

PREVALENCE OF INCIDENTAL BRAIN ANEURYSMS BETWEEN MEN AND WOMEN

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ABSTRACT: Verifying the prevalence of incidental cerebral aneurysm diagnosed by magnetic resonance imaging (MRI) between men and women. This research is a descriptive retrospective, database-based cohort study. The sample is composed of 1,545 patients. We use cross-tabulations to perform the absolute and relative frequencies. The Mann-Whitney U-Test was used to compare results between sexes. Incidental aneurysms have a higher relative frequency in women. The age of the highest incidence is 51 to 60 years for both genders. The risk factors present in both sexes are hypertension, dyslipidemia, smoking, diabetes, and polycystic kidneys. The women present a higher incidence of aneurysms in the posterior communicating arteries and internal carotid artery. For the men, there is a higher incidence of aneurysms in the anterior communicating arteries and the basilar artery. Modifiable risk factors are mostly responsible for the growth and development of aneurysms. In sum, the prevalence of incidental cerebral aneurysms in women occurs in a 3: 1 ratio to men, but this prevalence ranged from 2:1 to 9:1 among the years surveyed.

KEY WORDS: Intracranial Aneurysm; Cerebral hemorrhage; Stroke.

PREVALÊNCIA DE ANEURISMAS CEREBRAIS INCIDENTAIS ENTRE HOMENS E MULHERES

RESUMO: Verificar a prevalência de aneurisma cerebral incidental, diagnosticados por meio de ressonância magnética entre homens e mulheres. Trata-se de um estudo de coorte retrospectivo descritivo, baseado em banco de dados. A amostra é composta por 1.545 pacientes. Foram feitas tabulações cruzadas considerando as frequências absoluta e relativa. Utilizou-se o teste U de *Mann-Whitney* para comparar resultados entre sexos. Os aneurismas incidentais têm maior frequência relativa em mulheres. A idade de maior incidência é de 51 a 60 anos para ambos os sexos. Os fatores de risco presentes em ambos os sexos são hipertensão arterial, dislipidemia, tabagismo, *diabetes* e rins policísticos. As mulheres apresentam maior prevalência de aneurismas nas artérias comunicante posterior e artéria carótida interna. Os homens nas artérias comunicante anterior e artéria basilar. Os fatores de risco modificáveis são responsáveis em grande medida pelo crescimento e desenvolvimento de aneurismas. Em suma, a prevalência de aneurismas cerebrais incidentais em mulheres ocorre na proporção 3:1 em relação aos homens, porém esta prevalência variou de 2:1 a 9:1 entre os anos pesquisados.

PALAVRAS-CHAVE: Aneurisma intracraniano; Hemorragia cerebral; Acidente vascular cerebral.

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INTRODUÇÃO

Aneurysms are pathological dilations that occur at the most fragile points along the blood vessel wall (usually an artery) as a result of the increased hemodynamic pressure they are subject to.¹

Cerebral aneurysms are present in approximately 3.2% of the world population, with an average age of 50 years, proportionally in both sexes.² Intracranial aneurysms are of particular interest, due to the high rate of morbidity and mortality associated to its rupture, leading to subarachnoid hemorrhage (SAH).³⁻⁵

Approximately 5% of new strokes are due to subarachnoid hemorrhage (SAH), related to aneurysm rupture with nearly 500,000 deaths per year worldwide.⁶

SAH is responsible for almost 12% of patient deaths before undergoing treatment, and 30% of hospitalized patients die within a month after the event. Of those who survive, a third have neurological sequelae with loss of quality of life.⁷

This type of aneurysm is silent or asymptomatic, diagnosed incidentally through clinical examinations, family occurrence, complaints unrelated to the event and by neuroimaging.⁸⁻¹⁰ These aneurysms constitute 17% to 37% of all non-ruptured aneurysms.⁹

With the increase in life expectancy and the advancement of non-invasive and diversified technology, the detection and accuracy of incidental brain aneurysms have become more common. However, despite these research tools, studies on the prevalence of these aneurysms are still scarce. The literature describes great variation in the predominance of these aneurysms, as well as their natural history, possibly attributed by the evaluation methods employed.¹¹

The etiology of the aneurysm is multifactorial. In addition to environmental or modifiable factors, such as arterial hypertension, smoking, oral contraceptives, chronic alcoholism, hyperlipidemia, and diabetes mellitus, there are also non-modifiable risk factors. Non-modifiable risk factors may be the family genetic predisposition, hemodynamic and hormonal factors, sex, Ehlers-Danlos, and polycystic kidneys. All of these factors contribute to the formation of the aneurysm.¹²⁻¹⁴

Although it is not possible to act directly on these non-modifiable risk factors, it is essential to know about them to improve performance in risk groups. The

improvements may happen through the implementation of screening programs that contribute to reducing mortality and associated complications, as well as techniques for managing cerebral aneurysm in predicting patient prognosis.

Thus, this study aims to verify the prevalence of incidental cerebral aneurysm, diagnosed through computed tomography, among men and women at a referral service.

METHODOLOGY

This research is a descriptive retrospective cohort study, based on data from January 2006 to December 2017, in patients affected by intracranial aneurysms, seen at a referral hospital.

The database provided by the Hospital had a sample of 1,545 patients. We transferred the data to a spreadsheet for treatment and data presentation data using graphs and tables.

The parameters evaluated in this study were sex, age, aneurysm location, size, morphology, and registered risk factors.

Cross tabulations were made, considering the absolute and relative frequencies. To verify the differences between men and women, we used nonparametric tests for independent samples, such as the Mann-Whitney U test, with a p-value of less than 0.05 as a parameter. We used the statistical software SPSS (Statistical Package for Social Sciences) version 22 to perform the analysis.

As for ethical aspects, the study is approved by the Ethics and Research Committee (CEP) under protocol No. 14903519.0.0000.5370. This part of the project "Epidemiological Characteristics of Stroke in the Population of the municipality of Blumenau: retrospective and prospective study," registered at Plataforma Brasil

RESULTS

In the sample studied, there were 1,545 cases of aneurysms from 2006 to 2017. Of these, 938 cases were incidental, corresponding to 61% of the sample. The occurrence of incidental aneurysms was prevalent among women, corresponding to 76% of the sample, as shown in Table 1.

Table 1. Incidence of aneurysms by type and gender

Gender	Aneurysms				Total	
	Not incidental		Incidental		n	%
	n	%	n	%		
Female	427	70%	713	76%	1140	74%
Male	180	30%	225	24%	405	26%
TOTAL	607	39%	938	61%	1545	100%

Source: research data

The occurrence of incidental aneurysms over the years is higher among women. The case ratio between women and men varies between 2: 1 and 9: 1 representing, respectively, the years 2007 and 2016.

Concerning the age group, the highest incidence occurs in the age group 51 to 60 years, both for men and women. Although the percentage of men in this age group is higher than that of women, there is not a significant difference between the sexes (p-value = 0.084), according to Table 2.

We analyzed the risk factors between men and women to verify if there are significant differences between the sexes. Thus, the risk factors most present in patients with incidental aneurysms, men and women, are SAH (53%), dyslipidemia (31%), smoking (24%), DM (10%) and polycystic kidneys (1%). There were no statistically significant differences between men and women concerning the mentioned risk factors (p-value > 0.05).

Table 4 depicts the arteries affected by the aneurysm by gender. The highest frequency of aneurysms occurred in the bACM artery, with no differences between men and women (p-value = 0.503).

The rates of aneurysms in other arteries obtained statistical differences between genders. The incidence of incidental aneurysm occurs more frequently among women in the ACoP, ACI-O, and cv-ACI arteries. In contrast, for men, this frequency occurs in the ACoA and AB arteries. We did not mention the other arteries because the relative rate of incidental aneurysms in each one is less than 1%.

In terms of laterality, 54% of incidental aneurysms occur on the left side, between men and women. Thus, there was no statistical difference between men and women regarding the laterality of the aneurysm (p-value = 0.953).

Small aneurysms are more frequent (70%), followed by large (18%) and giant (12%). Regarding the size of the aneurysm, there was no significant difference between men and women (p-value = 0.177; 0.808 and 0.102, respectively).

Regarding the aneurysm type, 94% are saccular, with higher frequency in women (96% and p-value = 0.000), followed by fusiform with 3% relative frequency, occurring in most of the cases in men (9% and p-value = 0.000).

Table 2. Incidence of incidental aneurysms by sex and age group

Age group	Female		Male		Total		p-value
	n	%	n	%	n	%	
Up to 30 years	17	2%	8	4%	25	3%	0,342
31 - 40 years	61	9%	15	7%	76	8%	0,366
41 - 50 years	172	24%	48	21%	220	23%	0,389
51 - 60 years	204	29%	78	35%	282	30%	0,084
61 - 70 years	174	24%	48	21%	222	24%	0,345
71 - 80 years	76	11%	24	11%	100	11%	0,997
Over 80 years	9	1%	4	2%	13	1%	0,686
TOTAL	713	100%	225	100%	938	100%	

Source: research data

Table 3. Risk factors for incidental aneurysms by sex

Risk Factors	Sex						p-value
	Female		Male		Total		
	n	%	N	%	n	%	
DM	67	9%	27	12%	94	10%	0,254
SAH	380	53%	116	52%	496	53%	0,702
Smoking	169	24%	57	25%	226	24%	0,655
Dyslipidemia	218	31%	70	31%	288	31%	0,869
Polycystic kidneys	4	0%	1	0%	5	1%	1,000

Source: research data

Table 4. Arteries affected by incidental aneurysms by sex

Arteries	Female		Male		Total		p-value
	n	%	N	%	n	%	
	bACM	118	16,5%	33	14,7%	151	
ACoP	125	17,5%	25	11,1%	150	16,0%	0,022
ACI-O	114	16,0%	19	8,4%	133	14,2%	0,005
cv-ACI	93	13,0%	16	7,1%	109	11,6%	0,016
ACoA	62	8,7%	45	20,0%	107	11,4%	0,000
AB	28	3,9%	21	9,3%	49	5,2%	0,001
ACI-Po	29	4,1%	8	3,6%	37	3,9%	0,731
Other arteries	144	20,2%	58	25,8%	202	21,5%	-
TOTAL	713	100,0%	225	100%	938	100,0%	

Note: bACM: bifurcation of the middle cerebral artery; ACoP: posterior communicating artery; ACI-O: internal carotid artery-sec. Ophthalmic; cv-ACI: carotid artery sec. cavernous; ACoA: anterior communicating artery; AB: basilar artery; ACI-Po: internal carotid artery according to paraophthalmic

Table 5. Type of incidental aneurysms by sex

Type	Female		Male		Total		p-value
	n	%	n	%	n	%	
	Sacular	682	96%	198	88%	880	
Fusiform	11	2%	20	9%	31	3%	0,000
Dissecting	4	1%	3	1%	7	1%	0,241
Nipple	5	1%	2	1%	7	1%	0,776
Others	11	2%	2	1%	13	1%	-
TOTAL	713	100%	225	100%	938	100%	

Source: research data

The dissecting and nipple types have a relative frequency of 1% each, with no statistical differences between men and women (p-value = 241 and 0.776, respectively).

DISCUSSION

The present study raised the prevalence of incidental cerebral aneurysm among men and women. As a result, 76% of incidental aneurysms are present in women, against 24% in men. Similar studies evaluated the influence of risk factors on mortality from cerebral aneurysm¹⁵ and their anatomical distribution among men and women.¹⁶ The results obtained were more prevalent in women than in men, in both cases of 72%. Other studies¹⁷⁻¹⁹ also revealed the prevalence of incidental aneurysms in females.

We observed over the years, a growth rate of the aneurysm much higher in women than in men. In 2007, the ratio was 2: 1, and in 2016, 9: 1. Although the literature argues that there is a higher incidence of aneurysms in women, there is no explanation for this discrepancy between the sexes.

In addition to the prevalence, we identified the location of the aneurysms. A higher prevalence of aneurysms was observed among women in the posterior cerebral artery (ACoP) ($p = 0.022$), internal cerebral artery (ACI-o) ($p = 0.005$) and cavernous internal carotid artery (cv-ACI, p -value = 0.016).

In studies by Lindekleiv et al.,²⁰ and Horikoshi et al.,²¹ the hemodynamic mechanism in the blood vessels of the Willis circle between men and women are compared, they demonstrated a difference in the diameter of the blood vessels between the sexes. Since the vessels of a smaller caliber are found in women and have a higher blood flow speed, leading to greater tension in the vessel walls, especially in the ICA bifurcations, which favors aneurysmatic formation in women. This correlation has also been demonstrated in other studies,²² through mathematical models. The shear stress depends on the topography of the vessels.

Among men, the anterior communicating artery (ACoA) ($p = 0.000$) and basilar artery (AB) ($p = 0.001$) were more frequent, corroborating with previously published results,^{20,21} in which the highest incidence of aneurysm also occurred in these vessels.

Concerning laterality in the cerebral hemispheres, there was no statistical difference between men and women (p -value = 0.953). This study also found that

there is no significant difference between the sexes to the age range of incidental aneurysm. There is a great inclination in the ages group 41 to 50 years and 61 to 70 years, in women. In these age groups, there is the post-menopausal decline in the estrogen level. The drop in estrogen reduces endothelial protection, weakening vascular integrity and hemodynamic factors, causing vessel stress, leading to a possible risk of aneurysm formation²³.

This association is also present in research carried out on animals, proving the protective factor of β -estrogen against the formation of intracranial aneurysms in female ovariectomized mice²⁴ and humans, among women of older age^{18,25}.

In a meta-analysis,¹² environmental risk factors, such as hypertension, smoking, dyslipidemia, and diabetes, were the main predictors found for the formation of aneurysms, with an equal proportion between genders²⁶. Likewise, there are no statistically significant differences between men and women in this study. The risk factors raised were similar to those found in the literature. However, our analysis showed a prevalence of SAH, as a more prevalent predictor among patients, similar to other studies^{24,27}.

With the advent of modern diagnostic imaging techniques, the discovery of incidental aneurysms has been growing. However, we observed variations in the prevalence in previous studies, presumably due to the diversity of methods adopted and the use of the neuroimaging technique²⁸.

Studies carried out indicate that more than 75% of incidental aneurysms are small in size and saccular morphology²⁹. In this study, the results showed that 70% of aneurysms are small in size (<5 mm), followed by the large and giant. All with slight variation (not statistically significant differences) in percentage between genders.

As for morphology, there is a vast literature discussing saccular aneurysms¹⁷, which are responsible for 80% of non-traumatic subarachnoid hemorrhages (SAH)³⁰.

The prevalence of saccular aneurysm was significantly higher than other morphologies in our study, also with a predominance in females. Fusiform, on the other hand, has a less significant global proportion,

predominated in males, corroborating studies carried out²⁵.

Knowing that there is a difference in the investigation of cerebral aneurysm between men and women is important, as this can translate more dense information regarding the formation of the aneurysm. The risk factors raised in this study were similar between the sexes. However, they could have been better explored when identifying or diagnosing the aneurysm, such as genetic diseases and family history.

CONCLUSION

The study of cerebrovascular pathologies is essential, as it subsidizes the care and decision-making policies in the levels of health care for chronic non-communicable diseases. Women have a higher prevalence of cerebral aneurysms compared to men. Furthermore, hormonal and hemodynamic factors seem to explain the difference between the sexes. Predictor identification and health education are primary strategies for preventing aneurysm morbidity and mortality.

The limitations of this study refer to two points. The first is due to the retrospective nature of the research, using a secondary database; that is, the data were collected and tabulated by health professionals at the time of patient care, serving other purposes than the research. Thus, the analyzes were performed based on the available data, limiting the explanatory power of the phenomenon under study.

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