SURGERY FOR ADULT CARDIOVASCULAR DISEASE

THE “FIRST GENERATION” OF ENDOVASCULAR STENT-GRAFTS FOR PATIENTS WITH ANEURYSMS OF THE DESCENDING THORACIC AORTA

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Objective: Our goal was to determine whether endovascular stent-grafting is feasible and effective for patients with aneurysms of the descending thoracic aorta. **Methods:** Starting in July 1992, we conducted a prospective, uncontrolled clinical trial in 103 patients (mean age 69 years [range 34-89 years]) who underwent endovascular treatment of aneurysms of the descending thoracic aorta using a custom-fabricated, self-expanding stent-graft device. Follow-up was 100% complete and averaged 22 months. Sixty-two patients (60%) were judged not to be reasonable candidates for a conventional “open” surgical procedure. **Results:** Complete thrombosis of the aneurysm was ultimately achieved in 86 (83%) patients. The early mortality rate was $9\% \pm 3\%$ ($\pm 70\%$ CL). Multivariable analysis revealed that myocardial infarction or stroke was linked with a higher likelihood of early death ($P = .001$). Early serious complications included paraplegia in $3\% \pm 2\%$ and stroke in $7\% \pm 3\%$. Actuarial survival estimates at 1 year and 2 years were $81\% \pm 4\%$ and $73\% \pm 5\%$ (± 1 SE), respectively; being judged not to be a surgical candidate portended a higher probability of death ($P = .003$). According to the intent-to-treat principle, “treatment failure” (including all late sudden unexplained deaths) occurred in 38 patients; $53\% \pm 10\%$ of patients were free from treatment failure at 3.7 years. Stent-graft related complications occurred commonly and were linked with several anatomic, technical, and patient-related risk factors. **Conclusions:** This 5-year clinical trial involving use of a “first generation” device indicates that endovascular stent-grafting of descending thoracic aortic aneurysms is feasible with acceptable medium-term results. More refined, commercially developed devices available today offer less traumatic and more precise stent-graft deployment; these major technical advantages, coupled with important lessons we have learned over time and better patient selection, should be associated with more salutary clinical results in the future. (J Thorac Cardiovasc Surg 1998;116:689-704)

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The traditional treatment strategy for patients with aneurysm of the descending thoracic aorta is surgical intervention with graft interposition.¹ Since the first reports of successful operative repair more than 45 years ago,^{2,3} substantial clinical advances in the surgical management of these patients has led to a decline in the operative mortality risk to the range of 5% to 20%.⁴⁻⁶ Nevertheless, open surgical graft replacement of aneurysms is still associated with substantial morbidity and mortality for a patient population that is frequently elderly and debilitated with other serious medical problems. In addition, the

Fig 1. Histogram illustrating the number of endovascular stent-grafts carried out per year to repair descending thoracic aortic aneurysms. Also shown, for perspective, is the number of conventional open surgical graft replacement procedures each year for patients with descending thoracic aortic aneurysms on our service. S-G, Stent-graft.

operative mortality rate is nearly 50% in patients requiring emergency operative treatment.⁴⁻⁷

The endoluminal placement of stent-grafts is a new, less invasive alternative technique for repair of aortic aneurysms that was initially introduced by Dotter⁸ in 1969. Subsequently, other investigators experimented with stent-grafts in animal models of abdominal aortic aneurysms.⁹⁻¹² The first clinical use of stent-grafts for repair of abdominal aortic aneurysms was reported by Parodi, Palmaz, and Barone¹³ in 1991. Since then, endovascular stent-graft placement for the treatment of aneurysms in the abdominal aorta, descending thoracic aorta, subclavian or iliac arteries, as well as arteriovenous fistulas, has been clinically investigated in a number of centers.¹⁴⁻²¹ The initial results of these feasibility studies suggest that this approach is an attractive alternative to open surgical repair that may potentially reduce the operative risk, hospital stay, and procedural cost in selected patients.

In July 1992, we initiated this investigation into the feasibility of stent-graft treatment of patients with aneurysms of the descending thoracic aorta. This report summarizes our 5-year experience with an admittedly primitive "first generation," custom-made, self-expanding prosthesis in 103 patients, expands on previous reports^{16,21} conveying early results, and documents the many complications that arose during a mean follow-up period of 1.8 years (maximum 5.3 years). This report also summarizes clinical and anatomic factors that predicted adverse outcomes and thereby illuminates where the future challenges lie and focuses the direction of future research in this field.

Methods

From July 1992 through October 1997, 103 patients in whose treatment a cardiovascular surgeon from the

Department of Cardiothoracic Surgery was involved underwent transluminal endovascular stent-graft placement for repair of thoracic aortic aneurysms at Stanford University Medical Center. The procedures were performed with the use of an investigational protocol approved by the Institutional Review Board of Stanford University Medical Center. Informed consent was obtained from every patient before the procedure. All patients underwent chest radiography, spiral computed tomographic (CT) scanning with 3-dimensional vascular reconstruction, and arteriography before stent placement and at intervals afterward, as defined by protocol. Spiral CT and arteriography using a graduated catheter assessed the lengths and diameters of the aneurysm and its proximal and distal necks, or so-called "landing zones." In addition, these studies identified the relationship between the aneurysm and significant aortic branches, especially the left subclavian artery and the celiac axis. Abdominal and pelvic arteriography was used to determine the diameter and tortuosity of the abdominal aorta and the iliac and femoral arteries through which the stent-graft is delivered. Patient evaluation and selection was a true collaborative judgment effort involving both cardiovascular surgeons and interventional radiologists.

Ideally, the proximal and distal aneurysm necks (or "landing zones") should be longer than 20 mm and cylindrical. If the distance between the origin of the left subclavian artery and the proximal aspect of the aneurysm was insufficient, the left subclavian artery was moved to create a longer proximal neck. The procedures were performed in the operating theater or angiographic suite with the patient under general anesthesia. In the operating room, the procedure was guided by means of a portable digital C-arm image intensifier system and transesophageal echocardiography. In the angiographic suite, a stationary angiography unit capable of rapid-sequence computerized imaging and road map guidance was used. The implantations were performed by coordinated teams of interventional radiologists and cardiovascular surgeons working in concert.

The endovascular stent-graft was custom-fabricated on the basis of each patient's pathologic anatomy and composed of

Table I. Preoperative clinical characteristics of 103 patients with descending thoracic aortic aneurysms who were treated with transluminal endovascular stent-grafts

Characteristic	Value	Percent
Sex (No. of patients)		
Male	73	71
Female	30	29
Age (y)		
Mean	76 ± 12	
Range	34-89	
Operative status (No. of patients)		
Emergency	16	16
Nonemergency	87	84
Other medical problems (No. of patients)		
Angina		
Stable	17	17
Unstable	5	5
MI	10	10
CAD	31	30
Congestive heart failure	14	14
Renal failure*		
Mild-moderate	13	13
Severe, no dialysis	5	5
Severe, dialysis dependent	2	2
Hypertension	74	72
Diabetes mellitus	11	11
Chronic pulmonary disease	32	31
Stroke	11	11
Cigarette smoking	63	62
Previous cardiac, thoracic aortic, or vascular surgery	46	45
Previous thoracotomy (all reasons)	46	45
NYHA functional classification		
NYHA I	40	39
NYHA II	41	40
NYHA III	21	20
NYHA IV	1	1
Not open (thoracotomy) surgical candidate	62	60

MI, Myocardial infarction; CAD, coronary artery disease; NYHA, New York Heart Association.

*Mild-moderate renal failure was defined as a creatinine concentration of 1.3 to 2.3 mg/dL (115-203 μmol/L) and severe renal failure as a serum creatinine concentration of 2.4 mg/dL (212 μmol/L).

individual self-expanding Z-shaped stainless steel (2.5 cm long) stent bodies (Cook, Inc, Bloomington, Ind) interconnected by 2-0 polypropylene suture that ran circumferentially through the eyelets at the apex of each Z-bend. This cylindrical metallic endoskeleton was covered with uncrimped woven polyester graft material (Cooley Veri-Soft, Meadox Medicals/Boston Scientific Corporation, Oakland, NJ). The graft was attached to the stent at its ends by a series of 5-0 interrupted polypropylene sutures. The diameter of the stent-graft was oversized by 10% to 15% compared with the aortic neck diameter measured on CT to provide residual radial force and an effective friction seal against the aortic wall after stent-graft deployment. The device was sterilized with ethylene oxide.

Table II. Preoperative aneurysm characteristics

	No. of patients
Etiology	
Atherosclerotic/degenerative	64
Aortic dissection	8
Trauma	8
Penetrating ulcer	10
Other*	13
Size of aneurysm (mm, mean ± 1 SD)	
Main aneurysm (n = 103)	
Aneurysm length	86 ± 50 (range 10-220)
Aneurysm diameter	62 ± 13 (range 40-110)
Proximal neck diameter	31.9 ± 4.0 (range 20-45)
Distal neck diameter	31.7 ± 3.8 (range 22-40)
Secondary aneurysm (n = 6)	
Aneurysm length	80 ± 58 (range 35-190)
Aneurysm diameter	68 ± 24 (range 50-110)
Proximal neck diameter	30.3 ± 6.0 (range 24-38)
Distal neck diameter	29.7 ± 6.4 (range 22-38)

*Other: Mycotic (active in 1, healed in 1), anastomotic (n = 8), intramural hematoma (n = 3).

Patients were positioned in various degrees of the right lateral decubitus position on a radiolucent table and draped sterilely for emergency left thoracotomy in case serious complications ensued. The groins, pelvis, abdomen, and flanks were also prepared and draped to gain suitable femoral, iliac, or retroperitoneal abdominal aortic access, as determined individually for each patient. A double-lumen endobronchial tube, transesophageal echocardiography probe, and pulmonary artery catheter were introduced in most cases, and a cell salvage system and cardiopulmonary bypass (CPB) standby were available. With the patient under general anesthesia, the exposure and aortic access were performed by the surgeon, and the radiologist deployed the stent-graft after coordinated discussions took place concerning optimal positioning of the device. The details of the technique of inserting the stent-graft and postprocedural patient management have been described previously.^{16,21}

These selected 103 patients who received endovascular stent-grafts to treat a descending thoracic aortic aneurysm had a heterogeneous mix of aneurysm causes and risk factors. Table I lists the baseline clinical characteristics of the patients, and Fig 1 depicts the use of endovascular stent-grafts over time. Sixty-two of the 103 patients (60%) undergoing stent-grafting were judged by one of the surgeons not to be reasonable operative candidates for conventional "open" surgical repair because of a variety of pulmonary, cardiac, or other medical problems. During this same time interval, 186 other patients underwent open surgical graft replacement of descending thoracic aneurysms on our service; thus 36% ± 3% of patients treated in this time frame received an endovascular stent-graft. Twelve patients (12%) had stent-grafts placed for management of acute aortic rupture. A previously repaired or coexisting abdominal aortic aneurysm was identified in 47 (46%). Twenty-one additional patients

Table III. Location of proximal and distal aortic stent-graft "landing zones" in 103 patients

	Proximal stent-graft landing zone	Distal stent-graft landing zone
Distal arch*	8	3
Proximal third, descending aorta	71	15
Mid third, descending aorta	19	31
Distal third, descending aorta	4	40
Supraceliac abdominal aorta	0	13

*Distal arch was defined as the aortic segment from the left common carotid artery to 20 mm distal to the left subclavian artery.

had a stent-graft repair in which other surgeons at our institution were involved ($n = 16$) or at other institutions ($n = 5$) by one of us (M.D.D.) and were excluded from this analysis.

The preoperative aneurysm data, including etiology and size characteristics, are detailed in Table II. In 6 patients, a second (separate) descending thoracic aortic aneurysm was treated at the same procedure with an additional stent-graft. The average interval from stent-graft insertion to hospital discharge was 8 days (± 6.5 days [± 1 SD]; range 0-42 days). The median stay was 6 days, with one quarter of patients discharged on or before postoperative day 4 and one quarter on or after day 10. Some of this inpatient time was dedicated to completion of the protocol-mandated postprocedure imaging studies and optimizing renal function. The mean time spent in the intensive care unit was approximately 3 days.

The average stent-graft diameter was 3.5 cm (range 2.4-4.5 cm), and the average device length was 10.5 cm (range 4.5-22.5 cm). The femoral artery was the most common site for insertion (60 patients, or 58%), and the iliac artery was used in 9 cases (9%). Two patients undergoing simultaneous repair of an ascending aorta and arch aortic aneurysm or coronary artery bypass grafting had the stent-graft inserted through the transverse aortic arch in an antegrade manner with CPB and profound hypothermic circulatory arrest. A retroperitoneal approach to the infrarenal abdominal aorta was necessary to introduce the device in 31 patients (30%); access was gained through the native aorta in 10 of these patients, a previously implanted abdominal aortic tube graft in 2, and a concomitantly inserted aortic graft in 19 (18%). The endovascular procedure required placement of more than 1 stent-graft unit to treat the aneurysm adequately in 34 patients, or 33%. Twenty-six patients had 2 stent-grafts coaxially placed, 7 patients required deployment of 3 devices, and in 1 patient it was necessary to insert 4 devices. In 3 patients, the endovascular procedure for a descending thoracic aortic aneurysm was performed after previous surgical placement of an elephant trunk as part of arch aneurysm repair, that is, the dangling elephant trunk graft functioned as the proximal landing zone. The details of this combined approach have been previously reported.²² In 1 of these patients, the stent-graft was not actually deployed. In this case, the delivery sheath could not be

advanced into an appropriate position within the elephant trunk; further efforts to introduce the delivery sheath culminated in rupture of the proximal descending thoracic aorta, which mandated immediate surgical conversion.

In 8 patients, the proximal neck between the left subclavian artery and the aneurysm was judged to be too short or otherwise inadequate to allow a competent seal between the graft material and the aortic wall. In 3 patients the left subclavian artery was transposed to the left common carotid artery, and in 5 patients a left common carotid artery-left subclavian bypass graft was implanted to create a suitable proximal stent-graft landing zone before stent-graft deployment. The proximal and distal locations of the stent-graft landing zones are detailed in Table III. Stent-graft coverage of the intercostal arteries from the level of the ninth through the twelfth thoracic vertebral bodies was necessary in 18 patients. Coverage of more than 1 pair of intercostal arteries within this segment, which is traditionally deemed critical for a spinal cord perfusion, occurred in 44 cases.

The follow-up protocol included arteriography and spiral CT imaging either before hospital discharge or within 5 days of the initial procedure. Subsequently, spiral CT scans were performed 6 months after stent-graft placement and yearly thereafter. Patients underwent follow-up arteriography only if they had symptoms or CT evidence of a perigraft leak (endoleak) or other stent-graft abnormality.

Definitions and statistical analysis. Early mortality and morbidity included events occurring both in the hospital and after discharge, if they happened within 30 days. Patient information was compiled from retrospective chart review and by contacting the patient or family members or the treating physicians. Cause of death was determined from examination of death certificates, medical records, and, when available, autopsy reports. Current follow-up status was obtained between October 1997 and March 1998 and was 100% complete; follow-up averaged 1.8 ± 1.3 years, with a maximum of 5.3 years.

Many of the preoperative and intraoperative parameters inspected in the risk analyses are listed in Tables I to III. Additional variables were also entered and are listed in Appendix 1. When necessary, the hazard associated with each possibility was individually determined, and then the variables were ranked in logical order and entered into the multivariable Cox model analyses. Clinical outcome events of interest were defined thus: (1) treatment failure 1—all early deaths, late deaths related to complications arising in the treated aortic segment, endoleak, and need for subsequent intervention (catheter-based or surgical) in the treated aorta; (2) treatment failure 2—all of the above plus any sudden, unexplained late deaths. Nonfatal and fatal complications were subdivided into stent-graft-related and non-stent-graft-related complications; individual patients could have both types of nonfatal complications but could have only 1 type of fatal complication. To characterize how well the endovascular stent-graft worked, the following therapeutic definitions were used: (1) primary success, complete thrombosis of the aneurysm at the time of the first postoperative CT

Table IV. Parameters identified in the multivariable Cox model analysis to be associated with a higher probability of sustaining selected early and late post-operative adverse outcomes

	β	P value	e^{β}
Early death ($P = .0011$)			
MI	+2.1	.04	8.1
Stroke	+2.2	.01	9.1
No. of S-G units deployed	-6.1	.0003	.0022
Etiology	+1.2	.02	3.3
Treatment failure 1 ($P = .0155$)			
(Earlier) operative year	-.32	.017	.73
Treatment failure 2 ($P = .006$)			
(No) CAD	-.86	.034	.42
(Earlier) operative year	-.36	.007	.70
All deaths ($P = .003$)			
Not open surgical candidate	+2.0	.006	7.6
CPB	+2.9	.02	17.4
Without CPB covariate ($P = .003$)			
Not open surgical candidate	+1.7	.008	5.2
Late deaths ($P = .0000$)			
(Larger) aneurysm diameter	+.06	.006	1.1
(Larger) S-G proximal LZ diameter	+.2	.035	1.2
CPB	+3.0	.0207	19.5
(Older) age	+.10	.0107	1.1
Without CPB covariate ($P = .0001$)			
(Larger) aneurysm diameter	+.06	.0024	1.07
(Larger) S-G proximal LZ diameter	+.21	.023	1.2
(Older) age	+.08	.022	1.1
Nonfatal S-G complications ($P = .0007$)			
(More proximal) distal LZ site	-.38	.03	.68
Move LSCA	+.40	.03	1.5
Elephant trunk	+2.2	.006	8.9
(Earlier) operative year	-.28	.039	.75
Surgical access site	+.41	.0018	1.5
Without elephant trunk covariate ($P = .0035$)			
Move LSCA	+.44	.011	1.6
(Earlier) operative year	-.30	.032	.74
Surgical access site	+.31	.014	1.4
Nonfatal complications ($P = .0000$)			
Angina	-1.01	.025	.36
MI	+2.9	.0000	17.2
Surgical access site	+.80	.0001	2.2
Etiology	+1.08	.016	3.0
Fatal S-G complications ($P = .0009$)			
Stroke	+3.4	.054	30.9
(Larger) distal S-G LZ diameter	+.66	.025	1.9
More distal) S-G proximal LZ	+.76	.006	2.1

scan; (2) secondary success, endoleak with subsequent thrombosis; (3) unsuccessful, no secondary intervention attempted; (4) unsuccessful, persistent endoleak after secondary intervention; (5) endoleak with spontaneous thrombosis; and (6) aorta and/or stent-graft replaced or excluded. SPSS for Windows (version 6.1, SPSS Inc, Chicago, Ill) was used for all statistics. Continuous data are reported as mean $\pm$ 1 standard deviation (SD). Important ratios, for example, operative mortality rate, are reported with 70% confidence

Table IV. Continued

	β	P value	e^{β}
Fatal complications ($P = .0007$)			
Stroke	+2.3	.009	10.0
(More proximal) S-G distal LZ	-.75	.039	.47
CPB	+5.6	.0005	269
Etiology	+1.7	.007	5.5
Without CPB covariate ($P = .0013$)			
Stroke	+1.6	.02	4.9
Coil embolization of endoleak ($P = .0000$)			
MI	+2.1	.024	8.0
(Shorter) aneurysm length	-.043	.005	.96
Move LSCA	+1.4	.0000	4.0
Repeat stent-graft ($P = .0124$)			
Surgical access site	+1.3	.009	3.6
Surgical stent-graft removal ($P = .0001$)			
(Smaller) S-G distal diameter	-.18	.008	.84

S-G, Endovascular stent-graft; CAD, coronary artery disease; LZ, landing zone of stent-graft; CPB, cardiopulmonary bypass; LSCA, left subclavian artery; MI, myocardial infarction. The β coefficient is from the multivariable equation and its sign indicates whether the relationship with the hazard of the event is direct or indirect. The e^{β} term reflects relative risk; a value of 1.0 corresponds to no change in probability of sustaining the event risk, values greater than 1 indicate increased risk, and those less than 1 imply less risk. These estimates of relative risk only apply strictly to dichotomous covariates and need to be interpreted with caution in the case of categorical or continuous covariates.

limits ($\pm 70\%$ CL). The Cutler-Ederer life table method was used to generate actuarial estimates, which are reported as ± 1 standard error (SE). In the multivariable Cox proportional hazards model, statistical significance was inferred if $P < .03$, and the β coefficients from the equation are reported. The magnitude of the clinical impact of predictive covariates on outcome events in the Cox model is reported as an indicator of relative risk, e^{β} , but this can only be strictly interpreted for dichotomous covariates. If certain covariates made the model unstable or had tremendous clinical impact, then the model was re-run without this variable, and the results are reported separately.

Results

The results were compiled and analyzed according to the "intent-to-treat" principle. As such, the 1 patient described above who actually did not receive an endovascular stent-graft is included in this analysis; she is considered to have had a stent-graft-related death and treatment failure.

Early mortality. Including this patient (death attributed to aneurysm rupture), the operative mortality rate was $9\% \pm 3\%$. The other causes of early death were stroke due to intracerebral hemorrhage in 1, sepsis in 2, multisystem organ failure in 1, pulmonary insufficiency in 1, cancer in 1 (the patient had a contained aortic rupture caused by tumor invasion), hemorrhage in 1, and

Table V. Early postoperative complications and mortality among the 103 patients

	N	Rate (%)	$\pm 70\%$ CL (%)
Early death	9	9	± 3
Paraplegia/paraparesis	3	3	± 2
MI	2	2	± 1
Pulmonary insufficiency ($\pm$ tracheostomy)	12	12	± 3
Stent-graft misdeployment	3	3	± 2
Initial stent-graft endoleak	25	24	± 4
Arterial injury/replacement	4	4	± 2
DVT/venous injury/PE	1	1	± 1
Gut ischemia/infarction	1	1	± 1
Acute renal failure ($\pm$ dialysis)	5	5	± 2
Distal arterial thromboembolism	2	2	± 1
New aortic dissection (proximal)	1	1	± 1
Hemorrhage (local)	5	5	± 2
Hemorrhage (systemic/coagulopathy)	2	2	± 1
Wound infection	3	3	± 2
Other unrelated vascular operation	1	1	± 1
Other unrelated interventional procedure	4	4	± 2

MI, Myocardial infarction; DVT, deep venous thrombosis; PE, pulmonary embolism; 70% CL, 70% confidence limits.

pulmonary embolism in 1 patient. Multivariable Cox model analysis revealed that the presence of a prior myocardial infarction (MI) increased the probability of early death by 8-fold, and stroke increased the risk by 9-fold (see Table IV). In the absence of a remote MI, the 30-day survival estimate was $92\% \pm 3\%$, whereas it was $79\% \pm 3\%$ if the patient had had an MI; similarly, without a preoperative stroke it was $93\% \pm 3\%$ versus $71\% \pm 4\%$. Additionally, the need to use fewer stent-graft units to exclude the aneurysm was associated with a higher risk. Aneurysm etiology also influenced the early death hazard: The "other etiology" category carried the highest risk of death ($3/13 = 23\%$), whereas it was 10% in the 10 patients with a penetrating ulcer and 8% in the 64 patients with an atherosclerotic/degenerative aneurysm.

Early postoperative morbidity. Major early postoperative complications included stroke in 7 patients ($7\% \pm 3\%$), paraplegia/paraparesis in 3 ($3\% \pm 2\%$), MI in 2 ($2\% \pm 1\%$), and respiratory insufficiency in 12 ($12\% \pm 3\%$). Table V lists the incidence of these and other early morbid events, which occurred commonly. Surgical conversion was necessary in only 1 case. In 3 cases the stent-graft was deployed in the incorrect location, termed *stent-graft misdeployment*. One patient had a new, limited proximal aortic dissection.

Separate multivariable analyses were performed for stroke, paraplegia, MI, and respiratory failure: The only

significant, independent determinant of stroke was the use of CPB (β coefficient = 2.9, $P = .01$, $e^{\beta} = 17.9$); this strong influence of CPB was due to the fact that only 2 patients required CPB for insertion of the stent-graft through the arch, and 1 of them had a mild cerebellar stroke, yielding a 50% incidence. When the analysis was run without the covariate CPB, no covariates emerged as significant predictors of stroke. As one would expect, the only predictor of MI was the presence of coronary artery disease (CAD). The risk of paraplegia was higher according to surgical access site, with an incidence of 7% in those who required access via the abdominal aorta (2 of 29 patients). The third case of paraplegia occurred in the sole patient who had the stent-graft inserted via an old aorto-femoral bypass graft limb. Even though not statistically significant in the multivariable analysis, the paraplegia rate was $11\% \pm 7\%$ (2/19) in those patients who underwent simultaneous surgical repair of abdominal aortic aneurysm and stent-grafting of the descending thoracic aortic aneurysm compared with $1\% \pm 1\%$ for the 84 who did not; the third individual who had paraplegia had undergone repair of an ascending aortic aneurysm previously. Therefore the paraplegia/paraparesis rate was $6\% \pm 4\%$ among the 47 patients who either had had an ascending aortic aneurysm repair before or had a coexistent ascending aortic aneurysm (3/47) versus 0% (0/56) for the others. Finally, the risk of pulmonary insufficiency was linked to the presence of CAD ($e^{\beta} = 3.5$); furthermore, if the patient was judged not to be a suitable candidate for an open operation, the risk of respiratory failure was 6-fold higher ($e^{\beta} = 6.1$).

Early or late stent-graft endoleaks. An early endoleak was documented by angiography or CT scanning in $24\% \pm 4\%$ of cases, mostly during the first year of our experience. Primary success was achieved initially in 75 patients, or $73\% \pm 5\%$. Secondary success was accomplished in 11 other cases; therefore complete aneurysm thrombosis was eventually documented in 86 patients (or $84\% \pm 4\%$). An early or late stent-graft endoleak was not treated in 7 patients and persisted after coil embolization in 2 others. Three individuals had endoleaks that spontaneously thrombosed. At the time of this follow-up, 5 stent-grafts had been surgically removed or excluded.

Overall and late survival. There were 14 late deaths (MI in 2, documented ventricular tachyarrhythmia in 1, sudden/unexplained in 6, stroke in 2 [thromboembolic in 1 case], aneurysm rupture in 2, and respiratory failure in 1), in addition to the 9 early deaths. When all patients are considered, the actuarial survival estimates were $86\% \pm 4\%$ at 6 months, $81\% \pm 4\%$ at 1 year, and

73% $\pm$ 5% after 2 years (Fig 2). As shown in Table IV, the only significant, independent determinants of all deaths were “not open surgical candidate” ($e^{\beta} = 7.6$) and CPB ($e^{\beta} = 17.4$). To examine whether other predictors would emerge if the dominating covariate CPB (used in only 2 patients) was eliminated, re-running the Cox model without CPB yielded only “not open surgical candidate” ($e^{\beta} = 5.2$), that is, the risk of death was 5-fold higher. If an individual had been judged not to be a suitable candidate for an open operation, the survival estimate was 60% $\pm$ 7% at 2 years compared with 91% $\pm$ 5% at 1 year (Fig 2, B) for the others.

Focusing just on the 14 late deaths, the actuarial survival estimates were 89% $\pm$ 4% at 1 year and 80% $\pm$ 5% at 2 years. Interestingly, analyzing late deaths by means of the Cox multivariable model revealed 3 other determinants of late death in addition to CPB—larger aneurysm diameter, larger proximal stent-graft landing zone diameter, and older age. As was seen for all deaths, the influence of CPB, necessary in only 2 cases, was disproportionately large ($e^{\beta} = 19.5$); if CPB was excluded from the analysis, the same 3 other covariates remained, the goodness of fit was not substantially different, and the relative risks were similar. These other 3 predictors (larger aneurysm diameter, larger stent-graft proximal landing zone diameter, and older age), however, had only modest effects on the risk of late death, raising the hazard by only 10% to 20% (see Table IV).

Treatment failure. As noted earlier, 2 definitions of treatment failure were used. Thirty-six patients sustained treatment failure 1, and the only multivariable determinant of treatment failure 1 was earlier operative year ($e^{\beta} = 0.73$). Since sudden deaths could also be due to aneurysm rupture, all sudden, unexplained late deaths were considered in the definition of treatment failure 2, which added 2 patients.

Inasmuch as the numbers of patients sustaining treatment failures 1 and 2 were similar, only treatment failure 2 will be emphasized. Fig 3 illustrates the actuarial freedom from treatment failure 2 for all 103 patients. Most of these adverse events occurred early (average 84 days). The estimate of patients free from treatment failure 2 was 68% $\pm$ 5% at 30 days, 65% $\pm$ 5% at 1 year, and 53% $\pm$ 10% at 3.7 years. The significant, independent predictors of treatment failure 2 were the absence of CAD ($e^{\beta} = 0.42$) and earlier operative year ($e^{\beta} = 0.70$). The actuarial estimate of freedom from treatment failure 2 for patients without CAD was 53% $\pm$ 7% at 18 months compared with 63% $\pm$ 14% at 3.5 years for those with CAD. The influence of earlier operative year was more modest, reflecting only a 30% increased hazard.

Fig. 2. A, Actuarial curve depicting overall survival estimates for all 103 patients. B, Survival estimates according to whether the patient was judged not to be a reasonable candidate for open repair. SE, Standard error of the estimate.

Late complications. Complications were categorized according to whether they were directly related to the stent-graft or the operative procedure and whether they were fatal or nonfatal. Early and late complications were considered together in this analysis, and patients could have more than 1 complication. The predictors of need for coil embolization of stent-graft endoleaks, repeat stent-grafting, and surgical removal or bypass of the original stent-graft were also examined, as they are indicative of the durability of the stent-graft procedure.

Nonfatal stent-graft complications. Forty-nine nonfatal stent-graft complications occurred in 39 patients, including stent-graft misdeployment ($n = 3$), stent-graft removal ($n = 1$), initial endoleak ($n = 25$), late endoleak ($n = 1$), new aortic dissection ($n = 1$), arterial injury/replacement ($n = 2$), stroke ($n = 2$), paraplegia/paraparesis ($n = 3$), distal arterial thromboem-

Fig 3. Actuarial estimate of the freedom from treatment failure 2 (see text for definition) for all 103 patients. *SE*, Standard error of the estimate; *TF#2*, treatment failure 2.

bolism ($n = 1$), gut ischemia/infarction ($n = 1$), infection ($n = 2$), other aortic reoperations ($n = 3$), and catheter-based interventional procedures ($n = 4$), including stenting of the left subclavian artery. The most common complication was initial endoleak, and this was confined for the most part to the early phase of this series during our initial learning experience. On the other hand, no patient had stent-graft migration or distal embolization. Most of these stent-graft complications occurred during the first postoperative year; in actuarial terms, $61\% \pm 5\%$ of patients were free from a nonfatal stent-graft complication at 1.2 years, as were $52\% \pm 9\%$ at 3.7 years (Fig 4, A). Table IV shows that the significant, independent determinants of nonfatal stent-graft complication were more proximal distal stent-graft landing zone ($e^{\beta} = 0.68$), bypassing the left subclavian artery ($e^{\beta} = 1.5$, or a 50% increase in risk), use of an elephant trunk graft for the proximal landing zone ($e^{\beta} = 8.9$), (earlier) operative year ($e^{\beta} = 0.75$, a 25% higher risk), and more difficult surgical access sites ($e^{\beta} = 1.5$, or a 50% higher risk). Inasmuch as only 3 patients underwent attempted insertion of the stent-graft into an elephant trunk graft, the multivariable analysis was re-run without this covariate; the other 3 determinants remained (see Table IV). If the distal stent-graft landing zone was in the proximal descending aorta, for example, the shortest stent-grafts, only $17\% \pm 13\%$ of these 15 patients were free from a nonfatal stent-graft complication at 6 months, compared with 50% to 69% of patients in whom the distal landing zone was located more distally (Fig 4, B). As illus-

trated in Fig 4, C, the 5 patients who required a left subclavian artery–left carotid artery bypass graft had an estimate of freedom from a nonfatal stent-graft complication of only $20\% \pm 18\%$ at 6 months, whereas it was 100% free for the 3 patients who underwent carotid artery–left subclavian artery transposition and $53\% \pm 10\%$ at 3.5 years for the 95 individuals who did not require the left subclavian artery to be moved. Subdivided according to access site, these complications were seen less frequently in those who required native femoral arterial access ($19/60 = 32\%$); the incidence of nonfatal stent-graft complications was 41% in patients requiring access via the abdominal aorta and 56% ($5/9$) in those with iliac artery access.

Nonfatal complications. Twenty-four patients had a total of 31 nonfatal complications that were not directly related to the stent-graft. These included a new (distal) aortic dissection ($n = 1$), stroke ($n = 1$), deep venous thrombosis or pulmonary embolism ($n = 1$), distal arterial thromboembolism ($n = 1$), gut ischemia/infarction ($n = 1$), MI ($n = 2$), renal failure ($n = 5$), excessive local or systemic bleeding ($n = 5$), wound infection ($n = 1$), pulmonary failure ($n = 6$), tracheostomy ($n = 3$), unrelated aortic reoperation ($n = 3$), and other catheter intervention ($n = 1$). The life table estimate of freedom from a nonfatal complication was $72\% \pm 6\%$ at 2.8 years. Table IV lists the 4 covariates that had an impact on the risk of sustaining a nonfatal complication: angina, MI, more difficult surgical access site, and etiology. The presence of a preoperative MI markedly influenced the probability of a non-

Fig 4. **A**, Incidence of nonfatal stent-graft-related complications among all 103 patients. **B**, Nonfatal stent-graft complications as a function of the location of the distal stent-graft landing zone. **C**, Nonfatal stent-graft complications subdivided on the basis of manipulation of the left subclavian artery. *SE*, Standard error of the estimate; *S-G*, stent-graft; *Abd Ao*, abdominal aorta; *DsThAo*, descending thoracic aorta; *LSCA*, left subclavian artery; *LCCA*, left common carotid artery.

fatal complication: MI was associated with a 17-fold increase in hazard; similarly, the absence of angina was linked with a substantially lower risk. Inserting the stent-graft through the native femoral artery was associated with the lowest incidence of nonfatal complications. With respect to cause of the aneurysm, the highest rates of nonfatal complications were seen in the atherosclerotic/degenerative and aortic dissection categories.

Fatal stent-graft complications. A total of 5 fatal stent-graft complications occurred in 4 patients. These events included rupture of the treated aneurysm ($n = 2$), stent-graft erosion into the esophagus ($n = 1$), arterial injury necessitating graft replacement ($n = 1$), and excessive local bleeding ($n = 1$). Overall, $96\% \pm 2\%$ of patients were free from a fatal stent-graft complication

at 9 months. Multivariate analysis revealed that a preoperative stroke ($e^{\beta} = 30.9$) tremendously increased the likelihood of such a fatal complication. Other predictors that approximately doubled the hazard were larger distal stent-graft landing zone diameter ($e^{\beta} = 1.9$) and more distally located stent-graft proximal landing zone, that is, stent-grafts deployed starting farther down the descending thoracic aorta ($e^{\beta} = 2.1$).

Fatal complications. Nine patients had a total of 12 early or late fatal complications. These serious complications included stroke ($n = 3$), pulmonary embolism ($n = 1$), MI ($n = 1$), renal failure necessitating dialysis ($n = 1$), infection ($n = 1$), excessive local bleeding ($n = 1$), and pulmonary failure ($n = 4$). As seen before, most of these adverse events occurred in the early postoperative period; in actuarial terms, $90\% \pm 3\%$ of patients were

Fig 5. Actuarial incidence of the freedom from various stent-graft interventions, including need for coil embolization, repeat stent-graft insertion, and surgical removal* or exclusion of the initial stent-graft. *SE*, Standard error of the estimate; *S-G*, stent-graft. *The first patient to receive a stent-graft had the device removed at the time of emergency reoperation for contained rupture (previous coarctation repair 20 years before the stent-graft) 62 months later. This event is not indicated on the graph for stent-graft removal because he was the only remaining patient at risk at that time.

estimated to be free from a fatal complication at 9 months. Preoperative stroke increased the risk markedly ($e^{\beta} = 10.0$). It was about 50% higher for patients who required a shorter stent-graft (more proximal stent-graft distal landing zone) ($e^{\beta} = 0.47$), inordinately higher if CPB was necessary, and also higher according to etiology (Table IV). Patients with atherosclerotic or “other etiology” aneurysms (see Table II) had the highest risk of a fatal complication, whereas no patient with a penetrating ulcer, aortic dissection, or a traumatic false aneurysm had one. If the CPB covariate was excluded, the only predictor of a fatal complication was stroke ($e^{\beta} = 4.9$), which increased the chance of a fatal complication nearly 5-fold (see Table IV).

Ten patients required coil embolization for closure of stent-graft endoleaks at an average of 4.2 months after the operation; nine were proximal leaks, and 1 was a distal leak. Three years after the operation $87\% \pm 5\%$ of patients were free from coil embolization (Fig 5). Interestingly, one significant, independent predictor was MI ($e^{\beta} = 8.0$); the other risk factors—shorter aneurysm length ($e^{\beta} = 0.96$) and the need to move the left subclavian artery ($e^{\beta} = 4.0$)—were more intuitively plausible. That is, treating shorter aneurysms and the necessity to “create” a longer proximal stent-graft landing zone portended more endoleaks that necessitated coil embolization.

Only 5 patients ultimately required surgical removal or exclusion of the stent-graft, in 2 of them when the treated thoracic aortic aneurysm had leaked or ruptured. One patient counted here (intent-to-treat principle) never actually received a stent-graft, being the solitary surgical conversion case. One other individual with a chronic type A aortic dissection had enlargement of the arch component and received an extra-anatomic graft from the old ascending aortic graft to the abdominal aorta with exclusion of the entire descending thoracic aorta. (The descending thoracic aorta contained the stent-graft, which had been inserted for rupture of the false lumen.) The actuarial estimate of freedom from stent-graft removal was $86\% \pm 9\%$ at 3.7 years (Fig 5). Unexpectedly, (smaller) stent-graft distal diameter emerged as the sole predictor of a slightly higher probability of requiring subsequent operation to remove the stent-graft ($e^{\beta} = 0.84$, or a 16% higher risk, Table IV).

Fate of the aneurysm. This important question needs to be answered to determine whether stent-graft treatment of descending thoracic aortic aneurysms is efficacious over the long term; on the other hand, obtaining serial CT scans has been difficult, because few of these patients live locally. Nonetheless, in 1996 a limited analysis was performed in 85 of the initial patients who received a stent-graft. Among these, 63

had both a preoperative and an early (<10 days) postoperative CT scan; the average aneurysm diameter before stent-grafting was 59 mm, and it was 60 mm on the early postoperative scan. A subgroup of 23 patients had a subsequent late CT (average 1.1 years) available for comparison. With the use of a threshold of 3-mm increase or decrease to indicate a change in maximal aneurysm diameter, 6 of the 23 (26%) had an increase in size (3 with no demonstrable endoleak leak, 2 of 8 with a treated leak, and 1 of 2 with a persistent leak), 6 (26%) had no change (3 with no leak, 2 of 8 with a treated leak, and 1 of 2 with a persistent leak), and 11 (48%) had a decrease in aneurysm size (7 with no demonstrable endoleak leak, 4 of 8 with a treated leak).

Comparison with results in the entire patient series. During this time period an additional 21 patients received a stent-graft by one of us (M.D.D.), yielding a grand total of 124 patients. Some of these cases were included in previous publications.^{16,21} Among these other 21 patients, 1 additional case of paraplegia, 1 other stroke, and 1 additional early death occurred. Therefore the overall incidence of these adverse events in the entire series of 124 patients was 4 (3% $\pm$ 2%) for paraplegia, 8 (7% $\pm$ 2%) for stroke, and 10 (8% $\pm$ 3%) for early death; these figures are not different from the results reported herein for our selected 103 patients.

Discussion

Thoracic aortic aneurysm is a life-threatening condition with an estimated incidence of approximately 6 cases per 100,000 person-years.²³ Although the condition is relatively uncommon, the number of patients with thoracic aortic aneurysms is increasing, presumably because of the increase in life expectancy of the population and the availability of improved diagnostic modalities. Untreated thoracic aortic aneurysms are likely to expand over time and eventually rupture. Approximately 50% of patients with descending aortic aneurysms are free of symptoms when the initial diagnosis is made because thoracic aortic aneurysms rarely produce symptoms until progressive growth causes compression of adjacent structures or rupture.²⁴ Several reports have estimated that the risk of rupture in patients with thoracic aortic aneurysms ranges from 46% to 74%; therefore the actuarial 5-year survivals are very low, between 9% and 13%.^{23,25} The risk of rupture of thoracic aortic aneurysms mandates consideration of surgical treatment in all individuals who are suitable candidates for operation. Although no precisely defined, objective criteria prevail, operative repair is strongly recommended for any symptomatic aneurysm

or any aneurysm that exceeds 2 times the transverse diameter of an adjacent normal-caliber aortic segment or is 6 cm in diameter or larger. Elective surgical graft replacement is the traditional approach for the treatment of these patients and is currently associated with 5-year survivals ranging from 70% to 79%.^{1,4,26,27}

Transluminally placed endovascular stent-grafts offer an alternative approach to treatment that is potentially less invasive, less expensive, and less risky than standard open operative repair. Theoretically, endovascular repair of thoracic aortic aneurysms with stent-grafts will have lower morbidity and mortality rates than conventional surgical approaches because it avoids thoracotomy and aortic crossclamping. The operative mortality in our series was 9%, which is not lower than the average overall (emergency and elective) risk of 11% reported for surgical repair^{1,4,26-28}; however, in the context of the specific patient population described herein, which included 16% of patients being treated on an emergency basis and 60% not being considered to be reasonable operative candidates, we believe that this early mortality rate is quite acceptable. Although the placement of fewer stent-graft units to exclude the aneurysm was associated with a higher risk of mortality, all 9 patients in this group received a single stent-graft and died of other, unrelated causes (eg, intercerebral hemorrhage, sepsis, multisystem organ failure, pulmonary insufficiency, cancer, hemorrhage, and pulmonary embolism).

The incidence of most serious postoperative morbid events, including paraplegia/paraparesis (3%), MI (2%), and respiratory insufficiency (12%), was approximately what would be expected after open surgical repair. Of note, the incidence of paraplegia with the stent-graft procedure was not substantially different from that documented for open operative treatment.^{1,4,26-28} Conversely, the 7% occurrence of stroke in this series was disappointingly high. Although different causes (excessive anticoagulation, catheter, or surgical manipulations in the aortic arch, carotid, or subclavian arteries) were responsible for the strokes, it is intuitive that insertion of a large (24F-26F), relatively stiff delivery sheath into and across the origins of the brachiocephalic and carotid arteries within a diseased aortic arch is not desirable. Currently, the availability of lower profile, over-the-wire flexible delivery catheters allows stent-graft deployment without an overlying introducer sheath, which should minimize trauma to the aortic arch and the potential for cerebral embolization. Smaller stent-graft delivery systems also require less anticoagulation during the procedure, which may reduce the frequency of bleeding complications, including cerebral hemorrhage.

Since the initial popularization of endovascular stent-graft placement for the treatment of abdominal aortic aneurysms, perigraft leaks (endoleaks) have loomed as the Achilles' heel of this new technique. In the current series, an early endoleak was identified in 24% of cases. This rate appears alarmingly high; however, the majority occurred during the first year of our experience when predictive anatomic criteria for procedural success involving neck length, shape, angulation, and other factors were not yet identified. At that time, we accepted "benign appearing" minimal endoleaks on the initial CT scan, which was a mistake. Similarly, in the early days of our learning curve we did not fully appreciate the need to have back-up stent-graft devices available and, consequently, were not technically prepared to address unanticipated problems resulting from inadvertent errors in sizing and/or imprecise device deployment. Later on, additional stent-graft devices were coaxially deployed in such situations to extend graft coverage and successfully isolate the aneurysm from aortic blood flow.

Transcatheter coil embolization of the perigraft tract(s) causing the endoleak was performed in 10 patients.²⁹ The majority of these procedures were carried out before hospital discharge. In 9 cases, the leak was at the proximal margin of the device; in most it was located adjacent to the left subclavian artery or left common carotid artery, where its obliteration by proximal placement of an additional stent-graft extension was not feasible. Occasionally, balloon expansion of the initial stent-graft was performed before coil embolization. Balloon expansion alone successfully occluded the endoleak in only 1 case. Placement of an uncovered stent across the proximal aspect of the stent-graft and over the left subclavian and/or left common carotid origins was not attempted. One endoleak was located at the distal margin of the stent-graft. However, no cases of retrograde leak into the aneurysm sac from intercostal collateral flow were observed, as have been described in the abdominal aortic stent-graft experience with retrograde flow into the aneurysm sac via lumbar or inferior mesenteric arteries. The predominance of proximal leaks most likely reflects the use of a semi-rigid, segmented device that is incapable of accommodating to the curved anatomy of the distal aortic arch to secure a tight circumferential seal. Aortography and CT scans after coil embolization documented thrombosis of the aneurysm sac in 8 of the 10 cases; however, the long-term efficacy of this transcatheter embolization approach to the management of stent-graft endoleaks remains unknown.³⁰

Survival is of key importance when evaluating any

new alternative therapy for patients with aortic aneurysms. In this series there were 23 deaths. The actuarial survival estimates illustrated in Fig 2 are not dissimilar from those reported in large recent surgical series.^{1,4,26-28} The only relevant determinant of all deaths was the surgical judgment decision that a patient was "not an open surgical candidate." The risk of death was 5-fold higher in this subset, and their survival estimate was 60% at 2 years, compared with 91% at 1 year for those who were deemed appropriate surgical candidates (Fig 2, B). Although this raises the philosophical question of whether endovascular stent-graft therapy should even be offered to patients deemed not to be suitable candidates for an open operation, because of the poor postoperative survival statistics, the actuarial estimates presented in Fig 2 compare favorably with the natural history survival data for patients with thoracic aortic aneurysms.^{7,23}

Treatment failure 2 occurred in 38 patients. Most of these adverse events occurred in the early postoperative period (Fig 3). One of the 2 significant independent predictors of treatment failure was "earlier operative year," which reflects our learning how to use the device and our increasing ability over time to select which patients were best suited for the stent-graft procedure based on individual anatomy, including aneurysm location and neck morphology, aneurysm etiology, and vascular access for device introduction. For example, many of the treatment failures and some of the fatal stent-graft complications occurred in patients who had a very tortuous aorta; in retrospect, these patients did not have a satisfactory, tubular distal neck above the celiac axis. This point may be related to the findings that larger aneurysm diameter and larger stent-graft proximal landing zone diameter were significant predictors of late death, and patients with the more distally located stent-grafts had a higher incidence of fatal stent-graft complications (Table IV). Second, patients with *chronic* aortic dissections clearly are not good candidates for stent-grafts, because the distorted, non-circular true or false lumina do not lend themselves to a good circumferential friction seal. On the other hand, certain patients with *acute* type B aortic dissections may be suitable, as was the case in 4 patients in this series. It is clear that the best candidates for stent-grafting are those with fairly localized aneurysms (or anastomotic false aneurysms), including patients with giant penetrating ulcers. Surprisingly, the 1 patient with a ruptured aneurysm with active mycosis (*C. septicum*, with a colon carcinoma) did not become reinfected; however, in general, surgery should be avoided in patients with any active, infectious process.

In terms of late complications, 49 nonfatal stent-graft complications occurred in 39 patients, most during the first postoperative year. One half of these ($n = 25$) were initial endoleaks. More proximal distal stent-graft landing zone (eg, shorter stent-grafts), bypassing the left subclavian artery, and earlier operative year were all significant predictors of nonfatal stent-graft complications. The first 2 were most likely associated with the incidence of endoleaks, stroke, and stent-graft misdeployment related to our initial lack of full appreciation of the anatomic and technical challenges portended by distal arch aneurysms, which involve more catheter manipulations in the aortic arch and/or surgical transfer of the left subclavian artery. The frequency of endoleaks with this type of aneurysms is accentuated by the inability of these semirigid, segmented Z-stent prostheses to conform well to the curved geometry of the involved aorta and form a tight seal against the aortic wall within the aneurysm neck.

Currently, the improved, more flexible commercially developed stent-graft systems that are associated with less traumatic delivery and more precise targeting should lower the frequency of these complications. In theory, more refined devices in the future may actually permit the stent-graft to be retrieved or constrained after partial deployment. Finally, additional experience and enhanced understanding of the technical limitations and anatomic constraints associated with the procedure should facilitate more appropriate selection of patients, which should translate into better success rates. In this context, Fig 1 shows that the number of stent-graft procedures actually fell somewhat in the later 2 years of this study. This is due to several factors, but the chief cause was the more restricted patient selection criteria pivoting on anatomic and general considerations, for example, not offering stent-grafts to elderly patients who had other debilitating medical disorders, which limited their life expectancy, and continuing to prefer open surgical repair in younger, low-risk surgical candidates because of the unknown very long-term durability of the endovascular approach.

Thirty-one nonfatal, non-stent-graft-related complications were observed. The variety, severity, and frequency of these events were not unexpected given the patient substrate and type of aneurysms that were treated. Angina, MI, more difficult surgical access for stent-graft introduction, and etiology adversely affected these events. Five fatal stent-graft complications occurred in 4 patients. Three of these events occurred during the operation, including rupture of the descending aorta in 1 patient and avulsion of the iliac artery plus excessive bleeding during introduction of the

delivery sheath in another patient. Both of these complications are potentially avoidable in the future with smaller diameter, flexible stent-graft delivery catheters that do not require introduction of a large, relatively rigid introducer sheath. The 2 remaining fatal stent-graft complications occurred in the late postoperative period and were related to aneurysm rupture. In 1 case, a patient with a late endoleak (unknown to us) had continued aneurysm enlargement that culminated in rupture into the esophagus; in the other patient, erosion and infection of the stent-graft resulted in an aorto-esophageal fistula. Thus fatal aneurysm rupture occurred in 2 patients, or 2%. As reflected in Fig 5, intense serial imaging surveillance is required to detect any endoleaks that might occur around the stent-graft, such that interventional or surgical therapy can be carried out. Although the need for coil embolization, repeat stent-grafting, and definitive surgical excision of the stent-graft certainly detract from the long-term “durability” of this approach, they can be lifesaving.

Study limitations. Several factors exist that mandate continued caution in the interpretation of these results. For example, the lack of serial CT scans postoperatively at many points in time for all patients limits what can be said about whether one or both aneurysm necks might slowly dilate over the years, which conceivably could be associated with the appearance of late endoleaks. Such information would also allow one to comment on whether or not the aneurysm sac becomes smaller over time as the thrombus becomes transformed into fibrous scar tissue. Second, the absence of autopsy information in all patients who died makes it difficult to state with certainty whether the endovascular stent-graft failed to prevent aneurysm rupture. To err on the side of being conservative, we have included all late sudden unexplained deaths in the treatment failure 2 category to reflect this possibility; interestingly, this added only 2 patients to the total, implying that most of these patients had already been documented to have a stent-graft-related problem, that is, had qualified as meeting the treatment failure 1 criteria. Our postoperative follow-up can still only be considered to be early to medium term; 5- to 10-year results in larger numbers of patients will be required to assess the truly long-term effectiveness of this method of endovascular treatment. Finally, until we have more confidence in this endovascular approach beyond 5 years, it is probably prudent not to offer a stent graft to younger patients at low surgical risk, because the long-term durability of open surgical graft replacement remains the “gold standard” of care, and the likelihood of a good surgical outcome in these individuals is relatively good.

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Appendix 1. Additional preoperative and intraoperative variables not listed in Tables I to III examined in multivariate risk analyses

Operative year
 "Not an open surgical candidate"
 Aortic rupture
 Emergency operative status
 Surgical access route
 CPB
 Simultaneous repair of ascending aortic aneurysm
 Left subclavian artery moved
 Elephant trunk proximal landing zone

Length of the stent-graft
Proximal diameter of the stent-graft
Distal diameter of the stent-graft
Number of stent-graft units
T₉-T₁₂ intercostal arteries excluded by the stent-graft
Etiology of the aneurysm
Stent-graft landing zone

Discussion

Dr Randall B. Griepp (*New York, NY*). I congratulate Dr Miller and his coworkers on a major contribution to the treatment of patients with thoracic aortic aneurysms. This is the largest and the best-documented series of endovascular treatment of thoracic aortic aneurysms in the world, and it is also the best documented in terms of the long-term results.

However, if the role that stenting will play in the treatment of thoracic aortic disease is to be determined, a number of questions need to be asked, and comparisons with contemporary surgical series are appropriate.

First, an operative mortality of 9% is not bad in this extraordinarily sick group of patients, particularly in light of the fact that 60% were not deemed to be operative candidates. In the 40% who were operative candidates, however, only 91% were alive at 1 year, and this figure is not quite as good as the results of many contemporary series. Why then should a patient who is an operative candidate have a stent graft if the early risk is no lower?

Stroke occurred in 7% of the patients. This is higher than one sees in contemporary surgical treatment of this disease. In all fairness, 8 of these patients had aneurysms that involved the distal aortic arch or proximal descending thoracic aorta. Had they been treated surgically, they would have needed CPB and in all likelihood a period of hypothermic circulatory arrest to perform a safe and secure proximal anastomosis. Strokes do occur with a relatively high frequency in patients so surgically treated; however, even with a high estimate of 25% or so, this would have been only 2 strokes. In the remainder of the patients, that is, patients whose aneurysm began 2 cm or so beyond the arch, the risk of stroke is relatively low. Thus I think 7% is relatively high. Perhaps Dr Miller would like to state what he thinks can be done to reduce the risk of stroke in endograft-treated patients in the future.

Paraplegia occurred in 3%. This, again, is quite low, but it is not quite comparable with many contemporaneous series of aneurysms restricted to the descending thoracic aorta. As Dr Miller has pointed out, this complication occurred when the graft was deployed in the lower thoracic aorta and a large number of peridiaphragmatic intercostals were suddenly occluded. The complication occurred only in those patients who had undergone previous or were undergoing contemporaneous abdominal aortic aneurysm repair. Perhaps in these patients the stent devices should not be deployed in this area.

In patients who undergo surgical treatment of thoracic aortic aneurysms, treatment success is pretty much congruent with survival. It is unusual for patients, at least within the first few years, to have a form of treatment failure other than

death. A 47% treatment failure by 3.7 years, as seen in this series, is high compared with that of surgical patients.

Does placement of a stent graft treat the disease? This question brings up the only significant methodologic argument I have with Dr Miller's report. Only 23 of the patients had CT scans more than 1 year after the stent was placed. Why was this very important group of patients not followed up more closely? Nonetheless, among these 23 patients, 11 had a decrease in aneurysm size, but 12, or a slight majority, either had no change or an increase in aneurysm size. This failure to regress occurred in the presence or even in the absence of documented endoleaks. Do many of these patients have occult endoleaks? Might one anticipate that a certain proportion of these aneurysms will continue to expand and ultimately rupture?

To summarize, then, the stent graft does not work well in the proximal aorta because it occludes too many peridiaphragmatic intercostals and because of the tortuosity that frequently occurs in this area of the aorta. It does not work well in chronic aneurysms because of the eccentricity of the lumen. Its placement is associated with a mortality and morbidity that is not dissimilar from that of surgical treatment. It may not treat the disease. What then is its role?

Notwithstanding this tirade, I must state that I do believe that stenting will find a role in the treatment of thoracic aortic aneurysms. It is pioneering studies such as Dr Miller's that will help to define this role.

Dr Miller, can you speculate on the proportion of patients with descending thoracic aortic aneurysms who ultimately will be candidates for this endovascular repair?

This is a truly extraordinary paper in terms of its honest acknowledgment of the problems that have occurred. It sets a high standard for all of us who wish to report on innovative treatments.

Dr Miller. Thank you, Dr. Griepp, for that tirade. It is from one of my mentors, so I cannot get too angry.

We have to be honest when we enter these new eras. This is the only way we are ever going to learn. We were gratified to see that we actually had learned from our mistakes along the way within a very short interval of time. For example, early on we accepted these benign-appearing puffs of contrast, endoleaks, as a bad mistake, and we rapidly rectified that either using another stent graft or coil embolization.

The survival statistics speak for themselves. I do not know what the survival data would have been at Mount Sinai, but I am glad you pointed out that these distal arch aneurysms would have required profound circulatory arrest. That is not a walk in the park.

We admit the stroke rate is too high at 7%. This is readily explained by the fact that with this primitive device, not just the guidewire but also the dilator system and the sheath are wrenching around in the ascending aorta. I was fearful of aortic valve perforations with this chest tube up in the ascending aorta in these diseased aortas. The newer devices have totally rectified that. In the Gore Prograf device,* which are now in

*Registered trade mark of W L Gore & Associates, Inc, Elkton, Md.

use, the sheath is limited to the abdominal aorta. There is no dilator system and sheath in the ascending aorta, just the guidewire. Ideally, that will reduce the incidence of stroke.

We were expecting the paraplegia rate to be higher because we were deathly afraid that covering all these patent intercostals down low was going to wreak the havoc that one would predict. One might have predicted 10 to 13 cases of paraplegia whereas we saw only 3. Two of the 3 were in patients undergoing redo suprarenal abdominal aortic aneurysmectomy, which carries a risk of paraplegia in its own right. These were not simple cases. The third occurred in a patient who had had a prior abdominal aortic aneurysm repair and then had a rupture caused by intramural hematoma. We had no discrete surgical target and the entire descending thoracic aorta was covered.

Maybe this tells us that your premise from last year's meeting, that the artery of Adamkiewicz is a myth, is true without the ischemic preconditioning that your technique involves. I think we are lucky. Only more numbers and more time will tell.

The treatment failure rate is high. Most of the failures involved early endoleaks, a problem that we have rectified. Ideally, the new devices will be associated with fewer such leaks.

Does the stent-graft adequately treat the aneurysmal disease? That is a very important question. The data that Dr

Griep mentioned are in the manuscript: in half of the patients we actually documented a decrease of 3 mm or more in size, and in a quarter there was no change. Those results may not sound very good, but they are actually much better than what the vascular surgeons are reporting for stent-graft repair of abdominal aneurysms. Whether late ruptures may occur in a very slow, controlled fashion with any of these methods of treatment remains an open question. We do not know, but we are encouraged to see in 50% a demonstrable decrease in size, which is better than any other reported series in the abdominal aorta.

The reason for the sad return for CT scans is manifold. Patients came from all over the United States and abroad, and we simply could not get them back. That reflects an inadequacy on our part and we have to try harder.

Regarding the proportion of patients with descending thoracic aortic aneurysms who ultimately will be candidates for this endovascular repair, I think we have learned where and where not to use this procedure. However, we do have new opportunities. For example, for patients with acute type B dissection, endovascular repair might be the answer we have been looking for. Another potential use is for the repair of acute traumatic tear; none of us likes to do open operations in those patients. The stent-graft might be the answer.