



Aneurysmal Subarachnoid Hemorrhage Associated with Small Aneurysms in Smokers and Women: A Retrospective Analysis

Luisa F. Figueredo¹, María Camila Pedraza-Ciro², Juan Sebastian Lopez-McCormick¹, Roberto Javier Rueda-Esteban¹, Juan Armando Mejía-Cordovez³

■ **BACKGROUND:** Previous studies have shown low rupture rates for small aneurysms (<10 mm), suggesting that the risk of treatment could exceed the benefits. However, evidence has changed, showing crescent rates of aneurysmal subarachnoid hemorrhage (aSAH) associated with small aneurysms. We report trends in size, localization, clinical characteristics, and outcomes of intracranial aneurysms (IAs).

■ **METHODS:** In this retrospective study, a total of 200 clinical histories of patients diagnosed with IAs over an 8-year period were analyzed. Variables considered included age, sex, tobacco consumption, morphological characteristics of the aneurysm, complications, vasospasm, and mortality. Qualitative variables were assessed by measurements of absolute and relative frequency. Smoking behavior, aneurysm size, and aneurysm rupture (AR) were compared using 1-way analysis of variance. Categorical variables were analyzed using Pearson's χ^2 test.

■ **RESULTS:** The average age at presentation was 58 years. The average size of ruptured aneurysms in the general group was 2.5–7.5 mm, and AR was most common in women (76%) and in patients age 50–60 years (33%). The rate of vasospasm was 19%, and mortality was 37%. Smokers composed 32% of the cohort. Heavy smokers had a 57% rate of aSAH, with an average size of rupture of 5 mm. The most common location of aneurysms and AR was the AComA (33%).

■ **CONCLUSIONS:** Our results suggest increasing AR rates in aneurysms smaller than 10 mm. This trend is seen

especially in individuals with heavy tobacco consumption and in women of perimenopausal age. Our findings show a tendency of AR in accordance with previous results and are expected to serve as basis for further research on aneurysm management.

INTRODUCTION

Intracranial aneurysms (IAs) are potentially disabling and even life-threatening vascular dilations.^{1,2} Repercussions depend largely on whether or not the aneurysm ruptures, and management of unruptured aneurysms is based on the risk of aneurysm rupture (AR).^{1,3} The risk of AR varies according to the size and morphology of the aneurysm.^{4,5} However, there are considerable variations in the reported prevalence of AR in small (<5 mm) to medium (6–10 mm) aneurysms.^{4,6} Initial estimates considered a minimal risk of AR in aneurysms <7 mm, but new evidence suggests a higher prevalence of AR in this group than previously thought.⁶

Owing to this possibly higher prevalence of AR in small to medium aneurysms, earlier intervention than previously recommended may be called for. As technology improves, smaller aneurysms can be identified with more precision, providing an opportunity for early management, mainly in cases that coexist with known risk factors for AR,^{2,7} which are related mostly to inflammatory processes, such as lack of estrogens and smoking.^{8–10}

The possibly higher prevalence of AR in small aneurysms makes their characterization and analysis of potential associated risk factors of paramount importance. To address this, we sought to

Key words

- Intracranial aneurysm
- Menopausal
- Small aneurysm
- Smoker

Abbreviations and Acronyms

AComA: Anterior communicating artery

ANOVA: Analysis of variance

AR: Aneurysm rupture

aSAH: Aneurysmatic subarachnoid hemorrhage

IA: Intracranial aneurysm

ISUIA: International Study of Unruptured Intracranial Aneurysms

From the ¹School of Medicine, Universidad de los Andes, Bogotá; ²School of Medicine, Universidad El Bosque, Bogotá; and ³Department of General Surgery, Fundación Santa Fe de Bogotá, Bogotá, Colombia

To whom correspondence should be addressed: Roberto Javier Rueda-Esteban, M.D.
[E-mail: rj.rueda32@uniandes.edu.co]

Citation: *World Neurosurg.* X (2019) 4:100038.

<https://doi.org/10.1016/j.wnsx.2019.100038>

Journal homepage: www.journals.elsevier.com/world-neurosurgery-x

Available online: www.sciencedirect.com

2590-1397/© 2019 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

retrospectively analyze and describe trends in reported size, morphology, orientation, localization, clinical characteristics, and outcomes of IAs in a fourth-level university hospital over an 8-year period.

METHODS

In this retrospective analytical study, with previous Institutional Review Board approval, 200 clinical histories of patients diagnosed with IAs who presented to our institution between the years 2008 and 2016 were analyzed. Patient consent was not required, owing to the anonymous nature of the information collected. The information used in this study did not pose a risk or potential risk to patients' personal integrity.

Computed tomography and computed tomography angiography scan data were analyzed. For patients who presented with several aneurysms, each symptom was characterized separately, morphology was described, and intraoperative records and outcomes were considered.

Patient Selection: Inclusion and Exclusion Criteria

Institutional yearly records between January 2008 and January 2016 from the neurosurgery department were reviewed for patients with diagnosed IA or aSAH. A total of 200 clinical histories were chosen for analysis. Patients for whom no postsurgical follow-up data were available were excluded from the study, after which 189 remained for our analysis.

Database Construction

Data was obtained from our hospital's centralized patient history system. Variables considered were age and sex; admittance date; comorbidities; tobacco use; symptoms such as headache, nausea, hemiparesis, hemiplegia, sensitive disturbance, and consciousness diminishment before and after intervention for aneurysm; history of previous subarachnoid hemorrhage; Hunt and Hess grade and Fisher classification; morphological characteristics of the aneurysm (including orientation, lobulations, transverse diameter, anteroposterior diameter, and maximum reported diameter); intervention(s) provided; complications of intervention(s); vasospasm; prescribed medical treatment; and mortality.

Radiologic images were obtained from our institutional imaging database (IMPAX-AGFA Health Care; Agfa-Gevaert Group, Mortsel, Belgium). The Strengthening the Reporting of Observational Studies in Epidemiology statement guidelines for observational studies were followed.^{11,12}

Statistical Analysis

Qualitative variables were assessed by measurements of absolute and relative frequency, and quantitative data were assessed using central tendency measures, data dispersion, mean \pm SD in normal distribution models. Smoking, aneurysm size, and AR were compared using 1-way analysis of variance (ANOVA). Categorical variables, including aneurysm location, were analyzed using Pearson's χ^2 test. All data analyses were done using GraphPad Prism 8 for Mac OS X, version 8.01 (GraphPad Software, La Jolla,

Table 1. Demographic Data

Characteristic	Value
Number of patients	189
Age, years, mean \pm SD (range)	58 \pm 15.1 (16–91)
Female sex, <i>n</i> (%)	138 (73)
Diabetes, <i>n</i> (%)	18 (9.5)
Hypertension, <i>n</i> (%)	97 (51.3)
Hypercholesterolemia, <i>n</i> (%)	37 (19.6)
Smoking, <i>n</i> (%)	61 (32.3)

CA, USA). Patients with missing data were not included in our analysis.

RESULTS

A total of 189 patients were included in the study. The average patient age was 59 \pm 15 years (range, 16–91 years). The majority of patients were female (73%; *n* = 138), and 32.3% (*n* = 61) reported tobacco consumption (Table 1).

The most common vessel associated with aneurysm location was the anterior communicating artery (AComA; 33%; *n* = 189), followed by the internal carotid artery (23%; *n* = 43) and middle cerebral artery (13%; *n* = 23) (Figure 1). The most common location of AR was the AComA (34.8%; *n* = 66), followed by the middle cerebral artery (20.3%; *n* = 38) (Figure 2). The orientation of the aneurysms in AComA was most often anterior (24%; *n* = 15).

The average size of all (ruptured and nonruptured) aneurysms was 6 \pm 0.35 mm (range, 2–25 mm). The average size of ruptured aneurysms was 5 \pm 0.53 mm (range, 2.5–7.5 mm) (Figure 3). Of the 189 surgeries, 120 were elective procedures. AR occurred in 72 patients, who had an average age of 58 \pm 15.8 years (standard error, 1.9). The majority of these patients were female (76%; *n* = 55; *P* = 0.0752), with an average rupture size of 4 \pm 0.98 mm (Figure 4). In patients with AR, 15% (11 of 70) needed reintervention after rupture; 7 of these 11 patients required 1 additional surgery, and the other 4 required 2 or more interventions, including 1 decompressive craniotomy.

The mortality rate was 11.2% (8 of 71), predominantly in patients with an initial Hunt and Hess grade of 5 (38%; 3 of 8) and a Fisher scale score of 2 (25%; 2 of 8) (Table 2). Twenty-six patients had a Fisher scale score of 4, with a mortality rate of 2.55% (*P* = 0.5304) (Figure 5). Fisher scale score was also associated with the presence of vasospasm (*P* = 0.2670), with higher rates at Fisher 3 and 4 (Figure 6). Finally, the prevalence of hydrocephalus (*P* = 0.0132) was higher in the Fisher 4 group (18 of 26) (Figure 7). These findings are summarized in Table 3.

Patients who consumed tobacco composed 28% of the entire population (53 of 189) and 25% of the patients with aSAH (25 of 72) (Table 3). Heavy smokers (>16 packs/year) had an median AR size

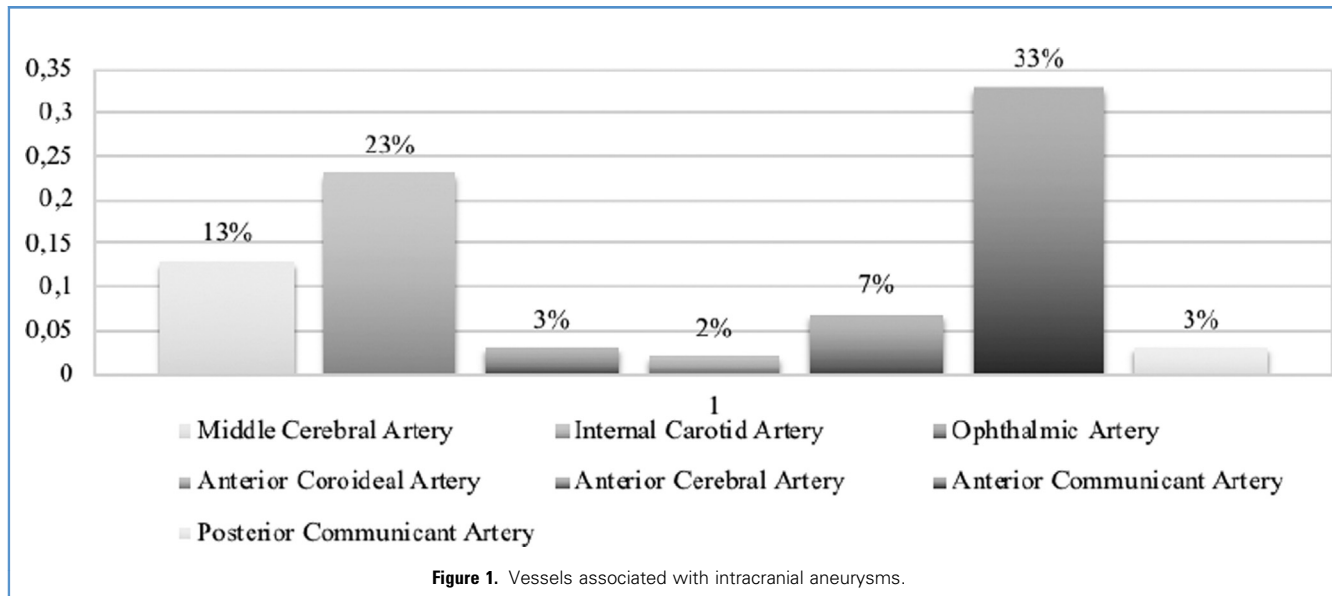


Figure 1. Vessels associated with intracranial aneurysms.

of 3 mm (range, 2–15 mm) ($R^2 = 0.0128$; $P = 0.4988$, ANOVA) (Figure 8).

In women, the average size of AR was nearly 5 mm for all groups (Figure 9). Finally, the evaluation for differences in ruptured aneurysm sizes between young smokers, young nonsmokers, old smokers, and old nonsmokers revealed a P value of 0.038 for differences between young smokers and young nonsmokers, but a P value of 0.36 for differences in all groups. Bartlett’s test for symmetry was 0.0088 (Figure 10). Vasospasm was reported in 17%

of the patients (32 of 189). The internal carotid artery was the most prevalent location associated with vasospasm (37%), followed by the anterior cerebral artery (22%) (Table 4).

DISCUSSION

In this 8-year retrospective descriptive study that included 189 patients presenting with IAs, most ruptures were observed in heavy smokers and women at the sixth decade of life. Age showed

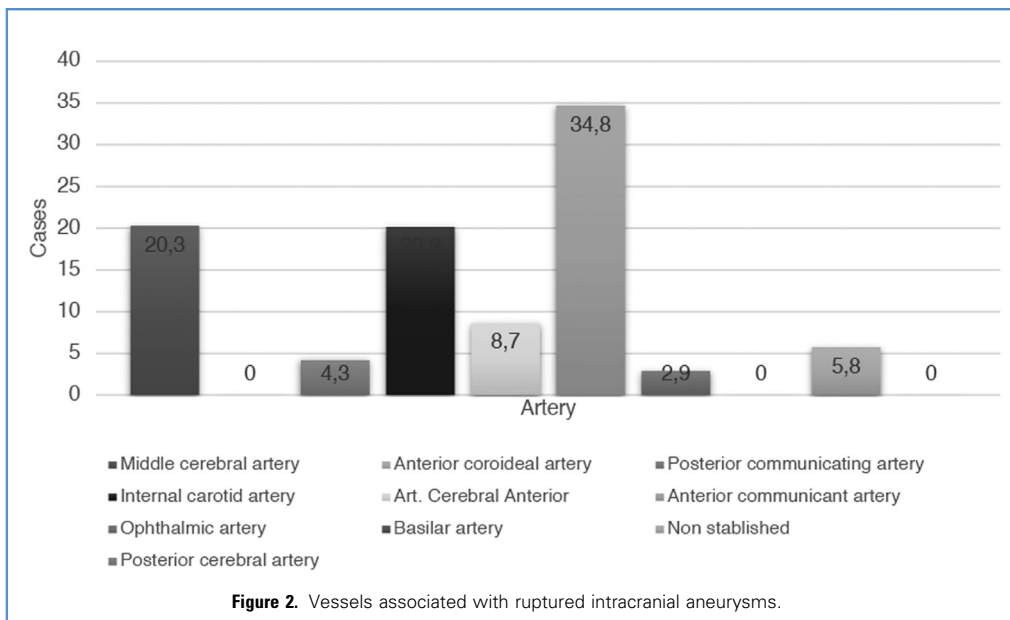


Figure 2. Vessels associated with ruptured intracranial aneurysms.

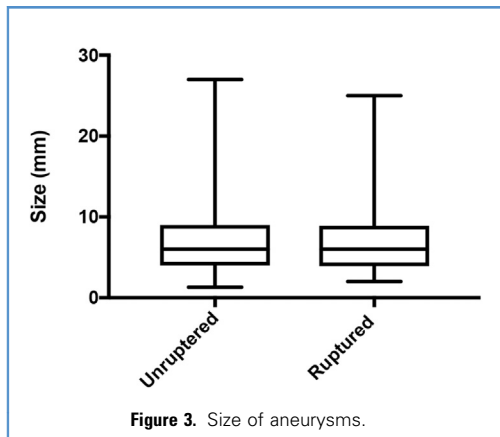


Figure 3. Size of aneurysms.

a wide range of distribution (16–91 years), with a parametric behavior at a mean of 59 ± 15 years. Vlák et al.^{13,14} described a similar distribution, with a high incidence at age 50 years. In addition, a monomodal behavior was observed for aneurysms frequency, with a peak in the sixth decade of life. This pattern could be associated with higher mortality by other causes in the older population, which may potentially present a confounding bias by obscuring potential AR later in life, which is supported by data reported by the World Bank in 2015, where the life expectancy for the study population was 74 years with mortality predominantly associated with coronary events, supporting the idea that the increased mortality due to other events (not aneurysms) could contribute to a bias for the risk of AR past the sixth decade of life. In addition, the International Study of Unruptured Intracranial Aneurysms (ISUIA) study found a relationship between increasing age and the risk of AR, essentially associated with aging mechanisms¹⁵ related mainly to vascular fragility and the accumulation of reactive oxygen species.^{16,17}

We found a higher prevalence of aneurysms in females, 73%, compared with males. Similar results were found by Vlák et al.,^{13,14}

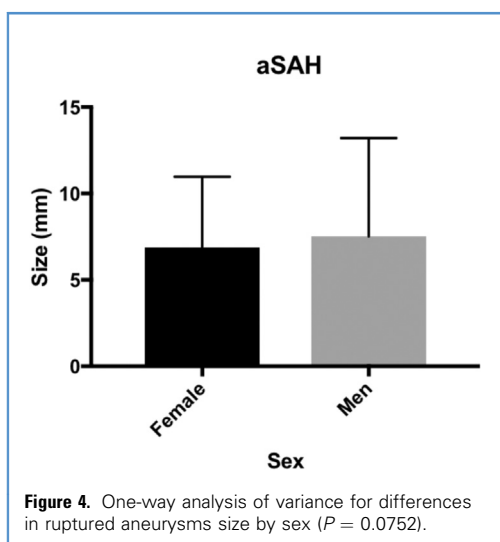


Figure 4. One-way analysis of variance for differences in ruptured aneurysms size by sex ($P = 0.0752$).

Table 2. Demographic Data for Patients with aSAH

Characteristic	Value
Number of patients	71
Age, years, n (%)	
10–30	4 (5.6)
31–40	3 (4.2)
41–50	12 (16.9)
51–60	23 (32.4)
61–70	13 (18.3)
>70	16 (22.5)
Sex, n (%)	
Female	54 (76)
Male	17 (24)
Mortality, n (%)	8 (11.2)
Hunt and Hess 1	1 (13)
Hunt and Hess 2	2 (25)
Hunt and Hess 3	1 (13)
Hunt and Hess 4	1 (13)
Hunt and Hess	3 (38)

who reported a prevalence of 6% (95% confidence interval [CI], 4.5%–8%) in females, compared with 1.57% (95% CI, 1.04%–2.37%) in males. Ghods et al.,¹⁸ the ISUIA study,⁴ and Rincon et al.^{19,20} have reported similar findings.

The heavy smokers in our cohort had an AR prevalence of 56%. Previously, Can et al.²¹ reported a similarly high prevalence (45%–75%) of aSAH in heavy smokers compared with a 30% rate in nonsmokers, which was also associated with small aneurysm size (median, 6 mm; range, 1–27 mm).²¹ Similar results have been published in Stroke, reporting that patients smoking >15 packs/year have a 43% risk of aSAH ($P = 0.05$).²² In our cohort, the average size of AR in women with a history of smoking

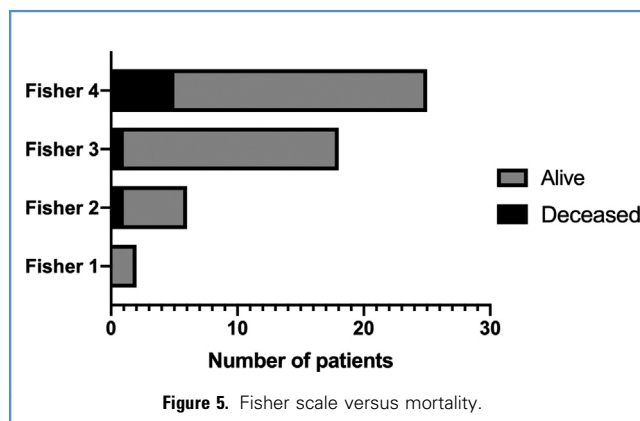


Figure 5. Fisher scale versus mortality.

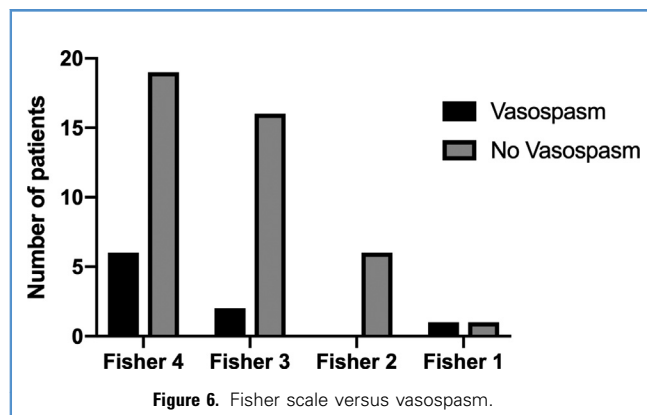


Figure 6. Fisher scale versus vasospasm.

suggests a higher incidence for smaller ruptures (4 mm in smokers vs. 5 mm in nonsmokers); however, these results were not statistically significant ($P = 0.877$, ANOVA) (Figure 5). The mechanisms behind this behavior may be related to tumor necrosis factor (TNF)- α , as a critical member of the immune system, associated with the activation of endothelial cells and macrophages.^{23,24} In other studies, a high phenotypic modulation in smooth muscle cells was observed, specifically in genes associated with vascular remodeling, such as MMP-3, VCAM-1, and IL-1 β .^{8,17,25} These results are in accordance with the reported decrease in the Aneurysm Rupture Index after treatment with a TNF- α inhibitor.²³

The average AR size in our population was smaller than that reported in previous studies (2.5 to 5 mm CI 95% 1.3 SD). These findings are in disagreement with previous studies such as that by Nabaweesii et al.,²⁶ who reported ARs of 1–27 mm, with an average size of 7–8 mm, but are supported by others, such as the Cooperative Aneurysm Study, which reported that 20% of ruptured aneurysms were <5 mm.²⁷ A literature review was performed (Table 5). The International Subarachnoid Aneurysm Trial (ISAT) reported an AR incidence of 53% ($P < 0.0001$) in surgically managed aneurysms measuring <5 mm and 40% in

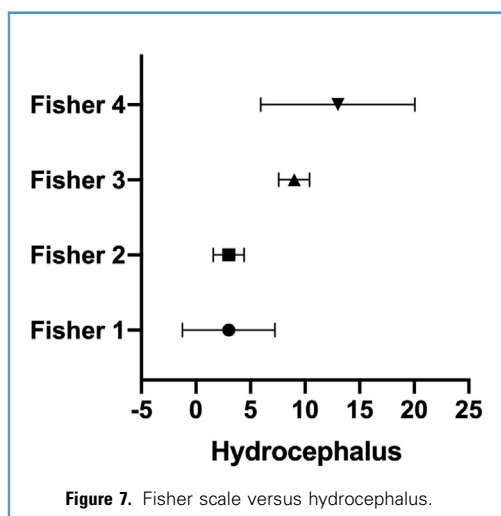


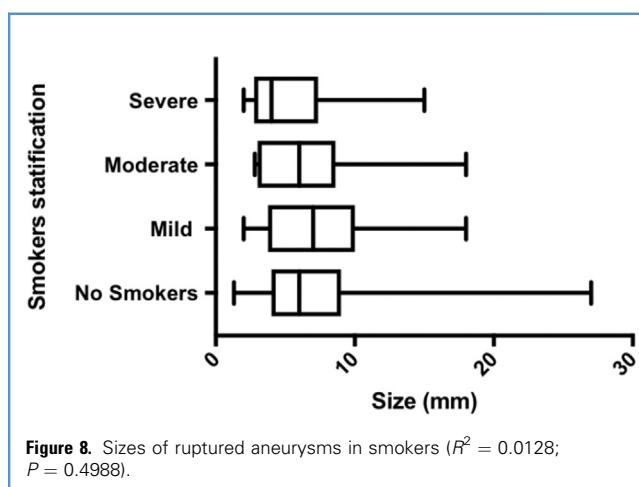
Figure 7. Fisher scale versus hydrocephalus.

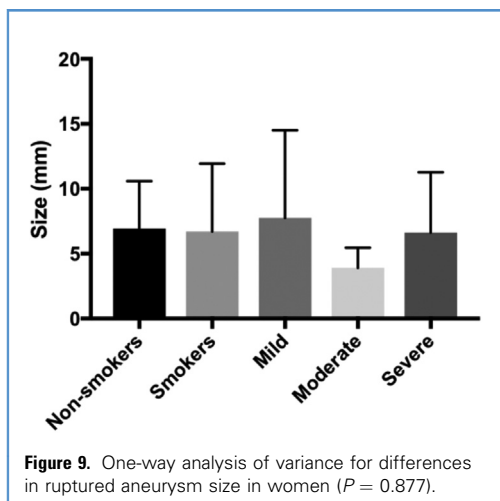
Table 3. Smoking Characterization by Amount of Calculated Packs/Year ($N = 53$)

Smoking Characterization	Size (mm)	Prevalence in the Population, % (n/N)	Prevalence of aSAH, %
Mild (0–5 packs/year)	6 (1–18)	13 (25/189)	25
Moderate (6–15 packs/year)	6.5 (1–18)	9 (15/189)	28
Severe (>16 packs/year)	3 (2–15)	7 (13/189)	56
No smokers	6 (1–27)		26

those measuring 6–10 mm.³⁶ In that same study, results for endovascular intervention showed an AR rate of 51% for aneurysms <5 mm. Some interesting results have been reported in the Japanese population. Morita et al.²⁹ reported an AR rate of 37% for aneurysms measuring 3–4 mm and 32.6% for those measuring 5–6 mm, with a total AR rate of almost 70% for aneurysms <7 mm. Ohashi et al.³² also reported a high prevalence of AR (74.3%) for aneurysms <10 mm (mean, 7.6 mm).³² Finally, Weir³⁴ reported a mean AR size of 5 mm. These findings suggest a trend toward smaller ruptured aneurysms than previously reported; however, possible confounding factors, including the tendency of the aneurysm wall to collapse after rupture, must be taken into account when considering this tendency. Bender et al.⁶ reported a decrease in average aneurysm size over a 25-year period, with an average size of 6 mm in 2012–2016, compared with 10.1 mm in 1991–1996, which may contribute to the lower average size of AR reported in more recent studies.

Hypotheses explaining the increasing rate of small ruptured aneurysms include improved aneurysm identification and endovascular innovations for treatment of large and giant aneurysms,³⁷ along with the recent more proactive approach to treating larger aneurysms with elective interventions, owing to the high risk associated with rupture.⁶

Figure 8. Sizes of ruptured aneurysms in smokers ($R^2 = 0.0128$; $P = 0.4988$).



In our center, which is classified as a reference center for neurosurgery in our country, the management of aneurysms includes an early intervention for aneurysms <10 mm, mainly in patients with such risk factors as hypertension and family history of AR. The choice between an endovascular treatment or a surgical approach is based on the feasibility of embolization, and difficult cases are revised weekly in an interdisciplinary meeting, including interventional radiology, to evaluate the best option available to the patient.

In the present study, the most common artery associated with symptomatic vasospasm was the internal carotid artery (37%; 10 of 27). In our cohort, mortality and the rate of vasospasm were higher at higher Fisher scale grades. However, in contraposition of the literature, the worst prognosis was found at Fisher grade 4 ($P = 0.2670$).

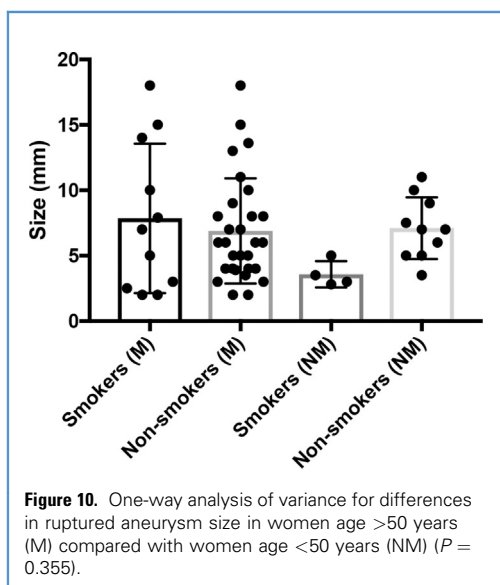


Table 4. Primary Area Involved in Symptomatic Vasospasm

Related Artery	%	n/N
Middle cerebral artery	15	5/32
Internal carotid artery		
General	37	11/32
Ophthalmic artery	45	5/11
Superior hypophyseal artery	9	1/11
Posterior communicating artery	9	1/11
Supraclinoidal portion	9	1/11
Anterior cerebral artery		
General	22	7/32
Pericallosal artery		
Anterior communicating artery	7	2/32
Basilar artery	15	5/32
Posterior cerebral artery	4	1/32
Posterior inferior cerebellar artery	4	1/32

Among pathological risk factors, hypertension was the most significant in our cohort (occurring in 51% of cases), in agreement with results reported by Tada et al.⁹ The ISUIA study reported a 43.6% prevalence of hypertension for the population with aneurysms in Europe, the United States, and Canada.⁴ A possible explanation for the relationship between hypertension and aneurysm formation could be associated with the nature of hypertension as a systemic inflammatory process in which endothelial remodeling is strongly affected^{9,15,38} and the disruption of normal hemodynamic behavior, which activates the renin-angiotensin pathway, changing vascular remodeling mechanisms¹⁰ and instigating migration of smooth muscle cells at sites of injury, contributing to destabilization of the aneurysm structure.^{5,10}

Limitations

A potential bias is related to our limited sample size. The individuals included in this study were patients with an existing clinical record in our institution, with no patients from private consult or public hospitals, thus limiting the sample. A probability test showed a 78% probability of finding an association in our sample. Although this is an acceptable reduction in the probability of type II error, we encourage future research with a multicentric prospective cohort, involving a larger sample size and including such variables as smoking cessation as well as morphological variables suggested by Zuan et al,³⁹ such as height-width ratio, flow angle, and aneurysm width-parent artery diameter ratio.

CONCLUSION

Our results suggest a trend toward an increasing rate of AR in aneurysms smaller than 10 mm, with higher rates in 5–7 mm

Table 5. Literature Review of SAH Associated with Aneurysms of <10 mm

Study	Country/Region	Treatment	Number (%)	Size, mm	P Value	Size, mm, mean \pm SD	Artery, % (n)
Molyneux et al., 2002 ²⁸	ISAT	Surgery	572 (53)	<5	<0.0001		AComA, 50.5 (1084)
			426 (40)	6–10			
		Endovascular	552 (51)	<5			
			438 (41)	6–10			
UCAS Japan Investigators, 2012 ²⁹	Japan	Surgery	554 (18.2)	7–9	<0.001	6.1 \pm 3.8	MCA, 39.8 (1215)
			993 (32.6)	5–6			
			1132 (37.1)	3–4			
Forget et al., 2001 ³⁰	USA	Surgery	86 (35)	<5			AComA, 67; PComA, 42
			124 (50.6)	6–10			
Dolati et al., 2015 ³¹	Canada		46 (37)	<5	<0.001		AComA, 86.5; MCA, 39
			52 (42)	>5–10			
Ohashi et al., 2004 ³²	Japan	Surgery	208 (74.3)	<10		7.6	AComA, 39.7 (29)
Orz et al., 1997 ³³	Japan	Surgery	475 (64.6)	<5			AComA, 70.8; PComA, 5.1
			681 (73.9)	>5–10			
Weir, 2002 ³⁴	USA		6 (20)	<3		5	AComA, 35.0; MCA, 28.8
			60 (80)	4–10			
Yasui et al., 1996 ³⁵	Japan		16 (64)	<5			MCA, 28; AComA, 20
			6 (24)	>5–10			
Inagawa, 1990 ¹⁵	USA		18 (17)	<4		9.5	AComA, 30; ICA, 40
			50 (46)	5–9			

AComA, anterior communicating artery; ICA, internal carotid artery; MCA, middle cerebral artery; PComA, posterior communicating artery.

aneurysms. This trend is most prominent in women with heavy tobacco consumption. In addition, women in the 6th decade of life show a trend toward a higher incidence of ruptures, likely associated with hormonal changes related to perimenopause. Studies including European, Asian, and American women suggest that the prevalence of AR in aneurysms <10 mm is increasing. In our analysis of AR morphology and outcomes, aneurysm size represents only one aspect of a complex evaluation. Future research with multicentric prospective cohorts is needed to further evaluate risk factors and possible cofounders.

DECLARATION OF COMPETING INTEREST

The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

ACKNOWLEDGMENTS

We thank the kind contribution of the Epidemiologic and Ethics Committee of the Santa Fe de Bogotá Foundation. We also thank Drs. Juan Fernando Ramon, Fernando Hakim, and Enrique Jimenez Hakim, without whom this work would not have been possible.

REFERENCES

- Yoneoka Y, Takeda N, Akira I, et al. Ruptured de novo intracranial aneurysms. *Acta Neurochir (Wien)*. 2004;146:979-981 [discussion: 981].
- Kayembe KN, Sasahara M, Hazama F. Cerebral aneurysms and variations in the circle of Willis. *Stroke*. 1984;15:846-850.
- Rahman M, Smietana J, Hauck E, et al. Size ratio correlates with intracranial aneurysm rupture status: a prospective study. *Stroke*. 2010;41:916-920.
- Allcock JM, Drake CG. Ruptured intracranial aneurysms—the role of arterial spasm. *J Neurosurg*. 1965;22:21-29.
- Bender MT, Wendt H, Monarch T, et al. Small aneurysms account for the majority and increasing percentage of aneurysmal subarachnoid hemorrhage: a 25-year, single institution study. *Neurosurgery*. 2018;83:692-699.
- Mason AM, Cawley CM, Barrow DL. Surgical management of intracranial aneurysms in the endovascular era: review article. *J Korean Neurosurg Soc*. 2009;45:133-142.
- Santiago-Dieppa DR, Pannell JS, Khalessi AA. Endovascular and surgical options for ruptured middle cerebral artery aneurysms: review of the literature. *Stroke Res Treat*. 2014;2014:315906.
- Tulamo R, Niemelä M. Smoking and cerebral aneurysms—potential pathobiologic mechanisms. *World Neurosurg*. 2014;82:e79-e80.
- Tada Y, Wada K, Shimada K, et al. Roles of hypertension in the rupture of intracranial aneurysms. *Stroke*. 2014;45:579-586.
- Peña Silva RA, Kung DK, Mitchell JJ, et al. Angiotensin 1-7 reduces mortality and rupture of

- intracranial aneurysms in mice. *Hypertension*. 2014; 64:362-368.
11. Morton SC, Costlow MR, Graff JS, Dubois RW. Standards and guidelines for observational studies: quality is in the eye of the beholder. *J Clin Epidemiol*. 2016;71:3-10.
 12. University of Bern. STROBE Statement: STROBE checklists. Available at: <https://www.strobe-statement.org/index.php?id=available-checklists>. Accessed July 30, 2017.
 13. Vlak MH, Algra A, Brandenburg R, Rinkel GJ. Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and time period: a systematic review and meta-analysis. *Lancet Neurol*. 2011;10:626-636.
 14. Vlak MH, Rinkel GJ, Greebe P, Algra A. Risk of rupture of an intracranial aneurysm based on patient characteristics. *Stroke*. 2013;44:1256-1259.
 15. Inagawa T. Risk factors for the formation and rupture of intracranial saccular aneurysms in Shimane, Japan. *World Neurosurg*. 2010;73:155-164 [discussion: e23].
 16. Yoshimoto Y, Tanaka Y, Hoya K. Acute systemic inflammatory response syndrome in subarachnoid hemorrhage. *Stroke*. 2001;32:1989-1993.
 17. Chalouhi N, Ali MS, Jabbour PM, et al. Biology of intracranial aneurysms: role of inflammation. *J Cereb Blood Flow Metab*. 2012;32:1659-1676.
 18. Ghods AJ, Lopes D, Chen M. Gender differences in cerebral aneurysm location. *Front Neurol*. 2012;3:78.
 19. Rincon F, Rossenwasser RH, Dumont A. The epidemiology of admissions of nontraumatic subarachnoid hemorrhage in the United States. *Neurosurgery*. 2013;73:217-222 [discussion: 212-213].
 20. Hamdan A, Barnes J, Mitchell P. Subarachnoid hemorrhage and the female sex: analysis of risk factors, aneurysm characteristics, and outcomes. *J Neurosurg*. 2014;121:1367-1373.
 21. Can A, Castro VM, Ozdemir YH, et al. Association of intracranial aneurysm rupture with smoking duration, intensity, and cessation. *Neurology*. 2017; 89:1408-1415.
 22. Bonita R. Cigarette smoking, hypertension and the risk of subarachnoid hemorrhage: a population-based case-control study. *Stroke*. 1986; 17:831-835.
 23. Starke RM, Chalouhi N, Jabbour PM, et al. Critical role of TNF- α in cerebral aneurysm formation and progression to rupture. *J Neuroinflammation*. 2014; 11:77.
 24. Jayaraman T, Paget A, Shin YS, et al. TNF-alpha-mediated inflammation in cerebral aneurysms: a potential link to growth and rupture. *Vasc Health Risk Manag*. 2008;4:805-817.
 25. Santiago-Sim T, Kim DH. Pathobiology of intracranial aneurysms. In: Winn HR, ed. *Youmans Neurological Surgery*. 6th ed. Vol. 4. Philadelphia, PA: Elsevier, Saunders; 2011:3747-3755.
 26. Nabaweesi-Batuka J, Kitunguu PK, Kiboi JG. Pattern of cerebral aneurysms in a Kenyan population as seen at an urban hospital. *World Neurosurg*. 2016;87:255-265.
 27. Kassell NF, Torner JC, Jane JA, Haley EC Jr, Adams HP. The International Cooperative Study on the Timing of Aneurysm Surgery. Part 2: Surgical results. *J Neurosurg*. 1990;73:37-47.
 28. Molyneux A, Kerr R, International Subarachnoid Aneurysm Trial (ISAT) Collaborative Group, et al. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomized trial. *J Stroke Cerebrovasc Dis*. 2002;11:304-314.
 29. UCAS Japan Investigators, Morita A, Kirino T, et al. The natural course of unruptured cerebral aneurysms in a Japanese cohort. *N Engl J Med*. 2012;366:2474-2482.
 30. Forget TR Jr, Benitez R, Veznedaroglu E, et al. A review of size and location of ruptured intracranial aneurysms. *Neurosurgery*. 2001;49:1322-1325 [discussion: 1325-1326].
 31. Dolati P, Pittman D, Morrish WF, Wong J, Sutherland GR. The frequency of subarachnoid hemorrhage from very small cerebral aneurysms (<5 mm): a population-based study. *Cureus*. 2015; 7:e279.
 32. Ohashi Y, Horikoshi T, Sugita M, Yagishita T, Nukui H. Size of cerebral aneurysms and related factors in patients with subarachnoid hemorrhage. *Surg Neurol*. 2004;61:239-245 [discussion: 245-247].
 33. Orz Y, Kobayashi S, Osawa M, Tanaka Y. Aneurysm size: a prognostic factor for rupture. *Br J Neurosurg*. 1997;11:144-149.
 34. Weir B. Unruptured intracranial aneurysms: a review. *J Neurosurg*. 2002;96:3-42.
 35. Yasui N, Magarisawa S, Suzuki A, Nishimura H, Okudera T, Abe T. Subarachnoid hemorrhage caused by previously diagnosed, previously unruptured intracranial aneurysms: a retrospective analysis of 25 cases. *Neurosurgery*. 1996;39: 1096-1100 [discussion: 1100-1101].
 36. Molyneux AJ, Kerr RS, Yu LM, et al. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. *Lancet*. 2005;366: 809-817.
 37. Thompson BG, Brown RD Jr, Amin-Hanjani S, et al. Guidelines for the management of patients with unruptured intracranial aneurysms: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2015;46:2368-2400.
 38. Weiss D, Taylor WR. Deoxycorticosterone acetate salt hypertension in apolipoprotein E^{-/-} mice results in accelerated atherosclerosis the role of angiotensin II. *Hypertension*. 2008;51:218-224.
 39. Duan Z, Li Y, Guan S, et al. Morphological parameters and anatomical locations associated with rupture status of small intracranial aneurysms. *Sci Rep*. 2018;8:6440.

Previous Presentations: XXVIII National Congress of Neurosurgery. Sponsoring society: Colombian Association of Neurosurgery, Date: April 18/ 2018, Location: Dann Carlton Hotel. Barranquilla – Atlántico, Colombia. Presentation type: Plenary.

Received 21 November 2018; accepted 13 May 2019

Citation: *World Neurosurg*. X (2019) 4:100038.
<https://doi.org/10.1016/j.wnsx.2019.100038>

Journal homepage: www.journals.elsevier.com/world-neurosurgery-x

Available online: www.sciencedirect.com

2590-1397/© 2019 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).