treatment, and outcomes. TAAAD was defined as any nontraumatic dissection of the aorta proximal to the left subclavian artery presenting within 14 days of symptom onset. Stroke was defined in the database lexicon as a cerebrovascular accident representing a loss of neurological function (loss or slurring of speech, altered state of consciousness) caused by an ischemic event, confirmed by computed tomography or MRI. This definition of stroke was formulated to be conservative, considering that not all patients had routine neurological consults postdissection. Therefore, we have probably somewhat underestimated the incidence of less obvious neurological injuries. Other definitions were similar to those in previous publications.[6–8]

Statistical Analysis

Data are shown as frequencies and percentages, mean±SD, or medians with first and third quartiles. Univariate comparisons between patients with and without stroke were performed using the χ^2 test for categorical data and Student t test for continuous variables with normal data distributions. Nonparametric test of medians was used for data with skewed distributions. In all cases, missing data were not defaulted to negative, and denominators reflect cases for which information was reported. Binary logistic regression analysis was performed to determine the independent correlates of presenting stroke and to assess the independent association of presenting stroke with in-hospital mortality. Cox proportional hazard models were used to identify the independent association of stroke with long-term mortality among patients discharged alive at hospitalization. Odds ratios and hazard ratios with their corresponding 95% confidence intervals were generated to provide an estimate of these associations. All P values were 2-sided, with values <0.05 considered statistically significant. Analyses were performed using SPSS 20.0 statistical analysis software (IBM Corporation).

Results

Incidence, Demographics, History, and Clinical Symptoms and Signs

Among 2202 patients with TAAAD enrolled in IRAD, 132 (6.0%) had stroke at presentation (Table 1). These patients were older, with only 1 stroke patient <40 years of age. A history of hypertension was 1.2× more common in patients with stroke, and atherosclerosis was ≈1.4-fold higher in the stroke cohort compared with nonstroke patients. Presentation with chest or back pain was less frequent, whereas presentation with syncope was 3-fold higher among TAAAD patients with stroke. Shock and pulse deficit were 2-fold higher, and the combination of shock, hypotension, and cardiac tamponade was 1.4× higher among patients with stroke. Other demographics, clinical features, and presenting symptoms were similar between groups (Table 2).

Table 1. Patient Characteristics in TAAAD Patients With and Without Presenting Stroke

Variable	Overall n (%)	Stroke n (%)	No Stroke n (%)	P
n (%)	n=2202 (100)	n=132 (6.0)	n=2070 (94.0)	Value
Demographics				
Age, mean±SD, y	61.9±14.4	65.0±11.5	61.7±14.6	0.002
Age <40 y	167 (7.6)	1 (0.8)	166 (8.0)	0.002
Male	1487 (67.5)	82 (62.1)	1405 (67.9)	0.17
White	1837(89.0)	109 (88.6)	1728 (89.1)	0.88
Transferred to IRAD sites	1654 (75.1)	95 (72.0)	1559 (75.3)	0.39
Medical history				
Marfan syndrome	88 (4.1)	2 (1.6)	86 (4.3)	0.14
Hypertension	1554 (72.3)	110 (85.9)	1444 (71.4)	<0.001
Cocaine abuse	27 (1.3)	2 (1.6)	25 (1.3)	0.68
Atherosclerosis	470 (22.1)	37 (29.4)	433 (21.6)	0.04
Bicuspid aortic valve	86 (4.6)	7 (6.4)	79 (4.5)	0.38
Iatrogenic dissection	56 (2.6)	1 (0.8)	55 (2.8)	0.26
Prior aortic dissection	89 (4.2)	4 (3.1)	85 (4.2)	0.56
Prior aortic aneurysm	269 (12.6)	13 (10.3)	256 (12.7)	0.43
Diabetes mellitus	125 (5.9)	10 (7.8)	115 (5.7)	0.33
Prior cardiovascular surgery	291 (13.8)	12 (9.5)	279 (14.0)	0.15

IRAD indicates International Registry of Acute Aortic Dissection.

Diagnostic Imaging and Use of Medications

The use of diagnostic imaging techniques was similar in patients with and without stroke. Chest radiograph, ECG, and imaging study findings were also similar between cohorts, with the exception of more arch involvement in patients with stroke (Table 3).

Patients with stroke had lower in-hospital β-blocker use; otherwise, use of evidence-based medical therapies at presentation and discharge was similar between groups (Table 4). Patients with stroke were twice as likely to undergo nonoperative management compared with those without stroke.

Complications and In-Hospital Mortality

In-hospital complications, such as hypotension and coma, were significantly higher in patients with stroke, who also demonstrated a trend toward greater incidence of malperfusion syndrome (Table 5). Although almost all other complications were higher in patients with stroke, these differences did not reach statistical significance. Median length of stay was 4.8 days longer in patients with stroke (17.8 days with stroke, Q1–Q3: 12.1–31.1 days; 13.0 days without, Q1–Q3: 8.6–21.0 days; P<0.001). Finally, overall mortality was 1.8-fold higher in patients with stroke (adjusted odds ratios, 1.62; 95% confidence interval, 0.99–2.65; P=0.055). Mortality was higher in patients with stroke compared with nonstroke patients with

Table 2. Presenting Sign and Symptoms in TAAAD Patients With and Without Stroke

Variable	Overall n (%)	Stroke n (%)	No Stroke n (%)	P Value
Presenting symptoms and signs				
Chest pain	1744 (81.6)	85 (69.7)	1659 (82.3)	<0.001
Back pain	889 (42.8)	36 (32.4)	853 (43.4)	0.023
Abrupt onset of pain	1729 (83.4)	95 (84.1)	1634 (83.4)	0.85
Migrating pain	284 (14.1)	17 (16.0)	267 (14.0)	0.56
Syncope	358 (17.0)	54 (43.5)	304 (15.3)	<0.001
Congestive heart failure	151 (6.9)	10 (8.1)	141 (6.9)	0.61
Mean systolic blood pressure±SD mm Hg	122.3±18.2	127.7±41.6	122.1±16.3	0.31
Mean diastolic blood pressure±SD mm Hg	69.7±11.4	69.3±10.3	69.7±11.4	0.80
Shock	154 (7.4)	17 (13.8)	137 (7.0)	0.005
Hypotension/tamponade/shock	565 (27.2)	46 (37.4)	519 (26.5)	0.009
Any pulse deficit	504 (29.9)	54 (50.5)	450 (28.5)	<0.001

TAAAD indicates type A acute aortic dissection.

Table 3. Diagnostic Imaging in TAAAD Patients With and Without Stroke

Variable	Overall n (%)	Stroke n (%)	No Stroke n (%)	*P* Value
Chest radiograph				
Normal	358 (22.0)	20 (20.8)	338 (22.0)	0.78
Widened mediastinum	832 (53.0)	55 (59.8)	777 (52.6)	0.18
Abnormal aortic contour	633 (41.6)	44 (47.8)	589 (41.2)	0.21
Abnormal cardiac contour	363 (23.8)	28 (30.8)	335 (23.3)	0.11
Pleural effusion	186 (12.2)	12 (13.0)	174 (12.2)	0.80
ECG				
Normal	648 (32.3)	35 (31.0)	613 (32.3)	0.76
NSST	752 (39.6)	37 (34.6)	715 (39.9)	0.28
LVH	382 (20.4)	29 (27.4)	353 (20.0)	0.07
Prior infarction	121 (6.5)	9 (8.3)	112 (6.3)	0.42
ST elevation or new infarct	132 (7.0)	9 (8.3)	123 (6.9)	0.60
Diagnostic imaging				
Any imaging study	2063 (98.4)	124 (97.6)	1939 (98.4)	0.46
Computed tomography	1784 (81.5)	113 (86.3)	1671 (81.2)	0.15
Echocardiography (TEE and TTE)	1609 (73.5)	88 (66.7)	1521 (73.9)	0.07
Aortography	249 (11.5)	22 (16.7)	227 (11.1)	0.054
MRI	88 (4.2)	8 (6.2)	80 (4.0)	0.23
Diagnostic imaging findings				
Widest diameter of ascending aorta median (Q1–Q3), cm	5.0 (4.5–5.7)	5.0 (4.2–5.4)	5.0 (4.5–5.8)	0.07
Pericardial effusion	819 (41.9)	53 (46.5)	766 (41.6)	0.30
Arch vessel involvement	628 (39.0)	66 (68.0)	562 (37.1)	<0.001
Aortic regurgitation	996 (54.3)	52 (49.1)	944 (54.6)	0.26

LVH indicates left ventricular hypertrophy; NSST, nonspecific ST-T changes; Q1–Q3, first quartile–third quartile; TAAAD, type A acute aortic dissection; TEE, transesophageal echocardiogram; and TTE, transthoracic echocardiogram.

similar management. Among hospital survivors, follow-up mortality (median follow-up 2 years, Q1–Q3: 1 –4 years) was not different between groups (adjusted hazard ratio, 1.15; 95% confidence interval, 0.46–2.89; P=0.76). Estimates using Cox proportional hazard model suggested excellent 5-year survival in 4 of 5 TAAAD surgically treated stroke patients who survived past index hospitalization; conversely, 5-year survival among medically managed stroke patients was dismal (estimated mortality of 100%).

Independent Clinical Correlates of Presenting Stroke and In-Hospital Mortality

Arch vessel involvement on imaging was the greatest predictor of stroke (Table 6). In addition, syncope, abdominal pain, presenting pulse deficit, abnormal chest radiograph without accompanying pain, and history of hypertension had significant independent adjusted correlations with stroke in our cohort.

In TAAAD patients presenting with stroke, surgical management had strong independent adjusted associations with improved survival (Table 7). Variables with independent adjusted associations with decreased survival included coma, pleural effusion, pulse deficit on presentation, and mesenteric ischemia.

Table 4. Treatment of TAAAD Patients With and Without Stroke

Variable	Overall n (%)	Stroke n (%)	No Stroke n (%)	*P* Value
Medical therapies: in hospital				
β-Blockers	1055 (53.6)	46 (42.6)	1009 (54.2)	0.018
ACE inhibitors	68 (10.3)	2 (6.1)	66 (10.5)	0.56
Angiotension II antagonist	27 (4.1)	2 (6.1)	25 (4.0)	0.64
Calcium antagonists	223 (11.8)	15 (14.0)	208 (11.6)	0.46
Statins	33 (5.8)	2 (8.0)	31 (5.7)	0.65
Medical therapies: discharge				
β-blockers	1269 (83.0)	57 (81.4)	1212 (83.1)	0.71
ACE inhibitors	599 (40.3)	25 (35.7)	574 (40.5)	0.43
Angiotension II antagonist	74 (13.0)	4 (16.0)	70 (12.9)	0.55
Calcium antagonists (Ca channel blocker)	536 (35.8)	21 (29.6)	515 (36.1)	0.26
Statins	127 (26.0)	9 (45.0)	118 (25.2)	0.048
Definitive management				
Surgery	1863 (84.6)	97 (73.5)	1766 (85.4)	<0.001
Medical therapy only	284 (12.9)	31 (23.5)	253 (12.2)	<0.001
Percutaneous	29 (1.3)	2 (1.5)	27 (1.3)	0.69

ACE indicates angiotension-converting enzyme; and TAAAD, type A acute aortic dissection.

Discussion

Our study, the largest to date, suggests that stroke at hospital admission is observed in 6% of patients with TAAAD. These patients were older, more often had hypertension and atherosclerosis, and presented more frequently with symptoms such as syncope rather than the more classic presentation of chest or back pain. Patients with stroke were also likely to have signs of hypotension, shock, and pulse deficit. Except aortic arch involvement, imaging study findings were similar between groups. Medical therapies in hospital and at discharge were similar in the 2 groups, with the lower use of in-hospital β-blocker among stroke patients likely a reflection of the more frequent hypotension and shock in these patients. Patients with stroke were more likely to be managed medically and had greater length of stay. In-hospital mortality was higher in patients with stroke compared with nonstroke patients, regardless of the management strategy; however, postdischarge mortality did not differ between groups.

Few studies have focused on stroke in patients with TAAAD, most of which are single-center case reports[9–15] evaluating a small number of patients with few stroke events.[2–5,16] These studies described a stroke incidence between 3% and 32% in 24 to 174 patients with TAAAD. Similar to our findings, some studies reported more frequent painless presentation, syncope, and hypotension in patients with stroke. Furthermore, most studies suggested a higher mortality for patients with stroke compared with those without it. Most of these reports focused primarily on patients undergoing surgery, and many did not characterize the factors associated with risk of presenting stroke and mortality in those with stroke.

Table 5. Outcomes in TAAAD Patients With and Without Stroke

Variable	Overall n (%)	Stroke n (%)	No Stroke n (%)	*P* Value
In-hospital complications				
Malperfusion	696 (33.1)	50 (41.0)	646 (32.6)	0.056
Coma	121 (5.5)	24 (18.2)	97 (4.7)	<0.001
Myocardial ischemia/ infarction	294 (14.0)	23 (19.2)	271 (13.6)	0.09
Mesenteric ischemia/ infarction	130 (6.2)	13 (11.0)	117 (5.9)	0.024
Acute kidney failure	521 (24.7)	36 (29.8)	485 (24.3)	0.18
Hypotension	641 (30.4)	52 (43.3)	589 (29.6)	0.002
Cardiac tamponade	388 (18.4)	28 (23.1)	360 (18.1)	0.17
Limb ischemia	273 (13.0)	20 (16.8)	253 (12.7)	0.20
In-hospital mortality				
Overall	555 (25.2)	56 (42.4)	499 (24.1)	<0.001
Surgically treated patients	371 (19.9)	30 (30.9)	341 (19.3)	0.005
Medically treated patients	160 (56.3)	24 (77.4)	136 (53.8)	0.012
5-year mortality estimate (Kaplan–Meier)				
Overall	17.6%	24.1%	17.2%	0.30
Surgery	14.1%	22.1%	14.1%	0.51
Medical therapy only	62.0%	100.0%	58.7%	0.56

TAAAD indicates type A acute aortic dissection.

Our findings may have several implications for patients with TAAAD and presenting stroke. In addition to chest or back pain preceding the stroke, this and other studies suggest that a high index of suspicion should also be made for TAAAD in stroke patients who present with syncope hypotension, pulse deficit, and a murmur of aortic regurgitation. In patients with these symptoms, early imaging would enable diagnosis of TAAAD if present and help prevent inadvertent use of fibrinolytic therapy that could lead to fatal outcomes in this cohort.[10,12,17–19]

Urgent surgical repair is required for TAAAD because conservative management is associated with a high incidence of early mortality.[6] However, some studies have suggested that immediate surgical repair of TAAAD in the presence of stroke has a prohibitive risk associated with hemorrhagic worsening of an ischemic infarction after reperfusion subsequent to cardiopulmonary bypass and full anticoagulation.[20,21] Others have suggested that delaying repair until cerebral injury stabilizes may minimize these concerns, albeit exposing patients to an early hazard of death from rupture.[22] However, Fann et al[3] reported no worsening of cerebral symptoms in 7 surgically treated patients with TAAAD. Several small studies have since corroborated the feasibility and safety of early surgical repair in TAAAD patients with stroke.[9,13,16,23,24] In fact, 1 study suggested no benefit of surgery beyond 12 hours when cerebral damage is almost complete.[16] Deeb et al[25] have suggested good results with a hybrid approach involving fenestrations for immediate percutaneous reperfusion followed by surgery after the brain tissue has healed. Although our data suggest that surgically treated TAAAD patients with stroke had higher mortality than those without stroke, surgical patients had much lower mortality than patients treated medically, regardless of whether they presented with stroke. Furthermore, adjusted survival estimates for patients with TAAAD suggested that among surgically treated patients with TAAAD discharged alive at index hospitalization, ≈4 of 5 patients survived at 5-year follow-up, whereas long-term outcomes were dismal among stroke patients treated medically (100% mortality). Our results and those of previous studies suggest, compared with medical therapy, that definitive early repair in TAAAD patients presenting with stroke is safe and likely associated with lower short- and long-term mortality. Further studies are warranted in TAAAD patients presenting with stroke to determine which stroke patients will benefit more from surgery and whether or not stroke severity impacts outcomes. In addition, analyses should be performed to determine the optimal timing of surgery (early versus late) and to compare outcomes between surgical strategies used in this cohort.

Table 6. Independent Clinical Correlate of Presenting Stroke Among These TAAAD Patients

Independent Adjusted Effects of Clinical Correlates of Presenting Stroke					
		95% CI for Odds Ratio			
Variable	Odds Ratio	Lower	Upper	Wald χ^2	*P* Value
Any arch vessel involvement	3.393	1.932	5.961	18.063	<0.001
Syncope on presentation	3.117	1.781	5.457	15.845	<0.001
History of hypertension	3.275	1.450	7.397	8.149	0.004
Abdominal pain on presentation	0.347	0.165	0.729	7.800	0.005
Any pulse deficit	2.019	1.172	3.479	6.410	0.011
Abnormal chest radiograph without associated pain	1.932	1.077	3.466	4.874	0.027

Hosmer–Lemeshow test *P*=0.525. C=0.780. CI indicates confidence interval; and TAAAD, type A acute aortic dissection.

Table 7. Independent Clinical Correlate of In-hospital Death Among TAAAD Patients Presenting With Stroke

Independent Adjusted Effects of Clinical Correlates of In-Hospital Death in Patients With Stroke					
		95% CI for Odds Ratio			
Variable	Odds Ratio	Lower	Upper	Wald χ^2	*U* Value
Age ≥70 y	1.622	0.379	6.937	0.426	0.514
Surgical management	0.015	0.002	0.129	14.555	<0.001
Coma	10.081	1.317	77.161	4.952	0.026
Pleural effusion on any test	4.303	1.031	17.959	4.007	0.045
Any pulse deficit	6.629	1.483	29.624	6.130	0.013
Mesenteric ischemia	47.605	3.458	655.452	8.336	0.004

Hosmer–Lemeshow test *P*=0.387. C=0.908. CI indicates confidence interval; and TAAAD, type A acute aortic dissection.

Limitations

Patients in this study had TAAAD and were admitted to centers specializing in aortic disease. Thus, our results may not be applicable to those with chronic TAAAD, type B AAD,

or those treated at smaller centers. IRAD data are collected retrospectively and prospectively through voluntary site participation and are subject to incomplete information, particularly with regard to long-term outcomes. As such, some strokes may have not been adequately captured in the registry. Furthermore, because IRAD is composed of tertiary care centers, patients with TAAAD and stroke who died at primary care centers or who were unable to be transferred secondary to their acute illness were not included. Treatment strategies were not protocol driven and were determined by the treating physicians. Thus, inference regarding the effectiveness of various strategies on outcomes in these patient cohorts should be made with caution. Imaging results were based on interpretation at the IRAD center and were not independently adjudicated. We are also unable to provide any details on stroke size, extent of debilitation after stroke, or improvement or resolution of neurological symptoms.

Conclusions

Stroke occurred in >1 of 20 patients with TAAAD and was associated with increased morbidity and in-hospital mortality, but not higher long-term mortality among survivors. Our data suggest that aggressive early intervention with rapid establishment of cerebral flow and surgical repair of dissection have significant potential for reducing morbidity and improving mortality.

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Disclosures

None.

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Extent of Preoperative False Lumen Thrombosis Does Not Influence Long–Term Survival in Patients With Acute Type A Aortic Dissection

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Extent of Preoperative False Lumen Thrombosis Does Not Influence Long-Term Survival in Patients With Acute Type A Aortic Dissection

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Background—Partial thrombosis of the false lumen has been related to aortic growth, reoperations, and death in the chronic phase of type B and repaired type A aortic dissections. The impact of preoperative false lumen thrombosis has not been studied previously. We used data from a contemporary, multinational database on aortic dissections to evaluate whether different degrees of preoperative false lumen thrombosis influenced long-term prognosis.

Methods and Results—We examined the records of 522 patients with surgically treated acute type A aortic dissections who survived to discharge between 1996 and 2011. At the preoperative imaging, 414 (79.3%) patients had patent false lumens, 84 (16.1%) had partial thrombosis of the false lumen, and 24 (4.6%) had complete thrombosis of the false lumen. The annual median (interquartile range) aortic growth rates were 0.5 (−0.3 to 2.0) mm in the aortic arch, 2.0 (0.2 to 4.0) mm in the descending thoracic aorta, and similar regardless of the degree of false lumen thrombosis. The overall 5-year survival rate was 84.7%, and it was not influenced by false lumen thrombosis (P=0.86 by the log-rank test). Independent predictors of long-term mortality were age >70 years (hazard ratio [HR], 2.34; 95% confidence interval [CI], 1.20 to 4.56, P=0.012) and postoperative cerebrovascular accident, coma, and/or renal failure (HR, 2.62; 95% CI, 1.40 to 4.92, P=0.003).

Conclusions—Patients with acute type A aortic dissection who survive to discharge have a favorable prognosis. Preoperative false lumen thrombosis does not influence long-term mortality, reintervention rates, or aortic growth. (***J Am Heart Assoc.*** **2013;2: e000112 doi: 10.1161/JAHA.113.000112)**

Key Words: aortic dissection • prognosis • surgery • thrombosis

Acute type A aortic dissection (AAAD) is a challenging clinical emergency. Despite continuous improvements in diagnosis, surgical treatment, and perioperative management, the latest report from the International Registry of Acute Aortic Dissection (IRAD) revealed an in-hospital surgical mortality of 23.9%.[1] This is similar to that found in a more recent study from another large registry,[2] while several single-center series report mortality well below 10%.[3–5] Patients who survive to discharge have reasonable intermediate and long-term survival rates.[6,7]

Several reports[8–12] have indicated that patients with a residual patent false lumen following an AAAD repair have an increased risk of distal aortic enlargement and death. In addition, the IRAD data have shown that in patients with acute type B aortic dissections, partial thrombosis, more than a completely patent false lumen, predicts a higher follow-up mortality.[13] As an extension of this observation, Song et al[14] found that partial thrombosis of the false lumen after an extensive Stanford type A (DeBakey type I) aortic dissection repair is a predictor of aortic enlargement, aorta-related procedures, and poor long-term survival. Different factors have been proposed to account for this increased risk, and one possible mechanism could be that the thrombus itself is a risk factor by enhancing the coagulation system.[15]

In this context, we anticipated that a partial thrombosis of the false lumen observed at the first hospitalization would negatively affect the remodeling of the distal aorta, increase

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the need for reintervention, and negatively influence the long-term survival of AAAD patients. To assess this hypothesis, in the IRAD database, we analyzed the patients with surgically treated AAAD who were discharged alive from their primary hospitalization.

Methods

IRAD Registry

IRAD is a multinational registry that collects consecutive and unselected cases of acute aortic dissection at 30 aortic centers in 10 countries. Participation in the registry does not per se imply treatment standardization. Further details about the IRAD structure and data collection have been previously published.[16] The study was approved by the institutional review board or ethics committee at each participating center.

Study Population

We screened the data records for all patients who were enrolled in IRAD between January 1, 1996 and January 31, 2011. We identified 2380 patients with an AAAD, which was defined as any nontraumatic dissection involving the ascending aorta and presenting within 14 days of symptom onset. Iatrogenic dissections were included. The patients were identified prospectively at presentation or retrospectively from discharge diagnoses. The diagnosis was based on imaging, intraoperative findings, and/or autopsy.

The patients who were exclusively managed medically, had intramural hematomas, died during the index hospitalization, or for whom follow-up or information on false lumen status was lacking were excluded from the analysis (Figure 1). Our final study population included 522 patients. Of these patients, 414 (79.3%) had a patent, 84 (16.1%) a partially thrombosed, and 24 (4.6%) a completely thrombosed false lumen.

Data Collection

A standardized form with 290 variables was used at all IRAD centers to describe the index hospital stay. This form included patient demographics, past medical histories, presenting symptoms, physical findings, imaging results, treatments, and outcomes (including complications and mortality).

All of the patients underwent computed tomography, magnetic resonance imaging, angiography, and/or echocardiography. The false lumen was classified as patent when flow was present without evidence of thrombus at any level of the aorta, as partially thrombosed when both flow and thrombus were present, and completely thrombosed in the absence of flow in the false lumen at any aortic level. Intramural

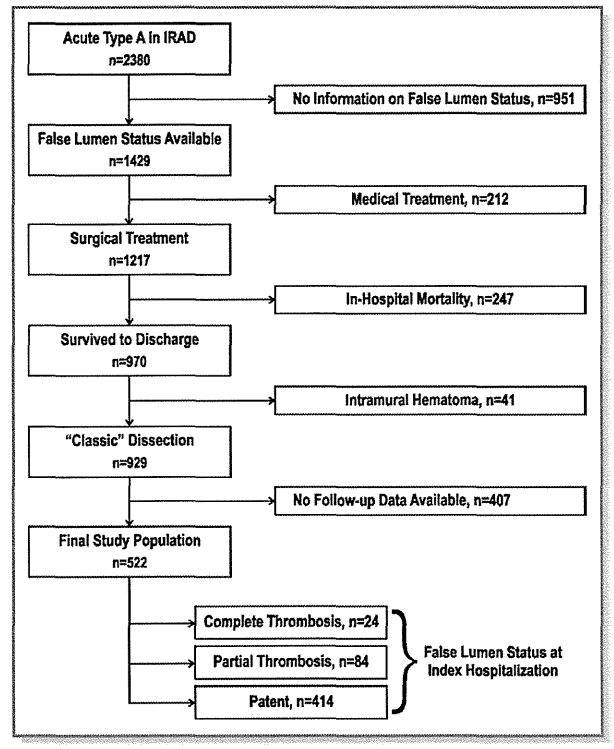

Figure 1. Study inclusion flow-chart. IRAD indicates International Registry of Acute Aortic Dissection.

hematoma was defined as an aortic wall hematoma without an intimal flap or tear on any imaging study. The distinction between an intramural hematoma and a classic double-barrel dissection with complete thrombosis of the false lumen was determined by experts at each IRAD center.

Follow-up data were obtained annually for up to 5 years using a standardized form to record clinical variables, imaging data, reoperations (including endovascular and/or open repair), and mortality.

Aortic Growth Analysis

The growth rate was calculated for the aortic arch and the descending thoracic aorta. Aortic size was measured as the largest transversal diameter perpendicular to the flow axis for each segment. Patients who underwent arch replacement at the index hospitalization were only included in the growth calculations for the descending thoracic aorta. For patients who underwent reintervention during follow-up, the latest diameter measure before reintervention was used. The growth rate was calculated as the difference between the most recent diameter measure and the diameter at the index hospitalization at the same aortic level, divided by the time interval between the 2 measurements and expressed as millimeters per year.

Statistical Analysis

Based on preoperative imaging at the index hospitalization, the patients were stratified into 3 groups according to the status of the false lumen: patent, partial thrombosis, and complete thrombosis. The clinical characteristics of each group are presented as frequencies and percentages for the categorical variables and as mean±standard deviation (SD) for the continuous variables. In cases of skewed distributions, the continuous variables are presented as the median and interquartile range (Q1 to Q3, the range between the 25th and the 75th percentile). For categorical variables, between-group differences were analyzed using the chi-squared or 2-sided Fisher's exact test, as appropriate. Continuous variables were compared with an analysis of variance or a Kruskal–Wallis test for data with skewed distributions. Missing data were not defaulted to negative and denominators reflect only those cases reported.

Univariate associations between clinical variables and mortality were calculated using a Cox regression analysis. Independent predictors of mortality were determined using a stepwise Cox proportional-hazards analysis. The initial model used variables with a P value of <0.15 in univariate testing and also included false lumen status. A backward stepwise selection of variables (after adjusting for sex and age) was performed sequentially with a default value for inclusion set at $P<0.05$.

Kaplan–Meier curves were created for the overall patient cohort and stratified according to the false lumen status. Curves were created for survival and for freedom from major adverse events (all-cause mortality, aortic rupture, and reoperation [including endovascular repair]). Between-group differences in survival and freedom from major adverse events were analyzed using the log-rank test.

All data analyses were performed using SPSS version 20 for Windows (SPSS Inc).

Results

Baseline Characteristics, Imaging, Treatment, and Complications

The mean age (±SD) of the 522 patients was 57.9±13.6 years, and 19.6% were aged >70 years (Table 1). The majority of patients (74.9%) were male and had a history of hypertension (70.9%). Other common comorbidities were atherosclerosis (19.1%), previous aortic aneurysm (11.7%), previous open-heart surgery (8.8%), and cardiac catheterization or percutaneous coronary intervention (7.8%). Marfan syndrome was present in 5.8% of the patients, and 30.0% were current smokers. Diabetes mellitus was rare in this patient cohort (4.9%), as were chronic renal insufficiency (3.6%) and chronic obstructive pulmonary disease (4.3%).

Almost a quarter of patients presented with hypotension, shock, or cardiac tamponade. Chest pain was common (85.3%); 15.0% of the patients presented with neurologic deficits, and 28.9% had a pulse deficit.

The mean number (±SD) of imaging studies per patient was 1.8±0.7, with a median (Q1 to Q3) number of studies of 2.0 (1.0 to 3.0). The most frequent procedure was computed tomography, which was performed in 81.0% of the patients, and 78.6% underwent a trans-esophageal echocardiography. Arch vessel involvement occurred in 40.3% of the patients. About one-third of the dissections were confined to the ascending aorta and aortic arch.

Complete arch replacement was performed in 12.3% of cases, and the aortic valve was replaced in 29.9% of patients (Table 2). Deliberate interruption of systemic perfusion was used in 86.0%, with a median (Q1 to Q3) circulatory arrest time of 44 (28 to 97) minutes.

Neurologic complications occurred in one quarter of the patients, acute renal failure in 19.3%, and limb ischemia in 13.4%. Mesenteric ischemia was rare, occurring in only 3.2% of patients.

Clinical Differences According to Preoperative False Lumen Status

Patients with a patent false lumen were on average 3 years younger than those with a partially thrombosed false lumen and 6 years younger than those with complete false lumen thrombosis. There were no differences with regard to previous medical history, presenting symptoms, or clinical findings. Patients with a patent false lumen had fewer imaging studies per patient, with a mean (±SD) of 1.7±0.6, versus 2.0±0.7 for those with partial thrombosis and 2.0±0.8 for those with complete thrombosis ($P=0.006$). Computed tomography was performed more frequently in the patients with partial thrombosis of the false lumen (90.5%) compared to the patients with complete patency or complete thrombosis of the false lumen (79.4% or 75.0%, respectively, $P=0.034$). The distal extension of the dissection was similar between the groups; however, extension merely to the aortic arch occurred more frequently in the partial thrombosis and complete thrombosis groups than in the patent false lumen group (31.8%, 37.5% and 17.1%, respectively, $P=0.005$). The surgical strategy did not differ between the groups.

Aortic Growth and Long-Term Outcome

The median aortic growth rate (Q1 to Q3) was 0.5 (−0.3 to 2.0) mm/year in the aortic arch and 2.0 (0.2 to 4.0) mm/year in the descending thoracic aorta (Table 3). Aortic growth was similar regardless of the degree of preoperative false lumen thrombosis.

Table 1. Patient Characteristics Stratified by False Lumen Status

	All Patients (n=522)	Status of the False Lumen			*P* Value
		Patent (n=414)	Partial Thrombosis (n=84)	Complete Thrombosis (n=24)	
Baseline patient characteristics					
Age, mean±SD	57.9±13.6	57.0±13.6	60.8±13.4	63.3±12.6	0.009*
Age ≥70 years, no./total no. (%)	102/521 (19.6)	73/413 (17.7)	20/84 (23.8)	9/24 (37.5)	0.036
Female gender, no./total no. (%)	131/522 (25.1)	96/414 (23.2)	26/84 (31.0)	9/24 (37.5)	0.12
Marfan syndrome, no./total no. (%)	30/514 (5.8)	25/407 (6.1)	4/83 (4.8)	1/24 (4.2)	0.93
Hypertension, no./total no. (%)	365/515 (70.9)	289/410 (70.5)	60/82 (73.2)	16/23 (69.6)	0.88
Atherosclerosis, no./total no. (%)†	98/513 (19.1)	82/406 (20.2)	10/83 (12.0)	6/24 (25.0)	0.16
Previous aortic dissection, no./total no. (%)	17/512 (3.3)	11/406 (2.7)	4/83 (4.8)	2/23 (8.7)	0.15
Previous aortic aneurysm, no./total no. (%)	60/513 (11.7)	52/407 (12.8)	5/82 (6.1)	3/24 (12.5)	0.21
Current smoking, no./total no. (%)‡	36/120 (30.0)	28/89 (31.5)	7/27 (25.9)	1/4 (25.0)	0.85
Diabetes mellitus, no./total no. (%)	25/513 (4.9)	19/407 (4.7)	5/82 (6.1)	1/24 (4.2)	0.84
COPD, no./total no. (%)	6/140 (4.3)	3/106 (2.8)	3/30 (10.0)	0/4 (0.0)	0.26
Chronic renal insufficiency, no./total no. (%)	5/140 (3.6)	4/106 (3.8)	1/30 (3.3)	0/4 (0.0)	1.00
Previous invasive cardiac procedures					
Open heart surgery, no./total no. (%)	44/499 (8.8)	33/396 (8.3)	8/81 (9.9)	3/22 (13.6)	0.53
Catheterization and/or PCI, no./total no. (%)	32/409 (7.8)	25/326 (7.7)	6/65 (9.2)	1/18 (5.6)	0.86
Clinical presentation					
Abrupt onset of pain, no./total no. (%)	439/498 (88.2)	350/395 (88.6)	67/79 (84.8)	22/24 (91.7)	0.60
Chest pain, no./total no. (%)	434/509 (85.3)	338/402 (84.1)	73/83 (88.0)	23/24 (95.8)	0.25
Migrating pain, no./total no. (%)§	72/478 (15.1)	57/380 (15.0)	12/78 (15.4)	3/20 (15.0)	1.00
Hypotension/shock/tamponade, no./total no. (%)¶	118/509 (23.2)	94/404 (23.3)	18/81 (22.2)	6/24 (25.0)	0.96
First systolic blood pressure (mm Hg), mean±SD	131.8±37.6	132.1±38.2	130.0±36.3	133.4±33.5	0.89
First diastolic blood pressure (mm Hg), mean±SD	73.0±22.0	72.9±21.8	72.7±23.9	74.7±19.3	0.93
Any pulse deficit, no./total no. (%)‖	122/422 (28.9)	102/338 (30.2)	18/68 (26.5)	2/16 (12.5)	0.30
Any neurologic deficit, no./total no. (%)**	77/513 (15.0)	65/405 (16.0)	10/84 (11.9)	2/24 (8.3)	0.49
Abnormal ECG, no./total no. (%)††	311/495 (62.8)	238/388 (61.3)	56/83 (67.5)	17/24 (70.8)	0.41
Diagnostic imaging					
Number of studies per patient, mean±SD	1.8±0.7	1.7±0.6	2.0±0.7	2.0±0.8	0.006
Computed tomography, no./total no. (%)	421/520 (81.0)	327/412 (79.4)	76/84 (90.5)	18/24 (75.0)	0.034
Magnetic resonance imaging, no./total no. (%)	25/492 (5.1)	15/391 (3.8)	8/77 (10.4)	2/24 (8.3)	0.037
Trans-esophageal echocardiography, no./total no. (%)	408/519 (78.6)	324/411 (78.8)	66/84 (78.6)	18/24 (75.0)	0.91
Arch vessel involvement, no./total no. (%)‡‡	183/454 (40.3)	147/357 (41.2)	30/78 (38.5)	6/19 (31.6)	0.66
Widest diameter of ascending aorta (cm), median (Q1 to Q3)§§	5.0 (4.4 to 5.8)	5.0 (4.4 to 5.6)	4.9 (4.1 to 6.0)	5.0 (4.1 to 6.1)	0.94
Widest diameter of descending aorta (cm), median (Q1 to Q3)§§	3.3 (3.0 to 3.7)	3.2 (3.0 to 3.6)	3.5 (3.0 to 4.0)	3.4 (2.9 to 4.0)	0.51

Continued

Table 1. Continued

	All Patients (n=522)	Status of the False Lumen			*P* Value
		Patent (n=414)	Partial Thrombosis (n=84)	Complete Thrombosis (n=24)	
Most distal extension of dissection					
Ascending aorta, no./total no. (%)	59/392 (15.1)	47/310 (15.2)	10/66 (15.2)	2/16 (12.5)	1.00
Aortic arch, no./total no. (%)	80/392 (20.4)	53/310 (17.1)	21/66 (31.8)	6/16 (37.5)	0.005
Left subclavian level, no./total no. (%)	22/392 (5.6)	19/310 (6.1)	3/66 (4.5)	0/16 (0.0)	0.74
Descending thoracic aorta, no./total no. (%)	103/392 (26.3)	86/310 (27.7)	12/66 (18.2)	5/16 (31.2)	0.24
Abdominal aorta, no./total no. (%)	128/392 (32.7)	105/310 (33.9)	20/66 (30.3)	3/16 (18.8)	0.41

SD indicates standard deviation; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; ECG, echocardiogram; ANOVA, analysis of variance.
*Analyzed using ANOVA. Independent T-test between groups: Patent vs partial thrombosis, *P*=0.019. Patent vs complete thrombosis, *P*=0.026. Partial vs complete thrombosis, *P*=0.411.
†Any history of PCI, coronary artery bypass graft surgery, or catheterization demonstrating >70% stenosis in coronary, cerebral, or peripheral vasculature.
‡Tobacco use during the last month.
§Pain changed location.
¶Hypotension defined as systolic blood pressure <100 mm Hg.
‖Diminution or absence of pulse in either right or left carotid, brachial or femoral arteries.
**Paraparesis, paraplegia, stroke, or coma.
††Showing signs of old or new infarction, nonspecific ST-T segment changes, left ventricular hypertrophy or low voltage.
‡‡Any imaging modality showing dissection extending into the brachiocephalic trunk, left common carotid artery or left subclavian artery.
§§Q1 to Q3 denotes interquartile range.

On univariate testing, age, preexisting renal failure and aortic aneurysm, presenting with chest or back pain, and the composite of postoperative cerebrovascular accident, coma, or renal failure were significantly associated with death during follow-up (Table 4). In the multiple regression models, only age and the composite of postoperative cerebrovascular accident, coma, or renal failure were statistically significant (Table 5). The preoperative status of the false lumen did not predict death after discharge in the univariate testing or when adjusted for age and gender.

Table 2. Surgical Treatment and In-Hospital Complications

	All Patients (n=522)	Status of the False Lumen			*P* Value
		Patent (n=414)	Partial Thrombosis (n=84)	Complete Thrombosis (n=24)	
Surgical treatment					
Complete arch replacement, no./total no. (%)	60/489 (12.3)	42/385 (10.9)	14/81 (17.3)	4/23 (17.4)	0.20
Descending aortic replacement, no./total no. (%)*	8/490 (1.6)	5/387 (1.3)	2/80 (2.5)	1/23 (4.3)	0.17
Aortic valve replacement, no./total no. (%)	145/485 (29.9)	124/384 (32.3)	16/78 (20.5)	5/23 (21.7)	0.080
Hypothermic circulatory arrest					
HCA used, no./total no. (%)	430/500 (86.0)	342/393 (87.0)	69/84 (82.1)	19/23 (82.6)	0.39
HCA duration (minutes), median (Q1 to Q3)†	44 (28 to 97)	44 (28 to 100)	42 (25 to 80)	46 (33 to 87)	0.52
In-hospital complications (pre- and postoperative)					
Neurologic deficit, no./total no. (%)‡	125/501 (25.0)	98/397 (24.7)	21/81 (25.9)	6/23 (26.1)	0.98
Mesenteric ischemia or infarction, no./total no. (%)	16/496 (3.2)	15/393 (3.8)	1/80 (1.2)	0/23 (0.0)	0.57
Acute renal failure, no./total no. (%)§	97/502 (19.3)	76/397 (19.1)	18/81 (22.2)	3/24 (12.5)	0.60
Limb ischemia, no./total no. (%)	67/499 (13.4)	55/395 (13.9)	11/80 (13.8)	1/24 (4.2)	0.48

HCA indicates hypothermic circulatory arrest.
*Replacement of at least part of the aorta between the left subclavian level and the diaphragm.
†Q1 to Q3 denotes interquartile range.
‡Stroke, coma, or spinal cord ischemia.
§Three-fold increase in serum creatinine, 75% reduction in glomerular filtration rate, serum creatinine ≥354 μmol/L, urine output <0.3 mL/kg per hour over 24 hours or anuria for ≥12 hours.

Table 3. Aortic Growth Rates (mm/year).

	All Patients (n=522)	Status of the False Lumen			*P* Value
		Patent (n=414)	Partial Thrombosis (n=84)	Complete Thrombosis (n=24)	
Aortic arch, median (Q1 to Q3)	0.5 (−0.3 to 2.0)	0.5 (−0.5 to 1.8)	1.7 (0.0 to 4.2)	0.3 (−1.0 to 9.2)	0.24
Descending thoracic aorta, median (Q1 to Q3)	2.0 (0.2 to 4.0)	1.8 (0.4 to 4.0)	2.1 (−0.1 to 4.9)	0.3 (−0.5 to 3.4)	0.29

Q1 to Q3 denotes interquartile range.

Table 4. Univariate Predictors of Long-Term Mortality

Variable	Hazard Ratio	95% Confidence Interval	*P* Value
Age	1.04	1.02 to 1.07	0.001
Age ≥70 years	2.96	1.65 to 5.31	<0.001
Female gender	1.24	0.66 to 2.35	0.51
Atherosclerosis*	1.48	0.78 to 2.82	0.23
Patent false lumen†	1.00		
Partially thrombosed false lumen	0.80	0.34 to 1.88	0.60
Completely thrombosed false lumen	0.87	0.21 to 3.61	0.85
Postoperative CVA, coma and/or acute renal failure‡	2.73	1.46 to 5.11	0.002
Postoperative spinal cord ischemia	0.93	0.13 to 6.80	0.95
Presenting diameter ascending aorta	1.02	0.80 to 1.31	0.86
Presenting diameter descending aorta	1.20	0.77 to 1.87	0.42
Chronic renal insufficiency	7.00	1.40 to 34.87	0.018
Previous aortic aneurysm	2.31	1.15 to 4.66	0.019
Peripheral artery disease	6.23	0.75 to 51.88	0.091
Postoperative mesenteric ischemia/infarction	5.66	0.77 to 41.77	0.089
Presenting syncope	0.50	0.20 to 1.27	0.14
Presenting CVA	1.87	0.67 to 5.23	0.23
Surgery on descending aorta	3.02	0.73 to 12.46	0.13
Presenting chest or back pain	0.44	0.21 to 0.92	0.029

CVA indicates cerebrovascular accident.
*Any history of percutaneous coronary intervention, coronary artery bypass graft surgery or catheterization demonstrating > 70% stenosis in coronary, cerebral or peripheral vasculature.
†Patent false lumen is the reference group.
‡Three-fold increase in serum creatinine, 75% reduction in glomerular filtration rate, serum creatinine ≥354 μmol/L, urine output <0.3 mL/kg per hour over 24 hours or anuria for ≥12 hours.

The Kaplan–Meier curves showed an overall 5-year survival of 84.7% (95% CI; 79.6% to 88.6%; Figure 2). The extent of preoperative false lumen thrombosis did not affect the 5-year survival rates (Figure 3). Nor did thrombosis of the false lumen preoperatively affect freedom of major adverse events (Figure 4).

Table 5. Independent Predictors of Long-Term Mortality After Multivariate Model Adjustments

Variable	Hazard Ratio	95% Confidence Interval	*P* Value
Female gender	0.90	0.43 to 1.87	0.78
Age ≥70 years	2.34	1.20 to 4.56	0.012
Patent false lumen*	1.00		
Partial thrombosis false lumen	0.78	0.30 to 1.99	0.60
Complete thrombosis false lumen	0.81	0.19 to 3.44	0.78
Postoperative CVA, coma and/or renal failure†	2.62	1.40 to 4.92	0.003

CVA indicates cerebrovascular accident.
*Patent false lumen is the reference group.
†Three-fold increase in serum creatinine, 75% reduction in glomerular filtration rate, serum creatinine ≥354 μmol/L, urine output <0.3 mL/kg per hour over 24 hours or anuria for ≥12 hours.

Discussion

The data included in the present analysis reject the hypothesis that a partially thrombosed false lumen on preoperative imaging was a predictor of an ominous clinical course in patients with surgically treated AAAD.

To our knowledge, the relationship between partial thrombosis of the false lumen and long-term outcome in patients with aortic dissection has been examined in 7 studies.[13–15,17–20] All of these studies have included patients with either type B dissections, postoperative AAAD, or a combination of both. The results have been divergent. Partial thrombosis was identified as an independent predictor for aortic enlargement, aortic-related procedures, or death in 2 studies.[13,14] In the remaining 5 studies,[15,17–20] partial thrombosis was not associated with a worse outcome, faster aortic growth, or higher incidence of aneurysm development compared to complete patency of the false lumen. However, in the

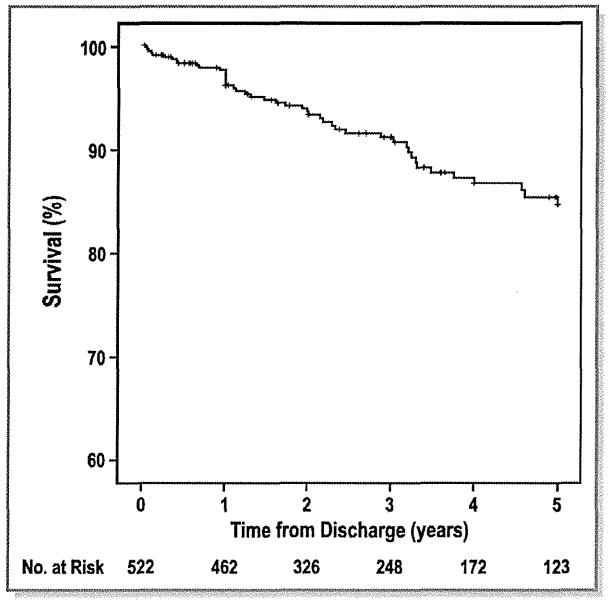

Figure 2. Kaplan–Meier postdischarge survival curve for all patients.

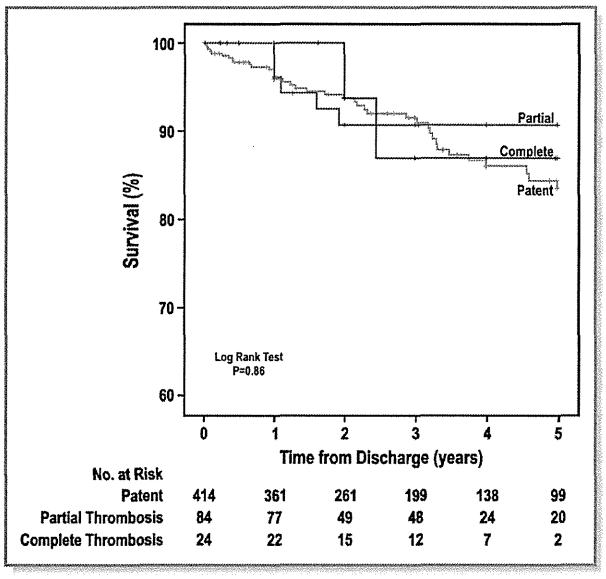

Figure 3. Kaplan–Meier postdischarge survival curves stratified according to the false lumen status.

study by Sueyoshi et al,[15] which compared aortic enlargement across different degrees of false lumen thrombosis in type B dissections, a subset within the partial thrombosis group with a blind pouch in the false lumen (ie, thrombosis covering the potential reentry site) had considerably faster growth rates. This group was small, only accounting for 15% of the patients with partial thrombosis of the false lumen.

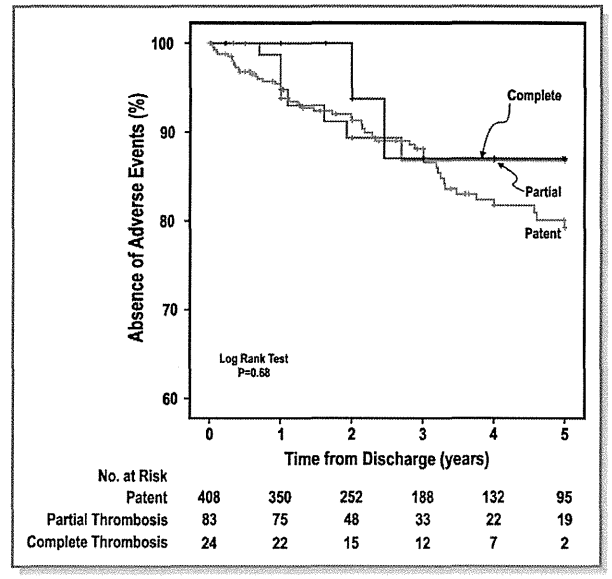

Figure 4. Kaplan–Meier curves of postdischarge freedom from major adverse events (all-cause mortality, aortic rupture and reoperation, including endovascular repair), stratified according to the false lumen status.

Results from previous studies on type B dissections and postoperative AAAD cannot readily be extrapolated to our data, as we examined the influence of preoperative false lumen thrombosis in AAAD. In addition, the fact that partial thrombosis of the false lumen seems to be unfavorable in type B dissections does not necessarily imply that this is the case in postoperative AAAD. The notion that an operated AAAD with a persistent false lumen in the descending aorta mirrors a type B dissection is not intuitive. In AAAD, the primary entry tear is typically located in the ascending aorta, whereas the area just distal to the subclavian artery is the predilection site in type B dissections.[21,22] This region is also most prone to dilation and rupture in the chronic phase.[20] By surgically removing the primary entry tear, the pathological process of an AAAD is fundamentally changed. Residual intimal tears, which maintain flow in the false lumen and remain distal after type A dissection repair, might have a different impact on flow and pressure dynamics compared to that associated with the primary entry in type B dissections. In fact, a residual primary entry tear independently predicts the need for reintervention in patients with operated AAAD only.[17] Moreover, patients with a patent false lumen distally to AAAD repair have better outcomes compared to type B dissections, which is potentially related to the size and location of intimal tears.[23] It is also to be noted, that the one study supporting partial thrombosis as a negative predictor in surgically treated AAAD[14] is based on 27 patients with a particularly high mortality of 60% at 5 years.

We observed that the degree of false lumen thrombosis appeared to increase with age. It is unknown why older

patients are more likely to have spontaneous complete thrombosis of the false lumen, but blood coagulability increases with age.[24] The group with complete thrombosis was small: 24 patients (4.6% of the total patient cohort). Traditionally, complete thrombosis of the false lumen has been thought to be a prerequisite for healing of the aorta postdissection, as flow and pressurization of the false lumen are thought to contribute to late dilation and rupture. Accordingly, one could expect lower mortality during follow-up in this setting. Our data did not show that there was any survival benefit associated with complete false lumen thrombosis. Because of the small number of patients, even in the IRAD database, adjusted comparisons with this group lacked statistical power. Of great practical importance, however, is that there are no definitive clinical epidemiological data supporting the traditional view that a persistent blood-flow in the false lumen is a definitive negative predictor for outome.[25] Thus, an extensive procedure with arch replacement and intraoperative stentgrafting of the descending aorta[3,4] has little support as a routine procedure in AAAD. Such an extensive operation is also at odds with the acceptable overall long-term survival rate of 85% at 5 years in surgically treated AAAD in the IRAD database.

The imaging characteristics in our material warrant further attention. Patients with partial or complete thrombosis of the false lumen were subjected to more imaging studies compared to those with no thrombosis of the false lumen. It could be argued that partial or complete thrombosis of the false lumen is more likely to be diagnosed with an increasing number of different imaging modalities and that a given portion of the patients who were categorized as having patent lumens may have actually had some degree of thrombosis. Conversely, diagnosing aortic dissection itself can be challenging, more so when there is no flow in the false lumen. In the case of a "classic" aortic dissection with flow in the false lumen and a clearly visible intimal flap, the diagnosis is straightforward. When the false lumen is void of flow, establishing the diagnosis can be difficult, particularly by echocardiography. Additional imaging is required in such circumstances.

A key aspect in the interpretation of our data is that the status of the false lumen was established once (at presentation, ie, before surgery). The main goal of surgery in AAAD is to prevent lethal complications, such as rupture, cardiac tamponade, and malperfusion. A secondary goal is to resect the entry tear and redirect the blood flow to the true lumen. Resection of the primary tear and aortic reconstruction will alter flow in the false lumen and might promote thrombosis. Thus, our classification (based on aortic morphology at presentation), may be altered postoperatively. However, a distal false lumen remains patent in as many as 79% of patients following the initial repair.[9,10,26–29]

Strengths and Limitations of the Study

The main strength of the study is that it included >500 patients in an orderly, prespecified manner during a limited time period. However, IRAD is an observational registry and selection bias is possible. Furthermore, follow-up data were not available for more than half of the survivors. As a result, our data might not be representative of the entire IRAD patient population but might represent a selection from the centers with the most systematic patient registration and follow-up.

Information on preoperative false lumen status was lacking for 40% of the AAAD patients in IRAD. In cases of iatrogenic dissections that occur during elective or emergency cardiac surgery for other reasons, preoperative imaging will not be relevant. Also, when a patient with AAAD present with cardiac tamponade, cardiac arrest, or other critical conditions, preoperative imaging will in many cases be limited to a screening echocardiography, and details regarding false lumen thrombosis will not be available.

Imaging techniques may have varied among the centers. Misclassification of false lumen status was possible as the imaging data were collected and reviewed at each participating center before the start of the study and were not reevaluated in a core laboratory. Likewise, patients with a completely thrombosed false lumen might have been excluded and patients with an intramural hematoma might have been included, as this distinction can be challenging. Furthermore, traditional first-pass imaging of the aorta might have overestimated the degree of thrombosis in the false lumen.[30]

We were unable to provide cause-of-death data and the distribution of aortic-related and nonaortic-related death could be different between the groups.

Conclusions

The present study revealed that preoperative partial thrombosis of the false lumen in surgically treated AAAD in the IRAD database was not an independent risk factor for aortic enlargement, intervention, or death in the follow-up period. The AAAD survivors had favorable prognoses, but the factors that influence aortic dilation and rupture following acute aortic dissections are still incompletely understood. New imaging techniques, for example, based on flow-dynamics[31] and/or bioimaging[32,33] can hopefully improve our ability to predict an ominous outcome in patients with aortic dissection.

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Disclosures

None.

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Risk Model of Cardiovascular Surgery in 845 Marfan Patients Using the Japan Adult Cardiovascular Surgery Database

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SUMMARY

The aim of this study was to evaluate the short-term operative results of patients with Marfan syndrome who underwent thoracic or abdominal aortic surgery in a 4-year period in Japan. Data were collected from the Japan Cardiovascular Surgery Database (JCVSD). We retrospectively analyzed the data of 845 patients with Marfan syndrome who underwent cardiovascular surgery between January 2008 and January 2011. Logistic regression was used to generate risk models. The early mortality rate was 4.4% (37/845). Odds ratios (OR), 95% confidence intervals (CI), and *P* values for structures and processes in the mortality prediction model were as follows: renal insufficiency (OR, 11.37; CI, 3.72-34.66; $P < 0.001$); respiratory disorder (OR, 11.12; CI, 3.20-38.67; $P < 0.001$); aortic dissection (OR, 13.02; CI, 2.80-60.60; $P = 0.001$); pseudoaneurysm (OR, 11.23; CI, 1.38-91.66; $P = 0.024$); thoracoabdominal aneurysm (OR, 2.67; CI, 1.22-5.84; $P = 0.014$); and aortic rupure (OR, 4.23; CI, 1.26-14.23; $P = 0.002$). The mortality prediction model had a C-index of 0.82 and a Hosmer–Lemeshow *P* value of 0.56. In conclusion, this study demonstrated that renal insufficiency and respiratory disorder had great impact on the operative mortality of Marfan patients undergoing cardiovascular surgery. Because patients with aortic dissection or aortic rupture showed high operative mortality, close follow-up to avoid emergency operation is mandatory to improve the operative results. Achieving good results from surgery of the thoracoabdominal aorta was quite challenging, also in Marfan patients. (Int Heart J 2013; 54: 401-404)

Key words: JACVSD

Marfan syndrome (MFS) is the most common multisystem disorder of connective tissue that affects 1 in 5000 individuals.[1)] It is inherited as an autosomal dominant trait and displays a variety of clinical manifestations in the ocular, musculoskeletal, and cardiovascular systems. Aortic root aneurysm and subsequent aortic dissection are the leading cause of morbidity and mortality in MFS patients. Aortic aneurysm in MFS is typically pear-shaped and involves progressive dilatation of the sinus of Valsalva. Early diagnosis and advances in surgical treatment, in particular the Bentall procedure and more recently the valve-sparing procedure, have significantly improved life expectancy in MFS.[2)] There has been no report of any nationwide study in Japan, presumably because the number of operations on MFS patients at each institute is limited. In the present study, risk analysis was performed for MFS patients who had undergone cardiovascular surgery between January 2008 and January 2011, using the Japan Adult Cardiovascular Surgery Database (JACVSD).

METHODS

Study population: The JACVSD was initiated in 2000 to estimate surgical outcomes after cardiovascular procedures in many centers throughout Japan. The JACVSD adult cardiovascular division currently captures clinical information from nearly half of all Japanese hospitals (235 hospitals) performing cardiovascular surgery. The data collection form has a total of 255 variables (definitions are available online at http://www.jacvsd.umin.jp), and these are almost identical to those in the STS National Database (definitions are available online at http://sts.org). The JACVSD has developed software for the Web-based data collection system through which the data manager of each participating hospital submits their data electronically to the central office. Although participation in the JACVSD is voluntary, data completeness is a high priority. Accuracy of the submitted data is maintained by a data audit that is achieved by monthly visits by administrative office members to the participating hospital to check data against clinical records. Data validity is further confirmed by an independent comparison of the volume of cardiac surgery at a particular

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hospital entered in the JACVSD versus that reported to the Japanese Association for Thoracic Surgery annual survey.[3]

We examined all MFS patients who had undergone cardiovascular surgery between 1 January 2008 and 31 December 2011. First, those JACVSD records that were obtained without informed consent were excluded from this analysis. Records with missing age (or which were out of range), sex, or 30-day status were also excluded. After this data cleaning, the population for this risk model analysis consisted of 845 patients from 235 participating sites throughout Japan.

Endpoints: The primary outcome measure of the JACVSD was 30-day operative mortality, which was defined exactly the same as the 30-day operative mortality in the Society of Thoracic Surgeons National Database. This includes any patient who died during the index hospitalization, regardless of the length of hospital stay, and any patient who died within 30 days of the operation after being discharged from the hospital. By using the definition from a previous study,[4,5] major morbidity was defined as any of the following 5 postoperative in-hospital complications: stroke, reoperation for any reason, need for mechanical ventilation for more than 24 hours after surgery, renal failure, or deep sternal wound infection.

Statistical analysis: The statistical model was multiple logistic regression; variables entered in the model were selected from all variables shown in Table I using bivariate tests. The chi-square test analyzed categoric covariates, and the unpaired *t* test or Wilcoxon rank-sum test was used for continuous covariates. A multivariate stepwise logistic regression analysis was then performed for each outcome. Stability of the model was checked every time a variable was eliminated. When all statistically nonsignificant variables had been eliminated from the model, "goodness-of-fit" was evaluated and the area under the receiver operating characteristic (ROC) curve was used to assess how well the model could discriminate between patients who lived and patients who had died. To evaluate model calibration, the Hosmer–Lemeshow test was applied.[6]

Results

Patient characteristics: Patient characteristics and outcomes of each procedure are shown in Table I. Patient median age was 41.9 ± 13.9 years, and the percentage of male patients was as 59.7%.

Early mortality and morbidity: As shown in Table II, 30-day operative mortality rates and composite rates for mortality or major morbidity were 4.4% and 23.0% respectively.

Model results and performance: Multiple regression analyses for all patients identified 6 preoperative risks affecting operative mortality (Table III). Preoperative comorbid conditions such as high creatinine levels ≧ 3.0 mg/dL or severe chronic lung disease significantly increased the surgical risks. Types of aortic disease such as dissecting aortic aneurysm, pseudoaneurysm, and thoracoabdominal aneurysm, and also mode of surgery such as emergency surgery for rupture of the aneurysm did as well. Model performance was evaluated using the C-index (area under the ROC curve) as a measure of model discrimination and the Hosmer–Lemeshow test as a measure of "goodness-of-fit." The C-index was 0.82 for the mortality model and 0.76 for the composite mortality or morbidity model; the Hosmer–Lemeshow test *P* value was 0.56 for the mortality model and 0.35 for the composite mortality or morbidity model. Details of model performance metrics are shown in Table IV.

Discussion

A clinical diagnosis of MFS is made according to the Ghent nosology when major manifestations are present in 2 organ systems and a third organ system is involved.[7] The cardinal features of MFS involve the ocular, cardiovascular, and skeletal systems,[1] but aortic enlargement and dissection, mostly of the ascending aorta, are the primary cause of early death.[8] In

Table I. Patient Characteristics ($n = 845$)

Variable	*n*	%
Male sex	507	59.7
Age (years)	41.9 ± 13.9	
Redo	326	38.4
Aortic dissection	487	57.4
Pseudoaneurysm	30	3.5
Rupture	24	2.8
Dilatation	560	66
Aortic root	432	50.9
Ascending aorta	359	42.3
Aortic arch	254	29.9
Descending aorta	165	19.4
Thoracoabdominal	118	13.9
Abdominal aorta	23	2.7
CABG	62	7.3
Mechanical valve	268	31.6
Bioprosthetic valve	48	5.7
Aortic regurgitation ≧ 2	371	43.7
Aortic regurgitation ≧ 3	245	28.9
Emergent operation	169	19.9
NYHA class ≧ 2	244	28.7
LVEF < 50%	18	2.1
Endocarditis	19	2.2
Hypertension	356	41.9
Associated coronary disease	18	2.2
History of myocardial infarction	19	2.2
Smoking	104	12.2
COPD	83	9.8
Diabetes	17	2
Renal insufficiency	24	2.8
Cerebrovascular accident	45	5.3
Aortic valve stenosis	4	0.5
Preoperative congestive heart failure	77	9.1
Prior cardiac operation	50	5.8
Hypercholesterolemia	89	10.5

Table II. Procedural Outcomes ($n = 845$)

	30-day operative mortality (%)	Composite results (%)
All patients	4.4	23
Thoracic aneurysm		
Root	2.1	23.1
Ascending	3.5	31
Arch	5.4	45.1
Descending	8.6	36.4
TAAA	12.4	68.6

Table III. Description of each prediction model ($n = 845$)

	30-day operative mortality				Composite mortality or major morbidity			
			95%CI				95%CI	
	P	OR	Lower	Upper	*P*	OR	Lower	Upper
Age	—	—	—	—	0.033	1.292	1.02	1.64
Gender	—	—	—	—	0.002	1.829	1.26	2.66
Myocardial infarction	—	—	—	—	0.011	3.566	1.34	9.52
Poor LV function	—	—	—	—	0.032	3.105	1.1	8.76
NYHA ≧ 2	—	—	—	—	0.007	1.688	1.15	2.47
Renal failure	0	11.37	3.727	34.66	—	—	—	—
Respiratory insufficiency	0	11.12	3.195	38.67	—	—	—	—
Reoperation	—	—	—	—	0.001	2.02	1.36	3.01
Rupture	0.02	4.225	1.256	14.22	0	6.975	2.61	18.7
Acute aortic dissection	—	—	—	—	0	2.339	1.53	3.59
Dissecting aortic aneurysm	0.001	13.02	2.796	60.6	—	—	—	—
Pseudoaneurysm	0.024	11.23	1.377	91.66	—	—	—	—
Aortic arch	—	—	—	—	0	2.376	1.61	3.51
Thoracoabdominal aneurysm	0.014	2.668	1.22	5.835	0	3.511	2.12	5.81

Table IV. Performance of each prediction model ($n = 845$)

	30-day operative mortality	Composite mortality or major morbidity
C-statistic	0.82	0.76
Hosmer-Lemeshow test	0.56	0.35

1968, Bentall reported a technique for the combined treatment of diseases of the aortic valve and the segment of the ascending aorta using a valvulated tube in which the coronary artery ostia were reimplanted.[2] In the years since, this technique has gone through several modifications and has become the procedure of choice for the treatment of aortic valve disease associated with the involvement of the ascending aorta.[9-12] Thus, the life expectancy of patients with MFS has dramatically improved from about 45 years in 1972[8] to 72 years in 1995.[13]

This study demonstrated that the 30-day operative mortality of aortic root surgery including both dissecting and nondissecting aneurysm in MFS patients was 2.1%. The JATS publishes an Annual Report of all Registry data, and the most recent version reported that the 30-day operative mortality of aortic root surgery performed for acute dissecting aneurysm and nondissecting, unrupturred aneurysm was 16.3% and 2.7%, respectively.[1] The better results in our study than the JATS Registry report might be attributed to the younger ages, less atherosclerotic changes of the aortic wall, and less opportunity for accompanying diseases in MFS patients. However, the operative mortality of thoracoabdominal aneurysm in MFS patients was 12.4%, which is not better than the number reported in the JATS Registry report; the 30-day operative mortality of thoracoabdominal procedures for chronic Stanford type B aortic dissection and nondissecting unruptured thoracoabdominal aneurysm was 10.7% and 6.9%, respectively.[1] It is likely that the thoracoabdominal aneurysms in MFS patietns in our study included more extensive types than the JATS Registry report, although classification of thoracoabdominal aneurysms was not clarified in either study.

There were two important variables affecting both the 30-day operative mortality rates and the composite results; ruputure for operative indication (OR, 3.67; 95% CI, 2.80 to 4.81 and OR, 3.67; 95% CI, 2.80 to 4.81) and thoracoabdominal aortic aneurysm (OR, 3.67; 95% CI, 2.80 to 4.81 and OR, 3.67; 95% CI, 2.80 to 4.81). Other factors, like preoperative high creatinine levels ≧ 3.0 mg/dL, severe chronic lung disease, dissecting aortic aneurysm, and pseudoaneurysm were also significant risk factors for the 30-day operative mortality in our study.

Aortic root dilatation, with subsequent aortic valve regurgitation, aortic dissection, or rupture, is a common and morbid cardiovascular abnormality in MFS patients.[14] As shown in our study, because the morbidity and mortality rates in MFS patients undergoing elective root surgery is low, and besides, emergency operation for aneurysmal rupure or acute dissection worsens the clinical results, early recognition of the disorder, identification of presymptomatic patients, and subsequent institution of surgical therapy is mandatory to reduce the frequency of catastrophic aortic events.

Symptomatic aneurysms have a much worse prognosis than asymptomatic ones, and should be resected regardless of size. There is an operative mortality of up to 20% for acute ascending aortic dissection in MFS. MFS patients who suffer aortic dissection have a significantly reduced long term survival, reported at 50–70% at 10 years.[15] These facts emphasise the importance of prophylactic aortic surgery before aortic dissection occurs in MFS. Recent guidelines have suggested that prophylactic aortic surgery be performed in adults with MFS when the aortic root diameter exceeds 5 cm.[15] Aortic surgery should also be considered in MFS when the aortic root exceeds 4.5 cm and there is a family history of aortic dissection, when there is rapid aortic growth (> 5–10 mm per year), and when significant aortic insufficiency is present. Aortic diameter should be measured serially by a transthoracic echocardiogram at multiple levels and compared to normal values based on age and body surface area. Unfortunately, there is no information about size criteria for operative indication in the study. Because Japanese people are generally smaller than people in western countries and the size of the vasculature might be accordingly smaller, further investigation is warranted to elucidate the true criteria of aortic size for operative indication in Japanese people.

Our study found that the operative mortality of thoracoabdominal aneurysm in MFS patients was not better than the JATS Registry report in the general population. Although en-

dovascular treatment has been demonstrated to be effective in type B aortic dissection and descending thoracic aneurysms in non-Marfan patients, it may have limited durability in MFS patients, because the aorta is prone to dilate in these connective tissue disorders.[16,17]

The validity of our study is limited because the odds ratio of several factors for the 30-day operative mortality were quite high (> 10) and suboptimal. These high odds ratios are attributed to the small number of each factor and therefore the figures themselves are not reliable, although these factors surely affect the results significantly. Additional limitation is that we did not divide our data into analyzing and validation data sets because of the relatively small volume of data. It would be possible to perform a validation of our risk model by dividing into the 2 data sets when the volume of data becomes large enough.

In conclusion, we have reported a risk stratification study on cardiovascular surgery that uses a nationwide cardiovascular surgery database. By analyzing 845 patients, the 30-day operative mortality rate was 4.4%. Renal insufficiency and respiratory disorder had great impacts on the operative mortality of MFS patients undergoing cardiovascular surgery. Because patients with aortic dissection or aortic rupture showed high operative mortality, close follow-up to avoid emergency operation is mandatory to improve the operative results in MFS patients. Achieving good results from surgery of the thoracoabdominal aorta was also quite challenging in MFS patients.

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the use of iliofemoral access for transcatheter aortic valve insertion. Although the aneurysm diameter in this patient did not meet criteria for repair (>5.5 cm), the use of a bifurcated aortic stent graft allowed more aggressive dilation of the aortic bifurcation in a controlled fashion to achieve larger luminal diameter. It is unclear whether the technique would work in patients with nonaneurysmal arteries, and vascular surgery consultation should be obtained before such intervention. Further cautious evaluation of the technique is warranted before more widespread use.

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Hybrid Repair of Subclavian-Axillary Artery Aneurysms and Aortic Arch Aneurysm in a Patient With Marfan Syndrome

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A patient with Marfan syndrome who had previously undergone a Cabrol procedure and thoracoabdominal aortic replacement had enlarging, symptomatic aneurysms in the subclavian-axillary artery and aortic arch. Both vessels were replaced with prosthetic grafts. A thoracic endoprosthesis was inserted bridging the aortic arch graft and the previously implanted descending aorta graft. Another stent graft was placed, bridging the axillary artery and a branch of the aortic arch graft. All the stent graft landing zones were within grafts, avoiding contact between the endoprostheses and fragile aortic wall. The aneurysms were excluded from the circulation, and the patient had no serious complications.

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Aneurysms of the subclavian or axillary artery are rare [1]. Large aneurysms have generally been treated with open surgical resection and placement of a prosthetic graft [2], but the sternotomy or lateral thoracotomy necessitated by this invasive procedure sometimes results in injury to the nerves or vessels [3]. Patients with Marfan syndrome probably have increased rates of morbidity and mortality after this operation, although this has not yet been clearly established [4]. Endovascular treatment of subclavian artery lesions is a less aggressive approach, and reduced death and complication rates and good patency outcomes have been reported with a variety of endovascular methods, devices, and access routes [4, 5]. However, the use of endovascular therapy in patients with Marfan syndrome is controversial because of the risk of possible adverse effects on the fragile aortic wall of the radial force exerted by stent grafts. We describe a case in which a hybrid procedure was used to repair subclavian-axillary and aortic arch aneurysms in a patient with Marfan syndrome.

A 49-year-old man with Marfan syndrome presented with a pulsatile mass in the right axilla and supraclavian region and numbness in the right arm that he first noticed 2 months earlier. Twenty-three years earlier, he had undergone a Cabrol procedure to treat an acute type A aortic dissection. Two years later, he had an elective repair of a dissection-related thoracoabdominal aortic aneurysm that included placement of a prosthetic graft. Approximately 9 years later, a pseudoaneurysm developed at the anastomosis of the prosthesis to the intercostal arteries. The graft was replaced with another synthetic graft, attached with the use of a side-to-end anastomosis, and the intercostal arteries were reconstructed. At about the same time, computed tomographic angiography (CTA) showed that the patient had an aneurysm of the right subclavian artery (maximum diameter, 3 cm). No intervention was performed, but the patient began to have routine annual CTA evaluations of the lesion. Approximately 12 years later, the patient underwent a mitral valve replacement and coronary artery bypass grafting. He had no symptoms associated with the aneurysm in the right subclavian artery for more than 15 years before the development of the pulsating mass and numbness.

CTA showed a subclavian artery aneurysm (4-cm diameter) and two axillary artery aneurysms (maximum diameters, 3.3 cm proximally and 2.5 cm distally). The subclavian artery aneurysm had a proximal neck, and there were necks between the three aneurysms (Fig 1). The aortic arch was dilated (5-cm diameter). We decided to repair the aneurysms by using a hybrid procedure because the procedure would be performed without thoracotomy and injury to the nerves and vessels.

A 10-mm–diameter Dacron graft (Hemashield; Boston Scientific, Natick, MA) was inserted into the axillary artery through a subclavian incision, and each end of the device was anastomosed to an aneurysm neck in an end-to-end fashion (Fig 2). A total arch replacement was performed through a median sternotomy by using a

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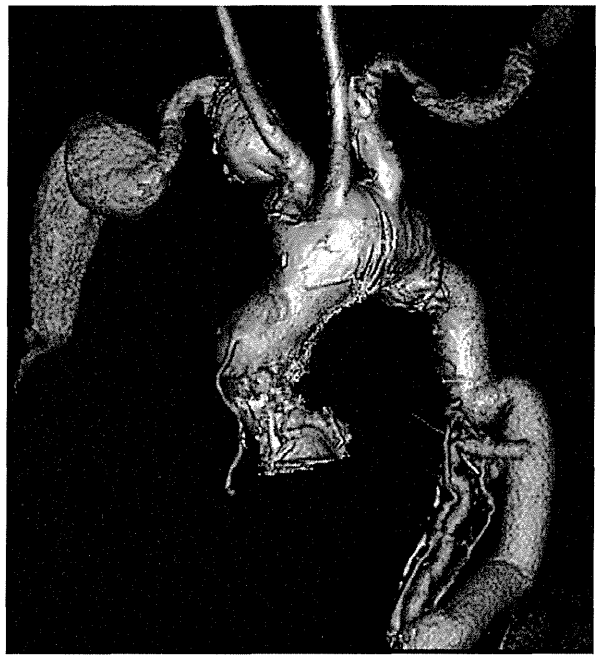

Fig 1. Baseline computed tomographic scan shows a subclavian-axillary artery aneurysm and dilation of the aortic arch. The prosthetic graft that was inserted previously to replace the middle portion of the descending thoracic aorta shows tortuosity.

Dacron graft (Hemashield) with four branches and the elephant trunk technique. A moderately hypothermic cardiopulmonary bypass (25°C) and selective antegrade brain perfusion were used during this procedure.

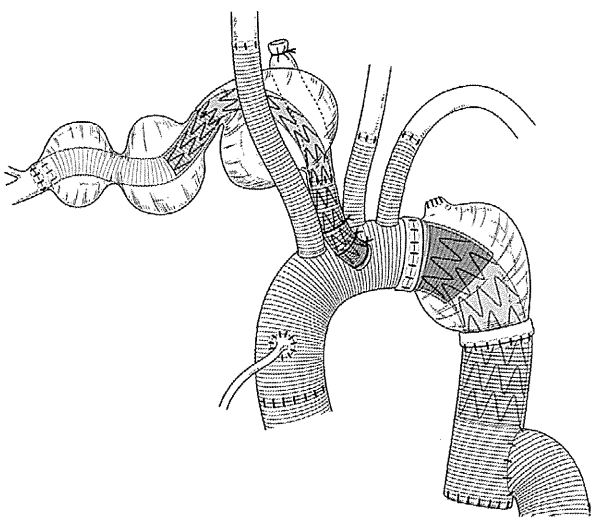

Fig 2. Diagram of the hybrid repair. The right axillary artery was replaced with a Dacron graft. The entire aortic arch was replaced with a four-branched Dacron graft. An endoprosthesis was placed in a bridging position between the aortic arch graft and the graft in the descending aorta. Another endoprosthesis was placed between the graft that replaced the axillary artery and one branch of the four-branched graft.

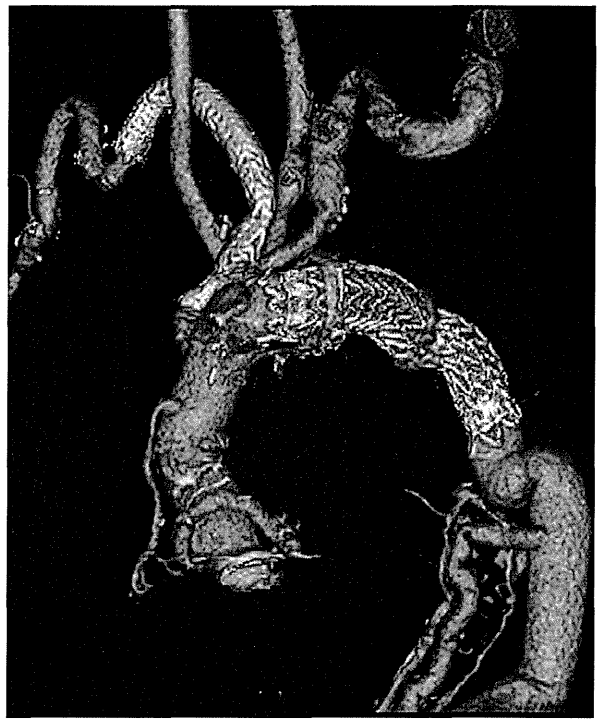

Fig 3. Computed tomographic scan obtained after the hybrid repair shows that all bypasses are patent and that the aneurysms are completely excluded from the blood flow.

The right common carotid artery was ligated, and an anastomosis was created between the vessel and one branch of the four-branched Dacron graft. Another branch of the graft was anastomosed to the neck of the subclavian artery aneurysm. A 28 mm × 15 cm stent graft (Gore TAG Thoracic Endoprosthesis; W.L. Gore and Associates, Flagstaff, AZ) was inserted through a branch of the four-branched graft and placed in a bridging position between the prosthetic graft in the aortic arch and that in the descending aorta. The proximal landing zone for the stent graft was just distal to the origin of the side branches. Two segments of a 12-mm–diameter endoprosthesis (contralateral legs of a bifurcated Excluder AAA device; W.L. Gore and Associates) were inserted into the Dacron graft that had replaced the axillary artery and were deployed in the branch of the graft that was anastomosed to the brachiocephalic artery.

The patient recovered fully from the operation, without any serious perioperative complications, and he remains well 1 year later. CTA performed 6 months after the procedure showed that all bypasses were patent and that the aneurysms were completely excluded from the blood flow (Fig 3).

Comment

Endovascular techniques have been used to treat aneurysms with a variety of causes. Using stent grafts to provide a bridge between the necks of synthetic grafts