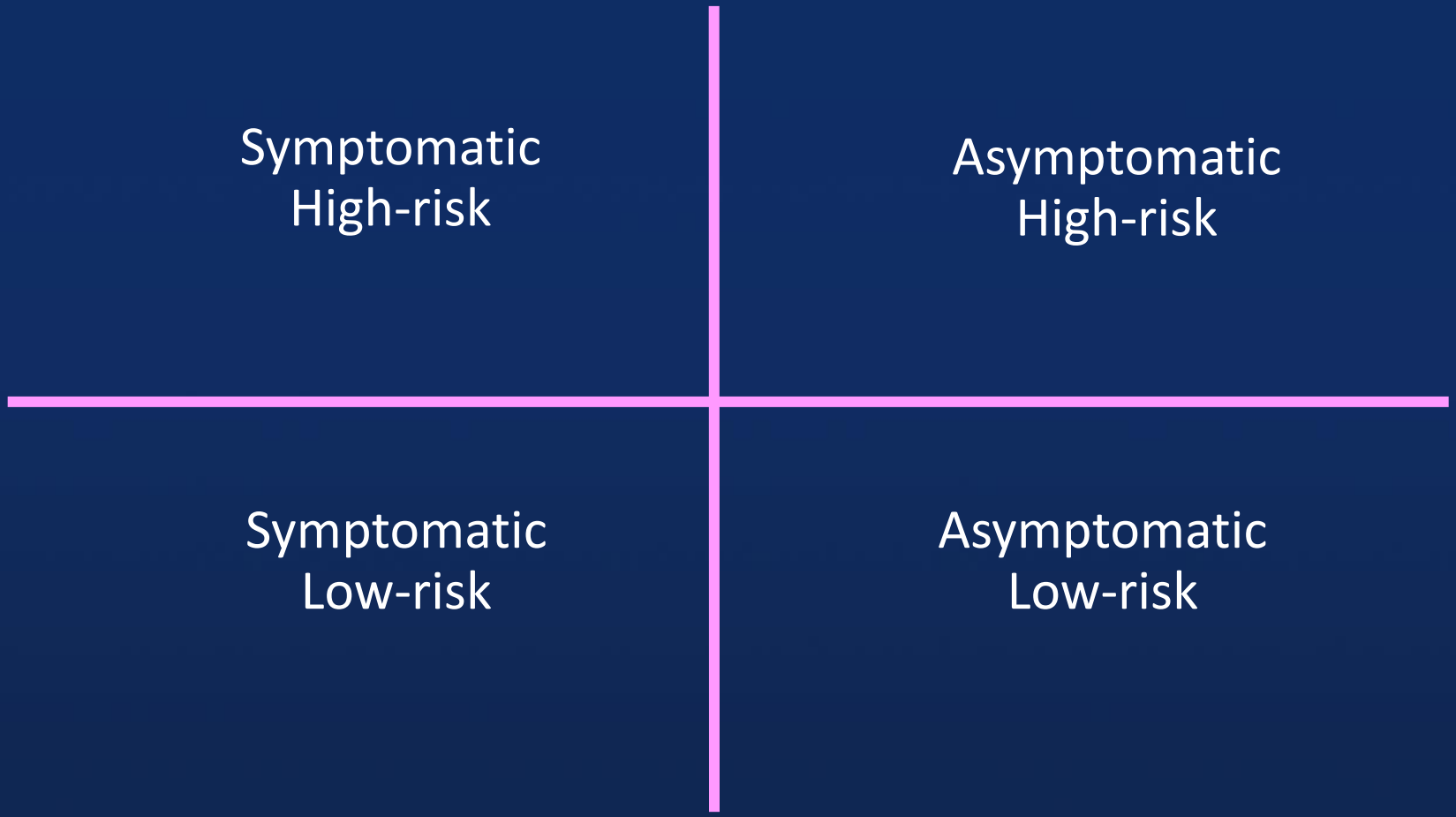
Carotid Artery Stenting

Carotid Artery Disease

Patient subsets



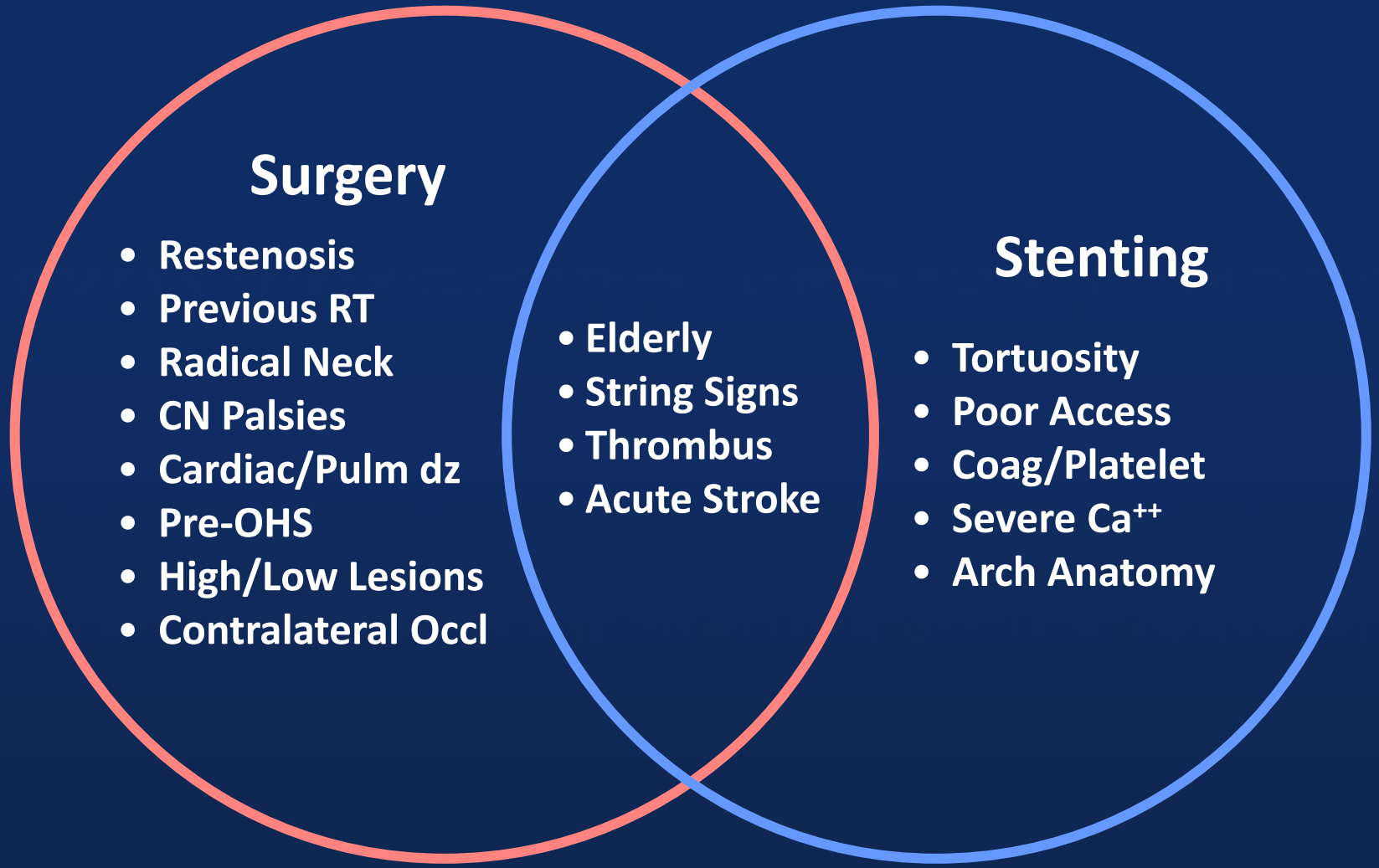
Clinical Criteria

- Age greater than 80
- Unstable angina CCS III-IV
- EF< 30%
- MI within past 6 wks
- Severe COPD (FEV1 < 30% predicted)
- Renarrowing after prior CEA (80% Asx; 50% Sx)
- Total occlusion of the contralateral ICA
- Two or more proximal or major coronary arteries with >70% stenosis

Anatomical Criteria

- Previous radiation treatment to neck
- Previous radical neck surgery
- Inability to extend neck
- Patient has a tracheostomy or tracheal stoma
- Laryngeal nerve palsy
- Lesion with difficult access

High Risk Features



Asymptomatic Carotid Stenosis

Which Asymptomatic Patients Benefit from CAS or CEA?

Standard Risk

- Stent
  - Young age, patients with heart problems, good anatomy for stent
- CEA
  - Old age, low cardiac risk, bad anatomy for stent
- Medical Alone
  - moderate steno**sis**

High Risk (for CEA)

- Stent
  - High anatomic risk, some physiologic high risk
- CEA
  - None
- Medical Alone
  - Over 80 years, moderate stenosis, women, some physiologic high risk, bad anatomy for stent

Patient Must Have Acceptable Anatomy

High Risk Factors for CAS

Physiologic	Anatomic
• Age >80	• Tortuous arch • Calcified arch • Diseased great vessels • Tortuous carotid artery • Pre-occlusive lesion • Heavy plaque burden • Circumferential calcification • Echolucent plaque • Thrombus in lesion • Isolated cerebral hemisphere

Pre-procedural Risk Quantification for Carotid

Stenting Using the CAS Score

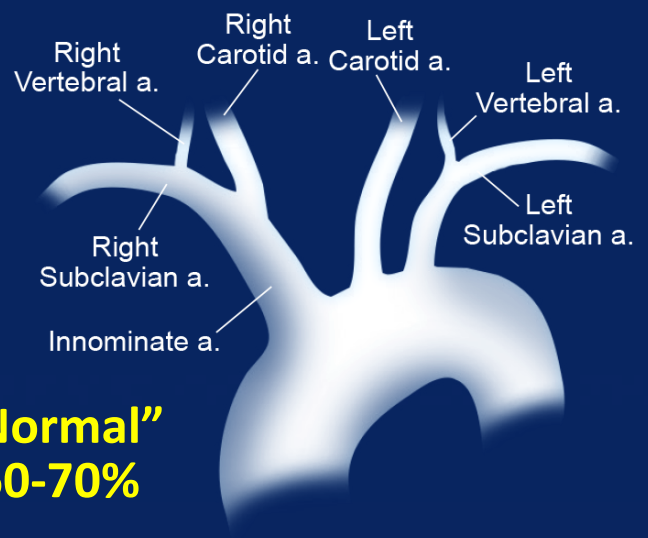
Risk model based on 11,122 carotid artery stenting (CAS) procedures from the NCDR CARE registry

Variable	Point Value
Impending major surgery	3
Previous stroke	3
Target lesion symptomatic in previous 6 months	2
Atrial fibrillation or flutter	1
Age, years	
<50	0
50–59	2
60–69	4
70–79	6
80–89	8
≥90	10
Previous ipsilateral CEA	–2

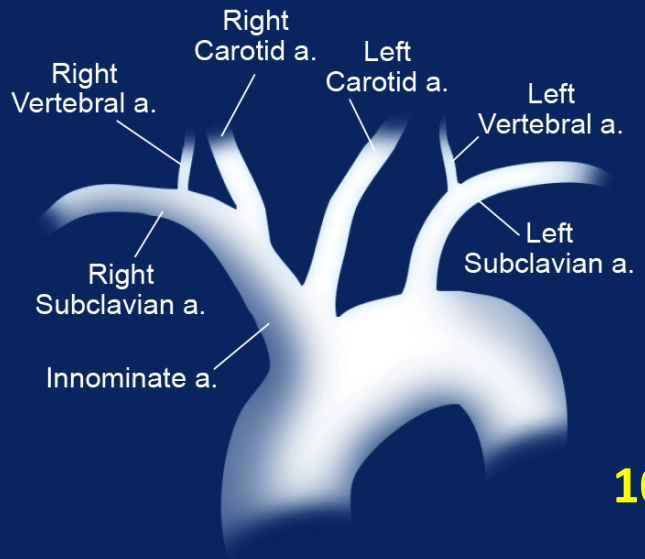
Scores above 5 exceeded the 3% threshold for 30-day events; Scores over 9 exceeded the 6% 30-day threshold

J Am Coll Cardiol 2012;60:1617–22

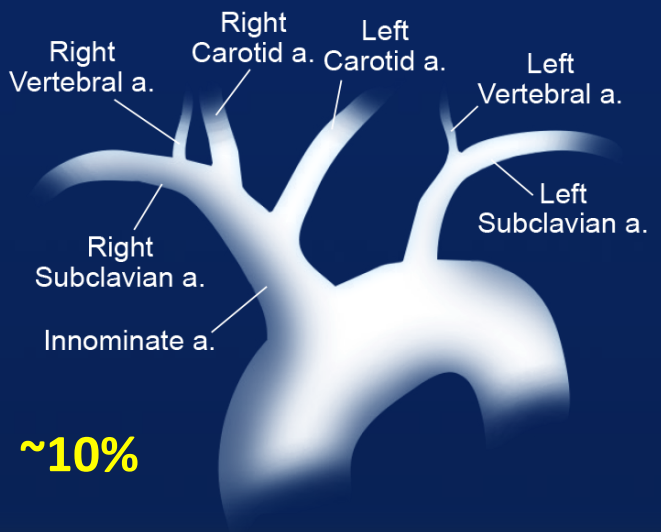
Aortic Arch Types



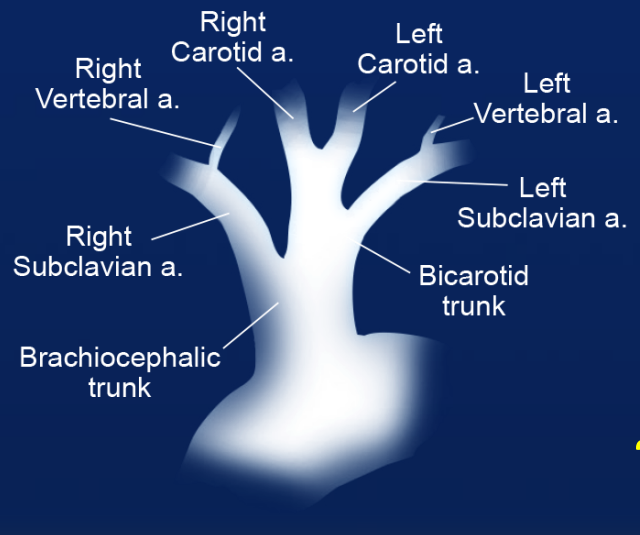
"Normal"
60-70%



10-15%



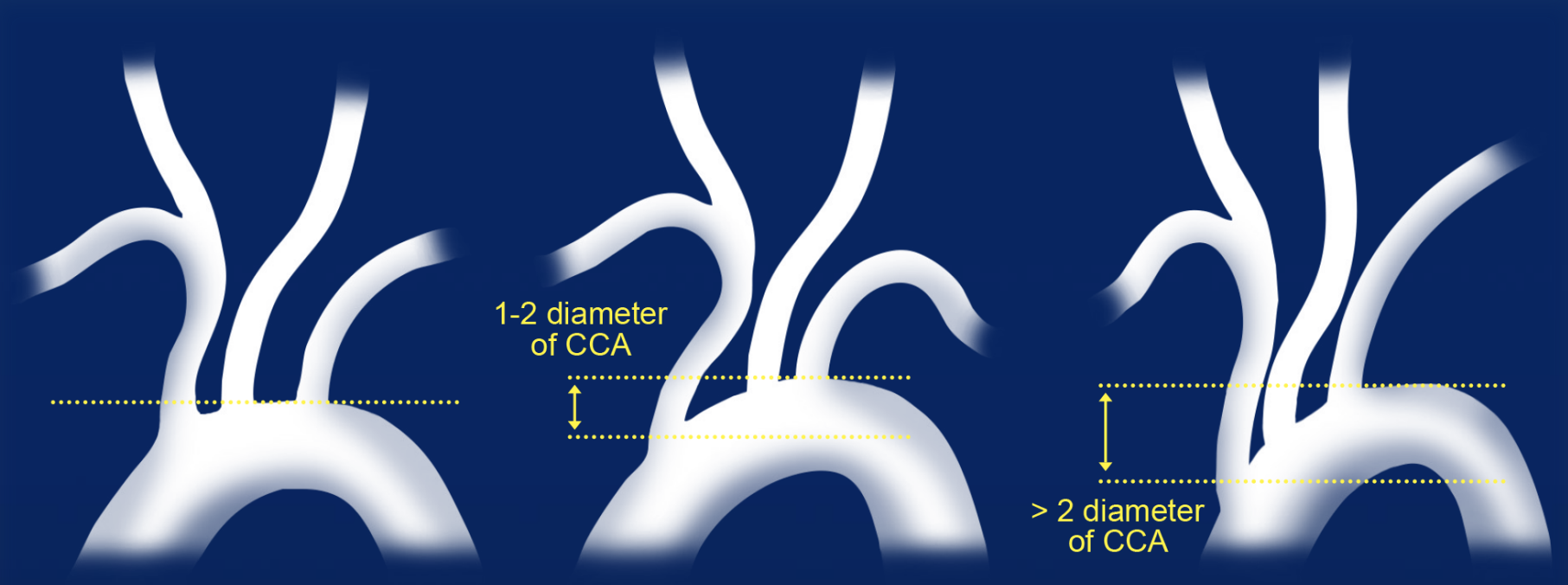
~10%



~5%

2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline
Circulation. 2011;124:e54-e130

Aortic Arch Classification



J Invasive Cardiol. 2008 May;20(5):200-4

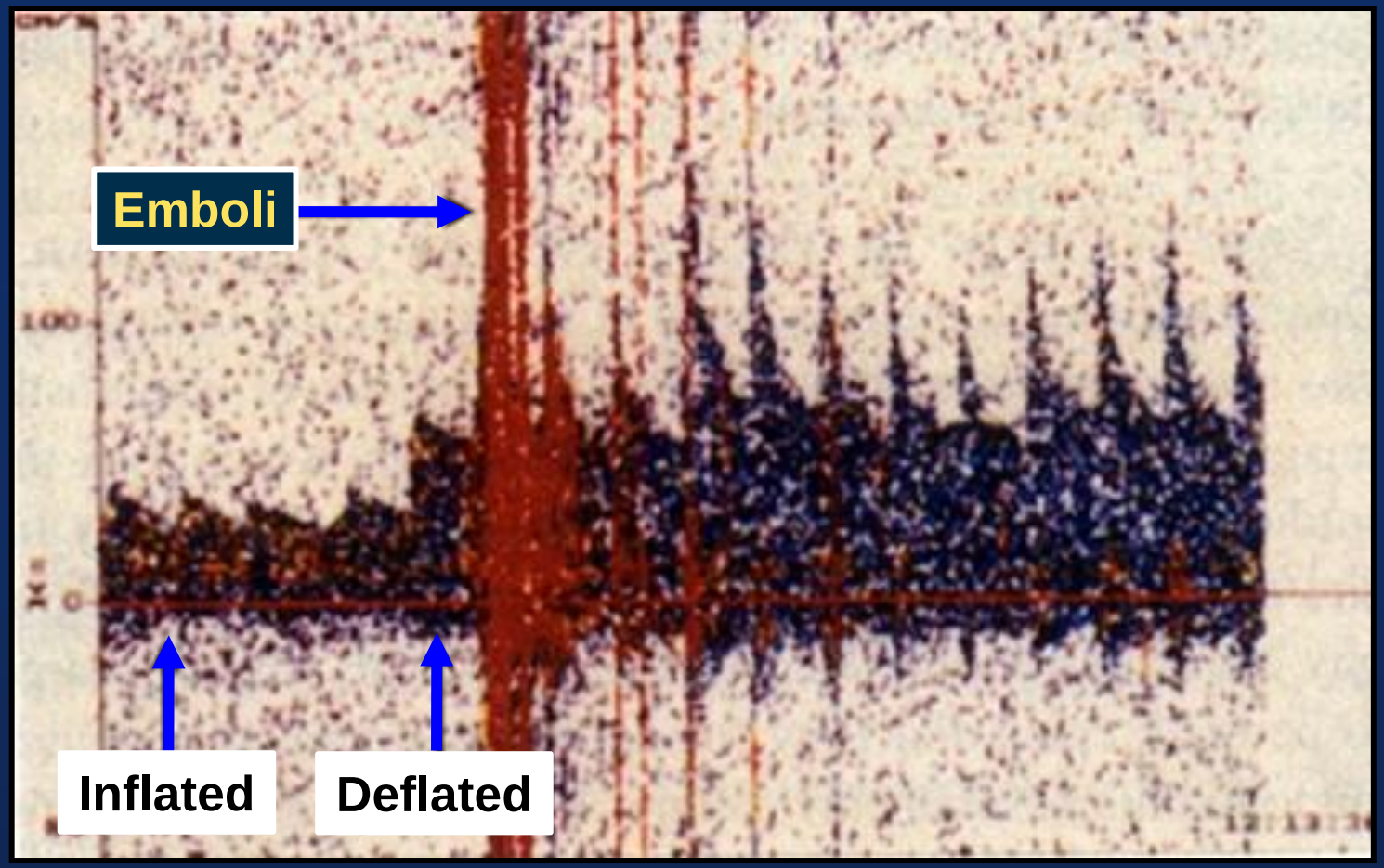
Features a/w increased procedural risks after carotid stenting

	Risk factors	Features
Clinical	Advanced age	Age ≥ 80 yrs
	Decreased cerebral reserve	- Dementia - Prior (remote) stroke - Multiple lacunar infarcts - Intracranial microangiopathy
Angiographic	Excessive tortuosity	≥ 2 90° bends within 5 cm of the lesion
	Heavy calcification	- Concentric circumferential calcification - Width ≥ 3mm

Circulation 2006;113:2021-2030

Embolic Protection Device (EPD)

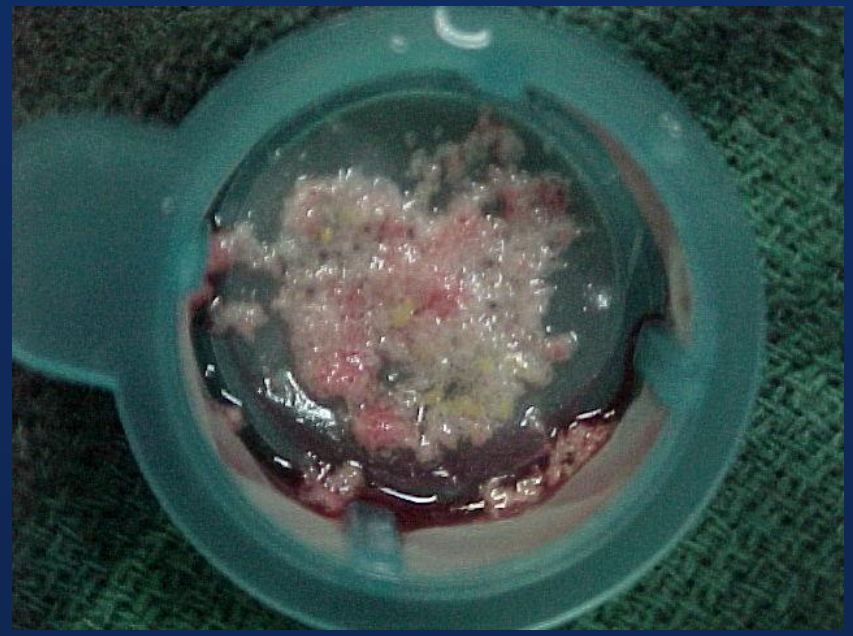
Trans Cranial Doppler During CAS



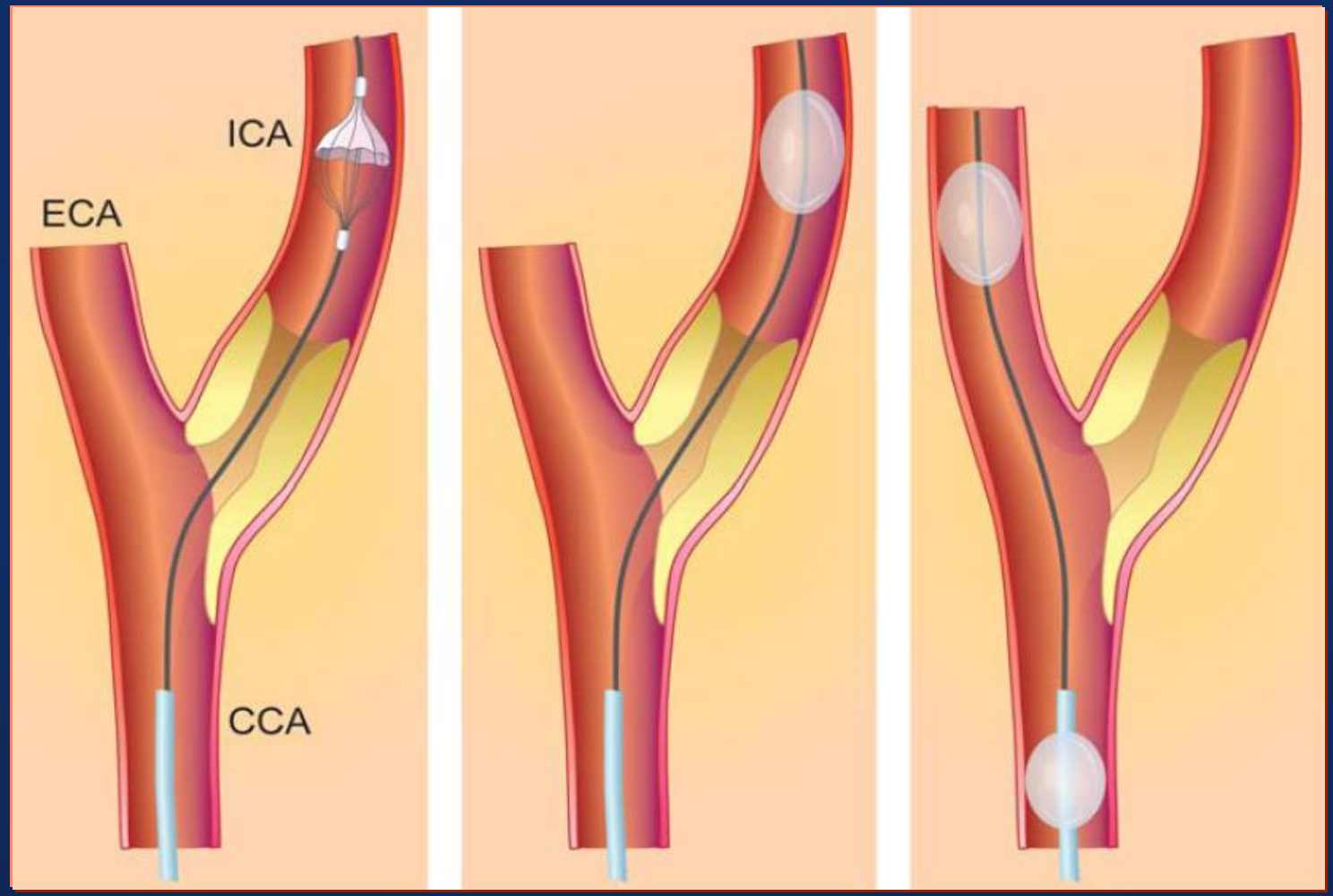
Carotid Artery Stenting

Current status

Embolic protection device (EPD)



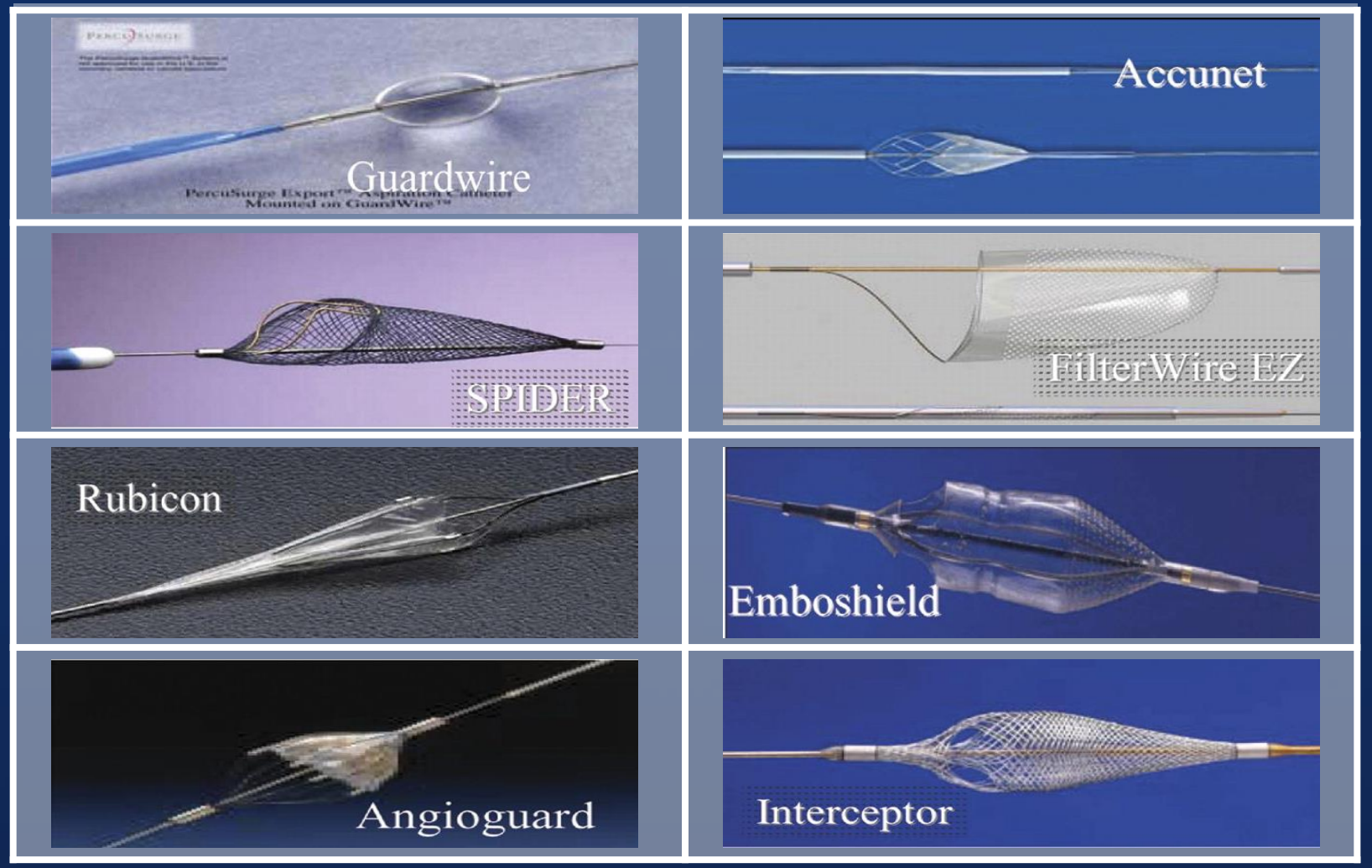
Strategies for Emboli Protection Devices



Filter Distal Occlusion Proximal Occlusion

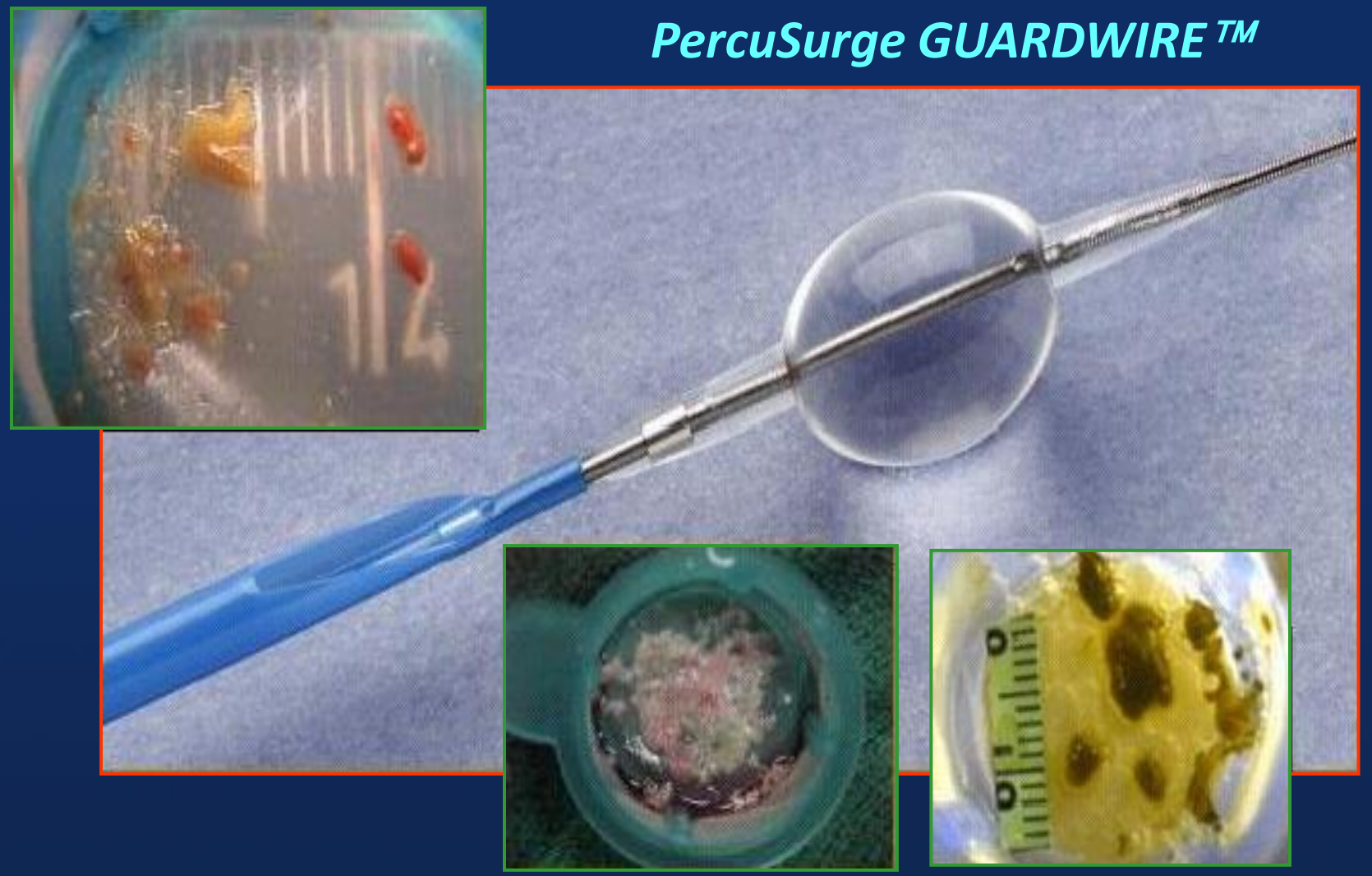
Eur Heart J. 2009; 30: 2693-2704

Embolic Protection Devices (EPD)



ACCF/SCAI/SVMB/SIR/ASITN 2007 Clinical Expert Consensus Document on Carotid Stenting J Am Coll Cardiol 2007;49:126–70

Distal Occlusion



EPD - Balloon Occlusion Devices

Advantages	Disadvantages
• Easy to cross lesion • Compatible with devices • Aspirate large and small particles • Reliably trap debris • Easy device retrieval	• No antegrade flow • 5–8% are intolerant • Balloon-induced injury • Not as steerable as PTCA wires • Difficult to image during the procedure

EPD - Filter Devices

Advantages	Disadvantages
• Preserve antegrade flow • Contrast imaging is possible throughout the procedure	• May not capture all debris • Filters may clog, cause spasm • Delivery catheters may cause embolization before filter deployment • Retrieval sheath may snag on stents

30-Day Events (TIA, Stroke, and Death)

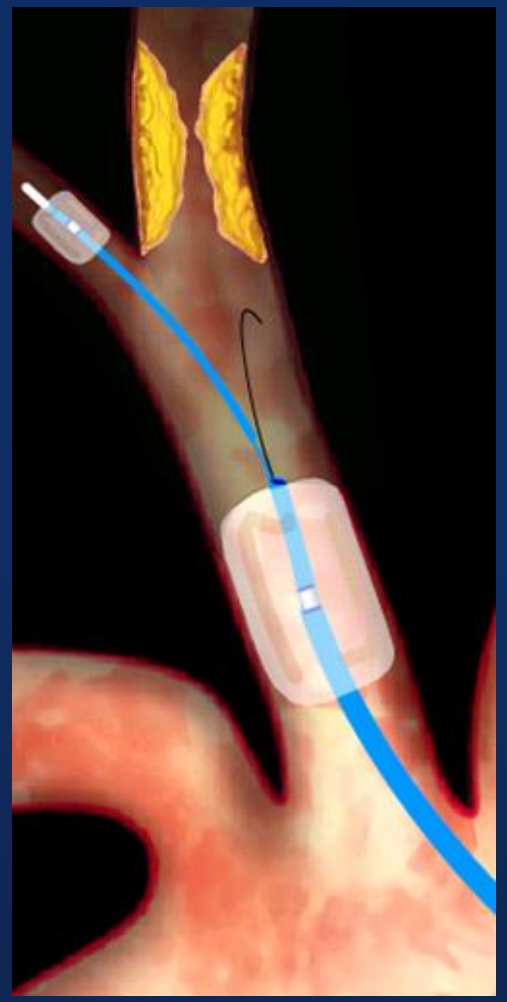
Comparison	RR	95% CI	*p*
Proximal occlusion vs. filter			
• Unadjusted	1.52	0.75–3.13	1.00
• Adjusted for RF, ST	1.59	0.71–3.10	1.00
Distal occlusion vs. filter			
• Unadjusted	2.72	0.71–10.51	0.96
• Adjusted for RF, ST	3.38	0.55–10.87	0.54
Distal vs. proximal occlusion			
• Unadjusted	1.79	0.40–7.96	1.00
• Adjusted for RF, ST	1.79	0.40–7.96	1.00
Eccentric vs. concentric filter			
• Unadjusted	0.59	0.38–0.92	0.04
• Adjusted for RF, ST	0.76	0.47–1.22	0.51

The Type of Embolic Protection **Does Not Influence the Outcome** in Carotid Artery Stenting

J Vasc Surg 2007;46:251–6

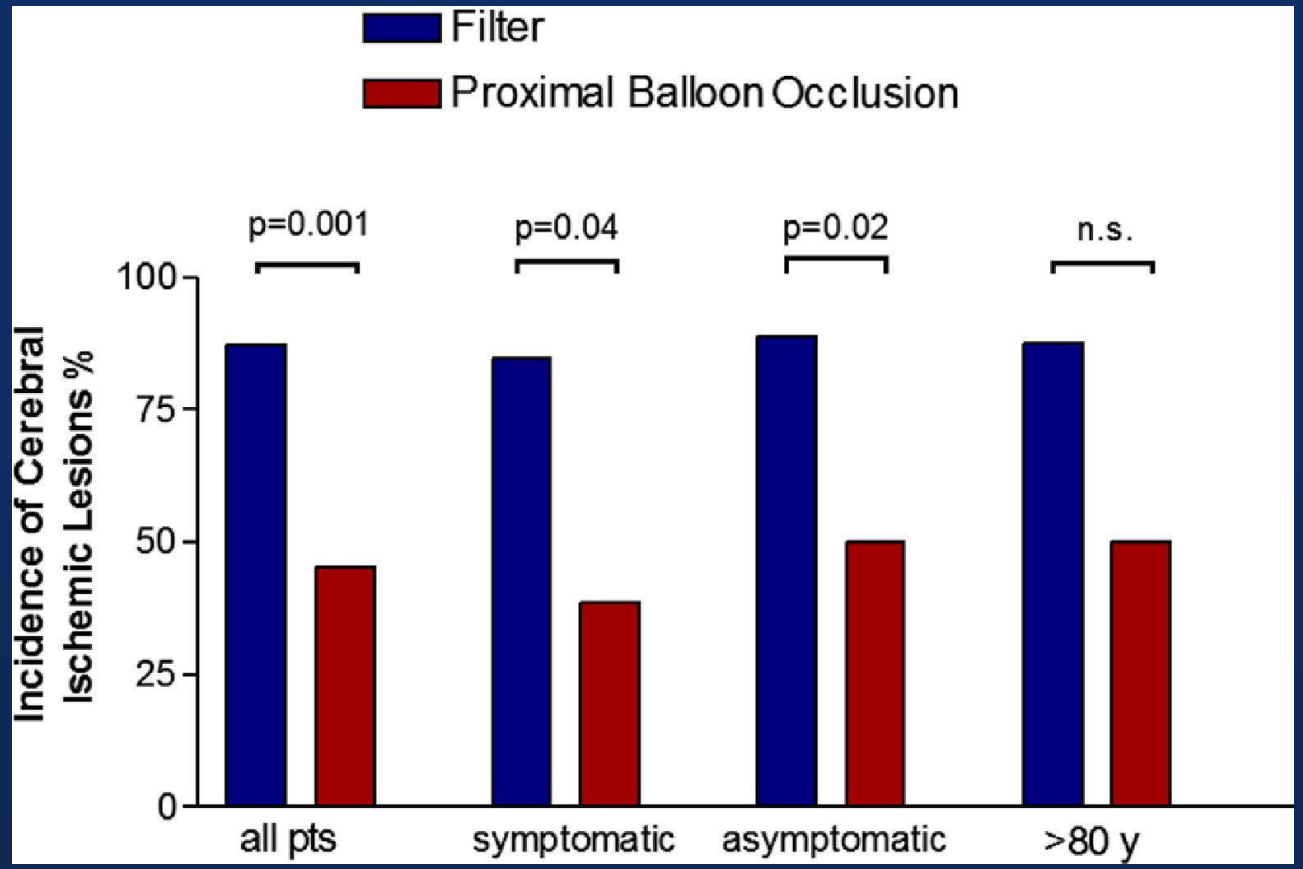
Proximal Balloon Occlusion - Mo.Ma

- **Endovascular Clamping**
- **Protects the brain from embolization**
  - Blocking antegrade blood flow from CCA
  - Blocking retrograde blood flow from ECA
- **Protection is established even before the ICA lesion is crossed**



The PROFI Study

Prevention of Cerebral Embolization by Proximal Balloon Occlusion Compared to Filter Protection During CAS) : A Prospective Randomized Trial



J Am Coll Cardiol. 2012 10;59(15) :1383–1389

The PROFI Study

Symptomatic and asymptomatic pts randomized to filter protection (n = 31) or proximal balloon occlusion (n = 31).

- The incidence of new cerebral ischemic lesions was higher in the filter group (87.1% vs. 45.2%; *P* = 0.001)
- These findings were consistent regardless of symptomatic (*P* = 0.04) or asymptomatic (*P* = 0.02) status
- Pts with filter protection also had a higher mean volume (*P* = 0.0001) and number (*P* = 0.0001) of new ischemic lesions

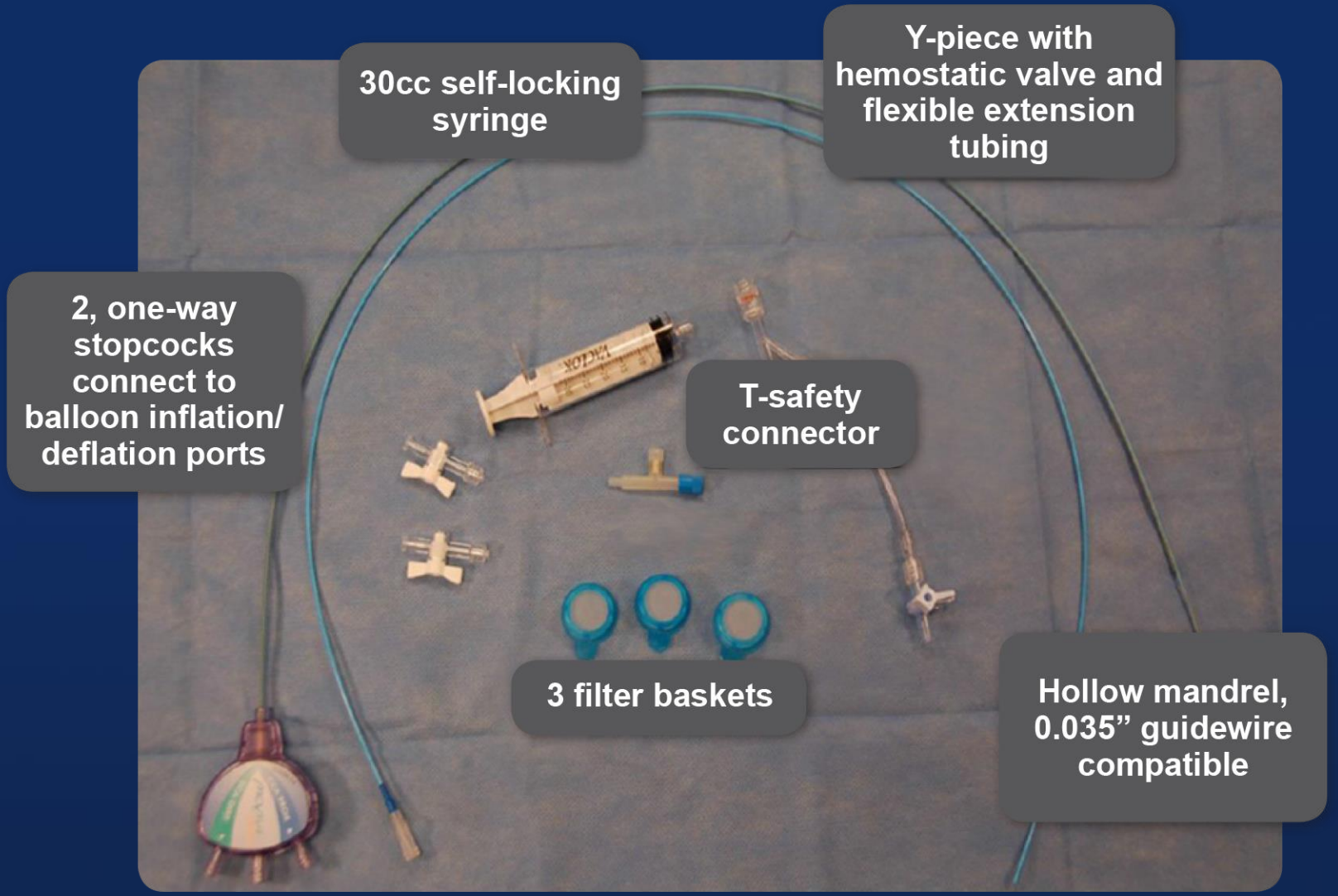
Conclusions: In patients undergoing carotid stenting, proximal balloon occlusion is associated with fewer new cerebral ischemic lesions than filter protection.

J Am Coll Cardiol. 2012 10;59(15) :1383–1389

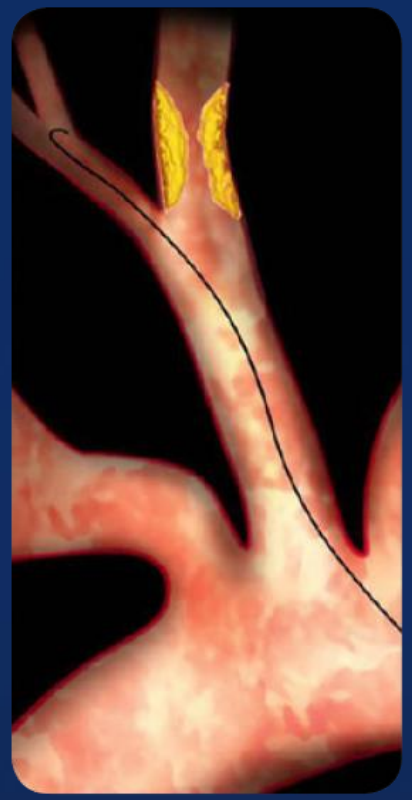
Mo.Ma Product Overview

Catheter design	Over The Wire (OTW) Multiple layers of Pebax with anti-kinking spiral coil and PTFE inner lumen
Range of diameter	1) Outer diameter 8F, Inner diameter 5F (1.76mm, 0.073") 2) Outer diameter 9F, Inner diameter 6F (2.12mm, 0.084")
Guidewire compatibility	0.035"
Usable shaft length	95 cm
Working channel length	104.5 cm
Distal shaft profile	5F (1.66 mm)
Introducer compatibility	1) 8F 2) 9F
Balloon material:	Compliant elastomeric rubber
Balloon occlusion range	up to 13 mm (prox.) up to 6 mm (dist.)
Balloon marker distance	60 mm

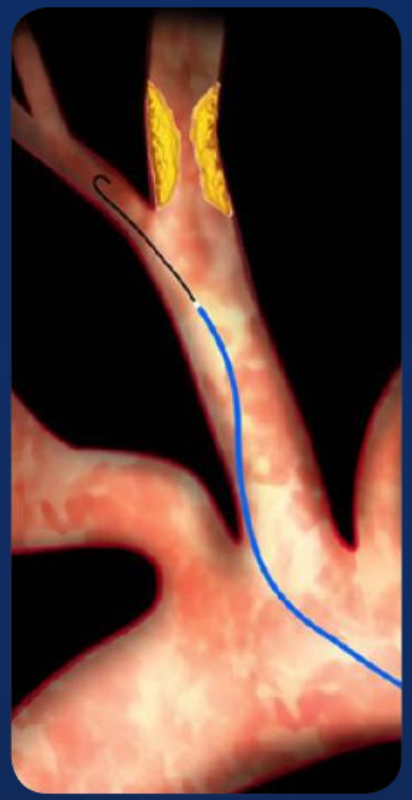
Mo.Ma


30cc self-locking syringe
Y-piece with hemostatic valve and flexible extension tubing
2, one-way stopcocks connect to balloon inflation/ deflation ports
T-safety connector
3 filter baskets
Hollow mandrel, 0.035” guidewire compatible

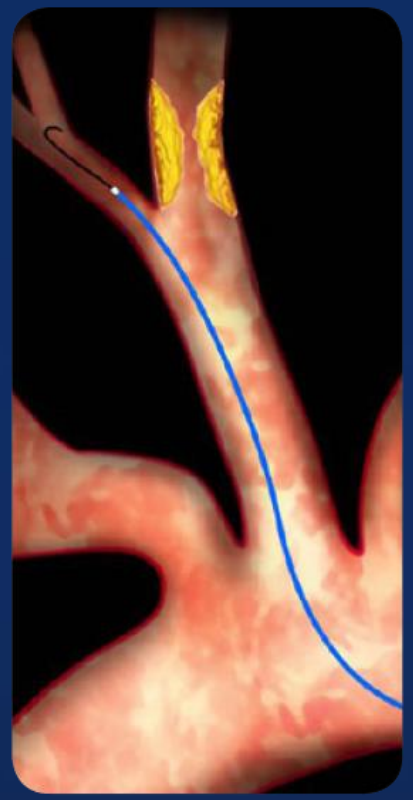
Mo.Ma step by step



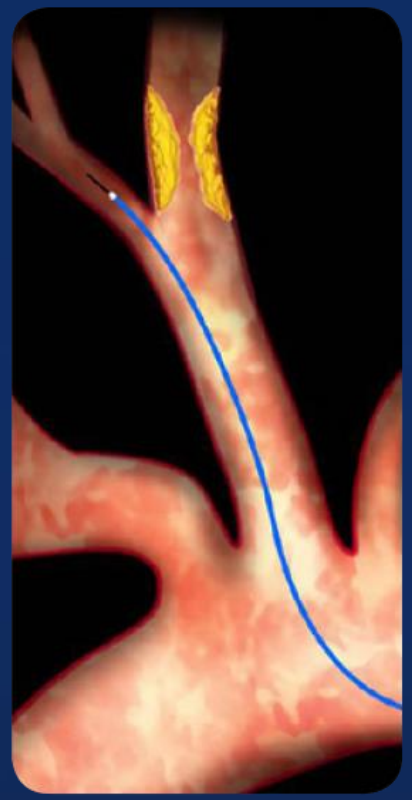
Introduction of steerable 0.035” wire into ECA



Introduction of diagnostic catheter into ECA

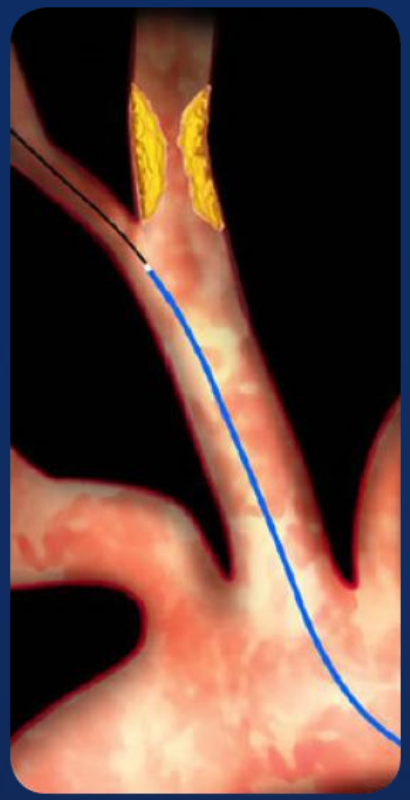


Remove steerable 0.035” guidewire

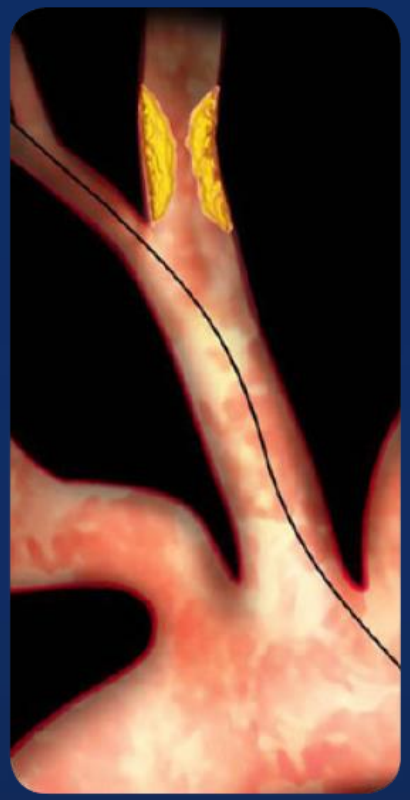


Introduce stiff 0.035” guidewire

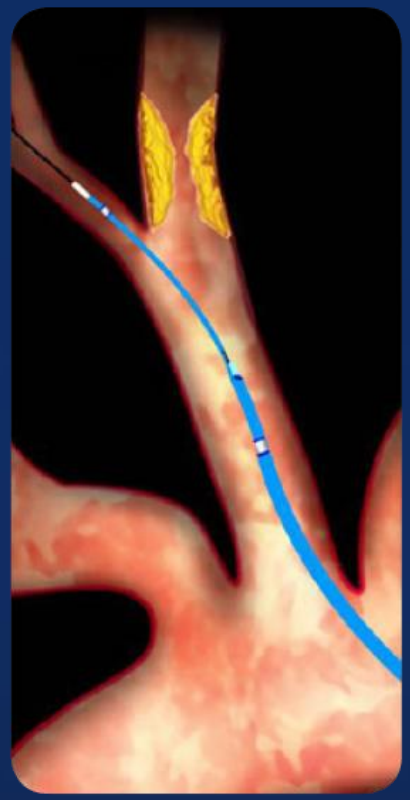
Mo.Ma step by step



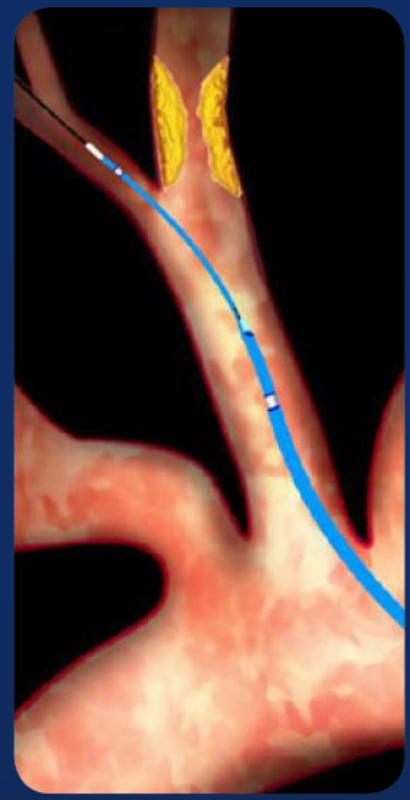
Remove diagnostic catheter



Retain 0.035” wire to introduce Mo.Ma Ultra device

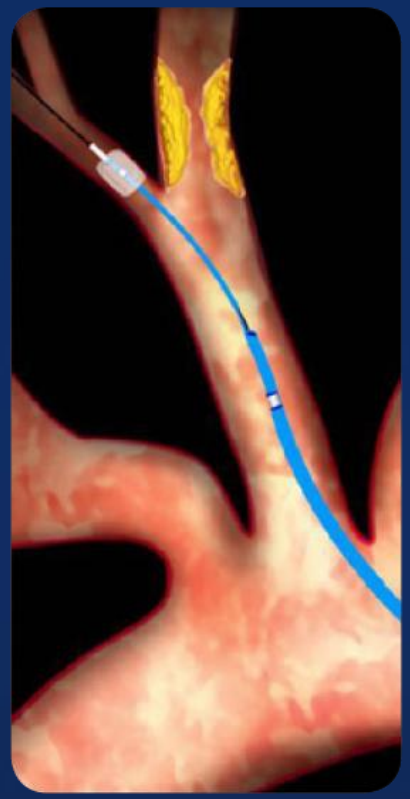


Introduce Mo.Ma Ultra device

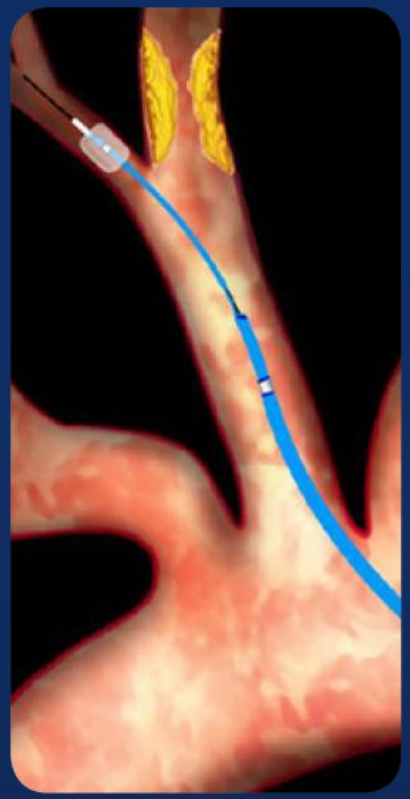


Advance Mo.Ma Ultra device 1cm - 1.5cm into ECA

Mo.Ma step by step



Remove mandrel; leave 0.035” guidewire in place. Inflate distal balloon in ECA

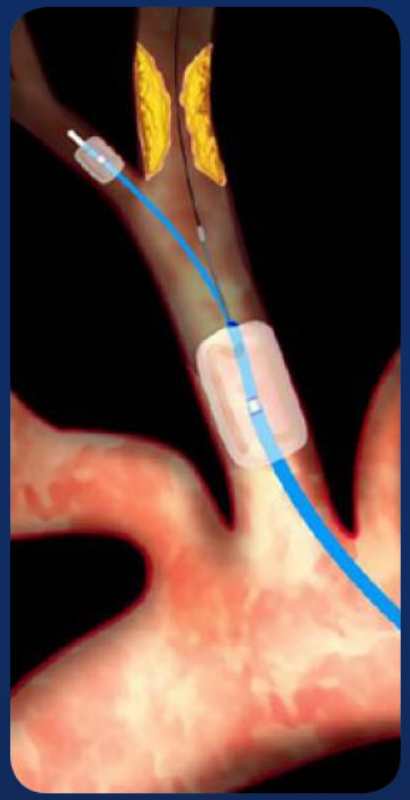


Remove 0.035” stiff guidewire

Inflate proximal balloon in the CCA

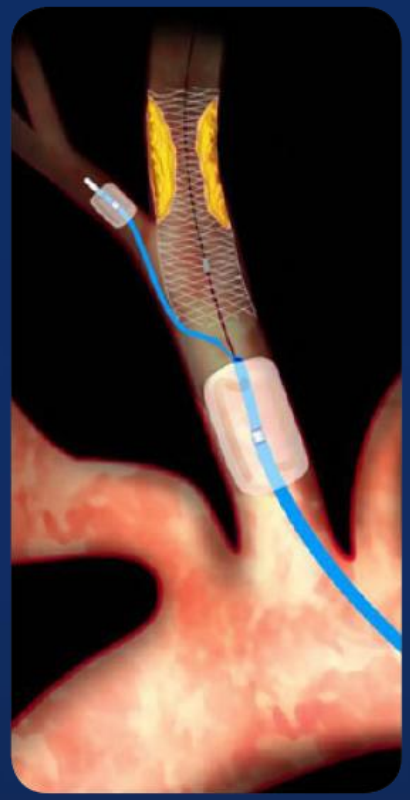
Advance 0.014” guidewire through lesion

Mo.Ma step by step



Predilate or primary stent

Place stent



Remove stent delivery system

Insert post-dilatation balloon

Mo.Ma step by step

Inflate
PTA balloon

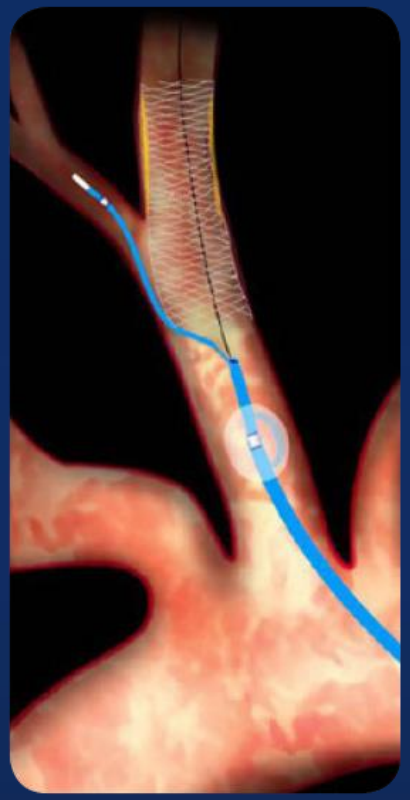
Deflate
PTA balloon

Retract
PTA balloon

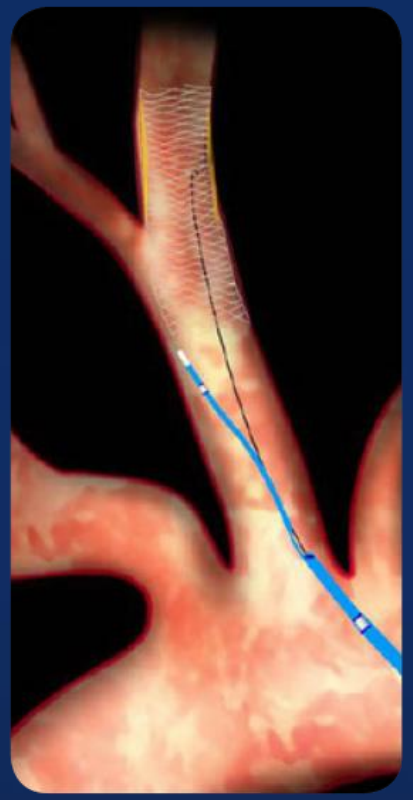
Aspirate to
remove debris

Mo.Ma step by step

Deflate distal (ECA) balloon



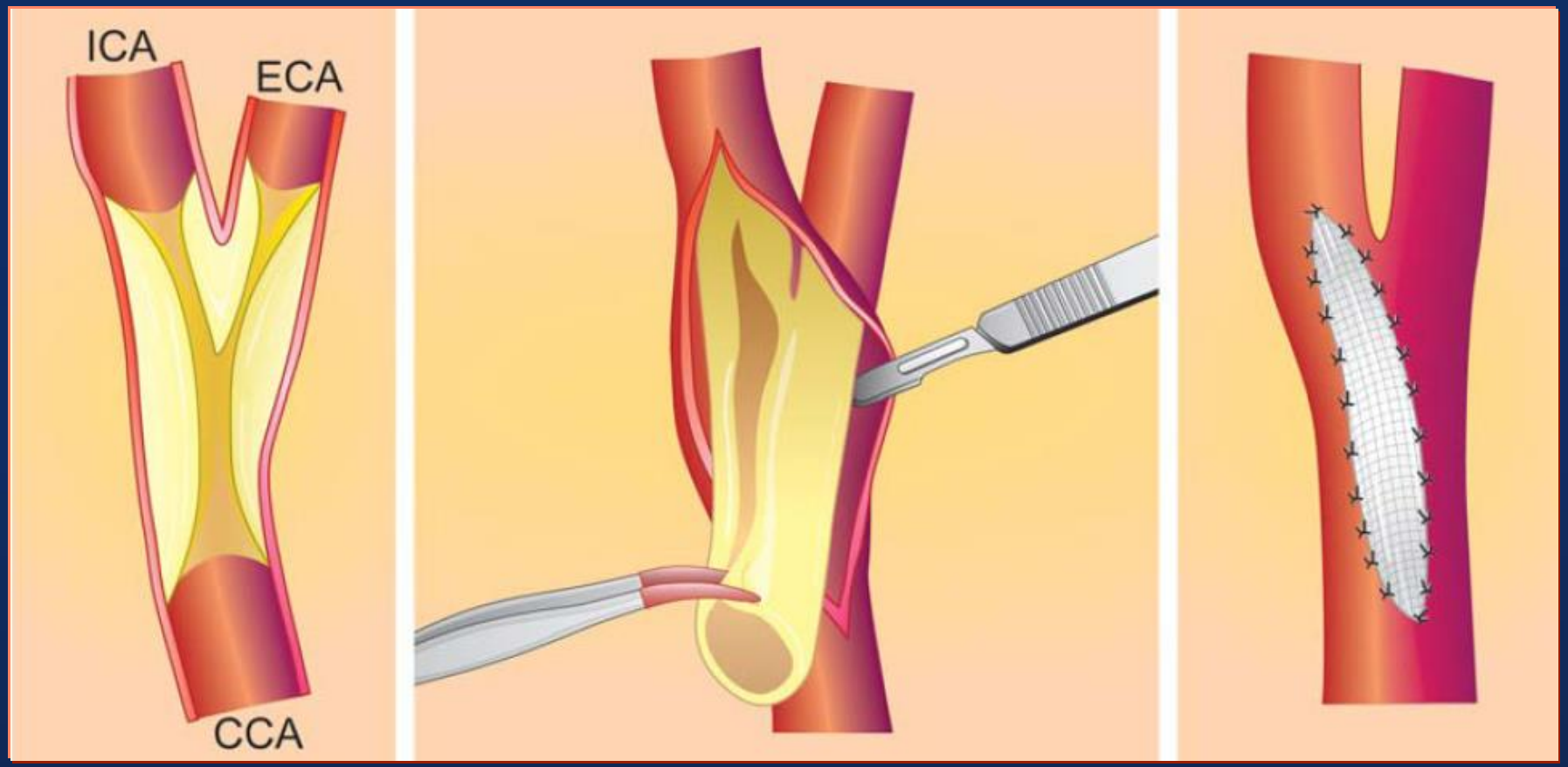
Deflate proximal (CCA) balloon



Retract Mo.Ma Ultra device and guidewire

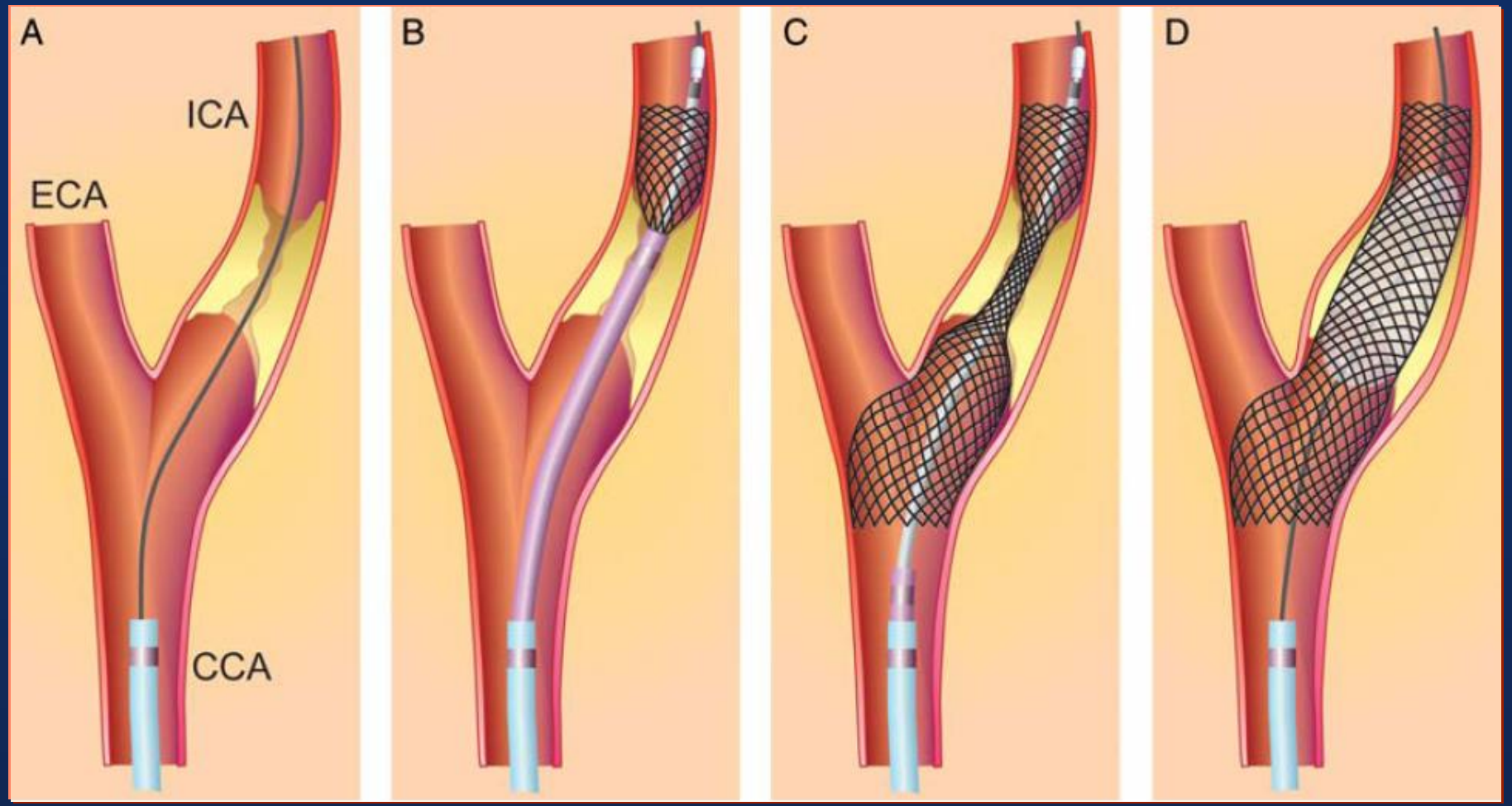
Carotid Endarterectomy
vs.
Carotid Stenting

Carotid Endarterectomy



Eur Heart J. 2009; 30: 2693-2704

Carotid Artery Stenting



Eur Heart J. 2009; 30: 2693-2704

Carotid Stent Randomized Trial Data

Pre-EPD

- Normal risk/randomized
  - WallStent trial-1999 (223)

Post-EPD

- Normal risk/symptomatic and asymptomatic/randomized
  - CREST, ACT 1
- Normal risk/symptomatic/randomized
  - EVA-3S, SPACE-1,
  - CAVATAS, ICSS
- High risk/symptomatic and asymptomatic/randomized
  - SAPPHIRE

Carotid Stent Registry Data – post EPD

High risk/registry

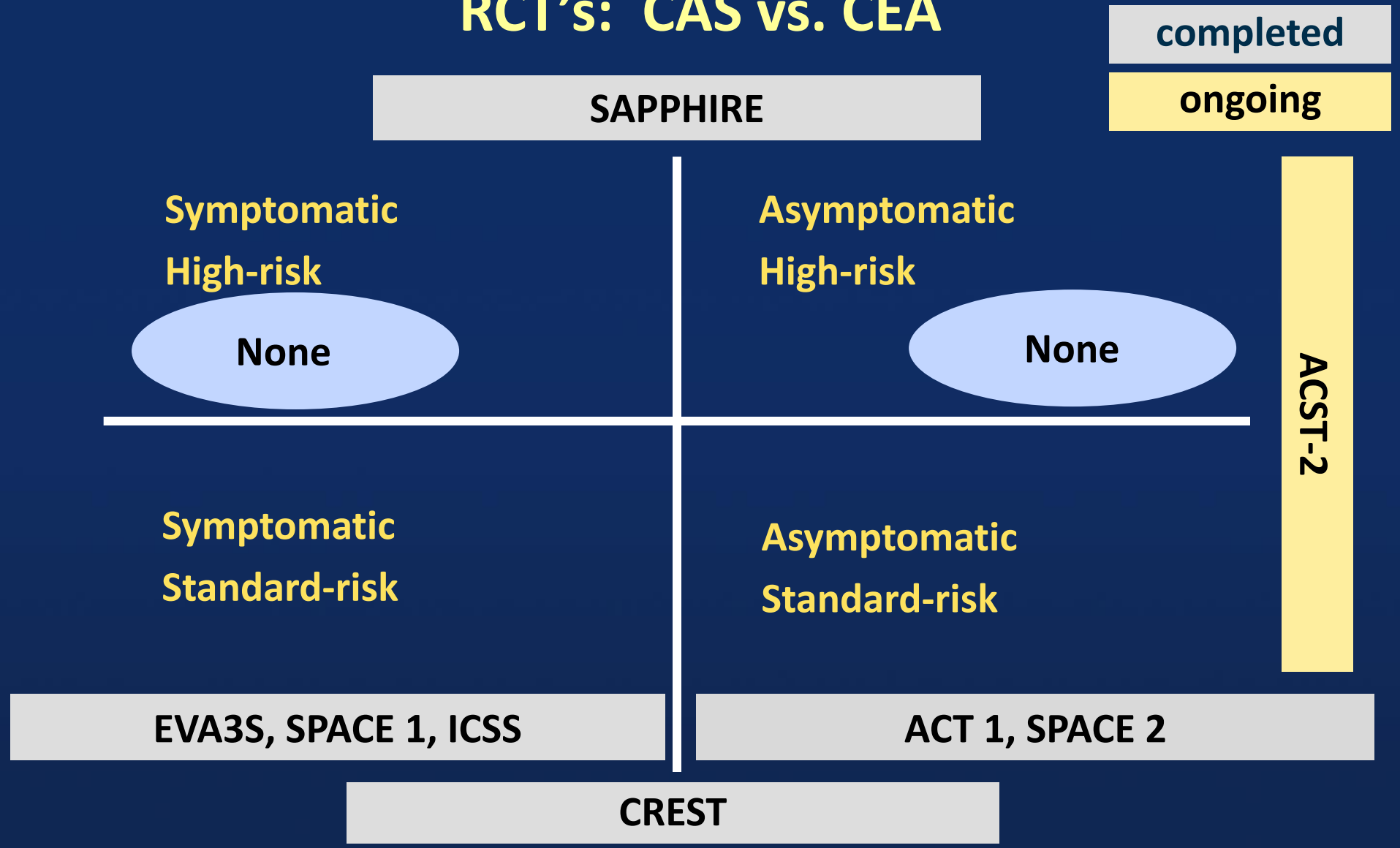
- SAPPHIRE-2002 (406)
- ARCHeR-2003 (581)
- SECuRITY-2003 (305)
- BEACH-2004 (408)
- CABERNET-2004 (454)
- CREATE -2005 (413)
- CAPTURE -2007 (3500)
- CASES PMS -2007 (1493)
- SAPPHIRE-W -2009 (2001)
- SVS -2009 (1450)
- EXACT -2009 (2145)
- CAPTURE 2 -2009 (4175)

Overview of major trials comparing CAE and CAS

Study	Year	Design	Symptomatic vs Asymptomatic	Results
SAPPHIRE	2004	Randomized, prospective, multicenter	96/238	CAS not inferior to CEA in symptomatic or nonsymptomatic patients in the high surgical risk group
SPACE	2006	Randomized, prospective, multicenter, European non inferiority trial	1,196/0	Ended after the second interim analysis owing to lack of recruitment
EVAS-3S	2006	Randomized, prospective, multicenter	527/0	CEA had better end point outcomes vs CAS for symptomatic stroke
ICSS	2010	Randomized, prospective, multicenter	1,710/0	CAS had a higher rate of stroke, death, and MI versus CEA for symptomatic stroke
CREST	2010	Randomized, prospective, multicenter, parallel, open label	1,326/1,176	CEA and CAS have similar safety and efficacy profiles

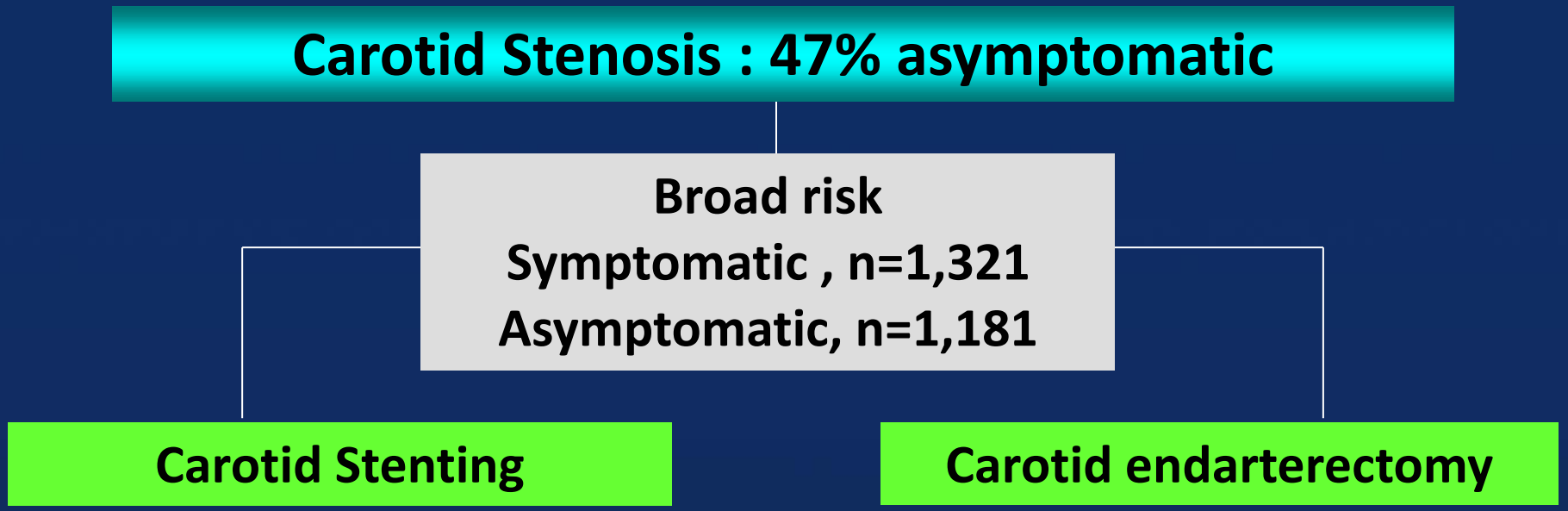
Curr Atheroscler Rep (2013) 15:345

Carotid Artery Disease
RCT's: CAS vs. CEA



CREST Trial

Carotid Revascularization Endarterectomy versus Stenting Trial



Primary Endpoint

: any stroke, MI, or death within 30 days plus subsequent ipsilateral stroke

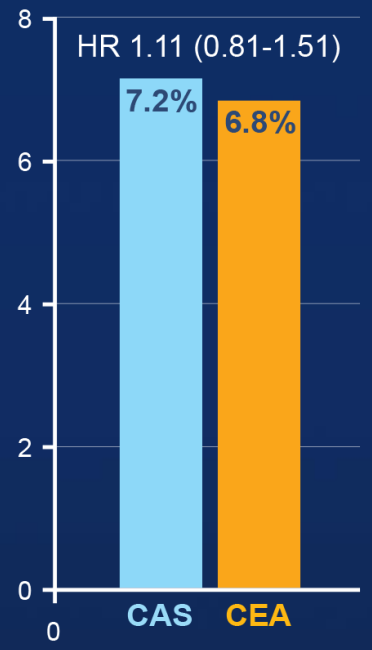
Follow-up was up to 4 years (median 2.5)

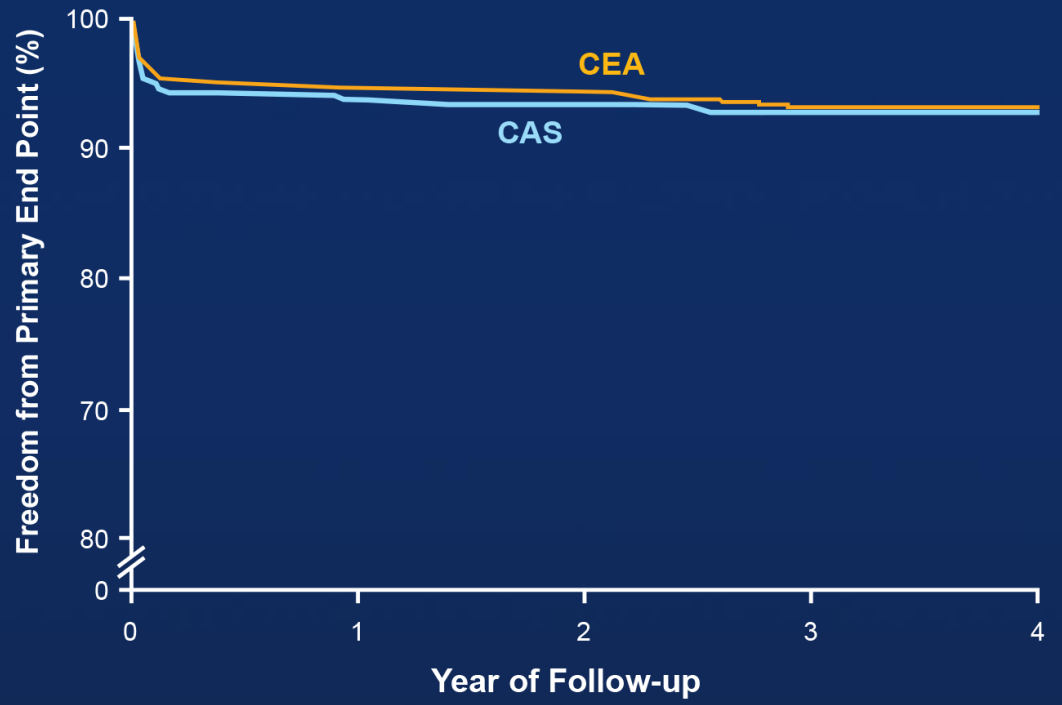
Int J Stroke. 2010;5:40–46

4-Year Outcomes of the CREST

Primary Endpoint :

any stroke, MI, or death within 30 days + subsequent ipsilateral stroke





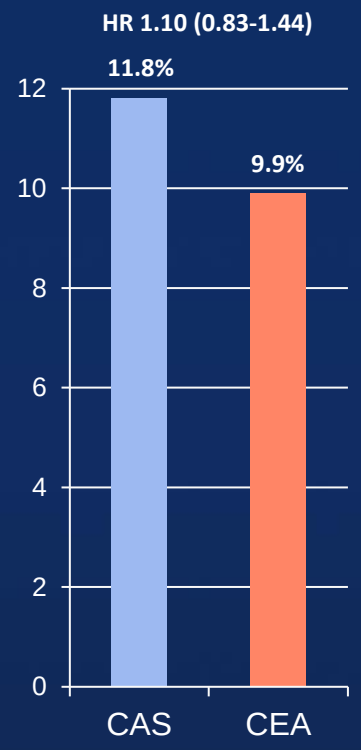
Number at Risk					
CAS	1262	1100	787	460	162
CEA	1240	1099	770	430	145

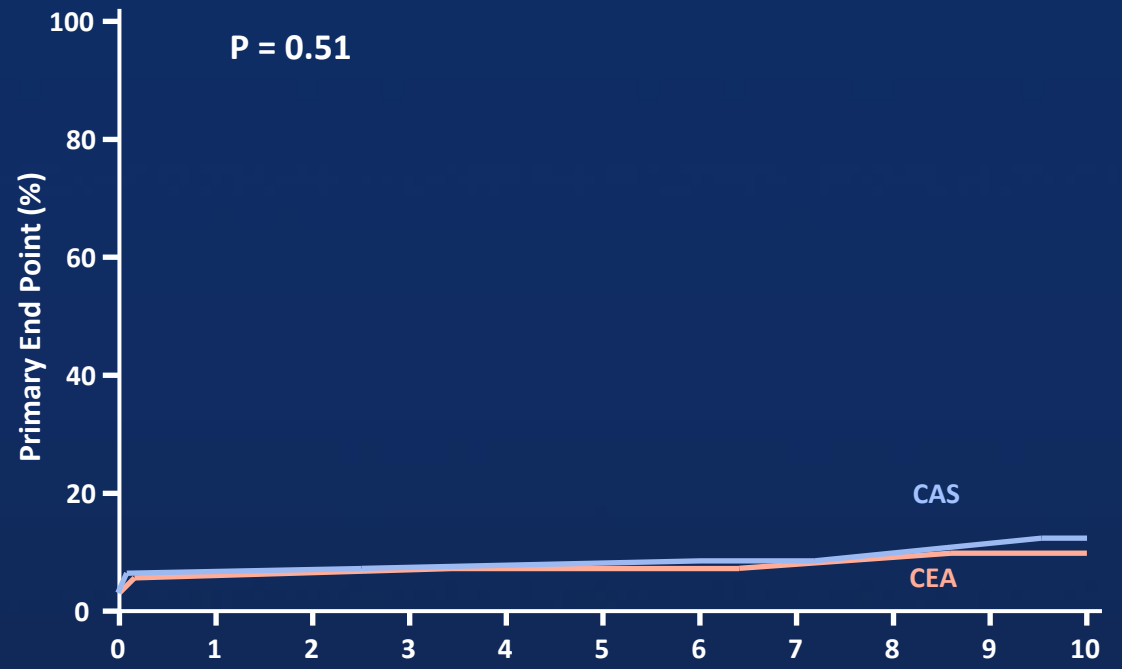
N Engl J Med 2010; 363(1):11-23

10-Year Outcomes of the CREST

Primary Endpoint :

any stroke, MI, or death during the periprocedural period + ipsilateral stroke



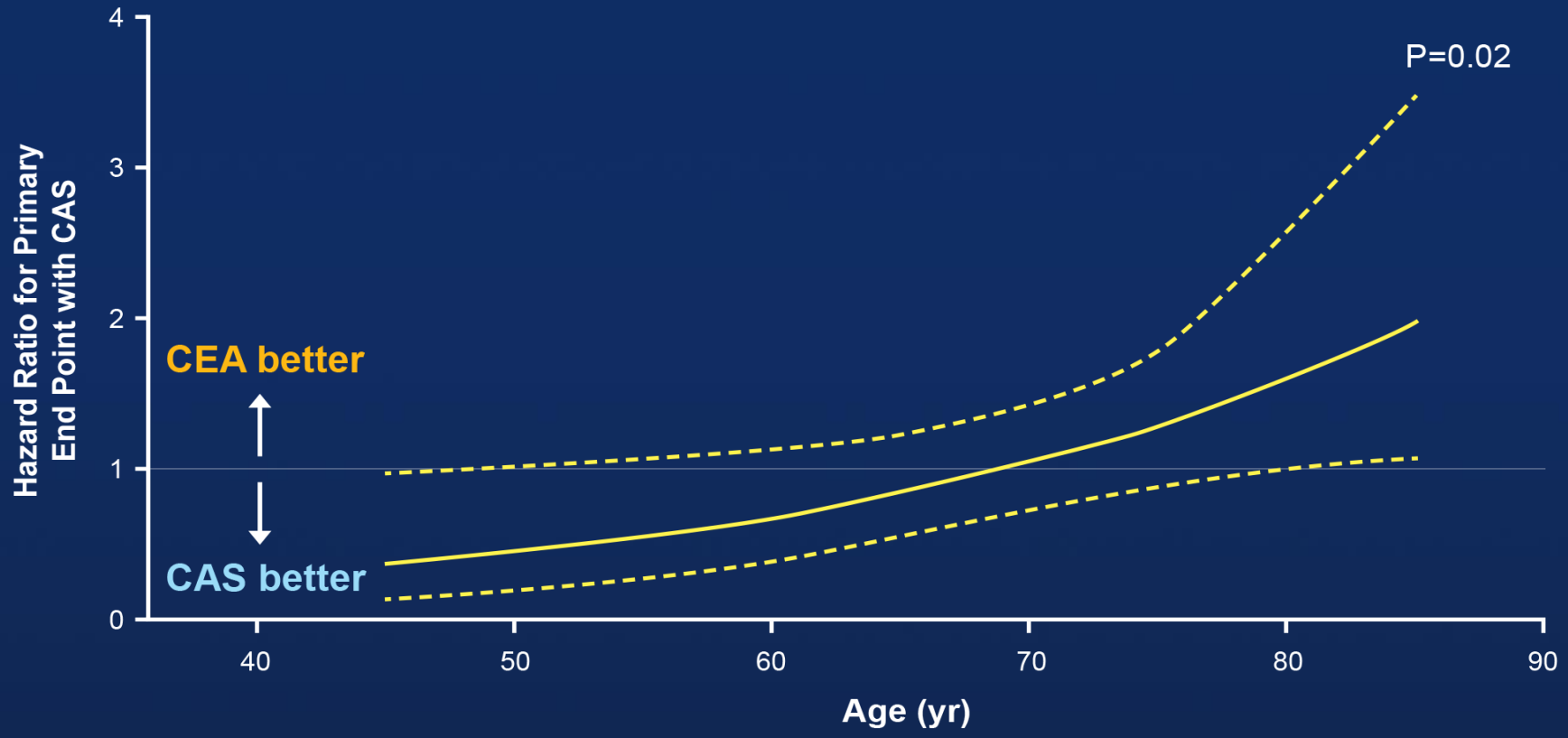


Number at risk											
CAS	1262	1103	1041	972	884	774	738	676	477	264	68
CEA	1240	1104	1036	949	833	736	695	620	438	243	66

N Engl J Med 2016; 374(11):1021-1031

Hazard Ratio for Primary Endpoint

4-Year Outcomes of the CREST



N Engl J Med 2010; 363(1):11-23

CREST Trial

Periprocedural (30-day) Complications

	CEA	CAS	HR (95% CI)	P Value
Stroke	2.3%	4.1%	1.79 (1.14-2.82)	0.01
Major	0.8%	1.4%		
Minor	1.4%	2.7%		
MI	2.3%	1.1%	0.50 (0.26-0.94)	0.03
CN Palsies	4.8%	0.3%	0.07 (0.02-0.18)	<0.0001

Overall death rate : 0.6%
Lowest reported in any randomized trials
Recurrent event rates 2.0% for CAS versus 2.4% for CEA

N Engl J Med 2010; 363(1):11-23

CREST Trial

Periprocedural (30-day) Complications

	CEA	CAS	HR (95% CI)	P Value
Stroke	5.6%	6.9%	0.99 (0.64-1.52)	0.96
Major	1.1%	2.7%	1.91 (0.71-5.10)	0.20
Minor	4.5%	4.2%	0.83 (0.51-1.34)	0.44

N Engl J Med 2016; 374(11):1021-1031

Safety of Stenting and CEA

by Symptomatic Status in the CREST

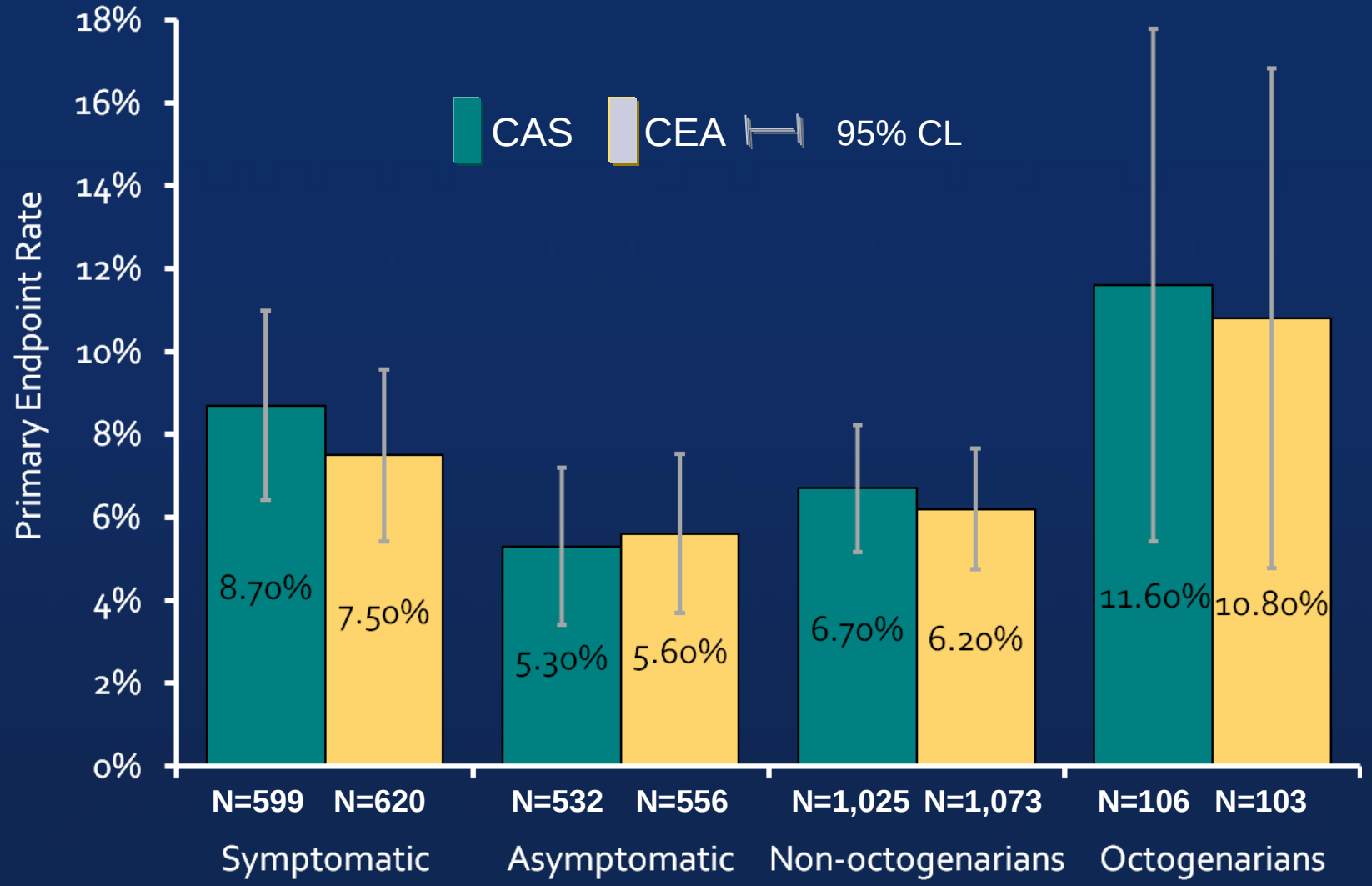
- 1,181 asymptomatic & 1,321 symptomatic pts
- Primary endpoint
  - periprocedural stroke, MI or death

	CAS	CEA	HR (95% CI)	*P Value*
Asymptomatic	3.5%	3.6%	1.02 (0.55-1.86)	0.96
Symptomatic	6.7%	5.4%	1.26 (0.81-1.96)	0.30

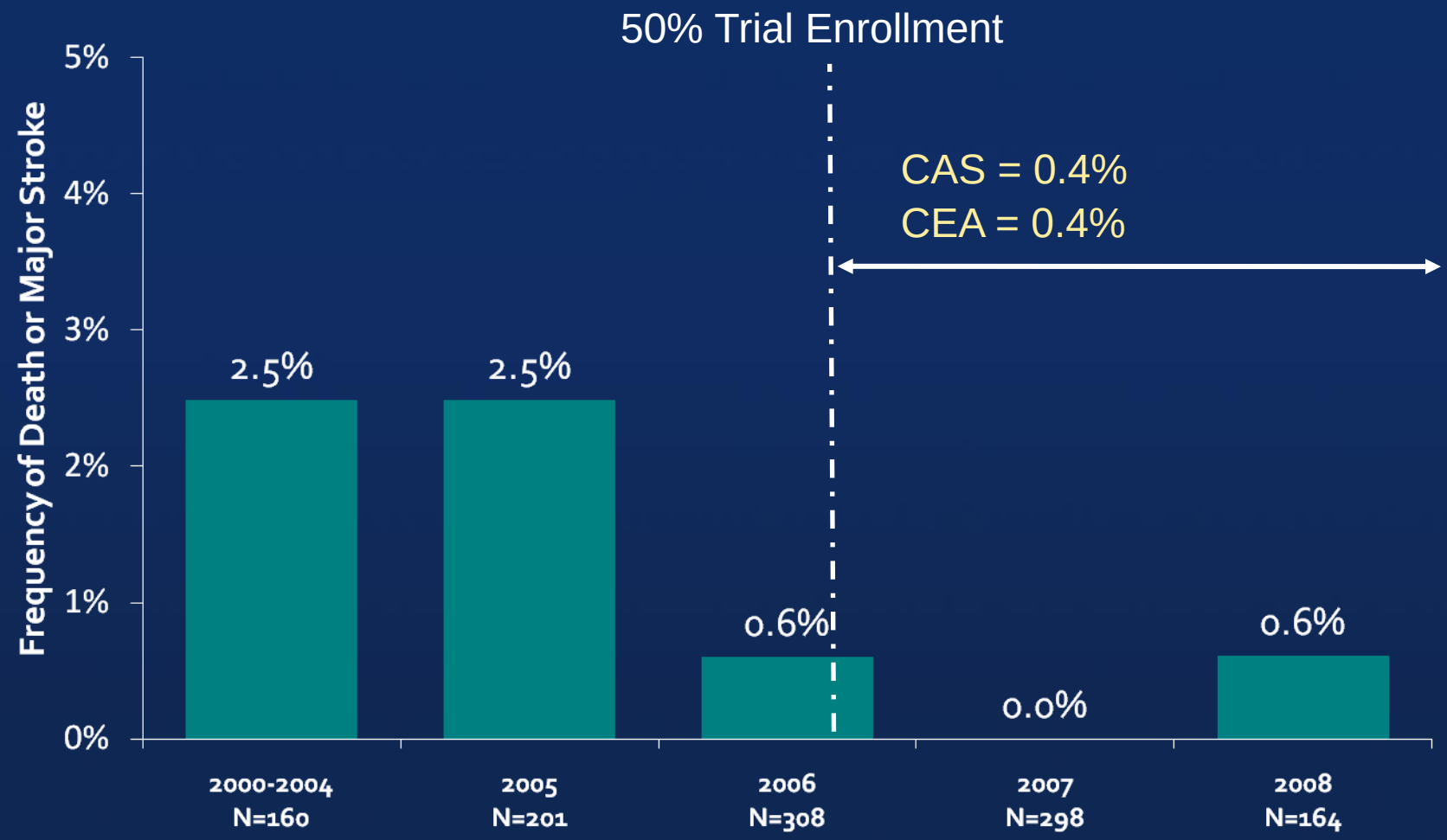
Stroke 2011; 42(3): 675-80

Primary Composite Endpoint

by Symptomatic or Octogenarian Statusin the CREST



Death or Major Stroke Rates Decrease for CAS over the Period of CREST Enrollment



Stroke and Death

by Age in the CREST

	Stroke Rate
<60 years (n=120)	2 (1.7%)
60-69 years (n=229)	3 (1.3%)
70-79 years (n=301)	16 (5.3%)
>80 years (n=99)	12 (12.1)%

Restenosis After Carotid Artery Stenting and Endarterectomy in the CREST trial

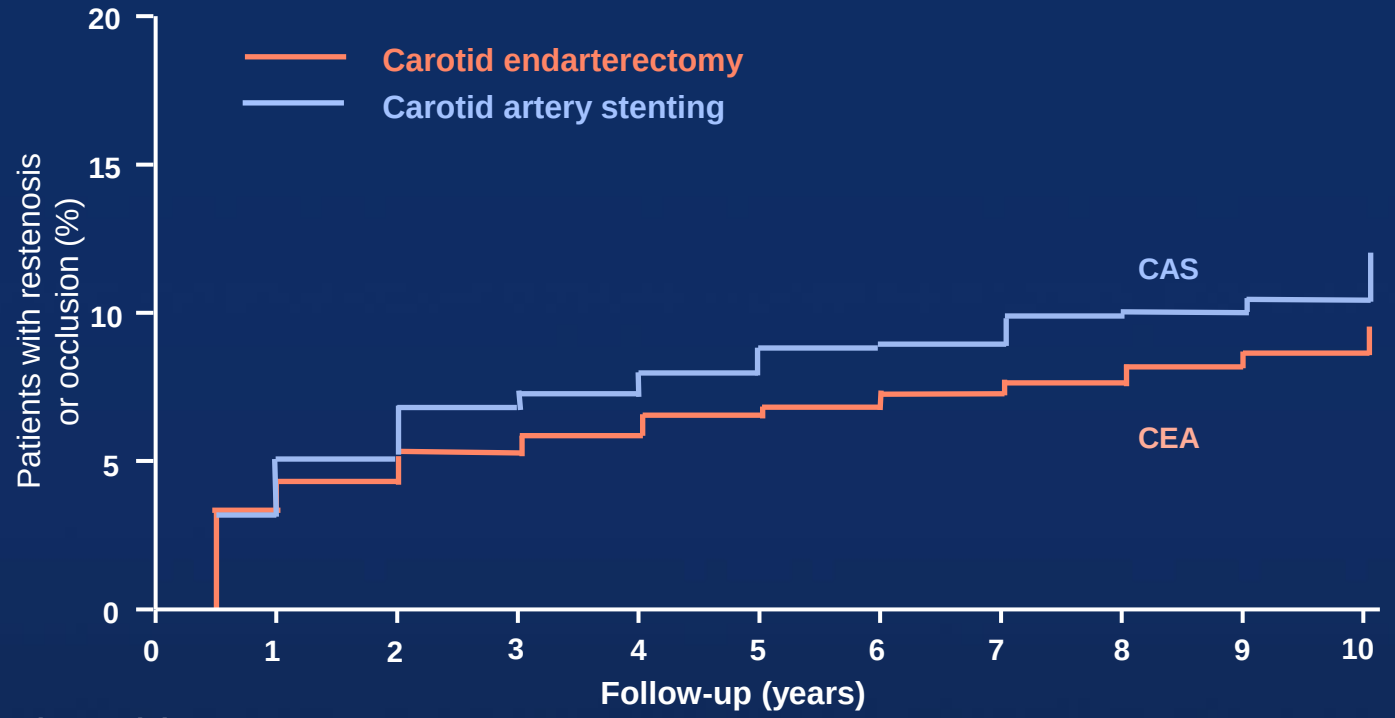
Pts who received assigned treatment ≤ 30 days after randomization and had core lab-reviewed duplex ultrasound (n = 1,086 CAS, n = 1,105 CEA)

- Restenosis occurred in 5.8% of both CAS and CEA patients at 2 years
- Repeat revascularization rates also were similar at 1.8% of the CAS group and 2.1% of the CEA group
- Multivariable analysis found that female sex, diabetes, and dyslipidemia independently predicted restenosis

Implications: Carotid stenting and surgery produce equivalent levels of restenosis out to 2 years after intervention.

Lancet Neurol 2012; 11: 755-63

Restenosis After Carotid Artery Stenting and Endarterectomy in the CREST trial



Number at risk											
CAS	1018	948	849	762	684	606	557	494	366	207	101
CEA	1014	939	849	750	654	558	514	460	334	197	89

HR (95% CI): 1.24 (0.91 – 1.70)

adjusted for age, sex, and symptomatic status

N Engl J Med 2016; 374(11):1021-1031

Frequency of restenosis after CAS or CEA

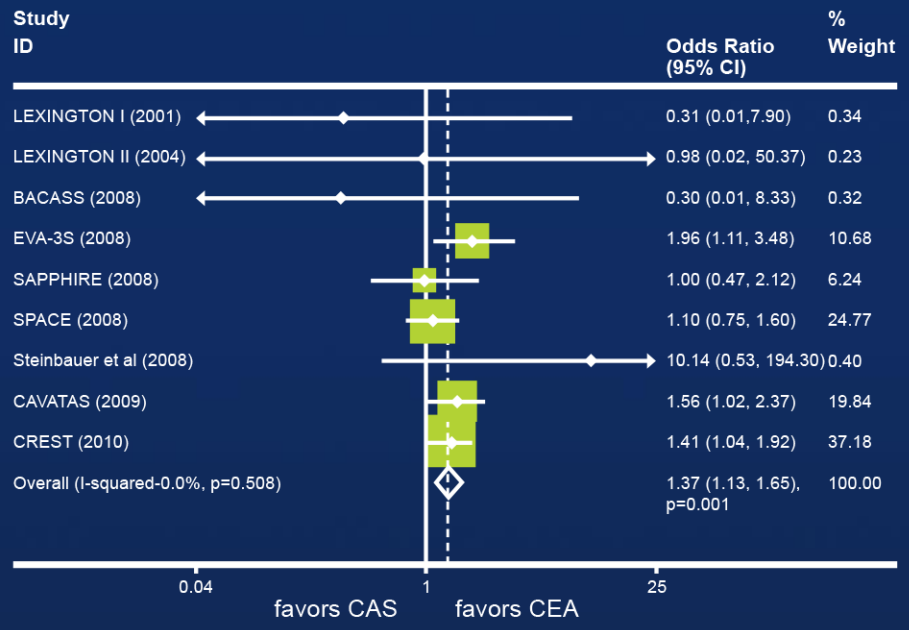
Trials	Definition of restenosis	Diagnostic criteria	No. of pts		Pts with restenosis		P Value
			CAS	CEA	CAS	CEA	
CAVATAS	Restenosis ≥70% or occlusion	PSV>2.1 m/s	50	213	16.6% in 5 years	10.5% in 5 years	Not reported
SAPPHIRE	Restenosis ≥50%(symptomatic) and ≥80% (asymptomatic)	Repeat revascularization procedure	143	117	3% in 3 years	7.1% in 3 years	0.08
EVA-3S	Restenosis ≥70% or occlusion	PSV>2.1 m/s (CEA) and ≥3.0 m/sec (CAS)	242	265	3.3% in 3 years	2.8% in 3 years	NS
CREST	Restenosis ≥70% or occlusion	PSV ≥3.0 m/sec	1086	1105	6.0% in 2 years	6.3% in 2 years	0.58
SPACE	Restenosis ≥70% or occlusion	Not specified	541	522	11.1% in 2 years	4.6% in 2 years	0.0007

Lancet Neurol 2012; 11: 755-63

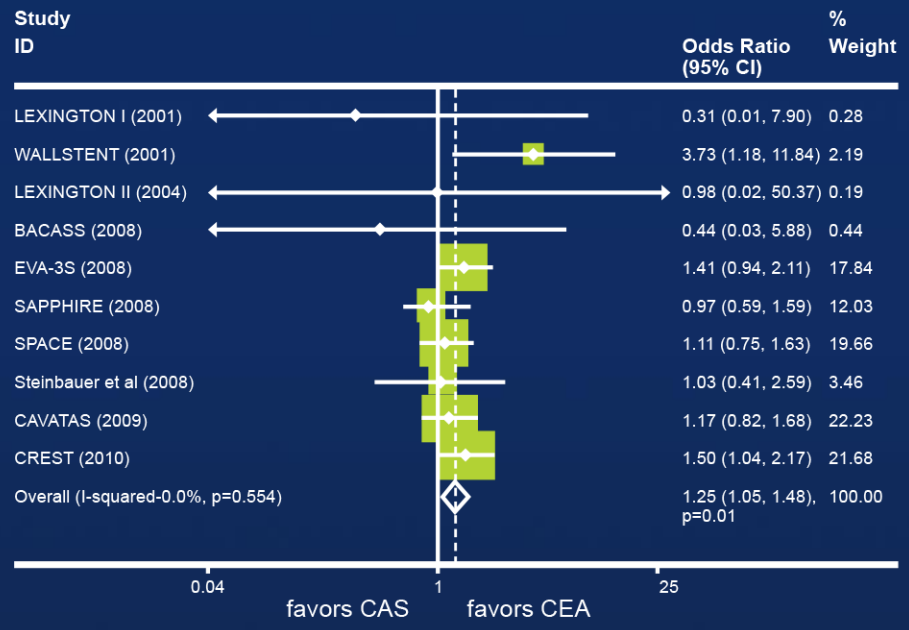
CEA vs. CAS : meta-analysis 13 RCTs included

Long-Term Outcomes (1-year)

Stroke



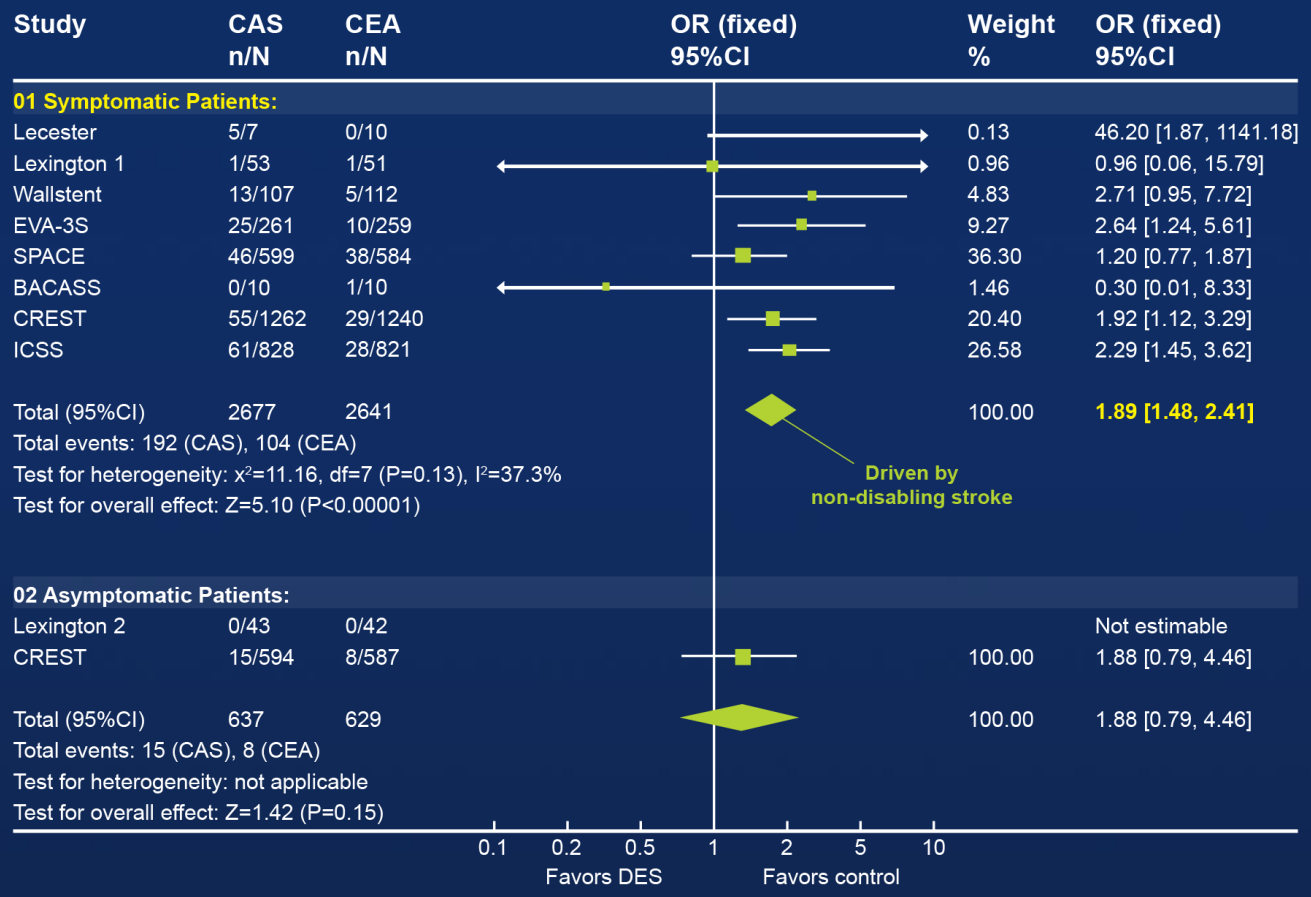
Death or Stroke



Stroke 2011; 42(3): 687-92

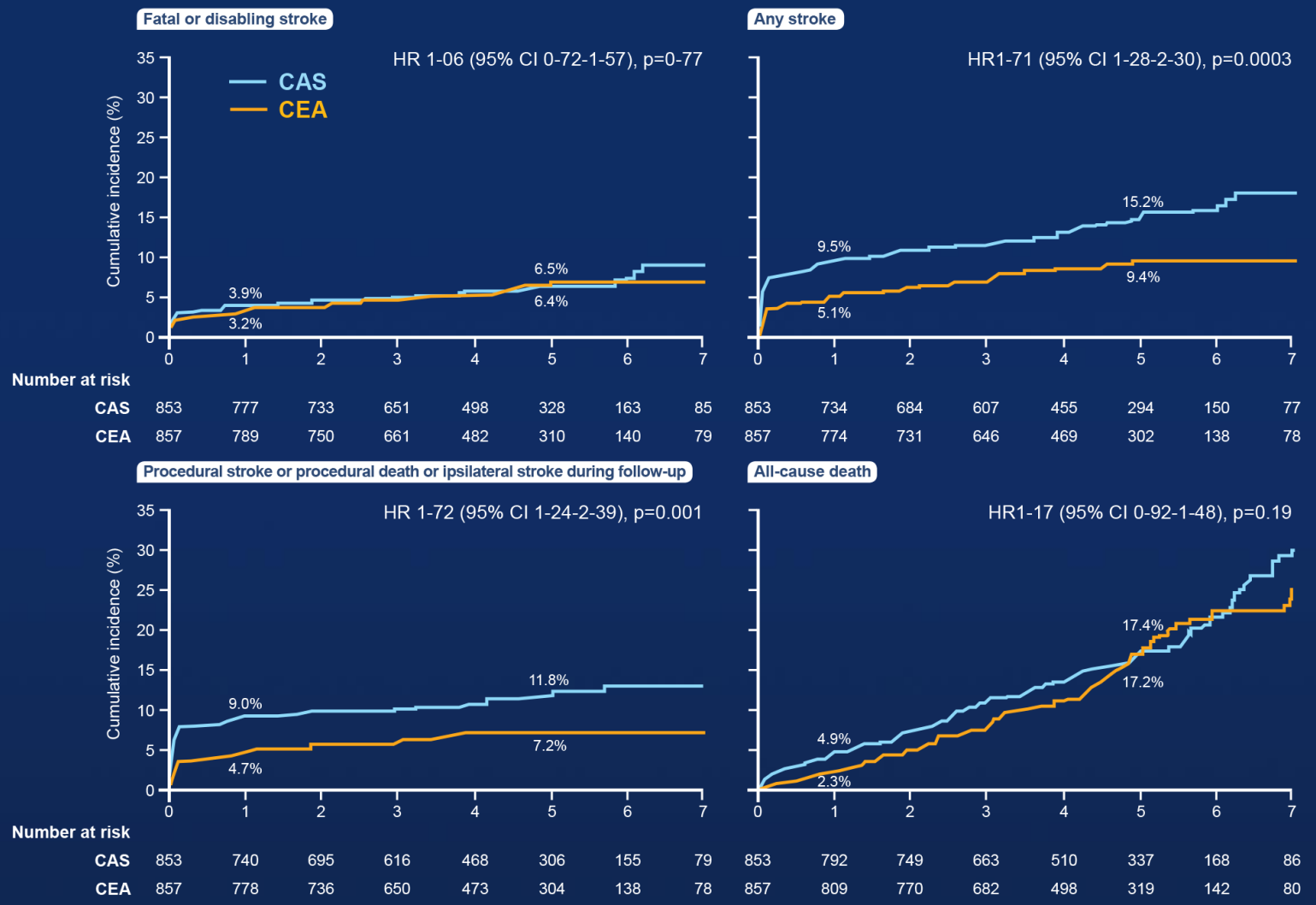
Safety Signal - Periprocedural Stroke or Death

Meta-Analysis of RCTs Comparing CEA and CAS



Ann Vasc Surg 2012;26:576-90

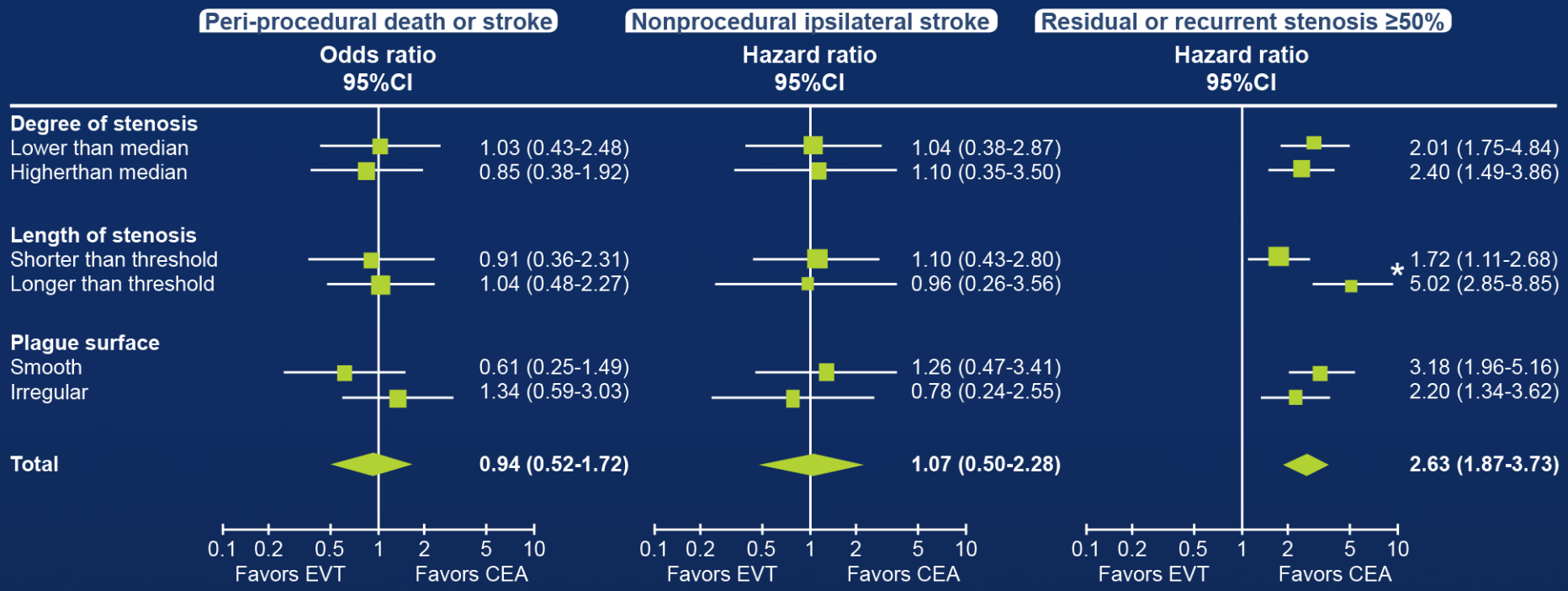
Long-term outcomes after stenting versus endarterectomy for treatment of symptomatic carotid stenosis: the International Carotid Stenting Study (ICSS) randomized trial



Lancet 2015; 385: 529–38

Length of carotid stenosis predicts peri-procedural stroke or death and restenosis

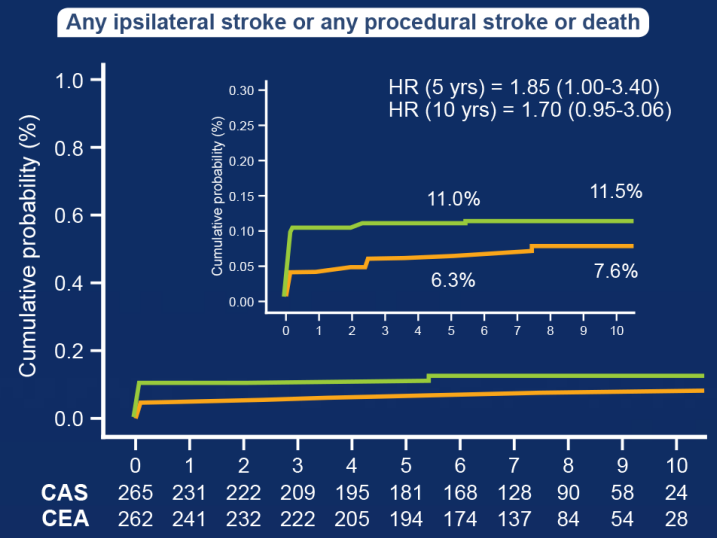
in patients randomized to endovascular treatment or endarterectomy

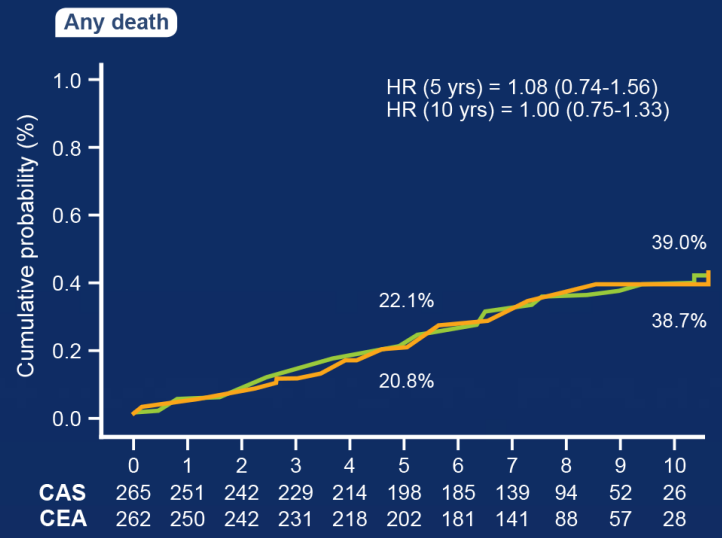


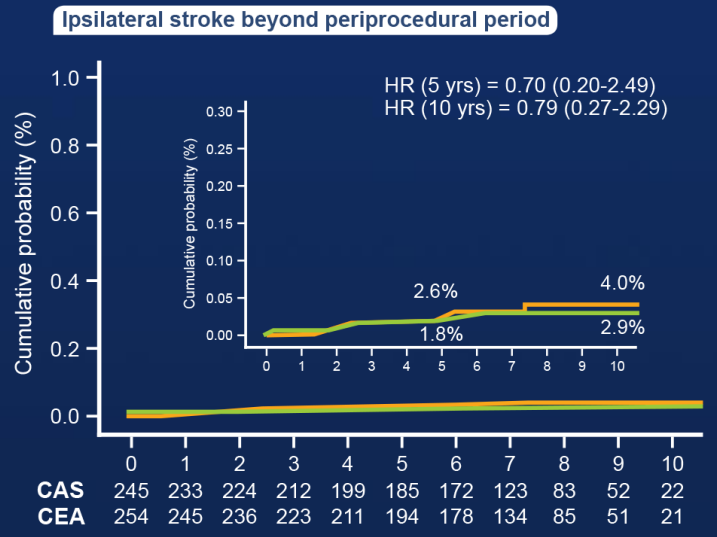
EVT, endovascular treatment; CEA, endarterectomy

Int J Stroke 2014 Apr;9(3):297-305

Endarterectomy Versus Angioplasty
in Patients With Symptomatic Severe Carotid Stenosis Trial (EVA3S)







Stroke. 2014;45:2750-2756

Carotid Stent

Carotid Stent Design

We need to make the first 30 days safer

- CAS related neurologic events are mutlifactorial

  - Arch and great vessel anatomy
  - Lesion morphology
  - Operator experience
  - Quality of embolic protection
  - Carotid stent attributes

Carotid Stent Design

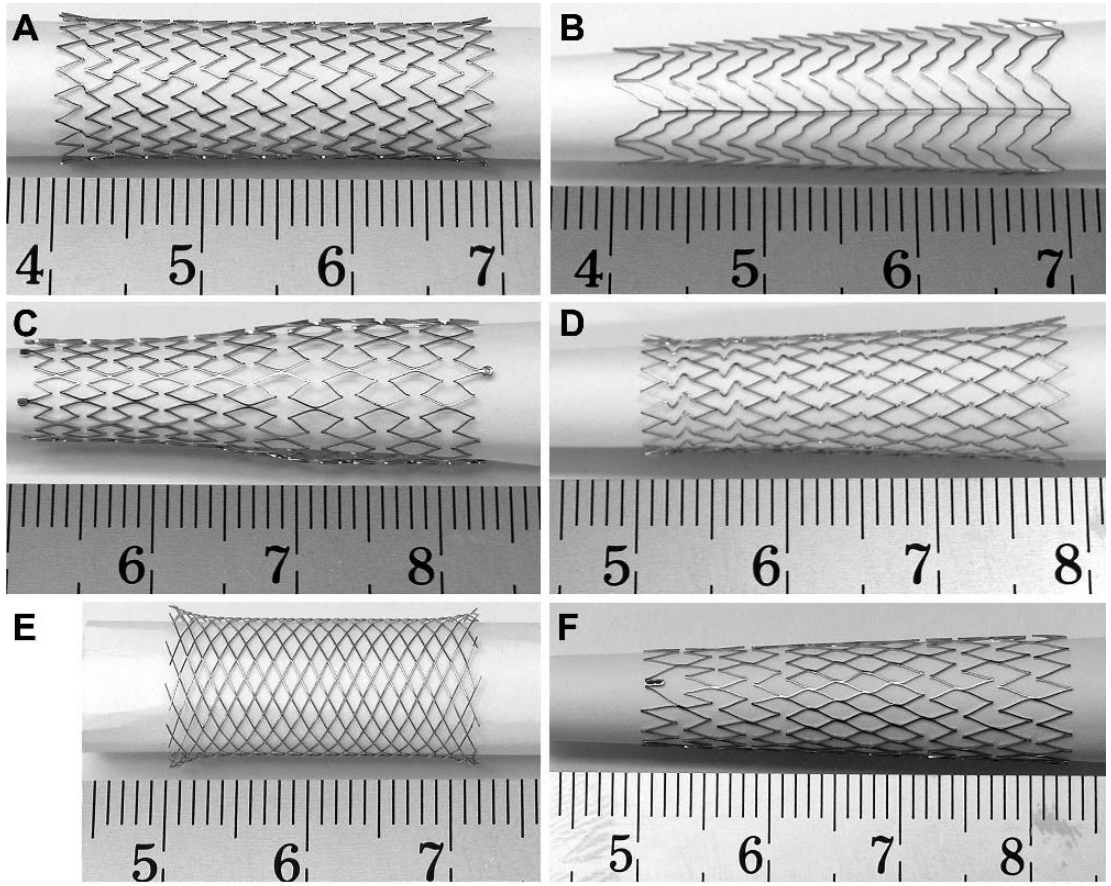


Figure 1 ◆ (**A**) Precise, (**B**) Acculink, (**C**) Protégé, (**D**) Xact, (**E**) Wallstent, and (**F**) Cristallo Ideale.

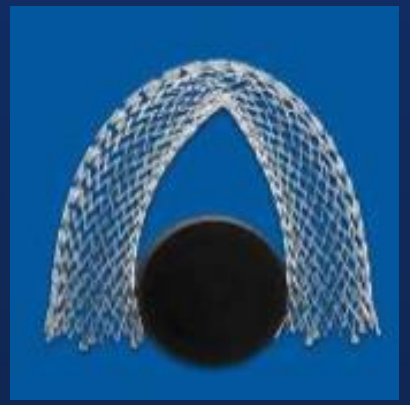
J Endovasc Ther 2009;16:168

What is the impact of the stent design?

PROTÉGÉ® RX
Carotid Stent (ev3)

WallStent
(Boston Scientific)

XACT
(Abbott)



SMART (Cordis)

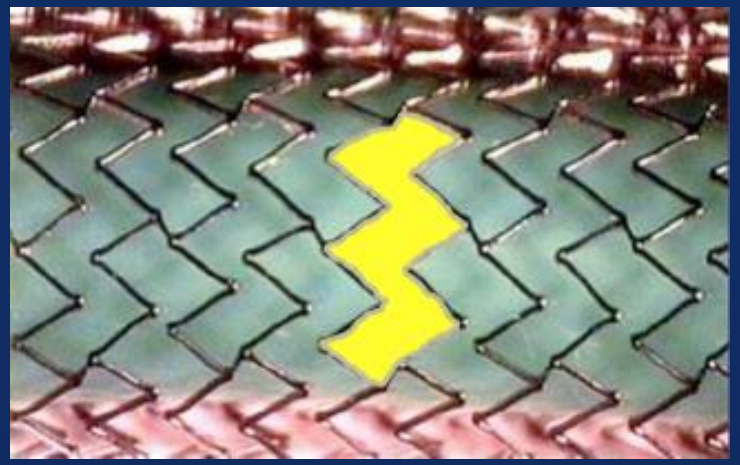
ACCULINK
(Abbott)

Closed vs. Open Cell Stenting

Closed Cell Stent

- Vessel wall scaffolding
- Plaque stabilization

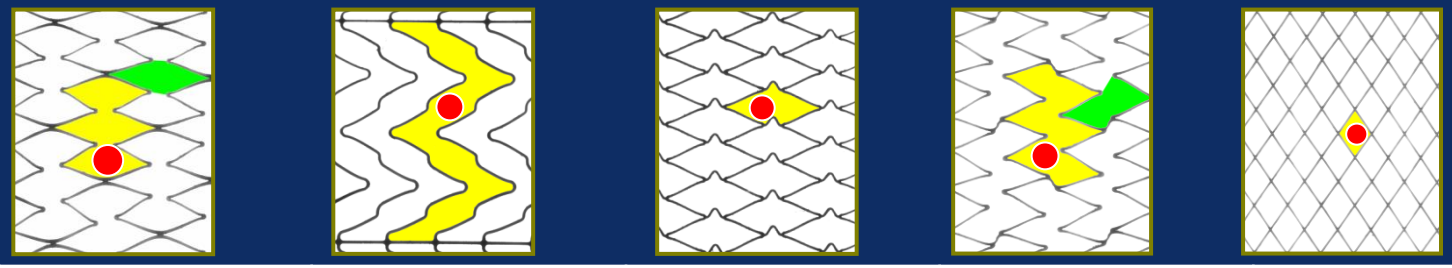
Open Cell Stent



- Flexibility
- Conformable to vessel anatomy

Carotid Stent Design

Proximal



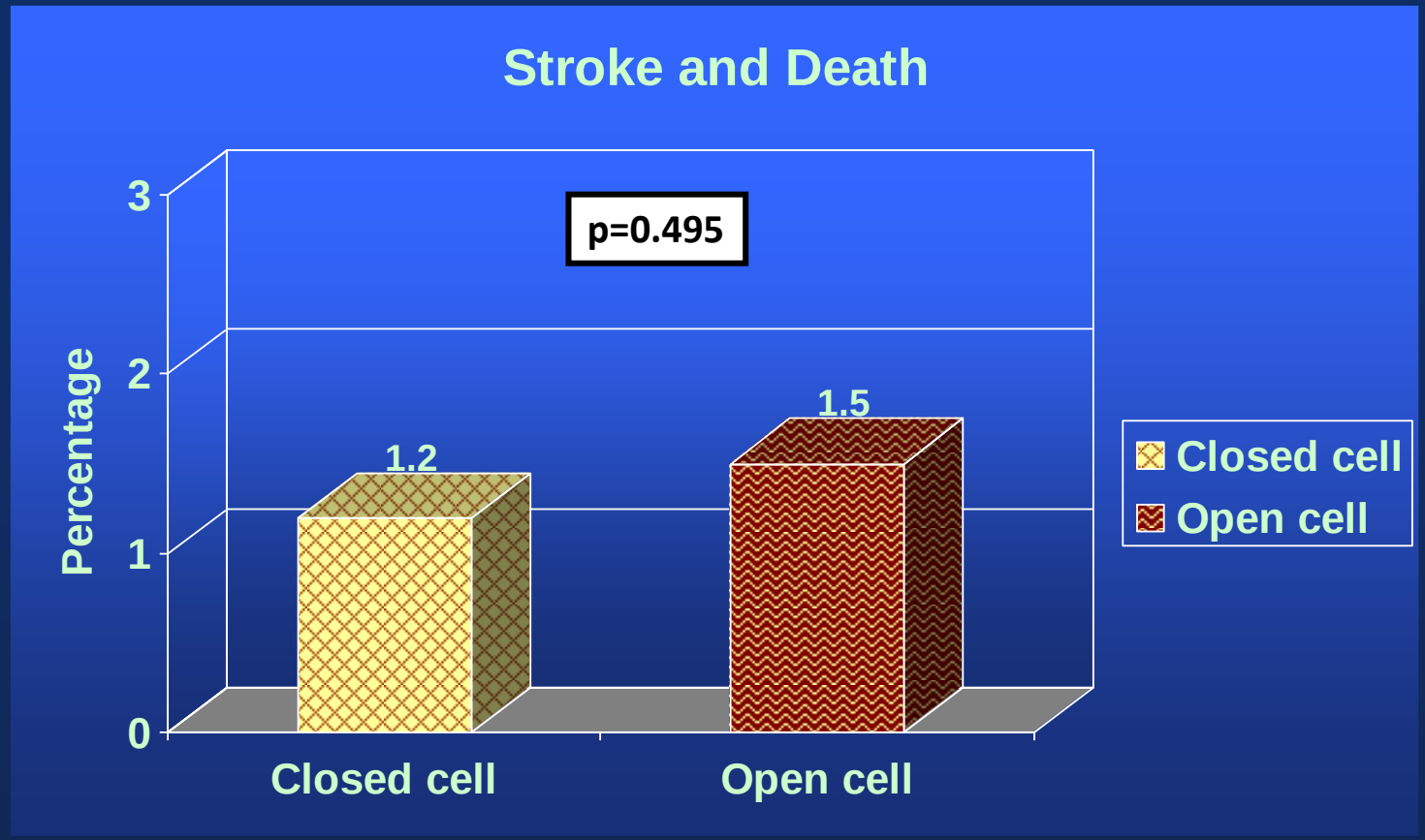
	PROTÉGÉ® RX (Tapered, 8-6mm)	RX ACCULINK™ (Tapered, 8-6 mm)	Xact® (Tapered, 8-6mm)	PRECISE® (Straight, 8 mm)	WALLSTENT® (Straight, 8 mm)
Pore Diam. (mm)	1.12	1.10	1.00	1.12	0.92
Pore Size (mm2)	**2.65**	**12.50**	**3.46**	**2.43**	**0.948**
Cell Area (mm2)	**7.19**	**12.50**	**3.46**	**7.39**	**0.948**

Distal

	PROTÉGÉ® RX (Tapered, 8-6 mm)	RX ACCULINK™ (Tapered, 8-6mm)	Xact® (Tapered, 8-6mm)	PRECISE® (Straight, 8 mm)	WALLSTENT® (Straight, 8 mm)
Pore Diam. (mm)	1.08	1.06	0.96	1.12	0.92
Pore Size (mm2)	**1.80**	**10.78**	**2.23**	**2.43**	**0.948**
Cell Area (mm2)	**4.48**	**10.78**	**2.23**	**7.39**	**0.948**

Bersin TCT 2008

30-Day Stroke (As Defined By the Authors) / Death Rates (no TIAs)



Difference: 0.3% (95% CI–0.5% to 1.4%, p=0.495)

Eur J Vasc Endovasc Surg 2007;33:135e–141

Increased in Neurologic Events With Open Cell Stents

SPACE Trial

Influence of Different Stent Types on OE Rate

Stent	Wallstent	Acculink	Precise
No. of patients	436	92	35
Pat. with OE	24	9	5
OE rate (95% CI)	5.5%(3.6-8.1%)	9.8%(4.6-17.8%)	14.3%(4.8-30.3%)

Combined OE rate: 11.0%(6.2-17.8%)

Stroke 2009;40:841

Increased in Delayed Neurologic Events With Open Cell Stents (1-30 days)

	Total population		
	Patients	All events	Post-procedural events
Open cell	937	39	32
Closed cell	2242	51	29
Total	3179	90	61
Open cell		4.2%	3.4%
Closed cell		2.3%	1.3%
Total	3179	2.8%	1.9%

Eur J Vasc Endovasc Surg 2007;33:135

Increase in Neurologic Events With Open Cell Stents

Symptomatic patients

P-values for the test that event rates differ between stents

Population	Outcome	p-value
Total	All events	0.018
	Post-procedural events	0.002
Symptomatic	All events	0.006
	Post-procedural events	<0.0001
Asymptomatic	All events	0.248
	Post-procedural events	0.790

Eur J Vasc Endovasc Surg 2007;33:135

Stent Design Trumps Embolic Protection

30-Day Follow-Up	Protection Device (n = 145)	No Protection Device (n = 418)	P value
Ipsilateral Stroke or Death	8.3 %	6.5 %	0.40
Disabling Stroke or Death	5.5 %	4.5 %	0.64

30-Day Follow-Up	Closed-cell Stent (n = 436)	Open-cell Stent (n = 127)	P value
Ipsilateral Stroke or Death	5.6 %	11.0 % (OR 2.13; 95% CI, 1.07-3.76)	0.029
Disabling Stroke or Death	5.5 %	4.5 %	0.64

*** Closed-cell stent: the Wall stent (Boston Scientific)**
Open-cell stent: Precise (Cordis) / Acculink (Guidant)

Stroke. 2009;40:841-846

CAS Outcomes Tied To . . .

ANATOMY

- Difficult Arch
- CCA/ICA Tortuosity
- Lesion anatomy

PATIENT

- Symptoms
- Octogenarians
- Cerebral Reserve

OPERATOR

- Early learning curve
- Case selection
- Stubborn persistence

DEVICE SELECTION TECHNIQUE

- Embolic Protection
- Stent design
- Cerebral protection

CAS Benefits Persisting at 5 Years

Single-center study of 2,202 carotid revascularization in either > 60% symptomatic or >70% asymptomatic

	CAS (n = 1,084)	CEA (n = 1,118)	*P Value*
30-Day Stroke or Death	2.8 %	2.0 %	0.27
30-Day Stroke/Death and 5-year ipsilateral Stroke	3.7%	4.7 %	0.4
Recurrent Stenosis (5-year)	3.4 %	5.8 %	0.7
Death (5-year)	18.0 %	12.3 %	0.05

J Am Coll Cardiol 2011;57:664-671

Intensive Medical Therapy

CEA versus Medical Therapy

Trial	N	Stenosis	Follow-Up	End POINT	Medical (%)	CEA (%)	p	RRR (%)	ARR (%)	NNT
Symptomatic										
ECST(38)	3,018	≥80%	3 yrs	Major stroke or death	26.5	14.9	<0.001	44	11.6	8.6
NASCET(18)	659	≥70%	2 yrs	Ipsilateral stroke	26	9	<0.001	65	17	5.9
VA 309(148)	189	>50%	1 yr	Ipsilateral stroke or TIA or surgical death	19.4	7.7	0.011	60	11.7	8.5
NASCET(19)	858	50-69%	5 yrs	Ipsilateral stroke	22.2	15.7	0.045	29	6.5	15.4
NASCET(19)	1,368	≤50%	5 yrs	Ipsilateral stroke	18.7	14.9	0.16	20	3.8	26.3
Asymptomatic										
ACAS(22)	1,662	>60%	5 yrs	Ipsilateral stroke, surgical death	11	5.1	0.004	54	5.9	16.9
ACST(23)	3,120	≥60%	5 yrs	Any stroke	11.8	6.4	0.0001	46	5.4	18.5
VA(149)	444	≥50%	4 yrs	Ipsilateral stroke	9.4	4.7	<0.06	50	4.7	21.3

CEA was significantly superior to Medical therapy, irrespective of symptom

ACCF/SCAI/SVMB/SIR/ASITN 2007 Clinical Expert Consensus Document on Carotid Stenting J Am Coll Cardiol 2007;49:126–70

RCT's: CAS vs. OMT

Symptomatic High-risk None	Asymptomatic High-risk None
Symptomatic Standard-risk None	Asymptomatic Standard-risk None

In absence of "head to head" trials vs. OMT, can only infer ability of CAS to prevent stroke based on:

a) registry studies of CAS

b) RCT's comparing it to CEA

Intensive Medical Therapy

Contemporary Results of Carotid Endarterectomy for Asymptomatic Carotid Stenosis

- CEA for asymptomatic stenosis from the 2005,2006, and 2007 NSQIP database
- 5,009 CEA for asymptomatic patients
- 5-Year stroke risk after CEA : 3.8% (ACST : Asymptomatic Carotid Surgery Trial)

  Average annual risk is 1%
- 0.8% for best medical management from the SMART : Second Manifestations of Arterial Disease Study trial
- → Stroke rates with CEA and best medical management for asymptomatic stenosis is similar

Stroke 2010;41(5):975-9

Intensive Medical Therapy

Effects of Intensive Medical Therapy on Micro-emboli and Cardiovascular Risk in Asymptomatic Carotid Stenosis

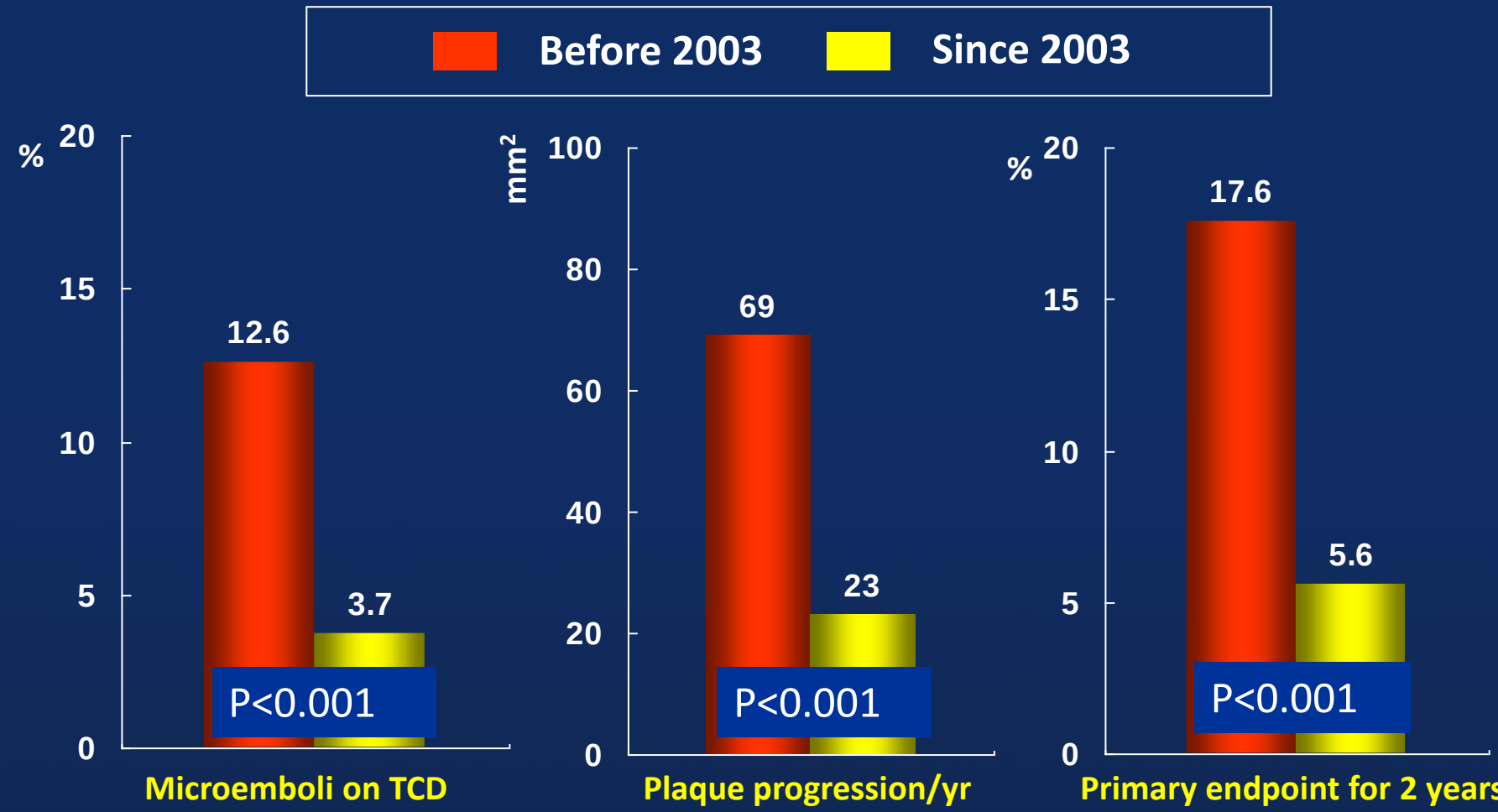
- Asymptomatic carotid stenosis (>60%)
- 199 patients, between Jan 2000 and Dec 2002
- 269 patients, between Jan 2003 and July 2007

  (Intensive medical therapy)
- Outcome values

  1. Micro-emboli on TCD
  2. cardiovascular events
  3. rate of plaque progression
  4. baseline medical therapy, before and since 2003

Arch Neurol. 2010;67(2):180-186

Clinical Outcomes

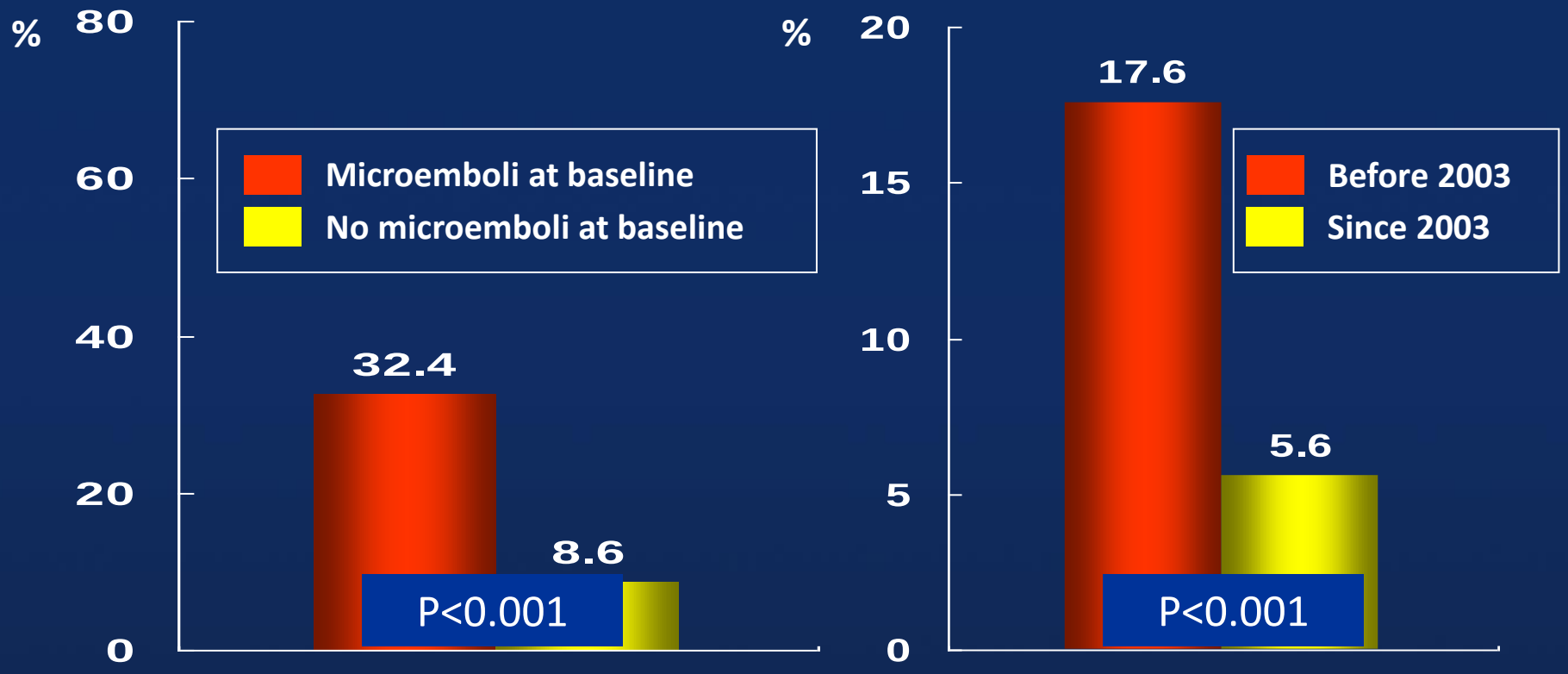


Primary endpoint: stroke, death, MI, or carotid endarterectomy upon symptom development

Arch Neurol. 2010;67(2):180-186

Clinical Outcomes for 2 years

Primary endpoint: stroke, death, MI, or carotid endarterectomy upon symptom development



- Less than 5% of Asymptomatic Carotid Stenosis patients can benefit from revascularization
- Only those with microemboli should be considered for endarterectomy or stenting

Arch Neurol. 2010;67(2):180-186

Medical Therapy for Carotid Artery Stenosis

- ASA 81 mg/d
  - No role for dual antiplatelet therapy for stroke prevention
- Antihypertensive Therapy
  - Angiotensin Converting Enzyme Inhibitor
  - Angiotensin Receptor Antagonist
- Lipid Lowering Therapy
  - LDL-Cholesterol <100 mg/dL
- Tobacco Cessation
- Glycemic Control (HbA1C <7.0%)

2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline
J Am Coll Cardiol 2011 Feb 22;57(8):1002-44

Optimal Medical Management of Asymptomatic Carotid Artery Stenosis

- Antithrombotic Therapy
  - ASA 75 – 325 mg/d
  - ASA + rivaroxaban 2.5mg bid
  - Clopidogrel 75mg OD or ticagrelor 90mg BID (if ASA-intolerant or allergic to ASA)

- Antihypertensive Therapy
  - Goal BP < 130/80
  - Prefer ACE inhibitor/ARB due to high prevalence of renovascular hypertension
  - May require combination therapy

- Glucose-lowering therapy
  - Goal HbA1c <7.0%
  - Metformin, GLP-1 agonist, SGLT-2 antagonist are preferred

Stroke, 2021;52:2191-2198

Optimal Medical Management of Asymptomatic Carotid Artery Stenosis

- Lipid Lowering Therapy
  - LDL-Cholesterol <70 mg/dL (<54mg/dL for very high risk
  - High dose statin
  - Add ezetimibe or Add PCSK9 inhibitor
  - Consider icosapent ethyl (high-dose EPA) for fasting triglyceride 1.52-5.63 mmol/L

- Mediterranean diet
- Exercise
  - Moderate intensity 4 to 7 days per week, for a total of at least 150 min per week
- Smoking Cessation

- Consider referral for carotid revascularization
  - TCD + for microemboli, plaque ulcer, reduced cerebrovascular reserve, intraplaque hemorrhage, silent embolic infarcts on CT/MRI, plaque echolucency, large JBA, progression in severerity of stenosis

Stroke, 2021;52:2191-2198

CEA vs. Intensive Medical Tx In Asymptomatic Stenosis

- Recently, intensive medical therapy may reduce event rate, compared with old, conventional medical therapy.
- The randomized, prospective trials comparing revascularization and best medical management for asymptomatic stenosis (SPACE 2, TACIT, ECST-2) will answer those issues

(TACIT : Transatlantic Asymptomatic Carotid Intervention Trial, optimal medical therapy alone, OMT plus stenting and OMT plus CEA in asymptomatic patients)

SPACE-2 Trial

- Prospective, randomized, controlled, multicenter trial
- Three parallel groups:
  Best medical treatment (BMT) (20%, n=540)
  CAS + BMT (40%, n=1550)
  CEA + BMT (40%, n=1550)
- About 100 certified centers
- N=3.640 patients with a follow-up of 5 years
  (duration 8-9 yrs)
- Funding by the German Ministry for Education and Research
  (BMBF, about € 4 Mi)

Int J Stroke. 2009;4(4):294-9

SPACE-2 Trial

- The three-arm study design was amended to become two parallel randomized studies (July 2013) because of slow patient recruitment
  - BMT alone vs. CEA plus BMT
  - BMT alone vs. CAS plus BMT

- Trial recruitment ceased after recruiting 513 patients over a 5 year period (2014) despite of the change in study design(2013)
  - CEA vs. BMT (n = 203); CAS vs. BMT (n = 197), and BMT alone (n = 113)
- Stroke and death rates (95% CI) within the first 30 days after undergoing CEA or CAS.

	CEA (*n* = 203)	CAS (*n* = 197)
Death within 30 days	0/203 (0%; 0.00–1.8%)	0/197 (0%; 0.00–1.86%)
Combined stroke and death rate within 30 days	4/203 (1.97%; 0.54%–4.97%)	5/197 (2.54; 0.83%–5.82%)

Eur J Vasc Endovasc Surg. 2016 51(6):761-5.

Medical Treatment for Asymptomatic Carotid Stenosis

Study	Reference	Patients	PSV	Details
SMART (>3000)	Goessens Stroke 2007	96 with ≥70% stenosis	150cm/s	Only 96 pts had PSV ≥210, 7% had carotid repair
OxVasc (>90,000)	Marquardt Stroke 2010	32 with ≥70%stenosis	150cm/s	Vascular death in 7.7%
ASED	Abbott Stroke 2005	202 with ≥50% stenosis	150cm/s	TCD

How To Treat Carotid Disease?

- **First and always….maximize medical therapy**
  - Antiplatelet Therapy
  - Antihypertensive Therapy
  - Lipid Lowering Therapy
  - Aggressive Glycemic Control

- **Revascularization**
  - Standard Risk Asymptomatic?
    - CEA = CAS (CREST)
  - High Risk Asymptomatic?
    - CEA ≤ CAS (SAPPHIRE)
  - Standard Risk Symptomatic?
    - CEA ≥ CAS (ICSS, CREST, EVA3S, SPACE1)
  - High Risk Symptomatic?
    - CEA ≥ CAS

Indications for carotid artery revascularization

Indication level	Symptomatic stenosis	Asymptomatic stenosis
Proven	• 70-99% stenosis • Peri-procedural complication risk <6%	• > 80% stenosis • Peri-procedural complication risk <3% • Life expectancy > 5yrs
Acceptable	• 50-69% stenosis • Peri-procedural complication risk <6%	• > 60% stenosis • Peri-procedural complication risk <3% • Planned CABG
Unacceptable	• <29% stenosis, or • Peri-procedural complication risk > 6%	• < 60% stenosis or • Peri-procedural complication risk >3% • No indication for CABG

Circulation 2006;113:2021-2030

Carotid Disease Guideline 2011

1. CAS is a safe and effective alternative to CEA in symptomatic patients with > 50% stenosis and low to average surgical risk.

2. Prophylactic CAS might be considered in highly selected patients with asymptomatic carotid stenosis (minimum 60% by angiography, 70% by validated Doppler ultrasound), but its effectiveness compared with medical therapy alone in this situation is not well established.

3. Selection of asymptomatic patients for carotid revascularization should be guided by an assessment of co-morbid conditions, life expectancy, and other individual factors and should include a thorough discussion of the risks and benefits of the procedure with an understanding of patient preferences.

4. It is reasonable to choose CEA over CAS when revascularization is indicated in older patients, “particularly when arterial patho-anatomy is unfavorable for endovascular intervention.”

5. It is reasonable to choose CAS over CEA when revascularization is indicated in patients with neck anatomy unfavorable for surgery

2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline
J Am Coll Cardiol 2011 Feb 22;57(8):1002-44

Class I
(Benefit >>>Risk)

- **>70% stenosis by non-invasive testing or >50% by angiography**
  - Symptomatic
    - TIA or CVA within 6 months should undergo CEA

      If at low risk for endovascular intervention CAS can be an alternative to CEA
  - Asymptomatic
    - Should be guided by assessment of comorbid conditions, life expectancy and individual risk vs. benefit

Class IIa
(Benefit >>Risk)

- **>70% stenosis of ICA and asymptomatic**
  - CEA→ low risk for perioperative CVA, MI or death
  - CEA over CAS→ Poor arterial pathoanatomy for endovascular intervention
  - CAS over CEA→ neck anatomy unfavorable for surgery

- **>70% stenosis of ICA and TIA/CVA within 2 weeks**
  - Favors early revascularization if no contraindications (CEA or CAS)

Class IIb
(Benefit = Risk)

- **>70% by Doppler or >60% stenosis by angiography**
  - Prophylactic CAS
  - CEA or CAS in asymptomatic or symptomatic patients at high risk of complications for revascularization
    - Effective is not well established (vs. medical therapy)

Class III
(No Benefit)

- **<50% stenosis**
  - Revascularization not recommended
  - Medical Therapy
  - Risk Factor Modification
  - Annual Evaluation

- **Chronic Total Occlusion (CTO)**
  - Revascularization not recommended

- **Severe Disability Cause by CVA**
  - Revascularization not recommended