The Gore TAG Pivotal Trial Results

Repair of descending thoracic aneurysm with the TAG device has shown improved short- and midterm results compared to open repair.

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The Gore TAG endoprosthesis (Gore & Associates, Flagstaff, AZ) is the only thoracic endoprosthesis that has gained FDA approval (March 2005) for commercial use for the treatment of descending thoracic aortic aneurysms (Figure 1). Through clinical trials, the safety and efficacy of the TAG endoprosthesis were proven and the midterm results were shown to be superior to those of open repair.

THE GORE TAG DEVICE

The TAG endoprosthesis is made of three layers of expanded polytetrafluoroethylene (ePTFE). It is externally reinforced with ePTFE/FEP (fluorinated ethylene propylene) film and a nitinol self-expanding stent that is fixed with ePTFE/FEP tape to the external surface of the graft. An ePTFE sealing cuff at both ends helps with sealing of the device to the aortic wall. Two radiopaque gold bands at the base of the flares serve as a marker during deployment and in surveillance.

Figure 1. The Gore TAG endoprosthesis is the only thoracic endoprosthesis that has gained FDA approval (March 2005) for commercial use for the treatment of descending thoracic aortic aneurysms.

The devices are available in diameters of 26 mm to 40 mm that accommodate aortic diameters between 23 mm and 37 mm. The introducer sheaths that are required are 20 F to 24 F, depending on the device diameter.

US TAG PIVOTAL TRIAL

After device safety was demonstrated with the feasibility study, the pivotal (phase II) trial was undertaken to determine the safety and efficacy of the device for the treatment of descending thoracic aortic aneurysms in comparison with open surgical repair.[1,2] The primary efficacy hypothesis was that freedom from any major device-related events at 1 year will be >80% after TAG repair. The efficacy for the open repair was assumed at 100%. The primary endpoint was the percentage of patients free from major device-related events through 1-year follow-up for the TAG group. The secondary endpoints were the operative blood loss, intensive care unit and hospital stay, and recovery-to-baseline activities.

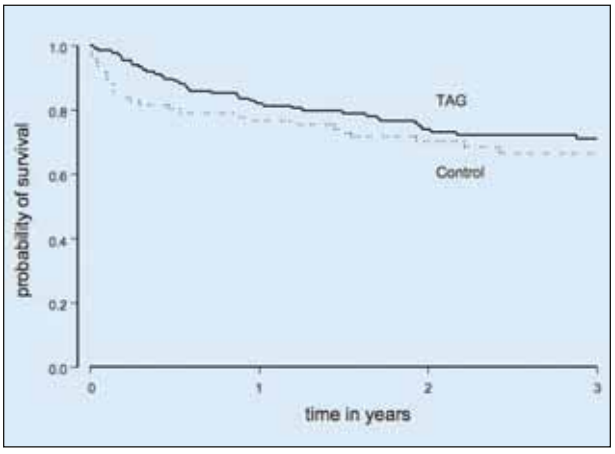

Figure 2. Kaplan-Meier estimates for probability of freedom from all-cause mortality.

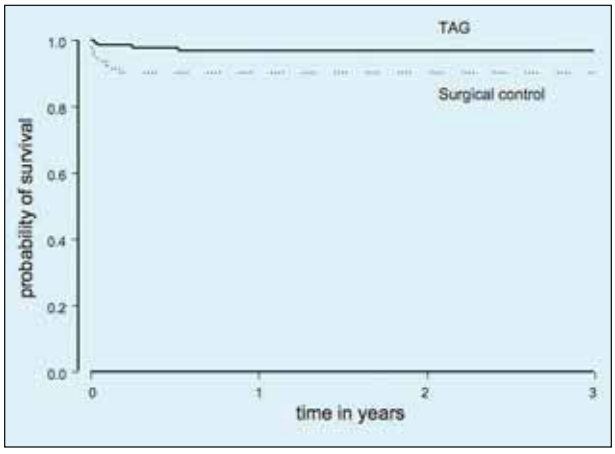

Figure 3. Kaplan-Meier estimates for probability of freedom from aneurysm-related death.

Design

This was a prospective, nonrandomized, controlled study conducted at 17 sites in the US. One hundred forty study patients (140 in the pivotal trial and two in extended access) and 94 control subjects were recruited between September 1999 and May 2001. The surgical control group consisted of two cohorts: 44 prospectively acquired patients and 50 historically acquired patients selected in reverse chronological order. Table 1 shows the inclusion and exclusion criteria.

Follow-Up

All patients are to be followed for 5 years with physical examinations and radiological imaging studies consisting of plain films and CT scans at 1-, 6-, and 12-month intervals, and yearly thereafter. Those with primary endoleaks were evaluated at the 3-month visit with a CT scan. A core laboratory reviewed all imaging studies. Clinical data were submitted by individual sites and monitored by sponsor representatives. A clinical events committee adjudicated major adverse events, defined as those that resulted in additional, unintended therapy, increased hospital stay, permanent adversity, or death.[3]

RESULTS

Clinical Materials

All major demographic and clinical variables were similar between the two groups. The average age in the TAG group was 71 years, and males constituted 57% of the patients, not unlike those in the control group, whose average age was 68 years and was composed of 51% males. With an exception of higher prevalence of symptomatic aneurysm in the control group, the comorbidities were equivalent between the groups (Table 2). There were no differences in the risk classifications as per American Society of Anesthesiologists classification and the Society for Vascular Surgery risk scores.

Operative Data

Technical success with TAG implantation was achieved in 98% (139 of 142) of the patients. Poor access accounted for all three failures. Conduits were constructed in 21 (15%) patients to provide access. Prophylactic revascularization of the left subclavian artery was performed in 28 (20%) patients who had proximal aneurysms that required coverage of the vessel with the device to ensure proper sealing. One subclavian and one visceral artery were covered unintentionally in one patient each. The latter patient was converted to an open explantation of the device and redeployment of another endograft without an adverse event.

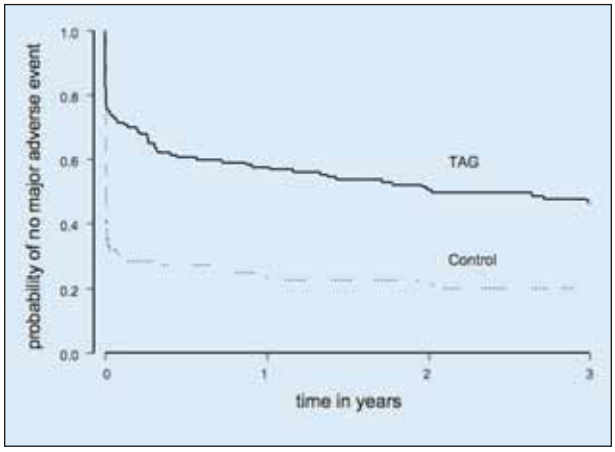

Figure 4. Kaplan-Meier estimates for probability of freedom from major adverse events.

TABLE 1. INCLUSION/EXCLUSION CRITERIA

Inclusion Criteria	
Sex	Males or infertile females
Age	>21 years
Life expectancy	>2 years
Pathology	Saccular Fusiform: descending thoracic aortic aneurysms at least twice the size of normal thoracic aorta Landing zone 2 cm of normal aorta proximal and distal to the descending thoracic aortic aneurysm

Exclusion Criteria

- Unstable rupture
- Mycotic aneurysm
- Penetrating ulcer
- Aortic dissection
- Connective tissue disorder
- Significant thrombus at landing zone
- Planned occlusion of carotid artery or celiac axis to seal
- Major surgery other than planned subclavian to carotid transposition or bypass
- Previous descending aortic surgery, endovascular or open
- Previous endovascular repair of AAA
- Myocardial infarction/cerebrovascular accident <6 weeks
- Creatinine level >2 mg/dL
- Participation in other investigational study within 1 year

Early Results

Overall early results were significantly better with TAG repair than with the open repair. Operative mortality (death within 30 days of the procedure or during the same hospitalization) occurred in three patients (2.1%) in the TAG group. A postoperative stroke and a cardiac event accounted for two early deaths. The cause of death in the third patient, who also had an anoxic brain injury from a respiratory arrest, was sepsis from aortoesophageal fistula after 7 months of hospitalization. The mortality rate in the open surgical group was significantly higher at 11.7% (11 of 94; *P*<.001).

The incidence rates of stroke were similar between the two groups (3.5% TAG vs 4.3% surgical controls; one resulted in death, three were right hemispheric). Notably, in the TAG group, four of the five strokes occurred in patients who had prophylactic left subclavian artery revascularization (four of 28; 14%). This is a significantly higher rate than that observed in those who did not have prophylactic left subclavian artery revascularization (one of 113; 1%; *P*<.001).

Spinal chord ischemia (SCI), manifested by paraplegia and paraparesis, developed in four patients (2.8%) after TAG repair; in one, paraplegia and paraparesis was immediate and permanent despite all supportive measures. The remaining three cases had delayed onset; all regained motor function (one complete and two partial) and were ambulatory at last follow-up. A significantly higher incidence rate of SCI (13.8%; 13 of 94) was noted in the control group compared to that of the TAG group (*P*<.001). A history of abdominal aortic aneurysm (AAA) repair did not contribute to an increased incidence of SCI: 4.7% with the history versus 2% without the history. It should be noted that cerebrospinal fluid drainage was not routinely used in either group.

Only intraoperative vascular complication occurred more commonly in the TAG group (14% TAG vs 4% controls). This was caused by passing a large sheath through the iliac arteries. Other common major adverse events (MAEs) were bleeding and cardiopulmonary events, both of which were significantly more frequent in the control group.

TABLE 2. COMORBIDITIES

	Proportion (%)		
	Surgical Control	TAG	*P* Value
Smoking	82	84	NS
Coronary artery disease	36	49	NS
Previous vascular intervention	55	45	NS
Chronic obtrusive pulmonary disease	38	40	NS
Other concomitant aneurysms	28	28	NS
Cardiac arrhythmia	31	24	NS
Symptomatic aneurysm	38	21	<.01
Malignancy	13	19	NS
Peripheral vascular disease	11	16	NS
Stroke	10	10	NS
Hepatic dysfunction	1	2	NS
Renal dialysis	0	1	NS
Paraplegia	0	1	NS

A significantly shorter average length of stay in the intensive care unit was noted in the TAG group as compared to the control group (2.6 ± 14.6 days vs 5.2 ± 7.2 days; *P*<.001). Similarly, the total length of hospital stay was shorter after TAG repair than with open repair (7.4 ± 17.7 days vs 14.4 ± 12.8 days; *P*<.001).

Late Outcome

Two-year all-cause mortality was 24% in the TAG group and 26% in the surgical control group (Figure 2). The causes of death were commensurate with comorbidities present in this elderly population. There have been no reported ruptures.

Aneurysm-related mortality occurred in one patient with aortoesophageal fistula 2 months after a TAG repair. The patient presented with a graft infection and aneurysm sac enlargement. During open conversion, aortoesophageal fistula was noted, and the endograft was removed followed by an extra-anatomic bypass grafting. Postoperatively, the patient developed respiratory failure and anoxic brain injury and died 1 day later. In the control group, three additional deaths were reported during the first 6 months. No deaths occurred after the first year in either group. Kaplan-Meier estimates of the probability of freedom from aneurysm-related death showed a significant advantage for the TAG group compared with the surgical controls (97% vs 90%; *P*=.024) at 3 years (Figure 3).

A majority (70%) of the MAEs occurred within 30 days of the original procedure (Table 3). At 1 year, the incidence of MAEs was significantly lower after TAG repair (42%) than after open surgical repair (77%). The same effects were seen through 3-year follow-up. The Kaplan-Meier estimates of the probability of freedom from MAEs at 3 years were 48% in the TAG group and 20% in the surgical control group (Figure 4).

No device-related deaths were noted through 3 years. Stent fractures were reported in 19 patients. Only one patient had an adverse effect (a type II endoleak), which was treated by placement of an additional endograft. Device migrations (three proximal and four components) were noted at a 2-year follow-up without clinical sequelae. At 3-year follow-up, five patients underwent secondary endovascular interventions, and one patient underwent surgical conversion. Sac shrinkage of >5 mm was noted in 38% (24 of 64) of patients, and sac expansion was noted in 17% (11 of 64) of patients. The probability of freedom from device-related events was 94% at 2 years after TAG repair, which is higher than the predefined limit of 80%.

DISCUSSION

The results of the Gore TAG trials have shown that endovascular treatment of descending thoracic aortic

aneurysms is superior to open surgical repair with respect to both short- and midterm results. Operative mortality and morbidity, including the incidence rates of SCI, were lower than those observed with conventional repairs. Device-related complications, aneurysm-related deaths, and major adverse events were all lower than those observed with open repair.

With that said, the device still requires close, life-long surveillance to ensure best long-term outcome, as several limitations have been noted. Aneurysm sac shrinkage, the only surrogate marker for successful repair of aneurysm, is not uniformly achieved.[1,4,5] This is not unlike what has been learned from experiences with endovascular repair of AAAs.[6,7]

Although the incidence rate of spinal cord ischemic injury was lower with repair using the TAG device, it remains a potential source of major morbidity and mortality. Although the Gore pivotal trial did not identify it as a risk factor, previous AAA repair and extensive exclusion of the thoracic aorta portend this devastating complication.[8-10]

The fact that the strokes were multicentric and right-hemispheric suggests that they were embolic in nature. This reflects potentially dangerous consequences of instrumentation of the aortic arch. This is particularly the case when the aneurysm extends proximally and requires coverage of the left subclavian artery to secure adequate sealing. Planned left subclavian coverage has served as a prognostic indicator for stroke in the pivotal trial, although European experience has suggested no such hazard with it.[11]

The device still requires a relatively large delivery system, and consequently may cause vascular trauma. This is of particular concern because women comprise approximately 50% of the descending thoracic aorta population. To prevent this problem, conduits should be used as a prophylactic measure rather than as a bail-out procedure. A smaller delivery system would also help reduce this complication.

TABLE 3. MAJOR ADVERSE EVENTS NOTED AT 1-YEAR FOLLOW-UP

	Open Surgical	Proportion (%) TAG	*P* Value
MAE	77	42	<.001
Bleeding	54	11	NS
Pulmonary	38	13	NS
Neurologic	33	11	NS
Cardiac	23	16	NS
Renal	15	4	NS
Wound	15	6	NS
Gastrointestinal	6	4	NS
Vascular	6	18	NS
Other	3	1	NS

CONCLUSION

The Gore TAG US trials have shown safety and efficacy with improved midterm results compared to open surgical repair. Long-term effects are essential to ensure the best outcome. The applicability of this technology to other aortic pathology such as aortic rupture, dissection, and traumatic transection await the results of a high-risk trial that is currently in progress. ■

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