ORIGINAL RESEARCH

Sex-Related Differences in Clinical Features and In-Hospital Outcomes of Type B Acute Aortic Dissection: A Registry Study

Toshiyuki Takahashi , MD, PhD; Hideaki Yoshino, MD, PhD; Koichi Akutsu, MD, PhD; Tomoki Shimokawa , MD, PhD; Hitoshi Ogino, MD, PhD; Takashi Kunihara , MD, PhD; Michio Usui, MD; Kazuhiro Watanabe, MD, PhD; Mitsuhiro Kawata , MD, PhD; Hiroshi Masuhara, MD, PhD; Manabu Yamasaki, MD; Takeshi Yamamoto, MD, PhD; Ken Nagao, MD, PhD; Morimasa Takayama, MD, PhD

BACKGROUND: The association between female sex and poor outcomes following surgery for type A acute aortic dissection has been reported; however, sex-related differences in clinical features and in-hospital outcomes of type B acute aortic dissection, including classic aortic dissection and intramural hematoma, remain to be elucidated.

METHODS AND RESULTS: We studied 2372 patients with type B acute aortic dissection who were enrolled in the Tokyo Acute Aortic Super-Network Registry. There were fewer and older women than men (median age [interquartile range]: 76 years [66–84 years], n=695 versus 68 years [57–77 years], n=1677; P<0.001). Women presented to the aortic centers later than men. Women had a higher proportion of intramural hematoma (63.7% versus 53.7%, P<0.001), were medically managed more frequently (90.9% versus 86.3%, P=0.002), and had less end-organ malperfusion (2.4% versus 5.7%, P<0.001) and higher in-hospital mortality (5.3% versus 2.7%, P=0.002) than men. In multivariable analysis, age (per year, odds ratio [OR], 1.06 [95% CI, 1.03–1.08]; P<0.001), hyperlipidemia (OR, 2.09 [95% CI, 1.13–3.88]; P=0.019), painlessness (OR, 2.59 [95% CI, 1.14–5.89]; P=0.023), shock/hypotension (OR, 2.93 [95% CI, 1.21–7.11]; P=0.017), non–intramural hematoma (OR, 2.31 [95% CI, 1.32–4.05]; P=0.004), aortic rupture (OR, 26.6 [95% CI, 14.1–50.0]; P<0.001), and end-organ malperfusion (OR, 4.61 [95% CI, 2.11–10.1]; P<0.001) were associated with higher in-hospital mortality, but was not female sex (OR, 1.67 [95% CI, 0.96–2.91]; P=0.072).

CONCLUSIONS: Women affected with type B acute aortic dissection were older and had more intramural hematoma, a lower incidence of end-organ malperfusion, and higher in-hospital mortality than men. However, female sex was not associated with in-hospital mortality after multivariable adjustment.

Key Words: female sex I intramural hematoma I mortality I sex difference I type B acute aortic dissection

Cute aortic dissection (AAD) is a life-threatening medical condition associated with high morbidity and mortality rates.¹ In a prior study from the IRAD (International Registry of Acute Aortic Dissection), the association between female sex and poor outcomes following surgery for type A AAD was reported; however, no significant difference in in-hospital mortality between the sexes was found in those with type B AAD.² More recent studies have shown conflicting results on the association between female sex and outcomes of AAD; some did not show a mortality difference between the sexes in patients with AAD, whereas others showed a higher short-term mortality rate after acute surgical repair in women than in men.^{3–10} In addition, few studies have reported on sex differences in outcomes for intramural hematoma (IMH), which

Correspondence to: Toshiyuki Takahashi, MD, PhD, Department of Cardiology, Tokyo Saiseikai Central Hospital, 1-4-17 Mita, Minato-ku, Tokyo 108-0073, Japan. Email: ttakahashi@saichu.jp

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CLINICAL PERSPECTIVE

What Is New?

- Women with type B acute aortic dissection (AAD) tended to be older, presented to the aortic centers later, had more intramural hematomas and less extension of dissection, and were less likely to experience end-organ malperfusion than men (2.4% versus 5.7%, P<0.001).
- In type B AAD, women were medically managed more frequently (90.9% versus 86.3%, P=0.002) and had a higher in-hospital mortality rate (5.3% versus 2.7%, P=0.002) than men.
- Multivariable analysis revealed that age, hyperlipidemia, painlessness, shock/hypotension, non-intramural hematoma, aortic rupture, and end-organ malperfusion were independent predictors of in-hospital mortality; however, female sex was not associated with in-hospital mortality (odds ratio, 1.67 [95% CI, 0.96–2.91]; P=0.072).

What Are the Clinical Implications?

- We clarified sex-related differences in clinical features, management, and in-hospital outcomes in patients with type B AAD, including classic aortic dissection and intramural hematoma.
- Our real-world data of type B AAD from a large Japanese AAD registry provide useful clinical information on the management of patients with type B AAD and insightful perspectives on sexrelated differences in AAD.
- Further research is warranted to determine sexspecific risk assessment and therapeutic strategies for patients with type B AAD.

Nonstandard Abbreviations and Acronyms

- IMH intramural hematoma
- TEVAR thoracic endovascular aortic repair

was traditionally regarded as a disease entity different from classic aortic dissection.^{11–13} Although there is no clear distinction between classic aortic dissection and IMH in terms of clinical presentation, IMH is associated with more favorable outcomes than classic aortic dissection.^{14–18}

During the past 2 decades, more patients have been managed with interventional procedures such as surgery for type A AAD and endovascular therapy for type B AAD. With these changes, a significant decrease has been noted in the overall in-hospital mortality for patients with type A AAD, but not for those with type B AAD.¹ Such temporal changes in diagnostic and therapeutic approaches for AAD may affect sexspecific effects on clinical features, management, and outcomes. It remains poorly understood whether sexrelated differences in clinical features and in-hospital outcomes for type B AAD exist and how they are influenced by in-hospital management.

Therefore, the present study aimed to assess sexrelated differences in clinical features, management, and in-hospital outcomes in patients with type B AAD, including classic aortic dissection and IMH, using a large Japanese multicenter registry database, representing the current real-world clinical practice of AAD in Japan. We also investigated whether female sex per se is independently associated with in-hospital outcomes of patients with type B AAD using multivariable analysis.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Aortic Network System and Database

The Tokyo Cardiovascular Care Unit Network is an emergent transfer system for patients with all types of cardiovascular diseases that covers the entire Tokyo metropolitan region except the island areas.¹⁹ Since November 2010, we inaugurated a regional aortic network system called the Tokyo Acute Aortic Super-Network, which was established on the basis of the Tokyo Cardiovascular Care Unit Network,¹⁴ with the aim to develop a safe and effective transfer system for patients with AAD and ruptured aortic aneurysm with the help of ambulance units through the control room of the Tokyo Fire Department. The Tokyo Acute Aortic Super-Network currently consists of 39 participating hospitals with specialized care for AAD and ruptured aortic aneurysm; patients with suspected or confirmed AAD are first referred to such hospitals, as reported elsewhere.^{20,21} Detailed data on all patients treated in their emergency departments, cardiovascular surgery departments, and cardiovascular care units were routinely recorded and submitted to the data management center on specific survey forms.

Ethical Statements

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki and the Ethical Guidelines for Epidemiological Research by the Japanese government. The study was approved by the institutional review board of the Tokyo Cardiovascular Care Unit Network Scientific Committee. According to the guidelines, the study satisfied the conditions for waiving the requirement for informed consent from individual participants.

Study Population and Design

We used the data from 2674 consecutive patients with type B AAD who were hospitalized from January 2013 to December 2017 and enrolled in the Tokyo Acute Aortic Super-Network registry database. The exclusion criteria were as follows: patients who were admitted >14 days from the symptom onset (n=35); patients who had cardiopulmonary arrest on arrival (n=8); and patients with no available data on the symptom onset date (n=28), in-hospital outcomes (n=16), false lumen status based on computed tomography (CT) findings (n=151), DeBakey classification or those with types other than DeBakey IIIa/IIIb (n=37), and blood pressure measurement at presentation (n=27). Finally, a total of 2372 patients with type B AAD were included in this study (Figure 1). Clinical features, management, and inhospital outcomes were compared between the sexes in patients with type B AAD.

We classified AAD with nonthrombosed or partially thrombosed false lumen as classic aortic dissection, whereas AAD with a completely thrombosed false lumen was classified as an IMH according to the CT findings. Aortic dissections with ulcer-like projection in the thrombosed false lumen on CT imaging were included in the IMH group as previously reported.¹⁴ AAD was categorized as types I, II, or III according to the DeBakey classification. Type III AADs were further subclassified, depending on whether the dissection was limited to the descending thoracic aorta (IIIa) or extended below the diaphragm to involve the abdominal aorta (IIIb).

Complicated type B AAD was defined by the presence of at least 1 of the following: aortic rupture or extra-aortic blood collection (impending rupture), intractable pain, uncontrolled hypertension despite full medications, early aortic expansion, progressive dissection, and malperfusion in the cerebral, spinal, renal, visceral, or peripheral vasculature. The best medical treatment was chosen as the initial management strategy for uncomplicated type B AAD. Interventional procedures such as endovascular or surgical treatment were indicated only for complicated aortic dissection, although operative procedures were selected at the discretion of surgeons and aortic teams in charge.

Statistical Analysis

We performed a power calculation to estimate the sample size required to detect a sex difference in the inhospital mortality of patients with type B AAD, assuming the ratio of men to women was 2.5, and the in-hospital mortality was 3.5% in men and 6.5% in women, based on the results of our previous study¹⁴ and the annual survey data of the Tokyo Cardiovascular Care Unit Network. The sample size needed to detect a prespecified difference in outcome with 80% power and an α level of 0.05 (2-sided) was calculated to be 1869 using the software package GPower (version 3.1.9.7; Kiel, Germany). The actual power calculated by a post hoc power analysis with an α level of 0.05 (2-sided) was 86.3%.

Categorical variables are expressed as the number of patients (%). Continuous data are presented

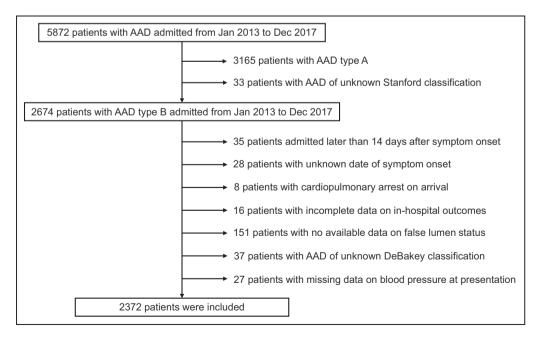


Figure 1. Flowchart of patient selection. AAD indicates acute aortic dissection.

as mean±SD if the data followed a normal distribution. Otherwise, data are shown as median (interquartile range). The χ^2 test or Fisher exact test was used to compare categorical variables, and the unpaired Student t test or Mann-Whitney U test was used to compare continuous variables. Multivariable logistic regression analyses were performed to determine the effects of female sex on aortic rupture, end-organ malperfusion, and in-hospital mortality in patients with type B AAD. Age, sex, and clinically relevant variables including shock/hypotension and classic aortic dissection, which had a P value < 0.05 on univariate analysis, were entered in a multivariable model. Hyperlipidemia and DeBakey classification were also included because women tended to be hyperlipidemic and had DeBakey type IIIb less frequently than men. Cigarette smoking was excluded because of multicollinearity (strong correlation with younger age and male sex). Additionally, aortic rupture, end-organ malperfusion, and medical management were entered into a different model to determine independent predictors of in-hospital mortality. Subgroup analyses were conducted in patients with complicated type B AAD or in the elderly group (patients aged \geq 70 years).

Statistical significance was defined as a *P* value of <0.05 (2-sided). All statistical analyses were performed using SPSS version 24 (IBM, Armonk, NY).

RESULTS

Baseline Characteristics

As presented in Table 1, the median (interguartile range) age of the patients was 70 years (60-79 years), and 695 (29.3%) patients were women. There were fewer and older women than men (76 years [66-84 years], n=695 versus 68 years [57-77 years], n=1677; P<0.001). The proportion of men and women by decade of age is shown in Figure 2. More women from the older age groups were admitted than were women from the younger age groups. Hyperlipidemia was more prevalent in women than in men (20.3%) versus 16.4%, P=0.025). The rate of cigarette smoking was lower in women than in men (16.2% versus 35.5%, P<0.001). Women had back pain more frequently and lower systolic blood pressures and heart rates on admission and were more likely to have IMH (63.7% versus 53.7%, P<0.001) and DeBakey type Illa AAD (27.5% versus 21.5%, P=0.002) than men. Among patients with IMH, ulcer-like projection was observed more frequently in men than in women (29.2% versus 20.8%, P=0.001).

In both the subgroups of patients with complicated type B AAD and elderly patients aged ≥70 years, women were significantly older, less likely to be

cigarette smokers, and had back pain more frequently than men (Tables S1 and S2).

Among patients who were admitted within 24 hours of symptom onset with available data on the exact times of symptom onset and hospital arrival, women presented to the aortic centers later than men (180 minutes [95–305 minutes], n=544 versus 159 minutes [80–280 minutes], n=1311; P=0.006). In addition, later presentation in women compared with men was also observed in patients with complicated type B AAD (216 minutes [134–355 minutes], n=98 versus 180 minutes [90–313 minutes], n=281; P=0.029) or in the elderly group (196 minutes [105–340 minutes], n=355 versus 165 minutes [83–283 minutes], n=562; P=0.006).

In-Hospital Management and Outcomes

As shown in Table 2, 2079 (87.6%) out of 2372 patients received medical treatment alone during hospitalization. Women were medically managed more frequently than men (90.9% versus 86.3%, P=0.002). The remaining 293 (12.4%) patients underwent interventional procedures including endovascular and open surgical therapies. Endovascular treatment and open surgery were performed in the acute phase (<14 days from the onset of AAD) in 17 (63.0%) women and 68 (64.8%) men and in 25 (69.4%) women and 80 (64.5%) men, respectively. In a subset of patients who underwent interventional procedures within 24 hours after admission, the time from hospital arrival to emergency operation did not differ between sexes (women: 186 minutes [88-520 minutes], n=29 versus men: 160 minutes [88-305 minutes], n=72; P=0.473). As for medications after admission, men were more likely to receive β-blockers, angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers, diuretics, and nitrates than women (Table 2).

The overall in-hospital mortality was higher in women than in men (5.3% versus 2.7%, P=0.002). In addition, the in-hospital mortality of the medically managed patients was higher among women than men (4.1% versus 1.8%, P=0.002). The in-hospital mortality of the endovascularly or surgically treated patients was also higher in women than in men (17.5% versus 8.7%, P=0.045). The most common cause of death was aortic rupture, which occurred in 38 (22 men and 16 women) out of 83 patients who were deceased. No significant difference was observed in aortic rupture between the sexes. In contrast, women were less likely to experience end-organ malperfusion than men (2.4% versus 5.7%, P<0.001), including renal ischemia (0.7% versus 2.0%, P=0.028) and mesenteric ischemia (0.7% versus 2.2%, P=0.012). In a subset of patients with classic aortic dissection, women had a higher incidence of aortic rupture than men (8.3% [21/252] versus 4.0% [31/777], P=0.006),

Table 1. Baseline Characteristics

| | Total | Men | Women | | |
|---|---------------|---------------|---------------|---------|--|
| | n=2372 | n=1677 | n=695 | P value | |
| Age, y | 70 (60–79) | 68 (57–77) | 76 (66–84) | <0.001 | |
| Hypertension | 1768 (74.5%) | 1263 (75.3%) | 505 (72.7%) | 0.175 | |
| Hyperlipidemia | 417 (17.5%) | 276 (16.4%) | 141 (20.3%) | 0.025 | |
| Diabetes | 187 (7.9%) | 135 (8.0%) | 52 (7.5%) | 0.643 | |
| Cigarette smoking* | 700 (29.9%) | 589 (35.5%) | 111 (16.2%) | <0.001 | |
| Previous coronary artery disease | 89 (3.8%) | 62 (3.7%) | 27 (3.9%) | 0.827 | |
| Previous stroke | 163 (6.9%) | 118 (7.1%) | 45 (6.5%) | 0.651 | |
| Previous peripheral artery disease | 26 (1.1%) | 20 (1.2%) | 6 (0.9%) | 0.486 | |
| Previous cardiac surgery | 36 (1.5%) | 28 (1.7%) | 8 (1.2%) | 0.347 | |
| End-stage renal disease on hemodialysis | 42 (1.6%) | 33 (2.0%) | 9 (1.3%) | 0.260 | |
| Time from onset to admission | | | | 0.548 | |
| <24 h | 2111 (89.0%) | 1497 (89.3%) | 614 (88.3%) | | |
| 1–6 d | 199 (8.4%) | 140 (8.3%) | 59 (8.5%) | | |
| 7–14 d | 62 (2.6%) | 40 (2.4%) | 22 (3.2%) | | |
| Back pain | 1689 (71.2%) | 1165 (69.5%) | 524 (75.4%) | 0.004 | |
| Chest pain | 938 (39.5%) | 675 (40.3%) | 263 (37.8%) | 0.275 | |
| Abdominal pain | 287 (12.1%) | 209 (12.5%) | 78 (11.2%) | 0.399 | |
| Lumbago | 183 (7.7%) | 126 (7.5%) | 57 (8.2%) | 0.568 | |
| Leg pain | 22 (1.2%) | 18 (1.3%) | 4 (0.7%) | 0.253 | |
| Painlessness | 115 (4.8%) | 74 (4.4%) | 41 (5.9%) | 0.125 | |
| Shock/hypotension | 63 (2.7%) | 43 (2.6%) | 20 (2.9%) | 0.666 | |
| Aortic rupture on admission | 48 (2.0%) | 32 (1.9%) | 16 (2.3%) | 0.525 | |
| Malperfusion on admission | 71 (3.0%) | 57 (3.4%) | 14 (2.0%) | 0.085 | |
| Systolic blood pressure, mm Hg | 161 (137–189) | 162 (139–190) | 159 (133–186) | 0.011 | |
| Heart rate, beats per min | 76 (66–88) | 77 (67–82) | 74 (65–86) | 0.012 | |
| Status of false lumen | | | | <0.001 | |
| Classic aortic dissection | 1029 (43.4%) | 777 (46.3%) | 252 (36.3%) | | |
| IMH | 1343 (56.6%) | 900 (53.7%) | 443 (63.7%) | | |
| DeBakey classification | | | | 0.002 | |
| Type Illa | 551 (23.2%) | 360 (21.5%) | 191 (27.5%) | | |
| Type IIIb | 1821 (76.8%) | 1317 (78.5%) | 504 (72.5%) | | |

Values are median (interquartile range) or n (percent). The χ^2 test or Fisher exact test was used to compare categorical variables, and the Mann-Whitney U test was used to compare continuous variables. IMH indicates intramural hematoma.

*Data on history of cigarette smoking are available on 1658 men and 684 women.

whereas no significant difference was found in endorgan malperfusion between the sexes (women: 4.4% [11/252] versus men: 7.5% [58/777], P=0.087). In a subset of patients with IMH, no significant difference was observed in aortic rupture between the sexes (women: 2.0% [9/443] versus men: 2.1% [19/900], P=0.924), whereas women had a lower incidence of end-organ malperfusion than men (1.4% [6/443] versus 4.1% [37/900], P=0.007).

Among patients with complicated type B AAD, women were medically managed more frequently than

men (49.2% versus 37.5%, *P*=0.022; Table S3). The in-hospital mortality of this subgroup was higher in women than in men (25.0% versus 10.9%, *P*<0.001). Women had aortic rupture and acute ischemic stroke more frequently than men, whereas women were less likely to experience end-organ malperfusion than men (Table S3).

In the elderly group, women had higher in-hospital mortality than men (7.3% versus 3.8%, P=0.007; Table S4). There were no significant differences in in-hospital complications including aortic rupture

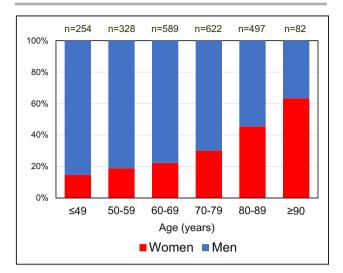


Figure 2. Proportions of men and women by decade of age.

and end-organ malperfusion between the sexes (Table S4).

Effects of Female Sex on Aortic Rupture, End-Organ Malperfusion, and In-Hospital Mortality in Type B AAD

Results of univariate analyses for aortic rupture, endorgan malperfusion, and in-hospital mortality are shown in Table S5. In multivariable analysis, age, shock/hypotension, and classic aortic dissection were significant predictors of aortic rupture. Female sex was not associated with aortic rupture after multivariable adjustment (Table 3). Additionally, shock/hypotension and classic aortic dissection were independent predictors of end-organ malperfusion. Female sex was inversely associated with end-organ malperfusion (odds ratio [OR], 0.47 [95% CI, 0.28–0.81]; *P*=0.006).

In the multivariable analysis for in-hospital mortality, age, hyperlipidemia, painlessness, shock/hypotension, classic aortic dissection, aortic rupture, and end-organ malperfusion were independent predictors of mortality, whereas female sex was not predictive of mortality after multivariable adjustment (OR, 1.67 [95% Cl, 0.96-2.91]; P=0.072; Model 2 in Table 3). The subgroup analysis of complicated type B AAD showed that age, classic aortic dissection, and aortic rupture were independent predictors of mortality; female sex was not significantly associated with mortality (Model 2 in Table S6). In addition, multivariable analysis, which was performed only for patients who underwent an interventional procedure (endovascular/surgical), showed that only aortic rupture was an independent predictor of mortality (Model 2 in Table S7). Female sex was a significant predictor of mortality, when multivariable analysis was conducted only in the elderly group (Table S8).

DISCUSSION

The main findings of our study were as follows: (1) Women were older, presented to the aortic centers later, and had IMH and DeBakey type IIIa AAD more frequently than men. (2) Women were less likely to experience end-organ malperfusion including visceral and limb ischemia than men. (3) Women were medically managed more frequently and had higher in-hospital mortality (unadjusted) than men. (4) Female sex per se was not associated with in-hospital mortality after multivariable adjustment.

As reported previously,⁴ women with type B AAD presented at an older age than men. The sex difference in age has also been reported to be observed in type A aortic dissections and ruptured aortic aneurysms.^{2,10,22,23} The pathogenic process of aortic disease may differ between the sexes through hormonal, molecular, and hemodynamic differences, although the pathophysiologic mechanisms remain unknown. Notably, women had IMH more frequently than men in the present study, where IMH was defined as aortic dissection with a completely thrombosed false lumen. The prevalence of IMH was as high as 57% in patients with type B AAD, which was consistent with the results from our previous report.¹⁴ The pathophysiology of IMH is thought to originate from a contained hemorrhage within the medial layer of the aorta because of either rupture of the vasa vasorum or an atherosclerotic plaque. The difference in the prevalence of IMH between our study and others may be explained by the different definitions of IMH, racial variance, and different availability of diagnostic image modalities, such as CT. In our study, aortic dissections with ulcer-like projection in the false lumen were included in the IMH group. Because ulcer-like projection is a sign of intimal tear on CT imaging, some studies may differentiate them as communicating dissections from IMH. As compared with those with classic aortic dissection, patients with IMH have been reported to be older,^{14,18,24,25} have a greater intima-media thickness,²⁶ experience dissection with limited extension to the supraceliac aorta more frequently, and exhibit lower incidences of leg ischemia and renal failure.^{16,24} The development of IMH may be associated with increased stiffness of the aortic wall, leading to limited extension of the dissection, particularly in older women than in older men. Previous reports focusing on sex differences in type B AAD^{4,8,9} did not provide detailed data on false lumen patency because their databases were created based on the coding system, which did not differentiate IMH from classic aortic dissection accurately; therefore, our data would provide additional information on the sex difference in IMH.

In the present study, women were medically managed more frequently than men, whereas men were

Table 2. In-Hospital Management and Outcomes

| | Total | Men | Women | |
|-----------------------------|--------------|--------------|-------------|---------|
| | n=2372 | n=1677 | n=695 | P value |
| Management | | | | |
| Medical therapy | 2079 (87.6%) | 1447 (86.3%) | 632 (90.9%) | 0.002 |
| Interventional therapy | 293 (12.4%) | 230 (13.7%) | 63 (9.1%) | 0.002 |
| Endovascular therapy | 132 (5.6%) | 105 (6.3%) | 27 (3.9%) | 0.022 |
| Open surgical therapy | 148 (6.2%) | 116 (6.9%) | 32 (4.6%) | 0.034 |
| Hybrid therapy | 13 (0.5%) | 9 (0.5%) | 4 (0.6%) | 0.907 |
| In-hospital death | | | | |
| Overall | 83 (3.5%) | 46 (2.7%) | 37 (5.3%) | 0.002 |
| Medically managed | 52 (2.5%) | 26 (1.8%) | 26 (4.1%) | 0.002 |
| Interventionally treated | 31 (10.6%) | 20 (8.7%) | 11 (17.5%) | 0.045 |
| Endovascularly treated | 12 (9.1%) | 8 (7.6%) | 4 (14.8%) | 0.265 |
| Surgically treated* | 19 (11.8%) | 12 (9.6%) | 7 (19.4%) | 0.107 |
| In-hospital complications | | | | |
| Aortic rupture | 80 (3.2%) | 50 (3.0%) | 30 (4.3%) | 0.130 |
| Hemothorax | 29 (1.2%) | 18 (1.1%) | 11 (1.6%) | 0.304 |
| Acute ischemic stroke | 38 (1.6%) | 23 (1.4%) | 15 (2.2%) | 0.165 |
| Acute coronary event | 29 (1.2%) | 21 (1.3%) | 8 (1.2%) | >0.999 |
| End-organ malperfusion | 112 (4.7%) | 95 (5.7%) | 17 (2.4%) | <0.001 |
| Renal ischemia | 38 (1.6%) | 33 (2.0%) | 5 (0.7%) | 0.028 |
| Mesenteric ischemia | 42 (1.8%) | 37 (2.2%) | 5 (0.7%) | 0.012 |
| Spinal cord ischemia | 16 (0.7%) | 14 (0.8%) | 2 (0.3%) | 0.109 |
| Limb ischemia | 38 (1.6%) | 32 (1.9%) | 6 (0.9%) | 0.065 |
| Redissection/extension | 92 (3.9%) | 70 (4.2%) | 22 (3.2%) | 0.248 |
| Medications after admission | t | | | |
| β-Blocker | 1884 (79.4%) | 1375 (82.0%) | 509 (73.2%) | <0.001 |
| ACEI/ARB | 1558 (65.7%) | 1129 (67.3%) | 429 (61.7%) | 0.009 |
| Calcium channel blocker | 1920 (80.9%) | 1362 (81.2%) | 558 (80.3%) | 0.600 |
| Nitrate | 940 (39.6%) | 687 (41.0%) | 253 (36.4%) | 0.039 |
| Diuretic | 487 (20.5%) | 366 (21.8%) | 121 (17.4%) | 0.015 |
| Statin | 536 (22.6%) | 368 (21.9%) | 168 (24.2%) | 0.237 |
| Antiplatelet | 250 (10.5%) | 188 (11.2%) | 62 (8.9%) | 0.098 |

Values are n (percent). The χ^2 test or Fisher exact test was used. ACEI indicates angiotensin-converting enzyme inhibitor; and ARB, angiotensin receptor blocker.

*The patients treated with hybrid therapy are included.

more likely to undergo interventional procedures than women. The sex difference in treatment could be explained by the higher incidence of end-organ malperfusion in men than in women. We also found an inverse association of female sex with end-organ malperfusion after multivariable adjustment. These results were in line with those of previous reports, which showed that men had a higher incidence of renal failure and mesenteric or limb ischemia than women.⁴ Although the exact mechanism underlying the sex difference in the incidence of end-organ malperfusion is unclear, it could be explained by the anatomical difference in the aorta involved with dissection between the sexes. Compared with women, men were more likely to have classic aortic dissection, which was also associated with the incidence of end-organ malperfusion. Because the proportion of DeBakey type IIIb dissections and the rate of end-organ malperfusion at initial presentation were comparable between the sexes, it is possible that men could be more susceptible to endorgan malperfusion during the hospital course. The development of malperfusion may be caused by distal extension of the aortic dissection, coexisting stenosis or dissection of the branch arteries, or progressive stenosis of the true lumen.

In the unadjusted analysis, we found that women had a higher in-hospital mortality rate than men. A difference in mortality was not only observed in the

| | Aortic rupture | • | | End-organ malperfusion | | | | |
|--|----------------|---------------------------------|--------|------------------------|---------------------------------|---------|--|--|
| Variables | OR | OR 95% CI P | | OR | 95% CI | P value | | |
| Age, per y | 1.05 | 1.03–1.07 | <0.001 | 0.99 | 0.97–1.00 | 0.111 | | |
| Female sex | 1.24 | 0.75–2.04 | 0.400 | 0.47 | 0.28-0.81 | 0.006 | | |
| Hyperlipidemia | 0.99 | 0.54–1.84 | 0.974 | 0.74 | 0.42-1.32 | 0.306 | | |
| Shock/hypotension | 12.3 | 6.54–23.3 | <0.001 | 5.92 | 3.06–11.4 | <0.001 | | |
| DeBakey type IIIb* | 1.11 | 0.63–1.96 | 0.729 | 0.98 | 0.60–1.61 | 0.933 | | |
| Classic aortic dissection [†] | 3.44 | 2.08–5.68 | <0.001 | 1.81 | 1.19–2.75 | 0.006 | | |
| | In-hospital m | In-hospital mortality (model 1) | | | In-hospital mortality (model 2) | | | |
| Age, per y | 1.06 | 1.04–1.09 | <0.001 | 1.06 | 1.03–1.08 | <0.001 | | |
| Female sex | 1.55 | 0.96–2.51 | 0.075 | 1.67 | 0.96–2.91 | 0.072 | | |
| Hyperlipidemia | 1.69 | 0.99–2.90 | 0.056 | 2.09 | 1.13–3.88 | 0.019 | | |
| Painlessness | 1.60 | 0.76-3.38 | 0.217 | 2.59 | 1.14–5.89 | 0.023 | | |
| Shock/hypotension | 11.0 | 5.64–21.3 | <0.001 | 2.93 | 1.21–7.11 | 0.017 | | |
| DeBakey type IIIb* | 1.40 | 0.78–2.50 | 0.260 | 1.44 | 0.75–2.76 | 0.274 | | |
| Classic aortic dissection [†] | 3.76 | 2.29-6.16 | <0.001 | 2.31 | 1.32-4.05 | 0.004 | | |
| Aortic rupture | | | | 26.6 | 14.1–50.0 | <0.001 | | |
| End-organ malperfusion | | | | 4.61 | 2.11–10.1 | <0.001 | | |
| Medical management | | | | 0.52 | 0.27-0.99 | 0.046 | | |

| Table 3. | Multivariable Analy | vses for Aortic Rupture. | End-Organ Malperfusion | , and In-Hospital Mortality |
|----------|---------------------|--------------------------|------------------------|-----------------------------|
| | | yses for Autile Hupture, | | |

OR indicates odds ratio.

*DeBakey type IIIa as a reference.

[†]Intramural hematoma as a reference.

medically managed patients (88%) but also in the patients who underwent an interventional procedure, including endovascular and open surgical therapies. Table 4 shows a list of prior studies on sex differences in mortality of patients with type B AAD. The study from the IRAD showed a significant mortality difference between the sexes in those with type A AAD but not in those with type B AAD.² Moreover, the study by Liang et al,⁴ which had the largest sample size, did not show a mortality difference between the sexes. Tolenaar et al⁷ showed a risk score calculation formula for mortality in type B AAD, in which age, shock/hypotension, malperfusion, and periaortic hematoma were positive independent risk factors for in-hospital mortality, whereas female sex was not significant. Only 0.3% was contributed by the female sex in such a risk calculation model for mortality. Therefore, we constructed a multivariable logistic regression model to assess the effect of female sex on mortality in the present study. As anticipated from the previous report by Tolenaar et al,⁷ age, shock/ hypotension, malperfusion, and aortic rupture were independent predictors of in-hospital mortality, whereas female sex was not associated with mortality in the total cohort. Female sex was a significant predictor of mortality when multivariable analysis was performed only in the elderly group. This suggests that older women are at higher risk of in-hospital death than older men. Women were less likely to experience malperfusion, which was not associated with mortality in the setting of invasively treated AAD. Therefore, the management of older women with type B AAD, compared with older men, should focus more on the prevention

 Table 4.
 Prior Studies With Available Data on Sex Differences in Mortality Among Patients With Type B Acute Aortic

 Dissection

| | | | Treatment | Treatment | | | In-hospital mortality | | | |
|------------------------------------|------|---------|-----------|-----------|--------------|-------|-----------------------|---------|--|--|
| Author, year | No. | % Women | Medical | Surgical | Endovascular | Men | Women | P value | | |
| Nienaber et al, 2004 ² | 403 | 29% | 72% | 18% | 10% | 12.3% | 14.4% | 0.56 | | |
| Tolenaar et al, 2014 ⁷ | 1034 | 35% | 65% | 10% | 23% | 10.4% | 11.0% | 0.77 | | |
| Maitusong et al, 2016 ⁵ | 246 | 26% | 30% | 2% | 68% | 3.8% | 7.9% | 0.19 | | |
| Liang et al, 2017 ⁴ | 9855 | 43% | 84% | 9% | 7% | 10.7% | 11.6% | 0.2 | | |
| McClure et al, 2018 ⁸ | 3632 | 39% | 83% | 10% | 7% | 6.9% | 9.9% | NA | | |

NA indicates not available.

and treatment of sex-related comorbid conditions and complications other than malperfusion, such as aortic rupture, during hospitalization.

In the present study, multivariable analyses showed that aortic rupture was one of the most life-threatening complications associated with increased in-hospital mortality, even in patients treated with interventional procedures. It would be reasonable that an initial therapeutic goal is to prevent the incidence of aortic rupture, the most common cause of death, in the setting of type B AAD regardless of male or female sex. Although female sex was not associated with aortic rupture after multivariable adjustment, age, shock/hypotension, and classic aortic dissection were independent risk factors for aortic rupture. Early interventional procedures such as thoracic endovascular aortic repair (TEVAR) may be optimal therapies for type B AAD with high-risk profiles of aortic rupture.

Study Limitations

There were some limitations to our study. First, this study was observational in nature; therefore, unmeasured confounders that affect mortality might be present. Second, responses to the treatment might be different between men and women. However, we did not directly compare these responses between the sexes. Third, patients with interventional procedures for type B AAD were included in only 12% of the total cohort. Although endovascular treatment such as TEVAR has been the first-line therapy for complicated type B AAD recently,²⁷ the risks of operation and comorbid conditions were considered when decisions for interventional therapies were made at each institution. A significant sex difference in in-hospital outcomes for such a high-risk patient group may not be detected because of the relatively small sample size. Fourth, long-term outcomes were not assessed in the present study. Further investigation is warranted to confirm sex differences in longterm outcomes, including aortic events in patients with type B AAD. Finally, pre-emptive TEVAR has now been increasingly used in patients with high-risk features to prevent late aorta-related complications.²⁸ However, the use of TEVAR was not indicated for uncomplicated type B AAD with high-risk features during the study period in Japan. The beneficial effect of preemptive TEVAR in the acute phase has not yet been established. It is uncertain whether our results are generalizable to other regions of the world where TEVAR is performed for different indications. Further study is needed to clarify the sex difference in the therapeutic effect of such intervention in patients with high-risk features.

Despite these limitations, we believe that our data from the large Japanese AAD registry will provide useful information on the management of patients with type B AAD and insightful perspectives on sex differences in AAD.

CONCLUSIONS

In type B AAD, women were older, presented later, had more IMH and less extension of dissection, and were less likely to experience end-organ malperfusion than men. The overall in-hospital mortality was higher in women than in men; however, female sex per se was not associated with in-hospital mortality after multivariable adjustment. Further research is warranted to determine sex-specific risk assessment and therapeutic strategies for type B AAD.

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Affiliations

Tokyo CCU Network Scientific Committee, Tokyo, Japan (T.T., H.Y., K.A., T.S., H.O., T.K., M.U., K.W., M.K., H.M., M.Y., T.Y., K.N., M.T.); and Department of Cardiology, Tokyo Saiseikai Central Hospital, Tokyo, Japan (T.T.).

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Disclosures

None.

Supplemental Material

Table S1-S8

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SUPPLEMENTAL MATERIAL

| | Total | Men | Women | P value |
|------------------------------------|---------------|---------------|---------------|---------|
| | (n = 492) | (n = 368) | (n = 124) | |
| Age (years) | 69 (58–78) | 66 (55–75) | 78 (70-84) | < 0.001 |
| Hypertension | 371 (75.4%) | 278 (74.7%) | 93 (75.0%) | 0.903 |
| Hyperlipidemia | 75 (15.2%) | 50 (13.6%) | 25 (20.2%) | 0.078 |
| Diabetes mellitus | 40 (8.1%) | 28 (7.6%) | 12 (9.7%) | 0.466 |
| Cigarette smoking* | 130 (26.7%) | 112 (30.9%) | 18 (14.8%) | 0.001 |
| Previous coronary artery disease | 18 (3.7%) | 12 (3.3%) | 6 (4.8%) | 0.414 |
| Previous stroke | 28 (5.7%) | 22 (6.0%) | 6 (4.8%) | 0.636 |
| Previous peripheral artery disease | 9 (1.8%) | 7 (1.9%) | 2 (1.6%) | 1.000 |
| Previous cardiac surgery | 7 (1.4%) | 6 (1.6%) | 1 (0.8%) | 0.685 |
| End-stage renal disease on HD | 6 (1.2%) | 3 (0.8%) | 3 (2.4%) | 0.171 |
| Time from onset to admission | | | | 0.054 |
| < 24 h | 436 (88.6%) | 328 (89.1%) | 108 (87.1%) | |
| 1–6 days | 40 (8.1%) | 32 (8.7%) | 8 (6.5%) | |
| 7–14 days | 16 (3.3%) | 8 (2.2%) | 8 (6.5%) | |
| Back pain | 324 (65.8%) | 230 (62.5%) | 94 (75.8%) | 0.007 |
| Chest pain | 195 (39.6%) | 146 (39.7%) | 49 (39.5%) | 0.975 |
| Abdominal pain | 66 (13.4%) | 52 (14.1%) | 14 (11.3%) | 0.422 |
| Lumbago | 42 (8.5%) | 35 (9.5%) | 7 (5.6%) | 0.183 |
| Leg pain | 14 (2.8%) | 12 (3.3%) | 2 (1.6%) | 0.367 |
| Painlessness | 30 (6.1%) | 23 (6.3%) | 7 (5.6%) | 0.808 |
| Shock/hypotension | 34 (6.9%) | 22 (6.0%) | 12 (9.7%) | 0.160 |
| Aortic rupture on admission | 48 (9.8%) | 32 (8.7%) | 16 (12.9%) | 0.172 |
| Malperfusion on admission | 71 (14.4%) | 57 (15.4%) | 14 (11.3%) | 0.250 |
| Systolic blood pressure (mmHg) | 150 (128–178) | 152 (131–180) | 142 (121–170) | 0.009 |
| Heart rate (beats per min) | 79 (68–91) | 80 (68–92) | 77 (66–89) | 0.249 |
| Status of false lumen | | | | 0.283 |
| Classic aortic dissection | 290 (58.9%) | 222 (60.3%) | 68 (54.8%) | |
| IMH | 202 (41.1%) | 146 (39.7%) | 56 (45.2%) | |
| DeBakey classification | | | . , | 0.089 |
| Type IIIa | 119 (24.2%) | 82 (22.3%) | 37 (29.8%) | |
| Type IIIb | 373 (75.8%) | 286 (77.7%) | 87 (70.2%) | |

Table S1. Baseline characteristics of patients with complicated type B AAD.

Values are median (interquartile) or n (%). AAD = acute aortic dissection; HD = hemodialysis; IMH = intramural hematoma. The Chi-square test or Fisher's exact test was used to compare categorical variables, and the Mann–Whitney U test was used to compare continuous variables. * Data on history of cigarette smoking are available in 365 men and 122 women.

| | Total | Men | Women | P value |
|------------------------------------|---------------|---------------|---------------|---------|
| | (n = 1201) | (n = 736) | (n = 465) | |
| Age (years) | 79 (74–84) | 78 (74–82) | 81 (74–86) | < 0.001 |
| Hypertension | 915 (76.2%) | 561 (76.2%) | 354 (76.1%) | 0.970 |
| Hyperlipidemia | 226 (18.8%) | 130 (17.7%) | 96 (20.6%) | 0.198 |
| Diabetes mellitus | 122 (10.2%) | 84 (11.4%) | 38 (8.2%) | 0.070 |
| Cigarette smoking* | 222 (18.7%) | 169 (23.2%) | 53 (11.6%) | < 0.001 |
| Previous coronary artery disease | 64 (5.3%) | 41 (5.6%) | 23 (4.9%) | 0.639 |
| Previous stroke | 117 (9.7%) | 76 (10.3%) | 41 (8.8%) | 0.390 |
| Previous peripheral artery disease | 20 (1.7%) | 15 (2.0%) | 5 (1.1%) | 0.204 |
| Previous cardiac surgery | 24 (2.0%) | 19 (2.6%) | 5 (1.1%) | 0.069 |
| End-stage renal disease on HD | 27 (2.2%) | 19 (2.6%) | 8 (1.7%) | 0.327 |
| Time from onset to admission | | | | 0.878 |
| < 24 h | 1062 (88.4%) | 653 (88.7%) | 409 (88.0%) | |
| 1–6 days | 111 (9.2%) | 67 (9.1%) | 44 (9.5%) | |
| 7–14 days | 28 (2.3%) | 16 (2.2%) | 12 (2.6%) | |
| Back pain | 826 (68.8%) | 490 (66.6%) | 336 (72.3%) | 0.038 |
| Chest pain | 468 (39.0%) | 294 (39.9%) | 174 (37.4%) | 0.382 |
| Abdominal pain | 125 (10.4%) | 76 (10.3%) | 49 (10.5%) | 0.907 |
| Lumbago | 80 (6.7%) | 50 (6.8%) | 30 (6.5%) | 0.817 |
| Leg pain | 4 (0.3%) | 2 (0.3%) | 2 (0.4%) | 0.643 |
| Painlessness | 81 (6.7%) | 49 (6.7%) | 32 (6.9%) | 0.880 |
| Shock/hypotension | 22 (1.8%) | 14 (1.9%) | 8 (1.7%) | 0.819 |
| Aortic rupture on admission | 32 (2.7%) | 19 (2.6%) | 13 (2.8%) | 0.822 |
| Malperfusion on admission | 25 (2.1%) | 14 (1.9%) | 11 (2.4%) | 0.584 |
| Systolic blood pressure (mmHg) | 160 (136–189) | 160 (138–188) | 159 (132–189) | 0.346 |
| Heart rate (beats per min) | 76 (66–87) | 76 (66–88) | 77 (65–86) | 0.467 |
| Status of false lumen | | | | 0.145 |
| Classic aortic dissection | 394 (32.8%) | 253 (34.4%) | 141 (30.3%) | |
| IMH | 807 (67.2%) | 483 (65.6%) | 324 (69.7%) | |
| DeBakey classification | | | 、 / | 0.204 |
| Type IIIa | 362 (30.1%) | 212 (28.8%) | 150 (32.3%) | |
| Type IIIb | 839 (69.9%) | 524 (71.2%) | 315 (67.7%) | |

Table S2. Baseline characteristics of the elderly group.

Values are median (interquartile) or n (%). HD = hemodialysis; IMH = intramural hematoma. The Chi-square test or Fisher's exact test was used to compare categorical variables, and the Mann–Whitney U test was used to compare continuous variables.

* Data on history of cigarette smoking are available in 727 men and 458 women.

| | Total | Men | Women | P value |
|-----------------------------|-------------|-------------|------------|---------|
| | (n = 492) | (n = 368) | (n = 124) | |
| Management | | | | |
| Medical therapy | 199 (40.4%) | 138 (37.5%) | 61 (49.2%) | 0.022 |
| Interventional therapy | 293 (59.6%) | 230 (62.5%) | 63 (50.8%) | 0.022 |
| Endovascular therapy | 132 (26.8%) | 105 (28.5%) | 27 (21.8%) | 0.140 |
| Open surgical therapy | 148 (30.1%) | 116 (31.5%) | 32 (25.8%) | 0.230 |
| Hybrid therapy | 13 (2.6%) | 9 (2.4%) | 4 (3.2%) | 0.746 |
| In-hospital death | | | | |
| Overall | 71 (14.4%) | 40 (10.9%) | 31 (25.0%) | < 0.001 |
| Medically managed | 40 (20.1%) | 20 (14.5%) | 20 (32.8%) | 0.003 |
| Interventionally treated | 31 (10.6%) | 20 (8.7%) | 11 (17.5%) | 0.045 |
| Endovascularly treated | 12 (9.1%) | 8 (7.6%) | 4 (14.8%) | 0.246 |
| Surgically treated* | 19 (11.8%) | 12 (9.6%) | 7 (17.5%) | 0.140 |
| In-hospital complications | | | | |
| Aortic rupture | 80 (16.3%) | 50 (13.6%) | 30 (24.2%) | 0.006 |
| Hemothorax | 29 (5.9%) | 18 (4.9%) | 11 (8.9%) | 0.104 |
| Acute ischemic stroke | 38 (7.7%) | 23 (6.3%) | 15 (12.1%) | 0.035 |
| Acute coronary event | 11 (2.2%) | 10 (2.7%) | 1 (0.8%) | 0.305 |
| End-organ malperfusion | 112 (22.8%) | 95 (25.8%) | 17 (13.7%) | 0.005 |
| Renal ischemia | 38 (7.7%) | 33 (9.0%) | 5 (4.0%) | 0.082 |
| Mesenteric ischemia | 42 (8.5%) | 37 (10.1%) | 5 (4.0%) | 0.038 |
| Spinal cord ischemia | 16 (3.2%) | 14 (3.8%) | 2 (1.6%) | 0.379 |
| Limb ischemia | 38 (7.7%) | 32 (8.7%) | 6 (4.8%) | 0.164 |
| Re-dissection/extension | 92 (18.7%) | 70 (19.0%) | 22 (17.7%) | 0.752 |
| Medications after admission | | | | |
| Beta-blocker | 362 (73.6%) | 280 (76.1%) | 82 (66.1%) | 0.030 |
| ACEI/ARB | 254 (51.6%) | 191 (51.9%) | 63 (50.8%) | 0.833 |
| Calcium channel blocker | 360 (73.2%) | 269 (73.1%) | 91 (73.4%) | 0.950 |
| Nitrate | 168 (34.1%) | 125 (34.0%) | 43 (34.7%) | 0.885 |
| Diuretic | 146 (29.7%) | 111 (30.2%) | 35 (28.2%) | 0.683 |
| Statin | 95 (19.3%) | 68 (18.5%) | 27 (21.8%) | 0.421 |
| Antiplatelet | 65 (13.2%) | 53 (14.4%) | 12 (9.7%) | 0.179 |

| Table S3. In-hospital management and outcom | nes of patients with complicated type B AAD. |
|---|--|
| | |

Values are n (%). AAD = acute aortic dissection; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker. The Chi-square test or Fisher's exact test was used. * The patients treated with hybrid therapy are included.

| | Total | Men | Women | P value |
|-----------------------------|--------------|-------------|-------------|---------|
| | (n = 1201) | (n = 736) | (n = 465) | |
| Management | | | | |
| Medical therapy | 1077 (89.7%) | 657 (89.3%) | 420 (90.3%) | 0.558 |
| Interventional therapy | 124 (10.3%) | 79 (10.7%) | 45 (9.7%) | 0.558 |
| Endovascular therapy | 72 (6.0%) | 49 (6.7%) | 23 (4.9%) | 0.224 |
| Open surgical therapy | 61 (5.1%) | 36 (4.9%) | 25 (5.4%) | 0.709 |
| Hybrid therapy | 9 (0.7%) | 6 (0.8%) | 3 (0.6%) | 1.000 |
| In-hospital death | | | | |
| Overall | 62 (5.2%) | 28 (3.8%) | 34 (7.3%) | 0.007 |
| Medically managed | 46 (4.3%) | 20 (3.0%) | 26 (6.2%) | 0.013 |
| Interventionally treated | 16 (10.6%) | 8 (10.1%) | 8 (17.8%) | 0.222 |
| Endovascularly treated | 5 (7.9%) | 2 (4.7%) | 3 (15.0%) | 0.315 |
| Surgically treated* | 11 (18.0%) | 6 (16.7%) | 5 (20.0%) | 0.747 |
| In-hospital complications | | | | |
| Aortic rupture | 56 (4.7%) | 30 (4.1%) | 26 (5.6%) | 0.225 |
| Hemothorax | 18 (1.5%) | 10 (1.4%) | 8 (1.7%) | 0.615 |
| Acute ischemic stroke | 18 (1.5%) | 8 (1.1%) | 10 (2.2%) | 0.139 |
| Acute coronary event | 14 (1.2%) | 9 (1.2%) | 5 (1.1%) | 0.816 |
| End-organ malperfusion | 40 (3.3%) | 28 (3.8%) | 12 (2.6%) | 0.250 |
| Renal ischemia | 13 (1.1%) | 11 (1.5%) | 2 (0.4%) | 0.082 |
| Mesenteric ischemia | 10 (8.3%) | 7 (1.0%) | 3 (0.6%) | 0.749 |
| Spinal cord ischemia | 8 (0.7%) | 6 (0.8%) | 2 (0.4%) | 0.718 |
| Limb ischemia | 14 (1.2%) | 9 (1.2%) | 5 (1.1%) | 0.816 |
| Re-dissection/extension | 43 (3.6%) | 26 (3.5%) | 17 (3.7%) | 0.911 |
| Medications after admission | | | | |
| Beta-blocker | 891 (74.2%) | 567 (77.0%) | 324 (69.7%) | 0.005 |
| ACEi/ARB | 728 (60.6%) | 462 (62.8%) | 266 (57.2%) | 0.054 |
| Calcium channel blocker | 949 (79.0%) | 579 (78.7%) | 370 (79.6%) | 0.709 |
| Nitrate | 429 (35.7%) | 272 (37.0%) | 157 (33.8%) | 0.261 |
| Diuretic | 224 (18.7%) | 141 (19.2%) | 83 (17.8%) | 0.571 |
| Statin | 277 (23.1%) | 168 (22.8%) | 109 (23.4%) | 0.805 |
| Antiplatelet | 153 (12.7%) | 101 (13.7%) | 52 (11.2%) | 0.198 |

Table S4. In-hospital management and outcomes in the elderly group.

Values are n (%). ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker. The Chi-square test or Fisher's exact test was used.

* The patients treated with hybrid therapy are included.

| | Aortic rupture | | End | End-organ malperfusion | | In-hospital mortality | | | |
|---|----------------|-----------|---------|------------------------|-------------|-----------------------|------|-----------|---------|
| Variables | OR | 95% CI | P value | OR | 95% CI | P value | OR | 95% CI | P value |
| Age (per year) | 1.04 | 1.02-1.06 | < 0.001 | 0.98 | 0.97-0.99 | 0.001 | 1.05 | 1.03-1.07 | < 0.001 |
| Female sex | 1.47 | 0.93-2.33 | 0.103 | 0.42 | 0.25-0.71 | 0.001 | 1.99 | 1.28-3.10 | 0.002 |
| Hypertension | 1.03 | 0.62-1.72 | 0.923 | 1.14 | 0.73-1.78 | 0.576 | 0.79 | 0.49-1.27 | 0.322 |
| Hyperlipidemia | 0.99 | 0.55-1.79 | 0.985 | 0.66 | 0.37-1.16 | 0.151 | 1.62 | 0.98-2.69 | 0.062 |
| Diabetes mellitus | 0.77 | 0.31-1.94 | 0.582 | 1.29 | 0.68-2.45 | 0.437 | 1.83 | 0.96-3.52 | 0.069 |
| Cigarette smoking | 0.69 | 0.40-1.17 | 0.164 | 0.95 | 0.62-1.45 | 0.807 | 0.36 | 0.19–0.69 | 0.002 |
| Previous coronary artery disease | 0.79 | 0.28-2.19 | 0.645 | 0.72 | 0.31-1.69 | 0.457 | 0.52 | 0.22-1.22 | 0.134 |
| Previous stroke | 0.71 | 0.26-1.96 | 0.503 | 1.12 | 0.59–2.41 | 0.618 | 1.06 | 0.45-2.47 | 0.896 |
| Previous peripheral artery disease | 1.15 | 0.15-8.58 | 0.893 | 1.69 | 0.40-7.26 | 0.478 | - | - | - |
| Previous cardiac surgery | - | - | - | 1.86 | 0.56-6.15 | 0.311 | 1.64 | 0.39-6.93 | 0.503 |
| End-stage renal disease on hemodialysis | 0.70 | 0.09–5.12 | 0.721 | - | - | - | 0.70 | 0.09-4.92 | 0.693 |
| Time from onset to admission <24 hours | 1.03 | 0.51-2.08 | 0.943 | 0.70 | 0.35-1.39 | 0.306 | 1.25 | 0.65-2.38 | 0.506 |
| Painlessness | 1.32 | 0.52-3.34 | 0.554 | 1.33 | 0.60-2.92 | 0.481 | 2.85 | 1.43-5.68 | 0.003 |
| Shock/hypotension | 23.6 | 12.0-46.6 | < 0.001 | 5.36 | 2.41-11.9 | < 0.001 | 22.5 | 11.4-44.4 | < 0.001 |
| DeBakey type IIIb [*] | 1.04 | 0.61-1.78 | 0.875 | 1.25 | 0.78 - 2.01 | 0.358 | 1.18 | 0.69-2.03 | 0.547 |
| Classic aortic dissection [†] | 2.50 | 1.57–3.99 | < 0.001 | 2.17 | 1.47-3.21 | < 0.001 | 2.51 | 1.59–3.97 | < 0.001 |
| Aortic rupture | | | | | | | 52.3 | 30.7-89.0 | < 0.001 |
| End-organ malperfusion | | | | | | | 5.46 | 3.05-9.77 | < 0.001 |
| Medical management | | | | | | | 0.22 | 0.14-0.34 | < 0.001 |

Table S5. Univariate analyses for aortic rupture, end-organ malperfusion, and in-hospital mortality.

OR = odds ratio; CI = confidence interval.

* DeBakey type IIIa as a reference. [†] Intramural hematoma as a reference.

| Variables | Model 1 | | | Model 2 | | |
|--|---------|-----------|---------|---------|-----------|---------|
| | OR | 95% CI | P value | OR | 95% CI | P value |
| Age (per year) | 1.06 | 1.03-1.08 | < 0.001 | 1.04 | 1.01-1.07 | 0.004 |
| Female sex | 1.76 | 0.97-3.17 | 0.062 | 1.78 | 0.93-3.43 | 0.083 |
| Hyperlipidemia | 1.55 | 0.77-3.10 | 0.219 | 1.62 | 0.75-3.46 | 0.218 |
| Painlessness | 1.61 | 0.59-4.41 | 0.352 | 1.98 | 0.65-6.07 | 0.233 |
| Shock/hypotension | 3.86 | 1.76-8.47 | < 0.001 | 2.00 | 0.81-4.93 | 0.134 |
| DeBakey type IIIb [*] | 1.75 | 0.88-3.49 | 0.113 | 1.69 | 0.80-3.59 | 0.169 |
| Classic aortic dissection [†] | 2.35 | 1.29-4.26 | 0.005 | 2.19 | 1.13-4.24 | 0.021 |
| Aortic rupture | | | | 8.79 | 4.65-16.6 | < 0.001 |
| End-organ malperfusion | | | | 1.36 | 0.65-2.86 | 0.416 |
| Medical management | | | | 1.73 | 0.92-3.25 | 0.087 |

Table S6. Multivariable analysis for in-hospital mortality in patients with complicated type B AAD.

AAD = acute a ortic dissection; OR = odds ratio; CI = confidence interval.

* DeBakey type IIIa as a reference. [†] Intramural hematoma (IMH) as a reference.

| Variables | Model 1 | | | Model 2 | | |
|--|---------|-----------|---------|---------|-----------|---------|
| | OR | 95% CI | P value | OR | 95% CI | P value |
| Age (per year) | 1.02 | 0.99–1.06 | 0.198 | 1.01 | 0.98-1.05 | 0.587 |
| Female sex | 2.10 | 0.87-5.07 | 0.100 | 1.87 | 0.71-4.97 | 0.210 |
| Hyperlipidemia | 0.98 | 0.33-2.86 | 0.965 | 1.03 | 0.33-3.24 | 0.965 |
| Painlessness | 0.38 | 0.04-3.39 | 0.384 | 0.55 | 0.06-5.22 | 0.603 |
| Shock/hypotension | 6.62 | 2.12-20.6 | 0.001 | 2.64 | 0.72-9.68 | 0.143 |
| DeBakey type IIIb [*] | 1.09 | 0.42-2.87 | 0.859 | 1.16 | 0.42-3.22 | 0.773 |
| Classic aortic dissection [†] | 2.60 | 0.98-6.92 | 0.055 | 2.11 | 0.76-5.89 | 0.153 |
| Aortic rupture | | | | 7.09 | 2.85-17.6 | < 0.001 |
| End-organ malperfusion | | | | 1.97 | 0.67–5.76 | 0.216 |

Table S7. Multivariable analysis for in-hospital mortality in patients treated with interventional procedures.

OR = odds ratio; CI = confidence interval.

* DeBakey type IIIa as a reference. [†] Intramural hematoma (IMH) as a reference.

| Variables | | Aortic rupture | | | End-organ malperfusion | | |
|--|--------|---------------------------------|---------|------|---------------------------------|---------|--|
| | OR | 95% CI | P value | OR | 95% CI | P value | |
| Age (per year) | 1.05 | 1.00-1.10 | 0.033 | 1.01 | 0.95-1.06 | 0.862 | |
| Female sex | 1.34 | 0.74–2.42 | 0.334 | 0.68 | 0.34–1.38 | 0.285 | |
| Hyperlipidemia | 1.03 | 0.49–2.14 | 0.943 | 0.78 | 0.32-1.90 | 0.586 | |
| Shock/hypotension | 24.0 | 9.48-60.9 | < 0.001 | 5.92 | 3.06-11.4 | 0.001 | |
| DeBakey type IIIb [*] | 1.00 | 0.53-1.90 | 0.729 | 1.09 | 0.53-2.23 | 0.821 | |
| Classic aortic dissection [†] | 3.62 | 2.01-6.52 | < 0.001 | 1.28 | 0.66–2.48 | 0.459 | |
| | In-hos | In-hospital mortality (model 1) | | | In-hospital mortality (model 2) | | |
| Variables | OR | 95% CI | P value | OR | 95% CI | P value | |
| Age (per year) | 1.07 | 1.02-1.12 | 0.004 | 1.06 | 1.01-1.11 | 0.028 | |
| Female sex | 1.94 | 1.11–3.40 | 0.020 | 1.95 | 1.05-3.63 | 0.036 | |
| Hyperlipidemia | 1.60 | 0.85-3.00 | 0.144 | 1.89 | 0.94-3.81 | 0.073 | |
| Painlessness | 1.46 | 0.62-3.40 | 0.387 | 2.25 | 0.88-5.75 | 0.090 | |
| Shock/hypotension | 11.3 | 5.09-25.1 | < 0.001 | 3.33 | 1.18–9.44 | 0.024 | |
| DeBakey type IIIb [*] | 1.23 | 0.66-2.29 | 0.518 | 1.23 | 0.62-2.45 | 0.554 | |
| Classic aortic dissection [†] | 3.74 | 2.14-6.53 | < 0.001 | 2.56 | 1.37-4.79 | 0.003 | |
| Aortic rupture | | | | 24.4 | 11.5–51.5 | < 0.001 | |
| End-organ malperfusion | | | | 3.84 | 1.32–11.7 | 0.013 | |
| Medical management | | | | 0.95 | 0.41–2.22 | 0.910 | |

Table S8. Multivariable analyses for aortic rupture, end-organ malperfusion, and in-hospital mortality in the elderly group.

OR = odds ratio; CI = confidence interval.

* DeBakey type IIIa as a reference. [†] Intramural hematoma (IMH) as a reference.