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Cardiovascular Surgery

Aortic Pathology Determines Midterm Outcome After Endovascular Repair of the Thoracic Aorta
Report From the Medtronic Thoracic Endovascular Registry (MOTHER) Database

Benjamin Patterson, BSc, MRCS; Peter Holt, PhD, FRCS; Chrisoph Nienaber, MD; Richard Cambria, MD; Ronald Fairman, MD; Matt Thompson, MD, FRCS

Background—Endovascular repair of the thoracic aorta has become an increasingly utilized therapy. Although the short-term mortality advantage over open surgery is well documented, late mortality and the impact of presenting pathology on long-term outcomes remain poorly reported.

Methods and Results—A database was built from 5 prospective studies and a single institutional series. Rates of perioperative adverse events were calculated, as were midterm death and reintervention rates. Multivariate analysis was performed with the use of logistic regression modeling. Kaplan-Meier survival curves were drawn for midterm outcomes. The database contained 1010 patients: 670 patients with thoracic aortic aneurysm, 195 with chronic type B aortic dissection, and 114 with acute type B aortic dissection. Lower elective mortality was observed in patients with chronic dissections (3%) compared with patients with aneurysms (5%). Multivariate analysis identified age, mode of admission, American Society of Anesthesiologists grade, and pathology as independent predictors of 30-day death ($P<0.05$). In the midterm, the all-cause mortality rate was 8, 4.9, and 3.2 deaths per 100 patient-years for thoracic aortic aneurysm, acute type B aortic dissection, and chronic type B aortic dissection, respectively. The rates of aortic-related death were 0.6, 1.2, and 0.4 deaths per 100 patient-years for thoracic aortic aneurysm, acute type B aortic dissection, and chronic type B aortic dissection, respectively.

Conclusions—This study indicated that the midterm outcomes of endovascular repair of the thoracic aorta are defined by presenting pathology, associated comorbidities, and mode of admission. Nonaortic mortality is high in the midterm for patients with thoracic aortic aneurysm, and managing modifiable risk factors appears vital. Endovascular repair of the thoracic aorta results in excellent midterm protection from aortic-related mortality, regardless of presenting pathology. (***Circulation***. 2013;127:24-32.)

Key Words: acute aortic syndrome ■ aneurysm ■ aortic dissection ■ endovascular surgery ■ pathology

The advent of endovascular repair of the thoracic aorta (thoracic endovascular aortic repair [TEVAR]) has altered the management algorithm for pathologies that affect the aortic arch and descending thoracic aorta. In recent years, the number of thoracic endovascular procedures has risen.[1,2] The increased use of TEVAR has been driven by the early mortality advantage reported when endovascular therapy is compared with open surgical treatment of the thoracic aorta.[3,4] TEVAR is now considered the first-line therapy for isolated aneurysms of the descending thoracic aorta and acute complicated type B aortic dissections.[2,5–8] In the abdominal aorta, the early mortality advantage associated with endovascular repair of abdominal aneurysms was lost as a result of late aortic rupture.[9] It has been suggested that long-term durability may be related to individual preoperative aneurysm morphology.[10] There is a concern that a

similar "catch-up" phenomenon might affect procedures in the thoracic aorta. At present, midterm to long-term data regarding the fate of patients treated with thoracic endografts are sparse, and it remains difficult to define whether TEVAR offers a durable solution to prevent aortic-related death. The fate of the aorta after endovascular treatment for chronic type B aortic dissection is of particular concern, and some experts suggest that TEVAR is not a viable alternative to open surgical repair in this pathology.[11]

Given the spectrum of different pathologies that affect the descending thoracic aorta, it is important to define whether the outcome of TEVAR is pathology specific to refine procedural technique and endograft design. Careful analysis of long-term

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results will be required to define which subsets of patients benefit most from endovascular therapy and to modify management algorithms according to the pathology treated.

Methods

Trials

Data from 5 prospective trials were obtained from Medtronic, Santa Rosa, CA, and collated with the addition of institutional data from a single UK center. The collated data were termed the *Medtronic Thoracic Endovascular Registry* (MOTHER). The registry consisted of the endovascular arm of 1 phase II/III trial (VALOR I[5]), the intervention arm of 1 randomized controlled trial (Investigation of Stent Grafts in Aortic Dissection [INSTEAD][12]), and 3 phase IV trials (VALOR II, Captivia, and Valiant Thoracic Stent Graft Evaluation For the Treatment of Descending Thoracic Aortic Dissections Trial [VIRTUE][13]). The institutional data included all TEVARs performed over a period of 8 years that used either the Talent or Valiant stent graft systems that were not entered into any of the registries (Table 1). All of the trials had stringent protocols for collection and validation. The institutional series was prospectively maintained, and follow-up was by computed tomography.

Patient Data

More than half of the data were from prospective, fully monitored trials with committee consensus adjudication of major adverse events. Two clinicians examined all of the adverse events in the St George's Vascular Institute (SGVI) series independently, and any disagreements were discussed before a final decision was made. There was emphasis on the occurrence of death, stroke (which included transient ischemic attack), acute spinal cord injury, and endograft-related events requiring reintervention. Deaths were classified as aortic or nonaortic. Aortic-related death was defined as any death that was directly attributable to the index procedure, any subsequent reintervention, aortic rupture, or aortic complication. The patient cohort was stratified into 3 groups determined by presenting pathology: thoracic aortic aneurysm (TAA), acute type B aortic dissection (<2 weeks after symptom onset), and chronic type B aortic dissection (>2 weeks after symptom onset). There were insufficient patients with other

pathologies (eg, transection, mycotic aneurysm) for individual subgroup analysis.

Statistical Analysis

Data from each source were pooled and analyzed with the use of SPSS 20 software (IBM, Armonk, NY). The preoperative characteristics of each group were examined with the ANOVA test for variance for continuous variables and the [chi]^2 test for categorical variables. The difference in the incidence of postoperative 30-day outcomes between each pathological group was tested with the [chi]^2 test. A univariate analysis for the strength of the association of preoperative characteristics with outcomes occurring before 30 days was performed with the Fisher exact test. Those variables with a *P* value of <0.1 were entered into a binary logistic regression model that incorporated backward variable selection to model 30-day death. The Wald test for significance was performed at each step to determine the contribution of each variable to the model based on the odds ratio (OR) and 95% confidence interval (CI). A significance level of 0.05 was set for entry, and 0.1 was used for removal of covariates. A maximum number of 20 iterations were set as criteria for termination of the process. For the deaths occurring at midterm follow-up, candidate variables were screened by plotting separate Kaplan-Meier curves for patients with and without that specific characteristic. Those variables that achieved a log-rank test of *P*<0.1 were entered into a Cox regression model. A backward selection technique was used to determine which factors would be included in the final model with the use of the Wald test for significant contribution to the model at each step. Hazard ratios were calculated with 95% CIs with a *P* value for significance from the Wald test. Kaplan-Meier curves were constructed for survival in each pathological group, and separate curves were plotted for all-cause death, aortic death, nonaortic death, and freedom from reintervention. The log-rank test was used to determine whether there was a difference between each pathological group.

Results

Demographics

The MOTHER database contained 1010 patients: 670 patients with TAA, 114 patients with acute type B aortic dissection,

Table 1. Sources of Information That Comprised the MOTHER Database

Registry	No.	NCT Identifier	Stent	Indication	Purpose/End Point	Duration
VALOR[5]	359	00604799	Talent	Test: TAA with low/moderate risk (comparator with OSR); registry: as for test but not for comparison; high-risk: not suitable for OSR or high risk (TAA = 333; chronic type B aortic dissection = 13; acute type B aortic dissection = 8)	Phase II/III study to determine success of aneurysm treatment	5-y follow-up (2003–2011)
VALOR II	160	00413231	Valiant	TAA only in patients who are candidates for OSR with low/moderate risk	Trial conducted under investigational device exemption to assess clinical performance	5-y follow-up (2006–2014)
Captivia	68	01181947	Valiant, Captivia	All indications (included TAA = 49; chronic type B aortic dissection = 23; acute type B aortic dissection = 19; other = 8)	Phase IV trial to evaluate midterm clinical performance	3-y follow-up (2010–2013)
VIRTUE[13]	100	01213589	Valiant, Xcelerant	Acute type B aortic dissection = 50; chronic type B aortic dissection = 50	Collection of safety, performance, and health economic data	3-y follow-up (2006–2012)
INSTEAD[12]	100	00525356	Talent	Chronic type B aortic dissection	Phase III comparison of stent vs medical therapy in chronic dissection	5-y follow-up (2002–2011)
SGVI	223	…	Talent/Valiant	All indications (included TAA = 128; acute type B aortic dissection = 37; chronic type B aortic dissection = 41; other = 17)	Institutional series of TEVAR with Medtronic stent grafts	Variable follow-up (2002–2010)

INSTEAD indicates Investigation of Stent Grafts in Aortic Dissection; MOTHER, Medtronic Thoracic Endovascular Registry; NCT, National Clinical Trial; OSR, open surgical repair; SGVI, St George's Vascular Institute; TAA, thoracic aortic aneurysm; TEVAR, thoracic endovascular aortic repair; and VIRTUE, Valiant Thoracic Stent Graft Evaluation For the Treatment of Descending Thoracic Aortic Dissections Trial.

and 195 patients with chronic type B aortic dissection. The demographics of the 3 pathological groups are tabulated in Table 2. There were significant differences in demographics between the 3 groups of patients, and patients with TAA were older and had significantly higher rates of comorbidity than patients with either acute or chronic dissection. Patients with acute type B aortic dissection were universally treated non-electively. Of additional interest was the low incidence of diabetes mellitus in patients with acute but not chronic dissection.

The Ishimaru zone classification refers to the final position of the leading edge of the stent graft after deployment. Overall, 394 patients had the left subclavian artery covered by the endografts, and 143 of these patients had a subclavian revascularization by either carotid-subclavian bypass or transposition. The policy toward revascularization was defined

by each institution involved in the individual studies. In the SGVI series, revascularization was performed in the majority of elective cases in which this was technically feasible.

Mean follow-up time for the TAA patients was 3.1 years (median, 2.7; interquartile range, 0.9–5.6), for chronic type B aortic dissection patients 2.4 years (median, 2.0; interquartile range, 1.5–3.2), and for acute type B aortic dissection patients 2.2 years (median, 2.0; interquartile range, 0.4–3.4).

Early Outcomes (30-Day and In-Hospital Results)

Death, stroke, and acute spinal cord ischemia were reported for elective and nonelective TEVAR with respect to pathology (Tables 3 and 4). In patients undergoing elective surgery, which consisted of patients with TAA and chronic type B aortic dissection only, there were more deaths (5% versus

Table 2. Demographics Between Patients Who Were Treated for Thoracic Aortic Aneurysm, Acute Type B Aortic Dissection, and Chronic Type B Aortic Dissection

	Thoracic Aortic Aneurysm	Chronic Type B Aortic Dissection	Acute Type B Aortic Dissection	P
n	670	195	114	
Male sex, n (%)	399 (59)	161 (83)	87 (76)	<0.001
Age, y (range)	71.4 (25–89)	63.1 (28–94)	61.4 (25–83)	<0.001
GAS (range)	79.1 (27–112)	68.3 (28–103)	66.3 (25–107)	<0.001
AAA, n (%)	167 (25)	22 (11)	17 (14)	<0.001
Renal impairment, n (%)	129 (20)	21 (12)	12 (11)	<0.001
Hypertension, n (%)	552 (83)	182 (83)	73 (93)	<0.001
Diabetes mellitus, n (%)	109 (17)	22 (11)	3 (3)	<0.001
COPD, n (%)	227 (34)	20 (11)	10 (9)	<0.001
Cerebrovascular disease, n (%)	115 (17)	6 (3)	5 (4.2)	<0.001
Smoking history, n (%)	452 (70)	109 (61)	56 (53)	<0.001
Cardiac disease, n (%)	269 (43)	33 (20)	18 (18)	<0.001
Peripheral vascular disease, n (%)	125 (22)	6 (6.7)	3 (4)	<0.001
Hyperlipidemia, n (%)	311 (52)	42 (48)	34 (43)	0.962
ACEi, n (%)	178 (26)	58 (31)	15 (13)	<0.001
[beta]-Blocker, n (%)	267 (62)	73 (65)	22 (55)	0.519
Calcium channel blocker, n (%)	146 (34)	23 (55)	13 (33)	0.018
Statins, n (%)	230 (53)	28 (62)	14 (35)	<0.001
Nonelective, n (%)	38 (6)	16 (8)	114 (100)	<0.001
ASA, n (%)				
1	17 (3)	26 (15)	4 (4)	<0.001
2	111 (18)	54 (28)	23 (22)	
3	345 (52)	72 (37)	31 (26)	
4	139 (21)	26 (14)	41 (35)	
5	11 (2)	1 (1)	8 (7)	
Missing	45 (7)	14 (7)	11 (9)	
Ishimaru, n (%)				
0	5 (1)	2 (1)	3 (3)	
1	44 (7)	16 (8)	4 (4)	
2	192 (29)	67 (35)	61 (54)	
3	260 (39)	101 (52)	38 (32)	
4	163 (24)	7 (4)	8 (7)	

AAA indicates abdominal aortic aneurysm; ACEi, angiotensin-converting enzyme inhibitor; ASA, American Society of Anesthesiologists score; GAS, Glasgow Aneurysm Score; and Ishimaru, Ishimaru landing zone classification. Statistical analysis used ANOVA and χ^2 test for difference in continuous and categorical variables, respectively. Percentages take into account missing data.

Table 3. Thirty-Day Outcomes For Patients Undergoing Elective Thoracic Endovascular Aortic Repair

	Thoracic Aortic Aneurysm (n = 625)	Chronic Type B Aortic Dissection (n = 179)
Death, n (%)	33 (5)	6 (3)
Stroke, n (%)	34 (5)	3 (2)
Spinal cord injury, n (%)	30 (5)	6 (3)

All acute type B dissections were treated nonelectively. Numbers in this table varied from those in Table 1 because 7 subjects were missing admission data for thoracic aortic aneurysm and 1 was missing data for chronic type B aortic dissection.

3%, respectively), strokes (5% versus 2%), and acute spinal cord injuries (5% versus 3%) after TEVAR for TAA. Twice as many patients were affected by a major adverse event in the TAA group (14% versus 7%). Nonelective surgery caused more deaths, with most occurring in the TAA group (18% versus 13% versus 11% in TAA, chronic type B aortic dissection, and acute type B aortic dissection, respectively). The rate of stroke was equivalent (5% versus 7% versus 6%, respectively), but there was a higher incidence of spinal cord injury in the TAA group (11% versus 0% versus 2%, respectively). Of the 42 incidences of spinal cord injury, 15 resulted in paraplegia and 27 in paraparesis. In the 20 patients in whom data were available, 12 had resolution of symptoms. The causes of death for each group of patients are illustrated in Table 5, tabulated according to whether the death occurred early (at 30 days) or later in follow-up.

Modeling 30-Day Outcomes

Regression modeling identified that the factors that predicted mortality at 30 days were as follows: age (OR, 1.048 [per additional year]); 95% CI, 1.016–1.080; $P=0.003$), American Society of Anesthesiologists (ASA) grade (OR, 2.339 [per additional point]; 95% CI, 1.563–3.500; $P<0.001$), and emergency admission (OR, 2.497; 95% CI, 1.270–4.908; $P=0.008$). If mode of admission was excluded from the analysis (because this was highly influenced by pathology), then a different model was generated with different significant predictor variables including age (OR, 1.051, 95% CI, 1.018–1.085; $P=0.002$), ASA grade (OR, 2.362, 95% CI, 1.615–3.455; $P<0.001$), and aortic pathology (TAA [OR, 1, assumed in comparison with dissection]; acute type B aortic dissection [OR, 2.32; 95% CI, 1.043–5.176; $P=0.0239$]; and chronic type B aortic dissection [OR, 1.124; 95% CI, 0.442–2.859; $P=0.81$]). The model that included mode of admission appeared to have slightly greater discriminatory power with a C statistic of 0.760 versus 0.733 in the pathology-based model (both $P=<0.005$).

Midterm Clinical Outcome

Life table analysis for all-cause mortality (Figure, panel A) showed that the early death rate was highest in the acute type B aortic dissection group and that after this initial period, the mortality curve assumed a similar trajectory and ran parallel to that of the chronic type B aortic dissection group. The TAA curve revealed an early death rate that lay between those of acute and chronic dissection but over the midterm continued to trend downward in a steeper trajectory than either acute or chronic dissection. Analysis of mortality from non–aortic-related (Figure, panel B) and aortic-related mortality (Figure, panel C) suggested that the excess mortality in the TAA group compared with the patients with dissection was principally accounted for by nonaortic death. Freedom from all-cause mortality by life table analysis over the whole period of follow-up was 56% in the TAA group, 64% in the chronic type B aortic dissection group, and 42% in the acute type B aortic dissection group. Freedom from aortic death was 93%, 96%, and 85%, respectively. All of the Kaplan-Meier plots for mortality demonstrated significant difference between the 3 pathology groups ($P<0.002$). The causes of deaths during the follow-up period are illustrated in Table 5; few of the late deaths in all groups were related to the primary, treated, aortic pathology.

The death rate per 100 patient-years at maximum follow-up was calculated for all patients in the 3 main pathology groups who had not died or been censored at [mtequ]90 days. The mortality rate was 8, 4.9, and 3.2 per 100 patient-years, and the aortic-related mortality rate was 0.6, 1.2, and 0.4 per 100 patient-years for TAA, acute type B aortic dissection, and chronic type B aortic dissection, respectively.

Statistical analysis with the use of Cox proportional hazards modeling revealed that the differences in overall mortality between the 3 groups of patients were influenced by variables that included age (hazard ratio, 1.037 per additional year; 95% CI, 1.021–1.054; $P<0.001$); the presence of previous cerebrovascular disease (hazard ratio, 1.48; 95% CI, 1.03–2.12; $P=0.034$); a history of renal failure (hazard ratio, 1.62; 95% CI, 1.17–2.24; $P=0.004$); and ASA grade (hazard ratio, 1.36 per additional grade; 95% CI, 1.11–1.68; $P=0.004$).

Reintervention and Aortic-Related Complications

The rate of aortic-related death in both dissection groups appears to plateau markedly before the 12-month time point; after that period, there appear to be relatively few aortic-related deaths. This is clearly of significance in defining whether endovascular therapy can prevent aortic-related deaths in type B aortic dissection.

Life table analysis of freedom from reintervention (Figure, panel D) showed that the highest rate of intervention in the postoperative period was in the acute

Table 4. Thirty-Day Outcomes For Patients Undergoing Nonelective Thoracic Endovascular Aortic Repair

	Thoracic Aortic Aneurysm (n = 38)	Chronic Type B Aortic Dissection (n = 15)	Acute Type B Aortic Dissection (n = 114)
Death, n (%)	7 (18)	2 (13)	13 (11)
Stroke, n (%)	2 (5)	1 (7)	7 (6)
Spinal cord injury, n (%)	4 (11)	0 (0)	2 (2)

Numbers in this table varied from those in Table 1 because 7 were missing admission data for thoracic aortic aneurysm and 1 was missing data for chronic type B aortic dissection.

Table 5. Causes of Mortality For Patients Undergoing Thoracic Endovascular Aortic Repair for Thoracic Aortic Aneurysm, Acute Type B Aortic Dissection, and Chronic Type B Aortic Dissection

	Thoracic Aortic Aneurysm, n (%)		Chronic Type B Aortic Dissection, n (%)		Acute Type B Aortic Dissection, n (%)	
Cause of death	<30 d (n=43)	>30 d (n=176)	<30 d (n=8)	>30 d (n=19)	<30 d (n=15)	>30 d (n=13)
Aortic related	13 (30)	16 (9)	1 (13)	3 (15)	5 (39)	5 (30)
Cardiac	7 (16)	48 (27)	2 (25)	4 (20)	3 (23)	0
Neurological	4 (9)	16 (9)	1 (13)	1 (5)	0	1 (6)
Noncardiac, nonneurological	8 (19)	63 (36)	0	3 (15)	1 (8)	0
Respiratory	2 (5)	6 (3)	0	1 (5)	1 (8)	1 (6)
Retrograde type A dissection	2 (5)	1 (1)	1 (13)	1 (5)	2 (16)	2 (12)
Other/unknown	7 (16)	26 (15)	3 (38)	6 (30)	1 (8)	6 (35)

The causes of mortality are given for early (<30 d) and midterm (>30 d) mortality. In this table, 3 patients had missing mode of admission data.

type B aortic dissection group followed by the chronic type B aortic dissection and TAA groups. Freedom from aortic reintervention at 6 years was 84% in the TAA group, 71% in the chronic type B aortic dissection group, and 46% in the acute type B aortic dissection group. The most common cause for reintervention in the TAA group was endoleak, most commonly type I (Table 6). This was reflected in the most common mode of reintervention, which was proximal or distal extension of the main endograft (Table 7). The most common reason for reintervention in both dissection groups was malperfusion (either ongoing or related to branch coverage by an endograft), followed by type II/III endoleak in the chronic type B aortic dissection group and further aneurysmal expansion in the acute type B aortic dissection group. The rate of late reintervention after 90 days was 2.1, 5.3, and 6.7 per 100 patient-years in TAA, chronic type B aortic dissection, and acute type B aortic dissection groups, respectively. There was no association between the need for aortic reintervention and midterm death.

Discussion

The database used in the present study contained >1000 patients who had undergone TEVAR with well-validated data collection and outcome definition.

The study demonstrated that outcomes after TEVAR were pathology specific. This finding has implications for future reporting standards because outcomes should be reported for specific pathologies rather than for generic procedures. Series reporting unstratified, unselected series are likely to miss subtle subgroup effects driven by aortic pathology, which will be increasingly important in defining the optimum treatment for patients with disease of the thoracic aorta.

Analysis of early outcomes demonstrated that patients with TAA had a higher rate of elective adverse outcomes than patients with chronic type B aortic dissection. The early mortality rate for TAA and chronic type B aortic dissection reported in the present study was similar to that described in several large series[14–16] and considerably better than that reported in community analyses.[17] The difference in adverse outcomes between the elective treatment of TAA and chronic type B aortic dissection was related to a higher incidence of stroke in patients with aneurysms. This difference may be related to the higher burden of cardiovascular disease observed in patients with TAA who had higher rates of comorbidities than patients with dissection.

All of the patients with acute dissection in the present study were treated nonelectively. This reflected that the indication for endovascular intervention in these cases was the treatment of complicated acute dissection. The mortality rate for acute type B aortic dissection was in agreement with previous reports[18,19] and, interestingly, was not significantly different from the mortality rate for the treatment of TAA or chronic type B aortic dissection in the nonelective setting. All groups studied exhibited higher adverse outcome rates when treated in the nonelective setting, which is intuitive and has been reported previously.[20]

The overall rate of neurological complications (stroke and spinal cord injury) in patients with nonelective TAA in the present study appears similar to that described elsewhere and is clearly a source of major morbidity in this group of patients,[21–24] although not in the patients with acute or chronic dissection. There is no proven explanation for the lower incidence of spinal cord injury in patients with type B aortic dissection, although the lower incidence of comorbidities and continued perfusion of the false lumen after TEVAR may play a role. Disruption of collateral blood supply can affect perfusion of the spinal cord, and patients who undergo a greater extent of aortic coverage may be more susceptible to spinal cord injury. Coverage of the left subclavian artery may have a similar effect, but more high-quality evidence is required before a consensus can be reached. Only 4 patients developed a spinal cord injury after 30 days, suggesting that this is chiefly a periprocedural problem.

Regression modeling revealed that age, ASA grade, mode of admission (elective versus nonelective), and type of aortic pathology were implicated in early mortality, which validates previous studies.[4,25,26]

The midterm results revealed considerable differences in mortality and reinterventions with reference to aortic pathology. Patients with TAA demonstrated poorer midterm survival compared with the patients with aortic dissection. Analysis suggested that patients with TAA had an increased rate of non–aortic-related mortality. The effectiveness of TEVAR in preventing aortic-related death in patients with TAA has been suggested by previous studies, which have revealed that >90% of patients remain free of aortic-related death 5 years after TEVAR.[7] These findings were confirmed

A		0	1	2	3	4	5	6
TAA	No. at risk	670	480	393	307	233	201	125
	Deaths	118	38	28	16	22	2	2
C-BD	No. at risk	195	152	105	50	26	17	14
	Deaths	19	3	3	1	1	1	1
A-BD	No. at risk	114	67	56	38	14	10	6
	Deaths	25	1	2	2	0	1	1

B		0	1	2	3	4	5	6
TAA	No. at risk	670	480	393	307	233	201	125
	Deaths	20	1	3	0	2	2	0
C-BD	No. at risk	195	152	105	50	26	17	14
	Deaths	5	1	0	0	0	0	0
A-BD	No. at risk	114	67	56	38	14	10	6
	Deaths	14	0	0	0	0	0	0

C		0	1	2	3	4	5	6
TAA	No. at risk	670	480	393	307	233	201	125
	Deaths	85	32	22	15	27	0	0
C-BD	No. at risk	195	152	105	50	26	17	14
	Deaths	10	2	2	0	1	1	0
A-BD	No. at risk	114	67	56	38	14	10	6
	Deaths	7	0	0	2	0	0	0

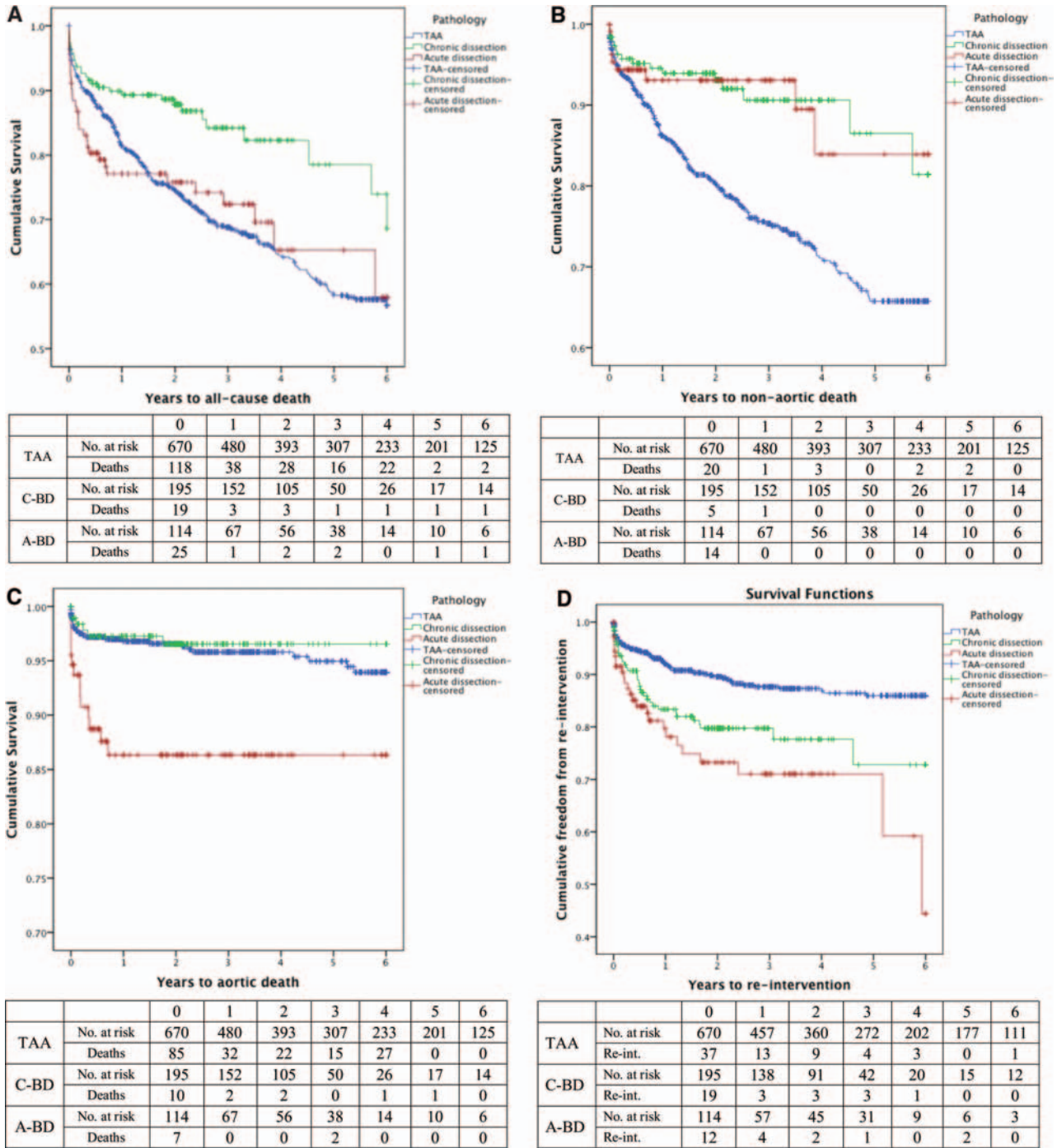| D		0	1	2	3	4	5	6
TAA	No. at risk	670	457	360	272	202	177	111
	Re-int.	37	13	9	4	3	0	1
C-BD	No. at risk	195	138	91	42	20	15	12
	Re-int.	19	3	3	3	1	0	0
A-BD	No. at risk	114	57	45	31	9	6	3
	Re-int.	12	4	2	1	0	2	0

Figure. A, Kaplan-Meier estimates for total survival in the 3 groups of patients up to 6 years of follow-up. The numbers of patients at risk are given below the graph. Log-rank test $P=0.002$. A-BD indicates acute type B aortic dissection; C-BD, chronic type B aortic dissection; and TAA, thoracic aortic aneurysm. **B**, Kaplan-Meier estimates for freedom from non–aortic-related death in the 3 groups of patients up to 6 years of follow-up. The numbers of patients at risk are given below the graph. Log-rank test $P<0.001$. **C**, Kaplan-Meier estimates for freedom from aortic-related death in the 3 groups of patients up to 6 years of follow-up. The numbers of patients at risk are given below the graph. Log-rank test $P<0.001$. **D**, Kaplan-Meier estimates for freedom from aortic-related reintervention in the 3 groups of patients up to 6 years of follow-up. The numbers of patients at risk are given below the graph. Log-rank test $P=<0.001$. Re-int. indicates reintervention.

by the present study. The majority of deaths after TEVAR for TAA were due to cardiac, respiratory, and miscellaneous causes (including cancer, which is not well defined in the data set), which has been reported previously in a series of patients undergoing treatment for both thoracic and abdominal aneurysms.[2,21,27] Patients with TAA have significant

comorbidity, which is reflected in a high non–aortic-related mortality rate after therapy for aneurysmal disease. It is perhaps relevant that only 53% of patients with TAA in the present study were taking statins. Interestingly, when the rate of death (8 deaths per 100 patient-years) was calculated for patients with TAA, it was remarkably similar to the rate of

Table 6. Causes of Reintervention for Patients Undergoing Thoracic Endovascular Aortic Repair for Thoracic Aortic Aneurysm, Acute Type B Aortic Dissection, and Chronic Type B Aortic Dissection

Indication for Intervention	Thoracic Aortic Aneurysm	Chronic Type B Aortic Dissection	Acute Type B Aortic Dissection
Total No.	70	34	29
Aneurysmal expansion of aorta	5 (7)	4 (12)	6 (21)
Continued perfusion of false lumen	0	5 (15)	0
Extension of dissection	0	4 (12)	4 (14)
Malperfusion	0	7 (21)	9 (31)
Rupture of aorta	0	1 (3)	1 (3)
Stent migration	4 (6)	0	0
Type I endoleak	25 (36)	4 (12)	1 (3)
Type II/III endoleak	20 (29)	8 (24)	2 (7)
Other endoleak	15 (21)	0	0
Unknown	1 (1)	1 (3)	6 (21)

Numbers in parentheses represent the percentage of total reinterventions each category contributes.

death reported for patients with abdominal aortic aneurysm in the Endovascular Aneurysm Repair (EVAR)-1 study.[9] Clearly, attention needs to be directed toward the medical management of cardiovascular risk factors in patients with aneurysms undergoing endovascular repair.

The 2 groups of patients with aortic dissection had differing patterns of midterm outcomes when subjectively compared with the patients with TAA. Importantly, after the initial differences in perioperative death, the curves for survival in acute and chronic dissection run parallel. This is a reflection of data quality because acute dissection becomes chronic after 2 weeks, and the natural history in the 2 groups might be expected to be similar after the effects of initial presentation and treatment have become manifest.

One of the crucial issues affecting endovascular therapy in patients with type B aortic dissection is whether TEVAR confers protection from aortic-related death in the mid to long term. It appears well established that TEVAR for both acute and chronic type B aortic dissection offers significant advantages over open surgery with respect to 30-day mortality and major morbidity.[19,28] However, open surgery offers a robust solution to preventing aortic-related death over long-term follow-up,[29] whereas the outcome after endovascular therapy is not as well defined, with uncertainty over the morphology of

the distal aorta after TEVAR.[30] The present study has revealed that patients with both acute and chronic aortic dissection have low rates of aortic-related mortality in the midterm after TEVAR. After the initial perioperative phase, aortic-related mortality is low, which suggests that endovascular therapy has the potential to confer prevention of aortic dissection and rupture over a reasonable time period. This effect appears to be dependent on aortic surveillance and subsequent intervention because rates of aortic reintervention in patients with acute and chronic type B aortic dissection were higher than those described for patients with TAA. However, patients can go on to develop complications at 5 to 10 years after endovascular surgery for aortic problems, and more long-term data are crucial in further characterizing the incidence of late aortic complications and mortality. A useful addition to the present study would have been more detailed morphological analysis of postoperative imaging to describe subsequent aortic remodeling because this remains relatively poorly studied. Unfortunately, access to individual preoperative and postoperative imaging was limited to the single-center series.

The occurrence of retrograde type A dissection should not be underestimated after TEVAR, and the present study has again demonstrated that this complication occurs with a higher incidence in patients with aortic dissection than in those with

Table 7. Mode of Reintervention for Patients Undergoing Thoracic Endovascular Aortic Repair for Thoracic Aortic Aneurysm, Acute Type B Aortic Dissection, and Chronic Type B Aortic Dissection

Mode of Reintervention	Thoracic Aortic Aneurysm	Chronic Type B Aortic Dissection	Acute Type B Aortic Dissection
Total No.	70	34	29
Open thoracic aortic surgery	1 (1)	2 (6)	2 (7)
Open abdominal aortic surgery	2 (2)	0	2 (7)
Endovascular repair of abdominal aorta	0	3 (9)	1 (3)
Supra-aortic bypass	0	1 (3)	4 (14)
Stent of other artery	0	5 (15)	2 (7)
Proximal/distal extension of stent graft/additional stent graft	48 (69)	12 (35)	8 (28)
Left subclavian artery embolization/plug	12 (17)	5 (15)	2 (7)
Hybrid open/endovascular procedure	3 (4)	2 (6)	0
Other	4 (6)	4 (12)	8 (28)

Numbers in parentheses represent the percentage of total reinterventions each category contributes.

aneurysmal disease. Data from the International Registry of Aortic Dissection suggest that the rate of retrograde type A dissection is 1.3% to 2.4%,[31] but a recent systematic review found the rate to be 3.2% after TEVAR for acute type B aortic dissection, 1.5% for chronic type B aortic dissection, and 0.5% for TAA. At midterm follow-up, this rate increased to 4.9% in acute type B aortic dissection patients and 2.3% in chronic type B aortic dissection patients, indicating that some patients are at risk of this devastating complication after the initial perioperative period (B. Patterson, MD, et al, unpublished data, 2011).

The factors that influenced midterm survival in the present study were advancing age, the presence of preoperative cerebrovascular and renal disease, and ASA grade. These factors appear to be a reflection of the burden of systemic disease and are not dissimilar to those reported by Lee et al[15] in a series of 400 patients.

An important limitation of our study is that the 5 trials that were used for pooled analysis all collected slightly different data, both preoperatively and postoperatively. This meant that some important elements could not be studied, such as the influence of medical risk factor control on midterm survival. Although most trials had independent adjudication of end points, it was not always possible to accurately record cause of death, which may have led to underestimation of the deaths in each category during the survival analyses. Importantly, some aneurysm-related deaths may have been recorded as "unknown," but on the basis of most reported series, it is unlikely that there were many. Surgeon experience and perioperative care have advanced over the last decade, and the care of patients operated on early in the registries may not reflect current practice. This is unavoidable when one studies midterm and long-term follow-up for most elements of medical practice. Many studies of this kind are criticized for studying obsolete first-generation stent graft technology at follow-up. In the present study, only 2 devices were used, and both of these are still commercially available. Another drawback was that access to original imaging was not possible. Analysis of such features may provide insight into the effect of morphology on outcomes (for example, the effect of transverse arch atherosclerotic load on the risk of subsequent neurological complications). In addition, many of these patients were operated on in high-volume centers, many of which were among the early adopters of TEVAR. This could reduce the generalizability of some of these results.

Although the data were derived from 6 individual studies, all but 1 were multicenter, multinational trials. Specific institution, surgeon, and year of the procedure probably had more influence than the study into which the patient was entered. Unfortunately, all of these factors cannot be controlled for, and this is an inherent weakness of data obtained in this fashion rather than the present study specifically. No specific methodology that applied to the selection of patients or the technical aspects of surgery was any different from that used in standard practice. Patients were treated as they would usually be at a specific institution. Subgroup analysis comparing demographics and adverse outcomes for patients with a specific pathology between registries showed that there appeared to be few differences between studies,

but this subdivision analysis resulted in relatively small numbers of events (Tables I and II in the online-only Data Supplement).

The present study has indicated that the midterm outcomes of TEVAR are defined by the aortic pathology treated, the associated comorbidities, and the nature of presentation (elective or emergent). Reporting of outcomes should stratify results according to these factors. In patients with TAA, the non–aortic-related mortality is high in the midterm, and attention must be focused on managing modifiable risk factors. TEVAR appears to offer excellent midterm protection from aortic-related mortality for both TAA and type B aortic dissection. This protection, however, appears dependent on a high rate of aortic reintervention, which should be the focus of practice and device development in the future.

References

1. Scali ST, Goodney PP, Walsh DB, Travis LL, Nolan BW, Goodman DC, Lucas FL, Stone DH. National trends and regional variation of open and endovascular repair of thoracic and thoracoabdominal aneurysms in contemporary practice. *J Vasc Surg*. 2011;53:1499–1505.
2. Goodney PP, Travis L, Lucas FL, Fillinger MF, Goodman DC, Cronenwett JL, Stone DH. Survival after open versus endovascular thoracic aortic aneurysm repair in an observational study of the Medicare population. *Circulation*. 2011;124:2661–2669.
3. Walsh SR, Tang TY, Sadat U, Naik J, Gaunt ME, Boyle JR, Hayes PD, Varty PD. Endovascular stenting versus open surgery for thoracic aortic disease: systematic review and meta-analysis of perioperative results. *J Vasc Surg*. 2008;47:1094–1098.
4. Jonker FH, Verhagen HJ, Lin PH, Heijman RH, Trimarchi S, Lee WA, Moll FL, Atamneh H, Rampoldi V, Muhs BE. Open surgery versus endovascular repair of ruptured thoracic aortic aneurysms. *J Vasc Surg*. 2011;53:1210–1216.
5. Fairman RM, Criado F, Farber M, Kwolek C, Mehta M, White R, Lee A, Tuchek JM. Pivotal results of the Medtronic Vascular Talent Thoracic Stent Graft System: the VALOR trial. *J Vasc Surg*. 2008;48:546–554.
6. Fattori R, Tsai TT, Myrmel T, Evangelista A, Cooper JV, Trimarchi S, Li J, Lovato L, Kische S, Eagle KA, Isselbacher EM, Neinaber CA. Complicated acute type B dissection: is surgery still the best option? A report from the International Registry of Acute Aortic Dissection. *J Am Coll Cardiol Cardiovasc Interv*. 2008;1:395–402.
7. Makaroun MS, Dillavou ED, Wheatley GH, Cambria RP. Five-year results of endovascular treatment with the Gore TAG device compared with open repair of thoracic aortic aneurysms. *J Vasc Surg*. 2008;47:912–918.
8. Brunt ME, Egorova NN, Moskowitz AJ. Propensity score-matched analysis of open surgical and endovascular repair for type B aortic dissection. *Int J Vasc Med*. 2011;2011:364046.
9. Greenhalgh RM, Brown LC, Powell JT, Thompson SG, Epstein D, Sculpher MJ; United Kingdom EVAR Trial Investigators. Endovascular versus open repair of abdominal aortic aneurysm. *N Engl J Med*. 2010;362:1863–1871.

10. Schanzer A, Greenberg RK, Hevelone N, Robinson WP, Eslami MH, Goldberg RJ, Messina L. Predictors of abdominal aortic aneurysm sac enlargement after endovascular repair. *Circulation*. 2011;123:2848–2855.

11. Svensson LG, Kouchoukos NT, Miller DC, Bavaria JE, Coselli JS, Curi MA, Eggebrecht H, Elefteriades JA, Erbel R, Gleason TG, Lytle BW, Mitchell RS, Nienaber CA, Roselli EE, Safi HJ, Shemin RJ, Sicard GA, Sundt TM III, Szeto WY, Wheatley GH III; Society of Thoracic Surgeons Endovascular Surgery Task Force. Expert consensus document on the treatment of descending thoracic aortic disease using endovascular stent-grafts. *Ann Thorac Surg*. 2008;85:S1–S41.

12. Nienaber CA, Rousseau H, Eggebrecht H, Kische S, Fattori R, Rehders TC, Kundt G, Scheinert D, Czerny M, Kleinfeldt T, Zipfel B, Labrousse L, Ince H. Randomized comparison of strategies for type B aortic dissection: the INVestigation of STEnt Grafts in Aortic Dissection (INSTEAD) Trial. *Circulation*. 2009;120:2519–2528.

13. VIRTUE Registry Investigators. The VIRTUE Registry of type B thoracic dissections: study design and early results. *Eur J Vasc Endovasc Surg*. 2011;41:159–166.

14. Leurs LJ, Bell R, Degrieck Y, Thomas S, Hobo R, Lundbom J; EURO-STAR, UK Thoracic Endograft Registry Collaborators. Endovascular treatment of thoracic aortic diseases: combined experience from the EUROSTAR and United Kingdom Thoracic Endograft registries. *J Vasc Surg*. 2004;40:670–679; discussion 679–680.

15. Lee WA, Daniels MJ, Beaver TM, Klodell CT, Raghinaru DE, Hess PJ Jr. Late outcomes of a single-center experience of 400 consecutive thoracic endovascular aortic repairs. *Circulation*. 2011;123:2938–2945.

16. Kang WC, Greenberg RK, Mastracci TM, Eagleton MJ, Hernandez AV, Pujara AC, Roselli EE. Endovascular repair of complicated chronic distal aortic dissections: intermediate outcomes and complications. *J Thorac Cardiovasc Surg*. 2011;142:1074–1083.

17. Orandi BJ, Dimick JB, Deeb GM, Patel HJ, Upchurch GR Jr. A population-based analysis of endovascular versus open thoracic aortic aneurysm repair. *J Vasc Surg*. 2009;49:1112–1116.

18. Eggebrecht H, Nienaber CA, Neuhäuser M, Baumgart D, Kische S, Schmermund A, Herold U, Rehders TC, Jakob HG, Erbel R. Endovascular stent-graft placement in aortic dissection: a meta-analysis. *Eur Heart J*. 2006;27:489–498.

19. Parker JD, Golledge J. Outcome of endovascular treatment of acute type B aortic dissection. *Ann Thorac Surg*. 2008;86:1707–1712.

20. Ehlert BA, Durham CA, Parker FM, Bogey WM, Powell CS, Stoner MC. Impact of operative indication and surgical complexity on outcomes after thoracic endovascular aortic repair at national surgical quality improvement program centers. *J Vasc Surg*. 2011;54:1629–1636.

21. Makaroun MS, Dillavou ED, Kee ST, Sicard G, Chaikof E, Bavaria J, Williams D, Cambria RP, Mitchell RS. Endovascular treatment of thoracic aortic aneurysms: results of the phase II multicenter trial of the GORE TAG thoracic endoprosthesis. *J Vasc Surg*. 2005;41:1–9.

22. Buth J, Harris PL, Hobo R, van Eps R, Cuypers P, Duijm L, Tielbeek X. Neurologic complications associated with endovascular repair of thoracic aortic pathology: incidence and risk factors: a study from the European Collaborators on Stent/Graft Techniques for Aortic Aneurysm Repair (EUROSTAR) registry. *J Vasc Surg*. 2007;46:1103–1110; discussion 1110–1111.

23. Feezor RJ, Martin TD, Hess PJ, Klodell CT, Beaver TM, Huber TS, Seeger JM, Lee WA. Risk factors for perioperative stroke during thoracic endovascular aortic repairs (TEVAR). *J Endovasc Ther*. 2007;14:568–573.

24. Jonker FH, Verhagen HJ, Lin PH, Heijmen RH, Trimarchi S, Lee WA, Moll FL, Athamneh H, Muhs BE. Outcomes of endovascular repair of ruptured descending thoracic aortic aneurysms. *Circulation*. 2010;121:2718–2723.

25. Bhamidipati CM, LaPar DJ, Mehta GS, Kern JA, Kron IL, Upchurch GR Jr, Ailawadi G. Have thoracic endografting outcomes improved since US Food and Drug Administration approval? *Ann Thorac Surg*. 2011;91:1314–1322; discussion 1322.

26. Baumgart D, Eggebrecht H, Herold U, Kuehl H, Piotrowski J, Niebel W, Jakob HG, Erbel R. Underlying aortic pathology and clinical health status determine success of endovascular stent-grafting for descending thoracic aortic disease. *Catheter Cardiovasc Interv*. 2006;67:527–534.

27. EVAR Trial Participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR Trial 1): randomised controlled trial. *Lancet*. 2005;365:2179–2186.

28. Trimarchi S, Nienaber CA, Rampoldi V, Myrmel T, Suzuki T, Bossone E, Tolva V, Deeb MG, Upchurch GR Jr, Cooper JV, Fang J, Isselbacher EM, Sundt TM III, Eagle KA; IRAD Investigators. Role and results of surgery in acute type B aortic dissection: insights from the International Registry of Acute Aortic Dissection (IRAD). *Circulation*. 2006;114:I357–I364.

29. Zoli S, Etz CD, Roder F, Mueller CS, Brenner RM, Bodian CA, Di Luozzo G, Griepp RB. Long-term survival after open repair of chronic distal aortic dissection. *Ann Thorac Surg*. 2010;89:1458–1466.

30. Sayer D, Bratby M, Brooks M, Loftus I, Morgan R, Thompson M. Aortic morphology following endovascular repair of acute and chronic type B aortic dissection: implications for management. *Eur J Vasc Endovasc Surg*. 2008;36:522–529.

31. Eggebrecht H, Thompson M, Rousseau H, Czerny M, L[uml]onn L, Mehta RH, Erbel R; European Registry on Endovascular Aortic Repair Complications. Retrograde ascending aortic dissection during or after thoracic aortic stent graft placement: insight from the European Registry on Endovascular Aortic Repair Complications. *Circulation*. 2009;120:S276–S281.

CLINICAL PERSPECTIVE

Endovascular repair is increasingly being adopted as the treatment of choice for many thoracic aortic conditions. As the application of this technology widens, developing an evidence-based understanding of which patients are most likely to benefit is a priority. A barrier to this has been the relatively few number of procedures that are performed, so that randomized controlled trials on the scale of those performed for infrarenal aortic aneurysm have not been feasible. At present, many published series fail to discriminate between different aortic pathologies when outcomes are reported, making pooled analysis difficult. This first report from the Medtronic Thoracic Endovascular Registry (MOTHER) combines raw data from 5 trials and 1 institutional series, characterizing the difference in early outcomes between the major pathology groups. Regional trends in practice suggest that thoracic endovascular repair has complemented open surgery rather than replaced it and has allowed more patients to be offered therapy than was previously possible. Significantly, some will have been deemed unfit for open surgery because of poor physiological reserve, and although thoracic endovascular aortic repair all but abolishes aortic death, individuals remain subject to an increased risk of mortality from all other causes in comparison with matched controls. Follow-up data collected for the component registries have allowed a description of midterm survival in such patients, and this report serves to highlight the importance of considering all-cause mortality in aneurysm patients and to reinforce the ability of thoracic endovascular aortic repair to prevent aortic-related death in both aneurysm and dissection patients.

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SUPPLEMENTAL MATERIAL

SUPPLEMENTAL TABLES 1

Elective TAA

	Captivia		SGVI		VALOR I		VALOR II		p
n	43		89		333		160		
Death	1	2.3%	11	12.4%	14	4.2%	7	4.4%	<0.05
Stroke	3	7.0%	8	9.0%	19	5.7%	4	2.5%	0.12
SCI	0	0.0%	4	4.5%	19	5.7%	5	3.1%	0.276

Elective C-BD

	Captivia		SGVI		VALOR I		INSTEAD		VIRTUE		
n	19		33		13		67		47		
Death	0	0.0%	3	9.1%	0	0.0%	3	4.5%	0	0.0%	0.273
Stroke	0	0.0%	1	3.0%	0	0.0%	1	1.5%	1	2.1%	0.964
SCI	0	0.0%	1	3.0%	1	0.0%	3	4.5%	1	2.1%	0.336

Emergency TAA

	Captivia		SGVI		p
n	6		32		
Death	1	16.7%	6	18.8%	0.904
Stroke	0	0.0%	2	6.3%	0.529
SCI	1	16.7%	3	9.4%	0.593

Emergency C-BD

	Captivia		SGVI		VIRTUE		p
n	4		8		3		
Death	1	25.0%	1	12.5%	0	0.0%	0.626
Stroke	0	0.0%	0	0.0%	1	33.3%	0.117
SCI	0	0.0%	0	0.0%	0	0.0%	-

	Captivia		Emergency A-BD SGVI		VALOR I		VIRTUE		p
n	19		37		8		50		
Death	2	10.5%	5	13.5%	2	25.0%	4	8.0%	0.637
Stroke	0	0.0%	2	5.4%	0	0.0%	5	10.0%	0.542
SCI	0	0.0%	1	2.7%	0	0.0%	1	2.0%	0.952

SUPPLEMENTAL TABLES 2

Chronic dissection

	Captivia	(%)	INSTEAD	(%)	SGVI	(%)	VIRTUE	(%)	Chi-sq
	23		68		40		50		
Age (STD)	62	9.6	60	10.1	64	13.0	59	10.9	0.058
GAS (STD)	70	11.1	62	12.0	75	20.0	62	11.8	<0.05
CVA	0	0.0%	1	1.5%	4 (37)	10.8%	0	0.0%	<0.05
Renal failure	4	17.4%	0	0.0%	9	22.5%	5	10.0%	<0.05
CAD	N/A	N/A	14	20.6%	8	20.0%	6 (49)	12.2%	0.467
Resp	1	4.3%	6	8.8%	3 (30)	10.0%	7	14.0%	0.723
Diabetes	1	4.3%	6	8.8%	6	15.0%	7 (49)	14.3%	0.526

Acute dissection

	Captivia	(%)	SGVI	(%)	VIRTUE	(%)	Chi-sq
	19		37		50		
Age	58	13.4%	66	12.5	63	14.1	0.272
GAS	67	13.8	72	15.5	66.3	15.0	0.314
Gender (M)	14	60.9%	27	67.5%	38	76.0%	0.946
CVA	1	4.3%	0	0.0%	2	4.0%	0.42
Renal failure	3	13.0%	5	12.5%	3	6.0%	0.36
Cardiac disease	N/A	N/A	7	17.5%	4	8.0%	0.2
Resp	1	4.3%	1	2.5%	7	14.0%	0.188
Diabetes	1	4.3%	2	5.0%	0	0.0%	0.226

	CAPTIVIA (%)		SGVI (%)		VALOR I (%)		VALOR II (%)		Chi-sq
	49		128		338		160		
Age (STD)	70	10.1	73	8.5	72	10.4	72	9.1	0.40
GAS (STD)	80	8.1	80	11.8	79	14.5	79	13.0	0.20
Gender (M)	38	77.6%	74	57.0%	194	57.4%	95	59.3%	0.06
CVA	5	10.2%	20 (124)	16.1%	59	17.5%	32	20.0%	0.446
Renal failure	12	24.5%	18 (115)	15.7%	73	21.6%	26	16.3%	0.274
CAD	**	-	39 (114)	34.2%	144	42.6%	71	44.4%	0.201
Resp	15(47)	31.9%	15 (108)	13.9%	141	41.7%	56	35.0%	<0.05
Diabetes	8 (47)	17.0%	8 (113)	7.1%	59	17.5%	34	21.3%	<0.05

TAA