

Is Standard Open Surgery Still Indicated
for TAA Involving the Descending
Thoracic Aorta: When?

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Disclosure Information

Jon Matsumura, M.D.

Research grant support, consultant, and training director:

Abbott, Abraxis, Bard, Cook, Cordis, ev3, Lumen, Medtronic, and WL Gore.

Stent grafts are only labeled for thoracic aneurysm, and other uses are off-label or investigational in the US.

Agenda

- Thoracic EndoVascular Aortic Repair (TEVAR)
 - Global Sample
 - US Clinical Trials
 - TX2
 - TAG
 - Talent

Global TEVAR Survey: n=1180

Pathology Treated & 30 d Mort

<u>Primary aortic pathology</u>	<u>%cases</u>	<u>30 d Mort (%)</u>
• Descending thoracic aneurysm	64.2	4.1
• Thoracoabdominal aneurysm	1.6	5.0
• Acute traumatic disruption	10.0	5.5
• Pseudoaneurysm	3.3	2.7
• Acute dissection	7.8	9.9
• Intramural hematoma	2.2	7.2
• Giant penetrating ulcer	1.0	0
• Chronic dissection	8.4	3.3
• Aortic fistula	0.9	2.6
• Embolizing lesion	0.3	0
• Stenosis/coarctation	0.1	0

Clinical Results

- 4.8% overall 30 day mortality
- 2.8% stroke
- 1.6% renal failure
- 2.5% paraplegia
 - 43% delayed
- 0.9% aneurysm rupture

US Regulatory Trials
Thoracic Aortic Aneurysm

TX2 Enrollment

Arm	N	% of Goal ^a	Completion Date ^b
TEVAR	160	100	June 6, 2006
OPEN	70	100	July 6, 2006
<i>Prospective</i>	<i>19</i>		
<i>Retrospective</i>	<i>51</i>		

^a42 institutions contributed to enrollment

^bEnrollment began on March 30, 2004

Patient Demographics

Item	TEVAR	OPEN	P-value
Age (years)	72 ± 9.6 (160)	68 ± 12 (70)	<0.01
Gender			0.09
Male	72% (115/160)	60% (42/70)	
Female	28% (45/160)	40% (28/70)	
Ethnicity			0.82
Asian	2.5% (4/159)	1.4% (1/70)	
African American	12% (19/159)	8.6% (6/70)	
Hispanic/Latino	3.8% (6/159)	4.3% (3/70)	
White/Caucasian	80% (127/159)	86% (60/70)	
Other	1.9% (3/159)	0.0% (0/70)	
Height (in)	67.5 ± 4.0 (154)	66.9 ± 3.6 (69)	0.26
Weight (lbs)	177 ± 35 (158)	167 ± 32 (70)	0.02
BMI	27.2 ± 4.9 (153)	25.9 ± 3.7 (69)	0.03

Morphology

Item	TEVAR	OPEN	<i>P</i>-value
Morphology			0.40
Aneurysm	86% (137/160)	90% (63/70)	
Ulcer	14% (23/160)	10% (7/70)	

Note: Based on core lab analysis

Clinical Utility

Measure	TEVAR	OPEN	P-value
Number of blood transfusions	0.3 ± 1.0 (160)	1.7 ± 1.9 (70)	<0.01
Duration of intubation (hrs)	2.8 ± 4.6 (147)	53.1 ± 85.4 (66)	<0.01
Duration of ICU stay (days)	2.2 ± 6.2 (153)	9.4 ± 16.9 (70)	<0.01
Days to ambulation	1.6 ± 2.5 (148)	5.5 ± 5.6 (63)	<0.01
Days to resumption of oral fluid intake	0.7 ± 1.9 (155)	4.0 ± 5.6 (60)	<0.01
Days to resumption of regular diet	1.9 ± 2.7 (156)	5.2 ± 3.7 (58)	<0.01
Days to resumption of bowel function	2.9 ± 2.3 (94)	5.5 ± 3.3 (61)	<0.01
Days to hospital discharge	5.0 ± 8.6 (159)	16.1 ± 18.7 (70)	<0.01

30-day Morbidity Score – All Events

Item	TEVAR	OPEN	<i>P</i> -value
Mean score (events per patient)	1.3 ± 3.0	2.9 ± 3.6	<0.01
% of patients with ≥1 event	41.9% (67/160)	68.6% (48/70)	<0.01

30-day Morbidity – Neurological Events

Event	TEVAR	OPEN	<i>P</i>-value
Stroke	2.5% (4/160)	8.6% (6/70)	0.07
Paraplegia	1.3% (2/160)	5.7% (4/70)	0.07
Paraparesis (weakness but able to walk)	4.4% (7/160) ^a	0% (0/70)	0.10

^aOf these seven patients, six had complete resolution

30-day Morbidity Scores – Pre-Specified Severe Events

Item	TEVAR	OPEN	<i>P</i> -value
Mean score (events per patient)	0.2 ± 0.7	0.7 ± 1.2	<0.01
% of patients with ≥ 1 event	9.4% (15/160)	32.9% (23/70)	<0.01

Freedom from Severe Morbid Events

Event	30 days		365 days	
	TEVAR	OPEN	TEVAR	OPEN
Q-wave MI	1.00	1.00	1.00	1.00
Cardiac event w/ arrest or resusc.	0.98 (0.01)	0.99 (0.01)	0.98 (0.01)	0.97 (0.02)
Ventilation >72 hours*	0.99 (0.01)	0.84 (0.04)	0.99 (0.01)	0.84 (0.04)
Re-intubation*	0.95 (0.02)	0.86 (0.04)	0.95 (0.02)	0.84 (0.04)
Event req. trach. or chest tube*	0.99 (0.01)	0.87 (0.04)	0.97 (0.01)	0.82 (0.05)
Permanent dialysis in pt. w/ normal baseline Cr	1.00	1.00	1.00	1.00
Bowel resection	0.98 (0.01)	0.99 (0.01)	0.97 (0.01)	0.99 (0.01)
Stroke*	0.98 (0.01)	0.91 (0.03)	0.97 (0.01)	0.90 (0.04)
Paraplegia*	0.99 (0.01)	0.94 (0.03)	0.99 (0.01)	0.94 (0.03)
PE w/ instability or surgery	1.00	1.00	1.00	1.00
Aneurysm/vessel leak req. surgery	1.00	0.99 (0.01)	1.00	0.99 (0.01)
DVT req. surgery or lytic therapy	1.00	1.00	0.99 (0.01)	1.00
Amputation of more than toes	1.00	1.00	1.00	0.98 (0.02)
Coagulopathy req. surgery	1.00	0.99 (0.01)	1.00	0.99 (0.01)
Wound comp. req. return to OR	1.00	1.00	0.99 (0.01)	1.00

*P-value (log-rank) ≤ 0.05 at 365 days

Migration

Item	% (n)
Migration (>10 mm)	2.8% (3/107)

^aTwo cases of caudal migration of the proximal graft and one case of cranial migration of the distal graft were identified. None have been associated with endoleak or increase in aneurysm size and none have had secondary intervention.

Endoleak

Type	Pre-dis.	30-day	6-mos.	12-mos.
Any	12.6% (17/135)	4.8% (6/126)	2.6% (3/114)	3.9% (4/103)
Multiple	0% (0/135)	0% (0/126)	0% (0/114)	0% (0/103)
Proximal Type I	0% (0/135)	0% (0/126)	0% (0/114)	0% (0/103)
Distal Type I	0.7% (1/135)	0.8% (1/126)	0.9% (1/114)	0% (0/103)
Type IIa	1.5% (2/135)	0.8% (1/126)	0% (0/114)	0% (0/103)
Type IIb	5.9% (8/135)	2.4% (3/126)	1.8% (2/114)	1.9% (2/103)
Type III	1.5% (2/135)	0.8% (1/126)	0% (0/114)	1.0% (1/103)
Type IV	1.5% (2/135)	0% (0/126)	0% (0/114)	0% (0/103)
Unknown	1.5% (2/135)	0% (0/126)	0% (0/114)	1.0% (1/103)

Note: Based on core lab analysis

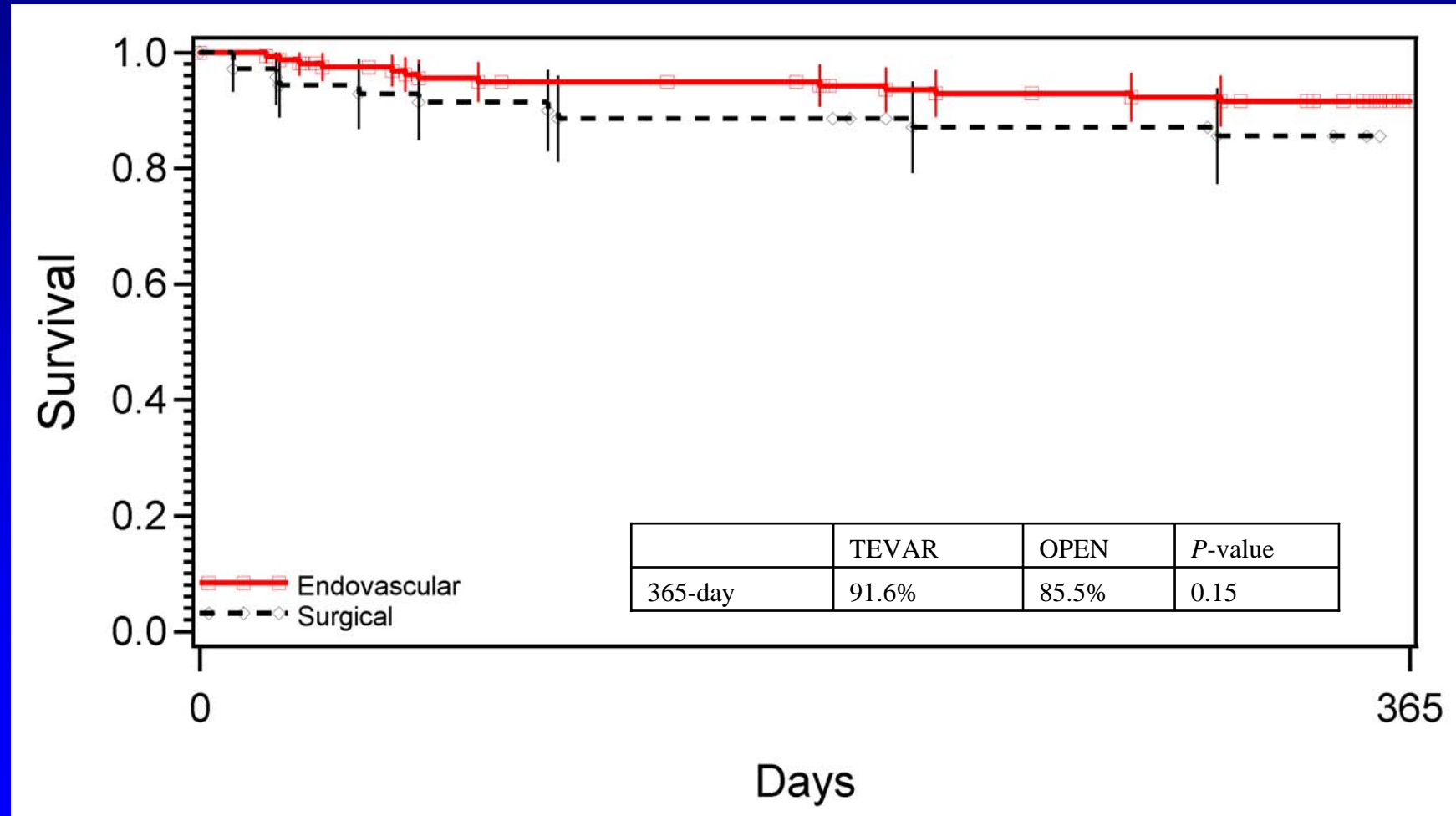
Secondary Interventions

Item	TEVAR	OPEN	<i>P</i> -value
Percent of patients with re-intervention (through 12 months)	4.4% (7/158) ^a	5.7% (4/70) ^b	0.74

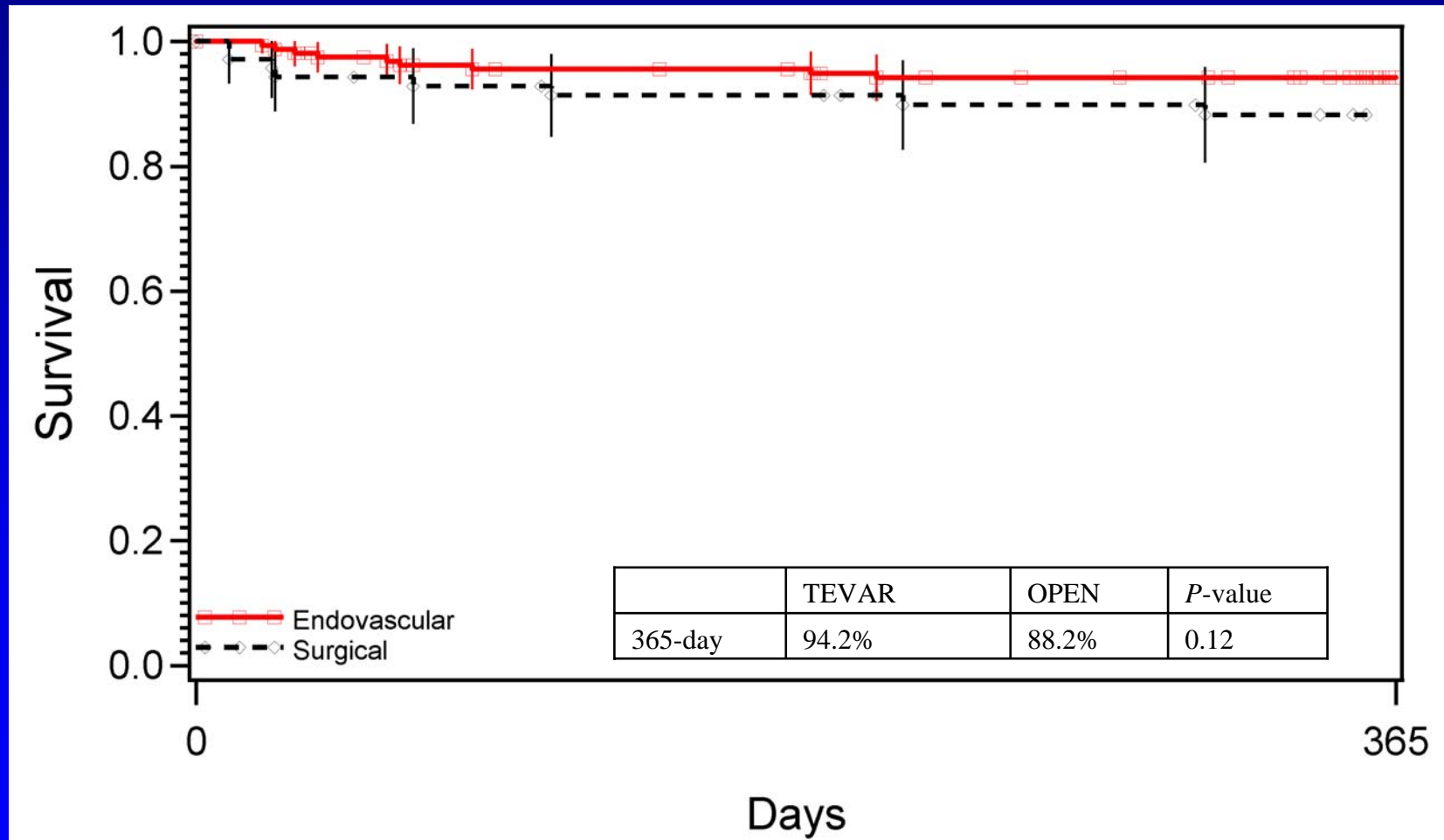
^aReasons include: Endoleak, iliac occlusion, aneurysm growth and proximal aortic pseudoaneurysm.

^bReasons include: intrapleural hematoma; continued bleeding/symptoms; bleeding and tamponade; and aorto-esophageal fistula.

All-cause Mortality



Aneurysm-related Mortality



Summary: 1 year Data

- Evaluation in a controlled trial.
- Similar overall and aneurysm-related survival with TEVAR compared to open repair.
- Major morbidity, severe morbidity, and clinical utility appear better with TEVAR.
- Sac enlargement, endoleak, migration, and other device issues were infrequent, but underscore the value of careful procedure planning and regular follow-up imaging before and after TEVAR.
- Similar reintervention rates in both groups, and no ruptures or conversions in TEVAR group.

Pivotal Study Design (TAG 99-01)

- Non-randomized, controlled clinical trial
 - 140 Test subjects treated with the TAG device
 - 94 Control subjects treated by open surgical repair
- 5-year follow-up complete May 2006

Pivotal Study (TAG 99-01)

Baseline Demographics

Variables	TAG Device (n=140)	Surgical Control (n=94)	<i>P</i>
Demographics			
-Gender (male, %)	57	51	0.42
-Age (yrs)	71	68	0.10
-Ethnicity (%)			0.79
Caucasian	87	86	
Black	8	10	
Other	5	4	
-Height (cm)	170	170	1.0
-Weight (kg)	76	78	0.54

Confirmatory Study (TAG 03-03)

Secondary Outcomes

Median Value Reported

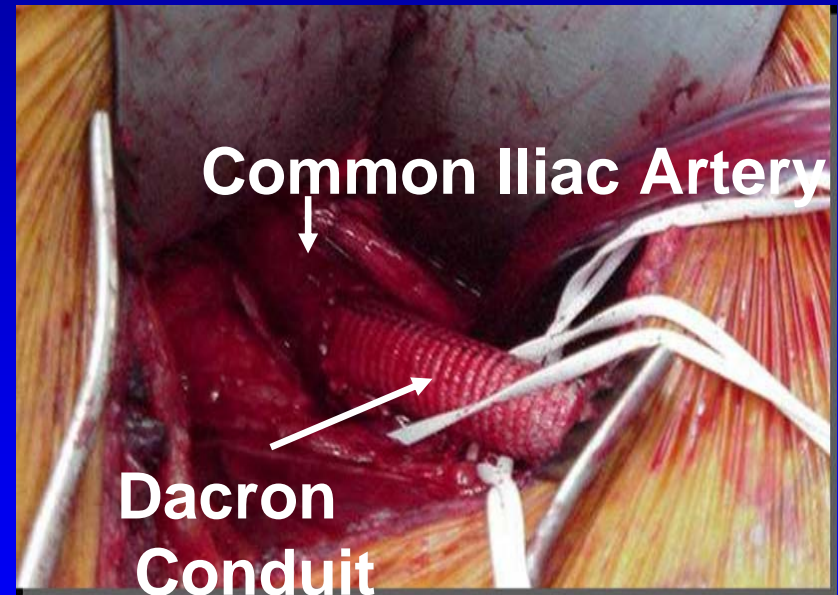
Secondary outcomes	TAG Device	Surgical Control
Procedural blood loss (ml)	200	1850
ICU stay (days)	1	3
Hospital stay (days)	3	10
Time to return to normal activity (days)	15	78

Pivotal Study (TAG 99-01)

Operative Results

140 TEVAR Patients Enrolled

- 137 successful implantation (98%)
- 3 failures due to poor iliac access
- 77 patients (55%) required >1 device to bridge the aneurysm
- 21 patients (15%) had a conduit to the aortoiliac segment for access



Operative Results

30 days or In-Hospital Events

	TAG Device	Surgical
Control		
• Operative Mortality	1%	6%
• Paraplegia / paraparesis	4%	13%
• Stroke	4%	4%

Primary SAFETY Endpoint Through 1 Year

Primary Safety Endpoints	Proportion (%)		<i>P</i>
	TAG Device	Surgical Control	
Any Major Adverse Event	42 (n=140)	77 (n=94)	< 0.001
Major Adverse Events			
-Bleeding	11	54	
-Pulmonary	13	38	
-Cardiac	16	23	
-Renal	4	15	
-Wound	6	15	
-Bowel	4	6	
-Vascular	18	6	
-Neurologic	11	33	
-Other	1	3	

Endoleaks

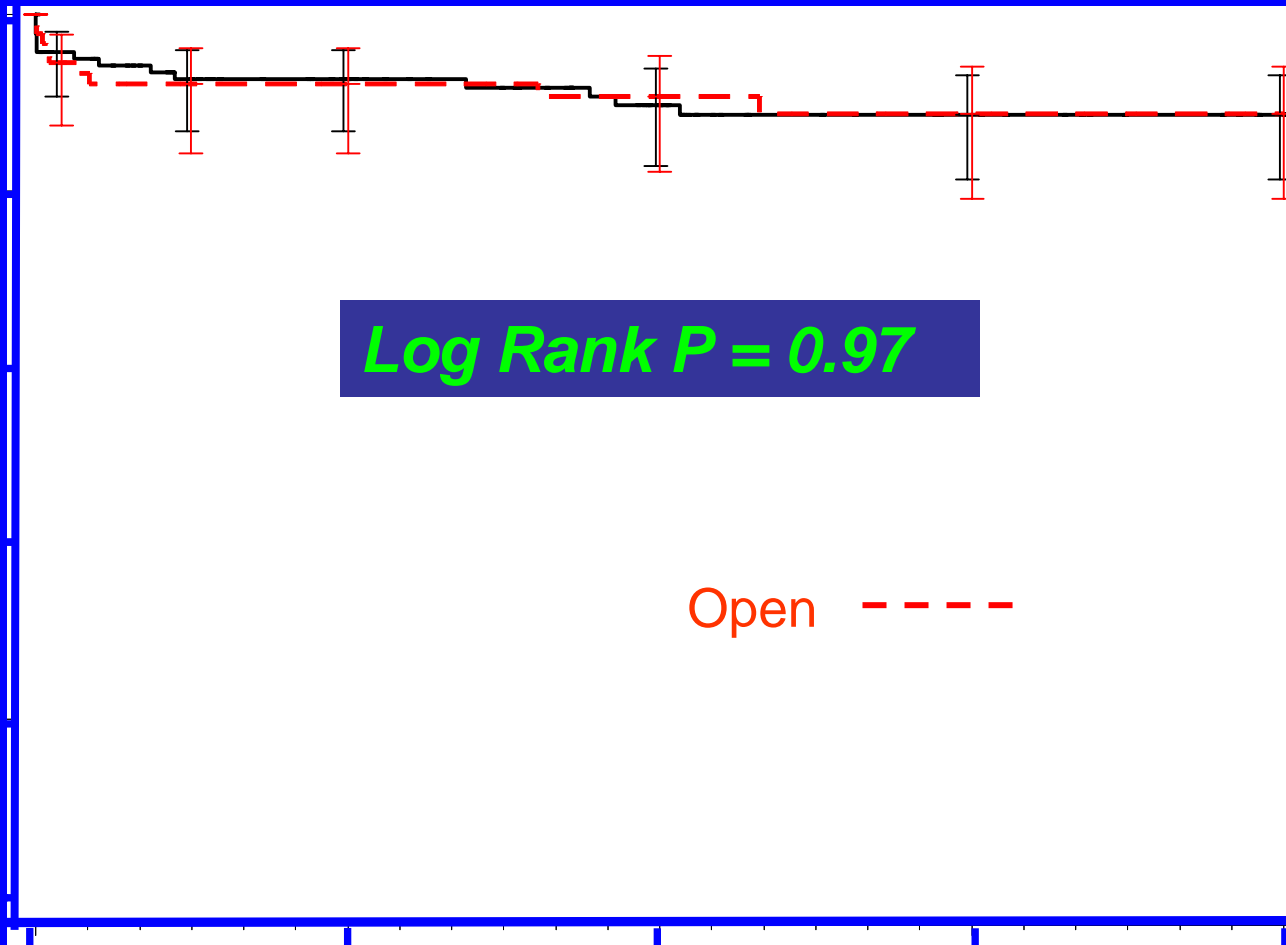
Follow-Up period	1 Month	12 Months	24 Months	36 Months	48 Months	60 Months
N	123	103	80	65	55	31
Number of patients (%)	10 (8.1%)	4 (3.9%)	5 (6.3%)	2 (3.1%)	3 (5.5%)	1 (3.2%)
Type IA	5	1	1	-	1	-
Type IB	1	1	1	2	2	-
Type II	1	1	1	-	-	1
Type III	1	-	1	-	-	-
Type IV	-	-	-	-	-	-
Indeterminate	2	1	1	-	-	-

*Site reported

*N = number of patients with adequate studies

Freedom from Re-Interventions

Freedom from Reintervention



Years Since Treatment

Major Re-interventions in the TAG Group

❑ One Arch aneurysm repair

✓ at 5 months for type I endoleak

❑ One Surgical conversion

✓ at 2 months for aneurysm enlargement

❑ 5 Endovascular Revisions in 3 patients

➤ Patient A with a spine fracture had 2 revisions for:

✓ Type I endoleak at 2 months

✓ Type III endoleak at 31 months

➤ Patient B had 2 revisions for

✓ Type I endoleak at 23 months

✓ Distal thoracic enlargement at 46 months

➤ Patient C had one revision for

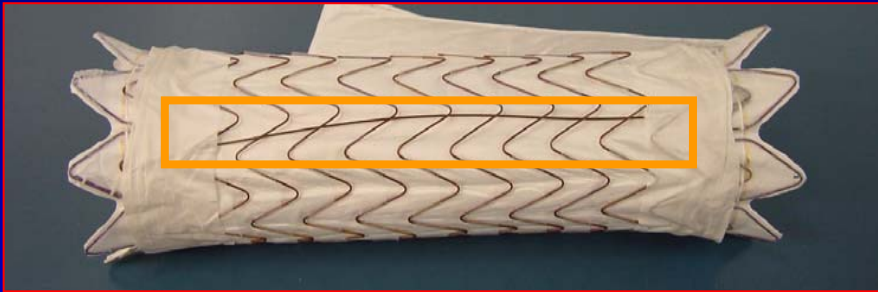
✓ Type I Endoleak at 26 months

Major TAG-Related Long Term Complications

5 Years Site Data

❑ Rupture	0
❑ Migration	1
❑ Any Endoleak @ any time	17%
❑ Endoleak @ 5 years	3%
❑ Size Increase @ 5 Years	23%

TAG Device Modifications

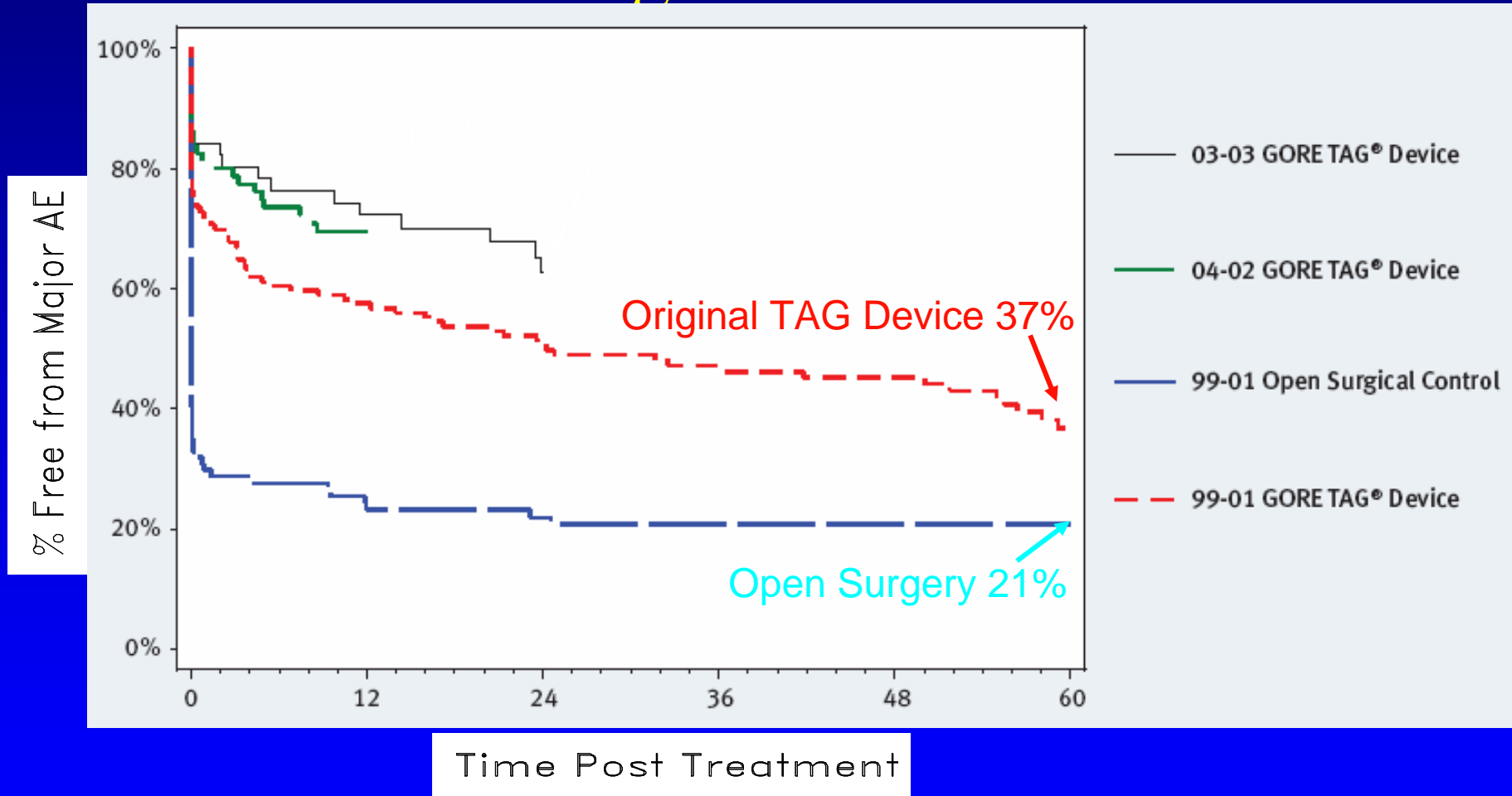


- Eliminated deployment wire from wire-frame
- Strengthened graft material for longitudinal stiffness by adding a stronger, less permeable ePTFE material
- No other device modifications

TAG Device Permeability Data: Change in Aneurysm Diameter From Baseline

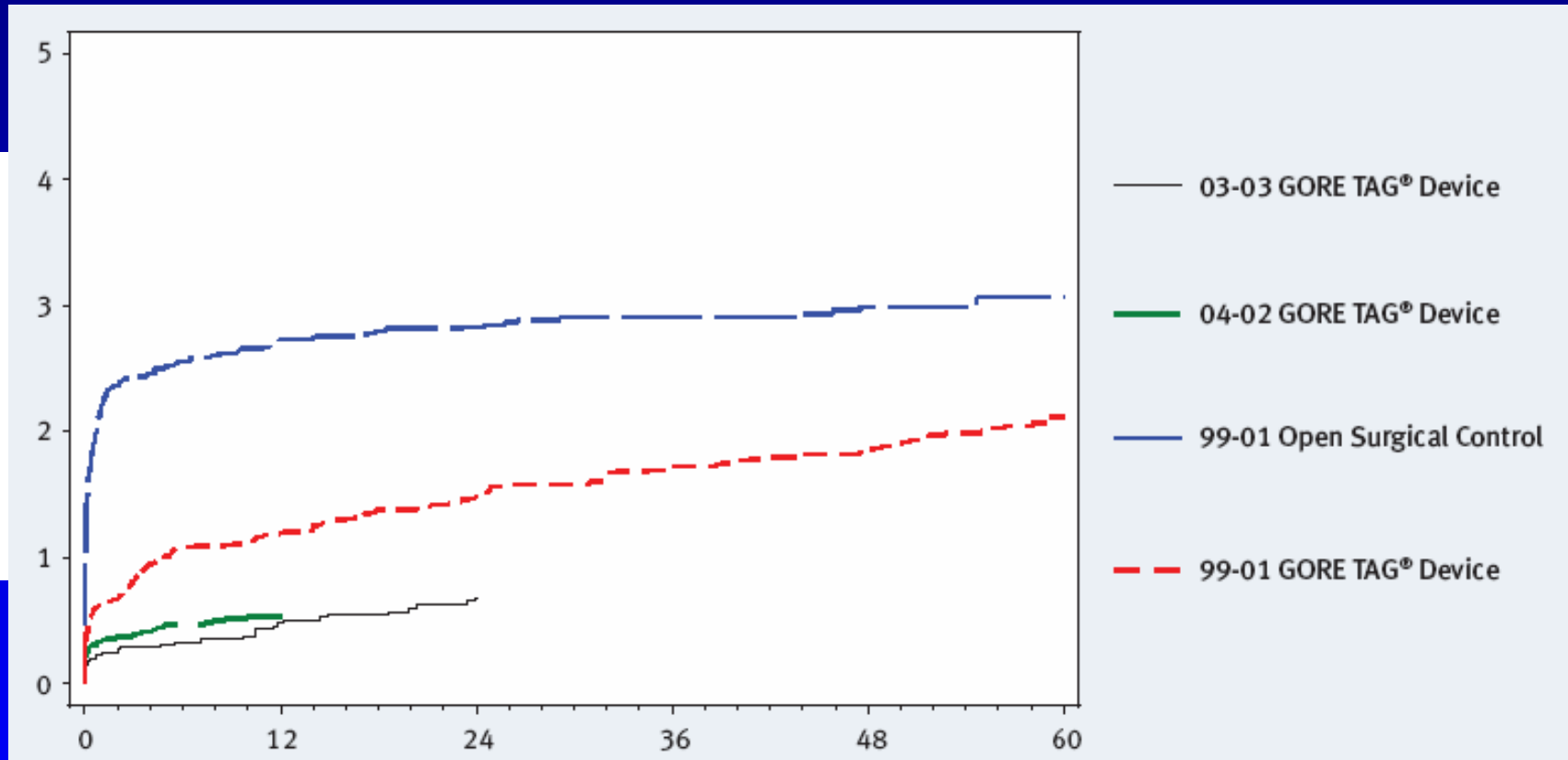
	12 Months	24 Months
99-01 GORE TAG® Device		
Number of Subjects with Available Data ¹	86	70
Change in Aneurysm Diameter from Baseline		
≥ 5 mm Decrease in Diameter	37 (43.0%)	32 (45.7%)
< 5 mm Change in Diameter	41 (47.7%)	29 (41.4%)
≥ 5 mm Increase in Diameter	8 (9.3%)	9 (12.9%)
03-03 GORE TAG® Device		
Number of Subjects with Available Data ¹	42	34
Change in Aneurysm Diameter from Baseline		
≥ 5 mm Decrease in Diameter	25 (59.5%)	20 (58.8%)
< 5 mm Change in Diameter	17 (40.5%)	13 (38.2%)
≥ 5 mm Increase in Diameter	0 (0.0%)	1 (2.9%)

Freedom from Major Adverse Events Through Five Years



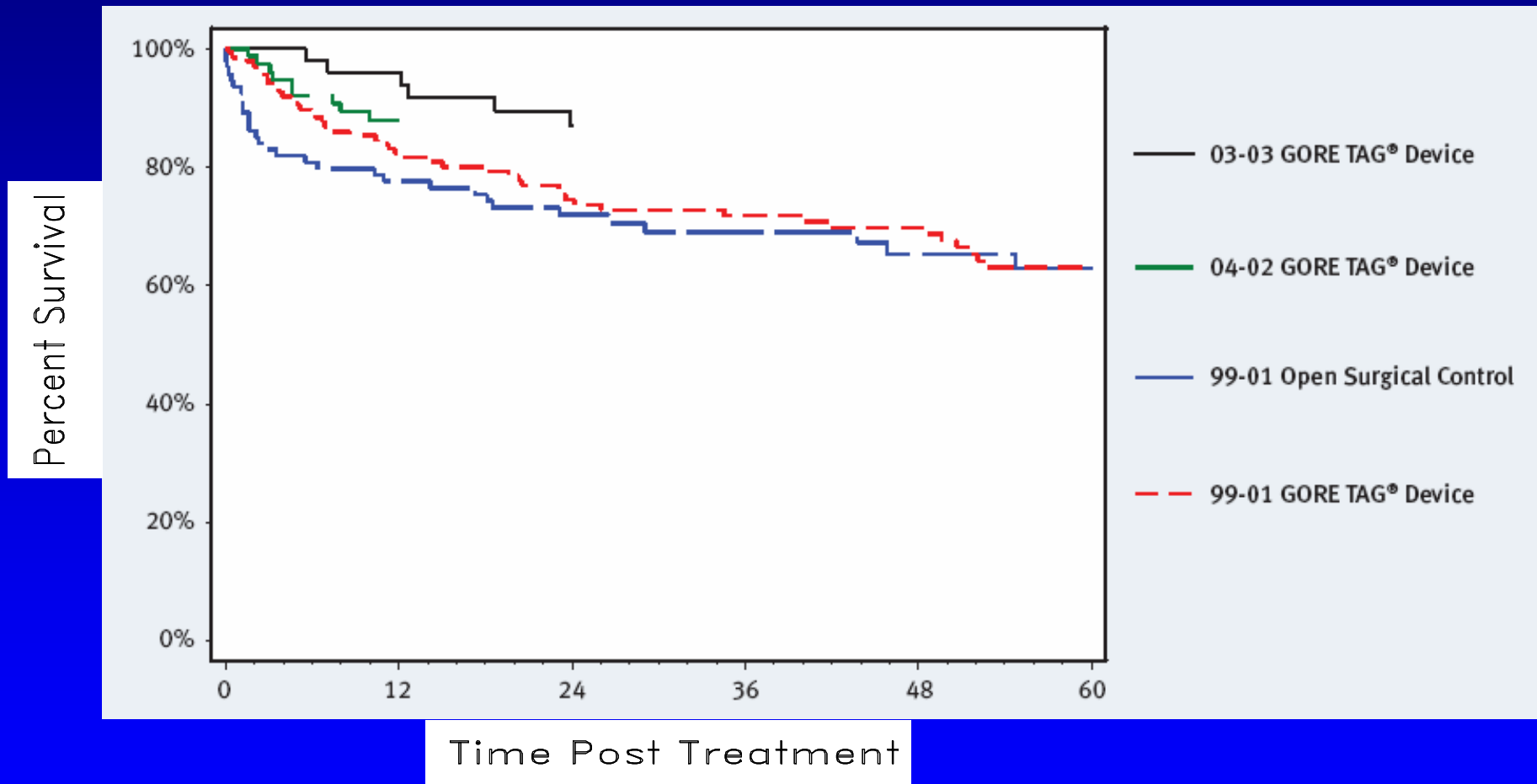
Cumulative Major Adverse Events Through Five Years

Cumulative Major AE

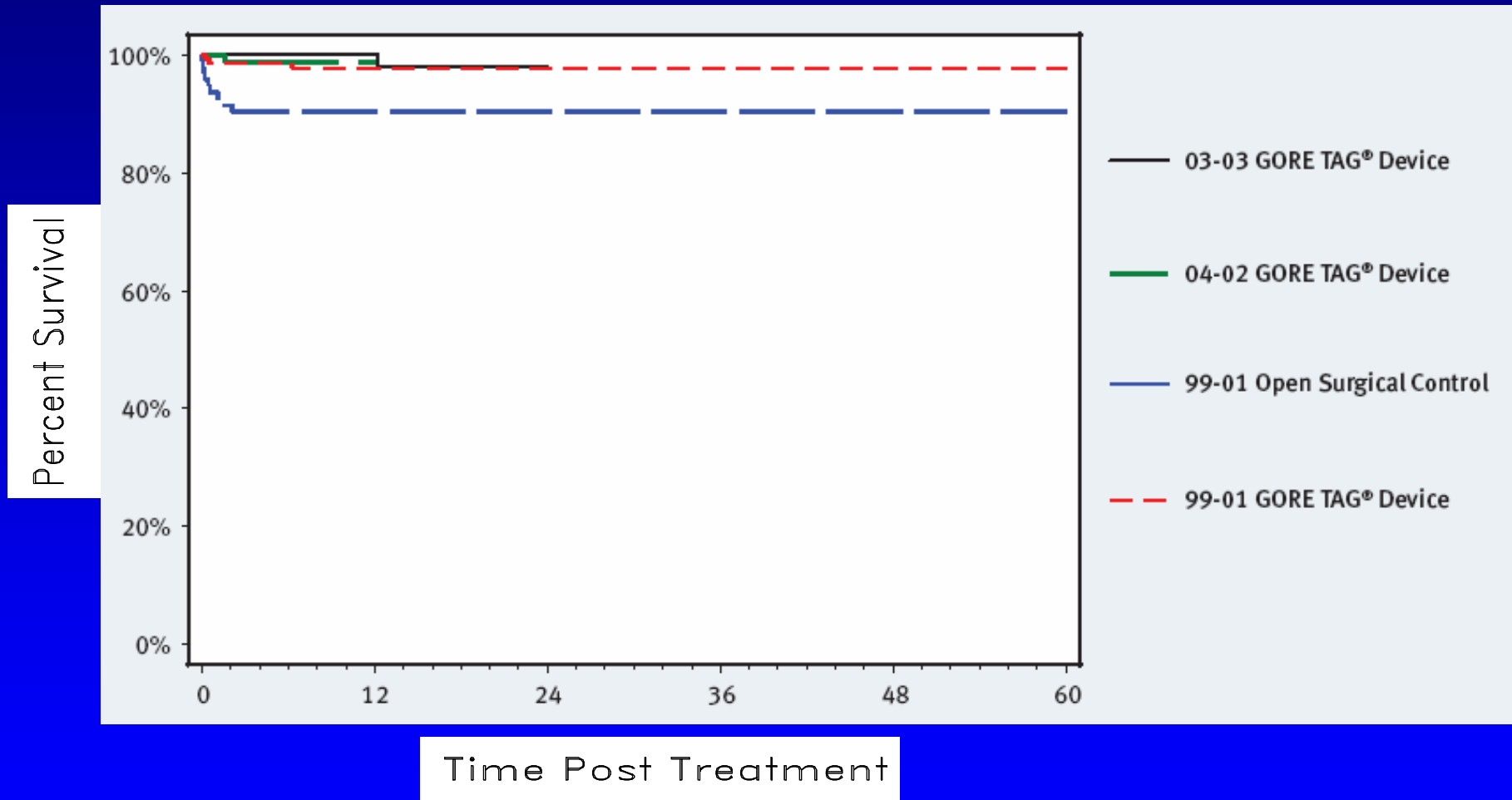


Time Post Treatment

All-Cause Mortality Through Five Years



Freedom from Aneurysm-Related Death Through Five Years



Pivotal Study (TAG 99-01)

Confirmatory Study (TAG 03-03)

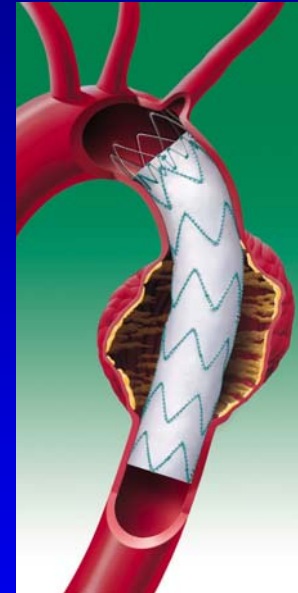
Summary of TAG Studies

In a 5 year controlled trial, treatment of aneurysms of the descending thoracic aorta with TAG is:

- Safer than open surgical repair
- Effective treatment for aneurysms of the DTA—no ruptures
- Less blood loss, shorter hospital and ICU stay and a quicker return to normal activities compared to open surgical repair
- Need for follow up and late reinterventions

US Trials--Nitinol/Polyester Standard Risk Arm

- 195 TEVAR
- Median age: 70.2 years
- Mean aneurysm diameter: 55.5 mm
- 12 month Results
 - Overall mortality: 16.1 % (Historic Control 29.8%)
 - Aneurysm-related mortality 3.1%
 - Major morbidity 43%
 - Conversion 0.5%
 - Aneurysm rupture 0.5%
 - Migration 3.9%
 - Endoleak 12.2%
 - Reintervention 6.5%
 - Loss of stent graft integrity: 4 patients
- SVS 2007



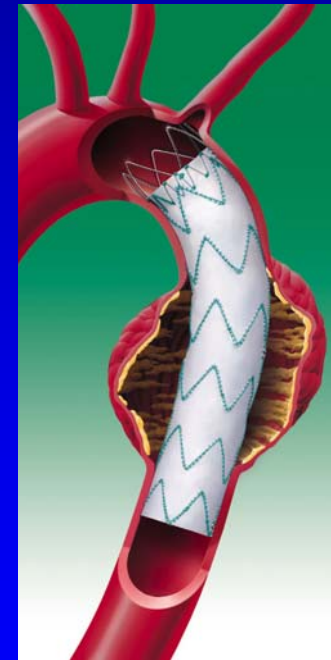
Summary of Standard Risk Trials

For treatment of aneurysms of the descending thoracic aorta, TEVAR is:

- Safer than open surgical repair
- Effective treatment for aneurysms of the DTA
- Less blood loss, shorter hospital and ICU stay and a quicker return to normal activities compared to open surgical repair
- Similar survival, lower aneurysm-related mortality
- Need for surveillance and late reinterventions

US Trials—Nitinol/Polyester High Risk, Non-Surgical Arm

- 137 patients
- Median age: 75 years
- Median aneurysm diameter: 64 mm
- Median follow-up: 8 months
- Results
 - 30 d mortality: 7.3%
 - Stroke: 7.3%
 - Paraplegia: 1%
 - Overall mortality at 12 months: 25%
- MVSS 2005



Is open surgery still indicated?

- Data available:
 - 5 year TAA results show TEVAR has persistent advantages
 - If anatomy for TEVAR, no open surgery
- Open surgery has a role compared to off-label TEVAR
- Technology continues to develop
 - Eventually most thoracic pathology that deserves invasive intervention will be TEVAR