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# Sex-related differences in patients with acute aortic syndromes

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## ABSTRACT

**INTRODUCTION:** Heterogeneity in the epidemiology, management, and in-hospital outcomes of patients with acute aortic syndromes can be found among male and female populations. This study aims to analyze sex-related differences in a cohort of patients treated in a tertiary university center.

**METHODS:** All patients admitted with acute aortic syndromes between January 2012 and January 2023 were retrospectively analyzed. A descriptive analysis of the data was performed, and the results were queried to explore sex-related differences according to the type of aortic syndrome, type of treatment (medical or surgical – conventional or endovascular), and the temporal phase of the disease in which this treatment occurred. A multivariable logistic regression was undertaken to identify variables associated with higher in-hospital mortality. Variables were included if statistically significant in the univariable analysis or if considered medically relevant.

**RESULTS:** A total of 116 patients (69% male) were included. Women were older (median age [interquartile range]: 64.6 years [40–85 years], n=36 versus 58.7 [23–84], n=80; P=0.034), had a higher proportion of intramural hematoma (19.4% versus 5.0%, P=0.014) and a lower proportion of aortic dissection (72.2% versus 88.8%, P=0.026) compared to men. Both sexes were more frequently treated with medical therapy alone (33.6%). However, women had a trend towards a lower proportion of open surgical management compared to men (16.7% versus 23.8%, P=0.391), as well as higher in-hospital mortality associated with this type of treatment (50.0% versus 21.1%, P=0.169). Additionally, women were associated with a higher conversion to endovascular or open surgery when first managed conservatively (13.9% versus 3.8%, P=0.046). In binary logistic regression, age was associated with higher in-hospital mortality (OR 1.056 [95% CI, 1.01-1.10]; P=0.014), but not female sex (OR 1.133 [95% CI, 0.39-3.30]; P=0.819).

**CONCLUSION:** Women were older, had more intramural hematoma, and were associated with a higher conversion from medical to surgical treatment. After multivariable regression, age was associated with higher in-hospital mortality, but female sex was not. Larger cohorts are needed to understand if intervention in female patients will have an impact on intra-hospital mortality.

**Keywords:** Aortic syndromes; type B aortic dissection; sex differences; gender differences; in-hospital mortality

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## INTRODUCTION

Aortic syndromes encompass three life-threatening conditions, including aortic dissection (AD), intramural hematoma (IMH), and penetrating aortic ulcer (PAU).[1] The incidence of AD varies between 2.6 to 7.2 per 100,000 patient-years, being associated with high morbidity and mortality rates.[1,2] Predisposing factors differ according to age, with the older population more commonly presenting with hypertension, atherosclerosis, and iatrogenic causes and, in contrast, younger patients, more likely to present with connective tissue disorders such as Marfan Syndrome, bicuspid aortic valves and cocaine use.[1]

Previous studies found differences in clinical profiles between male and female patients with AD.[3] In fact, most patients with type B AD tend to be male in the seventh decade of life, more commonly presenting with abrupt chest or abdominal pain.[1,3] Nevertheless, Takahashi et al. showed that women affected with type B acute AD tend to be older, to have more IMH, a lower incidence of end-organ malperfusion and higher in-hospital mortality compared with male patients, but female sex was not associated with in-hospital mortality after multivariable adjustment.[4]

However, published literature focusing on sex differences is scarce and heterogeneous, with most studies focused on investigating the impact of sex in both type A and B AD.[3-7] Improving knowledge of male-female differences can lead to recognizing high-risk patients and help shape optimal individualized care for both males and females. Accordingly, this study aims to analyze male-female differences in presentation, management, and outcomes of aortic syndromes, including type B AD, IMH, and PAU, in a cohort of patients treated in a tertiary center.

## METHODS

We examined data on all patients presenting with aortic syndrome (AD, IMH, and PAU) in a Portuguese tertiary center enrolled from January 2012 to January 2023. We excluded patients with type A AD and cases with aortic aneurysms without previous type B AD. No exclusion based on age was done.

Data were collected based on electronic medical records that included information on patient demographics, history, clinical presentation, imaging findings, management, and clinical events, including mortality. Completed data was stored in an Excel database stratified according to patient's sex, comorbidities, type of aortic syndrome (type B AD, IMH, and PAU), symptoms on admission, type of treatment (medical, endovascular, surgical or hybrid) and also according to the temporal phase of the disease in which this treatment occurred (hyperacute, acute, subacute or chronic phase).

Type B aortic dissection was defined as any dissection that involved the descending aorta. Complicated type B AD was defined by the presence of at least 1 of the following: aortic rupture or impending rupture, uncontrolled pain or hypertension despite full medications, early aortic expansion, progressive dissection, and end-organ malperfusion. The best medical treatment (BMT) was chosen as the initial management strategy for uncomplicated type B acute AD. Interventional procedures such as endovascular or surgical treatment were indicated only for complicated aortic dissection. Time from the onset of the symptoms to the presentation at the emergency department was defined according to the International Registry of Acute Aortic Dissection (IRAD), being 0-24 hours considered hyperacute, 2-7 days acute, 8-21 days subacute and chronic if more than 21 days.[8,9]

Statistical analyses were performed using the SPSS (version 27). Continuous variables were shown as median (interquartile range). Categorical variables were shown as frequencies. Continuous variables were compared using the Mann–Whitney U-test. Comparisons between groups for categorical variables were performed using Chi-square analysis or Fisher's exact test. Binary logistic regression analyses determined the variables associated with higher in-hospital mortality. Statistical significance was defined as a P value of <0.05.

## RESULTS

As presented in Table 1, a total of 116 patients were included (36 [31%] women versus 80 [69%] men). The median age was 60.5 years (23–85 years), and women were older than men (64.6 years [40–85 years] versus 58.7 years [23–84 years], P=0.034). Although not statistically significant, hyperlipidemia, connective tissue diseases, and positive family history were more prevalent in women (44.4% versus 30.0%, P=0.130; 8.3% versus 6.3%, P=0.682; 2.8% versus 2.5%, P=0.931).

Regarding imaging findings, women were more likely to have IMH (19.4% versus 5.0%, P=0.014) compared with men. However, men had more classic aortic dissection (88.8% versus 72.2%, P=0.026), and a trend towards more PAU in female patients was noted (8.3% versus 6.3%, P=0.682).

In general, patients presented more frequently in the chronic phase (34.5%). Although not statistically significant, a higher percentage of women presented in the chronic phase (41.7% versus 31.3%, P=0.275) compared to male patients. Nevertheless, men presented more frequently in the hyperacute phase (33.8%).

Differences between women and men regarding symptoms and complications at admission are shown in Tables 2 and 3. Chest pain was the most frequent presenting symptom (63.8%), followed by back pain (27.6%), abdominal pain (15.5%), and limb pain (5.2%). Although not statistically significant, men had chest and back pain more frequently than women (66.7% versus 57.9%, P=0.514; 28.2% versus 26.3%, P=0.880), whereas women had abdominal and limb pain more frequently compared with men (21.1% versus 12.8%, P=0.416; 5.3% versus 5.1%, P=0.983).

**Table 1.** Baseline characteristics of patients with acute aortic syndromes, comparing male and female

| | Male (n=80) | Female (n=36) | Total (N=116) | p-value |
|---|---|---|---|---|
| Age - mean | 58.7 | 64.6 | 60.5 | 0.034 |
| Hypertension - n (%) | 66 (82) | 29 (81) | 95 (82) | 0.801 |
| Hyperlipidemia - n (%) | 24 (30) | 16 (44) | 40 (35) | 0.130 |
| Connective tissue diseases – n (%) | 5 (6) | 3 (8) | 8 (7) | 0.682 |
| Active smokers – n (%) | 24 (30) | 7 (19) | 31 (27) | 0.106 |
| Renal insufficiency – n (%) | 12 (15) | 5 (14) | 17 (15) | 0.876 |
| Toxiphilic habits – n (%) | 4 (5) | 0 (0) | 4 (3) | 0.172 |
| Family history – n (%) | 2 (3) | 1 (3) | 3 (3) | 0.931 |
| Aortic dissection – n (%) | 71 (89) | 26 (72) | 97 (84) | 0.026 |
| Intramural hematoma – n (%) | 4 (5) | 7 (19) | 11 (10) | 0.014 |
| Penetrating aortic ulcer – n (%) | 5 (6) | 3 (8) | 8 (7) | 0.682 |
| Hyperacute – n (%) | 27 (34) | 12 (33) | 39 (34) | 0.965 |
| Acute – n (%) | 16 (20) | 3 (8) | 19 (16) | 0.116 |
| Subacute – n (%) | 12 (15) | 6 (17) | 18 (16) | 0.819 |
| Chronic – n (%) | 25 (31) | 15 (42) | 40 (35) | 0.819 |

**Table 2.** Complications at admission of patients with aortic syndromes, comparing male and female

| | Male (n=80) | Female (n=36) | Total (N=116) | p-value |
|---|---|---|---|---|
| Renal ischemia- n (%) | 12 (15) | 2 (5) | 14 (12) | 0.126 |
| Mesenteric ischemia - n (%) | 11 (14) | 1 (3) | 12 (10) | 0.064 |
| Limb ischemia – n (%) | 10 (13) | 2 (5) | 12 (10) | 0.232 |
| Refractory hypertension – n (%) | 8 (10) | 0 (0) | 8 (7) | 0.043 |
| Refractory pain – n (%) | 4 (5) | 0 (0) | 4 (4) | 0.161 |
| Aortic rupture – n (%) | 3 (4) | 2 (5) | 5 (4) | 0.702 |
| Rupture extension – n (%) | 6 (8) | 2 (5) | 8 (7) | 0.652 |
| Endoleak – n (%) | 1 (1) | 1 (3) | 2 (2) | 0.586 |

**Table 3.** Symptoms at admission of patients with acute aortic syndromes, comparing male and female

| | Male (n=39) | Female (n=19) | Total (N=58) | p-value |
|---|---|---|---|---|
| Chest pain- n (%) | 26 (67) | 11 (58) | 37 (64) | 0.514 |
| Back pain - n (%) | 11 (28) | 5 (26) | 16 (28) | 0.880 |
| Abdominal pain – n (%) | 5 (13) | 4 (21) | 9 (16) | 0.416 |
| Limb pain – n (%) | 2 (5) | 1 (5) | 2 (5) | 0.983 |

On admission, renal ischemia was the most frequent complication found in our study population (12.2%), being more frequent in men compared to women (15.4% versus 5.4%, P=0.126), followed by mesenteric and limb ischemia (10.3%), refractory hypertension and extension (7%), aortic rupture (4.3%), refractory pain (3.5%) and endoleak (1.7%). A trend towards more aortic rupture and endoleak in female patients was found (5.4% versus 3.8%, P=0.702; 2.7% versus 1.3%, P=0.586). Refractory hypertension occurred more frequently in men compared to women (10.3% versus 0.0%, P=0.043).

As shown in Table 4, 39 patients (34%) received medical treatment alone during hospitalization. Although not statistically significant, women were medically managed more frequently than men (39% versus 31%, P=0.420). Interventional procedures, including endovascular, open surgical, and hybrid therapies, were performed in the remaining 77 patients (66%). A trend towards more endovascular therapy in women was shown (18% versus 13%, P=0.692), but the opposite was noted regarding open surgical and hybrid therapy (24% in men versus 17% in women, P=0.391; 16% in men versus 13.9% in women, P=0.745; respectively).

Women showed a higher overall in-hospital mortality trend than men (16.7% versus 15.0%, P=0.819; Table 5). In addition, although not statistically significant, among the medically managed and hybrid therapy patients, the in-hospital mortality was higher in men (8.0% versus 0.0%, P=0.277; 23.1% versus 20.0%, P=0.888). In contrast, the in-hospital mortality of endovascular or surgically treated patients was higher in women than men (18.2% versus 13.0%, P=0.692; 50.0% versus 21.1%, P=0.169) (Table 3).

In general, conversion from best medical management to interventional procedures (endovascular or open surgery) occurred in 6.9% of patients, and it happened more frequently in female patients (13.9% versus 3.8%, P=0.046).

**Table 4.** Initial management of patients with aortic syndromes, comparing male and female

| | Male (n=80) | Female (n=36) | Total (N=116) | p-value |
|---|---|---|---|---|
| Medical management alone - n (%) | 25 (31) | 14 (39) | 39 (34) | 0.420 |
| Endovascular - n (%) | 23 (29) | 11 (31) | 34 (30) | 0.843 |
| Open surgery – n (%) | 19 (24) | 6 (17) | 25 (22) | 0.391 |
| Hybrid surgery – n (%) | 13 (16) | 5 (14) | 18 (16) | 0.745 |

**Table 5.** In-hospital mortality of patients with aortic syndromes, comparing male and female

| | Male (n=80) | Female (n=36) | Total (N=116) | p-value |
|---|---|---|---|---|
| Medical management alone - n (%) | 2 (8) | 0 (0) | 2 (5) | 0.277 |
| Endovascular - n (%) | 3 (13) | 2 (18) | 5 (15) | 0.692 |
| Open surgery – n (%) | 4 (21) | 3 (50) | 7 (28) | 0.169 |
| Hybrid surgery – n (%) | 3 (23) | 1 (20) | 4 (22) | 0.888 |
| Overall mortality – n (%) | 12 (15) | 6 (17) | 18 (16) | 0.819 |

**Table 6.** Multivariable analysis of predictors of in-hospital mortality of patients admitted for aortic syndrome

| | OR | 95% CI | p-value |
|---|---|---|---|
| Age, y | 1.056 | 1.01-1.10 | 0.014 |
| Female sex | 1.133 | 0.39-3.30 | 0.819 |
| Conversion BMT to EDV/CX | 0.000 | - | 0.999 |
| Aortic dissection | 0.976 | 0.25-3.76 | 0.971 |
| Intramural hematoma | 0.518 | 0.06-4.31 | 0.543 |
| Open surgical treatment | 2.828 | 0.96-8.30 | 0.058 |
| Medical treatment | 0.206 | 0.05-0.95 | 0.042 |

**BMT** - Best Medical Treatment; **EDV** - Endovascular; **CX** - Surgery; **OR** - Odds Ratio; **CI** - confidence interval

As presented in Table 6, after binary logistic regression, the patient's age was predictive of in-hospital mortality (OR, 1.056 [95% CI, 1.01–1.10]; P=0.014), but female sex was not (OR, 1.133 [95% CI, 0.39–3.30]; P=0.819).

## DISCUSSION

Few studies exist reporting sex differences in mortality among patients with aortic syndromes.[4,5,6] In the present study, we found that females were older, presented more frequently with HIM in the chronic phase, and showed a trend towards less end-organ malperfusion on admission.

Takahashi et al.[4] analyzed data from about 2372 (695 women, 29.3%) patients with type B acute AD enrolled in the Tokyo Acute Super-Network Registry and showed similar results. They noticed that in type B acute AD, women were older, presented later to the emergency department, had more IMH, less extension of dissection, and were less likely to experience end-organ malperfusion. Also, as shown in our study, the overall in-hospital mortality was higher in women compared with men. However, female sex was not associated with in-hospital mortality.

In 2021, a systematic review and meta-analysis encompassing 18 659 patients with type A and B AD showed that males were less often treated conservatively.[3] The same was noted in our study, where patients were more frequently treated with medical therapy (33.6%), but comparing both genders, men appear to be less frequently treated with BMT.

Women had a trend towards a lower proportion of open surgical therapy, as well as higher in-hospital mortality associated with this type of treatment. Additionally, women were associated with a higher conversion to endovascular or open surgery. Yang Zhou et al. noticed that females were more likely to experience a worse outcome after surgery, and the older age seems to be a possible explanation.[10]

This study has some significant limitations. First, the number of patients included in our database was relatively small, which could account for the lack of statistical significance of some of the analyses. Second, patients were included in different phases of the disease's natural history, adding to heterogeneity. Finally, the absence of registry information regarding clinical information at presentation was noted.

## CONCLUSION

Women were older, had more IMH, and were associated with a higher conversion from medical to endovascular or open treatment. After binary regression, age was associated with in-hospital mortality, but female sex was not. Larger cohorts are needed to understand if intervention in female patients will have an impact on intra-hospital mortality.

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## REFERENCES

**1.** Erbel R, Aboyans V, Boileau C, Bossone E, Bartolomeo RD, Eggebrecht H, et al. ESC Guidelines on the diagnosis and treatment of aortic diseases: document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. The Task Force for the Diagnosis and Treatment of Aortic Diseases of the European Society of Cardiology (ESC). Eur Heart J 2014;35:2873–926.

**2.** Bossone E, Carbone A, Eagle A. Gender Differences in Acute Aortic Dissection. J. Pers. Med. 2022;12:1148.

**3.** Frederike M, Arjen L, Carlijn T, Mostafa M, Jos B, Roland K, et al. Male–female differences in acute thoracic aortic dissection: a systematic review and meta-analysis. Interactive Cardiovasc Thor Surg 2022;34: 616–27.

**4.** Toshiyuki T, Hideaki Y, Koichi A, Tomoki S, Hitoshi O, Takashi K, et al. Sex-Related Differences in Clinical Features and In-Hospital Outcomes of Type B Acute Aortic Dissection: A Registry Study. J Am Heart Assoc 2022;11:e024149.

**5.** Liang L, Genovese A, Al-Khoury E, Hager S, Makaroun S, Singh J. Effects of Gender Differences on Short-Term Outcomes in Patients with Type B Aortic Dissection. Ann Vasc Surg 2017;38:78–83.

**6.** Maitusong B, Sun P, Xielifu D, Mahemuti M, Ma X, Liu F, et al. Sex-Related Differences Between Patients with Symptomatic Acute Aortic Dissection. Medicine 2016;95:e3100.

**7.** Liu J, Wang Z, Wang Y, He X, Yang L, Jing M, et al. Correlation between Sex and Prognosis of Acute Aortic Dissection in the Chinese Population. Chin Med J 2018;131:1430–5

**8.** Arturo E, Eric I, Eduardo B, Thomas G, Marco E, Udo S, et al. Insights From the International Registry of Acute Aortic Dissection 2018;137:1846-60

**9.** Hagan PG, Nienaber CA, Isselbacher EM, Bruckman D, Karavite DJ, Russman PL , et al. The International Registry of Acute Aortic Dissection (IRAD): new insights into an old disease. JAMA 2000;283:897–903.

**10.** Yang Z, Wen P, Guifang Y, Xiaogao P, Ning D, Hongliang Z, et al. Gender Difference is Associated with Short-Term Hypertension: A Retrospective Cohort Study. Risk Risk Manag Health Policy. 2021;14:323-30