Risk Factors Associated With the Presence of Unruptured Intracranial Aneurysms

Hyun Goo Kang, MD*; Bum Joon Kim, MD*; Jisung Lee, PhD; Mi-Jung Kim, MD; Dong-Wha Kang, MD; Jong S. Kim, MD, PhD; Sun U. Kwon, MD, PhD

Background and Purpose—With the increased investigation of cerebral arteries using magnetic resonance angiography in the general population, the detection of unruptured intracranial aneurysms (UIAs) has increased. Understanding the distribution and factors associated with UIAs might be helpful for understanding the pathomechanism.

Methods—Subjects who underwent magnetic resonance angiography with a health examination at the Health Screening and Promotion Center were enrolled. The incidence and risk factors of UIAs (age, sex, hypertension, diabetes mellitus, smoking, alcohol, and coronary artery disease) were investigated by comparing patients with and without UIAs. These risk factors were also investigated by the UIA location, distal internal carotid artery, anterior cerebral artery and middle cerebral artery (MCA), MCA bifurcation, anterior and posterior communicating artery, and posterior circulation.

Results—Among 187,166 subjects who received health examination, 18,954 underwent magnetic resonance angiography. Of them, 367 (1.93%) had UIAs. Age (odds ratio [OR], 1.02; \( P = 0.003 \)) women (OR, 2.00; \( P < 0.001 \)), hypertension (OR, 2.21; \( P < 0.001 \)), smoking (OR, 1.66; \( P = 0.001 \)), and coronary artery disease (OR, 0.23; \( P < 0.001 \)) were independently associated with the presence of UIAs. Hypertension was associated with most UIAs, except for those located at sidewalls (anterior cerebral artery and MCA). MCA aneurysms were associated with old age and smoking. Distal internal carotid artery, posterior communicating artery, and MCA-bifurcation aneurysms were associated with female sex. Anterior communicating artery aneurysms were associated with smoking and alcohol. Posterior circulation UIAs were only associated with hypertension. Coronary artery disease was negatively associated with anterior circulation aneurysms.

Conclusions—The risk factors for UIAs differ by their location, compared with the control. Interestingly, the presence of coronary artery disease was protective against the presence of UIAs. (Stroke. 2015;46:3093-3098. DOI: 10.1161/STROKEAHA.115.011351.)

Key Words: circle of Willis ■ coronary artery disease ■ intracranial aneurysm ■ middle cerebral artery ■ risk factors

An intracranial aneurysm is a vascular disorder that occurs in the weak point of an intracranial arterial wall to form a localized dilation. As neuroimaging has become more widely used, intracranial aneurysms are now being diagnosed with greater frequency before rupture (unruptured intracranial aneurysms [UIAs]). The prevalence of UIAs in the general population is 1.8% to 8.4% when diagnosed by magnetic resonance angiography (MRA). Because UIA rupture causes subarachnoid hemorrhage, which usually results in significant neurological deficits or death, there has been interest in evaluating the risk of aneurysm formation and enhancing the detection of UIAs before rupture.

UIAs occur in various locations around the Willis’ circle, some of which are predisposed to UIA formation. Bifurcation areas, where the arterial wall is weak and hemodynamic stress is altered, are known to be vulnerable sites. The hemodynamics of sidewall aneurysms might be different from that of aneurysms located at bifurcation sites. The most common histological findings of UIAs are a decreased thickness of the tunica media and middle muscular layer of the artery, which leads to structural defects. These defects, combined with hemodynamic factors, lead to aneurysmal outpouching. Previously, female sex, old age, active smoking, and hypertension were well established risk factors for the occurrence of...
UIAs. However, the relative importance of risk factors can be different according to the location of the UIA.

To determine the most appropriate treatment for UIAs, a better understanding of the risk factors and underlying pathophysiology of aneurysm occurrence is needed. The objectives of this study were to describe incidental UIAs on MRAs of healthy subjects at the Health Screening and Promotion Center and to identify specific risk factors for the presence of aneurysm at different locations.

Methods

Patient Population

All the subjects who underwent routine health examinations between September 2004 and May 2014 at the Health Screening and Promotion Center of Asan Medical Center were screened. The health screening and Promotion Center was not advertised, and the patients who visit the center were self-selected. Patients were consecutively enrolled if they had undergone MRA of the cerebral vessels (the health examination group). The prevalence of UIAs was determined from the MRAs, and UIAs >3 mm were considered true aneurysms. Subjects with UIAs <3 mm were excluded from both groups (Table 1 in the online-only Data Supplement). Subjects who had fusiform, mycotic, or traumatic aneurysms or UIAs who has been surgically or endovascularly treated before the first MRA were also excluded.

Clinical data were obtained through a review of the patient medical records and checklists and included demographic information, such as age and sex. We also recorded putative risk factors for aneurysm, including any personal history of hypertension, diabetes mellitus, coronary artery disease (CAD), past or current smoking, and alcohol consumption. Hypertension was defined as receiving antihypertensive medication or blood pressure >140/90 mm Hg on repeated measurement at Health screening and Promotion Center. Diabetes mellitus was also defined as taking diabetes mellitus medication or fasting blood glucose >126 mg/dL or 2-hour plasma glucose >200 mg/dL. Smoking and consumption of alcohol were obtained from the self-reported checklist. Personal history of CAD was defined as a diagnosis of CAD by a cardiologist and receiving medicine or with a history of percutaneous coronary intervention or bypass surgery.

To validate the distribution of UIAs in the health examination group, patients who visited the outpatient clinic of our Department of Neurology because of headache and underwent MRA were enrolled as a separate group (the outpatient group) that was then compared with the health examination group.

Imaging Analysis

Aneurysm diagnoses were based on MRA. Time of flight MRA was performed with 1.5-T (Siemens Avanto, Siemens Medical Solutions, Malvern, PA) and 3.0-T MR imagers (Philips Achieva; Philips Medical Systems, Andover, MA). The MR parameters for Time of flight MRA were as follows: echo time, 7 ms; repetition time, 25 ms; flip angle, 20°; 1 excitation; field of view, 160 or 200 mm; matrix size, 256x512; voxel size, ≥0.9x0.9x1.0 mm; and slab number, 4. In total, 36 images providing 12 stereoscopic images in 3 orthogonal directions were examined.

The size of the aneurysm was measured from the three-dimensional–reconstructed image. The length of aneurysm was measured from 3 points, that is, (1) neck width, which was defined as a virtual line separating the aneurysm from the parental artery; (2) the maximum height from the neck to the dome tip; and (3) the maximum width of the dome perpendicular to its height. Aneurysm size was defined as the largest of these measurements.

The location of aneurysms was classified as distal internal carotid artery (dICA), middle cerebral artery trunk (MCA), MCA bifurcation, anterior cerebral artery, anterior communicating artery (Acom), posterior communicating artery, or posterior circulation artery (including vertebral artery, basilar artery, posterior cerebral artery, and anterior and posterior inferior cerebellar arteries). In patients with multiple aneurysms, a single-index aneurysm with the largest size was selected. All MRA interpretations were performed by 2 neurologists (H.G.K. and M.-J.K.), independently. If there was a discrepancy between the original report and the reader’s interpretation or if the presence of an aneurysm was equivocal, another neurologist (B.J.K.) reviewed the records to reach a consensus.

Statistical Analysis

The prevalence of UIAs among patients who underwent MRA from the health examination group was calculated. Demographics and clinical data were compared between patients with and without UIAs. The Pearson χ² test and Student t test were used for categorical variables and continuous variables, respectively. To avoid variable selection caused by spurious correlations, only variables showing a potential association with aneurysms (P<0.2) in the univariate analysis were included as potential factors associated with UIAs in the multivariate logistic regression model.

Demographics and risk factors were also compared between patients with an aneurysm at a specific location and control subjects without an aneurysm. For comparisons, we performed ANOVA and then a χ² or Fisher exact test, as appropriate, with Bonferroni correction. Multinomial logistic regression was performed to estimate the adjusted odds ratios (ORs) of each variable at each location. UIAs at a specific location were first compared with the control group and with UIAs at other locations. Aneurysm locations from the health examination group were validated against aneurysms from the outpatient group. The comparison was done by the 2×6 χ² test. A 2-sided P value of <0.05 was considered statistically significant. All statistical analyses were performed using SPSS 21 (IBM Corp., Armonk, NY) and SAS 9.4 (SAS Institute, Cary, NC).

Results

Patient Characteristics

During the study period, 187,166 patients received a routine health examination at the Asan Medical Center. Among them, 18,954 (10.1%) patients underwent MRA. The mean age was 57.2±8.5 years, and 7392 patients (39.0%) were women. UIAs >3 mm were observed in 367 patients (1.94%; Figure 1). Among them, 29 patients (7.9%) had multiple UIAs, and 3 patients had >3 aneurysms.

During the same period, 59,081 patients visited our outpatient clinic. MRA was performed on 12,702 (21.5%) patients. The mean age of these patients was 63.1±12.5 years, and 8183 (64.4%) patients were women. Aneurysms >3 mm were observed in 302 patients (2.38%) of these outpatients (Figure 1). Among them, 29 patients (9.6%) were multiple aneurysms, including 5 patients with >3 aneurysms.

The prevalence of UIAs was significantly higher in patients from the outpatient clinic (P=0.007). Comparing the incidence of UIAs between the Health Examination and outpatient groups by each sex, there was no difference between men (181 of 11,381 [1.6%] versus 69 of 4,520 [1.5%]; P=0.83) or women (186 of 7,392 [2.5%] versus 233 of 8,182 [2.8%]; P=0.26). Finally, the trend of UIA incidence according to age and sex was similar between the 2 groups, showing an increase in women after their 50s (Figure 2).

Factors Associated With the Presence of Aneurysm

Among subjects who received a health examination, patients with aneurysms were older on average (57.2±8.5 versus 55.8±9.0; P=0.005), and the proportion of females was higher.
Health examination group

- Health screening patients (N = 187,166)
- Excluded patients w/o MRA (N = 168,212)
- Patients with MRA (N = 18,954)
- Patients with Aneurysm (N = 434)
- Excluded aneurysm size < 3mm (N = 67)

Outpatient group

- Patients with Headache (N = 59,081)
- Excluded patients w/o MRA (N = 46,379)
- Patients with MRA (N = 12,762)
- Patients with Aneurysm (N = 12,115)
- Excluded aneurysm size < 3mm (N = 85)

(50.7% versus 38.8%; P<0.001) compared with those without aneurysms. The prevalence of hypertension was also higher (40.9% versus 32.1%; P<0.001) among the aneurysm patients. On the other hand, the prevalence of CAD was lower in patients with aneurysms (10.1% versus 24.2%; P<0.001). The age, sex, hypertension, smoking, alcohol, and history of CAD variables identified by univariate analysis were entered into a multivariate logistic regression model that demonstrated that age, female sex, hypertension, smoking, and CAD were independently associated with aneurysms (Table 2).

Distribution of Aneurysm Location

UIAs were located at various sites around the Willis’ circle. The most common site was the distal ICA (n=166; 45.2%), followed by the MCA bifurcation (n=49; 13.4%) and the Acom (n=49; 13.4%). Posterior communicating artery aneurysms were observed in 38 patients (10.4%), whereas MCA and anterior cerebral artery aneurysms were observed in 24 patients (6.5%) and 21 patients (5.7%), respectively. Posterior circulation aneurysms were observed in 20 patients (5.4%).

The UIA distribution was not significantly different in the outpatient group (Table II in the online-only Data Supplement).

Risk Factors for UIA Formation by Location

The risk factors for UIAs varied at specific locations (Table 3). Compared with the control group, female sex (59.0% versus 38.8%; P<0.001) was more prevalent and a history of CAD (12.0% versus 24.2%; P<0.001) was less prevalent in patients with dICA aneurysms. Patients with MCA and Acom aneurysms demonstrated a higher prevalence of smoking (42.9% versus 17.9%; P=0.003 and 40.8% versus 17.9%; P<0.001, respectively). Patients with Acom aneurysms also showed a higher prevalence of alcohol consumption than the controls (73.5% versus 53.9%; P=0.006). Patients with posterior circulation aneurysms had a higher prevalence of hypertension than the controls (60.0% versus 32.1%; P=0.007).

By multinomial logistic regression comparative analysis comparing UIAs at a specific location with control, the independent risk factors for each UIA location were found to be different (Table 4). Female sex, hypertension, and CAD were independently associated with dICA, MCA bifurcation, and posterior communicating artery. MCA aneurysms were
associated with old age, smoking, and CAD. Acom aneurysms were associated with hypertension, smoking, alcohol consumption, and CAD. However, posterior circulation aneurysms were associated only with hypertension.

Compared with patients with UIAs at other locations, subjects with dICA aneurysm demonstrated more female subjects (OR, 1.851 [1.220–2.806]; P=0.004) compared with subjects with non-ICA UIAs. Subjects with MCA aneurysms had more smoking habits (OR, 3.123 [1.264–7.716]; P=0.01) compared with those with non-MCA aneurysms. Acom UIAs were associated with smoking (OR, 2.348 [1.197–4.606]; P=0.08) and alcohol (OR, 2.597 [1.282–5.262]; P=0.08) compared with non-Acom UIAs and posterior circulation UIAs with hypertension (OR, 2.836 [1.063–7.570]; P=0.04) and young age (OR, 0.921 [0.867–0.979]; P=0.008) compared with nonposterior circulation UIAs.

## Discussion

The prevalence of UIAs was 1.94% in the health examination group and 2.38% in the outpatient group. However, the incidence of UIAs in accordance with age and sex did not differ between these 2 study groups (Figure 2). The prevalence and distribution of UIAs were similar between the 2 groups and were also compatible with previous reports.2–5 Old age, hypertension, and smoking were associated with UIAs. Interestingly, the presence of CAD was found to be protective against UIAs. UIA prevalence increased sharply after their 50s and was significantly higher in the female patients. The risk factors associated with UIAs also varied by their location.

Hypertension, which is associated with hemodynamic stress, was associated with aneurysms at most of the sites. In fact, we found from our present analysis that hypertension was the only factor associated with aneurysms in the posterior circulation. On the other hand, sidewall (MCA and anterior cerebral artery) aneurysms were not associated with hypertension, but sidewall aneurysms of MCA were associated with smoking. Smoking induces an inflammatory response and proinflammatory phenotypic modulation of vascular smooth muscle cells, increases degradation of the extracellular matrix, and affects subsequent aneurysm formation.9,10 Female sex is also a well-known risk factor of UIAs, especially after menopause, which is consistent with our current results. This phenomenon can be explained by decreased estrogen, which enhances inflammatory reactions.11 UIAs located at the dICA, MCA bifurcation, and Acom might be at least partially associated with such mechanisms.

UIAs share risk factors with atherosclerosis development,12 and in some cases, atherosclerosis is associated with the occurrence of UIAs, especially in the abdominal aorta.13 However, intracranial aneurysms seem to be different from those of the abdominal aorta. Recently, intracranial aneurysms of the anterior circulation were found to be associated with aneurysms of the ascending aorta. Furthermore, ICA aneurysms, which are prone for atherosclerosis, were found to be associated with infrarenal aorta aneurysms.14 Interestingly, in our present analyses, the prevalence of CAD was lower in the patients with UIAs, and especially, patients with anterior circulation UIA were associated with a lower incidence of CAD. Our results are thus consistent with the findings of a previous study showing that anterior circulation UIAs are less frequently associated with atherosclerosis compared with other locations.

It is still unclear why vascular beds respond differently to similar risk factors. Previously, low cholesterol level was associated with intracerebral hemorrhage or subarachnoid hemorrhage,15 and the presence of hyperlipidemia showed a trend being protective for the rupture of cerebral aneurysm.16 However, still data showing the association between the presence of UIA and cholesterol level are lacking, and there was no difference between the levels of cholesterol in our data after adjusting for other variables. UIAs are mainly associated

### Table 1. Baseline Characteristics of the Study Patients With and Without Unruptured Intracranial Aneurysms

<table>
<thead>
<tr>
<th>Value</th>
<th>Control (n=18587)</th>
<th>Aneurysm (n=367)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>55.8 (9.0)</td>
<td>57.2 (8.5)</td>
<td>0.005</td>
</tr>
<tr>
<td>Women</td>
<td>7206 (38.8)</td>
<td>186 (50.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>122.8 (14.6)</td>
<td>122.6 (14.8)</td>
<td>0.802</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>77.4 (10.5)</td>
<td>76.9 (11.0)</td>
<td>0.386</td>
</tr>
<tr>
<td>Vascular risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>5961 (32.1)</td>
<td>150 (40.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2400 (12.9)</td>
<td>45 (12.3)</td>
<td>0.713</td>
</tr>
<tr>
<td>Smoking</td>
<td>3333 (17.9)</td>
<td>76 (20.7)</td>
<td>0.170</td>
</tr>
<tr>
<td>Alcohol drinking</td>
<td>10016 (53.9)</td>
<td>181 (49.3)</td>
<td>0.082</td>
</tr>
<tr>
<td>CAD</td>
<td>4493 (24.2)</td>
<td>37 (10.1)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are the number of patients (%) or mean (SD). P values were calculated by Pearson χ² test or Student t test as appropriate. BP indicates blood pressure; and CAD, coronary artery disease.

### Table 2. Factors Associated With the Occurrence of Unruptured Intracranial Aneurysms

<table>
<thead>
<tr>
<th>Value</th>
<th>Crude OR (95% CI)</th>
<th>P Value</th>
<th>Adjusted OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.18 (1.05–1.32)</td>
<td>0.005</td>
<td>1.02 (1.01–1.03)</td>
<td>0.003</td>
</tr>
<tr>
<td>Female</td>
<td>1.62 (1.32–2.00)</td>
<td>&lt;0.001</td>
<td>2.00 (1.55–2.56)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.46 (1.19–1.81)</td>
<td>&lt;0.001</td>
<td>2.21 (1.76–2.78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.20 (0.93–1.54)</td>
<td>0.171</td>
<td>1.66 (1.25–2.22)</td>
<td>0.001</td>
</tr>
<tr>
<td>Alcohol drinking</td>
<td>0.83 (0.68–1.02)</td>
<td>0.083</td>
<td>1.25 (0.98–1.59)</td>
<td>0.078</td>
</tr>
<tr>
<td>CAD</td>
<td>0.35 (0.25–0.50)</td>
<td>&lt;0.001</td>
<td>0.23 (0.16–0.33)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

P values represent the results of multivariable logistic regression. Variables with P<0.2 by univariate analysis were entered into the multivariate analysis model. CAD indicates coronary artery disease; CI, confidence interval; and OR, odds ratio.
with the degeneration of the tunica media and elastic lamina, which are the middle layers of the vessel wall.17,18 On the other hand, atherosclerosis is a disease of the endothelium that leads to lipid accumulation and growth of an atherosclerotic plaque inside the vessel.19 The individual vasculature responses to a similar risk factor might vary. Further studies comparing these 2 distinct vessel processes might help to reveal the exact reasons for these differences.

Although intra-arterial digital subtraction angiography remains the gold standard for aneurysm delineation, many reports have described MRA as having equivalent efficacy to digital subtraction angiography for the detection of most UIAs.20-22 The sensitivity of 1.5-T MRA for detection of intracranial aneurysms is between 79% and 97%.21,23,24 Three-T MRA is becoming more widely available and has been shown to be superior to 1.5-T MRA in the detection of intracranial aneurysms.25 This might increase the detection sensitivity of small aneurysms and the accuracy of size determination. In our present study, we excluded UIAs >3 mm because of the sensitivity limits of 1.5-T MRA. However, our findings indicate that MRA is an effective tool for cerebral aneurysm detection.

The strengths of our study include the large number of patients and aneurysms, rigorous measurement of size by the neurologist, ensuring representativeness through the comparison between the nature of the other 2 different groups, and the use of multivariate logistic regression models. However, there are some noteworthy limitations. First, our analyses were retrospective, and it must be considered that a selection bias may have been introduced. As smokers and heavy alcohol drinkers more likely refuse routine health examination, this can have lowered the prevalence of UIAs. However, we attempted to consecutively include all patients who underwent MRA during the study period from both the Department of Health Screening and Promotion and from the outpatient clinic at our hospital. We also compared UIA features from these 2 groups for external validation of health examination data. It is notable in this regard that the UIA distributions were similar in both groups.

Conclusions

Hemodynamic and degenerative factors both affect the occurrence of cerebral aneurysm, and the factors affecting the presence of UIAs differ by location. CAD demonstrates a protective effect against the occurrence of UIAs. This result may reflect the fact that although the risk factors are shared, vascular degeneration caused by different responses may lead to either a presence of aneurysm or atherosclerosis.

Table 3. Characteristics of the Control Patients and Patients With Unruptured Intracranial Aneurysms According to Location

<table>
<thead>
<tr>
<th>Aneurysm (n=367)</th>
<th>Control (n=18'587)</th>
<th>dICA (n=166)</th>
<th>MCA Bifurcation (n=49)</th>
<th>ACA (n=24)</th>
<th>Acrom (n=49)</th>
<th>Pcom (n=38)</th>
<th>Posterior Circulation (n=20)</th>
<th>Adjusted OR</th>
<th>Adjusted P</th>
<th>Value</th>
<th>Adjusted OR</th>
<th>Adjusted P</th>
<th>Value</th>
<th>Adjusted OR</th>
<th>Adjusted P</th>
<th>Value</th>
<th>Adjusted OR</th>
<th>Adjusted P</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>55.8 (8.0)</td>
<td>57.0 (8.9)</td>
<td>58.3 (6.5)</td>
<td>58.2 (6.9)</td>
<td>57.9 (11.4)</td>
<td>56.5 (8.0)</td>
<td>57.6 (8.0)</td>
<td>4.54 (4.6)</td>
<td>0.003</td>
<td>0.96</td>
<td>2.92 (2.0)</td>
<td>0.004</td>
<td>0.70</td>
<td>1.92 (1.2)</td>
<td>0.022</td>
<td>0.04</td>
<td>2.23 (2.0)</td>
<td>0.001</td>
<td>0.70</td>
</tr>
<tr>
<td>Women</td>
<td>7206 (38.8)</td>
<td>7220 (59.0)</td>
<td>7010 (57.1)</td>
<td>8333 (73.5)</td>
<td>76 (42.1)</td>
<td>7 (2.6)</td>
<td>8 (40.0)</td>
<td>12.60 (6.0)</td>
<td>0.007</td>
<td>0.91</td>
<td>10.0 (10.0)</td>
<td>&lt;0.001</td>
<td>0.91</td>
<td>9.45 (0.03)</td>
<td>0.003</td>
<td>0.91</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Vascular risk factors

Hypertension 5961 (32.1) 60 (36.1) 9 (42.9) 24 (49.0) 10 (41.7) 19 (38.8) 16 (42.1) 12 (60.0)* 0.007
Diabetes mellitus 2400 (12.9) 21 (12.7) 4 (19.0) 7 (14.3) 5 (10.2) 5 (13.2) 5 (13.2) 1 (5.0) 0.91
Smoking 3333 (17.9) 26 (16.7) 9 (42.9)* 10 (20.4) 4 (16.7) 4 (6.7) 5 (13.2) 1 (10.0) <0.001
Alcohol drinking 10'016 (53.9) 76 (45.8) 14 (66.7) 22 (44.9) 8 (33.3) 36 (73.5)* 16 (42.1) 9 (45.0) 0.003
CAD 4493 (24.2) 20 (12.0)* 1 (4.8) 5 (10.2) 4 (8.3) 4 (2.6)* 4 (20.0) <0.001

Values are the number of patients (%) or mean (SD). P values represent the results of ANOVA. ACA indicates anterior cerebral artery; Acrom, anterior communicating artery; CAD, coronary artery disease; dICA, distal internal carotid artery; MCA, middle cerebral artery; OR, odds ratio; and Pcom, posterior communicating artery.

*Represents factors with significant differences when comparing aneurysms at a specific location to the control after Bonferroni correction.

Table 4. Multinomial Logistic Regression Analysis of Risk Factors for Unruptured Intracranial Aneurysms at Each Location Compared With Control

<table>
<thead>
<tr>
<th>Aneurysm (n=367)</th>
<th>dICA (n=166)</th>
<th>MCA Bifurcation (n=49)</th>
<th>ACA (n=24)</th>
<th>Acrom (n=49)</th>
<th>Pcom (n=38)</th>
<th>Posterior Circulation (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.02 0.995</td>
<td>1.06 0.033</td>
<td>1.03 0.119</td>
<td>1.02 0.442</td>
<td>1.03 0.065</td>
<td>1.02 0.311</td>
</tr>
<tr>
<td>Women</td>
<td>2.59 &lt;0.001</td>
<td>1.25 0.702</td>
<td>2.78 0.004</td>
<td>1.00 0.999</td>
<td>1.17 0.678</td>
<td>2.23 0.041</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.74 0.002</td>
<td>2.34 0.066</td>
<td>3.10 &lt;0.003</td>
<td>2.12 0.089</td>
<td>2.02 0.025</td>
<td>2.71 0.004</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.35 0.212</td>
<td>3.93 0.007</td>
<td>2.02 0.083</td>
<td>1.25 0.712</td>
<td>2.98 0.001</td>
<td>1.05 0.929</td>
</tr>
<tr>
<td>Alcohol</td>
<td>1.22 0.280</td>
<td>2.00 0.203</td>
<td>1.25 0.521</td>
<td>0.50 0.154</td>
<td>2.54 0.012</td>
<td>1.15 0.539</td>
</tr>
<tr>
<td>CAD</td>
<td>0.33 &lt;0.001</td>
<td>0.08 0.018</td>
<td>0.20 0.038</td>
<td>0.21 0.043</td>
<td>0.17 0.001</td>
<td>0.05 0.004</td>
</tr>
</tbody>
</table>

Variables with P<0.2 by univariate analysis were entered into the multivariate analysis model. ACA indicates anterior cerebral artery; Acrom, anterior communicating artery; CAD, coronary artery disease; dICA, distal internal carotid artery; MCA, middle cerebral artery; OR, odds ratio; and Pcom, posterior communicating artery.
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Disclosures
None.

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Risk Factors for Development of Unruptured Intracranial Aneurysms

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Kang HG and Kim BJ equally contributed to this article as first authors.

This includes supplemental table I and II
**Supplemental table I** The characteristics of patients with UIA less than 3 mm.

<table>
<thead>
<tr>
<th></th>
<th>UIA (n=367)</th>
<th>UIA less than 3 mm (n=67)</th>
<th>Control (n=18,587)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>57.2 [8.5]</td>
<td>55.1 [8.2]</td>
<td>55.8 [9.0]</td>
</tr>
<tr>
<td>Female</td>
<td>186 (50.7)</td>
<td>32 (47.8)</td>
<td>7206 (38.8)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>150 (40.9)</td>
<td>22 (32.8)</td>
<td>5,961 (32.1)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>45 (12.3)</td>
<td>8 (11.9)</td>
<td>2,400 (12.9)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>37 (10.1)</td>
<td>9 (13.4)</td>
<td>4,493 (24.2)</td>
</tr>
<tr>
<td>Smoking</td>
<td>76 (20.7)</td>
<td>21 (31.3)</td>
<td>3,333 (17.9)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>181 (49.3)</td>
<td>32 (47.8)</td>
<td>8,571 (46.1)</td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dICA</td>
<td>166 (45.2)</td>
<td>25 (37.3)</td>
<td>-</td>
</tr>
<tr>
<td>MCA</td>
<td>21 (5.7)</td>
<td>8 (11.9)</td>
<td>-</td>
</tr>
<tr>
<td>MCA-bifurcation</td>
<td>49 (13.4)</td>
<td>11 (16.4)</td>
<td>-</td>
</tr>
<tr>
<td>ACA</td>
<td>24 (6.5)</td>
<td>3 (4.5)</td>
<td>-</td>
</tr>
<tr>
<td>Acom</td>
<td>49 (13.4)</td>
<td>10 (14.9)</td>
<td>-</td>
</tr>
<tr>
<td>Pcom</td>
<td>38 (10.4)</td>
<td>5 (7.5)</td>
<td>-</td>
</tr>
<tr>
<td>Posterior circulation</td>
<td>20 (5.4)</td>
<td>5 (7.5)</td>
<td>-</td>
</tr>
</tbody>
</table>

Values are the number of patients (%) or mean [SD]

dICA = distal internal carotid artery; MCA = middle cerebral artery; ACA = anterior cerebral artery; Acom = anterior communicating artery; Pcom = posterior communicating artery
**Supplemental table II** Location of unruptured intracranial aneurysms in health examination and outpatient groups

<table>
<thead>
<tr>
<th></th>
<th>dICA</th>
<th>MCA</th>
<th>MCA-bifurcation</th>
<th>ACA</th>
<th>Acom</th>
<th>Pcom</th>
<th>Posterior circulation</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health examination group (n=367)</td>
<td>166 (45.2)</td>
<td>21 (5.7)</td>
<td>49 (13.4)</td>
<td>24 (6.5)</td>
<td>49 (13.4)</td>
<td>38 (10.4)</td>
<td>20 (5.4)</td>
<td>0.07</td>
</tr>
<tr>
<td>Outpatient group (n=302)</td>
<td>155 (51.5)</td>
<td>8 (2.7)</td>
<td>49 (16.3)</td>
<td>10 (3.3)</td>
<td>28 (9.3)</td>
<td>32 (10.6)</td>
<td>19 (6.3)</td>
<td></td>
</tr>
</tbody>
</table>

Values are number of patients (%)

dICA = distal internal carotid artery; MCA = middle cerebral artery; ACA = anterior cerebral artery; Acom = anterior communicating artery; Pcom = posterior communicating artery;