Impact of antithrombotic therapy on clinical outcomes in patients with type B acute aortic syndrome

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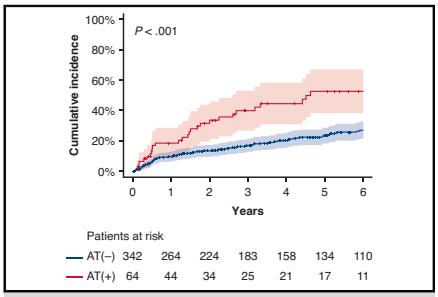
ABSTRACT

Objective: Antithrombotic therapy has the potential to interfere with false lumen thrombosis. In type B acute aortic syndrome, the degree of false lumen thrombosis affects clinical outcomes. We aimed to explore the association of antithrombotic therapy with the prognosis of patients with type B acute aortic syndrome.

Methods: We reviewed 406 patients with type B acute aortic syndrome who were discharged alive with and without antithrombotic therapy. The primary outcome was aorta-related adverse events, defined as a composite of aorta-related death, aortic rupture, aortic repair, and progressive aortic dilation.

Results: Of the 406 patients, 64 (16%) were discharged with antithrombotic therapy and 342 (84%) were discharged without antithrombotic therapy. A total of 249 patients (61%) presented with intramural hematoma with complete thrombosis of the false lumen, and 157 patients (39%) presented with aortic dissection. During a median follow-up of 4.6 years, 32 patients (50%) in the antithrombotic group and 93 patients (27%) in the nonantithrombotic group had a primary outcome event. Cumulative incidence of aorta-related events at 1 and 3 years with death as the competing risk was higher in the antithrombotic group than in the nonantithrombotic group (19% ± 5% vs 9% ± 2% at 1 year and 40% ± 7% vs 17% ± 2% at 3 years, $P < .001$).

Conclusions: Antithrombotic therapy might be associated with an increased risk of aorta-related events in patients with type B acute aortic syndrome. (JTCVS Open 2023;14:36-45)



Aorta-related adverse events in patients with and without antithrombotic therapy.

CENTRAL MESSAGE

In patients with type B AAS, antithrombotic therapy might be associated with an increased risk of aorta-related events.

PERSPECTIVE

Antithrombotic therapy might be associated with an increased risk of aorta-related events in patients with type B AAS. For patients with an indispensable need for antithrombotic therapy, careful follow-up is needed.

Video clip is available online.

Stanford type B acute aortic syndrome (AAS), including classic aortic dissection (AD) and aortic intramural hematoma (IMH), is a life-threatening disease, with a 5-year mortality rate of approximately 20%.[1-3] In contrast, a considerable portion of patients who survive the acute phase eventually experience aorta-related events that require surgical repair or thoracic endovascular aortic repair.[4,5] Initial conservative therapy and blood pressure control are recommended for patients with uncomplicated type B AAS; however, there is a lack of evidence supporting the efficacy of medical therapy in chronic aortic diseases.[6] Thus, predicting the risk factors for future aorta-related adverse events in patients with uncomplicated type B AAS is crucial in determining a therapeutic strategy. To date, several clinical and imaging-related risk factors have been shown to impact early disease progression. Among these risk factors, the degree of false lumen thrombosis is known to play an important role in disease progression.[7] In an ever-aging society, it is often the situation that patients taking an antiplatelet or anticoagulant develop type B AAS.

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Abbreviations and Acronyms
AAS = acute aortic syndrome
AD = aortic dissection
CAD = coronary artery disease
CT = computed tomography
IMH = intramural hematoma
PAD = peripheral artery disease

Antithrombotic therapy could modify the clinical course of AAS by interfering with thrombosis of the false lumen.

Currently, there has been no consensus on discontinuing antithrombotic therapy in patients who have been taking it before hospitalization or on starting antithrombotic therapy in patients who have been newly diagnosed with conditions with an indication for antithrombotic therapy such as coronary artery disease (CAD), cerebral ischemic disease, atrial fibrillation, and venous thromboembolism during hospitalization for AAS. To date, there have been no large-scale studies investigating the effects of antithrombotic therapy on the clinical outcomes in patients with type B AAS. The aim of this study was to explore the association of antithrombotic therapy with clinical outcomes in patients with type B AAS.

MATERIALS AND METHODS

Patient Characteristics

We retrospectively reviewed 431 consecutive patients admitted to our hospital who were diagnosed with uncomplicated type B AAS, including classic AD and IMH between 1991 and 2020. Of these, 406 patients were discharged alive and included in the study. This study was approved by the Institutional Review Board of the Kobe City Medical Center General Hospital (zn2102222; January 2021). The need to obtain informed consent was waived because of the retrospective nature of the study.

Patient and Public Involvement

There has been no patient and public involvement.

Treatment

All the patients initially received medical therapy. The therapeutic goals were pain relief and control of systolic blood pressure less than 120 mm Hg. Intravenous calcium channel antagonists are mainly used to control blood pressure during the acute phase. Oral antihypertensive drugs such as calcium channel blockers, beta-blockers, angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers (angiotensin-converting enzyme inhibitor/angiotensin receptor blocker) were added in the acute and chronic phase. Computed tomography (CT) or transesophageal echocardiography was performed approximately 2 weeks after symptom onset, and the patients were discharged unless they had abnormal imaging results or any complications. During hospitalization or outpatient follow-up, surgical or endovascular aortic repair was performed in cases of aortic rupture or progressive aortic enlargement.

Clinical Follow-up and Computed Tomography Evaluation

The patients had follow-up visits at the outpatient clinic every 4 to 8 weeks after discharge to check the adequacy of blood pressure control and the presence of symptoms. Multi-detector row CT or magnetic resonance imaging were performed at 1, 3, 6, and 12 months after discharge, and annually thereafter. Aorta-related adverse events were defined as a composite of aorta-related death, aortic rupture, surgical or endovascular aortic repair, and progressive aortic dilation ($\geq$55 mm or $\geq$5 mm per 6 months) as previously reported.[8,9] The cause of mortality was determined by review of the electronical health record, the physician's death summary, and the available autopsy reports. The cause of death was classified as aorta related if it had been due to aortic rupture, progression of dissection, malperfusion, or related to any aortic repair, as previously reported.[10,11] AD was defined as a double-channel aorta that typically showed contrast enhancement or a visible intimal tear. IMH was defined as crescentic aortic wall thickening without direct flow communication.[12,13] A comparison was made between patients with and without a prescription for antithrombotic therapy at discharge.

Statistical Analysis

Categorical variables were expressed as numbers and percentages and compared by chi-square test or Fisher exact test, as appropriate. For the continuous variables, normality of distribution was tested using Shapiro–Wilk test. Normally distributed variables were expressed as mean and standard deviation (mean $\pm$ standard deviation) and compared by unpaired *t* tests. Repeated measurements of aortic diameter during follow-up were compared by repeated analysis of variance. Non-normally distributed variables were expressed as median with interquartile range and compared between the groups using Wilcoxon rank-sum test. Nonparametric estimates of cumulative incidence (probability of aorta-related adverse events) were calculated considering non-aorta related death as competing-risk event. Survival regression used competing risk analysis with the Fine-Gray model. Results are presented as sub-hazard ratios and 95% confidence intervals. The following variables were selected: age, sex, comorbidities (hypertension, dyslipidemia, diabetes mellitus, end-stage renal disease with hemodialysis, previous CAD, peripheral artery disease [PAD] and stroke), medication at discharge (antithrombotic therapy, beta-blockers, angiotensin-converting enzyme inhibitor/angiotensin receptor blockers, and calcium channel blockers), type of aortic syndrome (AD or IMH), and cigarette smoking. No patients had missing data on these variables. We plotted log(time) vs log[-log(survival)] stratified by each significant risk factor and evaluated whether the plotted lines were parallel. The variables whose proportional assumptions were generally fair were included in the analysis.

All statistical analyses were performed using SPSS Statistics version 25.0 (IBM Corp, Armonk, NY) or R software package version 3.6.3 software.

RESULTS

Patient Characteristics

Of the 406 patients with type B AAS, 64 (16%) were discharged with antithrombotic therapy and 342 (84%) were discharged without antithrombotic therapy. The mean patient age was 68 $\pm$ 13 years. Of these, 275 (69%) were male. In relation to the types of antithrombotic therapy, 48 patients (75% of the antithrombotic group) were prescribed an antiplatelet, 25 patients (39%) were prescribed an anticoagulant, and 9 patients (14%) were prescribed both an antiplatelet and an anticoagulant. The baseline characteristics of patients in the antithrombotic and nonantithrombotic groups are shown in Table 1. In the antithrombotic group, the patients were significantly older compared with the nonantithrombotic group (73 $\pm$ 14 vs 67 $\pm$ 13 years, $P = .001$) and had more comorbidities such as diabetes mellitus (25% vs 10%, $P = .001$),

TABLE 1. Baseline characteristics of patients in the antithrombotic and nonantithrombotic groups

Characteristics	Antithrombotic therapy (+) (n = 64)	Antithrombotic therapy (−) (n = 342)	*P*
Age, y	73 ± 14	67 ± 13	.001
Male, n (%)	44 (69)	231 (68)	.85
Classic AD, n (%)	21 (33)	136 (40)	.29
Comorbidity			
Hypertension, n (%)	56 (88)	295 (86)	.79
Dyslipidemia, n (%)	24 (38)	88 (26)	.05
Diabetes mellitus, n (%)	16 (25)	35 (10)	.001
Smoking, n (%)	26 (41)	98 (29)	.06
Hemodialysis, n (%)	3 (5)	3 (1)	.05
Previous CAD, n (%)	24 (38)	0 (0)	<.001
Previous PAD, n (%)	4(6)	0 (0)	.001
Previous stroke, n (%)	17(27)	1 (0.3)	<.001
Medication at discharge			
ACEi/ARB, n (%)	19 (30)	175 (51)	.002
Beta-blocker, n (%)	46 (72)	265 (78)	.33
CCB, n (%)	48 (75)	287 (84)	.09

AD, Aortic dissection; *CAD*, coronary artery disease; *PAD*, peripheral artery disease; *ACEi*, angiotensin-converting enzyme inhibitor; *ARB*, angiotensin receptor blocker; *CCB*, calcium channel blocker.

previous CAD (38% vs 0%, $P < .001$), previous PAD (6% vs 0%, $P = .001$), and previous stroke (27% vs 0.3%, $P < .001$).

The most common reason for prescription of antithrombotic medication was CAD (n = 24, 38%), followed by atrial fibrillation (n = 20, 31%), cerebral infarction or transient ischemic attack (n = 17, 27%), venous thromboembolism (n = 6, 9%), mechanical valve replacement (n = 6, 9%), and peripheral artery disease (n = 4, 6%). A total of 249 patients (61%) presented with IMH with complete thrombosis of the false lumen, and 157 patients (39%) presented with classic AD.

Clinical Outcome

Follow-up was completed in 256 patients and the median follow-up period was 4.6 years (interquartile range, 2.0-8.6 years). A total of 150 (37%) patients were lost to follow-up. The reasons for lost follow-up were patients' refusal (n = 60), transfer to different hospital or clinic in another area (n = 68) and unknown (n = 22). A total of 125 patients (31%) had a primary outcome event after being discharged from the initial hospitalization. In total, 32 patients (50%) in the antithrombotic group and 93 patients (27%) in the nonantithrombotic group had a primary outcome event. Table 2 shows the aorta-related events in the antithrombotic and nonantithrombotic groups. Figure 1 and Figure E1 shows the cumulative incidence of aorta-related adverse events in patients with and without antithrombotic therapy, considering nonaorta-related death as the competing risk. Cumulative incidence of aorta-related

TABLE 2. Aorta-related adverse events in the antithrombotic and nonantithrombotic groups

Events	Antithrombotic therapy (+) (n = 64)	Antithrombotic therapy (−) (n = 342)	*P*
All-cause death, n (%)	9 (14)	41(12)	.20
Aorta-related adverse events, n (%)	32 (50)	93 (27)	<.001
Aorta-related death, n (%)	0 (0)	7 (2)	.62
Aortic rupture, n (%)	0 (0)	4 (1)	.62
Surgical repair, n (%)	14 (22)	46 (14)	.01
Endovascular repair, n (%)	6 (9)	15 (4)	.03
Progressive aortic dilation, n (%)	11 (17)	11 (3)	<.001
Redissection, n (%)	1 (2)	10 (3)	.77

events at 1 and 3 years with death as the competing risk was higher in the antithrombotic group than in the nonantithrombotic group (19% ± 5% vs 9% ± 2% at 1 year and 40% ± 7% vs 17% ± 2% at 3 years, $P < .001$).

In the competing-risk univariable analysis, initial presentation with classic AD, dyslipidemia, previous CAD, previous PAD, previous stroke, and antithrombotic therapy were significant risk factors for aorta-related adverse events (Table 3).

Subgroup Analysis

Figure 2 shows the cumulative incidence of aorta-related adverse events in patients with and without antithrombotic therapy in subgroups of IMH and AD, considering nonaorta-related death as the competing risk. In patients with IMH, the cumulative incidence of aorta-related events at 1 and 3 years with death as the competing risk was higher in the antithrombotic group than in the nonantithrombotic

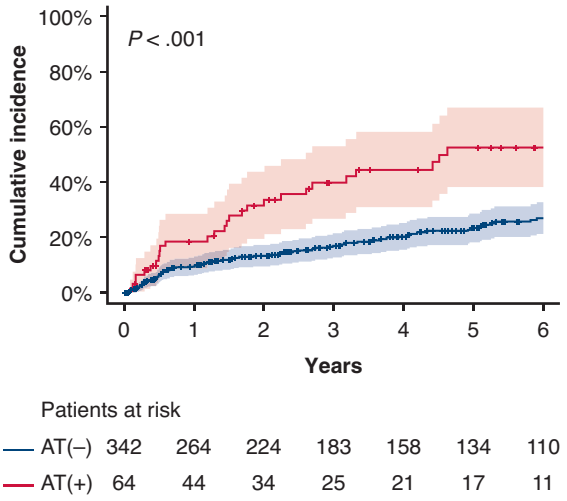

FIGURE 1. Considering nonaorta-related death as the competing risk, cumulative incidence of aorta-related adverse events between patients with and without antithrombotic therapy. The *shaded areas* represent 95% confidence interval (CI) for each outcome. *AT*, Antithrombotic therapy.

TABLE 3. Competing-risk univariable analysis of risk factors of aorta-related adverse events

Variables	Univariable model	
	Sub-hazard ratio (95% CI)	*P**
Age (≥75 y)	1.12 (0.76-1.63)	.57
Male	1.26 (0.86-1.85)	.24
Classic AD†	1.64 (1.15-2.32)	.006
Hypertension	0.89 (0.52-1.51)	.66
Dyslipidemia	1.56 (1.08-2.27)	.02
Diabetes mellitus	1.26 (0.73-2.18)	.41
Smoking	0.95 (0.64-1.40)	.78
Hemodialysis	1.10 (0.12-9.84)	.93
Previous CAD	2.51 (1.23-5.13)	.01
Previous PAD	3.10 (1.23-7.78)	.02
Previous stroke	1.89 (1.02-3.52)	.045
ACEi/ARB	0.78 (0.55-1.10)	.16
Beta blocker	0.71 (0.48-1.04)	.08
CCB	0.72 (0.47-1.12)	.15
Antithrombotic therapy	2.47 (1.64-3.71)	<.001

CI, Confidence interval; *AD*, aortic dissection; *CAD*, coronary artery disease; *PAD*, peripheral artery disease; *ACEi*, angiotensin-converting enzyme inhibitor; *ARB*, angiotensin receptor blocker; *CCB*, calcium channel blocker. *The Fine-Gray model with death as competing risk. †Reference: aortic intramural hematoma.

group (20% ± 6% vs 7% ± 2% at 1 year and 40% ± 8% vs 11% ± 2% at 3 years, $P < .001$). However, in patients with AD, there was no significant difference in the incidence of aorta-related events between the antithrombotic group and the nonantithrombotic group. Table 4 shows competing risk univariable analysis for aorta-related events in subgroups of IMH and AD. A trend was noted in which the effect of antithrombotic therapy was more apparent in patients with IMH; however, this was nonsignificant (P for interaction, .071).

Baseline characteristics and aorta-related adverse events according to subgroups of antithrombotic therapy including antiplatelet, anticoagulation, and both therapies are shown in Table E1. There were no significant differences in aorta-related adverse events among subgroups of antithrombotic therapy.

DISCUSSION

In the current study, the risk of aorta-related adverse events was significantly greater in the antithrombotic group than in the nonantithrombotic group in patients with type B AAS. In addition, it was significantly greater in the antithrombotic group particularly in the IMH subgroup (Figure 3 and Video 1).

There is a lack of evidence supporting the efficacy of medical therapy in chronic aortic diseases.[3,6] To date, there have been no randomized controlled trials studying the effect of antithrombotic therapy on clinical outcomes in

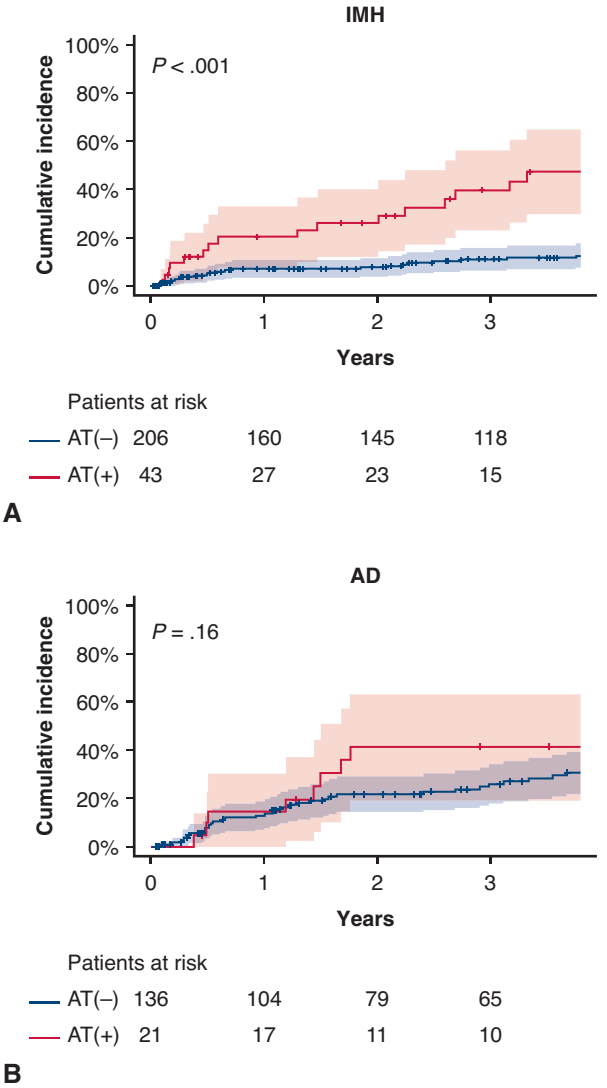

FIGURE 2. Considering nonaorta-related death as the competing risk, cumulative incidence of aorta-related adverse events between patients with and without antithrombotic therapy in patients with aortic IMH (A) and classic AD (B). The shaded areas represent 95% CI. *IMH*, Intramural hematoma; *AT*, antithrombotic therapy; *AD*, aortic dissection.

patients with AAS. At present, our study is the largest case series of patients with type B AAS focusing on antithrombotic therapy. Although many physicians inherently assume that antithrombotic therapy could have a negative effect on the healing process of the dissected lumen, there has been no consensus on discontinuing antithrombotic therapy in patients who have been taking it before hospitalization for AAS or on starting antithrombotic therapy in patients newly diagnosed with conditions with an indication for antithrombotic therapy such as atrial fibrillation, venous thromboembolism, or CAD during hospitalization for AAS.[14]

There have been 2 relevant case series focusing on the effect of anticoagulants in patients with type A AAS who

TABLE 4. Subgroup analysis for aorta-related events between intramural hematoma and classic aortic dissection

Variables	IMH (n = 249)		AD (n = 157)		*P* for interaction
	Sub-hazard ratio (95% CI)	*P**	Sub-hazard ratio (95% CI)	*P**	
Age (≥75 y)	1.64 (1.00-2.70)	.051	0.80 (0.40-1.59)	.52	.14
Male	1.28 (0.76-2.17)	.35	1.07 (0.61-1.90)	.81	.70
Hypertension	0.86 (0.41-1.79)	.68	0.92 (0.44-1.92)	.82	.94
Dyslipidemia	1.34 (0.79-2.29)	.28	1.75 (1.02-3.00)	.04	.46
Diabetes mellitus	1.65 (0.80-3.43)	.18	0.90 (0.40-2.03)	.80	.27
Smoking history	1.08 (0.63-1.86)	.78	0.77 (0.44-1.34)	.36	.38
Previous CAD	5.49 (2.44-12.34)	<.001	0.37 (0.05-2.65)	.32	.02
Previous PAD	2.87 (1.02-8.10)	.046	4.66 (3.20-6.80)	<.001	.34
Previous stroke	2.29 (1.15-4.59)	.02	2.26 (0.36-14.31)	.39	.90
ACEi/ARB	0.73(0.45-1.19)	.21	0.89(0.54-1.46)	.65	.27
Beta-blocker	0.63 (0.37-1.08)	.09	0.76 (0.44-1.31)	.32	.72
CCB	0.59 (0.32-1.10)	.10	0.91 (0.49-1.69)	.77	.34
Antithrombotic therapy	3.60 (2.13-6.08)	<.001	1.55 (0.80-3.00)	.19	.07

IMH, Intramural hematoma; *AD*, aortic dissection; *CI*, confidence interval; *CAD*, coronary artery disease; *PAD*, peripheral artery disease; *ACEi*, angiotensin-converting enzyme inhibitor; *ARB*, angiotensin receptor blocker; *CCB*, calcium channel blocker. *The Fine-Gray model with death as competing risk.

underwent surgical aortic repair. von Kodolitsch and colleagues[15] observed 243 patients with type A acute AD who survived after surgical repair and concluded that anticoagulation with warfarin was not related to late mortality or aortic events at a mean follow-up of 44 ± 26 months. Song and colleagues[16] reported the favorable effect of early anticoagulation after surgical repair of acute DeBakey type I AD in 136 patients on the onset or extension of thrombosis, aortic growth rate, need for repeat distal procedures, overall survival, and thrombosis-related complications during long-term follow-up. However, the 2 case series dealt with surgically managed type A AAS patients with the premise of having entry closure before initiation of antithrombotic therapy. Although false lumen could still not be thrombosed after surgical entry closure, the predisposing conditions of these patients differ from the clinical characteristics of the patients with type B AAS in our study, who had initially been managed medically and whose false lumen was possibly not completely thrombosed at the initiation of antithrombotic therapy. With respect to type B AAS, some authors reported untroublesome administration of antithrombotic therapy; however, the existing studies have so far been based on the observations of a few cases with the results being inconclusive.[17]

There are 2 possible mechanisms that could be associated with antithrombotic therapy and the worsening of clinical outcomes in type B AAS. One potential explanation is the interference of the thrombosis of the false lumen in the dissected aorta. Physiologically, thrombosis of the false lumen is thought to result in shrinkage and conceptually prevent aneurysmal degeneration and its rupture over time.[18] For example, in thoracic endovascular aortic repair, stent grafts are deployed with the aim of obliterating the proximal intimal tear and redirecting blood flow to the true lumen, simultaneously promoting thrombosis of the false lumen. In fact, in patients with type B AAS, the degree of false lumen thrombosis has been reported to affect clinical outcomes. A study conducted by Akutsu and colleagues[7] showed that patency of the false lumen is a strong independent prognostic factor for dissection-related death in patients with type B AD. Tsai and colleagues[19] showed that in patients with type B AD, partial thrombosis of the false lumen was associated with a significantly higher mortality rate than a completely patent false lumen.[20-22] In our subgroup analysis, antithrombotic therapy was associated with worse outcome only in patients presenting with IMH, not in AD, which could support the importance of prompt thrombosis of the false lumen in avoiding further aortic events.

Thus, we hypothesize that antithrombotic therapy delayed the remodeling process of the dissected false lumen by pharmacologically interfering with thrombosis, which consequently led to an increase in aortic dilation over time, resulting in an increase in aorta-related adverse events. In the current study, progressive aortic enlargement was more frequently observed in patients receiving antithrombotic therapy compared with those without antithrombotic therapy, which supports this hypothesis.

The other possible explanation behind the worse outcomes in the antithrombotic group is that the patients with an indication for antithrombotic therapy, especially antiplatelet therapy, had an atherosclerotic background. First, atherosclerotic comorbidities for which antithrombotic therapy was administered, such as CAD, PAD, or cerebral ischemic disease, might themselves be contributing factors for worsening outcomes in patients receiving

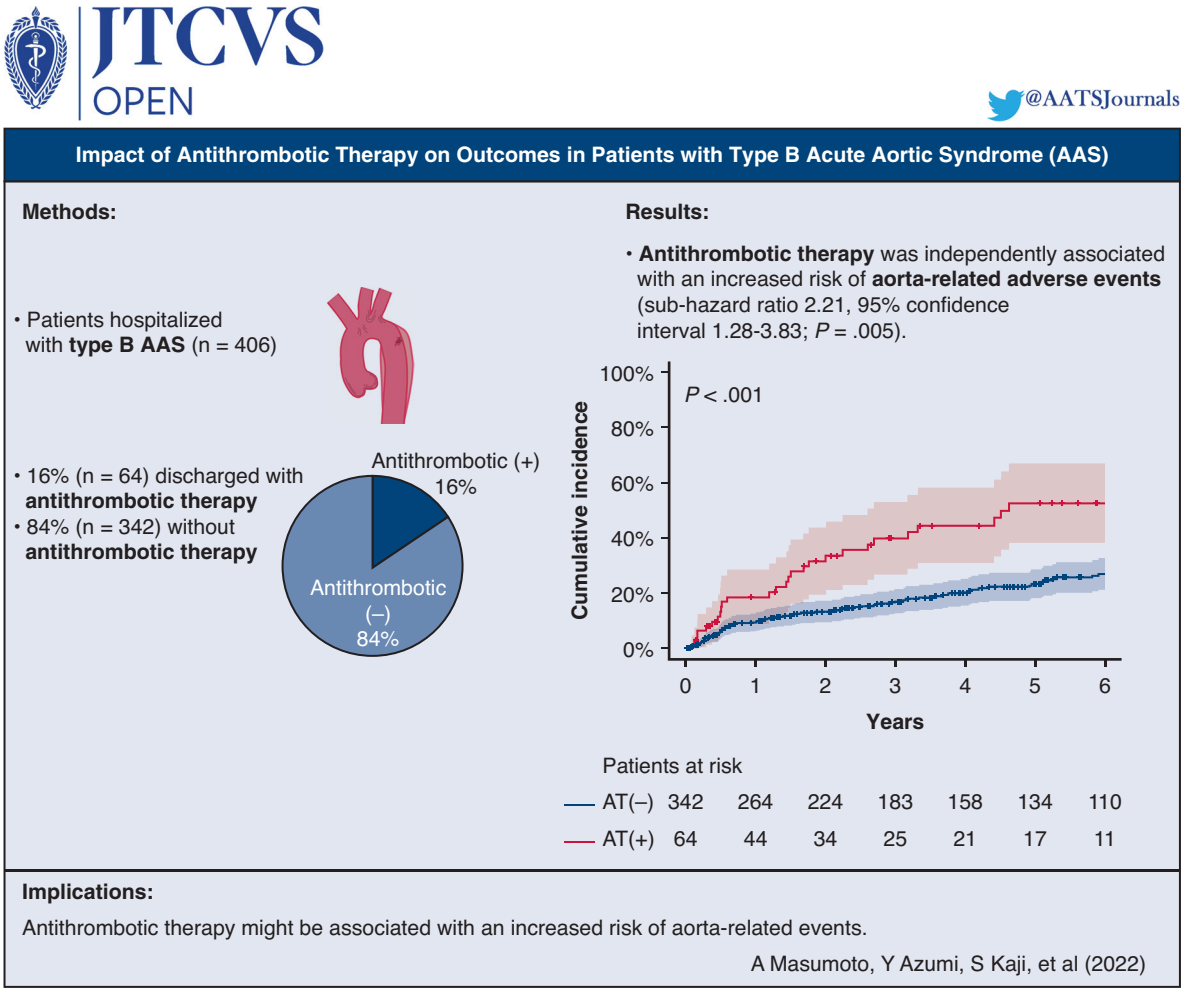

FIGURE 3. We aimed to determine the impact of antithrombotic therapy on outcomes in patients. Of the 406 patients who were hospitalized for type B AAS and discharged alive, 16% (n = 64) discharged with antithrombotic therapy 84% (n = 342) without antithrombotic therapy. The primary outcome was aorta-related adverse events, defined as a composite of aorta-related death, rupture, aortic repair, and progressive aortic dilation. Mean follow-up period was 4.6 years. Antithrombotic therapy was independently associated with an increased risk of aorta-related adverse events (sub-hazard ratio, 2.21, 95% CI, 1.28-3.83; $P = .005$). The Kaplan–Meier curves show the cumulative incidence of aorta-related adverse events in patients with and without antithrombotic therapy considering nonaorta-related death as the competing risk. This study implicates that antithrombotic therapy could be associated with an increased risk of aorta-related adverse events in patients with type B AAS. *AT*, Antithrombotic therapy.

antithrombotic therapy, although the difference in outcome persisted after adjustments for known comorbidities. Second, these patients, whose comorbidities needed antithrombotic therapy, could represent a cohort with a higher atherosclerotic burden. Historically, the most common risk factor associated with AD has been poorly controlled hypertension, observed in 65% to 75% of individuals.[23] The other established risk factors include heritable or genetic aortic disease, preexisting aortic valve disease, a family history of aortic diseases, history of cardiac surgery, cigarette smoking, direct blunt chest trauma, and the use of intravenous drugs.[24-27] Although the role of atherosclerosis has not been established in AD,[28] the formation of penetrating aortic ulcers is reported to be related to atherosclerosis, which could eventually result in AD in approximately 5% of patients.[13,29,30] Thus, the increased risk of aortic events in the antithrombotic group could be due to a preexisting atherosclerotic background.

Study Limitations

This study has several limitations. First, because there are so many unknown confounders and antithrombotic therapy itself is unrelated to the acute aortic syndrome, it is difficult to exclude potential confounding with statistical analysis. Therefore, we did not adjust possible confounding with multivariable analysis. Future prospective studies are warranted in a multicenter setting to confirm that antithrombotic activity is an independent risk factor for worsening outcomes in patients with type B AAS. Second, the blanket grouping of antithrombotic therapy is a classification that

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VIDEO 1. A brief presentation of the study methods, results, and discussions. Video available at: https://www.jtcvs.org/article/S2666-2736(23)00076-1/fulltext.

includes anticoagulants and antiplatelets, which act in different pharmacological manners, and therefore could have distinct effects in thrombosis of the dissected lumens. Although the study could still be relevant because there is a paucity of large-scale reports on the association of antithrombotic therapy with AAS, further knowledge should be accumulated for independent effects of anticoagulants and antiplatelets. Third, this was a single-center retrospective study. Because only 64 patients (16%) were discharged with antithrombotic therapy, there is a risk of type 1 error in group differences observed. Finally, because it was difficult to perform contrast-enhanced CT at every follow-up, we did not evaluate the size of the false lumen or progression of thrombosis.

CONCLUSIONS

Our study, with the largest number of patients with type B AAS focusing on antithrombotic therapy, showed that antithrombotic therapy might be a risk factor for aorta-related events. However, in many patients with conditions indicative of antithrombotic therapy, the indication for therapy often persists after onset of AAS. Thus, in patients with the indispensable need of antithrombotic therapy, careful follow-up with CT scans is required.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: acute aortic syndrome, antithrombotic therapy, aortic dissection, intramural hematoma

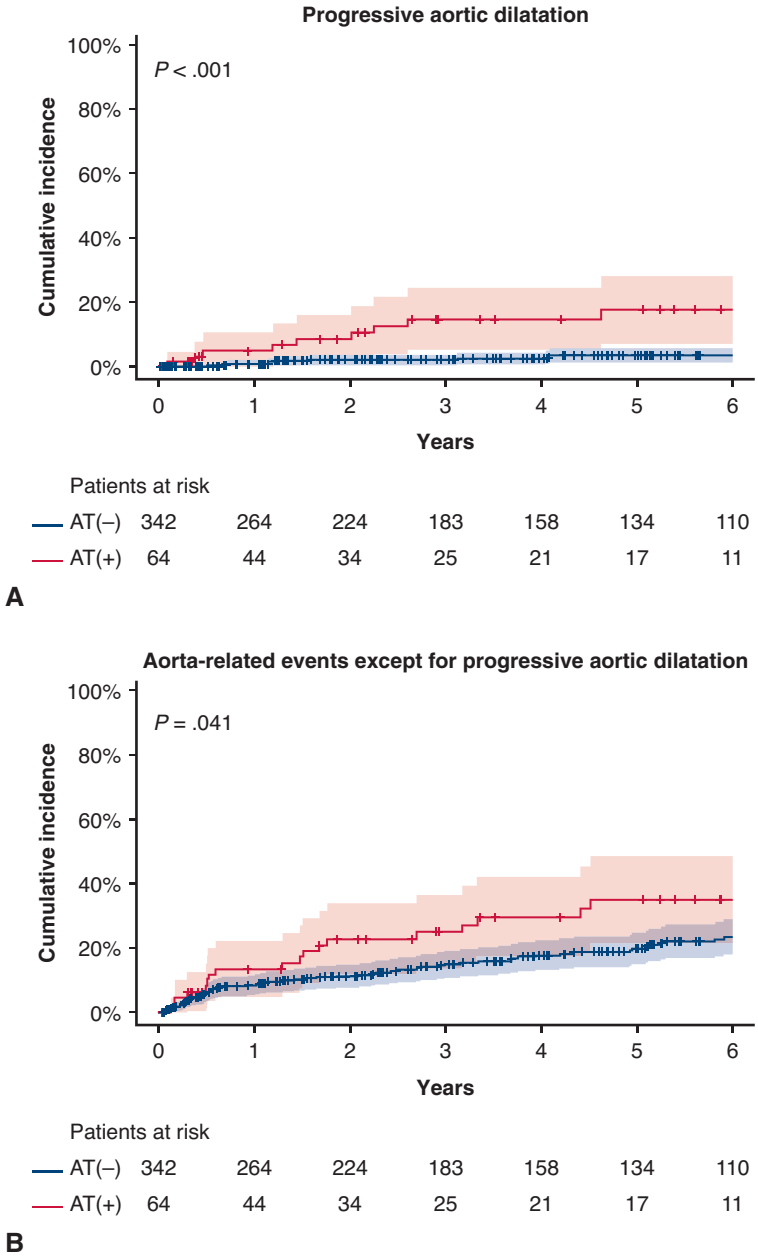

FIGURE E1. Cumulative incidence of progressive aortic dilatation between patients with and without antithrombotic therapy considering nonaorta-related death and composite adverse outcomes other than progressive aortic dilatation as the competing risk (A) and cumulative incidence of composite adverse outcomes other than progressive aortic dilatation (B). The shaded areas represent 95% CI. *AT*, Antithrombotic therapy.

TABLE E1. Baseline characteristics and aorta-related adverse events in patients with antiplatelet therapy or anticoagulation therapy

Characteristics	Antiplatelet (n = 39)	Anticoagulation (n = 16)	Antiplatelet+ Anticoagulation (n = 9)	*P*
Age, y	75 ± 8	63 ± 21	79 ± 10	.002
Male, n (%)	28 (72)	11 (69)	5 (56)	.64
Classic AD, n (%)	11 (28)	7 (44)	3 (33)	.54
Comorbidity				
Hypertension, n (%)	34 (87)	13 (81)	9 (100)	.42
Dyslipidemia, n (%)	14 (36)	4 (25)	6 (67)	.11
Diabetes mellitus, n (%)	9 (23)	3 (19)	4 (44)	.32
Smoking, n (%)	17 (44)	5 (31)	4 (44)	.68
Hemodialysis, n (%)	3 (8)	0 (0)	0 (0)	.72
Previous CAD, n (%)	16 (41)	0 (0)	8 (89)	<.001
Previous PAD, n (%)	2 (5)	0 (0)	2 (22)	.14
Previous stroke, n (%)	15 (39)	2 (13)	0 (0)	.02
Medication at discharge				
ACEi/ARB, n (%)	14 (36)	5 (31)	0 (0)	.10
Beta-blocker, n (%)	27 (69)	11 (69)	8 (89)	.57
CCB, n (%)	32 (82)	12 (75)	4 (44)	.08
All-cause death, n (%)	4 (10)	5 (31)	0 (0)	.08
Aorta-related adverse events, n (%)	20 (51)	9 (56)	3 (33)	.60
Surgical repair, n (%)	8 (21)	5 (31)	1 (11)	.57
Endovascular repair, n (%)	4 (10)	2 (13)	0 (0)	.84
Progressive aortic dilation, n (%)	8 (21)	1 (6)	2 (22)	.51
Redissection, n (%)	0 (0)	1 (6)	0 (0)	.39

AD, Aortic dissection; *CAD*, coronary artery disease; *PAD*, peripheral artery disease; *ACEi*, angiotensin-converting enzyme inhibitor; *ARB*, angiotensin receptor blocker; *CCB*, calcium channel blocker.