Endovascular stent grafting versus open surgical repair of descending thoracic aortic aneurysms in low-risk patients: A multicenter comparative trial

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Supplemental material is available online.

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Objective: Results are presented from the first completed multicenter trial directed at gaining approval from the US Food and Drug Administration of endovascular versus open surgical repair of descending thoracic aortic aneurysms.

Methods: Between September 1999 and May 2001, 140 patients with descending thoracic aneurysms were enrolled at 17 sites and evaluated for a Gore TAG Thoracic Endograft. An open surgical control cohort of 94 patients was identified by enrolling historical and concurrent subjects. Patients were assessed before treatment, at treatment, and at hospital discharge and returned for follow-up visits at 1 month, 6 months, and annually thereafter.

Results: One hundred thirty-seven of 140 patients had successful implantation of the endograft. Perioperative mortality in the endograft versus open surgical control cohort was 2.1% (n = 3) versus 11.7% (n = 11, $P < .001$). Thirty-day analysis revealed a statistically significant lower incidence of the following complications in the endovascular cohort versus the surgical cohort: spinal cord ischemia (3% vs 14%), respiratory failure (4% vs 20%), and renal insufficiency (1% vs 13%). The endovascular group had a higher incidence of peripheral vascular complications (14% vs 4%). The mean lengths of intensive care unit stay (2.6 ± 14.6 vs 5.2 ± 7.2 days) and hospital stay (7.4 ± 17.7 vs 14.4 ± 12.8 days) were significantly shorter in the endovascular cohort. At 1 and 2 years' follow-up, the incidence of endoleaks was 6% and 9%, respectively. Through 2 years of follow-up, there were 3 reinterventions in the endograft cohort and none in the open surgical control cohort. Kaplan–Meier analysis revealed no difference in overall mortality at 2 years.

Conclusions: In this multicenter study early outcomes with descending aortic endovascular stent grafting were very encouraging when compared with those of a well-matched surgical cohort. However, at 2 years' follow-up, there is an incidence of endoleaks and reinterventions associated with endovascular versus open surgical repair. Continued vigilant surveillance of patients treated with an endograft is important.

Although more than 10 years have passed since the first endovascular treatment of a descending thoracic aortic aneurysm (DTA), there has been only one comparative report of open versus endovascular repair.[1]

The prevalence of thoracic aortic aneurysms has appeared to triple in the 2 most recent decades.[2,3] Whether this represents an increase in the elderly proportion of our population, improved diagnostic capabilities, or an actual increase in incidence

Abbreviations and Acronyms
AAA = abdominal aortic aneurysm
ASA = American Society of Anesthesiologists
CT = computed tomography
CVA = cerebrovascular accident
DTA = descending thoracic aortic aneurysm

is unknown. Thoracic aortic aneurysms are now estimated to affect 10 of every 100,000 elderly adults, with 30% to 40% of these being DTAs. Although open repair has become a refined surgical procedure, with extracorporeal circulation for peripheral organ preservation and multiple techniques for spinal cord protection, it has nevertheless been associated with significant mortality, and the cumulative morbidity in this aged population frequently exceeds 50% to 70%.[4,5] The highly invasive nature of this procedure necessitates a prolonged recovery period, with return to well-being frequently delayed 4 to 6 months postoperatively. Additionally, high-risk patients previously denied surgical repair might become surgical candidates if a less-invasive endovascular option were possible. For the above reasons, an endovascular repair is highly attractive.

This report documents the results of the phase II W. L. Gore Tag Multi-Center Trial comparing the results of endovascular repair with those of an open surgical control group. The results of this study comprise the data presented for US Food and Drug Administration panel review.

Materials and Methods

Between September 1999 and May 2001, 140 patients with DTA who met strict inclusion and exclusion criteria (Table 1) were enrolled in a phase II study at 17 sites (Appendix A) across the United States and treated with a Gore TAG Endograft. An open surgical control cohort of 94 patients was identified by screening recent surgical cases for eligibility, beginning with the most recent procedure and working sequentially backward. Patients receiving the endograft were also required to be candidates for open surgical repair. DTAs deemed suitable for repair included all fusiform aneurysms greater than twice the diameter of the normal adjacent aorta or any saccular aneurysm of sufficient severity to warrant surgical repair. All patients were required to have at least a 2-cm length of nonaneurysmal aorta distal to the left carotid artery and proximal to the celiac axis. Specifically excluded were mycotic aneurysms, unstable patients with rupture, acute or chronic dissections, and all patients with a connective tissue disorder.

Endograft diameters ranged from 26 to 40 mm, allowing use in aortas 23 to 37 mm in diameter, with a 7% to 18% oversizing of diameter determined from the computed tomographic (CT) scan. Follow-up visits including plain radiographs and CT scans were scheduled at 1, 6, and 12 months and annually thereafter.

All adverse events were reported by individual sites. These events were then verified by independent study monitors. Finally, a clinical events committee consisting of 4 endovascular and cardiothoracic physicians reviewed selected adverse events to ensure consistent adverse event classification. This report includes data collected through the 24-month follow-up visit. Follow-up through 5 years continues.

Table 1. Inclusion and exclusion criteria for endograft and open surgical cohorts

Inclusion criteria
- Fusiform descending thoracic aortic aneurysm at least twice the size of the normal adjacent aorta or saccular aneurysm
- Life expectancy >2 y
- Surgical candidate
- Male or infertile female >21 years old

Specific to TAG device cohort
- Inner aortic diameter of 23-37 mm adjacent to aneurysm
- Lack of significant thrombus or calcification in landing zones
- Minimum 2 cm of normal thoracic aorta proximal and distal to aneurysm
- Aortic taper of no more than 4 mm or ability to treat with more than one graft

Specific to open surgical cohort
- Descending aorta must be clampable distal to the left carotid artery, and distal anastomosis must be performed proximal to the celiac axis.

Exclusion criteria
- Mycotic aneurysm
- Hemodynamically unstable ruptured aneurysm
- Major operation (other than planned subclavian to carotid transposition or bypass) within 30 d
- MI or CVA within 6 wk
- Creatinine >2.0 mg/dL
- Connective tissue disorder
- Acute or chronic aortic dissection
- Planned occlusion of carotid or celiac arteries
- Documented drug abuse within 6 mo
- Participation in another investigational device or drug study within 1 y

MI, Myocardial infarction; *CVA*, cerebrovascular accident.

Surgical Treatment

Open surgical repair was accomplished by means of the routine in place at each member institution. The use of spinal drainage was variable. The majority (82%) of the open surgical control group was composed of subjects with procedure dates ranging from January 1998 through May 2001. The remaining had a procedure date earlier than 1998.

Patients in the endograft group were treated with the Gore TAG endoprosthesis, a flexible polytetrafluoroethylene graft with a nitinol exoskeleton. The device is inserted through a 20F, 22F, or 24F (OD) sheath, depending on device size. Iliac and femoral vessel size and degree of calcification were assessed preoperatively on CT scan to allow for smooth introduction of the device. Procedures were performed in surgical or radiology suites with fluoroscopic control, usually after achievement of general anesthesia.

In June 2001, the sponsor received reports of fractures in the longitudinal support spine. Based on this, the device was voluntarily withdrawn from the market in November 2001. Of the 19 reported fractures, only 1 required further intervention. The device was modified and subsequently tested in a confirmatory study between January and June 2004.

Statistical Methods

Selected baseline characteristics are compared between the endograft and surgical control cohorts. Continuous variables are summarized by using means, standard deviations, and percentiles (eg, medians). Comparison of continuous variables between groups uses 2-sample *t* tests. Where normality does not hold, a Wilcoxon rank sum test was used. Categoric variables are summarized by using counts and percentages. Between-group comparisons for these variables use the Fisher exact test. Survival analyses use the Kaplan–Meier method. All tests use a 5% 2-tailed type I error rate. No statistical adjustment for multiple testing has been made, and *P* values are considered exploratory. Because of the limits of data collection in the open surgical control group, a large percentage of the aortic morphology characteristics are missing. For these variables, the distributions are presented, but no tests of significance are indicated.

Results

Patient Characteristics

One hundred forty patients satisfied all inclusion and exclusion criteria (Table 1) between September 1999 and May 2001 and were enrolled to receive the TAG thoracic endoprosthesis at 17 centers (endograft group). At the same centers, the open surgical control cohort enrolled 94 patients.

Subject demographics, previous medical history, and pretreatment aortic morphology are listed in (Tables E1 and E2). There was no significant difference in age, sex, body mass index, aneurysm size or aneurysm length, previous coronary artery disease, congestive heart failure, stroke, peripheral arterial disease, or American Society of Anesthesiologists class in the endograft group versus the open surgical control cohort. There was a higher incidence of symptomatic aneurysms (38% vs 21%, $P = .007$) in the surgical control group. The aortic diameter immediately proximal (30.8 ± 4.1 vs 33.9 ± 8.3 mm) and distal (29.8 ± 3.7 vs 33.6 ± 7.1 mm) to the aneurysm was larger in the surgical control group.

Historical Versus Concurrent Open Surgical Control Subjects

Of the 94 patients enrolled in the open surgical control cohort, 44 were concurrent control subjects and 50 were historically and retrospectively acquired by selecting the most recent surgical patients in reverse chronologic order. Appendices E1 through E3 list a comparison of the concurrent versus historical control subjects. The only significant difference between the 2 groups was that the concurrent cohort were older than the historical cohort (mean age, 71 ± 9.3 vs 65.7 ± 10.3 years; $P = .01$).

Early Outcome

Procedural data. One hundred thirty-seven of the 140 patients scheduled to receive the endograft had successful deployment of the device. Three patients could not get the device because of ileofemoral access limitations. During the initial procedure, 234 devices were implanted in the 137 subjects of the endograft cohort: 61 (45%) patients received 1 device, 60 (44%) patients received 2 devices, 11 (8%) patients received 3 devices, and 5 (4%) patients received 4 devices. The most common diameter size of graft implanted was 34 mm (44%). Grafts larger than 34 mm comprised 35% of the population, and grafts smaller than 34 mm made up only 21%. Fifteen percent of patients (n = 21) had a conduit constructed to insert the device. Of these, 62% had iliac conduits, 14% had infrarenal aortic conduits, 14% had femoral conduits, and 10% were not documented. One patient had an external iliac rupture requiring placement of wall stents. The left subclavian artery was covered in 28 (20%) cases. All patients had a left carotid to subclavian bypass before the subclavian artery was covered. There were no patients who had preparatory carotid-subclavian bypass and then failed to undergo endografting.

Patients in the open surgical control cohort underwent left thoracotomy and aneurysm resection with interposition graft placement. Seventy-eight percent of aneurysms were repaired with extracorporeal circulatory support. Spinal drainage was variable as per the protocol at each member institution.

Perioperative mortality. Operative mortality defined as death within 30 days of the procedure or on the same hospital admission was 2.1% (n = 3) in the endograft group versus 11.7% (n = 11) in the open surgical control cohort ($P = .004$).

ENDOGRAFT COHORT. One early death was due to a postoperative stroke, and another was due to a cardiac event on postoperative day 15. The third death occurred nearly 7 months after the procedure from septic complications after a long, complicated in-hospital course after respiratory arrest. At autopsy, this patient had an aortoesophageal fistula.

OPEN SURGICAL CONTROL COHORT. The causes of death among the 11 perioperative mortalities in the open surgical cohort were respiratory failure (n = 6), cerebrovascular accident (CVA; n = 3), cardiac arrest (n = 1), and aortoesophageal fistula (n = 1).

Spinal cord ischemia. The total spinal cord ischemia incidence was 2.9% (4/140) in the endograft cohort versus 13.8% (13/94) in the open surgical control group ($P = .003$). In the endograft cohort 3 patients had paraplegia, and 1 had paraparesis. Of the 4 patients, 2 were fully recovered, and 2 had residual weakness. Three of the 4 cases of spinal

Table 2. Early postoperative outcomes

	Endovascular group	Open surgical group	*P* value
Mortality: 30 d or in hospital	2.1% (n = 3)	11.7% (n = 11)	.004
Respiratory failure*	4%	20%	<.001
Postoperative MI	0%	1%	.40
Renal failure†	1%	13%	.01
Wound infection/dehiscence	4%	11%	.07
GI complication (ileus, bowel ischemia, or bowel obstruction)	2%	6%	.16
Peripheral vascular complications‡	14%	4%	.015
Neurologic complications			
CVA	4% (n = 5)	4% (n = 4)	1.00
Paraplegia/paraparesis	3% (n = 4)	14% (n = 13)	.003
Mean ICU length of stay (d)	2.6 ± 14.6	5.2 ± 7.2	<.001
Mean length of hospital stay (d)	7.4 ± 17.7	14.4 ± 12.8	<.001

MI, Myocardial infarction; *GI*, gastrointestinal; *CVA*, cerebrovascular accident; *ICU*, intensive care unit. *Mechanical ventilation for longer than 24 hours postoperatively or need for reintubation. †Thirty percent or greater increase in baseline creatinine level. ‡Includes embolism, thrombosis, and vascular trauma.

ischemia were diagnosed soon after surgical intervention, and 1 was clearly related to ileofemoral bleeding and postprocedural hypotension. Two of 4 patients with spinal cord ischemia had previous abdominal aortic aneurysm (AAAs) treated with aortobifemoral bypass. Forty-two (30%) patients in the endograft group had previous infrarenal aortic replacement, resulting in a 4.8% rate of spinal cord events in the AAA and endograft subgroup. Paraplegia in patients without previous abdominal aortic replacement was 2% ($P = .36$, not significant). Three of 4 patients with spinal ischemia had multiple devices placed for a full left subclavian to celiac DTA pavement.

In the open surgical control cohort, of the 13 cases of spinal ischemia, 8 were paraplegia, and 5 were paraparesis. Six of the 8 cases of paraplegia resulted in death.

CVAs. CVA was defined as a new neurologic deficit (lasting >24 hours), as determined by CT/magnetic resonance imaging, clinical examination, or both. The incidence of CVA was similar in the endograft and open surgical control cohorts (3.6% [n = 5] vs 4.3% [n = 4], $P = .58$). Four of the 5 patients with a stroke in the endograft group had coverage of the left subclavian artery with the endograft for a proximal aneurysm and a carotid-subclavian bypass. Of 28 patients undergoing subclavian coverage, 4 (14%) had a CVA compared with 1% of patients in whom the graft terminated distal to the subclavian artery ($P < .001$).

Other perioperative complications. For other perioperative complications, see Table 2. The endovascular cohort had a lower incidence of respiratory failure and renal failure and a higher incidence of peripheral vascular complications. The mean length of intensive care unit stay (2.6 ± 14.6 vs 5.2 ± 7.2 days, $P < .001$) and total length of hospital stay (7.4 ± 17.7 vs 14.4 ± 12.8 days, $P < .001$) were significantly shorter in the endovascular cohort.

Follow-up

The mean duration of follow-up was 25.8 months (range, 0.13-53.5 months) in the endograft cohort and 24.9 months (range, 0.48-66.3 months) in the open surgical control cohort. Through 2 years, follow-up was complete in 86% and 77%, respectively, of the endograft and open surgical control cohorts. The remaining patients either withdrew, were lost to follow-up, or missed the 24-month follow-up appointment.

Overall survival. Kaplan–Meier analysis reveals an estimated 2-year survival of 78% and 76% ($P = .48$) in the endograft group and the open surgical control cohort, respectively (Figure 1).

Endoleaks. At the 30-day follow-up visit, 11% (12/110) of patients had an endoleak documented. At 1 year of follow-up, there were no new endoleaks that had not been documented at 30 days, and there were 6 ongoing endoleaks, for an incidence at 1 year of 6% (6/103). At the 2-year follow-up visit, there were 2 new endoleaks present and 5 ongoing endoleaks, for a 2-year incidence of 9% (7/80). Of the diagnosed endoleaks, 60% were type I, 12% were type II, 12% were type III, and 16% were of an indeterminate cause.

Aneurysm regression. There were no cases of aneurysm rupture in either cohort. At 2 years' follow-up, 45% (30/67) of the endovascular patients had a decrease in aneurysm size of 5 mm or greater, 42% (28/67) had no change (<5 mm), and 13% (9/67) had an increase in aneurysm size of 5 mm or greater.

Stent migration and fracture. There was 1 case of stent migration diagnosed by 2 years' follow-up, with no clinical sequelae. Stent fractures were identified in 19 (14%) patients through 2 years after treatment. Only one fracture was

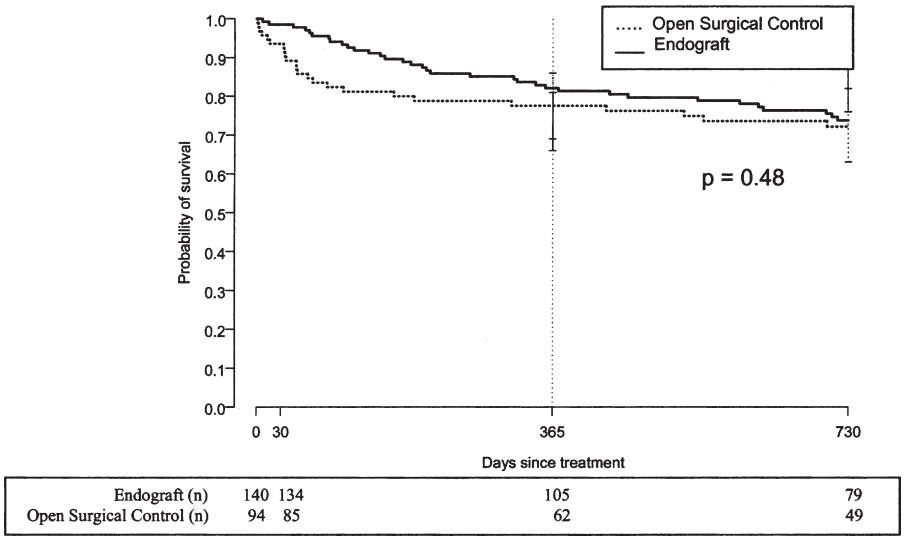

Figure 1. Kaplan–Meier survival curves for the endograft group versus the open surgical control cohort.

associated with a clinical sequela, an endoleak that was successfully treated with an additional endograft.

Aortic reoperation. There were 3 reinterventions in the endograft group through 2 years after treatment. Two of the 3 reinterventions involved a repeat endovascular procedure with no operative mortality. One patient in the endovascular group was operated on with an open surgical technique 73 days after the initial procedure, when he presented with recurrent infections and positive blood cultures, and a presumptive diagnosis of an infected stent graft was made. Intraoperatively, the patient was found to have an aortoesophageal fistula that was treated with graft removal and extra-anatomic bypass. Postoperatively, this patient had multisystem organ failure and died.

Discussion

Treatment of thoracic aneurysmal disease is a challenging entity. Nonoperative survival is dismal.[6,7] Although surgical resection is durable, perioperative mortality and morbidity are variable. Earlier reports suggest a perioperative mortality of 12% to 44%, depending on comorbid conditions[8,9] and urgency of operation. More recent literature from expert high-volume centers report mortality in the range of 4% to 9% and incidence of paraplegia of less than 3% for isolated DTAs.[10,11]

As "minimally invasive" endovascular treatment has become technically feasible, initially with homemade first-generation grafts and now with commercially available thoracic endografts, it is being offered as an attractive treatment option to patients. Thoracic aortic endografts have been used with early success in small- to moderate-sized, retrospective, single-center series.[12-17]

We previously reported on the initial results of the Gore TAG Endograft.[18] The present report includes a more in-depth and complete analysis of the initial data and, importantly, a comparative analysis with an open surgical control cohort. To our knowledge, this is the largest comparison of endovascular versus open surgical repair of DTA.

Although the open surgical control cohort in this study was not randomized, it is robust for several reasons:

1. It is a multicenter control cohort and not a single-surgeon experience, thus making it more applicable to results expected across the country.
2. The control group was subject to the same inclusion and exclusion criteria as the endograft group (apart from anatomic indications that make endograft repair technically unfeasible).
3. Forty-seven percent of the control group was concurrently enrolled. All demographic data and past medical history were compared between the concurrent and historical groups to try and ensure that the historical control subjects (53%) were "similar" patients to the concurrent group. The only variable that was significantly different was that the concurrent cohort was older than the historical cohort (mean age, 71 $\pm$ 9.3 vs 65.7 $\pm$ 10.3 years; $P = .01$).
4. The endograft and open surgical control groups were of similar age and comorbid status. The higher incidence of symptomatic aneurysms (38% vs 21%, $P = .007$) in the open surgical control group likely reflects the fact that endografts were not available in a timely fashion for these patients. The aortic diameter immediately proximal and distal to the aneurysm was larger in the open surgical control group. Aortic diameter greater than 37 mm in a proximal or distal landing zone was a contraindication to endovascular intervention because of the limitations of device size.

Specific Findings of This Study

Perioperative results were generally improved in the endograft cohort versus the open surgical control cohort. Perioperative mortality was lower (2.1% vs 11.7%, $P = .004$). Lengths of intensive care unit and hospital stay were shorter. Postoperative respiratory and renal failure was lower in the endograft cohort.

The incidence of spinal cord ischemia was 2.9% (n = 4) in the endograft cohort versus 13.8% (n = 13, $P = .003$) in the open surgical control cohort. Theoretical reasons for lower spinal cord ischemia rates with an endovascular technique include no period of aortic crossclamping; fewer periods of perioperative hypotension associated with blood loss or hemodynamic shifts; the ability to tolerate higher mean arterial pressures because there are no suture lines; earlier awakening from general anesthesia, which allows one to tailor blood pressure management to neurologic examination; and slow thrombosis of the aneurysmal sac versus acute occlusion of critical vessels in surgical patients. The 2.9% incidence of spinal ischemia in the endovascular cohort (and 4.8% rate in patients with a previous AAA) is consistent with DTA endograft rates published in the literature of 3.6% to 6.5%.[13-22]

Importantly, 2 of the 4 patients with spinal ischemia in this study made a full recovery. Spinal drainage was not consistently implemented in this series. Guidelines[19] for the use of cerebrospinal fluid drainage and somatosensory evoked potentials monitoring during DTA endograft procedures have been recently presented, and the recommendations for the use of these adjuncts are as follows: (1) patients with previous AAA repair and (2) full (subclavian artery to celiac axis) coverage of the descending aorta (DTA Extent C[23]).

The 13.8% incidence of spinal ischemia in the open surgical control cohort is higher than the recent best single-center published results of approximately 3%.[9,10] This study's higher rate might be due to several factors:

1. The surgeons performing the open procedures had various surgical backgrounds.
2. It is a multicenter trial, with variable volume of thoracic aortic surgery performed in each center.
3. This study excluded patients with aneurysmal dilatation of type B dissections, who are thought to have a reduced paraplegia rate in comparison with those with atherosclerotic aneurysms.[24]
4. There was a variable use of spinal cord protection techniques, as per surgeon preference.

For the above listed reasons, we believe this higher incidence of 13.8% probably better reflects the expected incidence throughout the country for all comers.

The incidence of CVA during the first 30 days was similar in both cohorts (3.6% for the endograft group vs 4.3% for the open repair group). However, strokes in the endovascular group clustered around those patients who underwent coverage of the left subclavian artery. This result might reflect a greater proximal atherosclerotic burden at the aortic arch and brachiocephalic vessels in patients who require coverage of the subclavian artery. Patients who require endografting at the level of the arch might need different adjunctive operative strategies in the future to decrease the incidence of CVA in this group.

Follow-up

Open surgical repair is known to be a durable and long-lasting operation with a very low incidence of reoperation, although the actual incidence of reoperation is unknown. Causes of reoperation with open repair include graft infection, pseudoaneurysm formation at suture lines, ongoing aortic aneurysmal disease, intercostal patch aneurysms, and the dreaded complication of aortic-enteric fistulas. The durability and long-term complication rate of thoracic endografts are yet to be determined. Recent publications have cautioned that late aortic complications do develop with thoracic endografts.[25,26] What is not clear is the acceptable frequency of reintervention with endografting. Reinterventions in the endograft group might be for reasons similar to those for open surgical repair or a new set of complications. In this study there were no reinterventions required in the open surgical group and 3 reinterventions in the endovascular group through 2 years of follow-up. As our knowledge of the nuances of endografting increases, along with technical improvements in graft design and delivery, it will be of interest to see whether the late complication rate will decrease.

There was no difference in overall survival between the 2 cohorts through 2 years of follow-up (Figure 1). There was one late aneurysm-related death (graft infection requiring conversion to open repair) in the endovascular group, and no late aneurysm-related deaths in the open surgical group. There were no aortic ruptures in either population.

Limitations of the Study

The main limitation of the study is that the groups were not randomized. In addition, 2-year follow-up was available in only 77% of the open surgical control cohort and 86% of the endograft cohort. DTAs are a slow-growing and indolent process. Until we have long-term follow-up data, it is difficult to know whether endografting has improved the natural history of these patients. This study was limited to a low-risk group of patients with isolated DTAs, and results might not be applicable to other pathologies for which endografting can be used.

Conclusions

In this study of 140 patients treated with endografts versus 94 open surgical control patients, we conclude the following:

1. Perioperative mortality and morbidity were significantly less with an endovascular approach.
2. Spinal cord ischemia was significantly less in the endograft cohort.
3. The overall stroke rate was similar in both the endograft and open surgical control cohorts.
4. The reintervention rate and continued presence of complications, such as endoleaks, is higher in the endograft group. The presence of endoleaks can lead to future complications, but their significance is still unclear.
5. There was no survival advantage associated with either strategy after 2 years of follow-up.

As technology continues to improve and we as surgeons progress along the learning curve, the long-term complications of endografting might or might not be mitigated. Therefore continued vigilant surveillance of patients treated with endovascular repair is important.

References

1. Najibi S, Terramani TT, Weiss VJ, et al. Endoluminal versus open treatment of descending thoracic aortic aneurysms. *J Vasc Surg*. 2002; 36:732-7.
2. Clouse WD, Hallett JW, Schaff HV, Gayari MM, Ilstrup DM, Melton LJ. Improved prognosis of thoracic aortic aneurysms. A population-based study. *JAMA*. 1998;280:1926-9.
3. Bickerstaff LK, Pairolero PC, Hollier LH. Thoracic aortic aneurysms: a population based study. *Surgery*. 1982;92:1103-8.
4. Hamerlijnck RP, Rutsaert RR, De Geest R, Brutel de la Riviere A, Defauw JJ, Vermeulen FE. Surgical correction of descending thoracic aortic aneurysms under simple aortic cross-clamping. *J Vasc Surg*. 1989;9:568-73.
5. Huynh TTT, Miller CC, Estrera AE, Porat EE, Safi HJ. Thoracoabdominal and descending thoracic aortic aneurysm surgery in patients aged 79 years or older. *J Vasc Surg*. 2002;36:469-75.
6. Davies RR, Goldstein LJ, Coady MA, Tittle SL, Rizzo JA, Kopf GS, et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size. *Ann Thorac Surg*. 2002;73:17-28.
7. Elefteriades JA. Natural history of thoracic aortic aneurysms: indications for surgery, and surgical versus nonsurgical risks. *Ann Thorac Surg*. 2002;74(suppl):S1877-80.
8. Kouchoukos NT, Dougenis D. Surgery of the thoracic aorta. *N Engl J Med*. 1997;336:1876-88.
9. Crawford ES, Hess KR, Cohen ES, Coselli JS, Safi HJ. Ruptured aneurysm of the descending thoracic and thoracoabdominal aorta. Analysis according to size and treatment. *Ann Surg*. 1991;213:417-26.
10. Coselli JS, LeMaire SA, Conklin LD, Adams GJ. Left heart bypass during descending thoracic aortic aneurysm repair does not reduce the incidence of paraplegia. *Ann Thorac Surg*. 2004;77:1298-303.
11. Estrera AL, Rubenstein FS, Miller CC, et al. Descending thoracic aortic aneurysm: surgical approach and treatment using the adjuncts cerebrovascular fluid drainage and distal aortic perfusion. *Ann Thorac Surg*. 2001;72:481-6.
12. Ramaiah V, Rodriguez-Lopez J, Diethrich EB. Endografting of the thoracic aorta: single center experience with technical considerations. *J Card Surg*. 2003;18:444-54.
13. Ehrlich M, Grabenwoeger M, Cartes-Zumelzu F, et al. Endovascular stent graft repair for aneurysms on the descending thoracic aorta. *Ann Thorac Surg*. 1998;66:19-25.
14. Ellozy SH, Carroccio A, Minor M, et al. Challenges of endovascular tube graft repair of thoracic aortic aneurysm: midterm follow up and lessons learned. *J Vasc Surg*. 2003;38:676-83.
15. Lepore V, Lonn L, Delle M, et al. Treatment of descending thoracic aneurysms by endovascular stent grafting. *J Card Surg*. 2003;18:436-43.
16. Inoue K, Iwase T, Sato M, et al. Clinical application of transluminal endovascular graft placement for aortic aneurysms. *Ann Thorac Surg*. 1997;63:522-8.
17. Criado FJ, Clark NS, Barnatan MF. Stent graft repair in the aortic arch and descending thoracic aorta: a 4-year experience. *J Vasc Surg*. 2002;36:1121-8.
18. Makaroun MS, Dillavou ED, Kee ST, et al. 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.
19. Cheung AT, Pochettino A, McGarvery ML, et al. Strategies to manage paraplegia risk after endovascular stent repair of descending thoracic aortic aneurysms. *Ann Thorac Surg*. 2005;80:1280-8.
20. Gravereaux EC, Faries PL, Burks JA, et al. Risk of spinal cord ischemia after endograft repair of thoracic aortic aneurysms. *J Vasc Surg*. 2001;34:997-1003.
21. Mitchell RS, Miller DC, Dake MD. Stent graft repair of thoracic aortic aneurysms. *Semin Vasc Surg*. 1997;10:257-71.
22. Leurs LJ, Bell R, Degrieck Y, et al. Endovascular treatment of thoracic aortic diseases: combined experience from the EUROSTAR and United Kingdom Thoracic Endograft registries. *J Vasc Surg*. 2004;40: 670-80.
23. Bavaria JE. Invited Commentary on: descending thoracic aortic aneurysm: surgical approach and treatment using the adjuncts cerebrospinal fluid drainage and distal aortic perfusion. *Ann Thorac Surg*. 2001;72: 486.
24. Coselli JS, LeMaire SA, de Figueiredo LP, Kirby RP. Paraplegia after thoracoabdominal aortic aneurysm repair: is dissection a risk factor? *Ann Thorac Surg*. 1997;63:28-35.
25. Doss M, Wood JP, Balzer J, et al. Emergency endovascular interventions for acute thoracic aortic rupture: four year follow up. *J Thorac Cardiovasc Surg*. 2005;129:645-51.
26. Demers P, Miller DC, Mitchell RS, et al. Midterm results of endovascular repair of descending thoracic aortic aneurysms with first generation stent grafts. *J Thorac Cardiovasc Surg*. 2004;127:664-73.

Discussion

Dr Joseph S. Coselli *(Houston, Tex)*. Scott, congratulations on an outstanding presentation and for bringing this information from a multicenter clinical trial to us. I believe that your report will be a seminal investigation into an evolving technology that stands to forever alter the way we therapeutically approach descending thoracic aortic pathology. Although I believe that aortic stenting is here to stay, we must shun the pressure of industry-driven initiatives and pursue good science and good medicine with, of course, industry support. We need to shoulder the responsibility of being the patient's primary advocate.

You and the coauthors importantly infer the problems associated with a nonrandomized multicenter trial. I continue to have problems with the control group. Most of the control subjects, 53%, were historically and retrospectively acquired. Not all institutions contributed patients to this cohort. Data on aortic characteristics were unavailable in many of the open reconstruction control patients. Proximal and distal aortic diameters and aneurysm length, for example, were reported in less than 35% of this cohort; even aneurysm diameter data were missing in 10%. The data support that the open repair group did not end up with more advanced disease because they had larger aortic diameters and were more likely to be symptomatic.

After endograft repair, 17% of the patients had expansion of their aneurysm of greater than 1/2 cm over 2 years. Considering the need for life-long monitoring after endograft repair, especially in the setting of a research protocol, incomplete 2-year follow-up of 14% is concerning. Do you think that 2 years really is enough?

The extent of aorta replaced and the location (ie, proximal or distal or the entire descending thoracic aorta) are related to morbidity, primarily stroke and paraplegia. Were comparisons made between these 2 groups accounts for these?

Seventy-eight percent of the open repairs had extracorporeal support. Was this need for cardiopulmonary bypass and hypothermic circulatory arrest suggestive of extensive disease and associated with increased morbidity or mortality?

One patient died of an aortoesophageal fistula. What do you believe the nature of that particular fistula was, how did it occur, and what lessons do you think were learned?

The incidence of paraplegia and paraparesis after endovascular repair was 5% in patients with prior AAA repair. What was the incidence of paraplegia or paraparesis after previous AAA repair in the open group?

The incidence of stroke in the treatment group was 4%. With the need to traverse the aortic arch with a stiff wire and, for proximal aneurysms, even advance the deployment device into the arch, do you and the authors see a need for transesophageal echocardiography to evaluate the arch for mobile atherosclerotic disease before implementation of the device?

Using a 30% increase in baseline creatinine level to define "renal dysfunction" as a cutoff point captures patients with clinically insignificant increases. Therefore what was the incidence of postoperative dialysis in the 2 groups?

The study excluded patients with recent myocardial infarction or recent stroke, renal insufficiency, and respiratory insufficiency, and interestingly enough, these are the patients in particular who might benefit the most from endovascular repair.

Once again, congratulations.

Dr Mitchell. Thank you, Dr Coselli. I will try and answer as many of your questions as I can remember.

First, is 2 years enough? Absolutely not. We do not know the exact hazard function, but I think these complications will be ongoing, hopefully decreasing with time, but we do not know that. Therefore these patients will require lifelong follow-up.

The question of the control group has been an energized discussion. It is not the best control group, we admit that, but it is the only one that we had, and I think all of us are aware of the difficulties in trying to get a very aware public to enroll in a randomized trial.

I cannot answer about the incidence of paraplegia in the open and control group as relates to previous abdominal aneurysm repairs.

As relates to cardiopulmonary bypass, that was used primarily as an adjunct for each individual site in their routine repair of descending thoracic aneurysms, and, in theory, circulatory arrest and hypothermia were not supposed to be used for these patient populations because they were supposed to be clampable.

Finally, we do agree that transesophageal echocardiography is an invaluable adjunct for the anesthetic management of these patients to look at the arch. There is no question that any manipulation in the arch does predispose this patient population to stroke, even as little as a stiff guide wire, and certainly, having to put your sheath through the arch increases that risk even more.

Dr Coselli. Scott, one quick follow-up. You and your group at Stanford have the longest and probably the largest experience with this particular technology. Would you just comment on your thoughts regarding connective tissue disease, particularly Marfan's syndrome, applying this approach?

Dr Mitchell. I think you noticed that patients with Marfan's syndrome were specifically excluded from this, and I would continue to urge that to be an exclusion with the exception of replacing some remnant aorta between 2 Dacron segments. Therefore if you are connecting Dacron to Dacron, I think that would be okay. Otherwise, I would be very pessimistic that this would be effective.

Dr Michael C. Maxwell *(Mesa, Ariz)*. The Achilles' heel of endoluminal grafting is the endoleak, and I noticed you had a 15% incidence. I talked to other investigators for this graft in the thoracic position, and endoleak, particularly type I, seems to be more common than it is in the abdominal position. Is that something you have also noticed, and if so, is it something that can be watched, unlike in the abdominal position, or does it have to be taken care of when identified?

Dr Mitchell. No, I think type I endoleaks should be managed on detection. Type II and III endoleaks perhaps can be followed, looking at aneurysmal sac size as a surrogate. But we have been very aggressive about trying to eliminate all type I endoleaks.

There was just one question I forgot to answer for Dr Coselli, that there were some aneurysm enlargements that were unassociated with endoleaks. This is the so-called endotension, which did occur with the old graft because it was thinner. The new revised graft has a stouter polytetrafluoroethylene column, and we do not think that these transmembrane leaks will occur, and hopefully this phenomenon will go away.

Appendix A. Subject enrollment by investigative site

Site name	Principal investigator	Endovascular (n = 140) Enrolled, n (%)	Surgical control (n = 94) Enrolled, n (%)	Total enrolled
University of Pennsylvania	Joseph Bavaria, MD	14 (10)	16 (17)	30
UCSF-Stanford Health Care	R. Scott Mitchell, MD Steven Kee, MD	18 (13)	9 (10)	27
Emory University	Elliot Chaikof, MD	15 (11)	10 (11)	25
Washington University	Gregorio Sicard, MD	14 (10)	10 (11)	24
University of Michigan	David Williams, MD	13 (9)	10 (11)	23
University of Pittsburgh	Michel Makaroun, MD	12 (9)	6 (6)	18
Massachusetts General	Richard Cambria, MD	11 (8)	6 (6)	17
Cleveland Clinic Foundation	Roy Greenberg, MD	10 (7)	4 (4)	14
Mt Sinai School of Medicine	Larry Hollier, MD	8 (6)	3 (3)	11
University of Florida	James Caridi, MD	7 (5)	3 (3)	10
Mayo Clinic Rochester	Kenton Zehr, MD	2 (1)	7 (7)	9
Northwestern University	Mark Marasch, MD	6 (4)	2 (2)	8
Hartford Hospital	Micheal Hallisey, MD	2 (1)	4 (4)	6
Johns Hopkins Hospital	Lawrence Hoffman, MD	2 (1)	3 (3)	5
Baylor College of Medicine	Joseph Coselli, MD	4 (3)	0	4
Medical University of South Carolina	Renan Uflatker, MD	1 (1)	1 (1)	2
Yale University	John Elefteriades, MD	1 (1)	0	1

Appendix E1. Historical versus concurrent control subjects: Demographics

Variable	Concurrent (n = 44)	Historical (n = 50)	*P* value, concurrent vs historical
Sex, n (%)			1.00
Female	22 (50)	24 (48)	
Male	22 (50)	26 (52)	
Age (y)			
n	44	50	
Mean ± SD	71.0 ± 9.3	65.7 ± 10.3	.011
Percentiles (25th, median, 75th)	66.0, 73.0, 77.0	60.0, 68.0, 72.0	
Range (min, max)	47.0, 88.0	35.0, 84.0	
Ethnicity, n (%)			.69
Asian	1 (2)	1 (2)	
Black	5 (11)	4 (8)	
White	36 (82)	45 (90)	
Hispanic	1 (2)	0 (0)	
Other	1 (2)	0 (0)	
Weight (kg)			
n	44	50	
Mean ± SD	79.5 ± 18.5	76.0 ± 16.7	.33
Percentiles (25th, median, 75th)	64.8, 78.3, 90.6	63.2, 76.1, 86.3	
Range (min, max)	53.0, 136.0	44.4, 114.4	
Height (cm)			
n	44	50	
Mean ± SD	169.8 ± 11.8	169.2 ± 11.0	.81
Percentiles (25th, median, 75th)	160.5, 169.0, 178.0	160.0, 170.0, 178.0	
Range (min, max)	145.0, 196.0	140.0, 188.0	
BMI (kg/m^2)			
n	44	50	
Mean ± SD	27.4 ± 4.9	26.4 ± 5.1	.34
Percentiles (25th, median, 75th)	23.9, 27.1, 29.8	22.5, 25.9, 29.2	
Range (min, max)	19.5, 39.6	18.6, 40.2	

SD, Standard deviation; *BMI*, body mass index.

Appendix E2. Historical versus concurrent control subjects: Pretreatment medical history

Variable	Concurrent (n = 44), n (%)	Historical (n = 50), n (%)	*P* value, concurrent vs historical
Coronary artery disease	15 (34)	19 (38)	.83
Cardiac arrhythmia	14 (32)	15 (30)	1.00
Valvular heart disease	4 (9)	5 (10)	1.00
Congestive heart failure	4 (9)	5 (10)	1.00
Stroke	3 (7)	6 (12)	.49
Peripheral arterial occlusive disease (infrainguinal)	5 (11)	5 (10)	1.00
Prior vascular intervention	23 (52)	29 (58)	.68
Thromboembolic event	1 (2)	5 (10)	.21
Aneurysm, symptomatic	16 (36)	20 (40)	.83
Aneurysm of traumatic origin	2 (5)	3 (8)	.18
Other concomitant aneurysm(s)	9 (20)	17 (34)	.17
COPD	18 (41)	18 (36)	.67
History of smoking (current or past)	37 (84)	40 (80)	.79
Renal dialysis	0 (0)	0 (0)	.79
Paraplegia	0 (0)	0 (0)	.79
Erectile dysfunction	5 (23)	0 (0)	.033
Hepatic dysfunction	1 (2)	0 (0)	.47
Bleeding disorder(s)	2 (5)	3 (6)	1.00
Cancer	4 (9)	8 (16)	.37
NYHA classification			1.00
I	10 (43)	12 (48)	
II	7 (30)	7 (28)	
III	6 (26)	6 (24)	
N/A	21 (48)	25 (50)	
ASA classification			.89
I	1 (2)	1 (2)	
II	3 (7)	2 (4)	
III	24 (55)	27 (54)	
IV	16 (36)	20 (40)	
Summary of mean SVS risk scores			
n	44	50	
Mean ± SD	0.6 ± 0.4	0.6 ± 0.3	.74
Percentiles (25th, median, 75th)	0.4, 0.5, 0.8	0.4, 0.5, 0.8	
Range (min, max)	0, 2	0, 2	

COPD, Chronic obstructive pulmonary disease; *NYHA*, New York Heart Association; *ASA*, American Association of Anesthesiologists; *SVS*, Society of Vascular Surgery.

Appendix E3. Historic versus concurrent control subjects: Pretreatment aortic morphology

Variable	Concurrent (n = 44)	Historical (n = 50)
Aorta diameter (mm)		
Immediately proximal to aneurysm		
n	14	20
Mean ± SD	34.5 ± 11.2	33.5 ± 5.9
Range (min, max)	22.0, 60.0	21.0, 45.0
Immediately distal to aneurysm		
n	12	21
Mean ± SD	32.4 ± 5.3	34.2 ± 8.0
Range (min, max)	21.0, 42.2	18.0, 55.0
Aneurysm diameter (mm)		
n	41	44
Mean ± SD	62.8 ± 18.4	63.7 ± 13.1
Range (min, max)	11.4, 113.0	33.0, 100.0
Aneurysm length (cm)		
n	14	18
Mean ± SD	11.0 ± 5.7	10.7 ± 5.5

SD, Standard deviation.

Table E1. Baseline characteristics

Variable	Endovascular TAG device (n = 140), n (%)	Surgical control (n = 94), n (%)	*P* value*
Demographics			
Mean age (y), mean ± SD	70.5 ± 10.4	68.2 ± 10.2	.096
Male sex, n (%)	80 (57)	48 (51)	.42
Mean BMI (kg/m^2), mean ± SD	26.4 ± 4.7	26.9 ± 5.0	.44
Medical history			
Coronary artery disease	69 (49)	34 (36)	.060
Congestive heart failure	13 (9)	9 (10)	1.00
Stroke	14 (10)	9 (10)	1.00
Peripheral arterial occlusive disease (infrainguinal)	22 (16)	10 (11)	.33
Prior vascular intervention	63 (45)	52 (55)	.14
Aneurysm, symptomatic	30 (21)	36 (38)	.007
Other concomitant aneurysm(s)	39 (28)	26 (28)	1.00
COPD	56 (40)	36 (38)	.89
History of smoking (current or past)	117 (84)	77 (82)	.86
Renal dialysis	2 (1)	0 (0)	.52
Paraplegia	1 (1)	0 (0)	1.00
Cancer	27 (19)	12 (13)	.21

Note: Denominators are the number of patients with known observations for each specific baseline variable. *BMI*, Body mass index. **P* values are based on the Fisher exact test for categoric variables and a 2-sample *t* test for continuous variables.

Table E2. Pretreatment aortic morphology

Variable	TAG device (n = 140)	Surgical control (n = 94)
Aorta diameter (mm)		
Immediately proximal to aneurysm		
N	140	134
Mean ± SD	30.8 ± 4.1	33.9 ± 8.3
Range (min, max)	22.0, 40.0	21.0, 60.0
Immediately distal to aneurysm		
N	140	33
Mean ± SD	29.8 ± 3.7	33.6 ± 7.1
Range (min, max)	20.0, 38.0	18.0, 55.0
Aneurysm diameter (mm)		
N	140	85
Mean ± SD	63.7 ± 15.2	63.2 ± 15.8
Range (min, max)	20.0, 110.0	11.4, 113.0
Aneurysm length (cm)		
N	140	32
Mean ± SD	10.2 ± 6.2	10.9 ± 5.5
Range (min, max)	1.0, 35.0	2.0, 22.0
Proximal length neck (cm)		
N	136	29
Mean ± SD	6.3 ± 3.9	5.8 ± 5.6
Distal neck length (cm)		
N	139	22
Mean ± SD	8.0 ± 5.5	7.0 ± 5.2

SD, Standard deviation.