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Original Article

Male gender and smoking are related to single, but not to multiple, human aortic aneurysms

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ABSTRACT

There is scanty information concerning multiple aortic aneurysms. Thus, we verified if clinical or pathological characteristics are different in patients with multiple (two or more) aortic aneurysms in comparison with those with only one. *Material and methods*: We selected at the necropsy files of the Heart Institute, São Paulo University School of Medicine, the last 100 cases with aortic aneurysms, comparing between the two groups: sex, age, presence of systemic arterial hypertension, diabetes, dyslipedemia, history of smoking habit, cause of the aneurysm, cause of death, and if the diagnosis was reached during life. Age was analysed by Mann–Whitney test, and the other variables by chi-square or Fisher's exact test. *Results*: Multiple aneurysms corresponded to 14% of cases. The proportion of women among patients with multiple aneurysms was higher than among those with single aneurysm (64.3% versus 20.9%, $P<.01$), even if only cases with atherosclerosis were taken into consideration (women among multiple—6/10, 60.0%; among single—14/70, 20.0%; $P=.01$). Smoking was less reported in cases with multiple (4/14, 28.6%) than with single aneurysm (53/86, 61.6%; $P=.04$); considering cases with atherosclerosis, such difference decreases (40.0% of multiple versus 68.6% of single, $P=.09$). *Conclusion*: although atherosclerosis is present in most cases of both single and multiple aortic aneurysms, male gender and smoking, considered highly influential in such lesions, are less frequent in patients with multiple than in patients with single aneurysms. Thus mechanisms underlying multiple aortic aneurysms are probably different from those related to single, more common aneurysms.

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1. Introduction

Aortic aneurysms are an important cause of mortality, but there are also many of them diagnosed only incidentally during image methods performed by other reasons or at necropsy. Abdominal aortic aneurysms are related to atherosclerosis and to smoking habit, and appear more in men than in women [1,2]. In contrast, concerning ascending aorta aneurysms the gender difference is not so marked, and patients have less atherosclerosis [3]; their histological aspects are similar to those from patients with aortic dissections [4]. Due to the diversity in epidemiologic and pathogenetic [5] factors, thoracic and mostly ascending aortic aneurysms are usually separated from abdominal aortic aneurysms, but there are some articles describing the concurrence of both [6–8].

The presence of more than one aortic aneurysm has been described, and is not uncommon, but usually not much attention is given to it. Most articles are case reports [9–11], usually in patients with rare diseases, such as Ehlers-Danlos [12,13] or Behcet [14] diseases, or focus on surgical techniques. [15,16] Otherwise, multiple aortic aneurysms are poorly explored, and a systematic approach, aiming to verify if the same conditions of aortic aneurysms in general apply to patients with multiple lesions, is still lacking.

To better understand the pathogenesis and clinical aspects of aortic aneurysms, in this study we investigated if are there differences in clinical and pathological features between patients with single or multiple (more than one) aortic aneurysms.

2. Methods

This study was approved by the Scientific and Ethical Committee of the Heart Institute (InCor), University of São Paulo, School of Medicine, São Paulo, Brazil.

We searched the necropsy files of the Laboratory of Pathology of this hospital for the last 100 cases in which aneurysm of the aorta was among the diagnosis. Diagnostic criteria usually used are the presence of a saccular lesion or a segmental >50% increase in the arterial diameter in relation to the adjacent region. Cases with aortic dissection were excluded, unless it was clearly documented that the processes did not take place at the same segment of the artery or occurred after the previous existence of the aneurysm. These 100 necropsies have been performed between November, 2001 and December, 2012, corresponding to 5.25% of the necropsies of the period. The following data were

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computed in each case: number of aneurysms, regions of the aneurysm(s), presence of atherosclerosis, non-atherosclerotic inflammation, presence of dissection in other aortic segment, presence of aneurysm in other artery (usually iliac, renal, carotid arteries), and cause of death (whether or not related to the aneurysms—these from rupture, dissection in one case, or complications during the postoperative period). Clinical files of the selected cases were also reviewed, and the following data collected: gender, age, presence of systemic arterial hypertension, diabetes, smoking habit (present either until hospitalisation, or in the past), hypercholesterolemia, hypertriglyceridemia, and if the aneurysm(s) was (were) diagnosed during life (cases with multiple aneurysms in which one was diagnosed, but not all of them, were classified as "not diagnosed during life"). The presence of a possibly related disease, such as Takayasu disease, Marfan syndrome, aortic coarctation, or bicuspid aortic valve, was also recorded. In many cases there was no information concerning family history, not even a statement about its absence, thus we decided to not consider this question.

Cases were separated in two groups, one in which there was only one aneurysm and other with two or more aneurysms. The number of aneurysms in each individual was independent of the areas affected by them. Thus, as examples, one single large aneurysm could take three segments of the aorta, or two or even more small aneurysms could be present in one single segment.

Additional analyses were done taking into account: (1) only cases with ascending aorta aneurysms (regardless of the presence or not of descending or abdominal aneurysms; (2) only cases with thoracic aneurysms (regardless of the presence or not of abdominal aneurysms); (3) only cases with abdominal aneurysms (regardless of the presence or not of thoracic aneurysms); (4) only cases with atherosclerosis; (5) only cases without atherosclerosis.

To further verify if there is any relationship between inflammation and number of aneurysmatic lesions, we analysed the number of aortas with and without inflammation in the two groups. Again, we made two analyses: in one, given the role of inflammation in atherosclerosis—in particular, in atherosclerosis-associated aneurysms—we gathered as inflammatory both atherosclerotic cases and inflammatory non-atherosclerotic cases; in the other, we considered only non-atherosclerotic cases.

2.1. Statistical methods

Age was analysed by Mann–Whitney test (since the distribution was not normal), and the other variables by chi-square or Fisher's exact test. The clinical and pathological variables with $P \leq .20$ entered a logistic regression model analysis, considering a confidence interval of 0.95. Concerning the location of the aneurysms, we could not use chi-square test because, according to the statistical program used (*Sigmastat 3.5*), at least one of the expected values in the contingency table is less than 1 and over 20% of the expected values in the contingency table is less than 5, and in this situation chi-square test can be quite inaccurate. Thus we tested by Fisher exact test the commitment or not of each location (abdominal aorta, thoracic aorta as a whole, thoracic ascending aorta, and thoracic descending aorta). Significance was established as $P \leq .05$.

3. Results

Fourteen of the 100 cases had more than one aneurysm.

Table 1 shows the location of the aortic aneurysms, and Table 2 the commitment of each segment. The descending thoracic aorta was the segment with fewer aneurysms, but the only with a significant difference between groups—a higher proportion in patients with multiple lesions. Eleven of the 69 patients with lesions at the abdominal aorta (16.0%) and 20 of the 42 with lesions at the thoracic aorta (47.6%) died as a consequence of the aneurysms ($P < .01$). Three of the patients with single lesions and two of the other group had thoracoabdominal aneurysms.

Table 1
Location of single and multiple aortic aneurysms

	Single (n=86)	Multiple (n=14)	Total
Ascending thoracic	18	1	19
Descending thoracic	7	2	9
Abdominal	57	1	58
Ascending + descending thoracic	1	2	3
Ascending + abdominal	0	1	1
Thoracic descending + abdominal	0	4	4
Thoracic unspecified + abdominal	0	2	2
Ascending + thoracic descending + abdominal	3	1	4
Total	86	14	100

Clinical and pathological findings are presented in Table 3. The only significant differences were the percentages of women (20.9% in single, 64.3% in multiple aneurysms, $P < .01$), and smoking habit (61.6% in single, 28.6% in multiple aneurysms, $P = .04$). These were also the only differences that fulfilled the criterium to enter the logistic regression analysis. At both univariate and multivariate analyses, men had a lower chance to present multiple aneurysms (odds ratio to women= 0.15 [confidence interval 0.04;0.50] in both analyses), as well as smokers (odds ratio to non-smokers=0.30 [confidence interval 0.07;0.80] at univariate analysis and=0.27 [confidence interval 0.07;0.90] at multivariate analysis). There was no interaction between these two variables (sex and smoking habit).

Possibly due to the small number of cases, no difference was significant among the patients with ascending aorta aneurysms, although there were less female patients with single lesions (18.2% versus 60.0%, $P = .09$), and there were 3 patients in the group of single ascending aorta aneurysms with syndromes (1 Marfan syndrome, 2 bicuspid aortic valve), and none among the cases in which there were more aneurysms (13.6% versus 0%, $P = 1.00$). Yet when considering all cases with commitment of the thoracic aorta, the differences between genders remained (20.1% female in single, 66.7% female in multiple aneurysms, $P = .01$), but smoking habit was low in both groups (31.0% in single, 25.0% in multiple aneurysms, $P = 1.00$). Concerning cases with commitment of the abdominal aorta, the differences in gender and smoking habit were significant (20.0% female in single, 66.7% female in multiple aneurysms, $P < .01$, and 75.0% smokers in single versus 33.3% in multiple aneurysms, $P = .02$). This subgroup showed an additional difference: atherosclerosis was detected in 100% of single legions, and in 77.8% of patients with more than one aneurysm ($P = .02$).

At the comparison excluding cases without atherosclerosis, the difference in gender remained significant (women among multiple—6/10, 60.0%; among single—14/70, 20.0%; $P = .01$); concerning smoking habit, there was less cases among multiple than single lesions, but the difference decreased: (4/10, 40.0% of multiple versus 48/70, 68.6% of single, $P = .09$). None of the other variables showed significant difference. Among the 20 cases without atherosclerosis, no difference was significant.

Taking into account the total extension of the artery, inflammation of any type (atherosclerotic or not, two of which with a diagnosis of Takayasu' arteritis) was detected in 86.0% of patients with a single aneurysm and in all but one (92.9%) of those with multiple aneurysms ($P = .69$). Yet at the thoracic aorta, the difference was significant: 58.6% of single and 92.3 of patients with multiple aneurysms ($P = .04$)

Table 2
Occurrence of single or multiple aneurysms in each aortic location

	Single (n=86)	Multiple (n=14)	P
Thoracic aorta	29	13	<.01
Ascending aorta	22	5	.30
Descending aorta	11	9	<.01
Abdominal aorta	60	9	.76

Observation: since a same aneurysm may compromise more than one region, the total number of commited regions is greater than the number of cases.

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