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Long-term Follow up of Patients with Acute Aortic Syndromes: Relevance of both Aortic and Non-aortic Events

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WHAT THIS PAPER ADDS

This study provides a detailed analysis of long-term follow up of patients discharged after type A and type B acute aortic syndromes. In particular, data about aorta related events (death, re-interventions) and non-aorta related events (cardiovascular and non-cardiovascular) were collected and analysed. Data collected over a long time interval (16 years) were analysed.

Background: The aim was to assess the long-term outcome of patients diagnosed with type A and type B acute aortic syndromes (AAS) and the mortality risk predictors.

Methods: A single centre retrospective observational study was performed on consecutive patients diagnosed with AAS and discharged between 2000 and 2016: 242 surgically treated type A, 87 uncomplicated, medically treated type B, and 80 complicated type B who received endovascular/surgical/hybrid treatment. Follow up of discharged patients (5 $\pm$ 3.9 years) was almost complete by the end of the study (December 2017).

Results: The mean age was 65.3 $\pm$ 12.5 years, and 70.2% were men. Long-term all cause mortality was 5.4 per 100 patients per year in surgically treated type A AAS patients and 6.7 per 100 patients per year in type B AAS patients ($p = .236$). The rates of major aorta related events were 6.1 per 100 patients per year and 13.4 per 100 patients per year, respectively ($p < .001$). Non-aorta related events during long-term follow up occurred in 18.2 per 100 patients per year in type A and 13.8 per 100 patients per year in type B ($p = .055$). At the end of follow up 279/409 (68.2%) patients (165/242 type A and 114/167 type B) experienced at least one event.

Conclusions: Among patients with either type A or type B AAS surviving the acute phase, the risk of adverse aorta and non-aorta related events, including death, persists during follow up, so that eventually two thirds of patients will experience at least one event. Notably, all cause mortality after type B AAS exceeds that of type A AAS after three years.

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INTRODUCTION

Acute aortic syndromes (AAS) include different conditions (intramural haematoma, penetrating aortic ulcer, and aortic dissection) that share aetiological substrates and clinical manifestations.

In type A AAS emergency surgery is the standard treatment and is associated with a 30 day mortality of around 30%.[1,2] Thoracic endovascular aortic repair (TEVAR) has become the treatment of choice for all type B AAS with clinical and/or anatomical complications.[3] Furthermore, recent data from multicentre randomised trials[4] and from the International Registry of Acute Aortic Dissection (IRAD) registry[5] suggest that TEVAR can offer long-term benefit in terms of aortic events even in uncomplicated type B patients, and this has been acknowledged in the most recent European guidelines.[1]

Although a number of studies have analysed long-term aortic complications in AAS[6,7] data regarding the incidence of non-aorta related events in the long term are limited.

The aim was to assess the long-term outcome of patients diagnosed with AAS, including all cause mortality, aorta and non-aorta related events, as well as risk predictors for mortality.

METHODS

Study design

The S. Orsola-Malpighi University Hospital is the referral centre for AAS treatment in a metropolitan hospital

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network that covers Bologna and its surrounding area (catchment area 1,000,000 inhabitants). The series includes all consecutive patients with a final diagnosis of spontaneous AAS (aortic dissection, intramural haematoma, penetrating aortic ulcer), with symptom onset <14 days, referred between January 1, 2000, and December 31, 2016.

Follow up after discharge was obtained through scheduled 1, 6, and 12 month computed tomography (CT) scans and visits, and yearly thereafter for both type A and type B patients. For those patients who were not followed in the centre, follow up information was obtained through telephone calls. The follow up ended in December 2017. The investigation conformed with the principles outlined in the Declaration of Helsinki and the study was approved by the local ethics committee.

Definitions

Major aorta related events included aorta specific mortality (defined as death from documented aortic rupture, heart failure secondary to cardiac tamponade or severe aortic regurgitation, malperfusion, proximal extension in type B patients, and peri-operative mortality), rehospitalisation for aortic complications (progression of aortic pathology causing malperfusion, increasing aortic diameter, progressive false lumen dilation, aortic rupture, redissection, moderate/severe aortic regurgitation) with or without re-intervention.

Non-aorta related events included non-aorta specific mortality (cardiovascular [CV] and non-CV related), rehospitalisation for other CV causes (including acute coronary syndrome [ACS], congestive heart failure, arrhythmia, cerebrovascular accident, bleeding, and other CV causes), and rehospitalisation for non-CV causes. Sudden death was considered aorta related when preceded by signs or symptoms suggestive of cardiac tamponade or aortic rupture. Sudden death was considered cardiac non-aorta related in the remaining cases.

Complications leading to invasive treatment in type B patients included persistent or recurrent pain, uncontrolled hypertension despite optimal medical treatment, malperfusion, early aortic expansion or signs of rupture such as haemothorax, increasing periaortic effusion or mediastinal haematoma.

ECG was considered to be ACS-like in the presence of ≥1 of the following characteristics: (a) ST segment elevation in two contiguous leads with the cut off point ≥0.1 mV in all leads other than V2V3, where the cut off point was ≥0.2 mV; (b) horizontal or down sloping ST segment depression ≥0.1 mV in two contiguous leads; and (c) T wave inversion ≥0.1 mV in two contiguous leads.[8] Shock was defined as a systolic blood pressure persistently lower than 90 mmHg. GFR (glomerular filtration rate) was estimated using the modified Modification of Diet in Renal Disease equation.[9]

Statistical analysis

Categorical variables are expressed as percentages and proportions, and continuous variables are reported as mean ± SD. The chi-square test or the Fisher exact test (for fewer than 5 observations) was used to compare groups for categorical variables, and the two-tailed Student *t* test was used for normally distributed continuous variables. The Benjamini–Hochberg procedure was used to control the familywise error rate in multiple comparisons.

Cox regression was performed to identify predictors of long-term outcome for patients discharged; non-correlated variables with $p < .2$ at univariable analysis were included in the multivariable analysis. Survival analyses were performed using the Kaplan–Meier method. For all statistical comparisons $p < .05$ was considered significant. All analyses were performed with the STATA/SE 12.1 software for Windows (StataCorp LP, College Station, TX, USA).

RESULTS

The study population consisted of 553 consecutive patients with a final diagnosis of spontaneous AAS (347 type A, 206 type B). Patents that died soon after admission and/or those with surgical/endovascular indications who did not undergo surgery because of excessive peri-operative risk were excluded from follow up analyses.

Optimal treatment during the index hospitalisation included surgery for type A AAS (295 patients, 85% of type A patients), medical treatment for uncomplicated type B AAS (91 patients, 44% of type B patients), and endovascular, surgical or hybrid endovascular/surgical treatment for complicated type B AAS (101 patients, 49% of type B patients). Among surgically treated type A patients 63% (186/295) were DeBakey type I.

All follow up analyses were performed on patients who received optimal treatment during the index hospitalisation and were discharged after the acute phase: 409 overall, 242 type A, 87 uncomplicated type B, 80 complicated type B (Supplementary Fig. 1). Average follow up of discharged patients was 5 ± 3.9 years (6 ± 3.8 years for type A and 5 ± 4.1 years for type B). The median follow up index was 1 (IQR 0.9–1) for the overall discharged patients, and for both type A and type B subgroups.[10]

Thirty day outcome

Details of surgical and endovascular treatments performed during the index hospitalisation are reported in Supplementary Table 1.

Of the 347 patients admitted with type A AAS, 85 died (30 day mortality 24.5%) including 50 out of 295 who underwent surgery (peri-operative mortality 16.9%). Of the patients who did not undergo surgery because of excessive surgical risk, 35/52 (67%) died at 30 days.

A total of 242 patients with type A AAS were discharged and included in long-term follow up analyses.

Of the 206 type B AAS patients, 29 died (30 day mortality 14.1%); specifically, 19 of 101 (18.8%) complicated patients who underwent endovascular/surgical/hybrid treatment and three of 91 (3.3%) uncomplicated patients who received medical treatment ($p = .001$).

A total of 167 type B patients (87 uncomplicated, 80 complicated) survived the index hospitalisation and were included in long-term follow up analyses.

Long-term outcome

Baseline characteristics of the study population are listed in Table 1.

Fig. 1 shows all cause mortality of the overall population according to Stanford subtype: while mortality of type A patients was higher during the acute phase, the two survival curves crossed around year 3, type B patients showing the highest mortality at the end of follow up.

Type A AAS

All cause mortality. Long-term all cause mortality in surgically treated type A AAS patients was 5.4/100 patients per year (Fig. 2).

Table 2 reports the risk factors for long-term mortality in patients discharged after type A AAS treated surgically. After multivariable analysis, age (HR 1.06 for each 1 year increase; 95% CI 1.03—1.08; $p < .001$), creatinine level at presentation (HR 2.99; 95% CI 1.96—4.56; $p < .001$), and peri/post-operative cerebral malperfusion (HR 2.08; 95% CI 1.14—3.78; $p = .016$) remained independent predictors of long-term mortality.

Table 1. Characteristics of patients discharged after type A and type B AAS.

Variable	Overall ($N = 409$)	Type A 59% ($N = 242$)	Type B 41% ($N = 167$)	p
Type of acute aortic syndrome				
Aortic dissection	80.4% (329)	86.4% (209)	71.9% (120)	<.001
Intramural haematoma	12.7% (52)	9.9% (24)	16.8% (28)	.058
Plaque rupture/ulceration	1.7% (7)	1.2% (3)	2.4% (4)	.619
Intramural haematoma plus plaque rupture/ulceration	5.1% (21)	2.5% (6)	8.9% (15)	.007
Patient characteristics				
Age (years), mean ± SD	65.3 ± 12.5	64.9 ± 12.1	65.9 ± 12.9	.424
Men	70.2% (287)	68.2% (165)	73.1% (122)	.343
Hypertension or antihypertensive therapy	75.3% (308)	71.5% (173)	80.8% (135)	.041
Hypercholesterolemia or lipid lowering drugs	26.7% (109)	21.1% (51)	34.7% (58)	.003
Diabetes	5.4% (22)	4.1% (10)	7.2% (12)	.262
Current smoking	27.1% (111)	21.9% (53)	34.7% (58)	.006
Marfan syndrome	1.5% (6)	1.2% (3)	1.8% (3)	.967
Bicuspid aortic valve	2.7% (11)	3.3% (8)	1.8% (3)	.538
Aortic coarctation	0.2% (1)	0% (0)	0.6% (1)	.852
Known thoraco—abdominal aortic aneurysm (surgically treated or not) and/or previous AAS	14.4% (59)	9.9% (24)	20.9% (35)	.003
Previous stroke	3.7% (15)	5.4% (13)	1.2% (2)	.052
Coronary artery disease (history)	7.6% (31)	8.3% (20)	6.6% (11)	.66
Disease complications				
Pleural effusion	21% (86)	19% (46)	24.4% (40)	.279
Periaortic effusion	14.9% (61)	12.4% (30)	18.6% (31)	.114
Pericardial effusion	28.1% (115)	38.8% (94)	12.6% (21)	<.001
Cardiac tamponade	6.6% (27)	11.2% (27)	0% (0)	<.001
Moderate/severe aortic regurgitation	19.8% (81)	28.5% (69)	7.2% (12)	<.001
Shock within 12 h of admission	10.3% (42)	15.7% (38)	2.4% (4)	<.001
Stroke	3.7% (15)	5.4% (13)	1.2% (2)	.052
Peri-/post-operative cerebral malperfusion	11.5% (47)	14.4% (35)	7.2% (12)	.035
Peri-/post-operative visceral malperfusion	13.9% (57)	19.8% (48)	5.4% (9)	<.001
ACS-like electrocardiogram	18.8% (77)	21.9% (53)	9.9% (24)	.074
Coronary ostial involvement	2.4% (10)	4.1% (10)	0% (0)	.02
Creatinine at presentation (mg/mL), mean ± SD	1.1 ± 0.6	1.1 ± 0.4	1.2 ± 0.8	.096
Medical therapy at discharge				
Antiplatelet drugs	56.2% (230)	52.5% (127)	61.7% (103)	.082
Anticoagulant drugs	27.8% (114)	37.2% (90)	14.4% (24)	<.001
Beta receptor blockers	81.9% (335)	76.9% (186)	89.2% (149)	.002
ACEIs/ARBs	48.4% (198)	47.9% (116)	49.1% (82)	.895
Calcium channel blockers	37.2% (152)	26% (63)	53.3% (89)	<.001
Diuretics	57.2% (234)	53.3% (129)	62.9% (105)	.069
Other antihypertensive drugs	21.3% (87)	9.1% (22)	38.9% (65)	<.001
Statins	17.8% (73)	16.5% (40)	13.8% (23)	.535

AAS = acute aortic syndrome; ACEIs = angiotensin converting enzyme inhibitors; ACS = acute coronary syndrome; ARBs = angiotensin receptor blockers; SD = standard deviation.

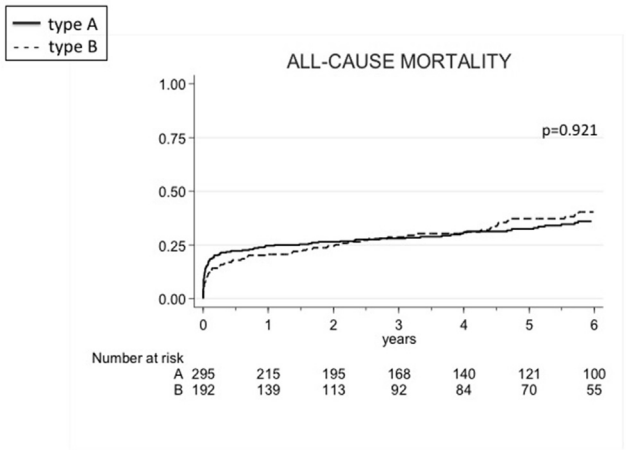

Figure 1. All cause mortality since hospitalisation according to Stanford subtype excluding early, pre-treatment deaths and patients with contraindication to the intervention (295 type A, 192 type B).

Major aorta related events. The long-term rate of major aorta related events after discharge was 6.1 per 100 patients per year (Fig. 2), including a 6.6% (16 patients) aorta specific mortality (Table 3, Supplementary Fig. 2).

A total of 52 patients (21.5%) underwent re-intervention on the aorta during follow up (Table 3): 37 patients for progressive aortic dilation, five for aortic pseudoaneurysm, two for severe aortic valve regurgitation, two for signs of impending aortic rupture, two for recurrent type B AAS, one for residual intimal flap in the aortic arch, one for residual symptomatic type B intramural haematoma, one for renal malperfusion, and one for endoleak.

Specifically, five of the 24 patients who underwent an "elephant trunk" procedure experienced a step-up re-intervention for dilatation of the descending aorta. As to the three patients with isolated type A plaque rupture/ulceration, one death was observed for an aortic cause (haemoptysis with documented progression of the aortic disease). This patient did not undergo further surgery as the surgical risk was considered excessive, and the two surviving patients did not require further surgery.

Non-aorta related events. Non-aorta related events after discharge occurred in 18.2 of 100 patients per year (Fig. 2), including a 23.6% (57 patients) non-aorta related mortality (Table 3, Supplementary Fig. 2).

Of the 57 patients who died of non-aorta related causes during follow up, 16 died of non-aortic CV causes (7 of stroke, 3 of infective endocarditis, 4 of sudden cardiac death, 2 of heart failure), 13 of infection, 12 of cancer, and 16 of other causes.

Regarding rehospitalisation, 85 patients (35.1%) had a rehospitalisation for non-aortic CV causes and 91 patients (37.6%) for non-CV causes, mainly infection and cancer (Table 3).

When considering the year of presentation (2000—2008 vs. 2008—2016), there were no differences in all cause mortality ($p = .736$) after long-term follow up (Supplementary Fig. 3).

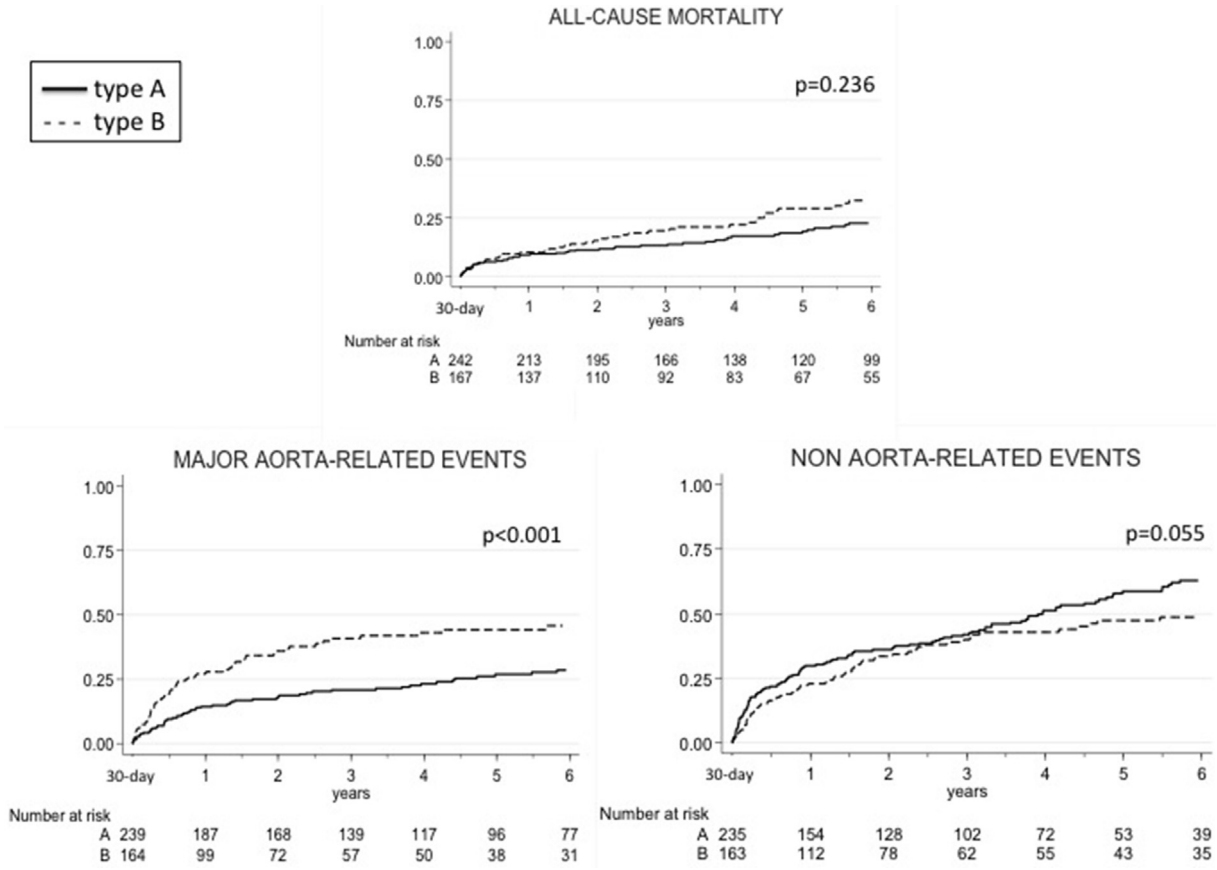

Figure 2. Long-term outcome of discharged type A (242) and type B (167) AAS patients.

Table 2. Risk factors for long-term mortality of patients discharged after surgically treated type A AAS.

Variable	Univariable analysis		Multivariable analysis	
	HR (95% CI)	*p*	HR (95% CI)	*p*
Age (for each one year increase)	1.06 (1.03–1.08)	<.001	1.06 (1.03–1.08)	<.001
Male gender	0.78 (0.48–1.25)	.312		
Hypertension (history)	2.54 (1.34–4.84)	.004	1.88 (0.91–3.89)	.086
Hypercholesterolemia	1.39 (0.8–2.4)	.231		
Diabetes	3.07 (1.23–7.66)	.016		
Current smoking	0.37 (0.16–0.87)	.022		
Known thoraco-abdominal aortic aneurysm (surgically treated or not) and/or previous AAS	1.7 (0.84–3.44)	.136		
Previous stroke	0.97 (0.35–2.67)	.958		
Coronary artery disease (history)	1.3 (0.59–2.84)	.506		
Aortic bulb diameter at presentation (for each 1 mm increase)	1.02 (0.95–1.08)	.537		
Ascending aorta diameter at presentation (for each 1 mm increase)	1.01 (0.98–1.03)	.471		
Aortic arch diameter at presentation (for each 1 mm increase)	0.98 (0.91–1.05)	.589		
Descending aorta diameter at presentation (for each 1 mm increase)	1.01 (0.99–1.03)	.143		
DeBakey type I	1.04 (0.63–1.73)	.851		
Creatinine at presentation (for each 1 mg/mL increase)	2.96 (1.9–4.61)	<.001	2.99 (1.96–4.56)	<0.001
Ascending aorta + arch replacement	0.83 (0.47–1.45)	.517		
Peri-/post-operative cerebral malperfusion	2.28 (1.3–4.01)	.004	2.08 (1.14–3.78)	.016
Peri-/post-operative visceral malperfusion	2.12 (1.29–3.49)	.003		
Shock	0.65 (0.32–1.31)	.235		
ACS-like ECG	1.15 (0.66–1.98)	.61		

Harrell's C = 76%. AAS = acute aortic syndrome; ACS = acute coronary syndrome; CI = confidence interval; HR = hazard ratio.

Type B AAS

All cause mortality. After discharge, long-term all cause mortality for type B patients was 6.7 per 100 patients per year; 5.9 per 100 patients per year for uncomplicated type B patients and 7.7 per 100 patients per year in complicated patients ($p = .351$) (Fig. 3).

Older age (HR 1.06 for each 1 year increase; 95% CI 1.04–1.09; $p < .001$), creatinine at presentation (HR 1.29; 95% CI 1.01–1.63; $p = .037$), and peri/post-operative visceral malperfusion (HR 4.05; 95% CI 1.37–11.95; $p = .011$) remained independent predictors of long-term mortality (Table 4).

Major aorta related events

After discharge, the long-term incidence of major aorta related events was 13.4 per 100 patients per year; 12.3 per 100 patients per year in uncomplicated type B patients and 14.8 per 100 patients per year in complicated patients ($p = .541$), (Fig. 3). Aorta specific mortality was 2.3% (2 patients) in the uncomplicated group and 8.8% (7 patients) in the complicated group ($p = .053$), (Table 5, Supplementary Fig. 2).

Among uncomplicated type B patients, who did not undergo invasive treatment during the index hospitalisation, 31 (35.6%) were treated with an endovascular/surgical/

Table 3. Outcome of patients after type A and type B AAS.

Variable	Overall	Type A	Type B	*p*
Short-term outcome				
30-day mortality	14.8% (72/487)	16.9% (50/295)	11.5% (22/192)	0.116
Long-term outcome after discharge				
Intervention/Re-intervention	27.4% (112/409)	21.5% (52/242)	35.9% (60/167)	0.002
Re-hospitalization for aortic causes	30.1% (123/409)	26% (63/242)	35.9% (60/167)	0.042
Re-hospitalization non-aortic CV causes:	29.8% (122/409)	35.1% (85/242)	22.2% (37/167)	0.007
- Re-hospitalization for ACS	2.4% (10/409)	2.1% (5/242)	2.9% (5/167)	0.786
- Re-hospitalization for CHF	4.4% (18/409)	6.2% (15/242)	1.8% (3/167)	0.059
- Re-hospitalization for tachyarrhythmia/bradyarrhythmia	2.9% (12/409)	3.7% (9/242)	1.8% (3/167)	0.404
- Re-hospitalization for CVA	3.7% (15/409)	4.9% (12/242)	1.8% (3/167)	0.16
- Re-hospitalization for bleeding	3.2% (13/409)	4.1% (10/242)	1.8% (3/167)	0.3
- Re-hospitalization for other CV causes	13.2% (54/409)	14% (34/242)	11.9% (20/167)	0.645
Re-hospitalization for non-CV causes	31.3% (128/409)	37.6% (91/242)	22.2% (37/167)	0.001
All-cause mortality	30.6% (125/409)	30.2% (73/242)	31.1% (52/167)	0.92
Aorta-related mortality	6.1% (25/409)	6.6% (16/242)	5.4% (9/167)	0.766
CV non-aorta-related mortality	8.1% (33/409)	6.6% (16/242)	10.2% (17/167)	0.264
Non-CV non-aorta-related mortality	16.4% (67/409)	16.9% (41/242)	15.6% (26/167)	0.816
Any event	68.2% (279/409)	68.2% (165/242)	68.3% (114/167)	0.928

ACS: acute coronary syndrome; CHF: congestive heart failure; CV: cardiovascular; CVA: cerebrovascular accident.

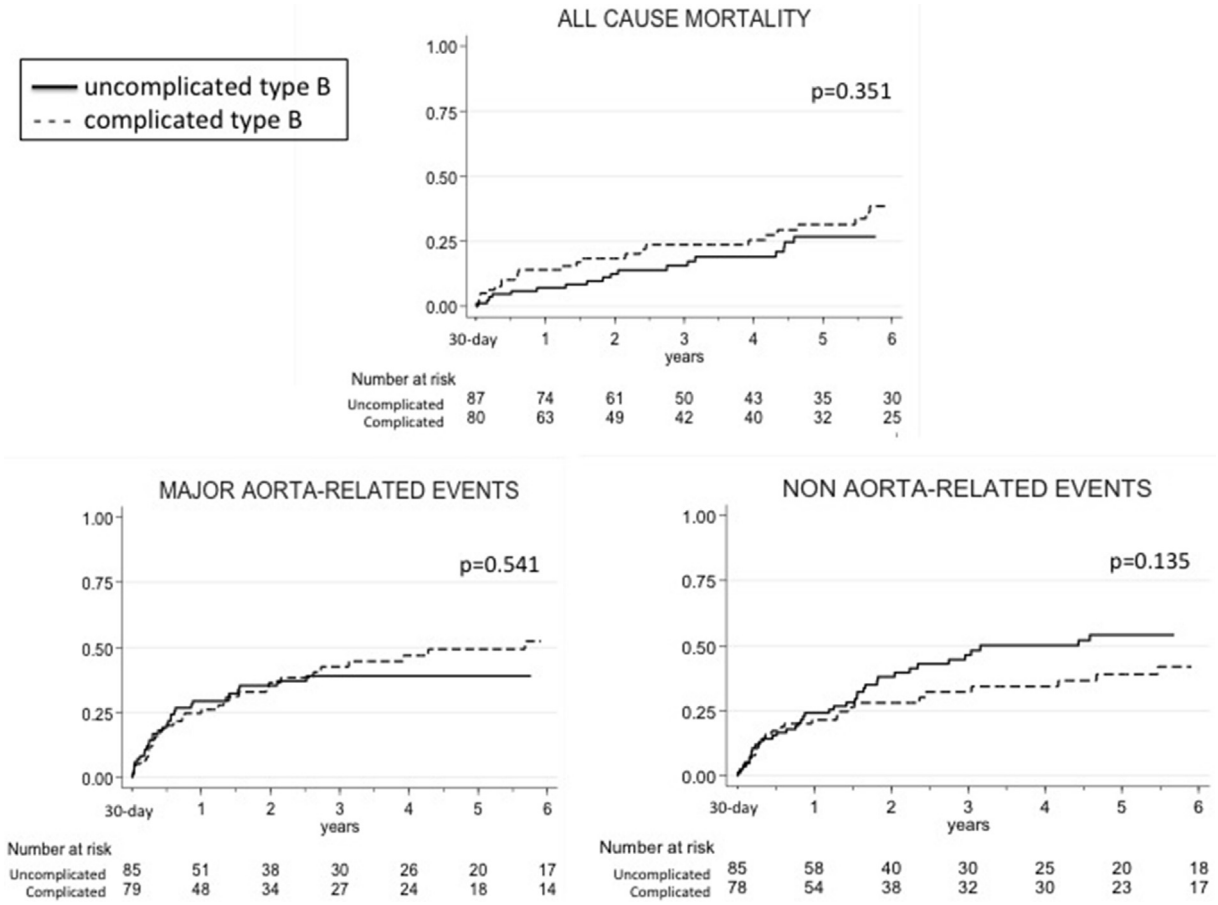

Figure 3. Long-term outcome of discharged uncomplicated type B (optimal medical therapy group, 87 patients) or complicated type B (endovascular/surgical/hybrid treatment group, 80 patients) AAS patients.

Table 4. Risk factors for long-term mortality of patients discharged after type B AAS.

Variable	Univariable analysis		Multivariable analysis	
	HR (95% CI)	*p*	HR (95% CI)	*p*
Age (for each one year increase)	1.06 (1.03—1.09)	<.001	1.06 (1.04—1.09)	<.001
Male gender	0.75 (0.42—1.35)	.35		
Hypertension (history)	1.3 (0.58—2.91)	.511		
Hypercholesterolemia	0.9 (0.47—1.72)	.756		
Diabetes	2.63 (1.02—6.73)	.044		
Current smoking	0.59 (0.3—1.13)	.114		
Marfan syndrome	0.49 (0.06—3.76)	.496		
Known thoraco-abdominal aortic aneurysm (surgically treated or not) and/or previous AAS	1.93 (1.05—3.54)	.033		
Coronary artery disease (history)	1.71 (0.73—4.02)	.214		
Aortic bulb diameter at presentation (for each 1 mm increase)	1.04 (0.99—1.1)	.09		
Ascending aorta diameter at presentation (for each 1 mm increase)	1.08 (1.03—1.13)	<.001		
Aortic arch diameter at presentation (for each 1 mm increase)	1.05 (0.99—1.11)	.089		
Descending aorta diameter at presentation (for each 1 mm increase)	1.05 (1.03—1.08)	<.001		
Creatinine at presentation (for each 1 mg/mL increase)	1.25 (1—1.56)	.046	1.29 (1.01—1.63)	.037
Endovascular/surgical/hybrid treatment	1.2 (0.69—2.07)	.504		
Peri-/Post-operative cerebral malperfusion	1.42 (0.56—3.57)	.456		
Peri-/Post-operative visceral malperfusion	2.01 (0.72—5.61)	.179	4.05 (1.37—11.95)	.011
Shock	1.59 (0.38—6.62)	.521		
ACS- like ECG	0.58 (0.24—1.37)	.217		

Harrell's C = 69%. AAS = acute aortic syndrome; ACS = acute coronary syndrome; CI = confidence interval; HR = hazard ratio.

hybrid procedure during follow up (Table 5): 28 patients for aortic dilation (with a maximum diameter exceeding 55 mm), three for signs of impending rupture.

In the complicated type B group, 29 patients (36.3%) underwent re-intervention (Table 5): 14 patients for descending aorta dilation distal to the endoprosthesis, 11 for endoleak, two for signs of impending rupture, one for recurrent type A AAS, and one for symptomatic retrograde extension of the aortic dissection. As for the four patients with type B plaque rupture/ulceration, only three were complicated at presentation and were treated with an endoprosthesis, two died for non-aortic causes, and none required surgical intervention or re-intervention.

Non-aorta related events. The long-term rate of non-aorta related events after discharge was 13.8 per 100 patients per year; 16.3 per 100 patients per year in the uncomplicated group and 11.1 per 100 patients per year in the complicated group ($p = .135$) (Fig. 3). Non-aorta related mortality was 26.4% (23 patients) in the uncomplicated group and 25% (20 patients) in the complicated group ($p = .861$) (Table 5, Supplementary Fig. 2).

Of the 43 patients who died of non-aorta related causes during follow up, 17 died of non-aortic CV causes (8 patients suffered sudden cardiac death, 4 heart failure, 2 stroke, 1 acute myocardial infarction, 1 pulmonary embolism, 1 haemorrhagic shock due to femoral puncture), nine died of cancer, eight of infection, and nine of other causes.

As for rehospitalisations (Table 5), in the uncomplicated group 27 patients (31%) were hospitalised for non-aortic CV causes compared with 10 (12.5%) in the complicated group ($p = .106$). Also the rates of readmission for non-CV causes did not differ significantly between the two groups: 24 patients (27.6%) in the uncomplicated group vs. 13 patients (16.3%) in the complicated group ($p = .573$).

Dividing the overall population of patients with type B AAS into two groups according to the year of presentation (2000–2008 vs. 2008–2016), there were no significant differences in all cause mortality ($p = .484$) at long-term follow up (Supplementary Fig. 3).

DISCUSSION

The present study provides a detailed analysis of contemporary long-term outcome of type A and type B AAS, considering both aorta- and non-aorta related events. The most significant findings are that:

1. All cause mortality after type B AAS exceeds that of type A AAS after three years.
2. Among patients with either type A or type B AAS surviving the acute phase, the risk of adverse aorta and non-aorta related events, including death, persists during follow up, so that eventually two thirds of patients will experience at least one event.
3. Despite an initial conservative strategy, with only complicated type B patients undergoing surgical or endovascular treatment, 69% of patients presenting with Type B AAS required surgical or endovascular treatment considering the whole follow up.

The main clinical characteristics of the population are similar to those of the IRAD registry (International Registry of Acute Aortic Dissection),[6,7] except for a lower prevalence of Marfan syndrome. Among type A patients, surgical in hospital mortality (17%) was similar to that reported in the IRAD registry, but differed in not having a decline in surgical mortality over time, probably because of the high volume surgical expertise achieved at the centre since the early 2000s.

The surgical strategy at the centre aimed to remove the primary entry tear, and is characterised by a high rate of hemi-arch and arch replacement (combined with replacement of the ascending aorta), preferably with open distal

Table 5. Outcome of patients after type B AAS according to therapeutic strategy at baseline.

Variable	Overall	Medical therapy	Medical therapy + endovascular/ surgical/hybrid treatment	*p*
Short-term outcome				
30 day mortality	11.5% (22/192)	3.3% (3/91)	18.8% (19/101)	.001
Long-term outcome after discharge				
Intervention/re-intervention	35.9% (60/167)	35.6% (31/87)	36.3% (29/80)	.255
Rehospitalisation for aortic causes	35.9% (60/167)	36.8% (32/87)	35% (28/80)	.393
Rehospitalisation for non-aortic CV causes	22.2% (37/167)	31% (27/87)	12.5% (10/80)	.106
Rehospitalisation for ACS	2.9% (5/167)	5.7% (5/87)	0% (0/80)	.158
Rehospitalisation for CHF	1.8% (3/167)	2.3% (2/87)	1.3% (1/80)	.746
Rehospitalisation for tachyarrhythmia/ bradyarrhythmia	1.8% (3/167)	3.4% (3/87)	0% (0/80)	.393
Rehospitalisation for CVA	1.8% (3/167)	3.4% (3/87)	0% (0/80)	.393
Rehospitalisation for bleeding	1.8% (3/167)	2.3% (2/87)	1.3% (1/80)	.746
Rehospitalisation for other CV causes	11.9% (20/167)	13.8% (12/87)	10% (8/80)	.876
Rehospitalisation for non-CV causes	22.2% (37/167)	27.6% (24/87)	16.3% (13/80)	.573
All cause mortality	31.1% (52/167)	28.7% (25/87)	33.8% (27/80)	.112
Aorta related mortality	5.4% (9/167)	2.3% (2/87)	8.8% (7/80)	.053
CV non-aorta related mortality	10.2% (17/167)	9.2% (8/87)	11.3% (9/80)	.432
Non-CV non-aorta related mortality	15.6% (26/167)	17.2% (15/87)	13.8% (11/80)	.962

ACS = acute coronary syndrome; CHF = congestive heart failure; CV = cardiovascular; CVA = cerebrovascular accident.

anastomosis technique without aortic clamping. In the current practice, if the aortic arch must be replaced end to end anastomosis is performed between the prosthetic graft and the aorta beyond the left subclavian artery, usually with the "frozen elephant trunk" approach, in order to stabilise the proximal portion of the descending aorta.[11,12] However, despite the "elephant trunk" technique being used increasingly to treat complex pathologies of the aortic arch and/or of the descending aorta, including AAS, the costs in terms of increased acute phase morbidity (bleeding, stroke, spinal cord injury, acute kidney injury) and mortality, and the effective number of patients needing a second intervention during follow up are still debated.[13] Five of 24 patients treated with this strategy also needed an endovascular re-intervention for dilation of the thoracoabdominal aorta during follow up.

Regarding the aortic valve, replacement was performed in a high number of patients (109/295, 36.9%) while valve reimplantation (David technique) was carried out only in 3.7% of cases (11 patients). This strategy has been shown to be protective for long-term aortic valve re-intervention, mainly for regurgitation,[14] which occurred in three of the patients.

In this series, despite 80% of patients undergoing surgery that extended beyond the ascending aorta, involving the aortic valve in 40%, the overall rate of long-term re-intervention was 20%, and in most cases this was elective.

In this series, the risk of developing a type B AAS among patients who previously underwent surgical treatment of type A AAS appears to be low, involving two of 295 patients, as is the risk of developing type A disease after type B AAS, involving one of 161 patients. These patients had hypertension as the single identified risk factor and no signs of connective tissue disease.

The high rate of long-term non-aorta related events, including mortality, is one of the main findings of the study. During a mean follow up of 5 years, the non-aorta related/aorta related events ratio was 3 in type A patients. Despite the relatively low mean age of the population (around 65) a moderately high rate of fatal non-CV events (cancer, infection) was observed.

In type B patients, in hospital mortality was higher among complicated than uncomplicated patients (23.8% vs. 3.4%, $p < .001$), and the trend was maintained during long-term follow up, although the difference does not reach statistical significance. Even though the usefulness of interventional treatment for uncomplicated cases remains under debate,[4,5] an initial "conservative strategy" has been adopted, with only complicated type B AAS patients undergoing surgical or endovascular treatment during the acute phase (49% in this series). Nevertheless, a considerably high number of patients treated with optimal medical therapy at the index hospitalisation required an interventional approach for late complications, so that in the long-term 69% of patients had undergone endovascular/surgical/hybrid treatment.[15] The need for a re-intervention among patients receiving interventional treatment in the acute phase is not uncommon,[16] and in the current population it reached 36.3%. The most common causes of delayed operation/reoperation were progressive aortic dilation in both groups. The majority of follow up interventions were elective.

As with type A patients, those with type B AAS also experience a high rate of non-aorta related events, including mortality, so that after an average follow up of 5 years, the non-aorta related/aorta related events ratio is 1. Despite the fact that this study was not designed to investigate the mechanisms of the follow up events, it is possible to hypothesise on the reasons behind some of the coronary and cerebrovascular events that occurred. First, the incidence of CV risk factors in the population is high (and even higher in type B patients with respect to hypertension, hypercholesterolaemia, and current smoking). Moreover, it has been shown that the aortic prosthetic material used in TEVAR can interfere with the generation and propagation of reflected waves, potentially leading to abnormal coronary perfusion and ventricular—aortic coupling.[17,18] It is also possible that the fear of redissection led to the avoidance of antiplatelet or anticoagulant drugs in patients who, for various reasons, would have had an indication for them.

Mortality independent predictors were related both to general risk factors (age, renal function) and to aorta specific complications such as cerebral and visceral malperfusion.

Conclusions and Clinical Implications

Despite type A AAS being a surgical emergency with a high mortality in the acute phase, the morbidity and mortality of type B AAS overtakes that of type A from the third year of follow up onward. For both type A and B the clinical relevance of non-aorta related events during long-term follow up is high and increases progressively over time. Long-term management of AAS patients discharged from hospital must take these observations into consideration. A close cooperation between surgeons, radiologists and interventional and clinical cardiologists is warranted.

Study limitations

The small sample size and the single centre, retrospective and non-randomised design of the study are the main limitations of the analysis. Data regarding therapy and blood pressure during follow up are missing, only the therapy at discharge being known. Finally, a small difference in follow up duration was found between type A and type B patients.

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CONFLICT OF INTEREST

None.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ejvs.2018.03.030.

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