Results with the Talent thoracic stent graft in the VALOR trial

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Objective: **We report the 5-year outcomes of thoracic endovascular aneurysm repair (TEVAR) using the Medtronic Vascular Talent Thoracic Stent Graft System (Medtronic Vascular, Santa Rosa, Calif) in patients considered low or moderate risk for open surgical repair.**

Methods: **The Evaluation of the Medtronic Vascular Talent Thoracic Stent Graft System for the Treatment of Thoracic Aortic Aneurysms (VALOR) trial was a prospective, nonrandomized, multicenter, pivotal study conducted at 38 U.S. sites. Between December 2003 and June 2005, VALOR enrolled 195 patients who were low or moderate risk (0, 1, and 2) per the modified Society for Vascular Surgery and American Association for Vascular Surgery criteria. The patients had fusiform thoracic aortic aneurysms (TAAs) and/or focal saccular TAAs/penetrating atherosclerotic ulcers. Standard follow-up interval examinations were conducted at 1 month, 6 months, 1 year, and annually thereafter.**

Results: **Over the 5-year follow-up, 76 deaths occurred (43.9%). Freedom from all-cause mortality was 83.9% at 1 year and 58.5% at 5 years. Most deaths were due to cardiac, pulmonary or cancer-related causes. Freedom from aneurysm-related mortality (ARM) was 96.9% at 1 year and 96.1% at 5 years. There was only 1 case of ARM after the first year of follow-up. Over the 5-year follow-up period, four patients were converted to open surgery and four patients experienced aneurysm rupture. The 5-year freedom from aneurysm rupture was 97.1% and the 5-year freedom from conversion to surgery was 97.1%. The incidence of stent graft migration (>10 mm) was ≤1.8% in each year of follow-up. The rate of type I endoleak was 4.6% at 1 month, 6.3% from 1 month to 1 year, and 3.8% during year 5. The rate of type III endoleak was 1.3% at 1 month, 1.9% from 1 month to 1 year, and 1.9% during year 5. Through 5 years, 28 patients (14.4%) underwent 31 additional endovascular procedures on the original target lesion. The 5-year freedom from secondary endovascular procedures was 81.5%.**

Conclusions: **Through 5-year follow-up in patients who were candidates for open surgical repair, TEVAR using the Talent Thoracic Stent Graft System has demonstrated sustained protection from ARM, aneurysm rupture, and conversion to surgery, and durable stent graft performance. Close patient follow-up remains essential after TEVAR. (J Vasc Surg 2012;56:1214-21.)**

Open surgical repair of thoracic aortic aneurysms (TAAs), even at centers of excellence, carries with it a significant risk of morbidity and mortality.[1-4] Early data from thoracic stent graft trials established thoracic endovascular aneurysm repair (TEVAR) as a safe and effective strategy for treating TAAs.[5-8] Data from nonrandomized clinical trials have demonstrated lower perioperative morbidity and mortality with TEVAR compared with open repair.[5,9-11] Thoracic endograft technology continues to evolve and yet there are only limited data available from prospective multi-institutional trials regarding long-term follow-up with TEVAR. Here we report the 5-year outcomes from The Evaluation of the Medtronic Vascular Talent Thoracic Stent Graft System for the Treatment of Thoracic Aortic Aneurysms (VALOR) trial using the Medtronic Vascular Talent Thoracic Stent Graft System (Medtronic Vascular, Santa Rosa, Calif).

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METHODS

Detailed descriptions of the VALOR trial design and the Talent Thoracic Stent Graft System have been reported previously.[5] Briefly, VALOR was a prospective, nonrandomized clinical trial of the Talent Thoracic Stent Graft System conducted at 38 U.S. sites, with enrollment occurring between December 2003 and June 2005. The pivotal test group, described here, consisted of 195 patients (VALOR also included high-risk and registry cohorts).

Follow-up protocol. At 1, 6, and 12 months, and annually thereafter, standard follow-up evaluations included physical examination, chest X-rays, and computed tomography (CT) scan or magnetic resonance angiogra-

phy. Imaging obtained through 1 year was evaluated by a core reference laboratory (M2S, Lebanon, NH).

Endoleaks were defined according to the type I to IV nomenclature.[12] Migration was defined as >10 mm proximal or distal movement of the stent graft relative to fixed anatomic landmarks. Aneurysm expansion was defined as an increase in diameter >5 mm between the 1-month and subsequent follow-up visits. Major adverse events (MAEs) were defined as death due to the procedure, any death within 30 days of the procedure, respiratory complications, renal insufficiency or failure, cardiac events, neurologic events, aneurysm rupture, bowel ischemia, major bleeding, or vascular complications. An MAE that was identified as a serious adverse event by the clinical investigator was defined as a serious MAE. All deaths and aneurysm ruptures through 5 years were adjudicated by an independent physician advisory group managed by Harvard Clinical Research Institute (Boston, Mass). All MAEs within 1 year, including deaths and ruptures, were adjudicated by the same group. After 1 year, potential MAEs were not adjudicated by an independent body; consequently, in this report, we provide an update on all serious adverse events as defined by the investigators.

Aneurysm-related death was defined as any death occurring within 30 days of the procedure or at any point as a consequence of aneurysm rupture, conversion to open surgery, or any other secondary endovascular procedure relative to the treated TAA as evidenced by CT scan, angiography, or direct observation at surgery or autopsy.

All statistical analyses were performed with SAS v. 9.1 (SAS Institute, Cary, NC). For continuous variables, the mean and standard deviation are provided; *P* values were calculated using standard *t*-tests. Kaplan-Meier curves were used to plot freedom from event over time. Cox proportional-hazard regressions were performed to identify potential risk factors.

RESULTS

Baseline patient characteristics and procedure data have been published previously.[5] Talent thoracic stent grafts were successfully deployed in 194 of the 195 patients enrolled in the VALOR test group (99.5%). Access failure prevented one patient from successfully undergoing TEVAR. Over the 5-year follow-up period, 76 patients died, 14 withdrew from the trial, and eight were lost to follow-up. A total of 96 patients had 5-year follow-up information available for analysis.

Mortality. There were 76 deaths (76/173, 43.9%) in the VALOR test arm over the 5-year follow-up period (Table I). The Kaplan-Meier estimate for freedom from all-cause mortality at 1 year and 5 years was 83.9% (standard error [SE] ± 2.6%) and 58.5% (SE ± 3.7%), respectively (Fig 1). Multivariate analysis revealed that a history of cerebrovascular accident (hazard ratio [HR], 2.3; 95% confidence interval [CI], 1.2-4.3) and a history of chronic obstructive pulmonary disorder (COPD) (HR, 1.9; 95% CI, 1.2-3.0) were associated with increased all-cause mortality during the 5-year follow-up period (Table II).

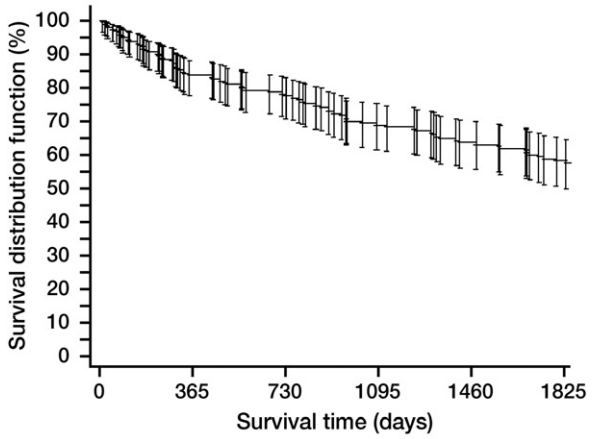
Table I. Cause of death within 5 years for VALOR test-group patients

Aneurysm-related deaths	
Stroke[a]	1
Cardiac arrest/MI[a]	1
Ruptured TAA	2
TAA dissection	1
Renal failure[a]	1
Sepsis[a]	1
All-cause mortality	
Cardiac arrest/MI	13
Respiratory failure	8
Cancer	7
Congestive heart failure	4
Hemorrhagic stroke	4
Multiorgan failure	4
Renal failure	4
COPD	3
Bowel ischemia	2
Ruptured AAA	2
Sepsis	2
Aortic infection	1
Acute morphine poisoning	1
Cirrhosis	1
Embolic stroke (>30 days)	1
Gastrointestinal bleed	1
Hemoptysis	1
Natural causes	1
Peripheral vascular disease	1
Unknown	8
Total deaths, 5 years	76

AAA, Abdominal aortic aneurysm, *COPD,* chronic obstructive pulmonary disease; *MI,* myocardial infarction; *TAA,* thoracic aortic aneurysm; *VALOR,* Vascular Talent Thoracic Stent Graft System for the Treatment of Thoracic Aortic Aneurysms.
[a]Death within 30 days.

Seven patients died of an aneurysm-related cause through 5 years (Table I). Estimated freedom from aneurysm-related mortality (ARM) at 1 year and 5 years was 96.9% (SE ± 1.3%) and 96.1% (SE ± 1.4%), respectively (Fig 2). Six of the aneurysm-related deaths (86%) occurred within the first year after TEVAR (four of these were within 30 days of the procedure) and one occurred during the third year. The four deaths <30 days were due to atheroembolic multisystem failure, stroke, periprocedural cardiac arrest, and sepsis. The two additional deaths within the first year were due to a retrograde type A dissection and an aneurysm rupture. The single aneurysm-related death after 1 year was due to a late aneurysm rupture. None of the seven patients whose deaths were aneurysm-related had a secondary procedure.

Aneurysm rupture. There were a total of four aneurysm ruptures over the 5-year follow-up period (mean, 27.3 months; range, 8-49 months). The Kaplan-Meier estimate of survival free from aneurysm rupture through 5 years was 97.1% (SE ± 1.5%) (Fig 3). Two ruptures resulted in death. There was one rupture in the first year of follow-up, two in the third year, and one in the fifth year. The first patient spent 7 months in the hospital following TEVAR secondary to multiple postoperative complications. At autopsy, a rupture was discovered at the distal end of the thoracic stent. This patient had both 1-month and 6-month CT scans in



	Time intervals (days)				
Statistics	*0–365*	*366–731*	*732–1096*	*1097–1461*	*1462–1826*
At risk[a]	195	160	141	123	111
Mortality	31	11	15	9	10
Censored[b]	4	8	3	3	101
Survival (2-sided 95% CI)	83.9% (78.0%, 88.4%)	78.0% (71.4%, 83.3%)	69.6% (62.4%, 75.6%)	64.4% (57.0%, 70.9%)	58.5% (51.0%, 65.3%)
SE[c]	2.6%	3.0%	3.4%	3.5%	3.7%

[a] At beginning of time interval.
[b] Patients are censored because they withdraw or are lost to follow-up.
[c] SE at end of interval.

Fig 1. Kaplan-Meier plot of freedom from all-cause mortality for the Vascular Talent Thoracic Stent Graft System for the Treatment of Thoracic Aortic Aneurysms (VALOR) test-group patients. *CI*, Confidence interval; *SE*, standard error.

the hospital, and each revealed no evidence of endoleak, migration, or device failure. Imaging core laboratory review of the patient's preoperative and 1-month imaging demonstrated that this patient had a thoracoabdominal aneurysm and should have been excluded from the trial. The second patient ruptured approximately 25 months following TEVAR and suffered a cardiac arrest on transfer to the enrolling facility. At autopsy this patient was noted to have a "gap" between the proximal and distal stent, consistent with a type III endoleak. This patient missed both 12- and 24-month follow-up visits and did not have any follow-up imaging during this interval. A 6-month CT scan did not demonstrate an endoleak. The third patient ruptured approximately 27 months after TEVAR and was successfully managed with the endovascular placement of a cuff. The fourth patient ruptured nearly 49 months after TEVAR in the setting of a transverse arch aneurysm and expanding descending TAA with a known proximal type I endoleak. This patient underwent successful hybrid repair consisting of a transverse arch repair and relining of the prior thoracic stent graft repair.

Conversion to surgery. Four patients were converted to open surgery over the 5-year follow-up period. The first patient was converted to open repair approximately 9 months after TEVAR for complications related to an infection in the stented segment of the aorta. This patient died near the end of the second year of follow-up due to hemoptysis. A second surgical conversion occurred approximately 16 months after TEVAR in a patient with aneurysmal expansion of the distal thoracic aorta, contiguous with the original aneurysm. There was no endoleak reported on either the 6- or 12-month CT scan. Core laboratory review of the preoperative CT demonstrated an inadequate distal landing and this patient should have been excluded from the trial. This patient was alive at 5-year follow-up. A third conversion occurred early in the third year, approximately 25 months after TEVAR, in a patient with aneurysm expansion due to a persistent type I endoleak after failure of a secondary endovascular procedure. This patient underwent partial conversion (proximal Dacron graft was sewn to the previously placed Talent stent graft distally) and was alive at 5-year follow-up despite having evidence of continued aneurysm growth. The fourth open conversion occurred approximately 49 months after device implantation in a patient who had a type I endoleak leading to aneurysm expansion and rupture. This patient was exited from the trial <30 days after open conversion. The Kaplan-Meier estimate of 5-year conversion-free survival was 97.1% (SE ± 1.4%) (Fig 4).

Predictors of a composite end point consisting of combined ARM, conversions, and ruptures are listed in Table II. Unresolved endoleaks at the conclusion of the procedure (HR, 6.3; 95% CI, 1.2-32.3) and a history of peripheral vascular disease (HR, 5.9; 95% CI, 1.7-20.3) were predictive of the composite end point.

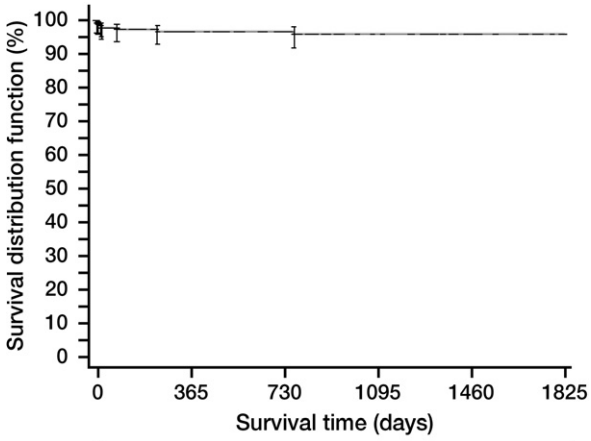
Endoleak. The occurrence of endoleaks through 5 years of follow-up is summarized in Table III. There were 32 site-reported type I endoleaks (19 proximal, 13 distal) documented over the 5-year follow-up period. Nine patients were reported to have persistent type I endoleaks (noted over at least two follow-up evaluations). Four of those patients (44%) had an associated increase in aneurysm diameter (>5 mm). Two of these patients went on to convert to open surgical repair (one patient ruptured). Four of the nine patients with persistent type I endoleaks died over the follow-up period; three deaths were from causes unrelated to the aneurysm, and one was from unknown causes. Two of the four patients that died had unresolved type I endoleaks. There were 49 site-reported occurrences of type II endoleaks. Eleven type III endoleaks were reported over the 5-year follow-up. All of these patients had junctional endoleaks; none had any kinking, twisting, fracture, or other loss of device integrity.

Migration and device integrity. Site-reported stent graft migration was noted in 0.6% in the first year, 1.8% in the second year, 1% in the third year, 1.2% in the fourth year, and 1.3% in the fifth year (Table III). There were eight observations of loss of stent graft integrity, all of which occurred after 24-month follow-up. There were six reports of stent graft kinking in the first year after initial device implantation and an additional nine reports out to 5-year

Table II. Results of Cox proportional-hazard regression analysis on selected events within 5 years for VALOR test-group patients

Baseline factor	*Hazard ratio*	*95% CI*	P *value*
Predictors of ARM, conversion to surgery, and rupture			
Endoleaks observed immediately after procedure	6.3	1.2-32.3	.030
Peripheral vascular disease	5.9	1.7-20.3	.005
Predictors of reinterventions within 5 years			
Maximum aneurysm diameter[a]	1.070	1.032-1.110	<.001
Aneurysm length[a]	1.006	1.001-1.011	.020
Predictors of all-cause mortality within 5 years			
Cerebrovascular accident	2.3	1.2-4.3	.010
COPD	1.9	1.2-3.0	.006
Predictors of major adverse events within 5 years			
Aortic tortuosity	15.9	4.4-57.7	<.001
Carotid artery disease	4.2	2.0-8.8	<.001
COPD	1.8	1.2-2.6	.003
Blood loss >200 mL[b]	1.7	1.2-2.4	.006
Tortuosity of access artery (moderate or severe)	1.7	1.1-2.6	.020
Implantation in zones 1 or 2	1.6	1.1-2.3	.020
Predictors of paraplegia and paraparesis within 5 years			
COPD	3.9	1.3-11.6	.010
Distal neck length[a]	0.2	0.1-0.7	.010

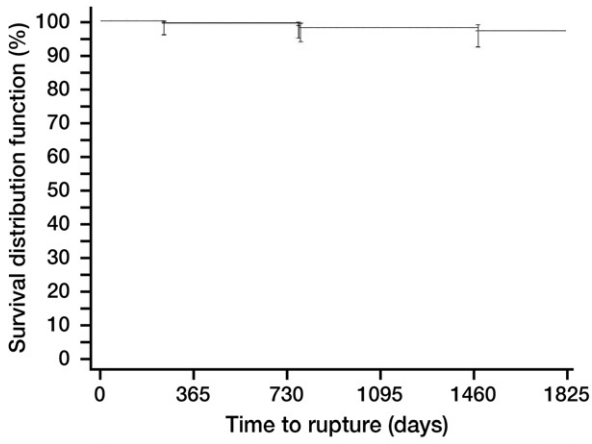
ARM, Aneurysm-related mortality; *CI,* confidence interval; *COPD,* chronic obstructive pulmonary disease; *VALOR,* Vascular Talent Thoracic Stent Graft System for the Treatment of Thoracic Aortic Aneurysms.
[a]For every additional mm.
[b]For every additional cc.



	Time intervals (days)				
Statistics	*0–365*	*366–731*	*732–1096*	*1097–1461*	*1462–1826*
At risk[a]	195	160	141	123	111
Mortality	6	0	1	0	0
Censored[b]	29	19	17	12	111
Survival (2-sided 95% CI)	96.9% (93.1%, 98.6%)	96.8% (93.1%, 98.6%)	96.1% (92.0%, 98.2%)	96.1% (92.0%, 98.2%)	96.1% (92.0%, 98.2%)
SE[c]	1.3%	1.3%	1.4%	1.4%	1.4%

[a]At beginning of time interval.
[b]Patients are censored because they withdraw or are lost to follow-up.
[c]SE at end of interval.

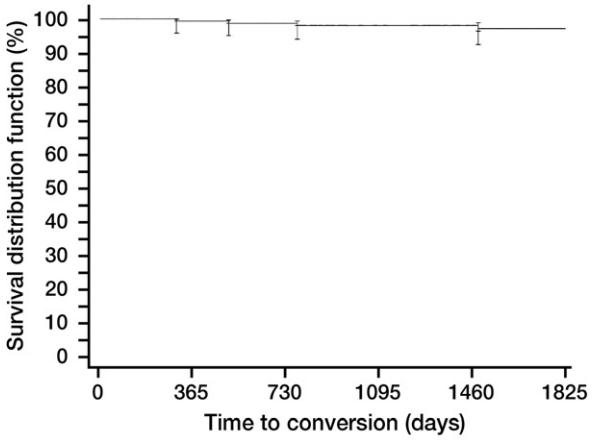
Fig 2. Kaplan-Meier plot of freedom from aneurysm-related mortality (ARM) for the Vascular Talent Thoracic Stent Graft System for the Treatment of Thoracic Aortic Aneurysms (VALOR) test-group patients. *CI*, Confidence interval; *SE*, standard error.



	Time intervals (days)				
Statistics	*0–365*	*366–731*	*732–1096*	*1097–1461*	*1462–1826*
At risk[a]	195	160	141	122	110
Ruptures	1	0	2	0	1
Censored[b]	34	19	17	12	109
Rupture-free (2-sided 95% CI)	99.4% (95.9%, 99.9%)	99.4% (95.9%, 99.9%)	98.0% (93.8%, 99.3%)	98.0% (93.8%, 99.3%)	97.1% (92.3%, 98.9%)
SE[c]	0.6%	0.6%	1.2%	1.2%	1.5%

[a]At beginning of time interval.
[b]Patients are censored because they withdraw or are lost to follow-up.
[c]SE at end of interval.

Fig 3. Kaplan-Meier plot of freedom from aneurysm rupture for the Vascular Talent Thoracic Stent Graft System for the Treatment of Thoracic Aortic Aneurysms (VALOR) test-group patients. *CI*, Confidence interval; *SE*, standard error.



	Time intervals (days)				
Statistics	*0–365*	*366–731*	*732–1096*	*1097–1461*	*1462–1826*
At risk[a]	195	159	140	121	109
Converted	1	1	1	0	1
Censored[b]	35	18	18	12	108
Conversion-free (2-sided 95% CI)	99.4% (95.8%, 99.9%)	98.7% (95.0%, 99.7%)	98.0% (94.0%, 99.4%)	98.0% (94.0%, 99.4%)	97.1% (92.4%, 98.9%)
SE[c]	0.6%	0.9%	1.1%	1.1%	1.4%

[a] At beginning of time interval.
[b] Patients are censored because they withdraw or are lost to follow-up.
[c] SE at end of interval.

Fig 4. Kaplan-Meier plot of freedom from conversion to surgery for the Vascular Talent Thoracic Stent Graft System for the Treatment of Thoracic Aortic Aneurysms (VALOR) test-group patients. *CI*, Confidence interval; *SE*, standard error.

follow-up. There were no reports of loss of device patency over the 5-year follow-up period.

Additional endovascular procedures. Twenty-eight patients (14.4%, 28/194) underwent 31 additional endovascular procedures on the original aneurysm over the 5-year follow-up period. Kaplan-Meier estimated freedom from secondary endovascular procedures was 81.5% (SE ± 3.3%) (Fig 5). Three patients each had two secondary procedures during that time. After 1 year of follow-up, 14 patients underwent 15 additional endovascular procedures on the original aneurysm. Thirteen (87%) of these were performed to resolve endoleaks (one patient also had concomitant device migration), and two were performed for aneurysm expansion. Two patients each had two secondary procedures after 1 year of follow-up, both to treat persistent endoleak. In addition to the 31 additional endovascular procedures performed on the original aneurysm over the 5-year follow-up period, there were two performed for a second thoracic aneurysm (one was ruptured), and one was performed to treat an abdominal aortic aneurysm. Cox regression analysis identified maximum aneurysm diameter (HR, 1.007 for each additional mm; 95% CI, 1.032-1.110) and aneurysm length at diagnosis (HR, 1.006 for each additional mm; 95% CI, 1.001-1.011) as predictors of additional endovascular procedures over the 5-year follow-up.

Changes in aneurysm diameter. Between 1 month and 5 years of follow-up, aneurysm sac diameter had decreased (>5 mm) or remained unchanged in 84.6% (Table IV). Increased aneurysm sac diameter (by >5 mm) was noted in 15.4% over the same time period. There were 48 separate observations of aneurysm sac expansion occurring in 27 patients. Seven of these patients underwent additional endovascular procedures, all of which were successful. One patient with documented sac expansion in the descending thoracic aorta and distal arch ruptured, resulting in an open conversion and hybrid stent graft repair. Another eight patients died over the follow-up period with none of the deaths being adjudicated as aneurysm-related.

Major adverse events. The relative distribution of MAEs occurring from 31 days through 5 years was cardiac complications in 29.8% of patients (57/191), pulmonary complications in 17.3% of patients (33/191), renal complications in 11.5% of patients (22/191), vascular complications in 11% of patients (21/191), and neurologic events in 7.9% of patients (15/191). Predictors of MAEs from index procedure through 5-year follow-up are listed in Table II. Patients with aortic tortuosity, defined as the ratio of the centerline length to straight line lengths between the subclavian and celiac arteries (HR, 15.9; 95% CI, 4.4-57.7), history of carotid artery disease (HR, 4.2; 95% CI, 2.0-8.8), history of COPD (HR, 1.8; 95% CI, 1.2-2.6), blood loss during procedure of more than 200 mL (HR, 1.7; 95% CI, 1.2-2.4), moderate or severe tortuosity of the access vessel as assessed by the investigational site (HR, 1.7; 95% CI, 1.1-2.6), and implantation in zone 1 or 2 (HR, 1.6; 95% CI, 1.1-2.3), had a higher risk of experiencing an MAE within 5 years.

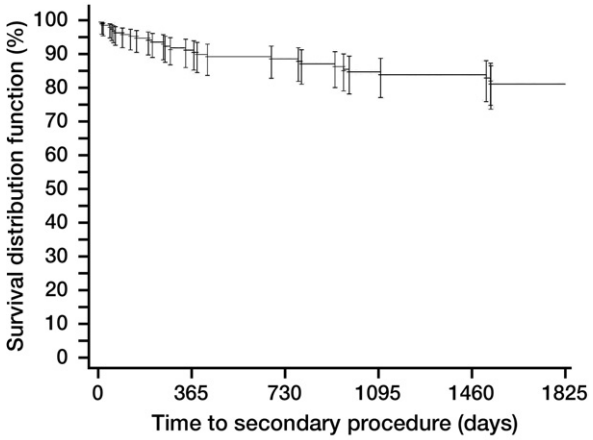
Neurologic complications. There were 23 strokes that occurred in 21 patients over the 5-year follow-up period (10.7%, 21/195). Eight of these events (seven patients) occurred within the first 30 days (3.6%, 7/195), and all were embolic in origin. Two of these events in the first 30 days after the stent graft implant were fatal, and the death of a third patient within 30 days was attributed to acute myocardial infarction and a cerebral infarct. None of these three patients had a history of stroke. Beyond 1 year, there were six strokes, three of them fatal. Three of the six strokes were embolic in origin, and the other three were hemorrhagic. The Kaplan-Meier 5-year estimate of freedom from stroke was 88.2% (SE ± 6.0%).

Seventeen patients experienced spinal cord ischemia (SCI) within 30 days after TEVAR (8.7%, 17/195). Three of these patients had paraplegia (1.5%, 3/195), and 14 patients had paraparesis (7.2%, 14/195). There were two cases of SCI after 30 days (1%, 2/195). One patient experienced paraplegia at 32 days post-TEVAR, and an additional case of paraparesis occurred 2 days following a patient's open repair of an aortic dissection that had been discovered at the 1-month imaging examination. Eight patients had resolution of paraparesis at 1-year or the last follow-up visit, but there was no resolution in the four cases

Table III. Site-reported endoleak and migration for VALOR test-group patients

Device-related event	*Through 1-month visit*[a]	*>1- to 12-month visit*[a]	*>12- to 24-month visit*[b]	*>24- to 36-month visit*[b]	*>36- to 48-month visit*[b]	*>48- to 60-month visit*[b]
Endoleak	16.4% (25/152)	17.7% (28/158)	12.0% (13/108)	14.7% (15/102)	11.3% (9/80)	10.8% (8/74)
Type I	4.6% (7/152)	6.3% (10/158)	3.7% (4/108)	5.9% (6/102)	3.8% (3/80)	2.7% (2/74)
Type Ia (proximal)	2.6% (4/152)	3.2% (5/158)	2.8% (3/108)	2.9% (3/102)	3.8% (3/80)	1.4% (1/74)
Type Ib (distal)	2.0% (3/152)	3.2% (5/158)	0.9% (1/108)	2.9% (3/102)	0.0% (0/80)	1.4% (1/74)
Type II	7.2% (11/152)	9.5% (15/158)	7.4% (8/108)	5.9% (6/102)	6.3% (5/80)	5.4% (4/74)
Type III	1.3% (2/152)	1.9% (3/158)	1.9% (2/108)	2.0% (2/102)	0.0% (0/80)	2.7% (2/74)
Type IV	0.7% (1/152)	0.0% (0/158)	0.0% (0/108)	0.0% (0/102)	0.0% (0/80)	0.0% (0/74)
Unknown	3.9% (6/152)	1.9% (3/158)	0.9% (1/108)	1.0% (1/102)	2.5% (2/80)	0.0% (0/74)
Migration >10 mm from 1 mo		0.6% (1/163)	1.8% (2/113)	1.0% (1/104)	1.2% (1/85)	1.3% (1/77)

VALOR, Vascular Talent Thoracic Stent Graft System for the Treatment of Thoracic Aortic Aneurysms.
[a]Core laboratory reported.
[b]Site reported.



	Time intervals (days)				
Statistics	*0–365*	*366–731*	*732–1096*	*1097–1461*	*1462–1826*
At risk[a]	194	145	124	103	92
Secondary procedures	15	4	5	1	3
Censored[b]	34	17	16	10	89
Secondary-procedure-free (2-sided 95% CI)	91.6% (86.5%, 94.9%)	89.0% (83.3%, 92.9%)	85.1% (78.5%, 89.8%)	84.3% (77.5%, 89.2%)	81.5% (74.0%, 87.0%)
SE[c]	2.1%	2.4%	2.9%	2.9%	3.3%

[a] At beginning of time interval.
[b] Patients are censored because they withdraw or are lost to follow-up.
[c] SE at end of interval.

Fig 5. Kaplan-Meier plot of freedom from secondary procedures for the Vascular Talent Thoracic Stent Graft System for the Treatment of Thoracic Aortic Aneurysms (VALOR) test-group patients. *CI*, Confidence interval; *SE*, standard error.

of paraplegia prior to the end of the study period or death of the patient. Predictors of SCI included a history of COPD (HR, 3.9; 95% CI, 1.3-11.6) and a shorter distal nonaneurysmal neck length (HR, 0.02; 95% CI, 0.1-0.7). The Kaplan-Meier 5-year estimate of freedom from SCI was 92.3% (SE ± 4.8%).

Table IV. Site-reported changes to aneurysm diameter during follow-up for VALOR test-group patients

Follow-up interval	*Increase >5 mm*	*No change ±5 mm*	*Decrease >5 mm*
1-6 months	7.9% (7/89)	66.3% (59/89)	25.8% (23/89)
1-12 months	7.0% (6/86)	55.8% (48/86)	37.2% (32/86)
1-24 months	8.7% (8/92)	48.9% (45/92)	42.4% (39/92)
1-36 months	8.3% (7/84)	46.4% (39/84)	45.2% (38/84)
1-48 months	13.9% (10/72)	37.5% (27/72)	48.6% (35/72)
1-60 months	15.4% (10/65)	35.4% (23/65)	49.2% (32/65)

VALOR, Vascular Talent Thoracic Stent Graft System for the Treatment of Thoracic Aortic Aneurysms.

Aortic dissection. Three of the 194 patients (1.5%) developed a retrograde type A dissection during the follow-up period. Two of these patients were diagnosed on routine 1-month follow-up imaging. One of these patients underwent open repair and died postoperatively secondary to respiratory failure after a protracted course. The other patient was observed due to significant medical comorbidities and expired approximately 3 months after TEVAR. The third patient was diagnosed 7 months following TEVAR after undergoing imaging for chest pain. This patient underwent open repair and died of an unknown cause at 32 months. There were no aortic dissections observed after this time, through the end of the study period.

DISCUSSION

Early data from multicenter reports confirmed the safety and efficacy of TEVAR and improved outcomes compared with open repair.[5,8,10,11,13] The VALOR test arm presented here was used as the pivotal data set to support Food and Drug Administration approval of the Talent Thoracic Stent Graft in 2008. The 5-year follow-up data on these patients adds to a very limited body of

literature from prospective multicenter TEVAR trials reporting on long-term outcomes.[9]

There were 76 deaths over the 5-year follow-up period, seven of which were aneurysm-related. Survival decreased steadily over the follow-up period with an estimated freedom from all-cause mortality of 58.5% at 5 years. Most deaths over the 5-year follow-up period were from cardiac, pulmonary, or cancer-related causes, leading to an estimated freedom from ARM of 96.1%. The majority of aneurysm-related deaths (4 of 6) occurred in the first 30 days after device implantation and only one occurred after the first year. The low rate of late ARM coupled with steadily decreasing survival over the length of the trial highlights the efficacy of TEVAR over the follow-up period but also speaks to the fragility of aneurysm patients in the post-TEVAR period. Similar findings have been reported in the literature.[14] Makaroun and colleagues reported an overall survival rate of 68% in the multi-institutional Gore TAG phase II trial (W. L. Gore, Inc, Flagstaff, Ariz).[9] The majority of deaths in that trial were attributed to cardiopulmonary, cerebrovascular, or cancer-related events. Only four aneurysm-related deaths were recorded in the TEVAR group of the Gore trial and all occurred in the first 3 months (compared with 11 in the open surgical group). Fattori and colleagues reported on outcomes of over 400 patients treated with the Talent Thoracic Stent Graft for a variety of aortic problems using retrospective registry data from seven European centers.[15] Kaplan-Meier estimated 5-year survival was 74.1%, and freedom from aneurysm-related death was 90.2% at 5 years. A number of single-center experiences have also been reported. Stone and colleagues reported 4-year survival estimates of 60% ± 8% for degenerative aneurysms that were fit for open repair and treated with TEVAR using a variety of different devices.[16] Czerny and colleagues published results on 113 TEVAR procedures performed for descending thoracic aneurysms with a mean follow-up of 54 months.[17] Kaplan-Meier survival estimates at 5 and 10 years were 60% and 42%, respectively. Five-year and 10-year aorta-related survival estimates were 90% and 83%, respectively. Single-institution data from high-risk patients treated with the Cook TX1 and TX2 devices (Cook Medical, Inc, Bloomington, Ind) demonstrated overall survival of 70% at 5 years, with ARM of <10%.[18] Lee and colleagues recently provided sobering data on the long-term outcomes of 400 TEVAR procedures at a single institution performed for various indications.[19] Estimated survival at 48 months was 53% ± 4.3%, with most explained deaths related to cardiac, pulmonary, or cerebrovascular events. When evaluated collectively, these data lend further support to the observation that in the post-TEVAR period the majority of patients are succumbing to their underlying comorbidities and not from aneurysm-related causes.

We observed a 15.4% rate of sac expansion over the 5-year follow-up period. An appropriate benchmark for this value is uncertain given the lack of long-term multicenter data. One important limitation of these data is that after 1 year only 55% to 62% of patients at each interval had measurements available on sac size. Makaroun and colleagues reported a 2.9% rate of sac enlargement at 2 years with the low-porosity TAG graft, but there have been no 5-year data published for this device.[9] Fattori et al reported a 17.1% rate of sac expansion with the Talent device over a mean follow-up period of 24 months.[15] These are data from a 7-center European registry over 8 years and are more consistent with our findings. Interestingly, 30% of patients in this registry had no recorded data for change in aneurysm dimensions during follow-up. Sac enlargement was noted in only two patients in long-term data with the TX2 graft, but this was a single-center experience with a mean follow-up time of 36 months (only 18 patients at 5-year follow-up interval).[18]

Type I and type III endoleaks continued to occur over each time interval of the study period (Table III) and were the indication for the majority of secondary interventions performed. The Talent stent graft used in the VALOR trial had an early generation delivery system and surgeon experience with the technology at the time was limited. Accuracy of device deployment and landing in the desired proximal and distal seal zones were likely to have been negatively impacted by these factors. Anatomic characteristics that make obtaining a proximal seal more difficult, such as aortic arch angulation, were not measured in this trial. As noted in the pivotal results for the VALOR trial,[5] there were no misaligned deployments wherein the proximal bare-stent portion of the device deploys in an asymmetric nonparallel fashion relative to the aortic wall and is then prone to flipping. Only short device lengths were available for the VALOR trial as demonstrated by an average number of implants per patient of 2.7 ± 1.3 (range, 1-7 devices). Short device lengths and the need for more devices to cover the full treatment length lead to an increase in the number of overlapping segments, thereby increasing the chance of junctional endoleaks. Aortic elongation, which may have contributed to the development of type III endoleaks over time, was not measured.

Long-term durability of TEVAR has been a concern since the inception of this technique, but stent graft technology has certainly evolved since the results with crude first-generation devices were reported.[20,21] The data presented here demonstrate very low rates of device migration, kinking, and/or twisting with the Talent Thoracic Stent Graft. There were no observations of loss of stent graft patency. However, continued occurrences of device-related complications over the 5-year follow-up period and the continued need for secondary interventions (half of all secondary endovascular interventions during the follow-up period were performed between 1 and 5 years) speak to the importance of close patient follow-up.

CONCLUSIONS

Through 5-years of follow-up, in patients who were candidates for open surgical repair, TEVAR using the Talent Thoracic Stent Graft System has demonstrated sustained protection from ARM, aneurysm rupture, and conversion to surgery. Close patient follow-up continues to be an essential component in achieving these results.

AUTHOR CONTRIBUTIONS

Conception and design: RF
Analysis and interpretation: PF, FC, MF, CK, MM, RW, AL, MT, RF
Data collection: PF, RF
Writing the article: PF, RF
Critical revision of the article: PF, FC, MF, CK, MM, RW, AL, MT, RF
Final approval of the article: PF, FC, MF, CK, MM, RW, AL, MT, RF
Statistical analysis: PF, RF
Obtained funding: Not applicable
Overall responsibility: RF

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Additional material for this article may be found online at www.jvascsurg.org.

Appendix (online only). The VALOR test-group trial sites and principal investigators

Principal investigator	*Site*	*City*	*Patients enrolled*
Michael Tuchek, DO	Loyola University Medical Center	Maywood, Ill	18
Alan Matsumoto, MD	University of Virginia	Charlottesville, Va	16
Mark Farber, MD	University of North Carolina	Chapel Hill, NC	14
Christopher Kwolek, MD	Massachusetts General Hospital	Boston, Mass	13
Ronald Fairman, MD	Hospital of the University of Pennsylvania	Philadelphia, Pa	11
Tomas Martin, MD	University of Florida	Gainesville, Fla	11
Manish Mehta, MD	Albany Medical Center	Albany, NY	10
Seyed-Mojtaba Gashti, MD	Union Memorial Hospital	Baltimore, Md	9
Rodney White, MD	Harbor UCLA	Torrance, Calif	9
Edward Garrett, MD	Baptist Memorial Hospital	Memphis, Tenn	7
Gregorio Sicard, MD	Washington University School of Medicine	St Louis, Mo	7
Tom Bower, MD	Mayo Clinic- Rochester	Rochester, Minn	6
Neal Cayne, MD	NYU Vascular Associates	New York, NY	5
Jim Swischuk, MD	St Francis Hospital	Peoria, Ill	5
Daniel Benckart, MD	Allegheny General Hospital	Pittsburg, Pa	4
Michael Hallisey, MD	Hartford Hospital	Hartford, Conn	4
Peter Lin, MD	Baylor College of Medicine	Houston, Tex	4
Richard McCann, MD	Duke University Medical Center	Durham, NC	4
James McKinsey, MD	New York Presbyterian Cornell University	New York, NY	4
Christopher Zarins, MD	Stanford University	Stanford, Calif	4
Lowell Satler, MD	Washington Hospital Center	Washington, DC	3
Paul Bove, MD	William Beaumont Hospital	Royal Oak, Mich	2
Mark Eskandari, MD	Northwestern Memorial Hospital	Chicago, Ill	2
Mark Fillinger, MD	Dartmouth- Hitchcock Medical Center	Lebanon, NH	2
Kim Hodgson, MD	Memorial Medical Center	Springfield, Ill	2
Matthew Jung, MD	Surgical Care Associates	Louisville, Ky	2
Barry Katzen, MD	Baptist Hospital of Miami	Miami, Fla	2
Zvonimir Krajcer, MD	St Luke's Episcopal Hospital – Houston	Houston, Tex	2
Sean Lyden, MD	Cleveland Clinic Foundation – Ohio	Cleveland, Ohio	2
Takao Ohki, MD	Montefiore Medical Center	Bronx, NY	2
Venkatesh Ramaiah, MD	Arizona Heart Institute	Phoenix, Ariz	2
Mark Bates, MD	Charleston Area Medical Center	Charleston, WV	1
Marc Glickman, MD	Sentara Norfolk General, Vascular, and Transplant Specialists	Norfolk, Va	1
Marc Kaye, MD	Physician's Regional Medical Center	Naples, Fla	1
Robert Rhee, MD	Shadyside Hospital – UPMC	Pittsburgh, Pa	1
Timothy Roush, MD	Carolinas Medical Center	Charlotte, NC	1
Cary Stowe, MD	Florida Hospital	Orlando, Fla	1
David Williams, MD	University of Michigan	Ann Arbor, Mich	1

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