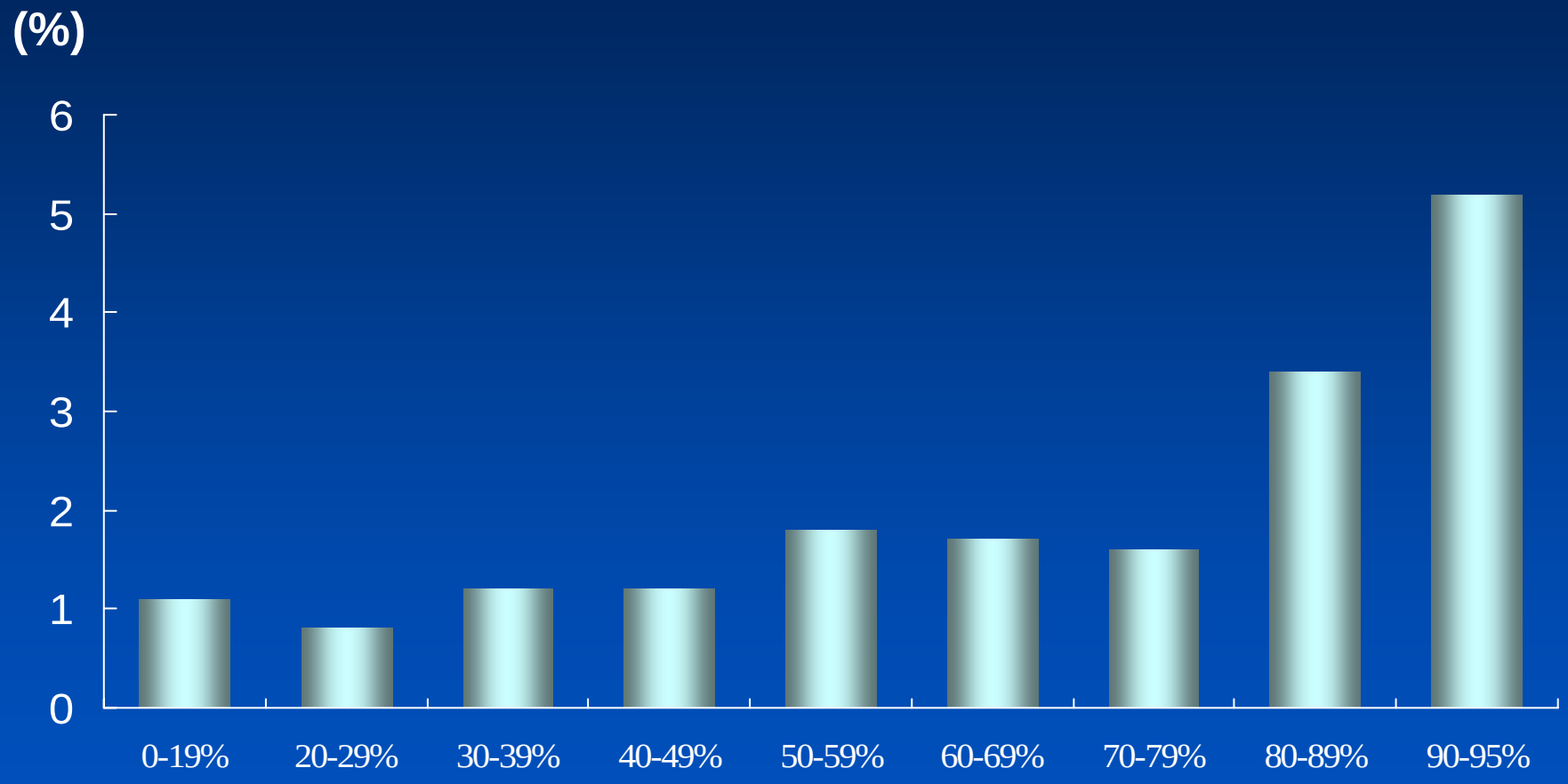
Percutaneous Intervention for Carotid Artery Stenosis

Natural Incidence of CVA In Carotid Stenosis

- Asymptomatic 80% carotid stenosis
  - 6% / year
- Symptomatic carotid stenosis
  - 10% / year
  - 40% / 5 years

Annual incidence of major stroke according to stenosis severity

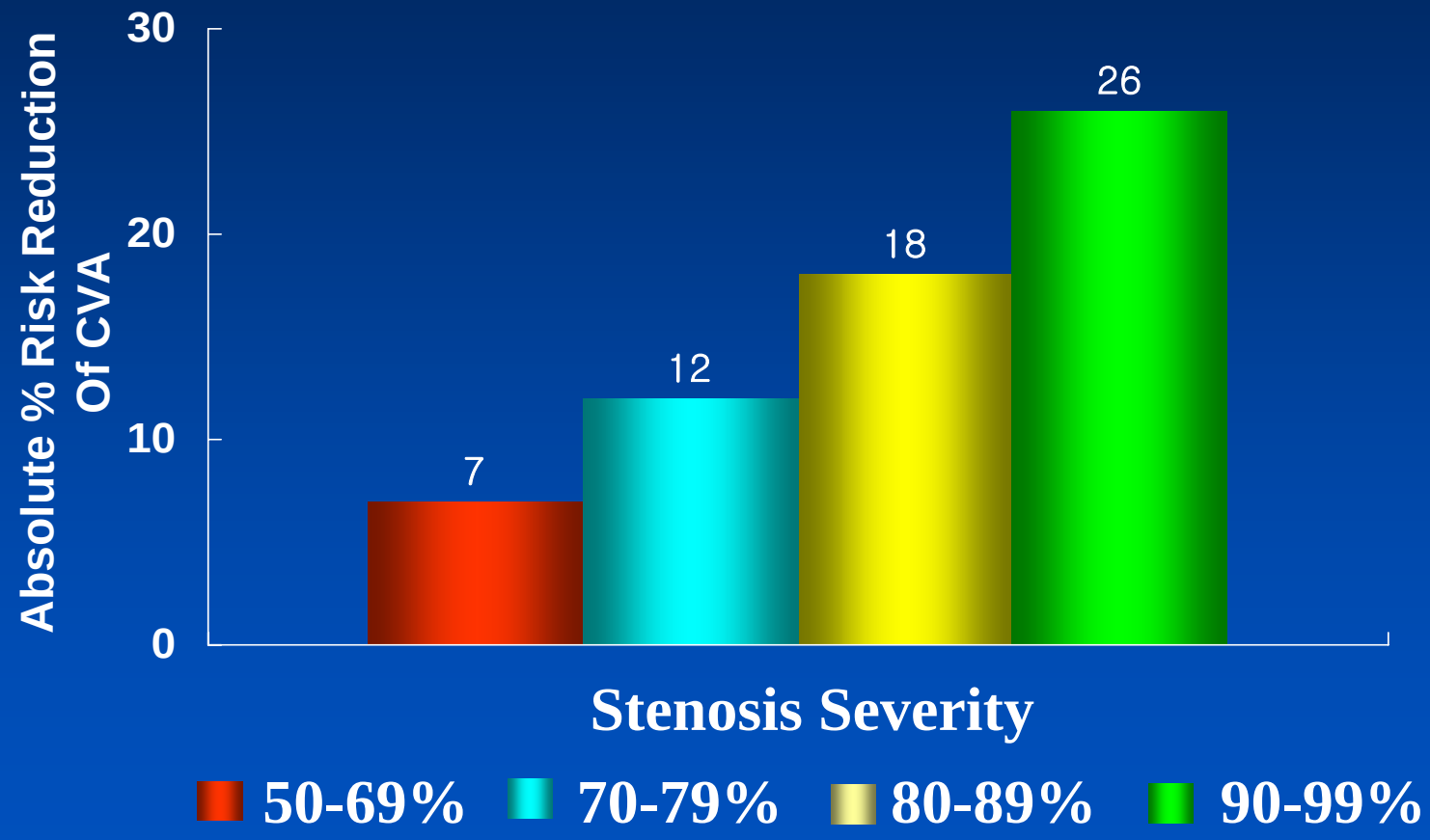


TCT 2005

Why should we open ?

Carotid End-Arterectomy
vs.
Medical Therapy

NASCET
Benefit of CEA by Stenosis Severity



CEA=carotid end arterectomy

Carotid End-Arterectomy

3,061 CEA during a 10-year period

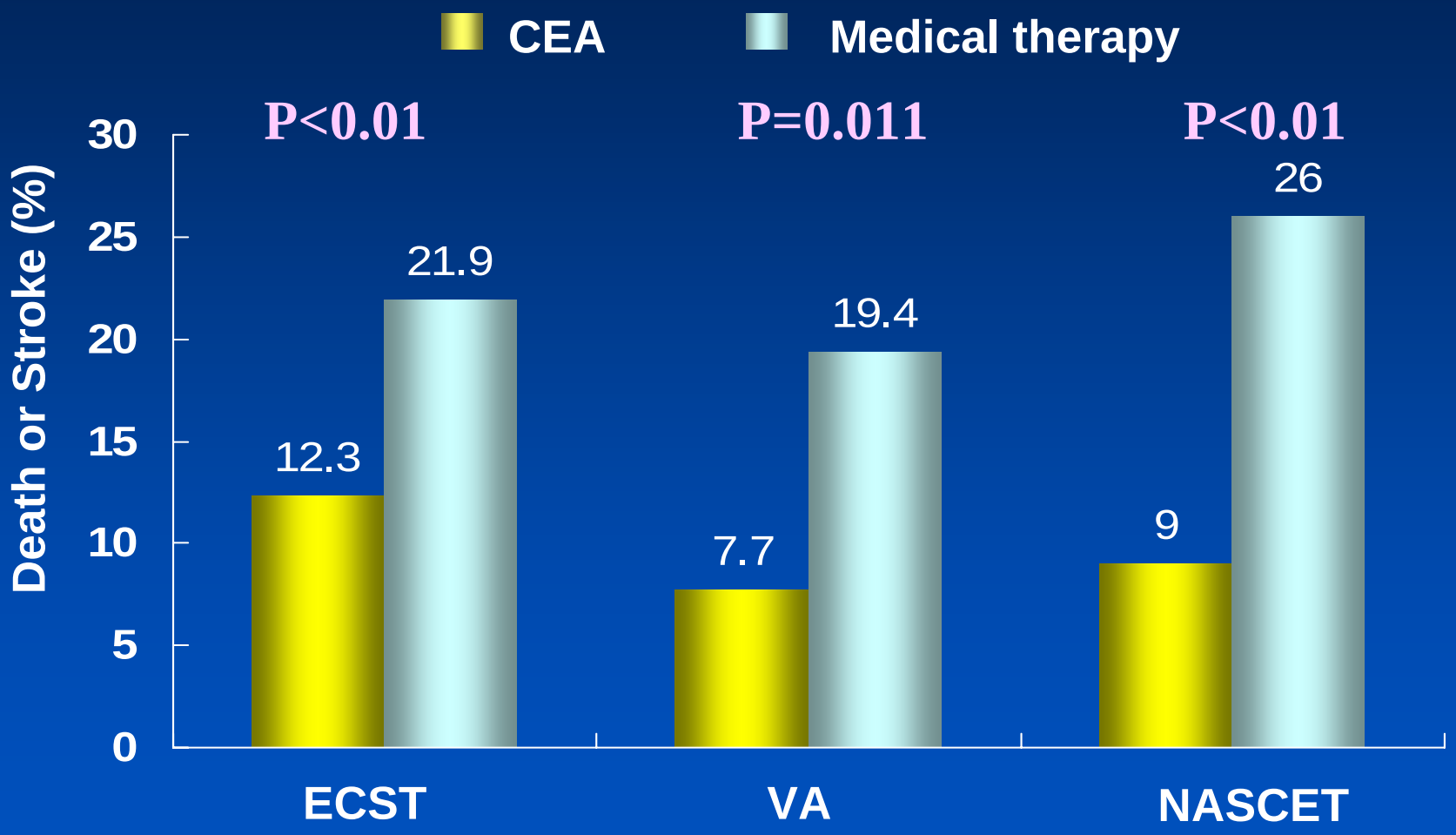
	Stroke	Death	Stroke, MI, Death
High Risk Patients	3.5%	4.4%	7.4%
Low Risk Patients	1.7%	0.3%	2.9%

* **High risk patients**: severe coronary disease, COPD, renal insufficiency

Ouriel K, et al. J Vasc Surg 2001;33:728

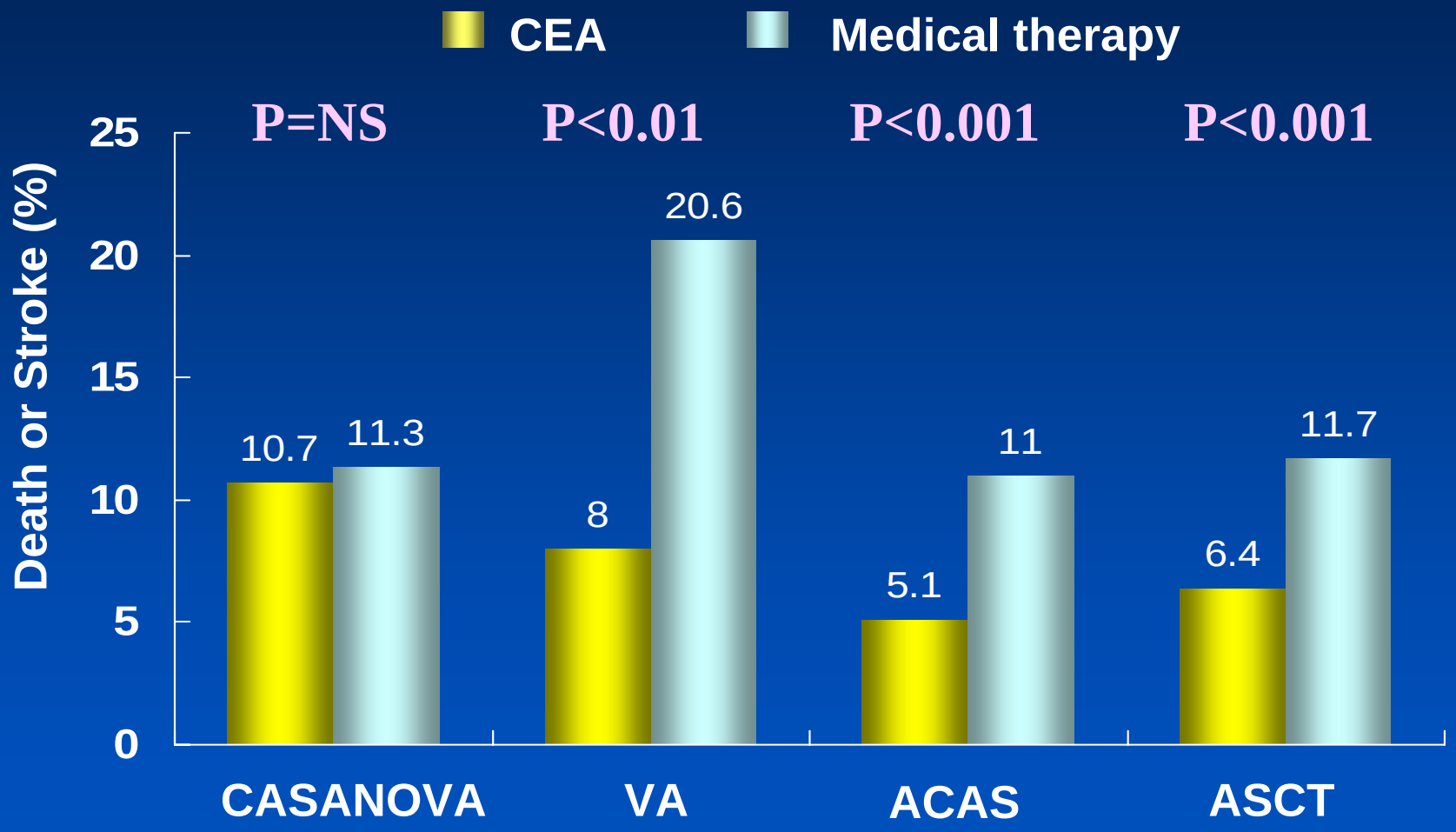
CEA vs. Medical Rx

Symptomatic Patients



CEA vs. Medical Rx

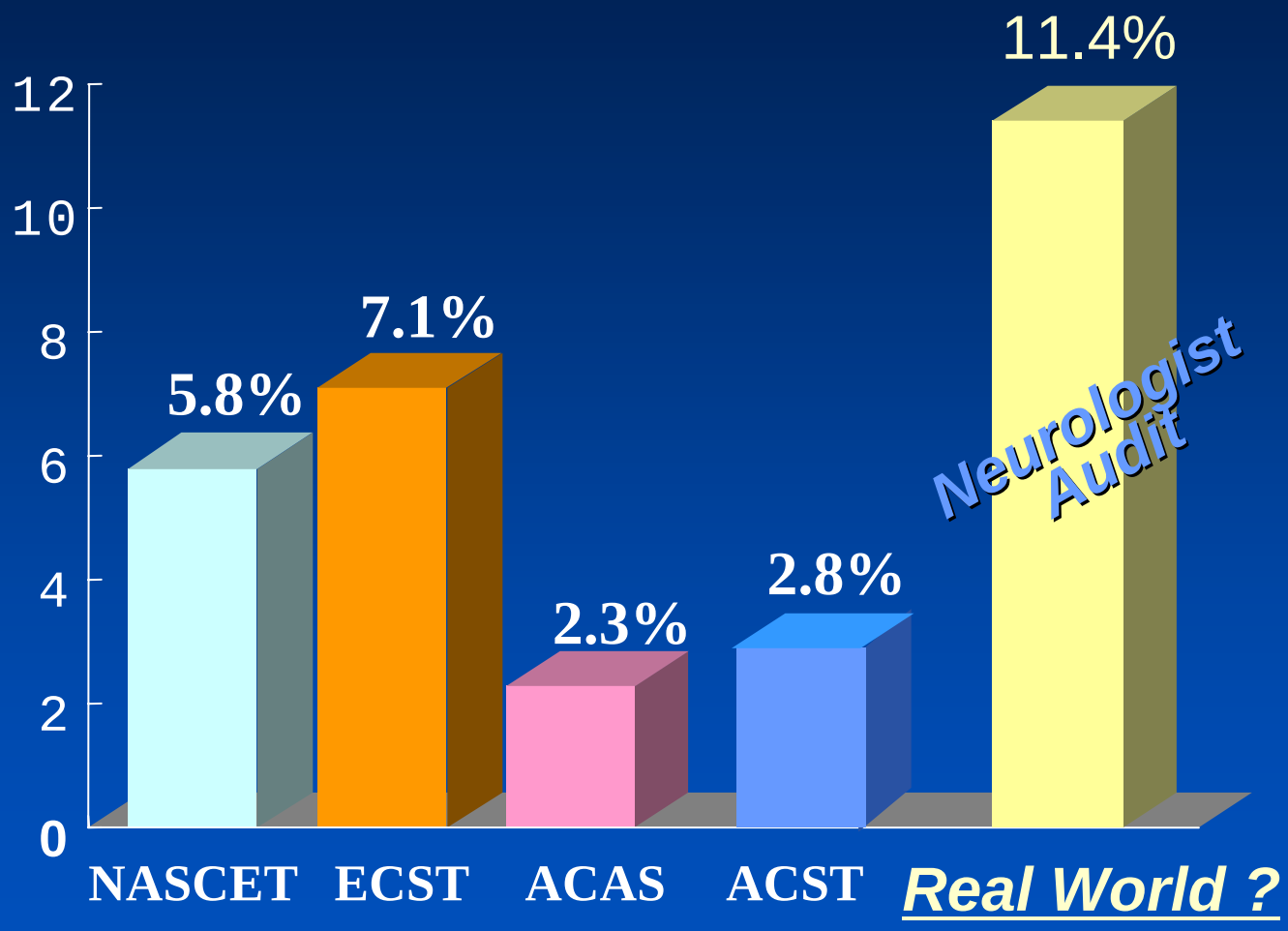
Asymptomatic Patients



Limitations of CEA

- Perioperative stroke for low risk patients : ~6%
- Anatomic considerations
- Cranial nerve palsies : 7~27%
- Restenosis : ~15%
- > 50% have severe coronary artery disease

Death or Stroke after CEA



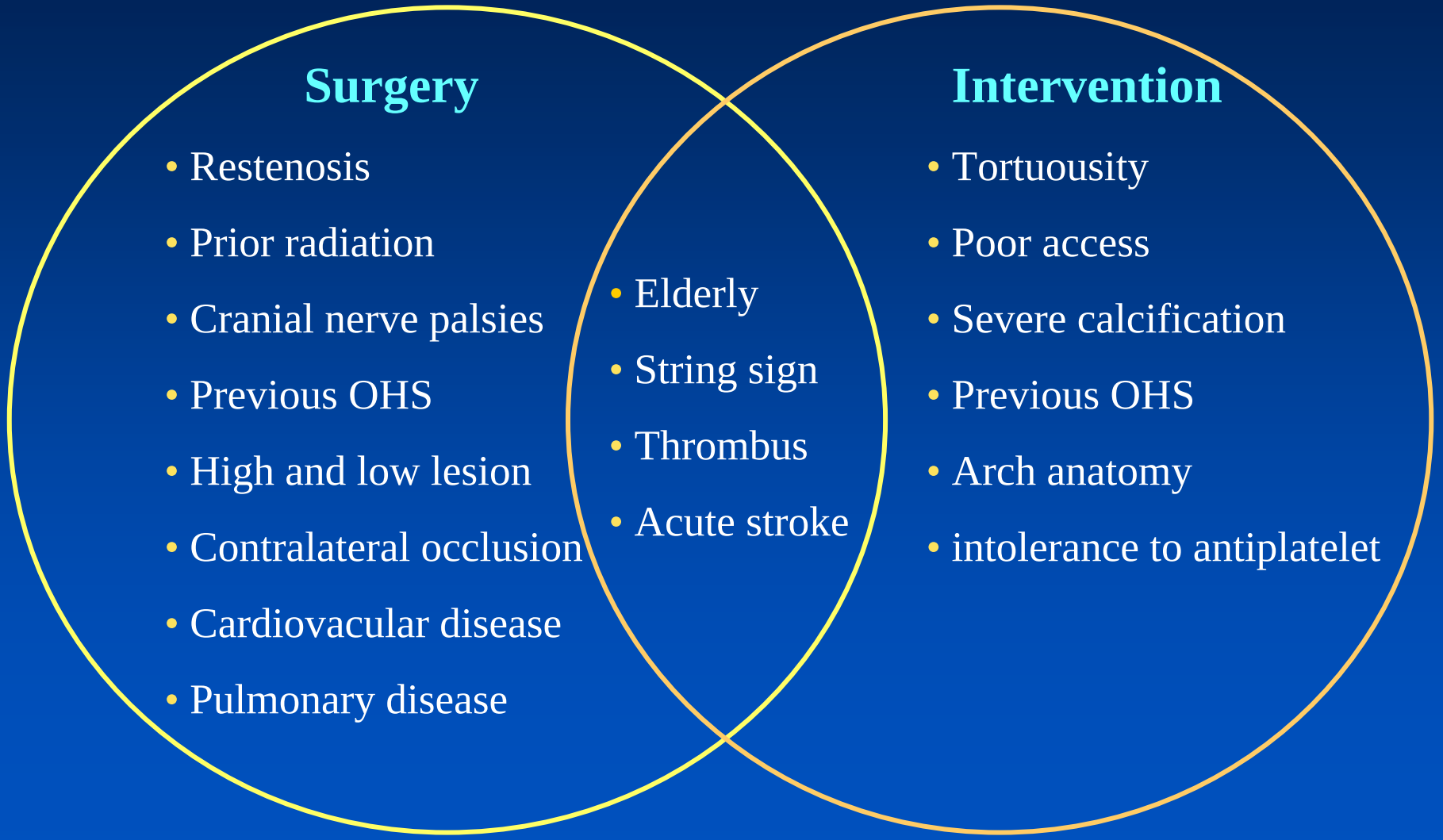
Chaturverdi, Neurology 2001 Sep
MRC ACST Collaborative group, Lancet 2004

Carotid Stenting

Carotid Stenting

- Reduced complication rates
- Less invasive
- Can reach essentially all blockages
- Very low restenosis rate
- Rapid return to daily life

High Risk Features of Surgery vs. Stenting for Carotid Stenosis



Carotid Stenting
Current Indications

- **Symptomatic stenosis $\geq$ 50% DS**
- **Asymptomatic stenosis $\geq$ 70% DS**

Consider patients' clinical status, Doppler hemodynamics, and operator's experience …

Carotid Stenting
Current Contraindications

- Severely tortuous, calcified and atheromatous aortic arch
- Pedunculated thrombus at the lesion site
- Recent stroke $\leq$ 3 weeks $\rightarrow$ anticoagulants and antiplatelets for 1 month
- Unable to tolerate antiplatelet agents

Carotid Stenting *Without* Protection

CAS without Protection

Success & Complications Rates

Study	Setting	No	Success Rate	Stroke & TIA*	Death
Roubin (1996)	High risk	146	99 %	6.2 %	0.7 %
Shawl (2000)	High risk	170	99 %	2.9 %	0 %
Wholey (2000)	Registry	5129	98.4 %	4.2 %	0.8 %
Roubin (2001)	High risk	428	99 %	4.6 %	0.2 %

**** Major stroke < 1%***

CAS without Protection

Complications Rates

4,757 pts, 36 major carotid centers, 1988-1997

TIAs	2.82 %
Minor Stroke	2.72 %
Major stroke	1.49 %
Deaths	0.86 %
Total stroke & death	6.29 %

*** 6-mo ISR = 1.99%**
12-mo ISR = 3.46%

Wholey MH, et al. CCI 2000;50:160

Long-term Outcomes

Enrollment: 1994-99, 528 patients with CAS

- 30-day stroke: 5.8% (major:1%, minor 4.8%)
- 30-day stroke and death: 7.4%
- Most of patients: high risk group
- Fatal and nonfatal stroke between 31days-3yrs : 3.2%
- The 3-year freedom from stroke: 92±1%

Most of all strokes occurred in periprocedural period.

Roubin GS et al. Circulation 2001;103:532-537

CAS without Protection

Long-term Outcomes
Compared to CEA

	CAS n=42	NASCET Med, n=331	NASCET CEA, N=328
Any ipsilat stroke	9.5%	26%	9%
Any stroke	14.3%	27.6%	12.6%
Any stroke or death	19%	32.3%	15.8%

Mean follow-up: 1.7 yrs, range (1-62 months)

CAS=carotid artery stenting
CEA=carotid endarterectomy

Fox DJ et al. Stroke 2002;33:2877-2880

Why distal protection ?

Carotid Stenting

With Protection

CAS with Embolic Protection for High Risk Patients

- **Randomized Trial**
  - SAPPIRE Trial
- **Non-randomized Trials**
  - ARCHER
  - SHELTER / BEACH
  - MAVERICK
  - CABERNET
  - SECURITY

Lesions at High Risk of Embolization

- Unstable plaque
  : break down of fibrous cap
- Soft plaque

- Long stenosis string sign
  : contain thrombus

Embolic Complications in Stenting

Periprocedural

- Angiography → Rare
- Access → Rare
- Wire Crossing → Rare if coronary wire
- Predilation → Rare
- Stent Placement → Potential and unpredictable
- Postdilation → Potential and unpredictable

Postprocedural → Rare

Methods for Prevention of Distal Embolization

- **Use embolic protection device (EPD)**
- No pre-dilatation with a peripheral balloon
- No oversizing of balloon
- Never use high pressures
- Never try to dilate the stent to in ulcerated area external to the stent

Independent Predictors of Embolic Stroke

30 days outcomes		*P* value
Minor stroke	Protection(-)	0.0182
	Hypertension	0.0216
Major stroke	Protection(-)	0.0892
	Age>80 yrs	<0.0001
Fatal stroke	Protection(-)	0.0892
	Prior TIA	0.0320
All stroke	Protection(-)	0.0009
	Hypertension	0.0102
	Age>80 yrs	0.0081
	Prior CEA	0.0822

AET 2003

Embolization during CAS

	Cerebral Protection	
	No (n=102)	Yes (n=142)
TCD-HITS*	100%	100%
Diffusion weighted-MRI	29%	7.1%
TIA	8%	2.7%
Stroke	3%	1.3%
TIA + Stroke	11%	4%

*Transcranial doppler-high intensity transient signals
Protection devices: Angioguard®, PercuSurge® & EPI

K. Mathias et al, AJNR 2001

Ideal Protection System

- Does not cause harm
  - Complete protection
  - Capture efficiency
- Protection at all time for all particles
- Wide applicability
- User friendly

Embolic Protection Devices

Distal occlusion	**Theron balloon** **PercuSurge Guardwire**
Filter	**MedNova NeuroShield** **EPI filter** **Angioguard filter** **Medtronic filter** **BSC Captura** **Bate's Floating Filter** **Accu-Filter** **E-Trap** **Microvena Trap**
Proximal occlusion	**Kachel balloon** **ArteriA Parodi Catheter**

Strength of Each System

Occlusion Device

- Mimics standard guidewire more than filters
- Ability to cross lesion
- Particles of all sizes can be blocked (ICA)

Filter Device

- User-friendly
- Preserves ICA flow

Weakness of Each System

Occlusion Device

- Unprotected
  1) During passage
  2) ECA
  3) Incomplete suction
- Does not preserve ICA flow
- Cumbersome procedure (cannot move wire during exchange, several added steps, aspiration)

Filter Device

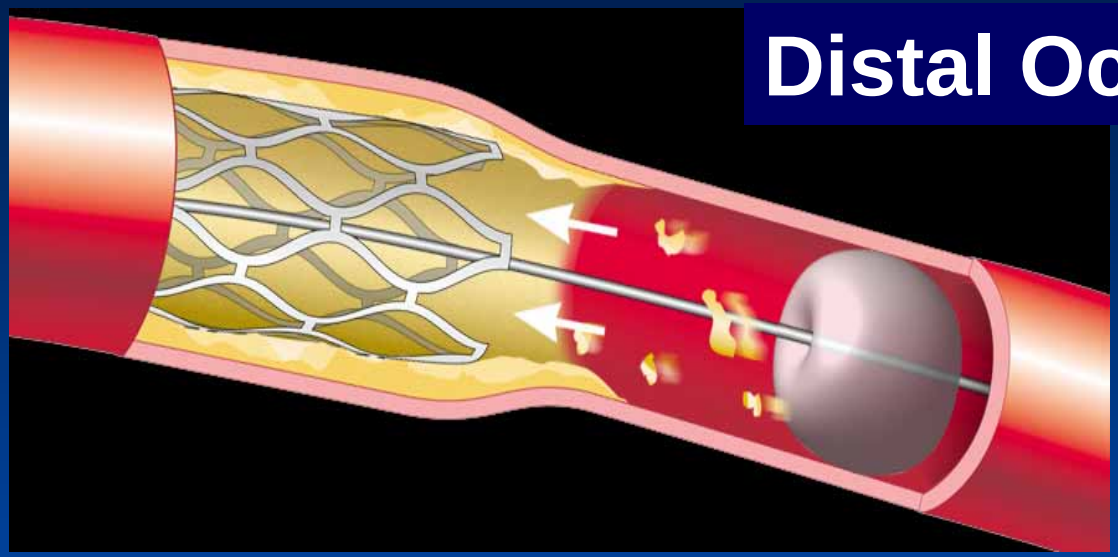
- Not same as standard guidewire
- Larger profile, less flexible
- Occasional need to predilate (recross PTA site)
- Unprotected
  1) during passage
  2) small particles
  3) flow around filter
  4) during filter retrieval
- May thrombose

Different Protection Devices

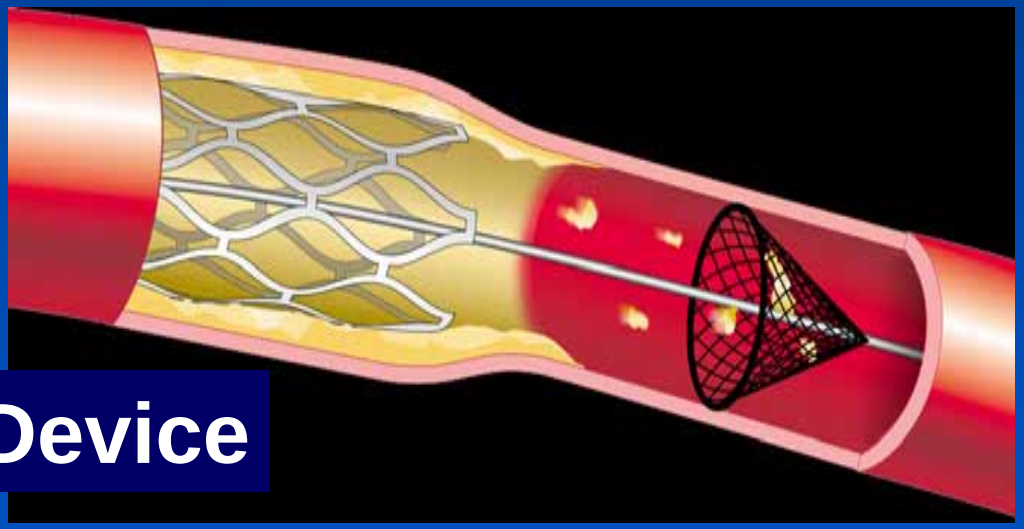
Advantages and Disadvantages

	Easy to use	Emboli during lesion crossing	Flow decrease	ICA protect	Angio during protection	Emboli through ECA	Spasm/ damage to ICA	Tolerance
Filters	+++	+	+	+	+++	-	+++	+++
Occlusion	++	+	++	++	-	+++	+++	+
Flow reversal	+	-	+++	+++	+++	-	-	+

Embolic Protection Devices

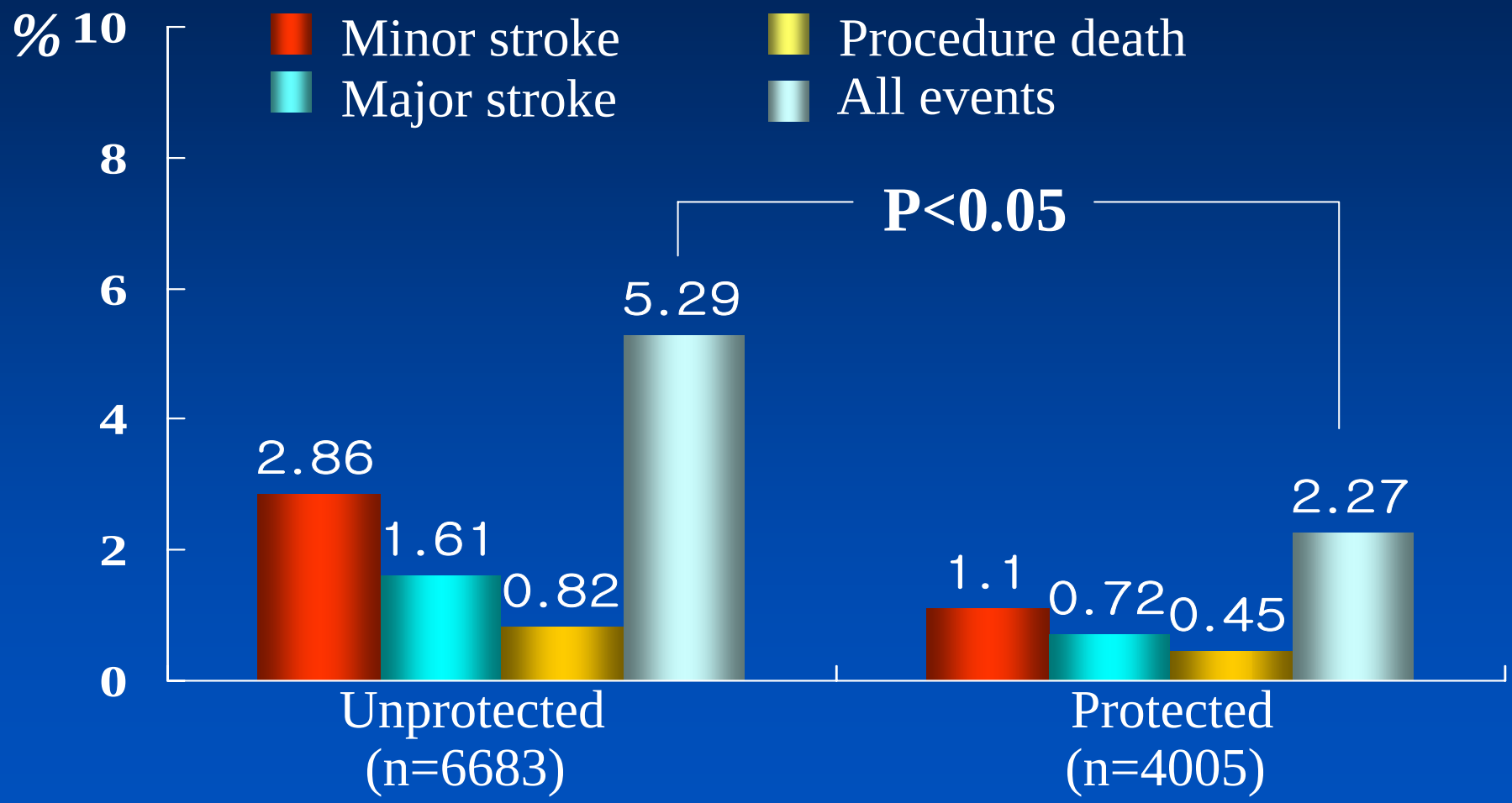


Distal Occlusion Device



Filter Device

Benefit of Distal Protection
Periprocedural Outcomes

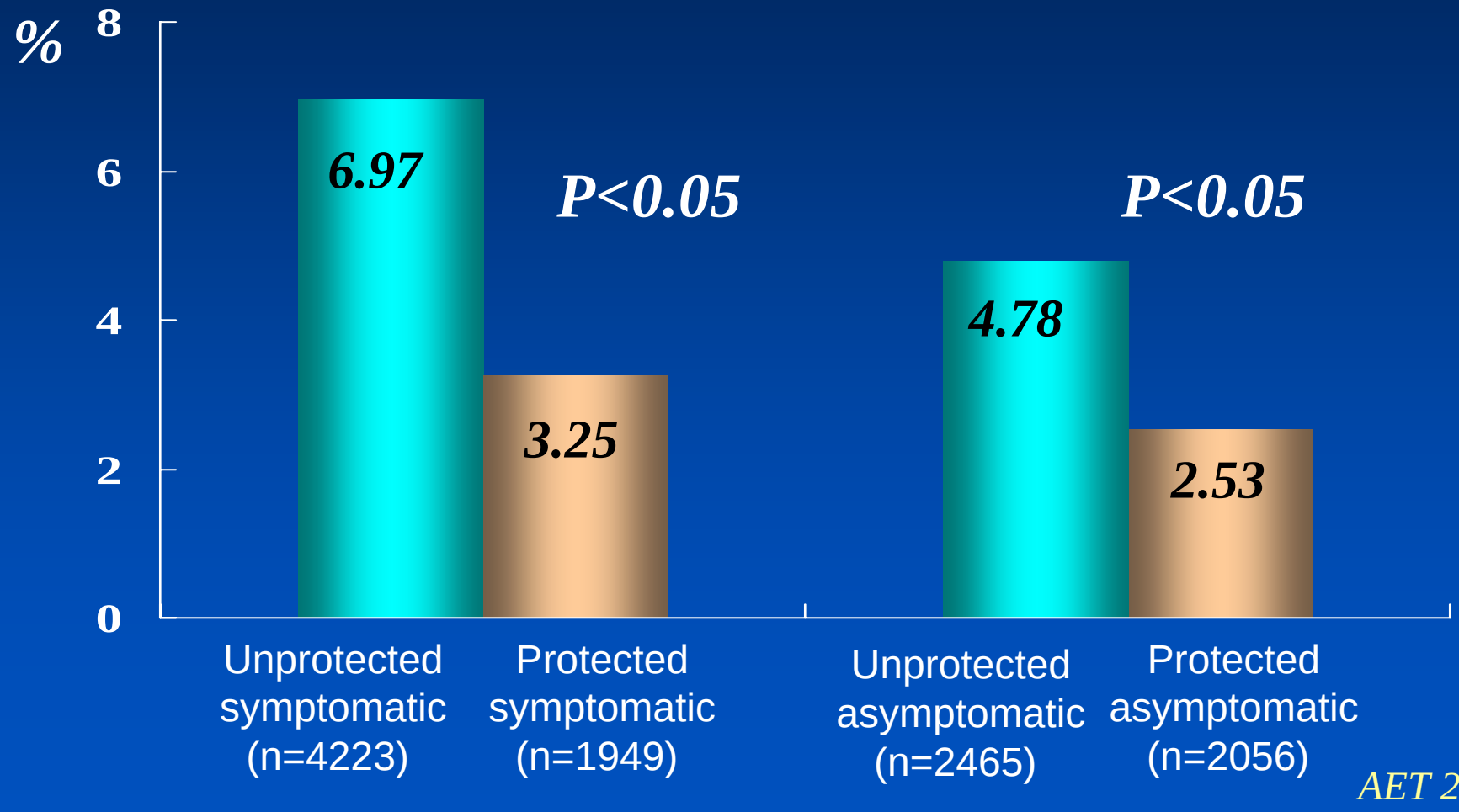


AET 2003

Benefit of Distal Protection

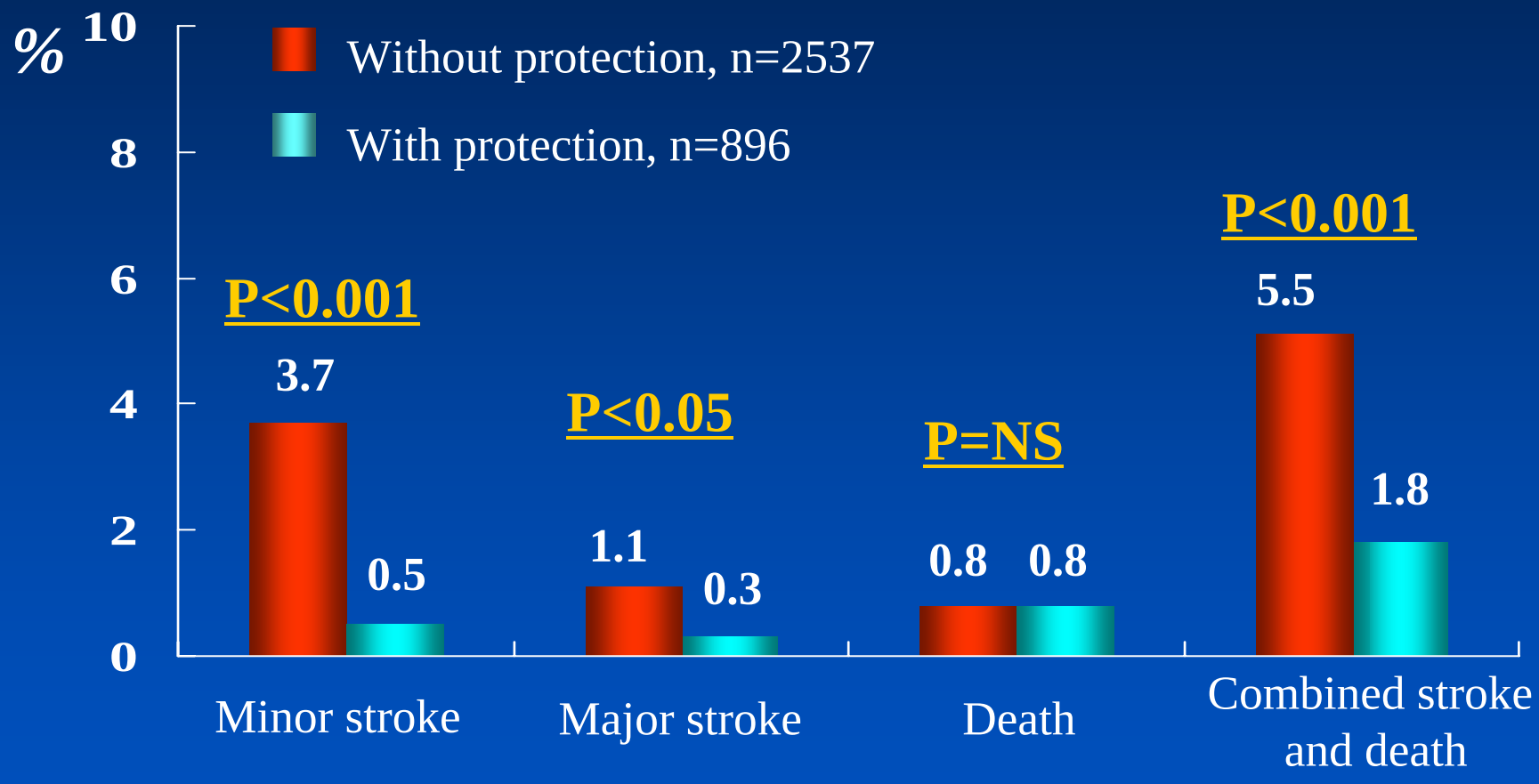
Periprocedural Outcomes

All cause death, major & minor stroke



AET 2003

Benefit of Distal Protection
30-Day Outcomes



Stroke 2003;34:813-819

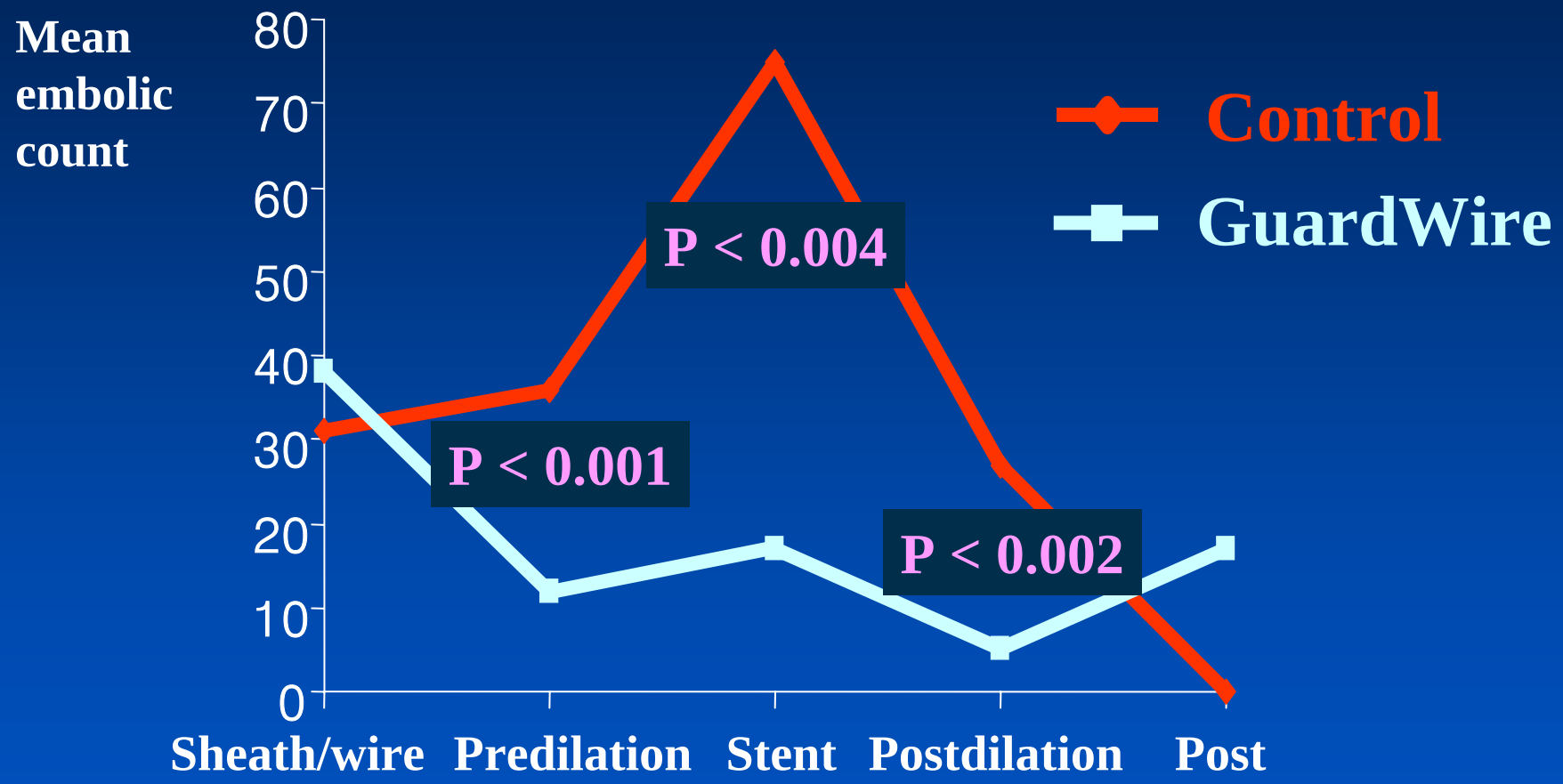
Embolic Protection Device

Distal Occlusion

PercuSurge GUARDWIRE ™

Distal Occlusion Device

PercuSurge GuardWire™



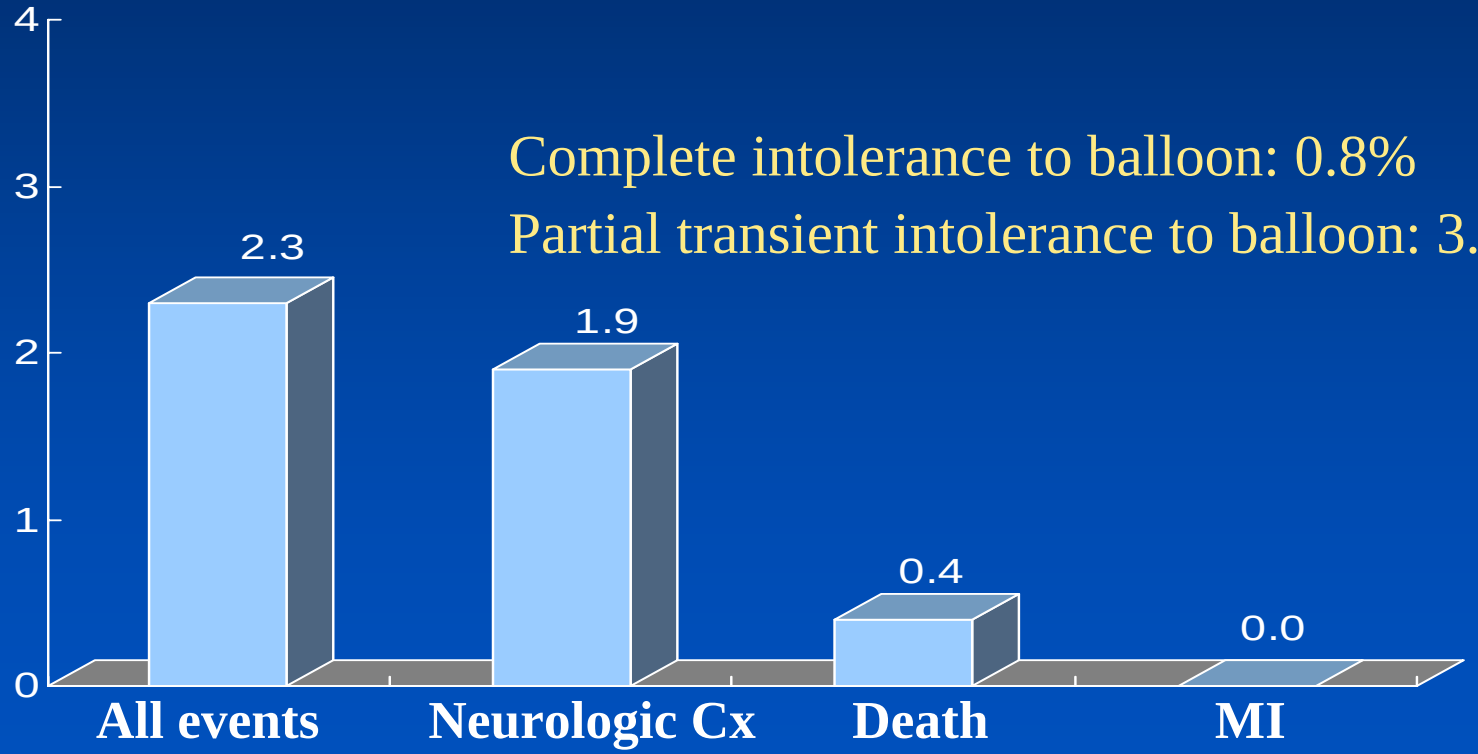
Al-Mubarak et al, Circulation, 2001

Distal Occlusion Device

PercuSurge GuardWire™

30-Day Event

246 patients with 272 lesions



Complete intolerance to balloon: 0.8%

Partial transient intolerance to balloon: 3.7%

J Interven Cardiol 2004;61:233-43

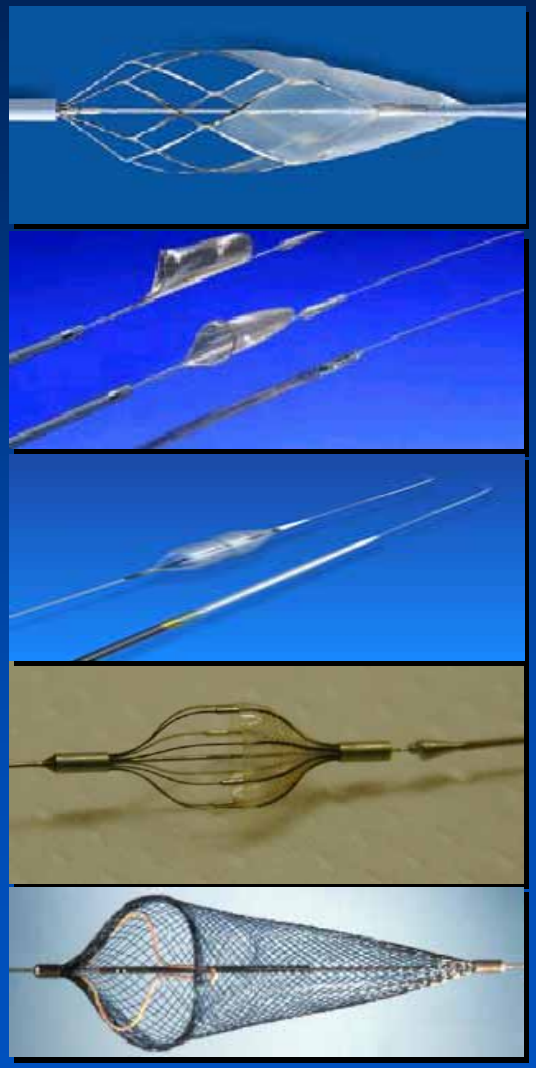
Distal Occlusion Device

PercuSurge GuardWire™

Number	179
Technical success	99.3 %
Overall mean balloon time (sec)	410 ± 220
30-day stroke rate	6 (2.3 %)
Minor stroke (TIA, retinal embolism)	4 (1.5%)
Major stroke	1 (0.4%)
Death (cardiac)	1 (0.4%)
36-month event (stroke & death)-free survival	97%
Death (AMI, stroke, cancer)	4 (1.5%)

Catheter Cardiovasc interv 2004;61:293-305

Embolic Protection Devices
Filter



Guidant - ACCUNET

BSC - FilterWire

ABBOTT - Emboshield

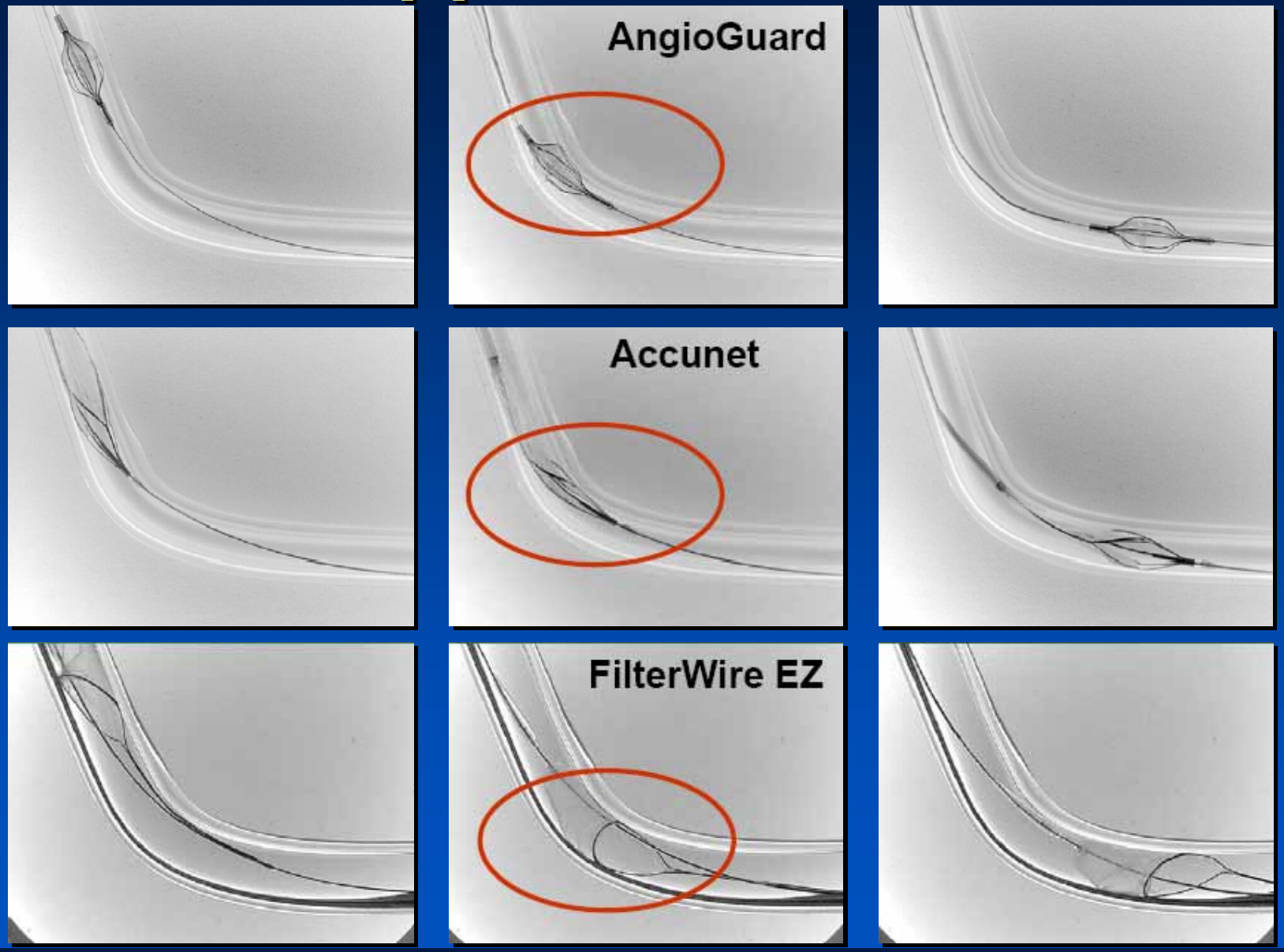
Cordis - Angioguard

EV3 - Spider

Features of Filter

- Delivery profile
- Steerability
- Vessel wall apposition
- Pore size
- Capture efficiency
- Ease of retrieval
- Clinical event rates

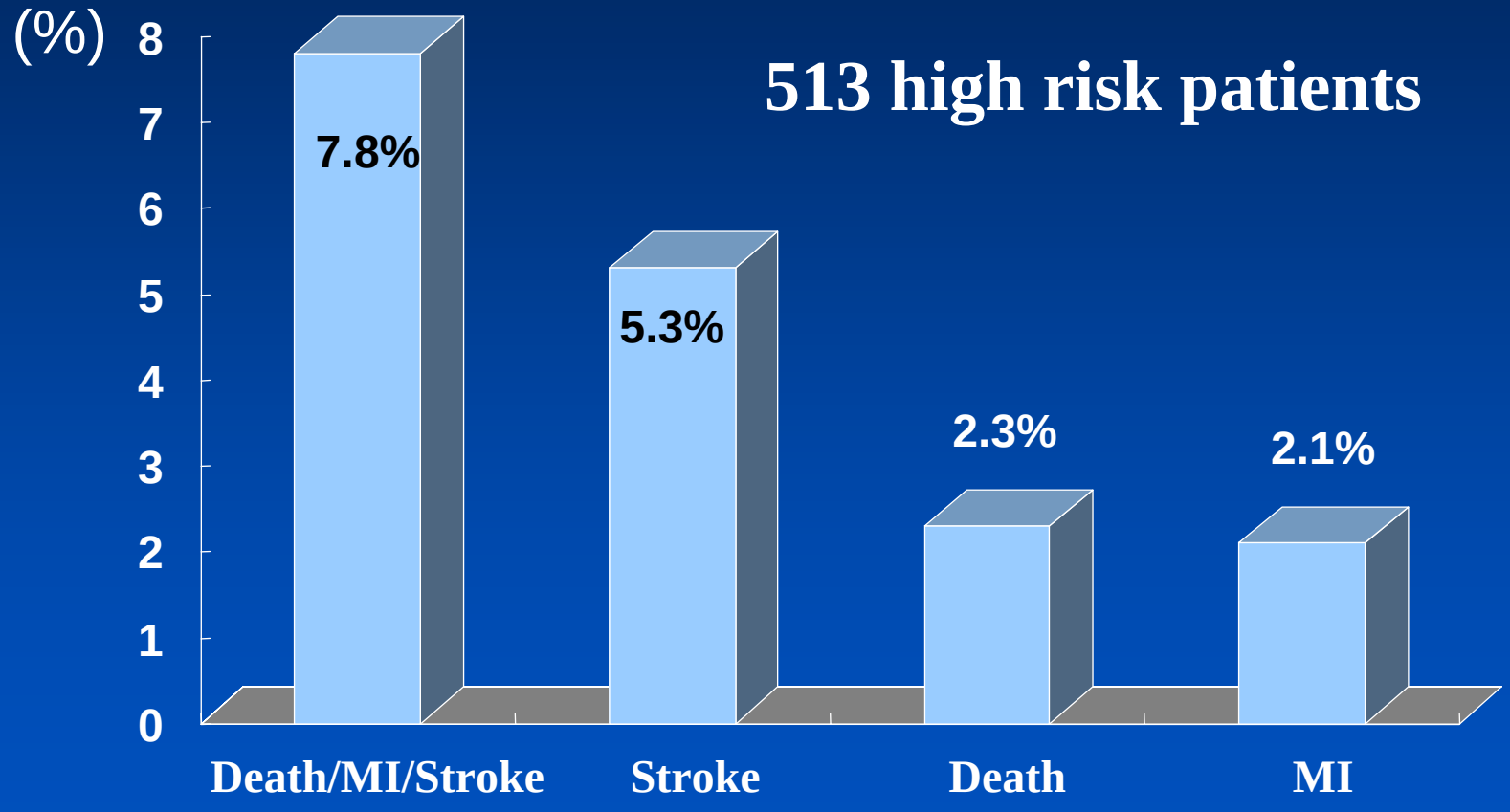
Wall Apposition in Curves



Accunet Filter

ARCHeR Trial

30-Day Event

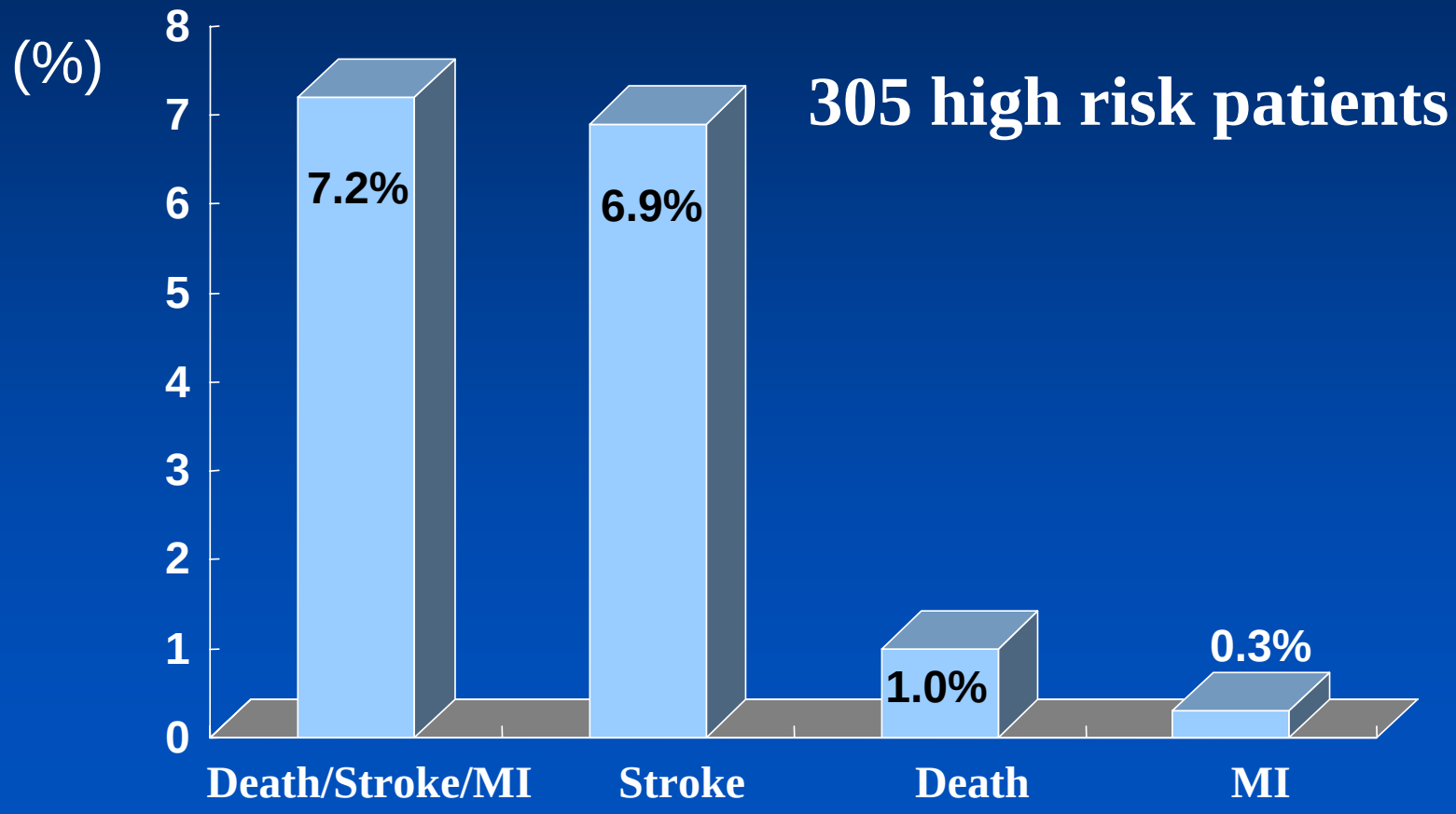


Illig KA et al. J Vasc Surg. 2003;37:575-81.

Mednova Filter

SECuRITY Trial

30-Day Event

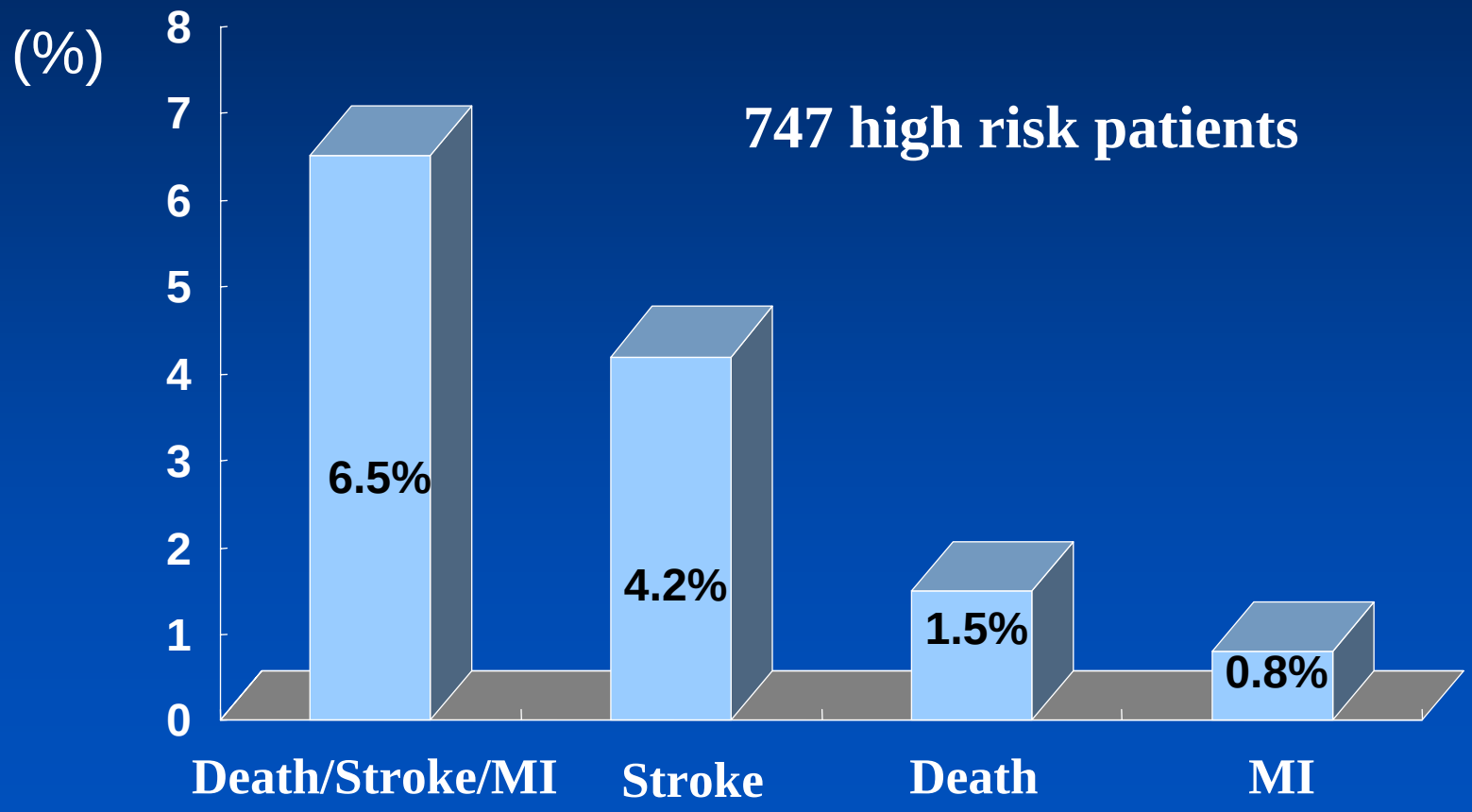


ACC 2003

Filter Wire

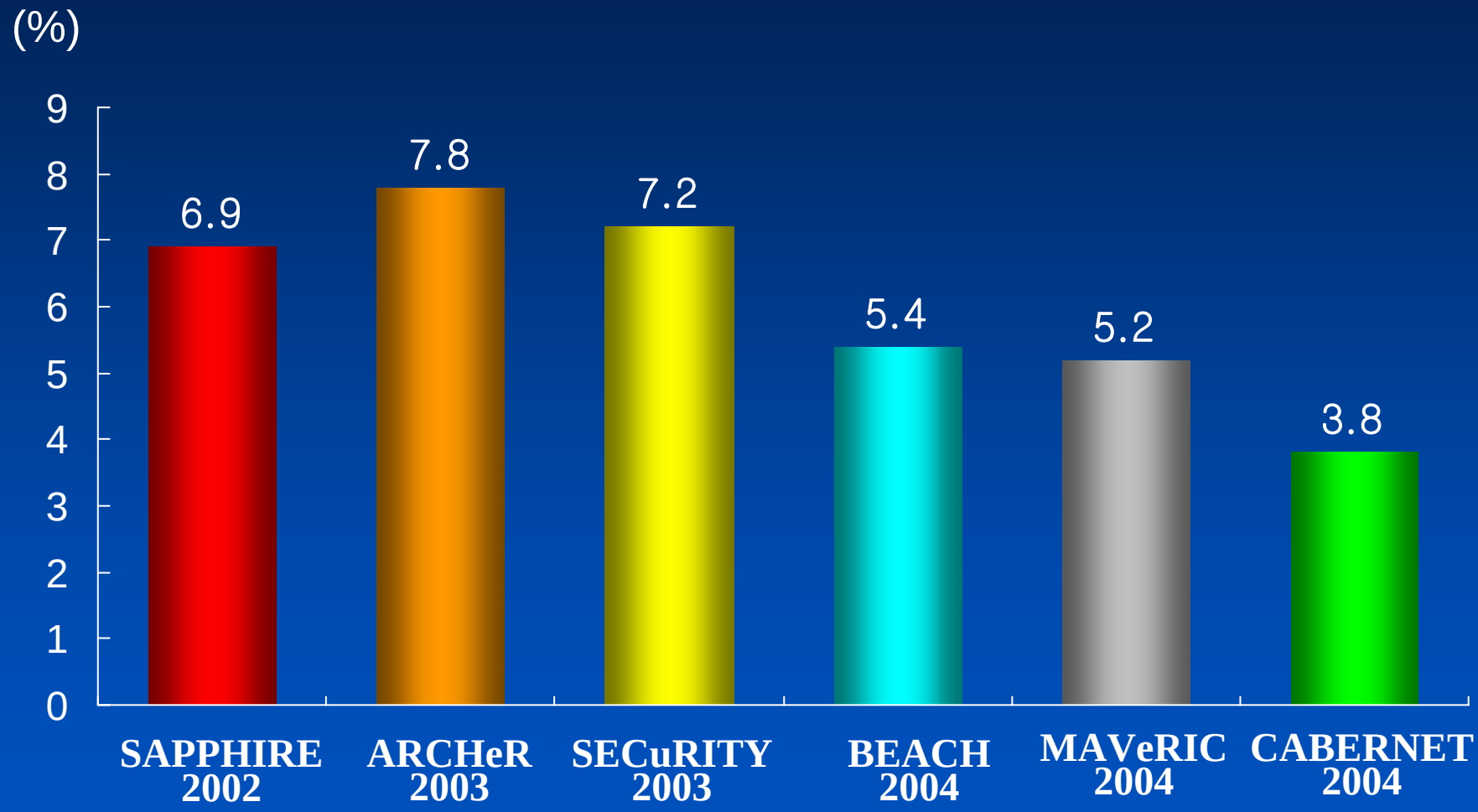
BEACH Trial

30-Day Event



White CJ et al. Catheter Cardiovasc Interv. 2006;67:503-12.

30 Day Stroke/Death/MI in High Risk Registry 2002-2004



TCT 2005

Practical Use of Distal Protection

CAPTURE 2500 Registry

- Stent; RX ACCULINK
- Protection device; RX ACCUNET™ filter system
- N=2,500 at 137 hospitals

  (less than maximal 40 patients per a hospital)
- More than 1/3 patients were enrolled at hospitals with a high level of experience.
- 1º Endpoint; composite of 1-month death / MI / stroke

ACC 2006

Practical Use of Distal Protection

CAPTURE 2500 Registry vs ARCHeR Trial

Primary Events < 30 days

Event	CAPTURE (N=2,500)	ARCHeR (N=581)	DIFFERENCE 95% CI
Death, Stroke, MI*	**5.7%**	**8.3%**	**-2.54% [-4.96, -0.13]**
Death	1.6%	2.1%	-0.47% [-1.72, 0.79]
Stroke-related death	0.8%	0.5%	0.24% [-0.43, 0.92]
All stroke	4.2%	5.5%	-1.27% [-3.28, 0.75]
Major stroke	1.7%	1.5%	0.13% [-0.99, 1.25]
Minor stroke	2.6%	4.0%	-1.32% [-3.02, 0.39]
MI*	0.9%	2.4%	-1.49% [-2.79, -0.19]
All stroke and death	**5.1%**	**6.9%**	**-1.80% [-4.04, -0.43]**
Major stroke and death	**2.5%**	**2.9%**	**-0.41% [-1.91, 1.10]**

* P<0.05

ACC 2006

Practical Use of Distal Protection

CAPTURE 2500 Registry vs ARCHeR Trial

Asymptomatic Patient Events < 30 days

Event	CAPTURE (N=2,267)	ARCHeR (N=443)	DIFFERENCE 95% CI
Death, Stroke, MI*	**4.9%**	**6.8%**	**-1.92% [-4.42, -0.58]**
Death	1.3%	2.0%	-0.71% [-2.10, 0.69]
Stroke-related death	0.5%	0.2%	0.26% [-0.27, 0.79]
All stroke	3.5%	3.8%	-0.31% [-2.25, 1.63]
Major stroke	1.3%	0.7%	0.65% [-0.25, 1.54]
Minor stroke	2.2%	3.2%	-0.91% [-2.65, 0.83]
MI*	0.7%	2.5%	-1.73% [-3.23, -0.24]
All stroke and death	**4.4%**	**5.4%**	**-1.05% [-3.32, 1.22]**
Major stroke and death	**2.2%**	**2.3%**	**-0.41% [-1.60, 1.41]**

* P<0.05

ACC 2006

Practical Use of Distal Protection

CAPTURE 2500 Registry vs ARCHeR Trial

Symptomatic Patient Events < 30 days

Event	CAPTURE (N=233)	ARCHeR (N=138)	DIFFERENCE 95% CI
Death, Stroke, MI*	**14.2%**	**13.0%**	**-1.12% [-6.06, 8.30]**
Death	4.3%	2.2%	2.12% [-1.44, 5.68]
Stroke-related death	3.4%	1.4%	1.98% [-1.09, 5.06]
All stroke	11.2%	10.9%	0.29% [-6.29, 6.87]
Major stroke	5.2%	4.3%	0.80% [-3.63, 5.23]
Minor stroke	6.4%	6.5%	-0.08% [-5.27, 5.10]
MI	2.6%	2.2%	0.40% [-2.77, 3.57]
All stroke and death	**12.0%**	**11.6%**	**0.42% [-6.36, 7.20]**
Major stroke and death	**6.0%**	**5.1%**	**0.94% [-3.83, 5.70]**

* P<0.05

ACC 2006

Practical Use of Distal Protection

CAPTURE 2500 Registry

Events < 30 days by Physician Experience

CAPTURE (N=2,500)	High (N=226)	Medium (N=1770)	Low (N=504)
Death, Stroke, MI	**6.2%**	**5.8%**	**5.4%**
Death	0.0%	1.7%	2.0%
All stroke	5.8%	4.2%	3.8%
Major stroke	1.3%	1.8%	1.6%
Minor stroke	4.4%	2.5%	2.2%
MI	0.4%	0.9%	1.2%
All stroke and death	**5.8%**	**5.1%**	**4.6%**
Major stroke and death	**1.3%**	**2.7%**	**2.4%**

* P<0.05

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Practical Use of Distal Protection

CAPTURE 2500 Registry: Conclusions

- Community based carotid stenting provides excellent results.
- Rollout of therapy to physicians with varying levels of experience achieved excellent results comparable to ARCHeR.
- Stroke/death rate (3.6%) for asymptomatic patients <80 years approaches ACAS/ACST outcomes in high risk patients.

ACC 2006

Carotid Endarterectomy

vs.

Carotid Stenting

CAVATAS

CEA vs. Angioplasty without protection in Low and High Surgical Risk group

	Angioplasty N=251	CEA N=253
30-day death & stroke	6.4%	5.9 %
Cranial neuropathy	0 %	8.7 %
1-year restenosis (>70% DS)*	14 %	4 %
3-year death or diabling stroke	14.3 %	14.2 %

* Stenting = only in 26%

Lancet 2001;357:1729-37

CEA vs. CAS without protection

Prospective Randomized Trial in Low and High Surgical Risk group

	CAS N=53	CEA N=51
Death/cerebral ischemia, n		
Death	0	1
Stroke	0	0
TIA	1	0
Other, n		
Arterial thrombosis/amputation	1	0
Hematoma	3	1
Cranial/cervical n injury	0	0
Bradycardia	7	7
Hypotension	12	3

Brooks et al. J Am Coll Cardiol 2001;38:1589-95

SAPPHIRE

CES vs. CAS with Filter

From August 2000 to July 2002

Carotid a stenosis with high risk (n=334)

Randomization (1:1)

Carotid stenting with filter device (n=167)

Carotid endarterectomy (n=167)

Primary endpint: composite of death, stroke, or MI within 30 days or death or ipsilateral stroke btw 31days and 1 year

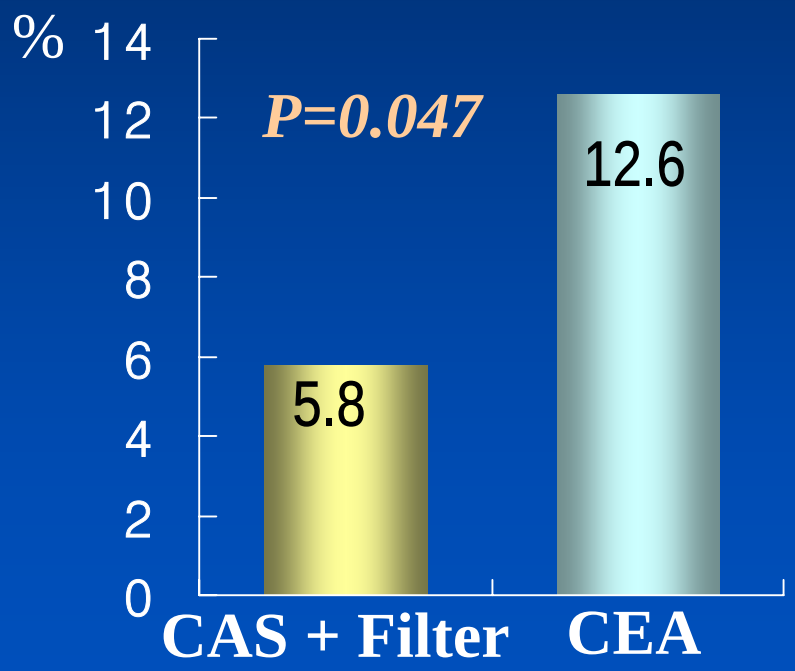
Yadav JS, et al. NEJM 2004;351:1493

SAPPHIRE

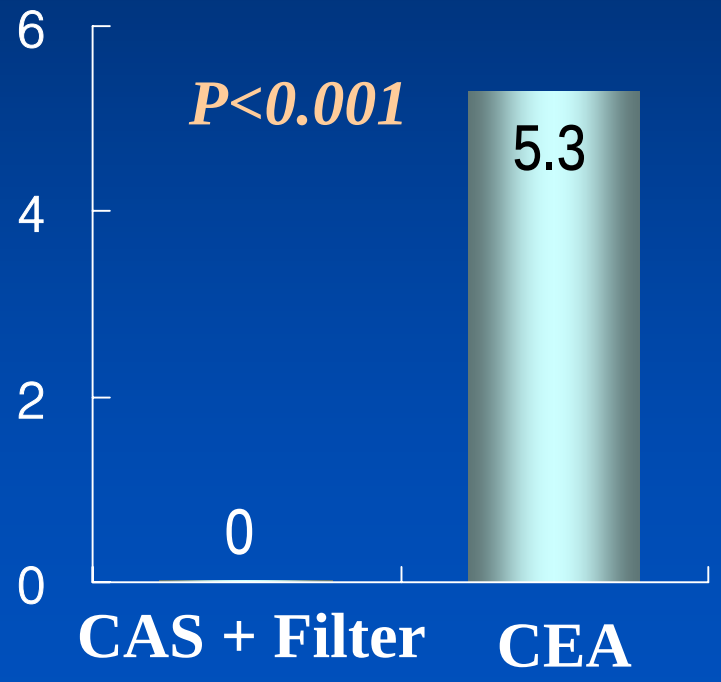
CEA vs. CAS with Filter

30-Day Outcomes

Death /MI /Stroke



Cranial nerve palsy

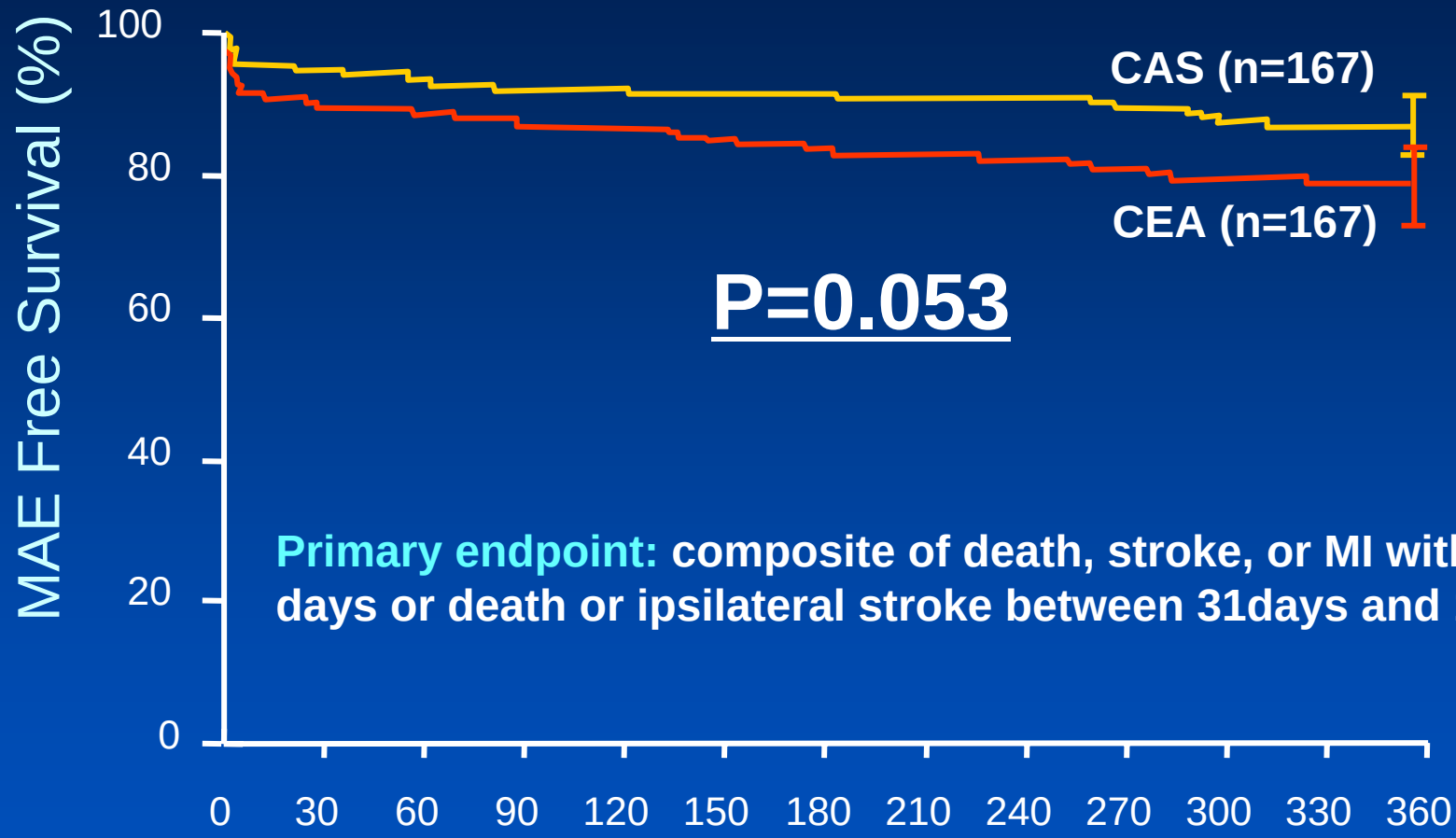


Yadav JS, et al. NEJM 2004;351:1493

CEA vs. CAS with Filter

SAPPHIRE

1-Year Clinical Outcomes



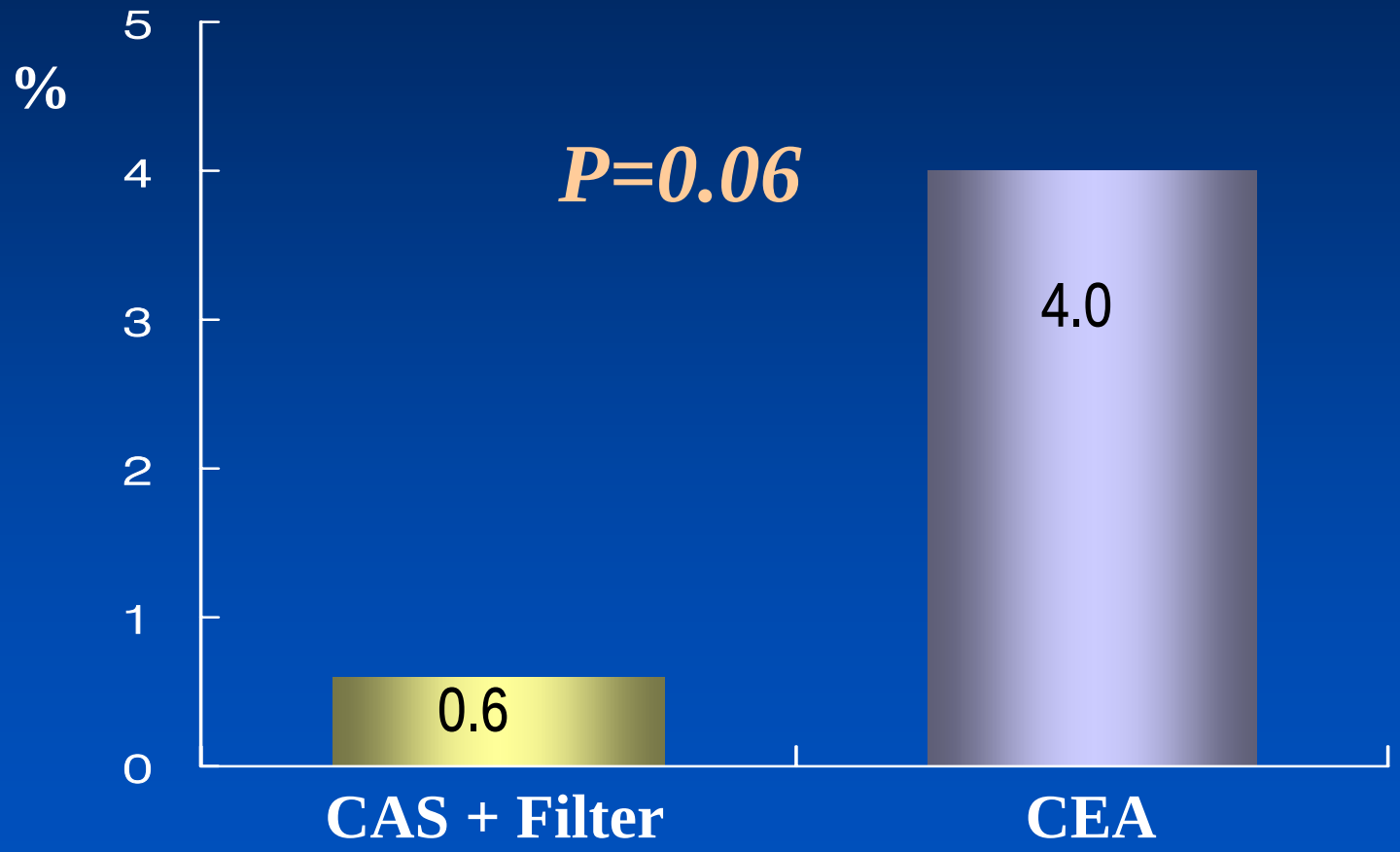
Primary endpoint: composite of death, stroke, or MI within 30 days or death or ipsilateral stroke between 31days and 1 year

Yadav JS, et al. NEJM 2004;351:1493

SAPPHIRE

CEA vs. CAS with Filter

1-Year TLR



Yadav JS, et al. NEJM 2004;351:1493

Conclusion

- Among patients with severe carotid-artery stenosis and coexisting conditions, CAS with the use of an emboli-protection device is not inferior to CEA.

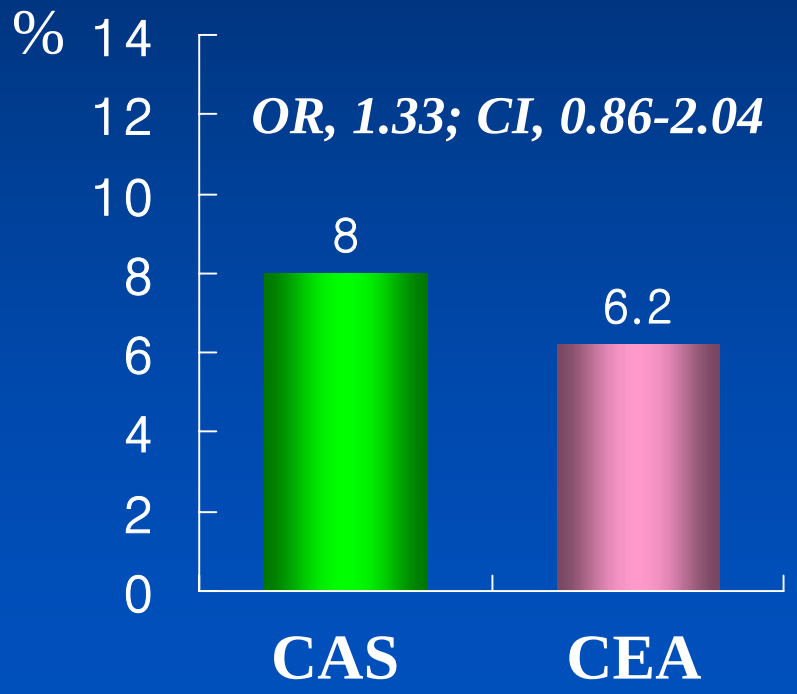
Yadav JS, et al. NEJM 2004;351:1493

CEA vs. CAS

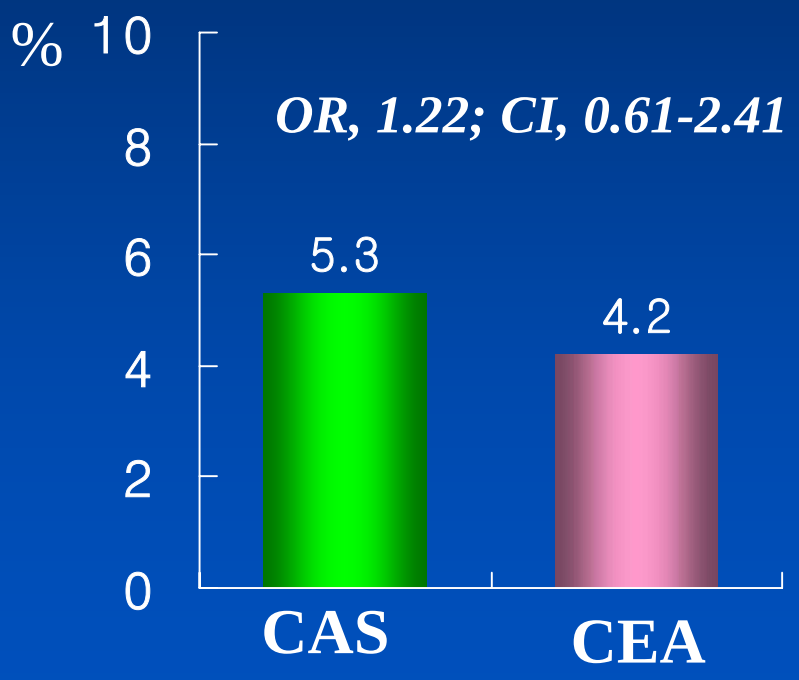
30 days outcomes from 5 RCT (n=1269)

(CAVATAS, Kentucky A&B, Leicester, WALL STENT, SAPPHIRE)

Death / any stroke



Death / disabling stroke



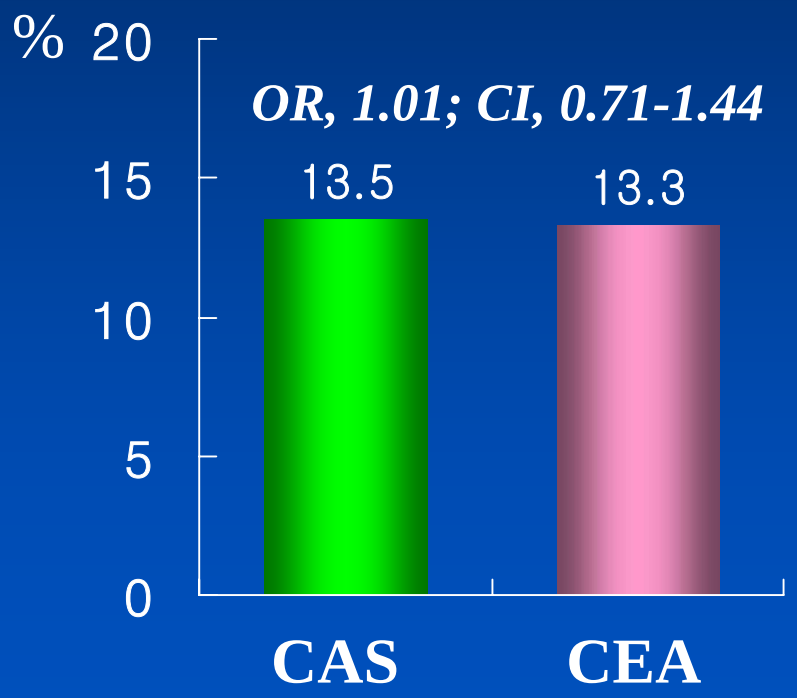
Coward LJ, et al. Stroke 2005;36:905-911

CEA vs. CAS

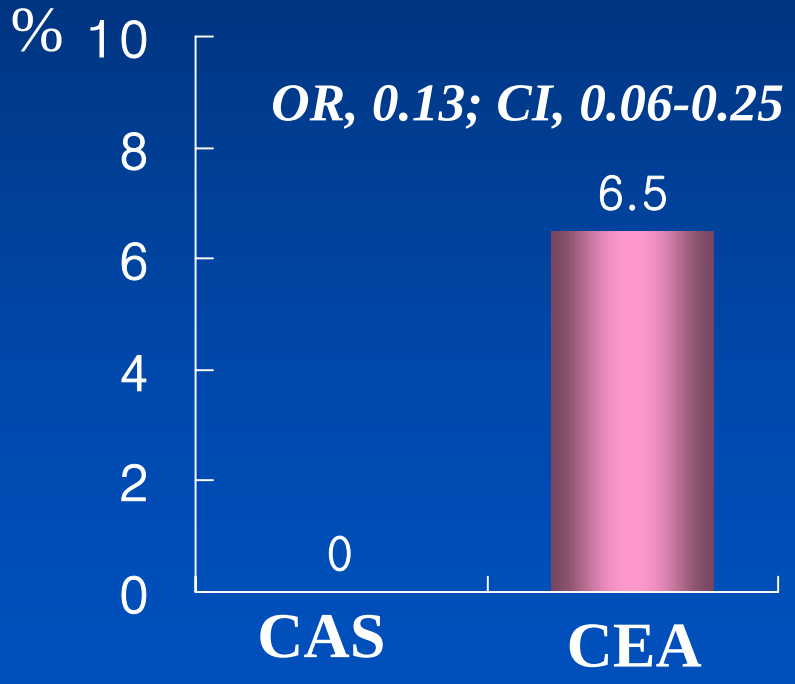
Outcomes from 5 RCT (n=1269)

(CAVATAS, Kentucky A&B, Leicester, WALL STENT, SAPPHIRE)

Death /any stroke at 1 year



Cranial nerve palsy



Coward LJ, et al. Stroke 2005;36:905-911

Case-control study

CES vs. CAS with Filter

From 2001 to 2004

Carotid a stenosis (n=602)

Concurrent-risk matched group

Carotid stenting with filter device (n=301)

Carotid endarterectomy (n=301)

Perioperative and midterm results of CAS vs. CEA

Cao P, et al. Stroke 2006;37:1221-1226

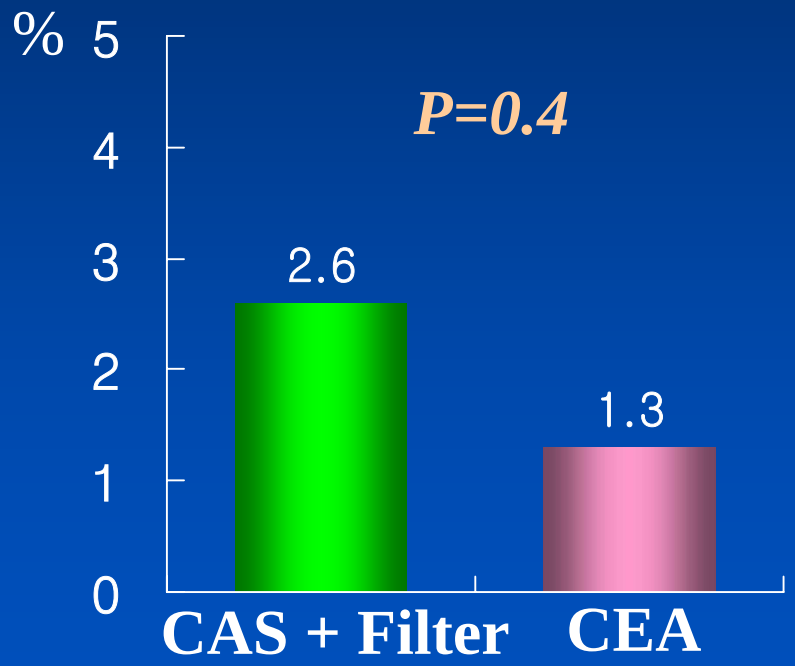
CEA vs. CAS with Filter

Case-control study

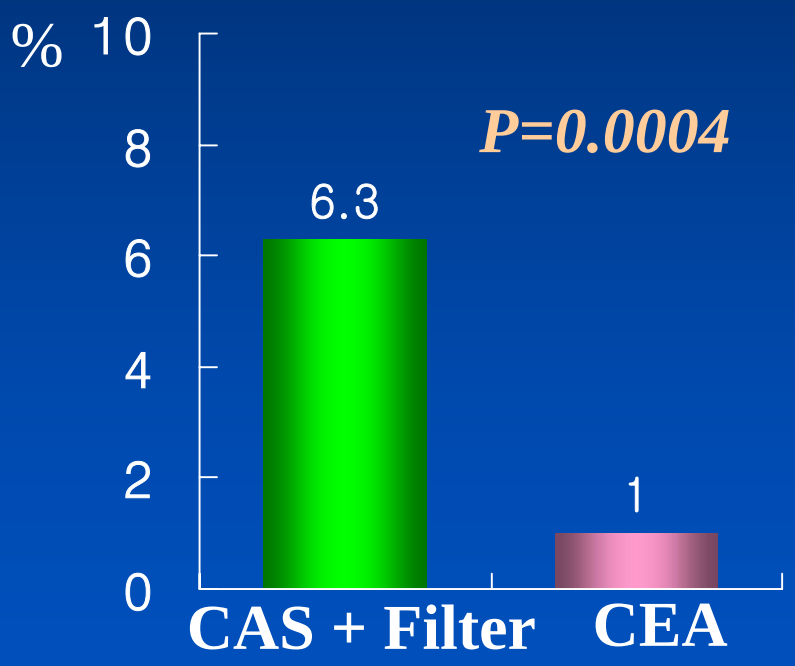
30-Day Outcomes

50% of CAS disabling strokes occurred during cannulation of epiaortic vessel

Death / disabling stroke



TIA



Cao P, et al. Stroke 2006;37:1221-1226

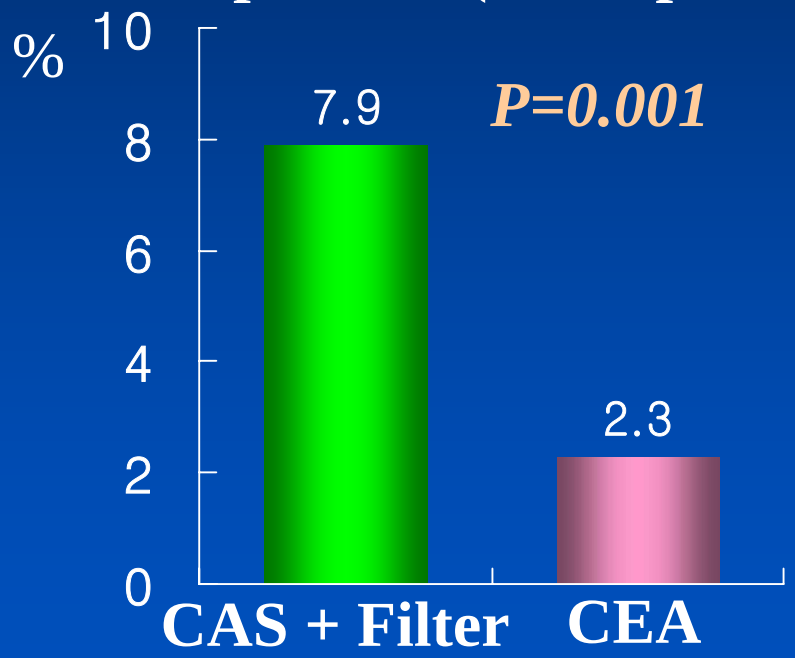
CEA vs. CAS with Filter

Case-control study

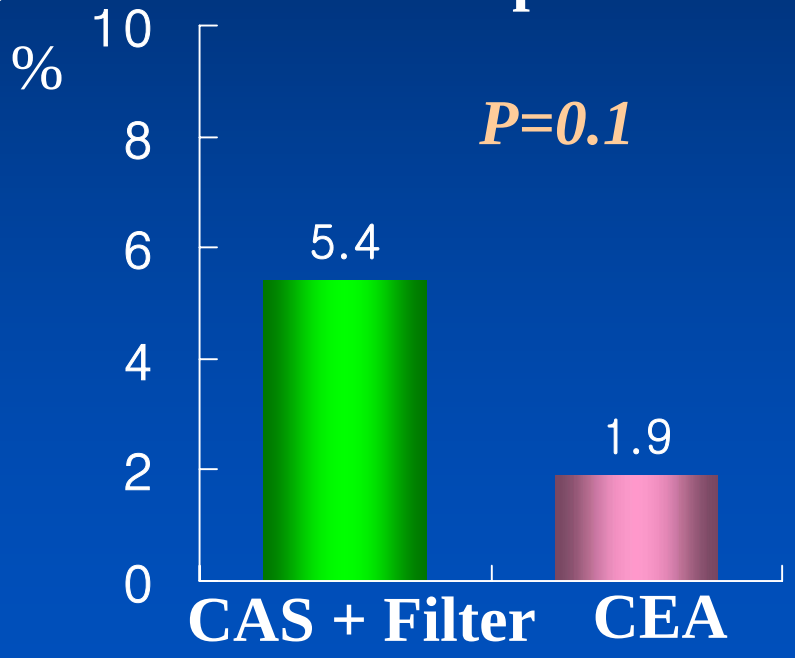
30-Day Outcomes

A decreasing trend in 30-day stroke with expertise

Any stroke
All patients (n=301pts/arm)



Any stroke
Last 201 pts/arm

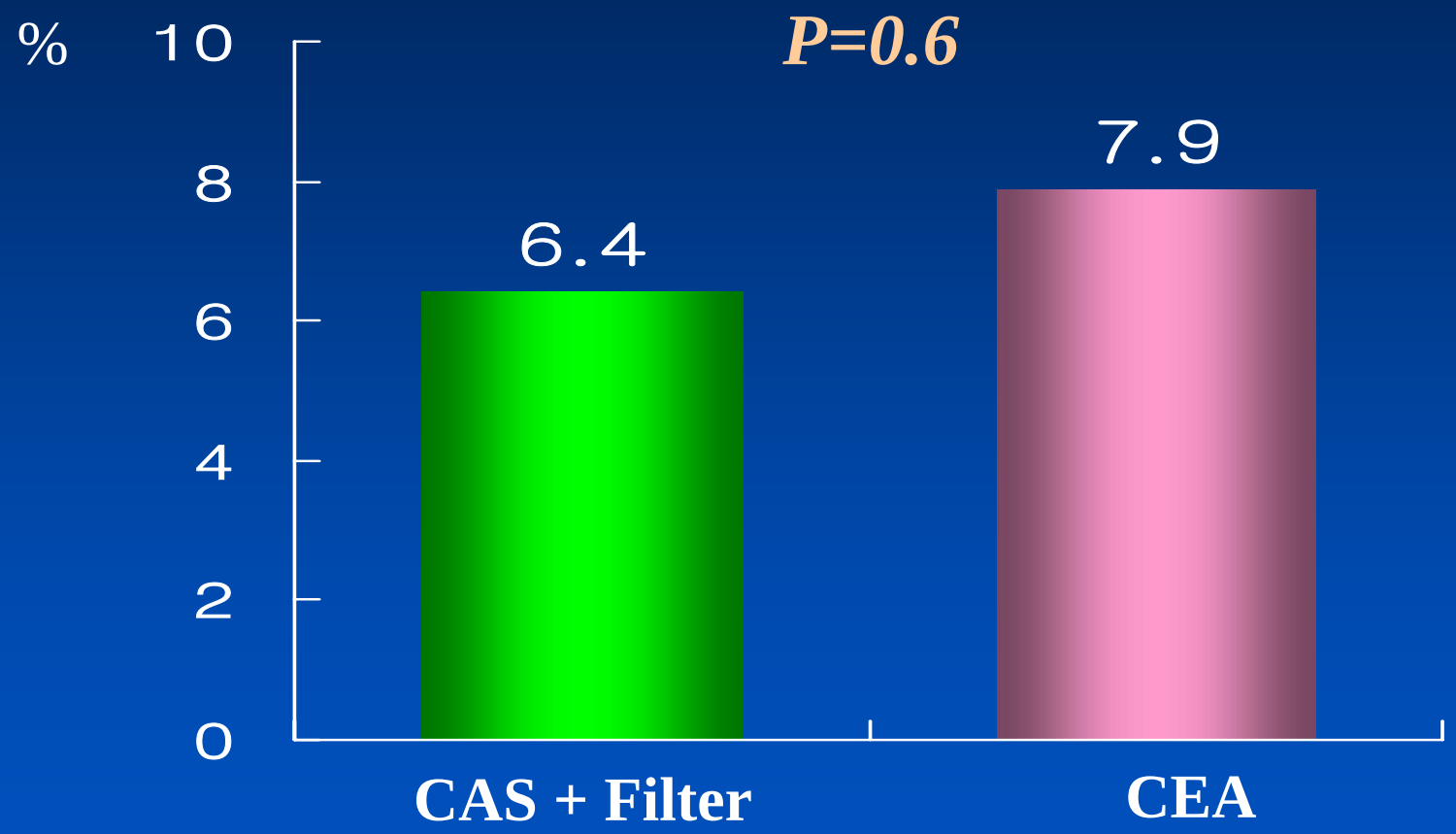


Cao P, et al. Stroke 2006;37:1221-1226

CEA vs. CAS with Filter

Case-control study

36-Month Restenosis



Cao P, et al. Stroke 2006;37:1221-1226

Case-control study

Independent Risk Factors

Predictors	Disabling stroke/death	Any stroke
CAS	HR 3.6 [0.93-13.9], p=0.06	HR 3.9 [1.6-9.4], p=0.002
Urgency	HR 8.9 [1.71-46.4], P=0.009	HR 4.6 [1.2-18.6], P=0.03
Diabetes		HR 2.2 [1.01, 4.83], P=0.045
Age		HR 1.06 [1.01, 1.1], P=0.02

Cao P, et al. Stroke 2006;37:1221-1226

Crotid Stenting vs. CEA before Open Heart Surgery

for Combined Severe Carotid and Coronary Stenosis

30-Day Event	CS + OHS N=56	CEA + OHS N=112	*P*
MI	2 (3.3%)	14 (12.6%)	0.06
Stroke	1 (1.8%)	10 (9.0%)	0.08
Death	3 (5.4%)	8 (7.2%)	0.65
Death/MI, or stroke	6 (10.7%)	24 (21.6%)	0.08

* CEA+OHS group had higher baseline risk profile

Am J Cardiol 2005;96:519-523

Carotid Stenting

- Although there is insufficient evidence to support CS, CS may be a more preferred therapy to CEA with appropriate learning curve and the use of the protection device
- Technical progress, advance in technical expertise and patients selection are important to reduce the risk of CS
- CS may be extended to all patients subsets, such as symptomatic, asymptomatic, high risk, and low risk subgroups.