CLINICAL RESEARCH STUDIES

Five-year results of thoracic endovascular aortic repair with the Zenith TX2

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Background: **This trial evaluated thoracic endovascular aortic repair (TEVAR) compared with open surgical repair of descending thoracic aortic aneurysms and large ulcers at 42 international sites. Whereas several studies demonstrate early safety and utility advantages with TEVAR, longer follow-up is important because of concerns about durability of TEVAR.**
Methods: **This prospective, nonrandomized study enrolled 160 TEVAR patients treated with the Cook Zenith TX2 and 70 open surgical repair patients.**
Results: **Although follow-up was limited, 5-year mortality rate was similar at 37% for both groups. Aneurysm-related mortality rate was 5.9% with TEVAR compared with 12% with open surgical repair ($P = .11$). There were no ruptures of the treated aneurysms in either group or open conversions in the TEVAR group. Predefined severe morbidity occurred at a significantly lower rate in TEVAR (21%) compared with open surgical repair (39%; $P < .001$). Aneurysm growth was seen by core laboratory in 5.9% of patients and endoleak in 5.7% of patients. Secondary intervention rates were similar between TEVAR (8%) and open surgical repair (12%; $P = .49$) patients.**
Conclusions: **Five-year results indicate similar all-cause mortality and aneurysm-related mortality with TEVAR compared with open repair. There was a persistent reduction of severe complications with TEVAR. Reinterventions occurred with similar frequency. TEVAR with the TX2 is a safe and effective alternative to open surgical repair for the treatment of anatomically suitable descending thoracic aortic aneurysms and ulcers. (J Vasc Surg 2014;60:1-10.)**

Thoracic endovascular aortic repair (TEVAR) is an example of less invasive approaches to vascular disease that has great potential to alter treatment paradigms. Thoracic aortic aneurysms (TAAs) and penetrating ulcers have been classically treated with risk factor control and observation until growth to a sufficient size that the risk of rupture justifies the risks of a major thoracic operation. Whereas these aortic diseases have been treated for many years with TEVAR, there are limited long-term data to address concerns about late failure rates with the newer technology.[1-7] There are specific concerns that late failure modes may mitigate striking early benefits. We conducted a large, multicenter trial with regulatory audit and detailed comparisons of 5-year outcomes between open surgical repair and TEVAR in the treatment of degenerative aneurysms and ulcers of the descending thoracic aorta.

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METHODS

Trial design. The Zenith TX2 pivotal study was a nonrandomized, controlled, multicenter, international trial designed to evaluate the safety and effectiveness of the Zenith TX2 TAA Endovascular Graft (William Cook Europe, ApS, Bjaeverskov, Denmark) in patients with descending TAAs ≥5 cm, rapid growth ≥5 mm/y, or ulcer ≥10 mm in depth and 20 mm in diameter. A detailed description of the TEVAR device, its deployment system, endovascular and open surgical repair techniques, and trial design with patient inclusion and exclusion criteria has been previously published.[8] Some facets of the trial design deserve repetition. Whereas a randomized design was

initially considered, TEVAR was clinically available with marked differences in short-term results, and the investigators did not have sufficient equipoise to justify randomization of patients. Few open surgical repairs were being conducted during the course of the study, limiting our ability to enroll prospective surgical control patients and thereby requiring enrollment of consecutive retrospective controls. Because of these design issues, we established anatomic criteria to enroll comparable patients in both cohorts. Per protocol, TEVAR patients were required to have a 3-cm proximal and distal neck length according to the site measurements. Patients undergoing open surgical repair needed to have planned sutured anastomoses between the left common carotid artery and celiac trunk artery. Patients with type I thoracoabdominal aneurysms were eligible for the study if the placement of endograft fabric was planned to be above the visceral vessels or if there was no planned mesenteric revascularization with open repair.

From 2002 to 2006, the pivotal study enrolled 160 patients for endovascular repair and 70 patients for surgical repair at 42 investigative sites in the United States, Canada, Europe, and Australia. Results through 1 year and 2 years have been published earlier.[1,2] All patients in this trial received treatment with the available technology at the time. Specifically, this was before introduction of modifications of the deployment system, such as the Pro-Form, which allows more parallel apposition of the proximal sealing stent in the inner curve of the aortic arch and more trackable and flexible delivery system introducers and sheaths. This report presents the final data set through 5-year follow-up, reflecting the data as of February 23, 2012.

The study was performed according to the Declaration of Helsinki II. Ethical approval was obtained from the relevant institutional review board or ethics committee at each institution. All subjects signed an informed consent.

Patient follow-up. Patients in the open surgical control group underwent clinical evaluation before discharge or at 1 month and then at 12 months and yearly thereafter up to 5 years. Of 70 surgical patients, 24 could not be observed beyond 1 year because the institutional review board/ethics committee-approved follow-up at their respective investigative sites was limited to 12 months. For endovascular patients, follow-up computed tomography (CT) scans, device radiographs, physical examinations, and laboratory studies were performed before discharge and at 1, 6, and 12 months and yearly thereafter up to 5 years. All CT images were analyzed by an independent core laboratory. Per protocol, core laboratory findings were confirmed by the independent clinical events committee (CEC). Unless otherwise indicated, imaging data reported in this manuscript reflect the results from core laboratory analysis.

Definitions. TAA-related mortality was defined as all deaths occurring within 30 days of implant procedure, secondary intervention, or conversion regardless of cause and those adjudicated as related to TAA repair by an independent CEC. The CEC reviewed all patient deaths and identified TAA-related deaths in cases in which the procedure, aneurysm disease progression, or sequence of events beginning within 30 days of the procedure may have contributed to the eventual death. Severe morbid events comprise 13 predefined morbid events as previously reported; they represent a subset from 57 predefined morbid events recorded in the study and are major complications commonly used by clinicians in comparing TEVAR and open aortic repair.[8] For example, the severe morbid events include paraplegia, return to operating room for bleeding, and permanent dialysis; morbid events also include transient weakness, postprocedure transfusion, and more than 30% elevation of serum creatinine concentration. Endoleaks were classified as type I through IV according to the standard definitions.[9] An increase in aneurysm or ulcer size was defined as a >5 mm increase in the major diameter of the aneurysm sac or the depth of the ulcer at follow-up time points compared with the predischarge CT scan. Radiographic device migration, which was identified by the imaging core laboratory and verified by the CEC, was defined as caudal or cranial movement of the proximal or distal components of the TX2 device >10 mm relative to anatomic landmarks identified on the first technically adequate postoperative CT scan.[9] Clinically significant migration was defined as migration resulting in the need for secondary intervention. Device integrity was assessed from follow-up CT scans and radiographic images by the core laboratory. Incidences of stent fracture and barb separation were confirmed by the CEC.

Data analysis. Data were managed by a centralized data coordinating center, MED Institute, Inc. Statistical analyses were performed with SAS for Windows (release 9.3 or higher; SAS Institute, Cary, NC). Continuous variables were reported as means and standard deviations unless otherwise indicated, and *P* values were calculated with standard *t*-tests. Dichotomous and other categorical variables were reported as percentages. The Kaplan-Meier method was used to estimate freedom from all-cause mortality, aneurysm-related mortality, severe morbid events, morbid events, and secondary interventions.

RESULTS

Patients and follow-up availability. The Zenith TX2 pivotal study enrolled 160 endovascular patients and 70 open surgical control patients. The details of these two patient groups were published previously.[1] Twenty-six sites enrolled at least one open surgical patient, including one site that enrolled 14. Poolability analysis for open surgical patients indicated homogeneity of mortality results from multiple sites. In the endovascular group, 158 of 160 patients were successfully implanted with the TEVAR device. Two patients did not undergo TEVAR because of inability to insert or to advance the introducer system, completed 30-day follow-up, and have no further follow-up.[1] Another 32 TEVAR subjects and 28 control subjects were lost to follow-up, withdrew, or had limited consent to follow-up. At 5 years, among patients eligible for follow-up, 93% (68 of 73) of the endovascular patients and 48% (12 of 25) of the surgical patients received clinical examinations, and

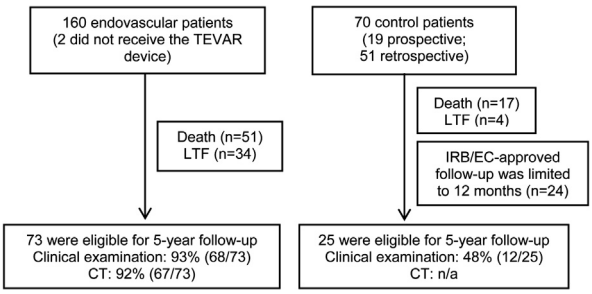


Fig 1. Subject follow-up availability at 5 years. *CT,* Computed tomography; *IRB/EC,* institutional review board/ethics committee; *LTF,* lost to follow-up; *n/a,* not applicable; *TEVAR,* thoracic endovascular aortic repair.

92% (67 of 73) of the endovascular patients underwent CT scans (Fig 1).

Mortality. During follow-up through 5 years, 51 deaths occurred in the endovascular group and 17 deaths occurred in the open surgical control group. The survival estimate from all-cause mortality was 62.9% for the endovascular treatment group and 62.8% for the open surgical control group at 5 years (1825 days), with no significant difference in the survival curves between the two groups (Fig 2; log-rank: $P = .88$). Causes for all deaths are summarized in Table I.

The Kaplan-Meier analysis indicated a trend that was not statistically significant (log-rank, $P = .11$) toward higher survival estimates from TAA-related mortality in the endovascular group (Fig 3). The survival estimate from TAA-related mortality was 94.1% for the endovascular treatment group and 88.3% for the control group at 5 years. A summary of deaths included in the TAA-related mortality analysis is provided in Table II. Ascertainment of cause of death is often uncertain, and for nine deaths in the study (six in the endovascular group, three in the surgical group), the independent CEC could not determine whether they were related to aneurysm treatment (ie, indeterminate). In most of these cases, the deaths were reported by the family or the Social Security Death Index. To avoid missing some aneurysm-related deaths, a sensitivity analysis was performed to include these indeterminate deaths as TAA related in the Kaplan-Meier analysis. A similar trend of higher survival from TAA-related mortality was observed for the endovascular group (88.7% at 5 years) than for the surgical group (76.7% at 5 years), again without statistical significance (log-rank, $P = .07$). In summary, there was no difference in all-cause or aneurysm-related mortality at 5 years.

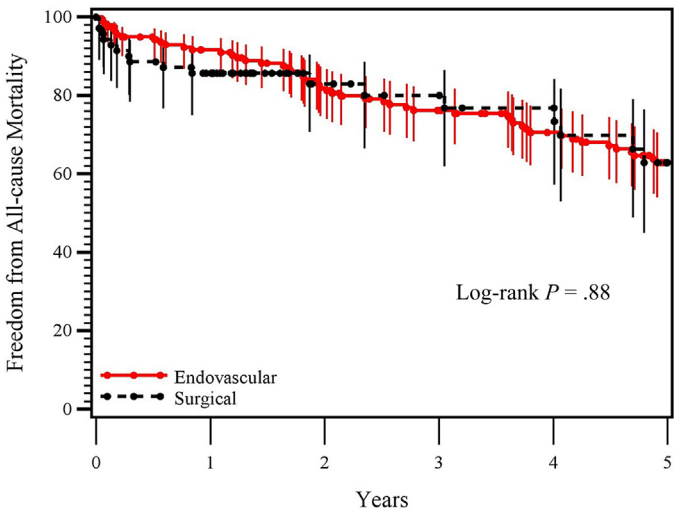
Rupture and conversion. There were no ruptures of the treated aneurysm in either group or conversions to open repair in the TEVAR group.

Morbidity. The early results of the TX2 study demonstrated a striking reduction of prespecified severe morbidity for endovascular patients at 30 days.[2] Kaplan-Meier analysis of freedom from severe morbid events indicates that this benefit was maintained through 5 years of follow-up (Fig 4; log-rank test, $P < .001$). The Kaplan-Meier estimates of freedom from severe morbid events for endovascular and open surgical control patients were 87.3% vs 64.3% at 1 year and 79.1% vs 61.2% at 5 years. Overall, 30 endovascular patients and 26 surgical patients experienced at least one severe morbid event within 5 years. Among these patients, the average number of severe morbid events per patient was 1.9 ± 1.3 (range, 1-5) in the endovascular group and 2.7 ± 2.4 (range, 1-13) in the control group ($P = .15$).

In addition, the Kaplan-Meier analysis of predefined morbid events by category shows that endovascular patients had similar rates of renal, gastrointestinal, wound, and neurologic morbidity compared with the open surgical control patients. However, endovascular patients had significantly lower cardiovascular morbidity (log-rank, $P = .003$), pulmonary morbidity (log-rank, $P < .001$), and vascular morbidity (log-rank, $P = .01$) during the 5-year follow-up. Furthermore, although neurologic morbidity (comprising stroke, transient ischemic attack/reversible ischemic neurologic deficit, carotid artery embolization/occlusion, paraparesis, and paraplegia) was similar between the two groups, an examination of individual neurologic events showed that the endovascular patients had a significantly lower occurrence of strokes (log-rank, $P < .05$) and paraplegia (log-rank, $P < .05$). There was only one late paraparesis that occurred in the fifth year in a TEVAR patient; a spinal drain was placed and the patient discharged to home after rehabilitation and ambulating without assistance 8 months later.

Endoleaks. Results of endoleaks are summarized in Table III. The occurrence of type I or III endoleak was low: only nine patients were found to have a type I or III endoleak during 5 years of follow-up. There were no proximal type I endoleaks in the first 3 years; only two patients at the 4-year and 5-year follow-up had a proximal type I endoleak. These two patients did not experience aneurysm growth or secondary interventions. Both patients had an inverted funnel-shaped proximal neck on preprocedural imaging and an insufficiently oversized proximal component placement on retrospective imaging review, and both had experienced a device migration during earlier follow-up (1-year and 2-year, respectively). Distal type I endoleak was observed in three patients, and two have undergone reintervention. In both these patients, a funnel-shaped distal neck and insufficient device oversizing at the distal end were observed. Type III endoleak was detected in four patients; three resolved spontaneously, and the fourth patient experienced component separation and underwent a reintervention that successfully bridged the separated components. None of the patients with a type II endoleak underwent secondary intervention.

Change in aneurysm or ulcer size. The aneurysm sac size or ulcer depth decreased or remained stable in more than 90% of patients through 5 years (Table IV). A total of 14 patients were found to have an increase >5 mm in their pathology during follow-up. Six of these experienced



	Years	0	1	2	3	4	5*
TEVAR	Survival (%)	100	91.6	82.0	76.2	70.5	62.9
	SE (%)	0	2.23	3.15	3.53	3.86	4.20
	Deaths	0	13	27	35	42	51
	Censored	0	11	16	23	33	47
	Remaining	160	136	117	102	85	62
Surgical	Survival (%)	100	85.6	83.0	80.0	76.8	62.8
	SE (%)	0	4.20	4.85	5.51	6.15	8.07
	Deaths	0	10	11	12	13	17
	Censored	0	4	29	32	34	38
	Remaining	70	56	30	26	23	15

*An additional death occurred at 1855 days in an endovascular patient who did not undergo 5-year follow-up; the K-M estimate was 61.9% for the endovascular treatment group at 1855 days.

Fig 2. Kaplan-Meier (*K-M*) estimate of survival for the endovascular group and surgical control group. There is no difference in survival by univariate analysis (log-rank, $P = .88$). The *vertical lines* represent 95% confidence intervals. The standard error (*SE*) is less than 10% through 5 years. *TEVAR*, Thoracic endovascular aortic repair.

spontaneous decrease in the aneurysm sac size or ulcer depth (to below the extent of 5 mm increase) at later follow-up. Five patients underwent reintervention: one died after two reinterventions for continued growth without detectable endoleak, and the other four had stabilized (ie, no further growth) or decreased aneurysm size after the reinterventions. Of the remaining three patients, one expired with a non-TAA-related death (pancreatitis) without further follow-up, and two who experienced late growth (one at 4 years and 5 years and one at 5 years) did not have endoleaks or require secondary intervention at the 5-year follow-up.

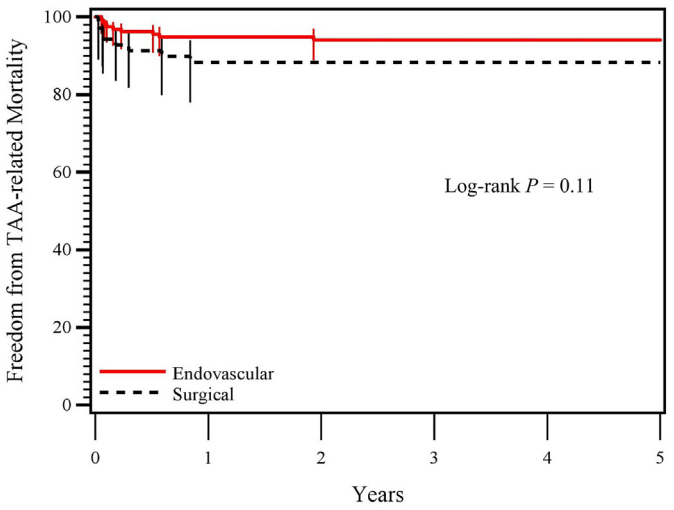
Migration. CEC-confirmed radiographic graft migration >10 mm occurred in 12 patients. Caudal migration of the proximal component was observed in nine patients, and among them, one patient also had a concomitant cranial migration of the distal component. In addition, two patients had a cranial migration of the distal end of the stent graft, and one patient had caudal migration of the proximal end and cranial migration of the distal end of the same stent graft. Retrospective imaging review revealed that all 12 patients had inadequate aortic neck anatomy at the location where the device was deployed: 11 patients had an inverted funnel-shaped proximal neck, 10 of whom also had a funnel-shaped distal neck, and one patient had

Table I. Causes of deaths included in the all-cause mortality analysis

Cause of death (reported by site)	*Endovascular, No. (% of all deaths)*	*Surgical, No. (% of all deaths)*
Cancer	3 (6)	1 (6)
Cardiac	9 (17)	5 (29)
Organ failure	6 (12)	0
Paralysis	0	2 (12)
Pneumonia	3 (6)	0
Respiratory failure	4 (8)	1 (6)
Rupture (nonstudy aneurysm)	2 (4)[a]	0
Sepsis	8 (15)	1 (6)
Shock	0	1 (6)[b]
Stroke	7 (13)	3 (18)
Surgical complications	1 (2)	0
Unknown	9 (17)	3 (18)
Total	52	17

[a]Two patients died of rupture of a nonstudy aneurysm: one patient had a rupture of a femoral artery aneurysm (a preexisting condition), and one patient had a rupture of a known enlarging distal thoracoabdominal aneurysm unrelated to the initial endovascular repair with the TEVAR device and for which the patient refused treatment.

[b]This patient exhibited sudden signs of shock, including cold and clammy skin, decreased blood pressure, and decreased level of consciousness. It was suspected that the patient experienced aneurysm leaking or rupture.



	Years	0	1	2	3	4	5
TEVAR	Survival (%)	100	94.9	94.1	94.1	94.1	94.1
	SE (%)	0	1.77	1.92	1.92	1.92	1.92
	Deaths	0	8	9	9	9	9
	Censored	0	16	34	49	66	89
	Remaining	160	136	117	102	85	62
Surgical	Survival (%)	100	88.3	88.3	88.3	88.3	88.3
	SE (%)	0	3.88	3.88	3.88	3.88	3.88
	Deaths	0	8	8	8	8	8
	Censored	0	6	32	36	39	47
	Remaining	70	56	30	26	23	15

Fig 3. Kaplan-Meier estimate of freedom from thoracic aortic aneurysm (*TAA*)-related deaths for the endovascular treatment group and open surgical control group (log-rank, $P = .11$). The *vertical lines* represent 95% confidence intervals. *TEVAR*, Thoracic endovascular aortic repair; *SE*, standard error.

irregularly shaped proximal and distal necks. Circumferential thrombus in the proximal or distal neck was also seen in five patients. In addition, insufficient stent graft oversizing at the location of actual graft placement was observed in all but one patient (less than 10% oversizing, which was the minimum labeled oversizing).

Among the 12 cases of confirmed device migration, two cases were clinically significant and required secondary intervention. One patient underwent a secondary intervention, and the aneurysm size had decreased to the level of baseline size at the 60-month follow-up. In the second patient, a cranial migration of the distal end of the stent graft required a secondary intervention (placement of a distal main body extension), which successfully resolved an associated distal type I endoleak.[3]

Device integrity. Twenty-one patients had device integrity issues on the basis of core laboratory analysis and confirmed by the CEC (for barb separation and stent fractures). One patient had a distal bare stent strut entanglement from predischarge through 12 months,[1] which was not associated with migration, endoleak, aneurysm growth, or the need for secondary intervention before the patient was lost to follow-up. There were four cases of stent fractures (single fracture in three cases and two fractures of a distal stent in one case); none resulted in type I or III endoleak or migration of the affected device component, and none required secondary interventions. Barb separation occurred in 18 patients (single-barb separation in 16 cases and multiple-barb separation in two cases), and most of these patients (12 of 18) did not have device migration, type I or III endoleak related to the affected device component, or the need for secondary intervention. Six patients experienced caudal migration of the proximal component from which a single barb separation occurred. Barb separation was observed before migration in two patients, after migration in two patients, and at the same time point as migration in two patients. Of note, all these six patients had an inverted funnel-shaped proximal neck as well as insufficient device oversizing on the proximal end, conditions likely contributing to suboptimal apposition of the sealing stent to the aortic wall. Under these conditions, some barbs may not have fully engaged into the aortic wall or may have been subjected to disproportional force.

Secondary interventions. Secondary interventions occurred at similar rates between the endovascular and open surgical control patient groups during follow-up through 5 years, as shown in Fig 5 (log-rank, $P = .49$). The Kaplan-Meier estimate of freedom from secondary intervention was 91.5% for the endovascular patients and 88.4% for the open surgical control patients at 5 years. Eleven patients in the endovascular group underwent 14 secondary interventions (three patients underwent two

Table II. Deaths included in the thoracic aortic aneurysm (*TAA*)-related mortality analysis

	Cause of death as reported by site	*CEC adjudication*
Endovascular		
≤30 days	1 Cardiac arrest	TAA related
	1 Multisystem organ failure	TAA related
	1 Adult failure to thrive, cerebrovascular disease	TAA related
31-365 days	1 Sepsis and respiratory failure	TAA related
	2 Multisystem organ failure	TAA related
	1 Respiratory failure	TAA related
	1 Cardiopulmonary arrest due to pneumonia	TAA related
	1 Coronary artery disease	Indeterminate
1-2 years	1 Respiratory distress	TAA related (secondary intervention)[a]
	1 Unknown[b]	Indeterminate
2-3 years	1 Unknown[b]	Indeterminate
3-4 years	2 Unknown[b]	Indeterminate
4-5 years	1 Unknown[b]	Indeterminate
Surgical		
≤30 days	1 Myocardial infarction	TAA related
	1 Prolonged cerebral hypoperfusion	TAA related
	1 Respiratory failure and sepsis	TAA related
	1 Respiratory failure related to paralysis	TAA related
31-365 days	1 Respiratory failure and paraplegia	TAA related
	1 Cardiopulmonary arrest, aortoesophageal fistula, TAA	TAA related
	1 Unknown[b,c]	TAA related
	1 Respiratory failure, cardiac arrest, aspiration, pneumonia	TAA related
1-2 years	None	
2-3 years	None	
3-4 years	1 Unknown[d]	Indeterminate
4-5 years	1 Cardiac arrest	Indeterminate
	1 Shock (possible leaking/rupture of aneurysm)	Indeterminate

CEC, Clinical events committee.

[a]This patient died within 30 days after the latter of two secondary interventions for continued increase in aneurysm size without detectable endoleak.

[b]Death notification by Social Security Death Index for these six patients.

[c]In this patient, a chain of events beginning within 30 days (including tracheoinnominate fistula requiring surgical intervention, pleural effusion, pericardial effusion, and multiple infections) led to prolonged hospitalization and may have contributed to the eventual death.

[d]The patient died during sleep without recent health issues and the death notification was provided by the patient's family.

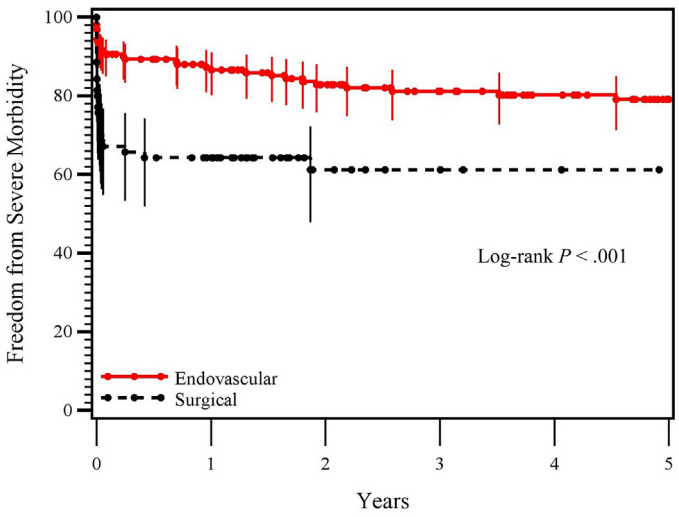
reinterventions each). Most of these reinterventions were placement of additional stent grafts for the treatment of proximal or distal type I endoleak (n = 6), component separation with or without associated type III endoleak (n = 3), device migration (n = 1), aneurysm growth (n = 2), and pseudoaneurysm (n = 1). In addition, one patient underwent angiography for assessment of endoleak (with no endoleak detected), and one patient underwent a femoral-femoral bypass for a right iliac artery occlusion. Most of the reinterventions (11 of 14) occurred within the first 2 years after the initial endovascular repair. Six patients in the surgical group underwent secondary interventions. These reinterventions included treatment of bleeding complications in four patients, one stent graft placement for aortoesophageal fistula, and one subsequent thoracoabdominal aortic aneurysm. Details of the secondary interventions are summarized in Table V.

DISCUSSION

This and other trials have demonstrated that TEVAR with the TX2 has striking early benefits with reduced complications and faster recovery.[1] Five-year radiographic follow-up captures endoleak, migration, aneurysm sac growth, and device integrity issues with TEVAR, yet reintervention rates are similar in both groups, and the early benefits are not attenuated by late complications. Late survival and aneurysm-related survival are not statistically different between endovascular and open repair. However, the current study shows a trend with half as much aneurysm-related mortality with TEVAR (6% vs 12% with open repair), which is consistent with the findings of another prior multicenter controlled trial of TEVAR and open repair that demonstrated similar 5-year all-cause mortality and improved aneurysm-related survival with TEVAR.[4]

Despite reduction of aneurysm-related mortality with TEVAR, these patients often have severe comorbid diseases, and death due to these comorbid diseases is frequent. In this unadjusted analysis, 5-year survival rates from all-cause mortality were 63% in both groups, similar to the 68% with TEVAR and 67% with open repair reported in the literature.[4] This implies that TEVAR should not alter the indication thresholds used to treat aneurysms or large ulcers.

This trial was designed with a prespecified list of severe complications that experienced clinicians have traditionally used to measure progress in treatment of thoracic aortic disease. This was thought to be essential to avoid



	Years	0	1	2	3	4	5
TEVAR	Survival (%)	98.1	87.3	82.9	81.2	80.2	79.1
	SE (%)	1.07	2.66	3.07	3.24	3.34	3.48
	Patients with events	3	20	26	28	29	30
	Censored	0	14	29	42	55	76
	Remaining	157	126	105	90	76	54
Surgical	Survival (%)	88.6	64.3	61.2	61.2	61.2	61.2
	SE (%)	3.80	5.73	6.22	6.22	6.22	6.22
	Patients with events	8	25	26	26	26	26
	Censored	0	4	25	29	31	33
	Remaining	62	41	19	15	13	11

Fig 4. Kaplan-Meier estimate of freedom from severe morbid events for the endovascular treatment group and control group (log-rank, $P < .001$). The *vertical lines* represent 95% confidence intervals. Thoracic endovascular aortic repair (*TEVAR*) patients have fewer major complications. *SE,* Standard error.

Table III. Percentage of patients with endoleaks at each follow-up time point based on core laboratory analysis

	Time points,[a] *% (No.)*							
Patients available	*Predischarge (n = 135)*	*1-month (n = 126)*	*6-month (n = 114)*	*1-year (n = 105)*	*2-year (n = 90)*	*3-year (n = 83)*	*4-year (n = 60)*	*5-year (n = 53)*
Proximal type I	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1.7 (1)	3.8 (2)
Distal type I	0.7 (1)	0.8 (1)	0.9 (1)	0 (0)	1.1 (1)	1.2 (1)	1.7 (1)	1.9 (1)
Type IIa	1.5 (2)	0.8 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1.7 (1)	0 (0)
Type IIb	7.4 (10)	3.2 (4)	2.6 (3)	1.9 (2)	1.1 (1)	0 (0)	0 (0)	0 (0)
Type III	1.5 (2)	0.8 (1)	0 (0)	1.0 (1)	0 (0)	0 (0)	1.7 (1)	0 (0)
Type IV	1.5 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Unknown	2.2 (3)	0 (0)	0 (0)	1.0 (1)	0 (0)	1.2 (1)	1.7 (1)	0 (0)
Any	14.8 (20)	5.6 (7)	3.5 (4)	3.8 (4)	2.2 (2)	2.4 (2)	8.3 (5)	5.7 (3)
Multiple	0.7 (1)	0.8 (1)	0.9 (1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

[a]In some patients, the same endoleak was detected at multiple time points.

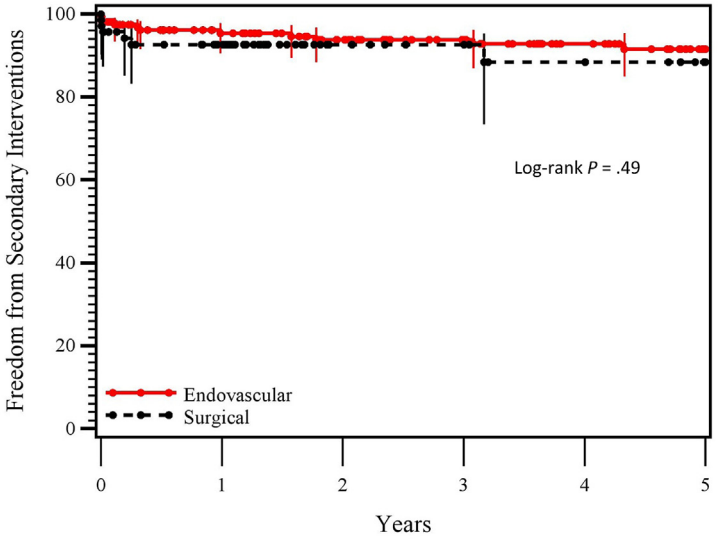
"dilution" of a composite adverse event rate with clinically unimportant reductions of minor complications. For example, a composite measure might show reduction of postoperative ileus, anemia, or other minor laboratory abnormalities but miss important differences in severe complications. In regard to this predefined severe morbidity index at 5 years, open repair patients are about twice as likely to suffer a severe complication compared with TEVAR patients. Further, if the patient is affected by at least one severe complication, the average number of complications is three with open repair compared with two with TEVAR.

In the analysis of all morbid complications, cardiovascular, pulmonary, and vascular complications were reduced with TEVAR. Gastrointestinal, renal, wound, and neurologic morbidity were similar, although stroke and paraplegia were both less frequent with TEVAR compared with open repair. The reductions in severe complications, stroke, and paraplegia are substantial advantages of TEVAR that lead to improved clinical utility. This trial

Table IV. Number of patients with increase, decrease, or no change in aneurysm or ulcer size at each follow-up time point based on core laboratory analysis

	Time points,[a] *% (No.)*						
Patients available	*1-month (n = 121)*	*6-month (n = 117)*	*1-year (n = 114)*	*2-year (n = 90)*	*3-year (n = 83)*	*4-year (n = 65)*	*5-year (n = 51)*
Decrease	5.8 (7)	32.5 (38)	47.4 (54)	52.2 (47)	59.0 (49)	61.5 (40)	62.7 (32)
No change	93.4 (113)	64.1 (75)	45.6 (52)	44.4 (40)	36.1 (30)	33.8 (22)	31.4 (16)
Increase	0.8 (1)	3.4 (4)	7.0 (8)	3.3 (3)	4.8 (4)	4.6 (3)	5.9 (3)

[a]In some patients, an increase in aneurysm or ulcer size was detected at multiple time points.



	Years	0	1	2	3	4	5
TEVAR	Survival (%)	100	95.4	93.8	93.8	92.8	91.5
	SE (%)	0	1.71	2.01	2.01	2.23	2.53
	Patients with events	0	7	9	9	10	11
	Censored	0	23	40	55	71	95
	Remaining	160	130	111	96	79	54
Surgical	Survival (%)	100	92.6	92.6	92.6	88.4	88.4
	SE (%)	0	3.18	3.18	3.18	5.11	5.11
	Patients with events	0	5	5	5	6	6
	Censored	0	11	37	41	44	50
	Remaining	70	54	28	24	20	14

Fig 5. Kaplan-Meier estimate of freedom from secondary interventions for the endovascular treatment group and open surgical control group (log-rank, $P = .49$). The *vertical lines* represent 95% confidence intervals. *TEVAR,* Thoracic endovascular aortic repair; *SE,* standard error.

and other data have shown improved recovery time and more frequent discharge to home with TEVAR.[1-7]

It is interesting that there was one late paraparesis after the first year with good recovery, and this occurred in the TEVAR group. It is speculative that a subgroup of patients who avoid paraplegia with TEVAR will continue to be at risk for late spinal cord ischemia because of relative subclinical collateral reduction.

Radiographic follow-up was mandatory in the TEVAR arm of this trial. Several radiologic events were identified by the core laboratory in the TEVAR group and include endoleaks, aneurysm sac enlargement, device migration, and device integrity events. The majority of these findings are not noted by sites and do not lead to clinical sequelae or reintervention. Subclinical migration is not uncommon after TEVAR and has been previously reported with this device and others.[10,11] Detailed imaging analysis of many of the endoleak and migration cases reveals that the device had been deployed in a neck location that is not ideal or properly sized. This emphasizes orthogonal preprocedure imaging, careful patient and device selection, and deployment at the intended neck location. This is facilitated with modern image postprocessing systems, greater physician experience, and improved delivery systems, previously described, that were not available at the time of this trial enrollment.

Table V. Secondary interventions occurring within 5 years

Patient	*Days*	*Reason for intervention*	*Type of intervention*	*Outcome of reintervention*
Endovascular				
1	2	Proximal type I endoleak[a]	Stent graft placement	Endoleak resolved
2	3	Evaluation of endoleak	Angiogram	No endoleak detected
3	3	Distal type I endoleak[a]	Stent graft placement; molding balloon angioplasty	Endoleak resolved
	1545	Component separation, type III endoleak	Stent graft placement	Successful bridge of components
4	42	Pseudoaneurysm of thoracic aorta	Stent graft placement	Pseudoaneurysm excluded; patient died within 30 days of reintervention
5	111	Right iliac artery occlusion	Femoral-femoral bypass	Improved pulses
6	119	Distal type I endoleak	Stent graft placement	Endoleak resolved
	290	Distal type I endoleak	Stent graft placement; coil embolization	Endoleak resolved
7	361	Aneurysm growth	Stent graft placement	Aneurysm stable after procedure
	697	Persistent aneurysm growth	Stent graft placement	Components placed successfully; patient died within 30 days of reintervention
8	575	Component separation,[b] type III endoleak,[a] and symptoms	Stent graft placement	Endoleak resolved
9	650	Component separation[b]	Stent graft placement	Lumen widely patent
10	1125	Distal type I endoleak	Stent graft placement	Endoleak resolved
11	1581	Device migration	Stent graft placement	Components placed successfully
Surgical				
1	1	Bleeding and tamponade	Intercostal vessel ligation	Bleeding resolved
2	2	Persistent bloody drainage from chest tubes	Exploratory thoracotomy and evacuation of intrapleural hematoma	No significant bleeding sources discovered
3	6	Bleeding into left pleural cavity	Reexploration and reseal	Bleeding resolved
4	71	Tracheal stoma bleeding	Emergent sternotomy and patch repair of tracheoinnominate fistula	Bleeding resolved
5	92	Aortoesophageal fistula	Stent graft placement	Bleeding unresolved; patient died within 30 days of reintervention
6	1157	Extensive thoracoabdominal aortic aneurysm	Hybrid repair with branch vessel reconstruction followed by stent graft placement	Aneurysm excluded; no endoleak detected

[a]These endoleaks were not reported by core laboratory analysis of regular follow-up imaging. They were reported by the investigative sites at the time of secondary interventions (two occurred shortly after the index procedure and one occurred between follow-up visits).
[b]These two cases of component separation were reported by the investigative sites at the time of secondary interventions that occurred between follow-up visits. The core laboratory analysis of follow-up imaging noted decreased device overlap but did not report component separation.

Established early benefits of TEVAR have led to its becoming the treatment of choice for anatomically suitable patients with TAAs and large ulcers. Randomized controlled studies of endovascular vs surgical repair of abdominal aortic aneurysms have suggested that higher rates of secondary interventions erased early benefits after endovascular repair during long-term follow-up.[12-14] In contrast, this study has shown that although late complications and reinterventions occur with TEVAR, they occur at rates similar to those of open repair. Reintervention is infrequent, and the early benefits of TEVAR persist through 5 years.

Limitations of this trial include the smaller number of patients available for follow-up at 5 years, especially in the surgical group. Standard techniques to improve research compliance like the Social Security Death Index were used, but follow-up may have been hampered in some patients who travel significant distances to receive their care in units that are specialized in thoracic aortic diseases. Another limitation is the nonrandomized design, which resulted in imbalance of anatomic, clinical, and unknown characteristics.

CONCLUSIONS

This trial evaluated 5-year follow-up of patients after TEVAR and open repair and found similar all-cause mortality and aneurysm-related survival with TEVAR compared with open repair. There were no ruptures of the treated aneurysm in either group and no conversions of TEVAR to open repair. There is a persistent reduction in severe and major complications with TEVAR compared with open repair. Endoleak, migration, and aneurysm growth are observed in routine radiographic follow-up after TEVAR, yet reintervention rates are similar in both groups. Taken together, when repair is indicated, TEVAR is the preferred treatment option for patients with

anatomically suitable descending thoracic aneurysms and penetrating ulcers.

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Overall responsibility: JM

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