20$); inability to find the digital subtraction angiography image ($n = 12$); fusiform, traumatic, or dissecting aneurysm ($n = 16$); or aneurysms that were related to cerebral arteriovenous malformation, arteriovenous fistula, or moyamoya disease ($n = 18$). The patient inclusion flowchart is shown in Figure 1.

Baseline Characteristics

The IAs were divided into the ruptured group and the unruptured group based on computed tomography findings. The baseline demographic data of the patients included in this study are shown in Table 1. The basic characteristics of UIAs and RIAs are shown in Table 2.

Univariate Analyses

In univariate analysis, factors that were significantly associated with the incidence of aneurysm rupture in small IAs were sex (OR, 1.816; 95% CI, 1.299–2.539; $P < 0.001$), age (OR, 1.529; 95% CI, 1.100–2.126; $P = 0.011$), smoking (OR, 1.568; 95% CI, 1.079–2.279; $P = 0.018$), hypertension (OR, 1.396; 95% CI, 1.014–1.922; $P = 0.041$), AR (OR, 2.138; 95% CI, 1.528–2.991; $P < 0.001$), higher SR (OR, 4.492; 95% CI, 3.042–6.633; $P < 0.001$), irregular shape (OR, 1.628; 95% CI, 1.086–2.439; $P = 0.018$), maximum aneurysm width (OR, 1.422; 95% CI, 1.028–1.968; $P = 0.033$), location at the bifurcation of the circle of Willis (OR, 5.427; 95% CI, 3.834–7.681; $P < 0.001$), and location in the posterior circulation (OR, 1.561; 95% CI, 0.929–2.624; $P = 0.093$) (Table 3).