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Epidemiological analysis of 1404 patients with intracranial aneurysm followed in a single Brazilian institution

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ABSTRACT

Background: We sought to evaluate the epidemiology of intracranial aneurysms in relation to location, gender, age, presence of multiple aneurysms, and comorbidities in the Brazilian population.

Methods: We performed a prospective analysis of a cohort of 1404 patients diagnosed with intracranial aneurysm admitted to the Hospital das Clinicas of the University of Sao Paulo, a referral hospital for the treatment of cerebrovascular diseases in Brazil. Patients admitted between September 2009 and September 2018 with radiological diagnosis of intracranial aneurysm were included in the study.

Results: A total of 2251 aneurysms were diagnosed. Females accounted for 1090 aneurysms (77.6%) and the mean age at diagnosis was 54.9 years (ranging 15–88). The most common location was middle cerebral artery (MCA) with 593 aneurysms (26.3%) followed by anterior cerebral artery (ACA) with 417 aneurysms (18.5%) and internal carotid artery in the posterior communicating segment with 405 aneurysms (18.0%). Males had higher rates of ACA aneurysms (29.7%) while females had higher rates of MCA aneurysms (26.1%). Sorting by size, 492 aneurysms were <5 mm (21.8%), 1524 measured 5–10 mm (67.7%), 119 size 11–24 mm (5.3%), and 116 were >24 mm (5.2%). The occurrence of multiple aneurysms was associated with female gender ($P < 0.001$) and smoking ($P < 0.001$), but not with hypertension ($P = 0.121$).

Conclusion: In this population, the occurrence of intracranial aneurysm is related to several factors, including gender, age, smoking, and hypertension. Our study brought to light important characteristics of a large number of Brazilian patients regarding epidemiology, location, size, and multiplicity of intracranial aneurysms.

Keywords: Epidemiology, Gender, Intracranial aneurysms, Risk factors, Smoking, Vascular disorders

INTRODUCTION

Intracranial aneurysms are the leading cause of spontaneous subarachnoid hemorrhage (SAH) accounting for up to 85% of cases.[5] It is estimated that half a million people every year suffer from aneurysmal SAH.[9] The mortality rate in SAH is 25–50% and half of the survivors become dependent on activities of daily living.[23] Several risk factors appear to be associated with the development of intracranial aneurysms, including age, female gender, genetic factors, smoking, and hypertension.[2]

Several epidemiological studies evaluated the prevalence of aneurysms and the risk of rupture.[10,12,21] Among the observed factors, aneurysm location, age, female gender, hypertension, history of SAH, aneurysm size, and symptomatic aneurysms have an increased risk of rupture.[7,24] Geographic location, probably due to genetics specific environmental, factors are an another important risk factor. Finnish or Japanese patients have a greater risk of aneurysm rupture than the European or North American population.[7] Although geographic location is an important risk factor for the development and rupture of intracranial aneurysm, few studies on this subject are performed in Brazil or in Latin America.[9,22]

In this study, we sought to analyze the epidemiology of intracranial aneurysms regarding location, gender, age, presence of multiple aneurysms, and comorbidities in the Brazilian population. These data might bring to light singular epidemiologic characteristics regarding intracranial aneurysm in the Brazilian and Latin American population.

PATIENTS AND METHODS

This study was carried out through a prospective analysis of a cohort of 1404 consecutive patients diagnosed with intracranial aneurysm admitted to the Hospital das Clinicas of the School of Medicine of the University of Sao Paulo, a referral hospital for the treatment of cerebrovascular diseases in Brazil. Data collection occurred between September 2009 and September 2018. Patients admitted to the emergency department with a history of SAH and ruptured aneurysm or patients evaluated at the outpatient clinic with unruptured intracranial aneurysms were included in the study. All patients underwent a digital subtraction angiography or a computed tomography angiography and only those with a confirmed diagnosis of intracranial aneurysm remained in the study.

Information on the location, size, and number of aneurysms were obtained by reports of neuroradiologists. The size used in the analysis corresponds to the biggest diameter of the aneurysm. Patients or family members reported the presence of comorbidities such as smoking and hypertension.

Data analysis was carried out using JASP 0.9.0.1 (2018, Amsterdam, The Netherlands). Student's *t*-test was the standard test choice, but in most cases, Mann–Whitney U-test was the chosen test due to violation of equal variances assumptions evidenced by Levene's test. Significance was established at $P < 0.05$.

RESULTS

Patient characteristics are listed in Table 1. A total of 1404 patients were included in the study. Females accounted for 1090 (77.6%), and the mean age was 54.9 years ranging from 15 to 88 years. The mean age of men and women was 52.4 years and 55.6 years, respectively, accounting for a significant difference ($P < 0.001$). The overall distribution of ages is shown in Figure 1. Among the patients, 773 (57.3%) were smokers and 929 (66.2%) of them reported a history of systemic arterial hypertension. The majority of the aneurysms measured between 5 mm and 10 mm (67.7%). Table 1 presents the size of aneurysms, grouped by gender, smoking status, and systemic arterial hypertension.

Location

The most common location was middle cerebral artery (MCA) with 593 aneurysms (26.3%), followed by anterior cerebral artery (ACA) with 417 aneurysms (18.5%) and posterior communicating segment (PComm) of the internal carotid artery with 405 aneurysms (18%). Posterior circulation (Post) aneurysms accounted for only 6.7% (152) of all aneurysms in this study. All other locations are depicted in Figure 2.

Aneurysm location prevalence was different among males and females, as shown in Tables 2 and 3. Males had higher rates of ACA aneurysms (29.7%), followed by MCA aneurysms (27.3%), PComm aneurysms (14.6%), and posterior circulation aneurysms (12%). Females, on the other hand, had higher prevalence of MCA aneurysms (26.1%), followed by PComm aneurysms (18.8%), ophthalmic segment of the internal carotid artery aneurysms (17%), and ACA aneurysms (16%).

In sum, males were more prone to posterior circulation aneurysms when compared to females (10.2% vs. 3.4%), and this difference was statistically significant ($\chi^2 = 21.400$, $P < 0.001$). Neither hypertension ($\chi^2 = 3.464$, $P = 0.18$) nor smoking ($\chi^2 = 4.801$, $P = 0.09$) were significantly associated with location differences.

Multiple aneurysms

We diagnosed 2251 aneurysms, which yield a ratio of approximately 1.6 aneurysms per patient. Altogether, 511 (36.4%) patients had multiple aneurysms.

Table 1: Characteristics of patients.

Characteristics	Patients (*n*=1404)
Age	
Mean – years (±SD)	55.9 (±12.3)
>70 years – *n* (%)	138 (9.8)
Gender	
Female – *n* (%)	1090 (77.6)
Male – *n* (%)	314 (22.4)
Hypertension – *n* (%)	929 (66.2)
Former or current smoking – *n* (%)	773 (57.3)
Multiplicity of aneurysms	
Single – *n* (%)	893 (63.6)
Multiple – *n* (%)	511 (36.4)

SD: Standard deviation

Table 2: Number of aneurysms depicted by location and size in female patients.

Location	<5 mm	5–10 mm	11–24 mm	>24 mm	Total (%)
ICA	195	606	69	89	959 (52.3)
Cav	60	63	25	64	212 (11.6)
Opht	70	201	23	18	312 (17)
PComm	38	285	16	5	344 (18.8)
ACh	18	26	0	0	44 (2.4)
Bifurcation	9	31	5	2	47 (2.6)
MCA	130	325	18	6	479 (26.1)
ACA	69	220	3	1	293 (16)
Post	31	63	2	6	102 (5.6)
Total (%)	425 (23.2)	1214 (66.2)	92 (5)	102 (5.6)	1833

ICA: Internal carotid artery, Cav: Cavernous segment, Opht: Ophthalmic segment, PComm: Posterior communicating segment, ACh: Anterior choroidal segment, MCA: Middle cerebral artery, ACA: Anterior cerebral artery, Post: Posterior circulation

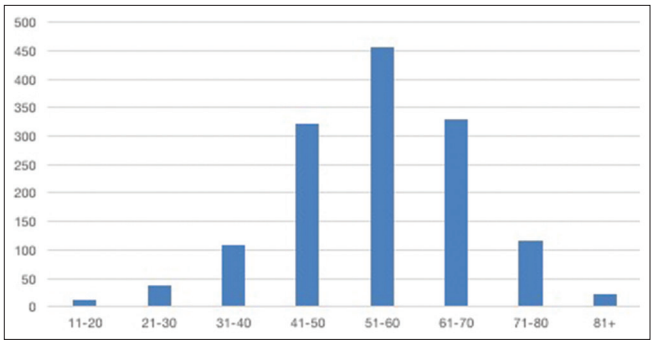

Figure 1: Distribution of patients with intracranial aneurysms according to age.

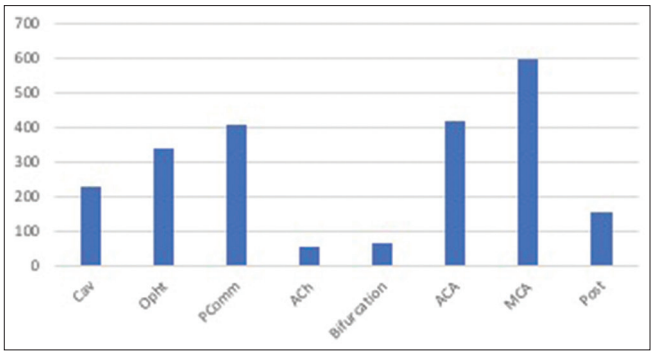

Figure 2: Number of aneurysms depicted by location. ICA: Internal carotid artery, Cav: Cavernous segment, Opht: Ophthalmic segment, PComm: Posterior communicating segment, ACh: Anterior choroidal segment, MCA: Middle cerebral artery, ACA: Anterior cerebral artery, Post: Posterior circulation.

Female gender was associated with a higher prevalence of multiple aneurysms, with an average 1.682 against 1.331 aneurysms among men (W = 202,856.0, $P < 0.001$).

Smoking was also associated to higher number of multiple aneurysms (W = 219,393.0, $P < 0.001$), with smokers harboring an average 1.691 aneurysms against 1.496 for nonsmokers (W = 219,393.0, $P < 0.001$).

Systemic arterial hypertension was not associated to multiple aneurysms (W = 211,110.5, $P = 0.121$, respectively).

DISCUSSION

We performed an epidemiological analysis of Brazilian patients diagnosed with cerebral aneurysms during almost a decade. In this study, we found 2251 aneurysms in 1404 patients with a 3.4 female/male ratio. Among the females, we found a higher incidence of MCA aneurysms. The preferential location of aneurysm in males was the ACA. The vast majority of the aneurysms was located in the anterior circulation and measured between 5 mm and 10 mm. About a third of the patients had more than one intracranial aneurysm.

To the best of our knowledge, this is the largest study involving Latin American patients diagnosed with intracranial aneurysms. Other studies have demonstrated the burden of the geographic location for the development and rupture of intracranial aneurysms.[7,10,21] The lack of data regarding cerebral aneurysms in certain geographical areas has been brought to light by Hughes *et al.*[9]

In our study, we found a higher rate of female patients with cerebral aneurysms (77.6%). This trending was also true in other studies performed worldwide. When analyzing studies that stratify the gender percentage in a series of patients with intracranial aneurysms,[22] the female rates were 54% in Finnish studies,[10,21] 62% in a Chinese study,[26] 68% in a Japanese study,[21] and about 72% for the populations of North America and Europe.[25] Therefore, even though our data are consistent with those studies, it seems that the Brazilian percentage of female patients with cerebral aneurysm is much higher than in other countries.

The mean age of the patients studied was 54.9 years, consistent with other studies that show an average age of 50 years for the world population diagnosed with intracranial aneurysm.[22] Another interesting finding was that the

Table 3: Number of aneurysms depicted by location and size in male patients.

Location	<5 mm	5–10 mm	11–24 mm	>24 mm	Total (%)
ICA	20	90	12	8	130 (31.1)
Cav	6	5	1	4	16 (3.8)
Opht	6	15	5	2	28 (6.7)
PComm	5	48	6	2	61 (14.6)
ACh	0	9	0	0	9 (2.2)
Bifurcation	3	13	0	0	16 (3.8)
ACA	19	103	2	0	124 (29.7)
MCA	20	83	8	3	114 (27.3)
Post	8	34	5	3	50 (12)
Total (%)	67 (16)	310 (74.2)	27 (6.5)	14 (3.3)	418

ICA: Internal carotid artery, Cav: Cavernous segment, Opht: Ophthalmic segment, PComm: Posterior communicating segment, ACh: Anterior choroidal segment, MCA: Middle cerebral artery, ACA: Anterior cerebral artery, Post: Posterior circulation

average age of female was greater than that of male (55.6 and 52.4 years, respectively). This finding may result from the hypothesized protective vascular effects of estrogen until menopause.[16] This happens presumably through inhibition of nuclear factor kappa-B and other inflammatory cytokines, impairing adhesion of leukocytes to cerebral vascular endothelium.[3]

Smoking and hypertension were reported in 57.3% and 66.2% of the patients, respectively. Both risk factor rates are significantly higher than nationwide or even state-based general statistics on smoking[15] and hypertension[1] in the Brazilian population, sustaining the association of these factors with intracranial aneurysms.

Aneurysms from the anterior circulation were far more common than vertebrobasilar aneurysms (93.2% vs. 6.7%) reproducing international findings.[22] The most common location among females was the MCA, but males presented higher rates of ACA aneurysms. This higher prevalence of ACA aneurysms in male was previously evidenced in other studies.[22] However, the higher prevalence of MCA aneurysms among females seems to be a singular feature of Brazilians.[6,8,19]

The reasons behind this distinctness remain subject of debate. Recent studies of computational fluid dynamics highlight the hemodynamics of blood flow as an important contributor to the development and rupture of intracranial aneurysms.[13] Lindekleiv *et al.*[14] described a significant difference in the diameter of the intracranial arteries, with females presenting smaller diameter arteries than males. Moreover, in simulations with computational fluid dynamics, a higher wall shear stress was found at the MCA bifurcation of females compared with males. These findings may help clarify the differences in intracranial aneurysms regarding gender.

Our results showed that most of the aneurysms found were between 5 mm and 10 mm in size. The previous studies have shown a higher rupture rate between aneurysms larger than 5 mm in size.[24] However, when we analyzed the relationship between the size of the aneurysm and hypertension, smoking status, or gender, we did not find a significant correlation.

Multiple aneurysms were found in 36.4% of patients, a slightly higher prevalence than the previous studies has shown.[4,11] Multiplicity was associated with female gender and smoking ($P < 0.001$), as described in other international studies.[17,18,20]

Data like these provide relevant data on the distribution of aneurysm's prevalence worldwide, help to understand specific features of a given population, and delineate public health policies. Significant limitations of our study include being conducted in a single institution, although a referral center for cerebrovascular diseases. However, we encompass a large number of individuals and have provided important insights into cerebral aneurysm epidemiological characteristics for Brazilian and Latin American population.

CONCLUSION

The occurrence of intracranial aneurysm is related to several factors, including gender, age, smoking, hypertension, and geographical location. Our study brought to light important characteristics of a large number of Brazilian patients regarding epidemiology, location, size, and multiplicity of intracranial aneurysms. In addition, this paper fulfills a lack that existed when studying the prevalence of intracranial aneurysms in our continent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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