

13th Annual Angioplasty Summit
TCT Asia Pacific
Seoul, Korea
April 24, 2008



A Teaching Affiliate
of Harvard Medical School



Which Patients Are Good Candidates for Carotid Artery Stenting or Carotid Endarterectomy

Michael R. Jaff, DO, FACP, FACC
Associate Professor of Medicine
Harvard Medical School
Medical Director, Vascular Center
Massachusetts General Hospital
Boston, Massachusetts, U.S.A.



MASSACHUSETTS
GENERAL HOSPITAL

VASCULAR CENTER

Michael R. Jaff, DO

Conflicts of Interest

- **Consultant**
 - Abbott Vascular
 - Atheromed
 - Bacchus Vascular, Inc
 - Baxter, Incorporated
 - FlexStent, Incorporated
 - Harvard Clinical Research Institute
 - Hypermed, Incorporated
 - I.C.Sciences, Incorporated
 - Micelle, Incorporated
 - Paragon IP
 - Pathway Medical
- **Equity**
 - Access Closure, Inc
 - Icon Interventional, Inc
 - Sadra Medical
 - Setagon
 - Square One, Inc
 - Vascular Therapies, Inc
- **Research Support**
 - Abbott Vascular
 - Genzyme
- **Board Member**
 - VIVA Physicians
 - www.vivapvd.com



A Teaching Affiliate
of Harvard Medical School

April, 2008



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

Burden of Stroke in the U.S.

- 1 stroke every 45 seconds (700,000 per year)
- 2.4 million non-institutionalized stroke survivors
- Stroke causes 1 in 15 deaths
- Approximately 30 % aged 70-80 have silent brain infarction
- Stroke cost= 58.8 billion/year



Treatment Options

- Optimize medical intervention
- Carotid Endarterectomy
- Carotid Artery Stent



Carotid Endarterectomy

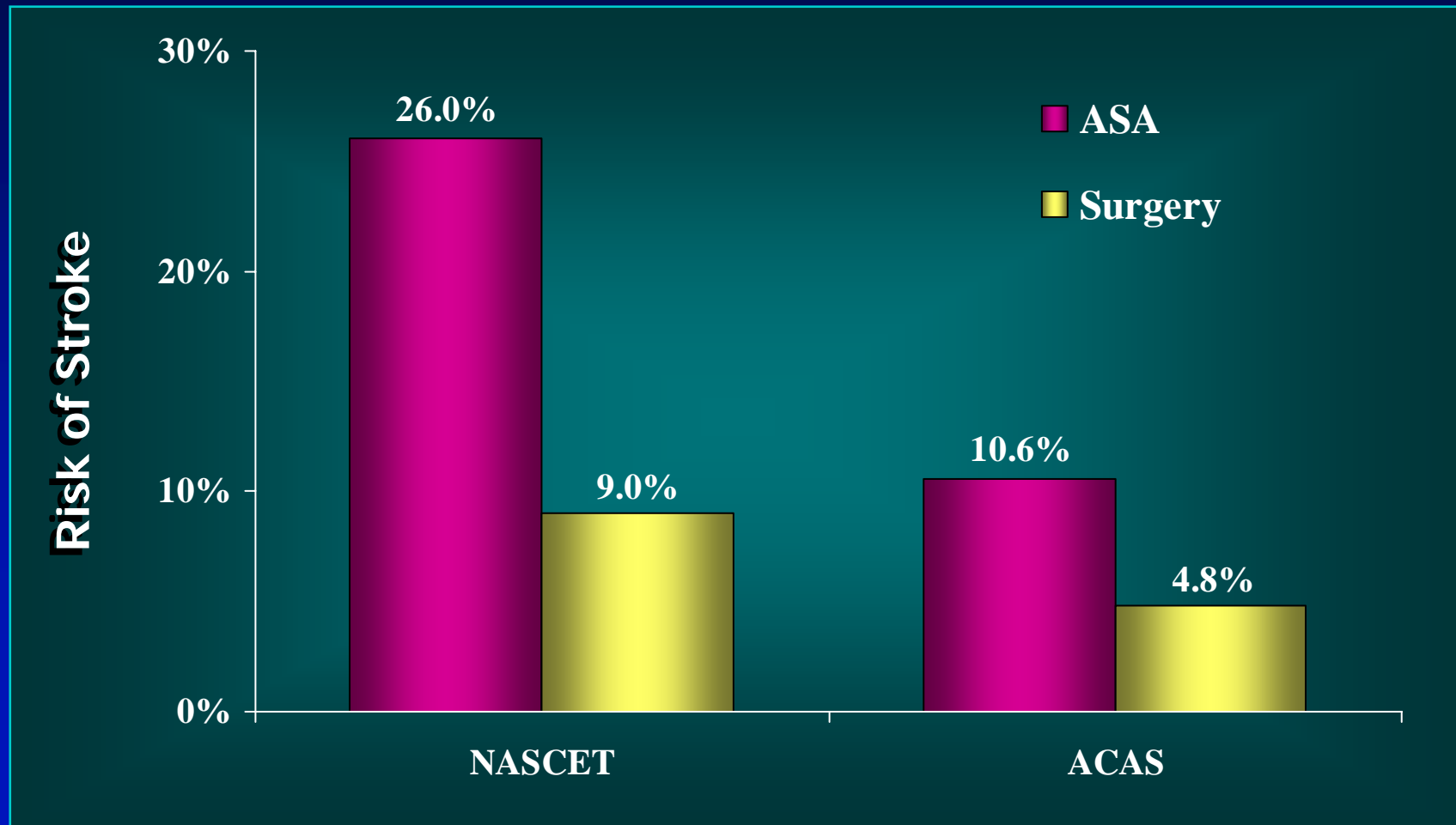


A Teaching Affiliate
of Harvard Medical School



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

Surgery for Carotid Stenosis



Early vs Deferred Carotid Endarterectomy in Asymptomatic Patients with >70% ICA Stenosis

- Prospective randomized multicenter trial in Europe
 - 126 hospitals in 30 Countries
 - Surgeons with documented perioperative CVA/Death rate <6% in prior 50 CEAs
- 3120 asymptomatic patients with asymptomatic ICA stenosis >60%
- Randomized to
 - Immediate CEA
 - Indefinite deferral of CEA
- Followed for up to 5 years (mean 3.4 y)



A Teaching Affiliate
of Harvard Medical School



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

ACST Investigators. Lancet 2004;363:1491-1502

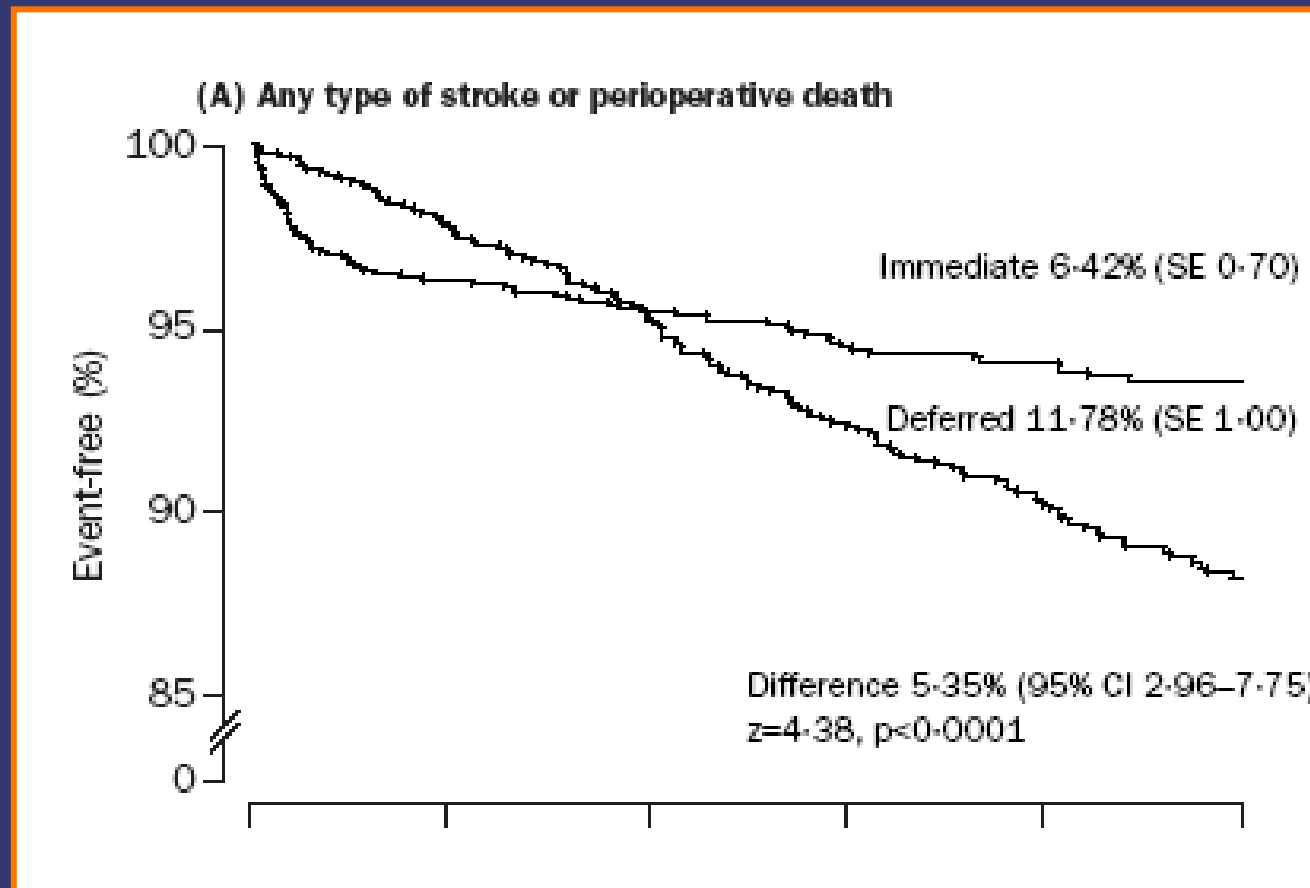
Early vs Deferred Carotid Endarterectomy in Asymptomatic Patients with >70% ICA Stenosis

- Risk of CVA/Death within 30 days of CEA
 - 3.1%
- 5-year CVA risk
 - 3.8% immediate CEA
 - 11% deferred CEA (p<0.0001)
 - Half of all CVAs were disabling
- Combining peri-op and non-peri-op CVA
 - 5-year CVA risk
 - 6.4% vs 11.8% (p<0.0001)



Early vs Deferred Carotid Endarterectomy in Asymptomatic Patients with >70% ICA Stenosis

Any Stroke or Perioperative Death



Carotid Endarterectomy

- **Complications**

- Wound Complications

- Hematoma 0.7-1.5%
- Infection/Pseudoaneurysm 0.15%
- Cranial Nerve Dysfunction
 - Hypoglossal Nerve 5-8%
 - All other Cranial Nerves <2%
- Perioperative Stroke

- Cleveland Clinic

1.5% Asymptomatic

2.7% Prior TIA

3.8% Prior CVA



A Teaching Affiliate
of Harvard Medical School



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

Carotid Artery Stenting



A Teaching Affiliate
of Harvard Medical School



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

Why Carotid Stenting?

- Potential Advantages
 - Less Invasive Technique
 - More Widely Accepted by Patients
 - Less Discomfort
 - Faster Recovery Time
 - Less Expensive
 - Treat Difficult Lesions
 - Post Radiation ICA Stenosis
 - Restenosis after Endarterectomy
 - High Bifurcation Stenosis
 - Serious Co-Morbid Medical Conditions



Who Should Receive a Carotid Stent?

- It all depends on who you ask...



Who Should Receive a Carotid Stent?

- Centers for Medicare/Medicaid Services



A Teaching Affiliate
of Harvard Medical School



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER



Who Will Be Covered?

- Patients at **high risk for CEA** with a SYMPTOMATIC carotid artery stenosis $\geq 70\%$
- Patients at **high risk for CEA** with a SYMPTOMATIC carotid artery stenosis between 50% and 70% AND are enrolled in a Category B IDE Clinical Trial
- Patients at **high risk for CEA** with an ASYMPTOMATIC carotid artery stenosis $\geq 80\%$ AND are enrolled in a Category B IDE Clinical Trial

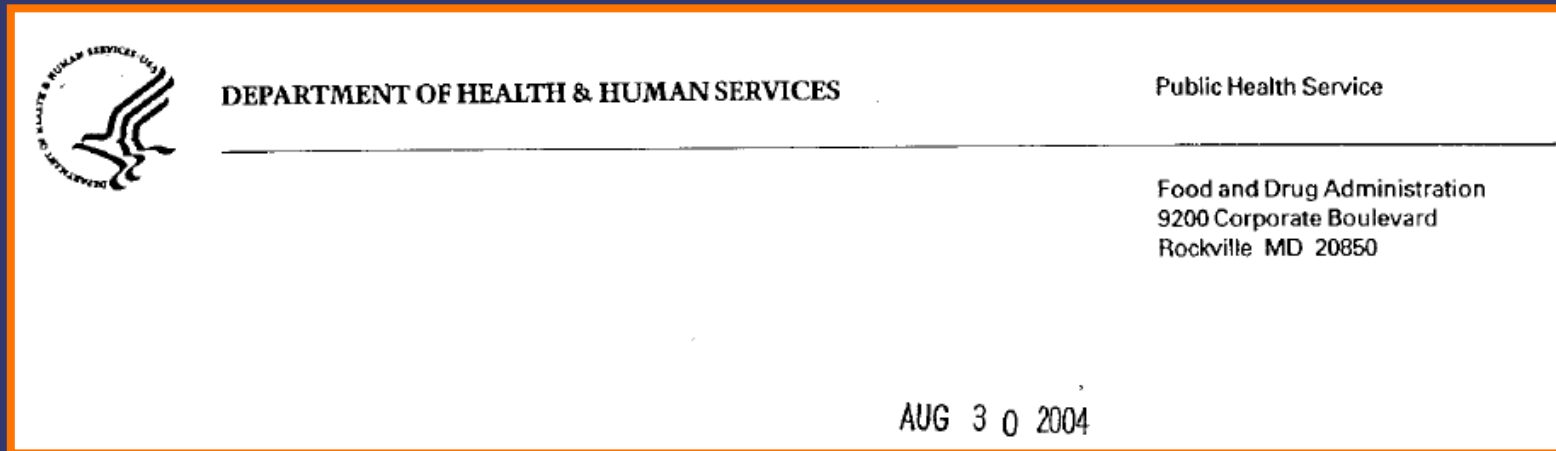


Who Should Receive a Carotid Stent?

- Centers for Medicare/Medicaid Services
- U.S. Food and Drug Administration



FDA Approval of Guidant Acculink Carotid Stent System



P040012
ACCULINK™ Carotid Stent System

We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions described below and in the "Conditions of Approval" (enclosed).

FDA-Approved Indications

The ACCULINK™ Carotid Stent System and the RX ACCULINK™ Carotid Stent System, used in conjunction with Guidant carotid embolic protection systems, is indicated for the treatment of patients at high risk for adverse events from carotid endarterectomy who require carotid revascularization and meet the criteria outlined below.

1. Patients with neurological symptoms and $\geq 50\%$ stenosis of the common or internal carotid artery by ultrasound or angiogram OR patients without neurological symptoms and $\geq 80\%$ stenosis of the common or internal carotid artery by ultrasound or angiogram, AND
2. Patients must have a reference vessel diameter within the range of 4.0 mm and 9.0 mm at the target lesion.



What is “High Risk”?

- **Co-Morbid Medical Conditions**

- Congestive heart failure (class III/IV) and/or known severe left ventricular dysfunction
LVEF <30%
- Open heart surgery needed within six weeks
- Recent MI (>24 hrs. and <4 weeks)
- Unstable angina (CCS class III/IV)
- Severe pulmonary disease

- **Anatomic Factors**

- Contralateral carotid occlusion
- Contralateral laryngeal nerve palsy
- Radiation therapy to neck
- Previous CEA with recurrent stenosis
- High cervical ICA lesions or CCA lesions below the clavicle
- Severe tandem lesions
- Age > 80 years



Who Should Receive a Carotid Stent?

- Centers for Medicare/Medicaid Services
- U.S. Food and Drug Administration
- Neurologists



Asymptomatic carotid stenosis: what to do

Jessica N. Redgrave and Peter M. Rothwell

Purpose of review

Patients with asymptomatic carotid stenosis are at increased vascular risk but optimal treatment is

Optimal medical treatment is the most important aspect of management of patients with asymptomatic carotid stenosis. On the basis of previous trials, endarterectomy is only of overall benefit in men, and this benefit may now be obviated by improved medical treatment. There is insufficient evidence to advocate the routine use of carotid angioplasty or stenting in patients with asymptomatic stenosis. Inaccuracy in the measurement of carotid stenosis

are lacking.

Summary

Absolute benefit from endarterectomy for asymptomatic carotid stenosis is small, but can sometimes be justified in men. Further research is required to determine long-term benefit in women and to risk stratify patients, particularly in the light of advances in medical treatment.

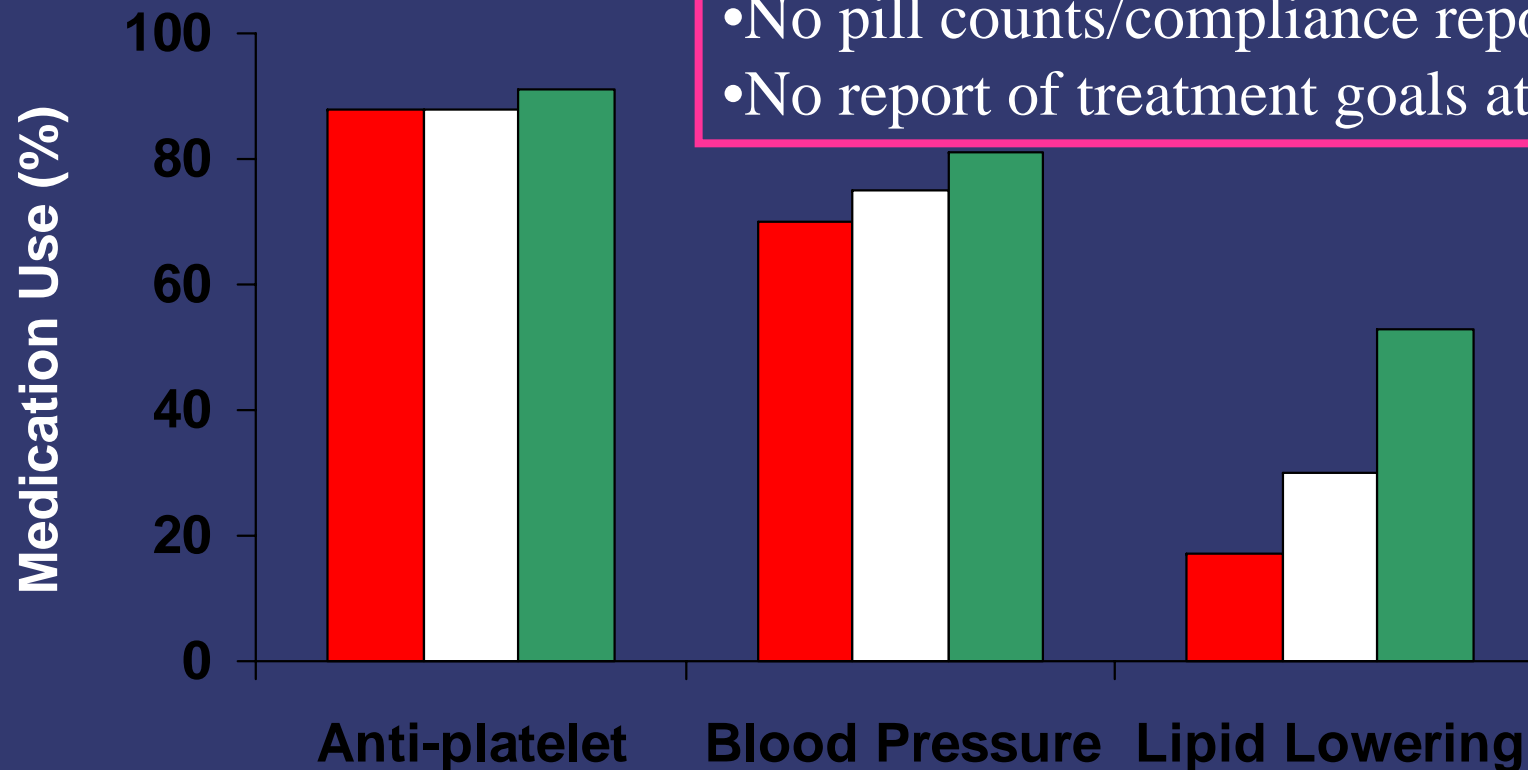


A Teaching Affiliate
of Harvard Medical School



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

MRC Asymptomatic Carotid Surgery Trial (ACST): Medical RX



Problems:

- No pill counts/compliance reports
- No report of treatment goals attained



A Teaching Affiliate
of Harvard Medical School

■ 93 - 96 ■ 97 - 99 ■ 00 - 03



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

Who Should Receive a Carotid Stent?

- Centers for Medicare/Medicaid Services
- U.S. Food and Drug Administration
- Neurologists
- Vascular Surgeons



Long-term results of 442 consecutive, standardized carotid endarterectomy procedures in standard-risk and high-risk patients

D. Preston Flanigan, MD, Meghan E. Flanigan, Andrew L. Dorne, Timothy R.S. Harward, MD, Mahmood K. Razavi, MD, and Jeffrey L. Ballard, MD, *Orange, Calif*

<i>Category</i>	<i>Standard risk</i>	<i>High risk</i>	<i>Total (%)</i>	<i>P</i>
All strokes	1	1	2 (0.45)	.982
Death	0	0	0 (0)	NA
MI	1	0	1 (0.23)	.347
All strokes or death	1	1	2 (0.45)	.982
All strokes or death or MI	2	1	3 (0.68)	.638



A Teaching Affiliate
of Harvard Medical School

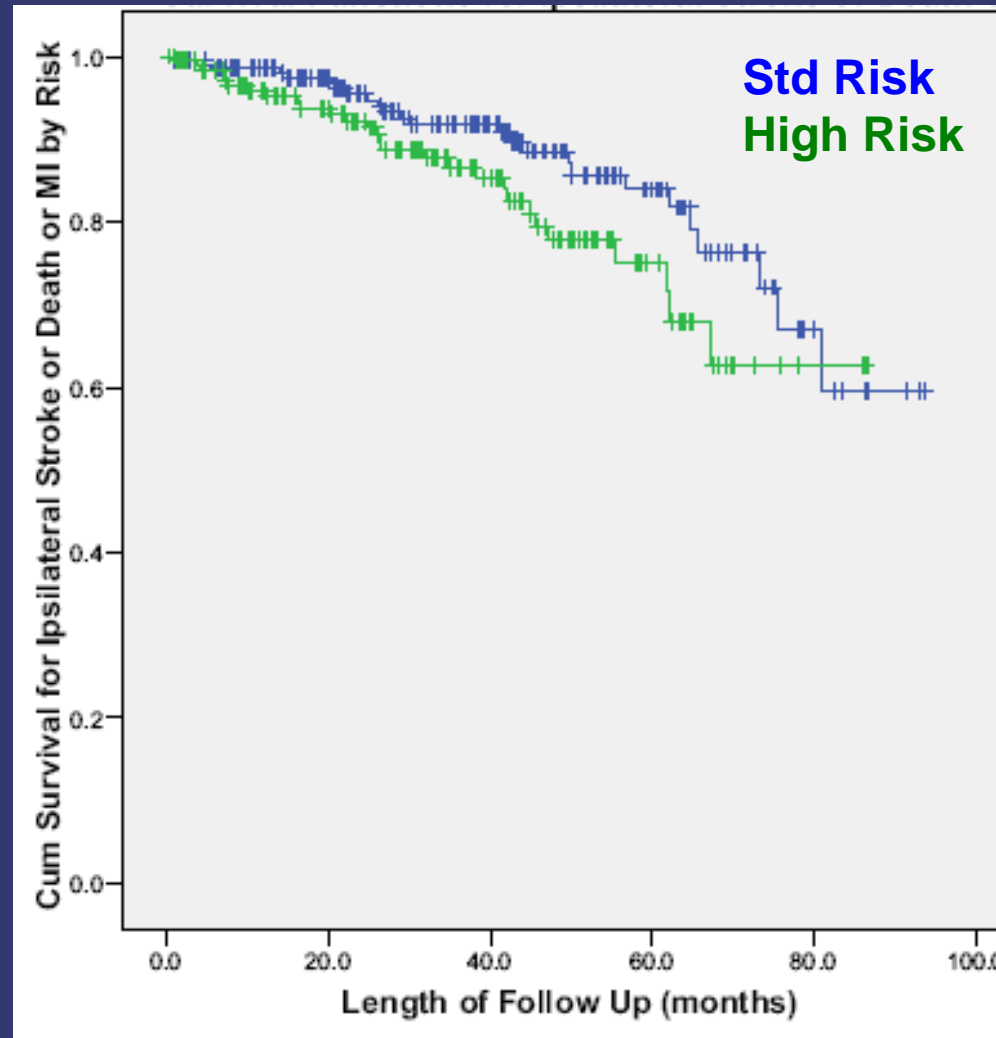
J Vasc Surg 2007;46:876



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

Long-term results of 442 consecutive, standardized carotid endarterectomy procedures in standard-risk and high-risk patients

D. Preston Flanigan, MD, Meghan E. Flanigan, Andrew L. Dorne, Timothy R.S. Harward, MD, Mahmood K. Razavi, MD, and Jeffrey L. Ballard, MD, *Orange, Calif*



MGH RECENT RESULTS -- CEA

	<u>2003–04</u>	<u>2004–05</u>	<u>2005–06</u>	<u>2006–07</u>
Total CEA	292	268	256	251
All strokes	4 (1.4 %)	3 (1.1%)	1 (0.4%)	1 (0.5%)
Deaths	0	1	1	0
Stroke/Death	1.4%	1.5%	0.4%	1 (0.5%)



A Teaching Affiliate
of Harvard Medical School

Courtesy of Richard Cambria, MD
March 2008



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

NATIONAL INPATIENT SAMPLE DATA

Carotid endarterectomy was performed with lower stroke and death rates than carotid artery stenting in the United States in 2003 and 2004

James T. McPhee, MD,^a Joshua S. Hill, MD, MS,^b Rocco G. Ciocca, MD,^b Louis M. Messina, MD,^b and Mohammad H. Eslami, MD,^b *Worcester, Mass*

Objective: Although carotid endarterectomy (CEA) is the gold standard for the treatment of carotid artery stenosis, the recent United States Food and Drug Administration approval of carotid artery stenting (CAS) may have led to its widespread use outside of clinical trials and registries. This study compared in-hospital postoperative stroke and mortality rates after CAS and CEA at the national level.

Methods: The Nationwide Inpatient Sample (NIS) was queried to identify all patient-discharges that occurred for revascularization of carotid artery stenosis. The *International Classification of Diseases, 9th Revision, Clinical Modification* procedure codes for CEA (38.12), CAS (00.63), and insertion of noncoronary stents (39.50, 39.90) were used in conjunction with the diagnostic codes for carotid artery stenosis, with (433.11) and without (433.10) stroke. Primary outcome measures included in-hospital postoperative stroke and death rates. Multivariate logistic regressions were performed to evaluate independent predictors of postoperative stroke and mortality. Adjustment was made for age, sex, medical comorbidities, admission diagnosis, procedure type, year, and hospital type.

Results: During the calendar years 2003 and 2004, an estimated 259,080 carotid revascularization procedures were performed in the United States. CAS had a higher rate of in-hospital postoperative stroke (2.1% vs 0.88%, $P < .0001$) and higher postoperative mortality (1.3% vs 0.39%) than CEA. For asymptomatic patients (92%), the postoperative stroke rate was significantly higher for CAS than CEA (1.8% vs 0.86%, $P < .0001$), but the mortality rate was similar (0.44% vs 0.36%, $P = .36$). For symptomatic patients (8%), the rates for postoperative stroke (4.2% vs 1.1%, $P < .0001$) and mortality (7.5% vs 1.0%, $P < .0001$) were significantly higher after CAS. By multivariate regression, CAS was independently predictive of postoperative stroke (odds ratio [OR], 2.49; 95% confidence interval [CI], 1.91 to 3.25). CAS was also associated with in-hospital postoperative mortality for asymptomatic (OR, 2.37; 95% CI, 1.46 to 3.84) and symptomatic (OR, 2.64; 95% CI, 1.89 to 3.69) patients.

Conclusions: As determined from a large representative national sample including the years 2003 and 2004, the in-hospital stroke rate after CAS for asymptomatic patients was twofold higher than after CEA. For symptomatic patients, the respective in-hospital stroke and mortality rates were fourfold and sevenfold higher. These unexpected results indicate that further randomized controlled trials with homogenous symptomatic and asymptomatic patient groups should be performed. (*J Vasc Surg* 2007;46:1112-8.)



A Teaching Affiliate
of Harvard Medical School



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

J Vasc Surg 2007;46:1112-8

National Inpatient Sample Data

Variable	CAS	CEA	p Value
In Hospital CVA	2.1%	0.88%	<0.0001
Mortality	1.3%	0.39%	NS
Asymp CVA	1.8%	0.86%	<0.0001
Symp CVA	4.2%	1.1%	<0.0001



A Teaching Affiliate
of Harvard Medical School

J Vasc Surg 2007;46:1112-8



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

Who Should Receive a Carotid Stent?

- Centers for Medicare/Medicaid Services
- U.S. Food and Drug Administration
- Neurologists
- Vascular Surgeons
- Interventionists



A Teaching Affiliate
of Harvard Medical School



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

ACCF/SCAI/SVMB/SIR/ASITN 2007 Clinical Expert Consensus Document on Carotid Stenting

Randomized Trials of CAS vs CEA

Trial	N	Patient Subset	EPD Stent	Primary End Point	Comment
Wallstent (184)	219	Low risk Symptomatic	None Wallstent	1 yr stroke/D	CAS 10.4%, CEA 4.4%; stopped prematurely
SAPPHIRE (160)	334	High risk Symptomatic, Asymptomatic	AngioGuard Precise	30 days MI/stroke/D plus 1 yr ipsilateral stroke/D	CAS 12.2%, CEA 20.1%; stopped prematurely for slow enrollment
CREST	2,500	Low risk Symptomatic, Asymptomatic	AccUNET Acculink	30 days MI/stroke/D and 4 yr ipsilateral stroke	Active enrollment
SPACE (196a)	1,183	Low risk Symptomatic	Various Various	30 days ipsilateral stroke/D	CAS 6.8%, CEA 6.3%; stopped prematurely
EVA-3S (198a)	527	Low risk Symptomatic	Various Various	30 days stroke/D and 4 yr ipsilateral stroke	CAS 9.6%, CEA 3.9%; stopped prematurely
ICSS (CAVATAS II)	1,500	Low risk Symptomatic	Various Various	30 days MI/stroke/D and 3 yr disabling stroke/D	Active enrollment
ACT-1	1,540	Low risk Asymptomatic	Emboshield Xact	30 days MI/stroke/D plus 1 yr ipsilateral stroke	Active enrollment
ACST-2	5,000	Any risk Asymptomatic	Various Various	30 days MI/stroke/D 1 yr stroke/D	Active enrollment



A Teaching Affiliate
of Harvard Medical School



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

OCTOBER 7, 2004

VOL. 351 NO. 15

Protected Carotid-Artery Stenting versus Endarterectomy in High-Risk Patients

Jay S. Yadav, M.D., Mark H. Wholey, M.D., Richard E. Kuntz, M.D., M.Sc., Pierre Fayad, M.D., Barry T. Katzen, M.D., Gregory J. Mishkel, M.D., Tanvir K. Bajwa, M.D., Patrick Whitlow, M.D., Neil E. Strickman, M.D., Michael R. Jaff, D.O., Jeffrey J. Popma, M.D., David B. Snead, Ph.D., Donald E. Cutlip, M.D., Brian G. Firth, M.D., Ph.D., and Kenneth Ouriel, M.D., for the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy Investigators*



A Teaching Affiliate
of Harvard Medical School



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

SAPPHIRE Data

Event	Intention-to-Treat Analysis			Actual-Treatment Analysis		
	Stenting (N=167) no. (%)	Endarterectomy (N=167) no. (%)	P Value	Stenting (N=159) no. (%)	Endarterectomy (N=151) no. (%)	P Value
Death	12 (7.4)	21 (13.5)	0.08	11 (7.0)	19 (12.9)	0.08
Stroke	10 (6.2)	12 (7.9)	0.60	9 (5.8)	11 (7.7)	0.52
Major ipsilateral	1 (0.6)	5 (3.3)	0.09	0	5 (3.5)	0.02
Major nonipsilateral	1 (0.6)	2 (1.4)	0.53	1 (0.6)	1 (0.7)	0.97
Minor ipsilateral	6 (3.7)	3 (2.0)	0.34	6 (3.8)	3 (2.2)	0.37
Minor nonipsilateral	3 (1.9)	4 (2.7)	0.64	3 (2.0)	3 (2.1)	0.89
Myocardial infarction	5 (3.0)	12 (7.5)	0.07	4 (2.5)	12 (8.1)	0.03
Q-wave	0	2 (1.2)	0.15	0	2 (1.3)	0.15
Non-Q-wave	5 (3.0)	10 (6.2)	0.17	4 (2.5)	10 (6.7)	0.08
Cranial-nerve palsy	0	8 (4.9)	0.004	0	8 (5.3)	0.003
Target-vessel revascularization	1 (0.6)	6 (4.3)	0.04	1 (0.7)	6 (4.6)	0.04
Conventional end point (stroke or death at 30 days plus ipsilateral stroke or death from neurologic causes within 31 days to 1 yr)	9 (5.5)	13 (8.4)	0.36	8 (5.1)	11 (7.5)	0.40
Primary end point (death, stroke, or myocardial infarction at 30 days plus ipsilateral stroke or death from neurologic causes within 31 days to 1 yr)	20 (12.2)	32 (20.1)	0.05	19 (12.0)	30 (20.1)	0.05



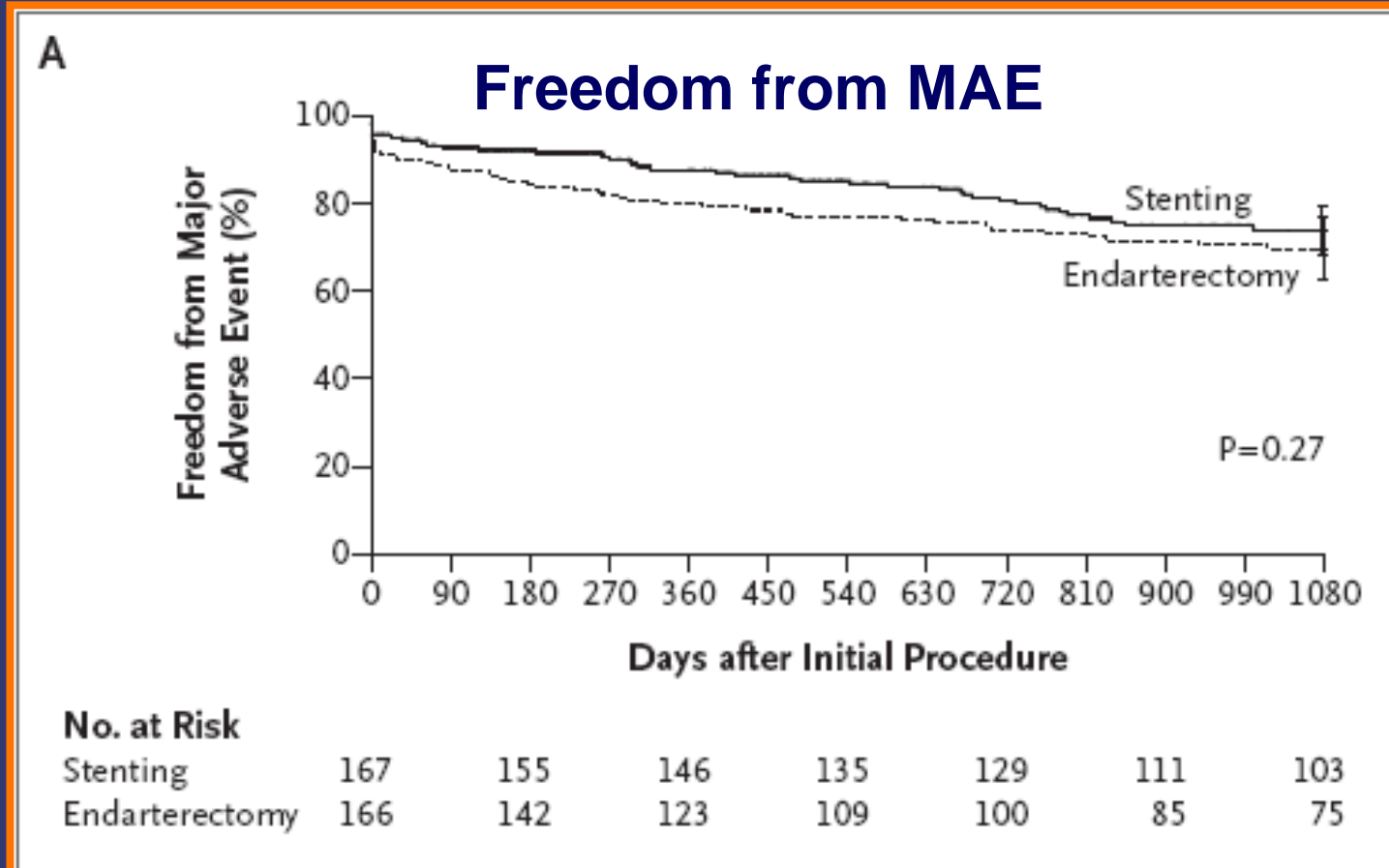
A Teaching Affiliate
of Harvard Medical School

N Engl J Med 2004;351:1493-501.



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

SAPPHIRE 3-Year Outcomes



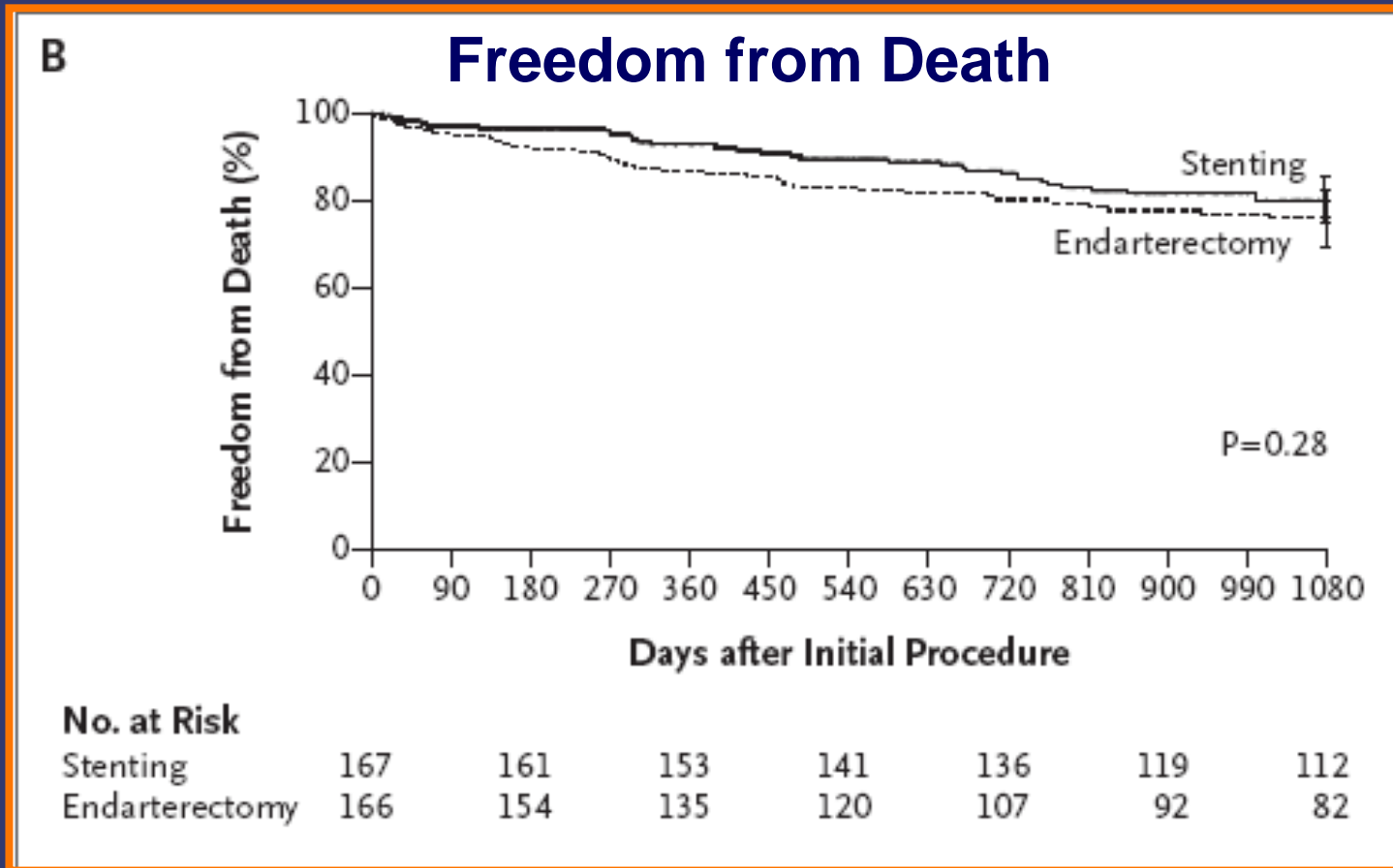
A Teaching Affiliate
of Harvard Medical School

N Engl J Med 2008;358:1572-9



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

SAPPHIRE 3-Year Outcomes



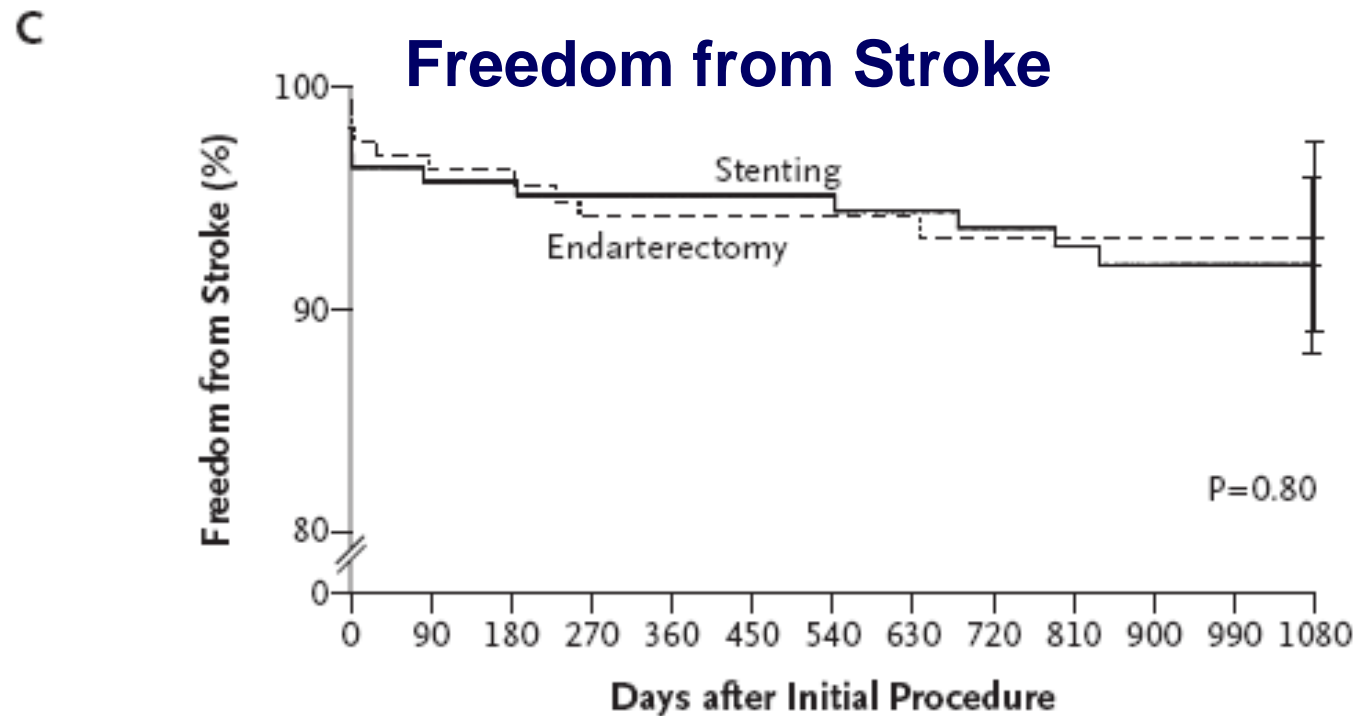
A Teaching Affiliate
of Harvard Medical School

N Engl J Med 2008;358:1572-9



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

SAPPHIRE 3-Year Outcomes



No. at Risk

Stenting	167	154	145	135	128	111	103
Endarterectomy	166	146	128	113	102	87	77



A Teaching Affiliate
of Harvard Medical School

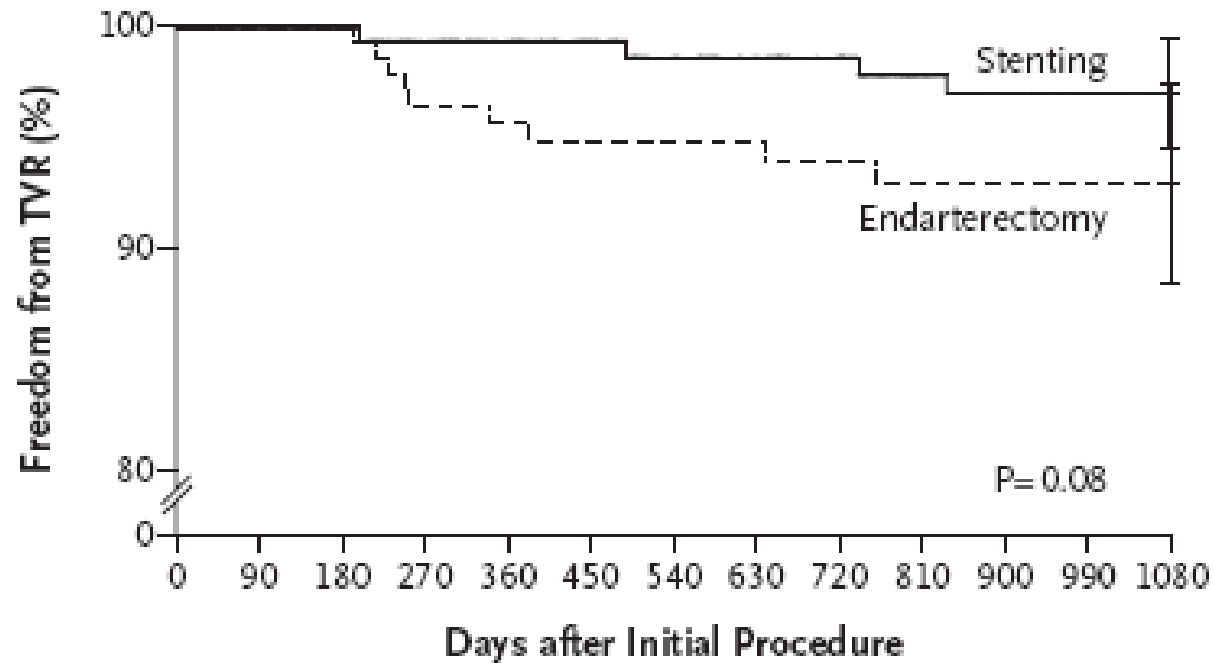
N Engl J Med 2008;358:1572-9



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

SAPPHIRE 3-Year Outcomes

Freedom from TVR



No. at Risk

Stenting	167	157	151	140	133	116	108
Endarterectomy	166	147	128	112	100	83	74



A Teaching Affiliate
of Harvard Medical School

N Engl J Med 2008;358:1572-9



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER

Mortality Rate ACST vs ArCHER

Study	Mortality Rate (%)
ACST (3.4 yr) Standard Risk	16.9
ArCHER (3.0 yr) High Risk	19.1



We Still Don't Know....

- The role of *modern* primary medical intervention in patients with carotid artery stenosis when compared head-to-head with
- Carotid Endarterectomy
- Carotid Artery Stent



How To Choose

- Asymptomatic Standard Risk Patient
 - Enrollment in prospective clinical trial
 - Carotid Endarterectomy



How To Choose

- Asymptomatic Standard Risk Patient
 - Enrollment in prospective clinical trial
 - Carotid Endarterectomy
- Asymptomatic High Risk Patient
 - Enrollment in prospective clinical trial
 - Carotid Endarterectomy
 - Carotid Stent (self pay, coverage)



How To Choose

- Asymptomatic Standard Risk Patient
 - Enrollment in prospective clinical trial
 - Carotid Endarterectomy
- Asymptomatic High Risk Patient
 - Enrollment in prospective clinical trial
 - Carotid Endarterectomy
 - Carotid Stent (self pay, coverage)
- Symptomatic Standard Risk Patient
 - Carotid Endarterectomy
 - Enrollment in prospective clinical trial



How To Choose

- Asymptomatic Standard Risk Patient
 - Enrollment in prospective clinical trial
 - Carotid Endarterectomy
- Asymptomatic High Risk Patient
 - Enrollment in prospective clinical trial
 - Carotid Endarterectomy
 - Carotid Stent (self pay, coverage)
- Symptomatic Standard Risk Patient
 - Carotid Endarterectomy
 - Enrollment in prospective clinical trial
- Symptomatic High Risk Patient
 - Carotid Stent
 - Carotid Endarterectomy



How Controversial Is This???

Circulation 2007;116:October 2

CONTROVERSIES IN CARDIOVASCULAR MEDICINE

Has the expanded use of carotid stents been justified?

Carotid Stents
Frank W. LoGerfo, MD

The CAS technique continues to evolve into a safer and more effective treatment as new technology becomes available. However, CAS is now at a point in its development in which the focus of future clinical research should change. With the availability of embolic protection, improved stent designs, and added endovascular physician experience, outcomes for CAS now consistently parallel those for CEA.

The Argument to Support Broader Application of Extracranial Carotid Artery Stent Technology

Rodney M. Samuelson, MD; Junichi Yamamoto, MD, PhD; Elad I. Levy, MD; Adnan H. Siddiqui, MD, PhD; L. Nelson Hopkins, MD



A Teaching Affiliate
of Harvard Medical School

Why Is This So Controversial?

Is It The Lack of Data?
I Think Not...

Politics

Ego

Lack of Unified Voice Among
the Medical Community



A Teaching Affiliate
of Harvard Medical School



MASSACHUSETTS
GENERAL HOSPITAL
VASCULAR CENTER