Angiographic Features of Intracranial Aneurysms in Ecuador

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Background: Most of the literature describing morphological features of intracranial aneurysms (IAs) is from North-America, East-Asia, and Europe. There is limited data from South-America. We describe the epidemiologic and angiographic features of ruptured and unruptured IAs in a cohort of patients from Ecuador.

Methods: We conducted a retrospective analysis of prospectively acquired databases from 3 different tertiary hospitals over a 3-year period (2014-2017). In a per-patient basis, odd ratios (ORs) of ruptured presentation for each variable using a univariate logistic regression model were calculated. An aneurysm-based multivariate analysis was performed to calculate rupture ORs for each variable.

Results: Our sample included 557 patients with 761 IAs. Mean patient age was 52.2 years (range 18-82). Sixty-eight percent were women, and almost 90% presented with ruptured aneurysms and concomitant subarachnoid hemorrhage (SAH). Mean size of all the IAs was 6.4 mm ± 3.98 mm. Most IAs were located in anterior circulation (96.6%): 28.4% medial cerebral artery, 24.4% anterior cerebral artery or anterior communicating artery (ACOM), and 23.5% posterior communicating artery (PCOM). Only 6 basilar tip aneurysms (0.8%) were reported. In the adjusted analysis, aneurysms located in the ACOM (OR 1.89, 95% CI 1.29-2.78) and PCOM (OR 1.84, 95% CI 1.25-2.71), size larger than 5 mm (OR 2.84, 95% CI 2.04-3.93) and 7 mm (OR 2.28, 95% CI 1.64-3.19), and those with non-saccular morphology (OR 9.87, 95% CI 2.21-44.14) were significantly associated with ruptured presentation.

Conclusions: The prevalence of posterior circulation IAs in Ecuador, particularly basilar tip aneurysms, is low when compared to previous reports from developed countries. In our sample, IAs greater than 5 mm (and ≥7 mm) in size, ACOM and PCOM locations, and IAs with nonsaccular morphologies (blister and fusiform) were significantly associated with SAH presentation.

Key Words: Intracranial aneurysm—subarachnoid hemorrhage—Ecuador—Hispanic—South-America

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Introduction

The current angiographic features used to assess the risk of rupture of intracranial aneurysms (IAs) are size, location, and aneurysm morphology.[1,2] The large pooled-analysis study PHASES [Population, Hypertension, Age, Size, Earlier subarachnoid hemorrhage (SAH), and Site][3] introduced the variable "geographic region" as an important factor in determining the natural history of IAs. Based on this study, the Finnish and Japanese populations have a 3.6- and 2.8-fold increased risk of rupture, when compared to the North American population. However, the risk of rupture of IAs in other areas of the world such as the South American Andean region remains unclear. There are no large English written reports describing the morphological characteristics of IAs in countries of this region such as Ecuador. Previous reports from Ecuador and surrounding countries of the Andean region are limited to anecdotal small case-series (Table 1).[4-9] Until now, the epidemiology of IAs in the Ecuadorian population has not been assessed objectively. Moreover, the Ecuadorian ancestry radically differs from the surrounding larger South American countries such as Brazil and Argentina where IAs have been better characterized. Ecuador has a strong trihybrid influence from Kichwa, Mestizo, and Afro-American ethnic groups.[10] This unique ethnic ancestry may influence vascular disease and morphological characteristics of brain aneurysms. In this study, we aim to describe the morphological features of IAs in Ecuadorian patients admitted to 3 large hospitals.

Methods

Population

We reviewed and analyzed digital subtraction angiography (DSA), computational tomographic angiography, and magnetic resonance angiography reports of patients with IAs who presented over a 3-year period (2014-2017) at 3 large tertiary hospitals in Quito-Ecuador. Patients were referred for evaluation of ruptured IAs or due to the incidental finding of an unruptured IA. Aneurysms were classified as ruptured when a noncontrast head CT demonstrated the presence of SAH accompanied by acute symptoms such as: worst headache of their life, loss of consciousness, and neck rigidity. Patients who were less than 18 years old, those with non-aneurysmal SAH, and

Table 1. *Epidemiological studies of intracranial aneurysms in South America*

Author (y)	Country	Number of aneurysms	Presentation	Main epidemiological findings
Rocca et al* (2001)[4]	Peru	731	Ruptured and unruptured	Women (63%). The most common location was PCOM (24.4%), MCA (22.2%), and ACOM (18.5%). Only 2.6% of aneurysms were located in the posterior circulation and 1.2% in basilar tip. Multiple aneurysms were found in 16.1% subjects.
Vigueras et al* (2003)[5]	Chile	38	Ruptured	Women (73.7%). Median age was 48.8 ± 13.7 years old. The most common location was ICA (39.47%), MCA (31.58%), ACOM (21.01%), and PCOM (7.9%). No aneurysms reported in the posterior circulation.
Pena-Tapia et al* (2003)[6]	Ecuador	62	Ruptured	Women (67.2%). The average age was 45.9 years old. The most common location was PCOM (44%), ACOM (26%), MCA (17%), ICA (9%), and pericallosal artery (2.6%).
Costa LB Jr. et al (2004)[7]	Brazil	630	Ruptured and unruptured	Women (72.1%) in the fourth or fifth decades of life. The most common location was MCA (32.5%), PCOM (24.6%), and ACOM (17.5%). In the posterior fossa, the most common location was the basilar tip (3.1%).
Vargas et al* (2010)[8]	Colombia	473	Ruptured and unruptured	Women (74.4%). The average age was 51.7 years old. The most common location was ACA (18%), MCA (17%), and PCA (2.1%). Small aneurysms (<5 mm) accounted for 17.3% of the series. Approximately 44% aneurysm measured between 5 mm-9 mm, 36.4% between 10 mm-25 mm, and 2.3% >25 mm.
Romano Flores et al* (2017)[9]	Venezuela	82	Ruptured	Women (89.3%). The majority of aneurysms were located in the MCA (32.9%), ACA (19.5%), ACOM (11%) and PCOM (8.6%). 85% had a saccular morphology. 32% of patients had ≥2 intracranial aneurysms.

ACA, anterior cerebral artery; ACOM, anterior communicating artery; MCA, medial cerebral artery; PCA, posterior cerebral artery, PCOM: posterior communicating artery.

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those with incomplete angiographic description of the IAs were excluded from the analysis. Institutional review board approval was obtained from the Ethics Committee of Universidad San Francisco de Quito in Ecuador. Patient consent was waived as no identifiable information was included. Information was obtained from a prospectively collected database of IAs.

Data Collection

Basic demographic information was collected from DSA reports and medical records of all the individuals referred for ruptured and unruptured IAs evaluation. Comorbidities such as hypertension, hyperlipidemia, diabetes, or smoking were not available in every report, and were excluded from the analysis. Angiographic characteristics of every aneurysm such as size, location, and morphology were collected following reporting standards and current consensus.[11,12] Aneurysms were classified in 3 categories: "saccular": IAs with a characteristic dome and neck configuration; "fusiform": dilated IAs involving the entire circumference of an arterial segment and without a neck; and "blister": IAs arising from the anterior wall of the internal carotid artery. For location, IAs were stratified in 7 different categories as described in the International Study of Unruptured Intracranial Aneurysms (ISUIA): cavernous carotid artery, internal carotid artery, anterior communicating, or anterior cerebral artery (ACOM), middle cerebral artery (MCA), posterior communicating artery (PCOM), vertebrobasilar or posterior cerebral artery, and basilar tip.[13] For patients who presented with SAH, when available, we used both Fisher and Hunt & Hess grading scales as reported and scored by neurologists and emergency trained physicians.

Statistical Analysis

We used descriptive statistics to estimate overall proportions of the epidemiological characteristics of the sample. Collected demographic data were normally distributed based on Shapiro-Wilk normality test's nonsignificant results. We plotted a univariate logistic regression model to analyze ruptured presentation odd ratios (ORs) for demographic variables in a per-patient basis, and ORs for angiographic variables in a per-aneurysm basis, making sure we do not duplicate any of the data. When a patient had multiple aneurysms, the largest and/or ruptured aneurysm was used to categorize the patient. An aneurysm-based multivariate analysis was performed to calculate ruptured presentation ORs for each variable. This adjusted model included as covariates age, gender, and all other variables with significant P values (<0.05) in the prior unadjusted analysis. Those variables were also included as interaction terms when assessing the ruptured presentation and aneurysm size relationship in the multivariate model. Observed effect size and power of this study final sample were 0.16 and 1.0, respectively. Statistical analysis was performed

Table 2. *Population characteristics*

Variable			Overall patients (N=557)	Unruptured (n = 56)	Ruptured (n = 501)
Age (Mean ± SD), years			52.29 ± 14.93	54.28 ± 13.98	52.51 ± 14.87
Age	<70-year-old		487 (87.4%)	50 (89.3%)	437 (87.2%)
	≥70-year-old		70 (12.6%)	6 (10.7%)	64 (12.8%)
Gender	Male		178 (32%)	17 (30.4%)	161 (32.1%)
	Female		379 (68%)	39 (69.6%)	340 (67.9%)
Clinical presentation	SAH (ruptured)		501 (89.9%)	NA	501 (100%)
	Fisher Scale (Mean ± SD)*		NA	NA	3.02 ± 0.958
	Hunt & Hess (Mean ± SD)*		NA	NA	2.16 ± 0.920
	Unruptured	Headache	NA	32 (57%)	NA
		III CN paralysis	NA	14 (25%)	NA
		Seizure	NA	6 (10%)	NA
		IPH/AIS	NA	4 (0.7%)	NA
Aneurysms	1 aneurysm		418 (75%)	41 (73.2%)	377 (75.2%)
	2 aneurysms		94 (16.9%)	10 (17.9%)	84 (16.8%)
	3 aneurysms		31 (5.6%)	4 (7.1%)	27 (5.4%)
	≥4 aneurysms		14 (2.5%)	1 (1.8%)	13 (2.6%)
Treatment	Endovascular		423 (75.9%)	38 (67.9%)	385 (76.8%)
	Observation		124 (22.3%)	17 (30.4%)	107 (21.4%)
	Clipping		10 (1.8%)	1 (1.8%)	9 (1.8%)

AIS, Acute ischemic stroke; III CN, third cranial nerve; IPH, intraparenchymal hemorrhage; NA, not applicable; SAH, subarachnoid hemorrhage.

*Ninteen patients with SAH did not have Fisher or Hunt & Hess scores.

using Statistical Package for the Social Sciences (SPSS) version 22 software.

Results

A total of 605 patient records were reviewed. Of these, we excluded 48 based on our study criteria. Our final analysis included 557 patients with 761 aneurysms. Descriptive characteristics of the studied population are summarized in Table 2. Briefly, mean patient age was 52.2 years (SD 14.93, range 18-82) with most cases being younger than 70 year-old. Almost 90% (501 patients) presented with SAH, and 68% were women. Of the patients who presented with SAH, the median Fisher CT score was 3 [interquartile range (IQR) 2], and the median Hunt & Hess score was 2 (IQR 1). The most common symptom in patients who presented with unruptured IAs was headache (57.1%), followed by III cranial nerve palsy (25%), seizures (10.7%), and intraparenchymal hemorrhage/acute ischemic stroke (7.2%). Twenty-five percent of patients had multiple IAs (range 2-8). Endovascular surgery was the most common treatment (75.9%) of ruptured and unruptured aneurysms.

Mean size of all the IAs was 6.4 mm (SD 3.98): 48.5% were small (≤5 mm), 47% medium (6 mm-15 mm), 3.5% large (15 mm-25 mm), and 0.9% giant (≥25 mm) (Table 3). Following the size cutoff of 7 mm used in ISUIA: 63.2% IAs were smaller than 7 mm and 36.8% were equal to or larger than 7 mm. Most IAs were located in anterior circulation (96.6%): 28.4% in the MCA, 24.4% in the ACOM distribution, and 23.5% in the PCOM. Only 6 basilar tip aneurysms (0.8%) were reported. Twenty-nine aneurysms had nonsaccular morphology: 23 blister (3%) and 6 fusiform (0.8%).

The most common location of the 501 ruptured IAs was the anterior circulation: ACOM (27.3%), MCA (25.9%), and PCOM (26.7%). Only 2.8% ruptured IAs were located in the posterior circulation. Non-saccular morphology was observed in 5.4% ruptured IAs. The mean size for ruptured IAs was 6.94 mm ± 3.77 mm. However, most patients who presented with SAH had IAs of 5 mm or less in size (200 cases, 40%). In patients with unruptured IAs (n = 260), the mean size was significantly smaller (5.42 mm ± 3.77 mm, $P < 0.001$). Fifty-seven aneurysms (22%) were located in either PCOM or the posterior circulation and only six aneurysms (0.8%) had nonsaccular morphology.

Clinical and morphological features of ruptured IA are summarized in Table 4. In multivariable analysis, aneurysms greater than 5 mm and equal to/greater than 7 mm in size (OR 2.84, 95% CI 2.04-3.93; and OR 2.28, 95% CI 1.64-3.19, respectively), located in the ACOM (OR 1.89, 95% CI 1.29-2.78) and PCOM (OR 1.84, 95% CI 1.25-2.71) were significantly associated with ruptured presentation after adjusting for age, size, location, morphology, and gender (Fig 1A). Such association remained significant in a stratified analysis for aneurysms smaller than 7 mm (Fig 1B). Aneurysms with non-saccular morphology (blister and fusiform) were more likely to present with rupture (OR 9.87, 95% CI 2.21-44.14). Cavernous aneurysms were associated with unruptured presentation, with protective ratios in both unadjusted and adjusted

Table 3. *Angiographic characteristics of 761 aneurysms*

Variable			Aneurysms (N = 761)	Unruptured (n = 260)	Ruptured (n = 501)
Size (Mean ± SD), mm			6.42 ± 3.98	5.42 ± 3.77	6.94 ± 3.77
Size	Small (≤5 mm)		369 (48.5%)	169 (65%)	200 (39.9%)
	Medium (5 mm-15 mm)		357 (47%)	82 (31.5%)	275 (54.9%)
	Large (15 mm-25 mm)		28 (3.5%)	7 (2.7%)	21 (4.2%)
	Giant (>25 mm)		7 (0.9%)	2 (0.8%)	5 (1%)
Location	Anterior	Cavernous carotid artery	18 (2.4%)	13 (5%)	5 (1%)
		Internal carotid artery (ICA)	136 (17.9%)	55 (21.2%)	81 (16.2%)
		Anterior communicating or anterior cerebral artery (ACOM)	186 (24.4%)	49 (18.8%)	137 (27.3%)
		Middle cerebral artery (MCA)	216 (28.4%)	86 (33.2%)	130 (25.9%)
		Posterior communicating segment of ICA (PCOM)	179 (23.5%)	45 (17.3%)	134 (26.8%)
	Posterior	Vertebrobasilar or posterior cerebral artery (PCA)	20 (2.6%)	8 (3%)	12 (2.4%)
		Basilar tip	6 (0.8%)	4 (1.5%)	2 (0.4%)
Morphology	Saccular		732 (96.2%)	258 (99.2%)	474 (94.6%)
	Blister		23 (3%)	1 (0.4%)	22 (4.4%)
	Fusiform		6 (0.8%)	1 (0.4%)	5 (1%)

ACOM, anterior communicating; ICA, internal carotid artery; MCA, middle cerebral artery; PCOM, posterior communicating; PCA, posterior cerebral artery.

Table 4. *Demographic and morphological features associated with rupture of intracranial aneurysms in the Ecuadorian population*

Variable		Ruptured	Univariate analysis		Multivariate analysis	
			OR (95% CI)	*P*	OR (95% CI)	*P*
Age	<70-year-old	437/487	Reference			
	≥70-year-old	64/70	1.22 (.50-2.96)	.659		
Gender	Male	161/178	Reference			
	Female	340/379	.92 (.51-1.68)	.787		
Size	Continuous (mm)	NA	T = 5.082	<.001	NA	NA
Size	Small (≤5 mm)	200/369	Reference			
	Medium or larger (>5 mm)	301/392	2.79 (2.05-3.82)	<.001	2.84 (2.04-3.93)	<.001
Size (ISUIA)	< 7 mm	286/481	Reference			
	≥ 7 mm	215/280	2.25 (1.62-3.14)	<.001	2.28 (1.64-3.19)	<.001
Location*	Cavernous carotid artery	5/18	.19 (.07-.54)	.002	.15 (.05-.46)	.001
	Internal carotid artery (ICA)	81/136	.72 (.49-1.05)	.089	.60 (.40-.90)	.014
	Anterior communicating or anterior cerebral artery (ACOM)	137/186	1.62 (1.12-2.34)	.01	1.89 (1.29-2.78)	.001
	Middle cerebral artery (MCA)	130/216	.71 (.51-.98)	.039	.69 (.49-.97)	.031
	Posterior communicating segment of ICA (PCOM)	134/179	1.74 (1.2-2.54)	.004	1.84 (1.25-2.71)	.002
	Posterior circulation	14/26	.59 (.27-1.30)	.194	.51 (.22-1.19)	.12
Multiple	No	377/418	Reference			
	≥2 aneurysms	124/139	.89 (.48-1.68)	.739		
Morphology	Saccular	474/732	Reference			
	Nonsaccular (blister-like, fusiform)	27/29	7.35 (1.73-31.15)	.002	9.87 (2.21-44.14)	.003

ACOM, anterior communicating; ICA, internal carotid artery; ISUA, international Study of Unruptured Intracranial Aneurysms; MCA, medial cerebral artery; PCOM, posterior communicating.

*For this variable, displayed odd ratios compare the proportion of ruptured aneurysms in the respective location versus that of all other locations.

models (OR 0.19 and 0.15, *P* 0.002 and 0.001, respectively). Age, gender, and the presence of multiple IAs did not significantly correlate with rupture status at presentation.

Discussion

It is important to determine epidemiological characteristics of IAs in different patient populations to have a better understanding of the disease process and deliver targeted treatments. Most of the epidemiological studies of IAs are from Europe, North America, and Asia. There are almost no—if any—studies of IAs in the Andean region of South America reported in the English literature. We describe a very low proportion of IAs in the posterior circulation, particularly affecting the basilar tip (0.8%). The ISUIA retrospective cohort showed a 3.9% and 5.1% proportion of BA tip aneurysms in patients with and without history of SAH, respectively.[13] We report a 6-fold difference in the incidence of these aneurysms in the Ecuadorian population.

Similar to what has been reported, ACOM and PCOM aneurysms were more likely to present with SAH in our sample.[2,14] However, contrary to ISUIA, posterior circulation aneurysms were not significantly associated with rupture status on presentation. This probably could be explained by the low prevalence of these aneurysms in the Ecuadorian population: 3.4% in the posterior circulation and only 0.8% in the basilar tip. This differs significantly not only from ISUIA, but also from previous studies reporting a 5%-7% incidence of basilar tip aneurysms in European and Japanese populations.[11,15,16] Moreover, in recent years, an increased number of ruptured posterior circulation aneurysms has been described in the Finnish population, with up to 12% of the total number of ruptured IAs.[17] We only report a 2.8% rate of ruptured IAs in the posterior circulation.

A large meta-analysis by Wermer et al of 6,556 unruptured aneurysms (4,705 patients) found higher risk of rupture in patients older than 60 years-old (RR 2.0, 95% CI 1.1-3.7).[18] The PHASES study also exhibited a trend of rupture in older patients, especially those older than 70 years of age.[3] In Ecuador, older patients (≥70 year-old) did not exhibit a significant association with rupture status (Table 4). This may be influenced by epidemiological variables such as life expectancy and age distribution of the population.

Female gender as a risk factor of IAs rupture has been assessed in many prior studies, and results have not been reproducible in all populations. A systematic review by Rinkel et al that included 56,304 patients, as well as a meta-analysis by Wermer et al, found a higher risk of

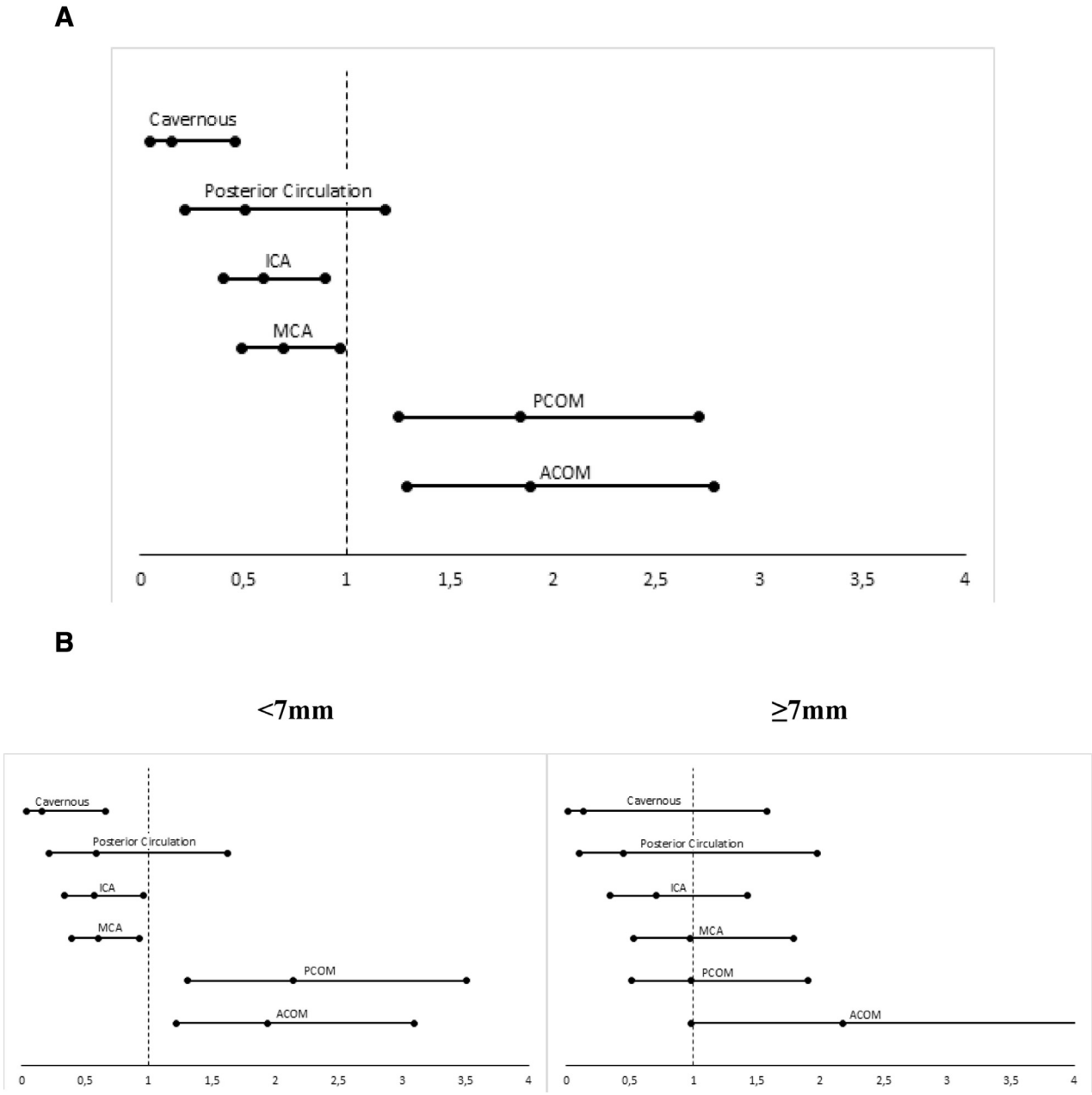

Figure 1. *(A) Odd ratios for SAH presentation by location in multivariate analysis – each location is compared to all other remaining locations. (B) Odds ratios for SAH presentation by location in the multivariate analysis stratified by size. Abbreviations: SAH, subarachnoid hemorrhage.*

rupture in women (RR 2.1, 95% CI 1.1-3.9; and OR 1.6, 95% CI 1.1-2.4, respectively).[1,18] In our population, most ruptured and unruptured aneurysms were found in women. However, women were not more likely to present with ruptured IAs when compared to men (Table 4).

Evidence suggests a direct proportional relationship between IA size and risk of rupture.[2,11,16] Our results showed a 40% of SAHs due to small aneurysms (≤5 mm), but larger IAs showed significant association with ruptured presentation when compared to small aneurysms in both uni- and multivariate analysis (Table 4). The fact that almost half of SAHs are seen in patients with small IAs can be explained by the overall high prevalence of small IAs in our sample (48.5%). This has been replicated in other series, with approximately 50% of ruptured IAs being smaller than 5 mm in size.[19] Unlike the Small Unruptured Intracranial Aneurysms Verification (SUAVe) study,[15] the presence of 2 or more aneurysms was not significantly associated with ruptured presentation in the Ecuadorian population.

The foremost limitation of this study is its observational and retrospective nature. Subjects were treated at different hospitals, generating sample bias. Moreover, follow-up information was quite limited, and patient

comorbidities such as hypertension, hyperlipidemia, diabetes, and smoking were not available for statistical analysis. The nature of the sample may predispose to biases of aneurysm identification, as ruptured IAs may be identified more often due to the need to perform more imaging studies such as DSA.

Conclusion

The distribution of IAs in the Ecuadorian population differs from what has been reported in other large observational studies from Europe, North America and Asia. The incidence of posterior circulation IAs, particularly basilar tip aneurysms, is considerably lower compared to what has been reported in developed countries. We found that IAs greater than 5 mm (and ≥7 mm) in size, ACOM and PCOM locations, and IAs with non-saccular morphologies (blister and fusiform) are significantly associated with SAH presentation.

Statement of Ethics

Institutional review board (IRB) approval was obtained from the Ethics Committee of Universidad San Francisco de Quito in Ecuador. Patient consent was waived as no identifiable information was included.

Disclosures

E.A.S. is a consultant for Microvention and Medtronic. S.O.G. is a consultant for Stryker. J.A.R., B.M.B., D.M.H., M.J., J.C.T., and N.M. have nothing to disclose.

Author Contributions

E.A.S. and J.A.R.: study design, acquisition of data, data analysis and manuscript preparation, critical revision of the manuscript, and guarantors of the study. B.M.B.: acquisition of data. All authors reviewed and approved the manuscript.

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