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Essentials of Carotid Artery Disease

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Disclosure Statement of Financial Interest

I, Jose M. Wiley, MD DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.



Outline

1. Anatomy
2. Presentation
3. Evaluation
4. Treatment
 - Medical Rx
 - Revascularization
5. Unusual causes of carotid disease



AHA/ASA Guideline

Guidelines for the Prevention of Stroke in Patients With Stroke or Transient Ischemic Attack

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

The American Association of Neurological Surgeons and Congress of Neurological Surgeons have reviewed this document and affirm its educational content.

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Deidre Wentworth, MSN, RN; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Clinical Cardiology, and Interdisciplinary Council on Quality of Care and Outcomes Research

Abstract—The aim of this updated statement is to provide comprehensive and timely evidence-based recommendations on the prevention of ischemic stroke among survivors of ischemic stroke or transient ischemic attack. Evidence-based recommendations are included for the control of risk factors, interventional approaches for atherosclerotic disease, antithrombotic treatments for cardioembolism, and the use of antiplatelet agents for noncardioembolic stroke. Further recommendations are provided for the prevention of recurrent stroke in a variety of other specific circumstances, including arterial dissections; patent foramen ovale; hyperhomocysteinemia; hypercoagulable states; sickle cell disease; cerebral venous sinus thrombosis; stroke among women, particularly with regard to pregnancy and the use of postmenopausal hormones; the use of anticoagulation after cerebral hemorrhage; and special approaches to the implementation of guidelines and their use in high-risk populations. (*Stroke*. 2011;42:227-276.)

Key Words: AHA Scientific Statements ■ ischemia ■ transient ischemic attack ■ stroke ■ stroke prevention

ACCF/SCAI/SVMB/SIR/ASITN CLINICAL EXPERT CONSENSUS DOCUMENT

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

A Report of the American College of Cardiology Foundation Task Force
on Clinical Expert Consensus Documents (ACCF/SCAI/SVMB/SIR/ASITN
Clinical Expert Consensus Document Committee on Carotid Stenting)

*Developed in Collaboration With the American Society of Interventional & Therapeutic
Neuroradiology, Society for Cardiovascular Angiography and Interventions, Society for Vascular
Medicine and Biology, and Society of Interventional Radiology*

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2. Presentation

3. Evaluation

4. Treatment

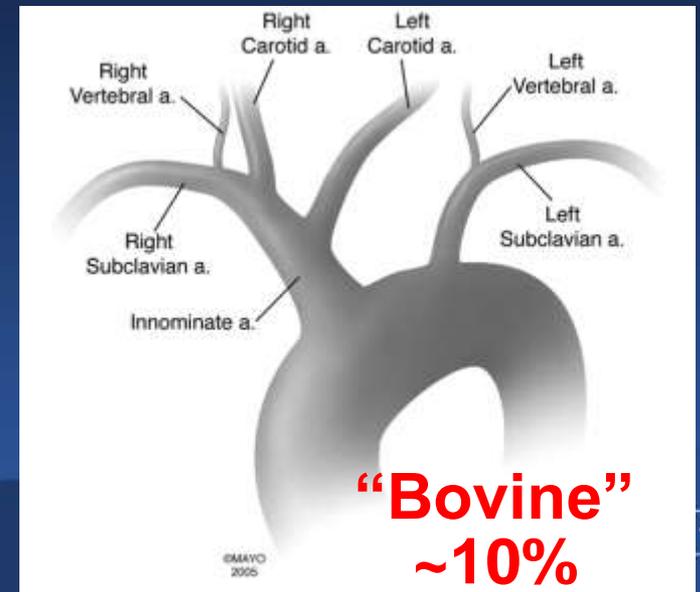
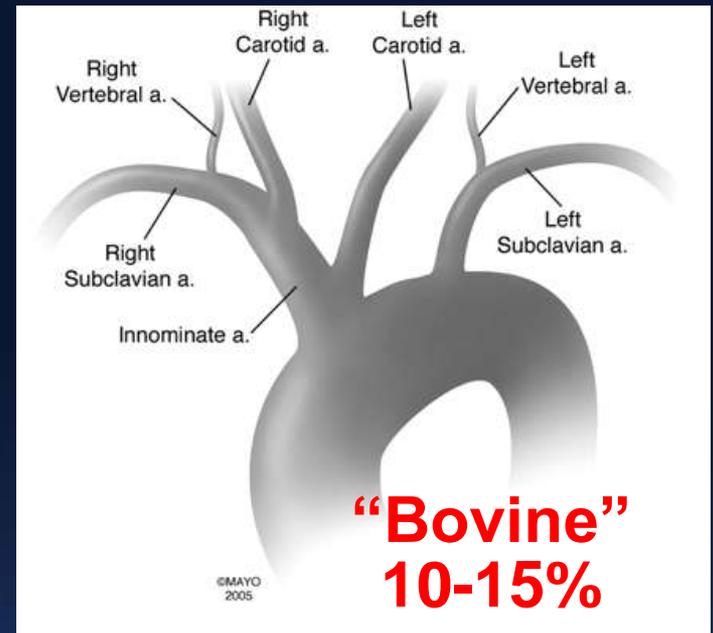
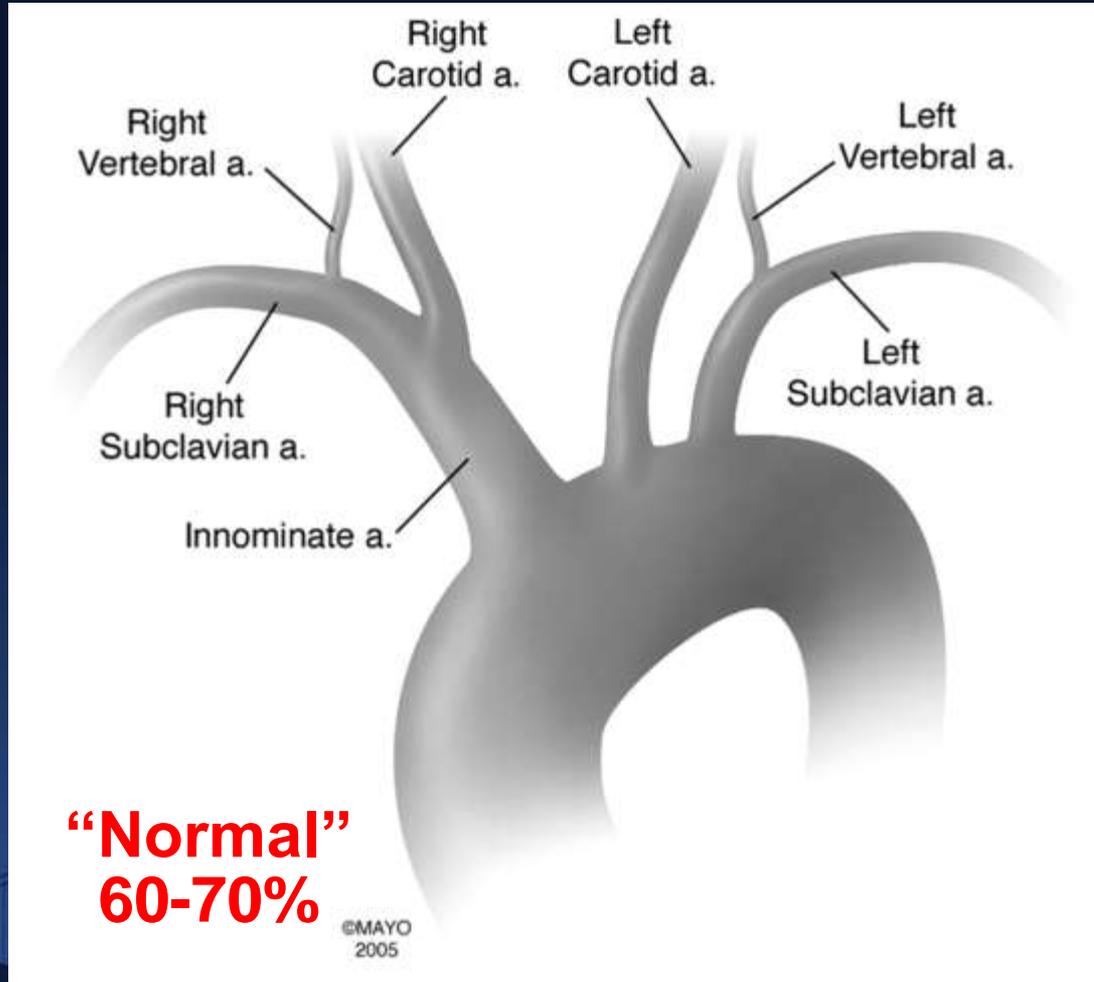
Medical Rx

Revascularization

5. Unusual causes of carotid disease

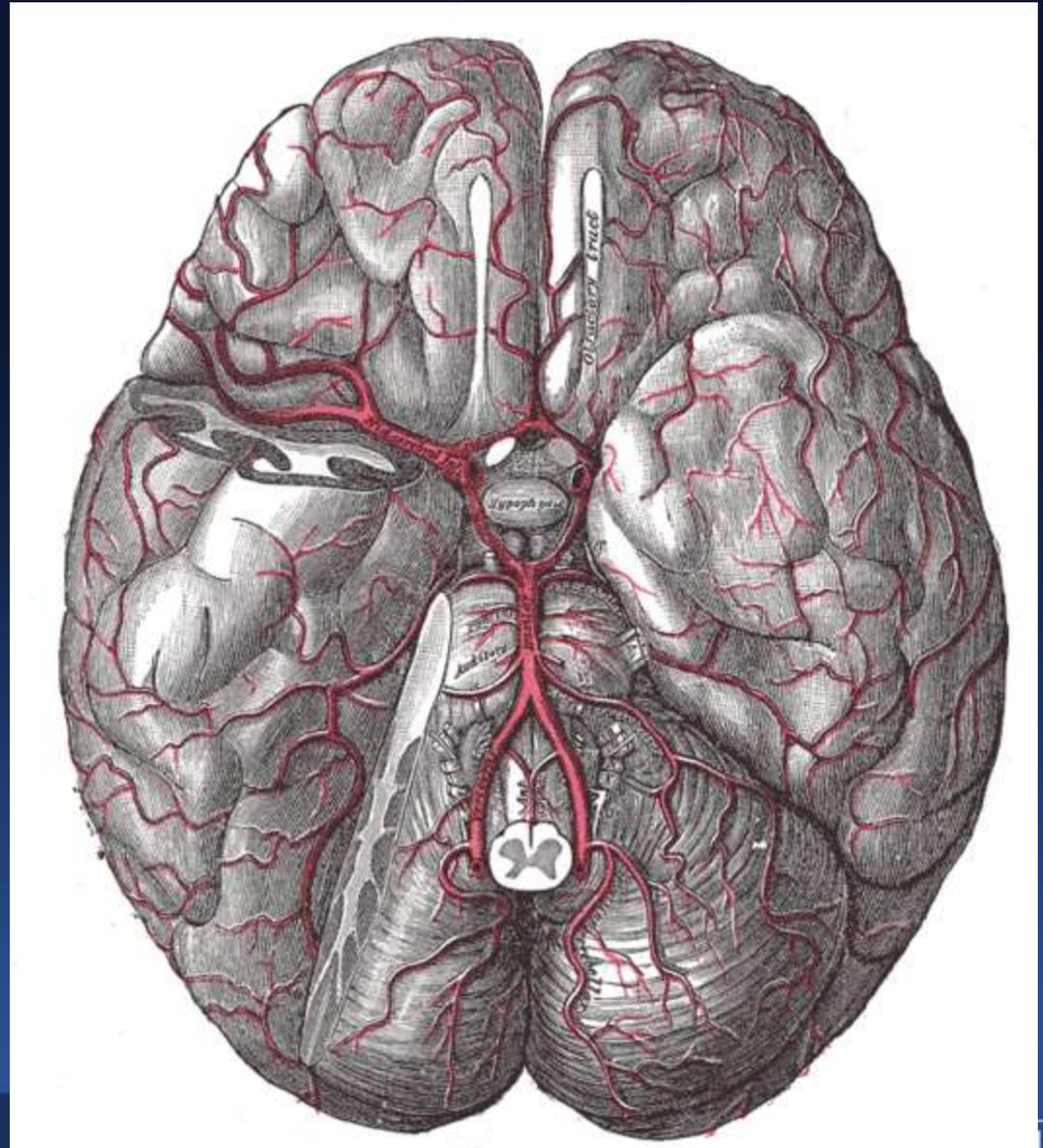
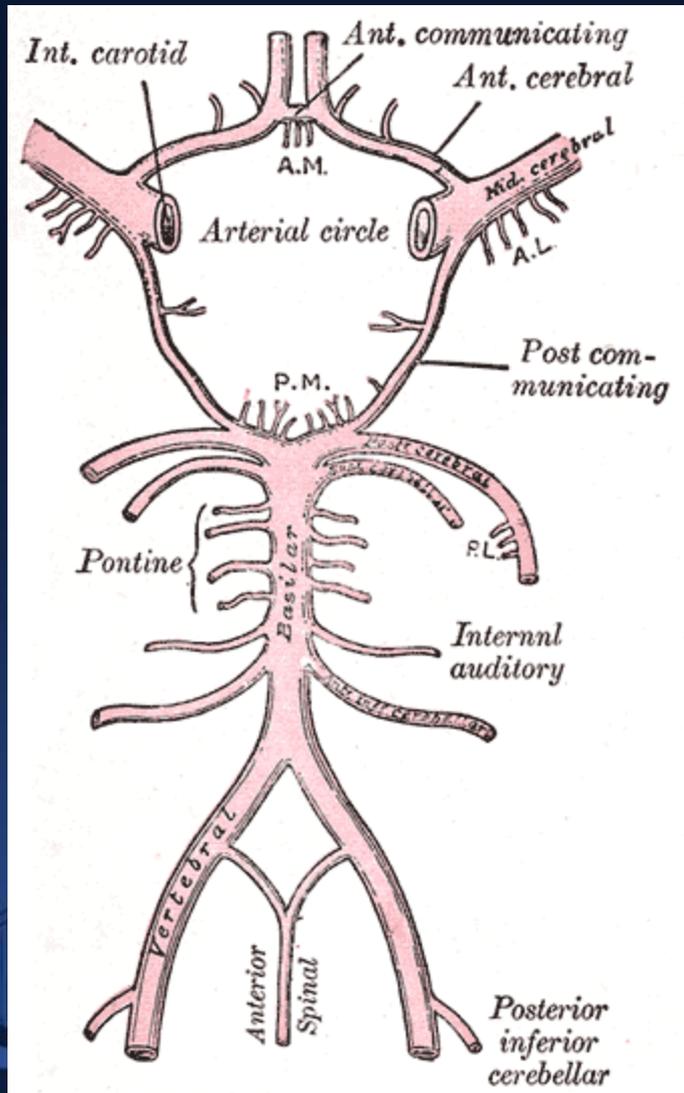


1. Anatomy



Layton: AJNR 2006

Extracranial and Intracranial Circulation



Outline

1. Anatomy

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Stroke Mechanism

Ischemic (83%)

Hemorrhagic (17%)

Intracerebral (59%)

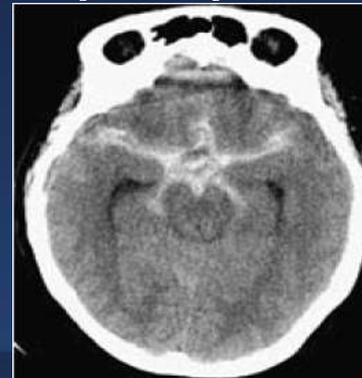
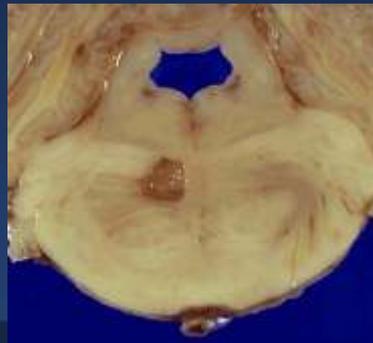
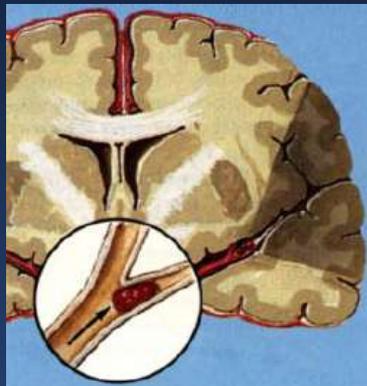
Atherosclerotic cerebrovascular disease (20%)

Cryptogenic (30%)

Embolism (20%)

Lacunar (25%)

Subarachnoid hemorrhage (41%)



Carotid Disease: Presentation

Retinal syndromes

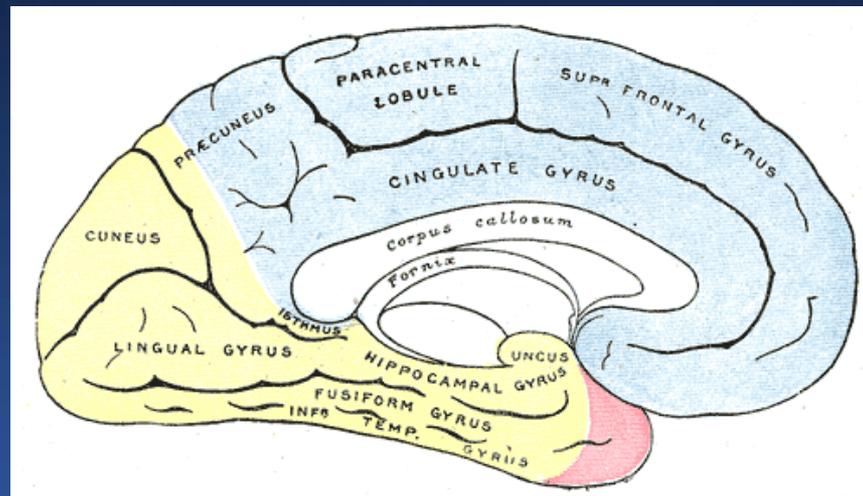
1. Amaurosis fugax

2. Retinal infarction

Hemispheric symptoms

1. TIA

2. Stroke



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Physical Examination

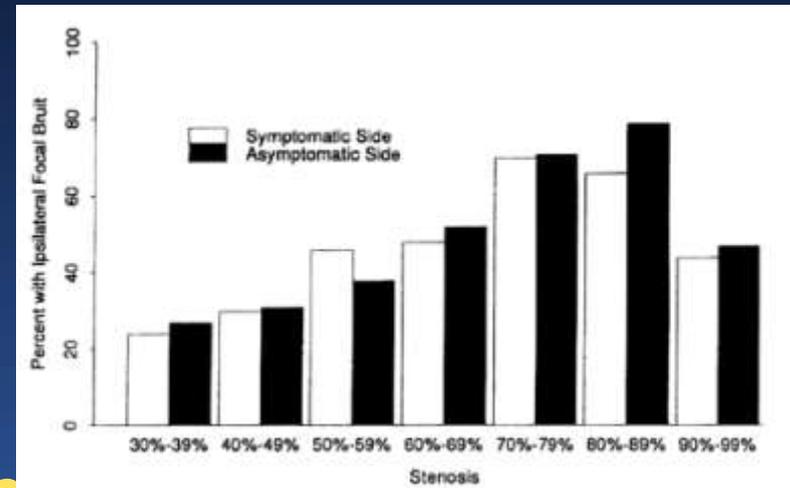
1. Fundoscopy

?retinal embolization



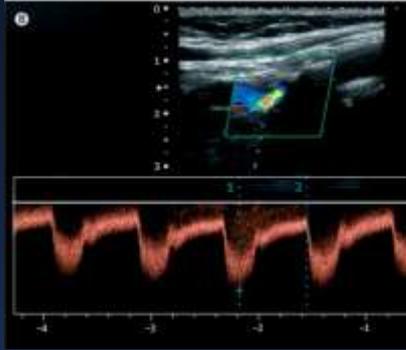
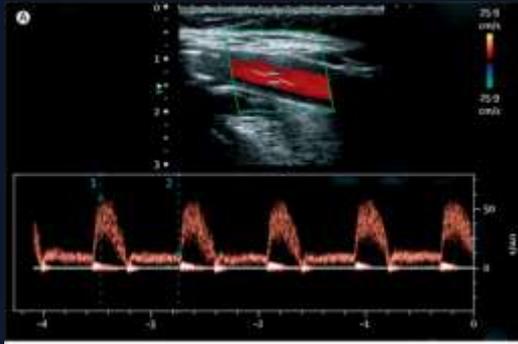
2. Neck auscultation

Carotid bruit: 63% sensitivity,
61% specificity for high-grade
stenosis



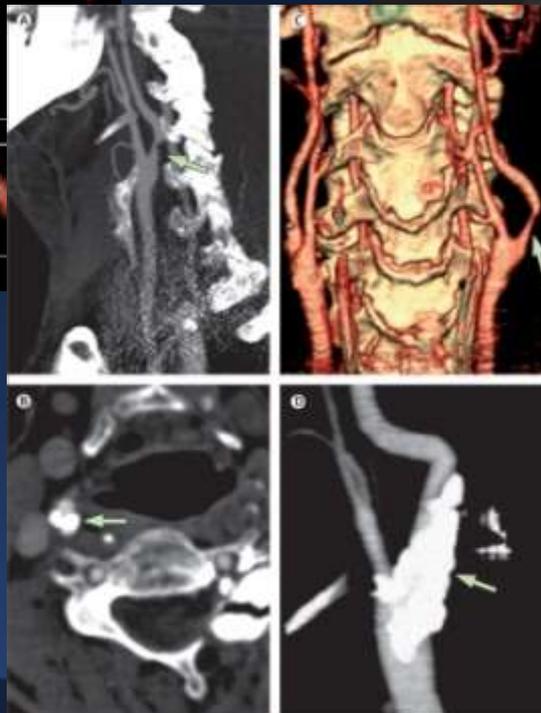
3. Neurologic evaluation

DUS - CTA - MRA Angiography



MRA

Invasive
Angiography



CTA

Duplex US



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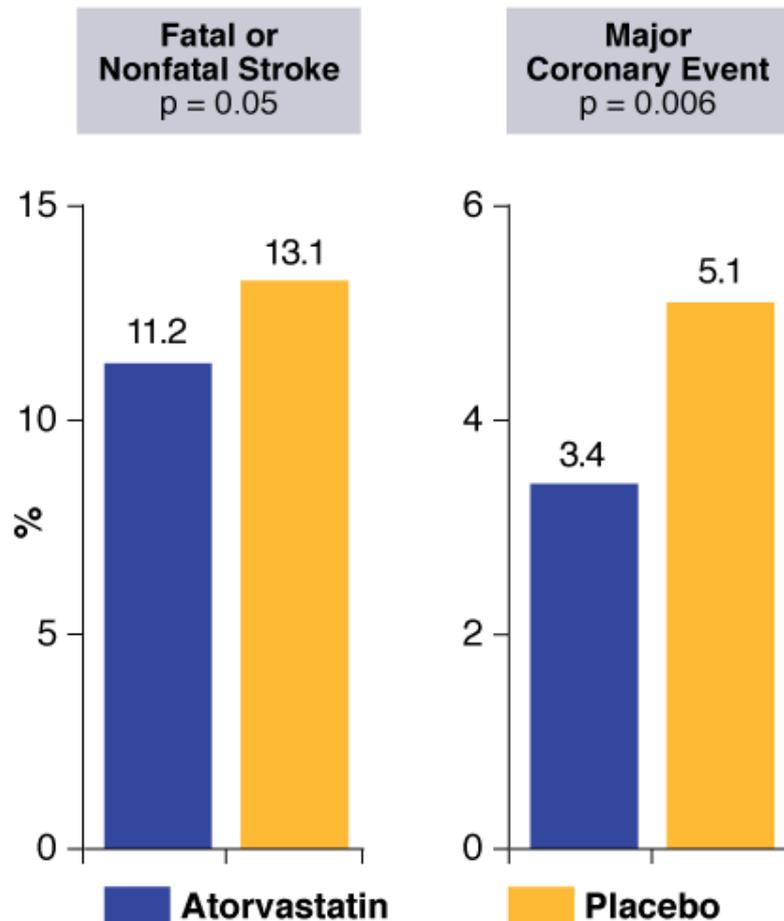
Medical Rx to Prevent Stroke

- Hypertension control
- Cessation of Tobacco Use
- ? Diabetes control
- Reduction in Serum Cholesterol
- Antiplatelet Therapy



SPARCL

Trial Design: SPARCL was a randomized, double-blind trial of atorvastatin (80 mg daily, n=2365) or placebo (n=2366) in patients with prior stroke or TIA. Primary endpoint was fatal or nonfatal stroke at a median follow-up of 4.9 years.



Results

- At 1 month, LDL levels ↓ from 133 mg/dl at baseline to 61.3 mg/dl in atorvastatin group ($p < 0.0001$) but no change in placebo group (133.5 mg/dl)
- Primary endpoint of stroke ↓ in atorvastatin group vs placebo (Figure)
- Reductions in 2° endpoints of TIA (6.5% vs 8.8%, $p = 0.004$), major coronary event (Figure), major CV event (14.1% vs 17.2%, $p = 0.005$) also ↓ for atorvastatin
- No difference in mortality (9.1% for atorvastatin vs 8.9% for placebo, $p = 0.77$)
- Persistent ALT/AST elevations ↑ in atorvastatin group (2.2% vs 0.5%, $p < 0.001$)

Conclusions

- Among patients with prior stroke or TIA, treatment with atorvastatin was associated with reduction in recurrent stroke compared with placebo, as well as reductions in major coronary events
- Prior studies such as 4S, CARE, and CARDS showed ↓ coronary events with statin in patients with coronary heart disease
- Present trial extends findings to setting of cerebrovascular disease

2011 Stroke Guidelines

1. Treatment with a statin medication is recommended for all patients with extracranial carotid or vertebral atherosclerosis to reduce low-density lipoprotein (LDL) cholesterol below 100 mg/dL (**Class I, LOE B**)
2. Treatment with a statin medication is reasonable for all patients with extracranial carotid or vertebral atherosclerosis who sustain ischemic stroke to reduce LDL-cholesterol to a level near or below 70 mg/dL (**IIA, LOE B**)



Antiplatelet Rx for Stroke Prevention Synopsis

- 1996 **CAPRIE:** Clopidogrel > ASA alone
- 1996 **ESPS 2:** ASA + ER-DP > ASA alone
- 2004 **MATCH:** Clopidogrel alone > Clopidogrel + ASA
- 2006 **ESPRIT:** ASA + ER-DP > ASA alone
- 2006 **CHARISMA:** Clopidogrel + ASA = ASA alone
- 2008 **PRoFESS:** Clopidogrel = ASA + ER-DP

CONCLUSIONS

(Clopidogrel = ASA + ER-DP) > ASA alone

\$136/m

\$162/m

\$4/m

QD

BID - Headache

QD

TCTT2011

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Carotid Endarterectomy

RISKS

Cardiovascular

Hypertension (20%)

Hypotension (5%)

Myocardial infarction (1%)

Wound

Infection (1%)

Hematoma (5%)

Neurological

Hyperperfusion syndrome

Intracerebral hemorrhage

Cranial nerve injury (7%)

Seizures

Stroke (2%–6%)

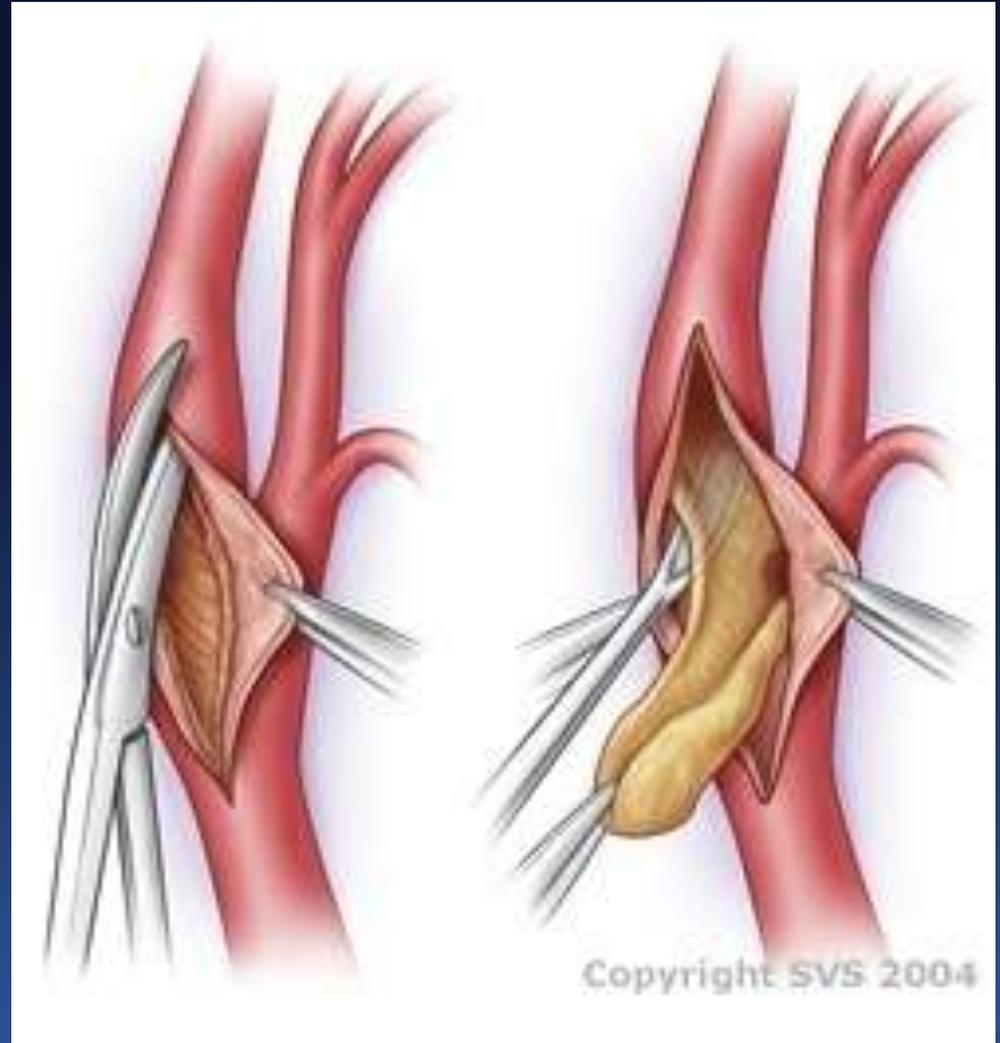
Carotid artery

Carotid artery thrombosis

Carotid artery dissection

Restenosis (5%–10%)

Death (1%)



RISKS

Carotid Stenting

Cardiovascular

Vasovagal reaction (5%–10%)

Vasodepressor reaction (5%–10%)

Myocardial infarction (1%)

Carotid artery

Dissection (<1%)

Thrombosis (<1%)

Perforation (<1%)

ECA stenosis or occlusion (5%–10%)

Transient vasospasm (10%–15%)

Restenosis (3%–5%)

Neurological

TIA (1%–2%)

Stroke (2%–3%)

Intracranial hemorrhage (<1%)

Hyperperfusion syndrome (<1%)

Seizures (<1%)

General

Access site injury (5%)

Blood transfusion (2%–3%)

Contrast nephropathy (2%)

Contrast reactions (1%)

Death (1%)



CEA vs. Medical Rx

Table 5. Randomized Trials of CEA Versus Medical Therapy for Carotid Artery Stenosis

Trial	N	Stenosis	Follow-Up	End Point	Medical (%)	CEA (%)	<i>p</i>	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

ACAS = Asymptomatic Carotid Atherosclerotic Study; ACST = Asymptomatic Carotid Surgery Trial; ARR = absolute risk reduction; CEA = carotid endarterectomy; ECST = European Carotid Surgery Trial; NASCET = North American Symptomatic Carotid Endarterectomy Trial; NNT = needed to treat; RRR = relative risk reduction; TIA = transient ischemic attack; VA = Veterans Affairs.



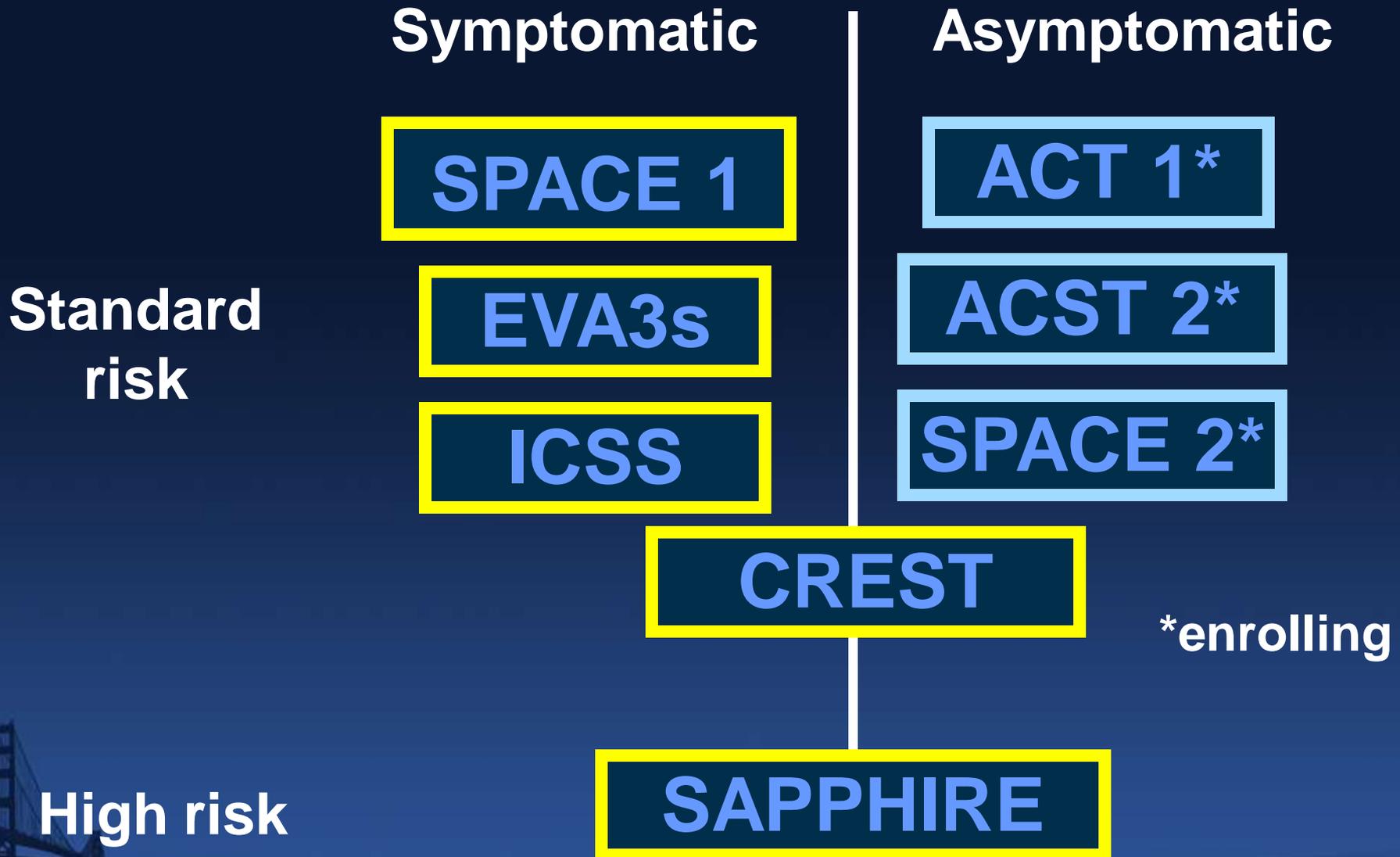
Table 6. Risk Reduction of Any Stroke or Operative Death at 5 Years After CEA in Symptomatic Patients From 3 Randomized Clinical Trials

Stenosis (%)	ARR (% , 95% CI)	<i>p</i>	RRR (95% CI)
Near-occlusion	−0.1 (−10.3 to 10.2)	0.6	0.98 (0.61 to 1.59)
70–99	15.6 (9.8 to 20.7)	0.00001	0.52 (0.40 to 0.64)
50–69	7.8 (3.1 to 12.5)	0.002	0.72 (0.58 to 0.86)
30–49	2.6 (−1.7 to 6.9)	0.7	0.90 (0.75 to 1.04)
<30	−2.6 (−6.2 to 0.9)	0.03	1.17 (0.90 to 1.43)

Modified with permission from Rothwell PM, Eliasziw M, Gutnikov SA, et al. Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. *Lancet* 2003;361:107–16 (87).

ARR = absolute risk reduction; CEA = carotid endarterectomy; CI = confidence interval; RRR = relative risk reduction.

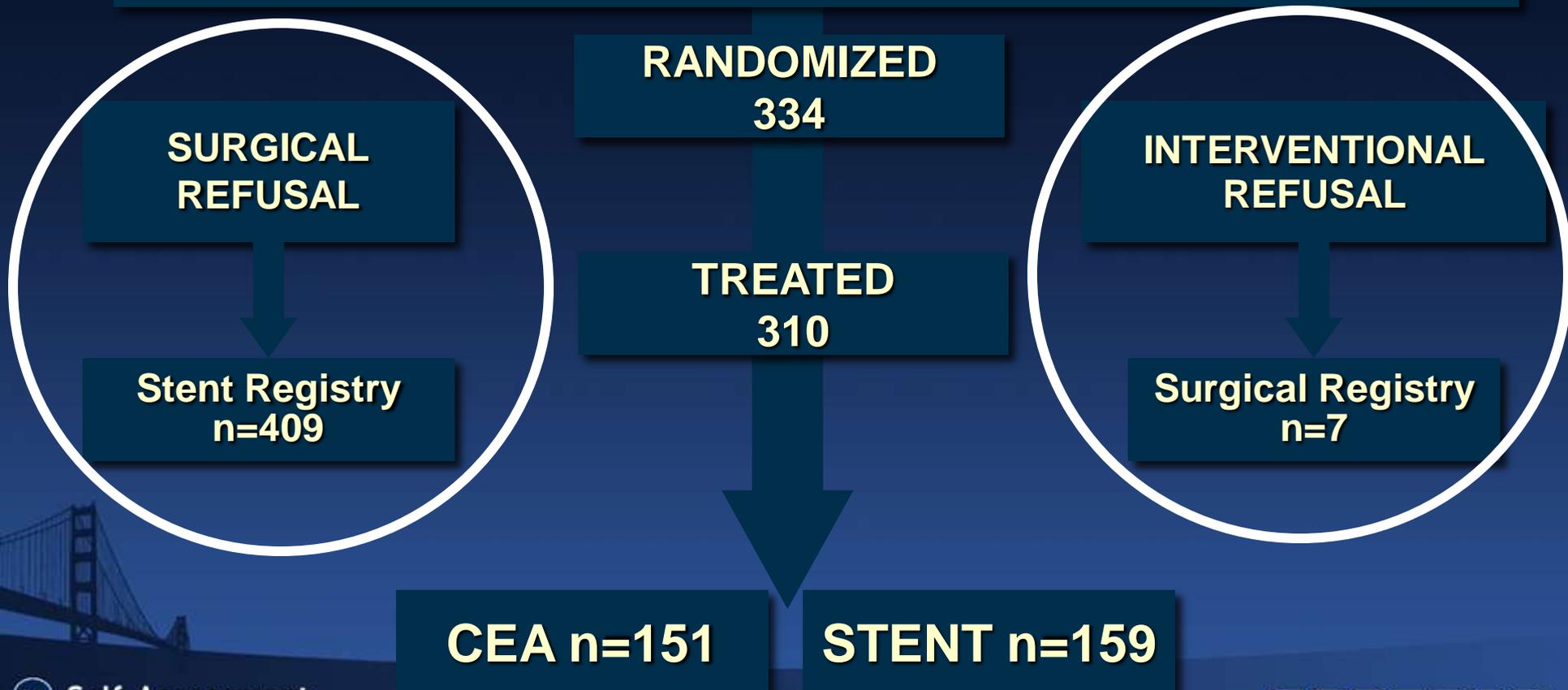
CAS vs. CEA Trials



SAPPHIRE

>50% Stenosis Sx (29%)
≥80% Stenosis Asx (71%)
≥1 Comorbid Conditions

Physician Team: Neurologist, Surgeon, Interventionalist
CONSENSUS: 747 pts enrolled



CEA n=151

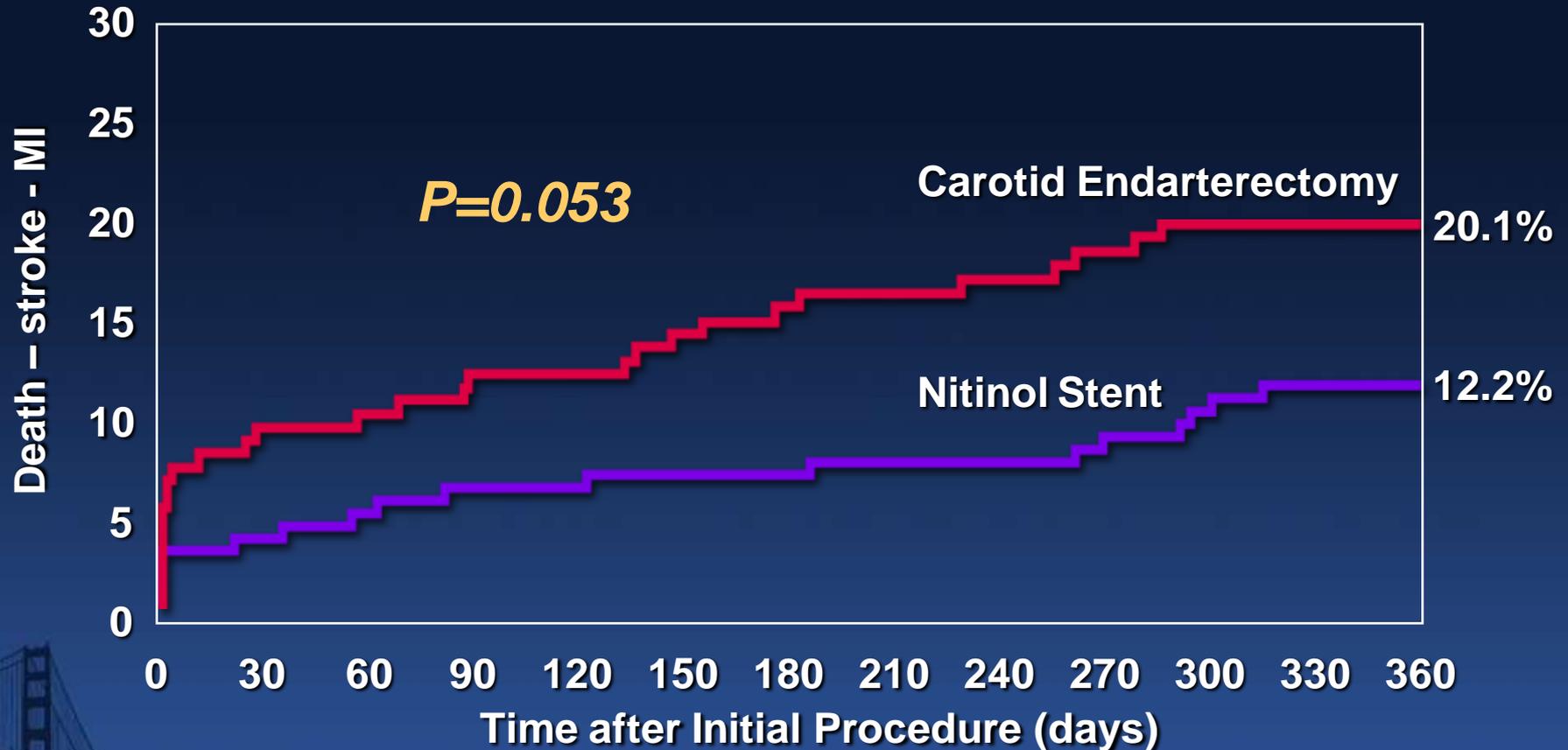
STENT n=159

SAPPHIRE – High Risk Criteria

1. Age ≥ 80
2. Severe cardiac disease (CHF, +ve stress test, need for open-heart surgery)
3. Severe pulmonary disease
4. Contralateral carotid occlusion
5. Contralateral laryngeal nerve palsy
6. Previous radical neck surgery or radiation therapy to the neck
7. Recurrent stenosis after endarterectomy

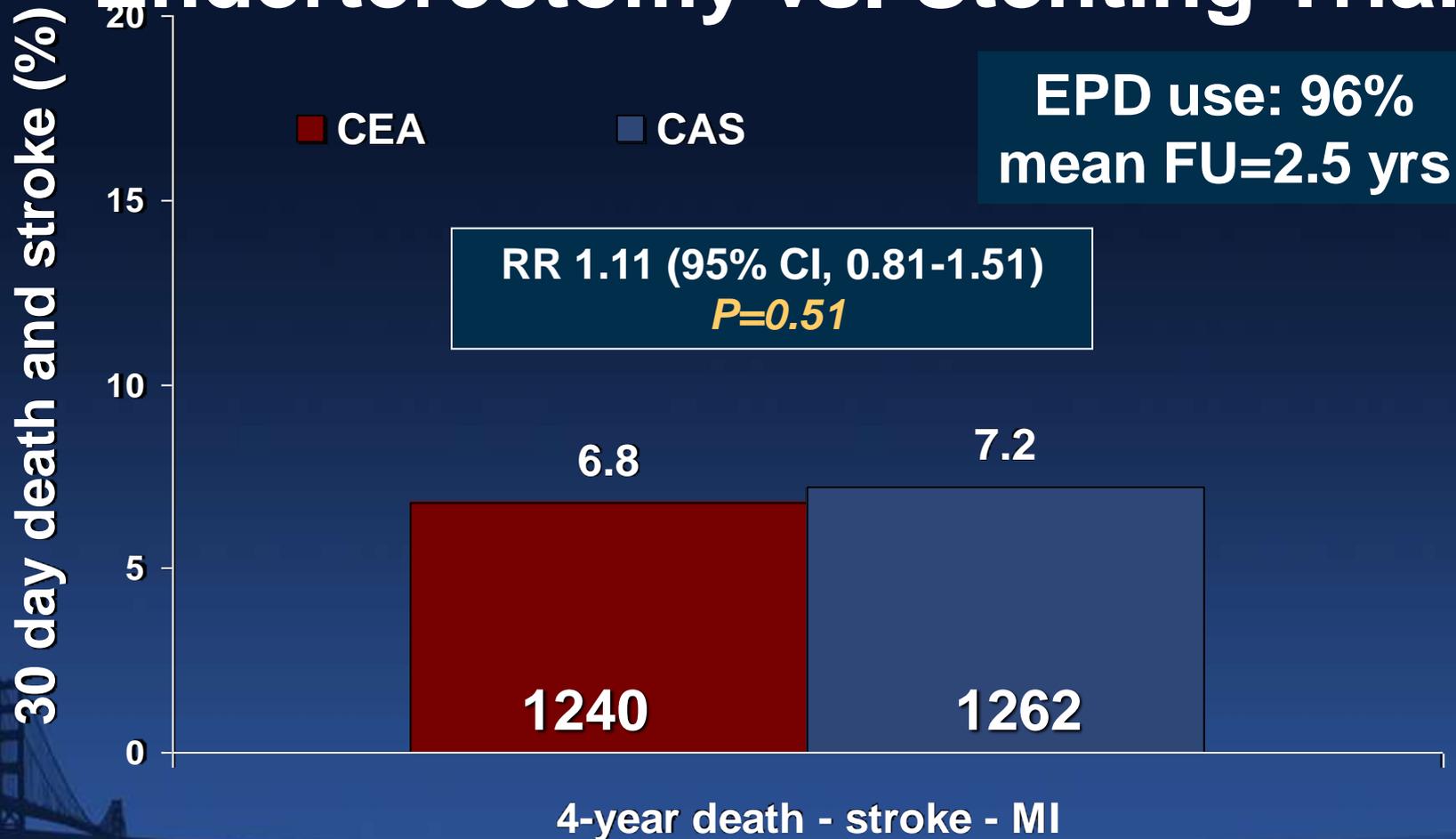


SAPPHIRE Trial: 1-Year Outcome Sx and Asx



CREST (47% asymptomatic) Carotid Revascularization

Endarterectomy vs. Stenting Trial



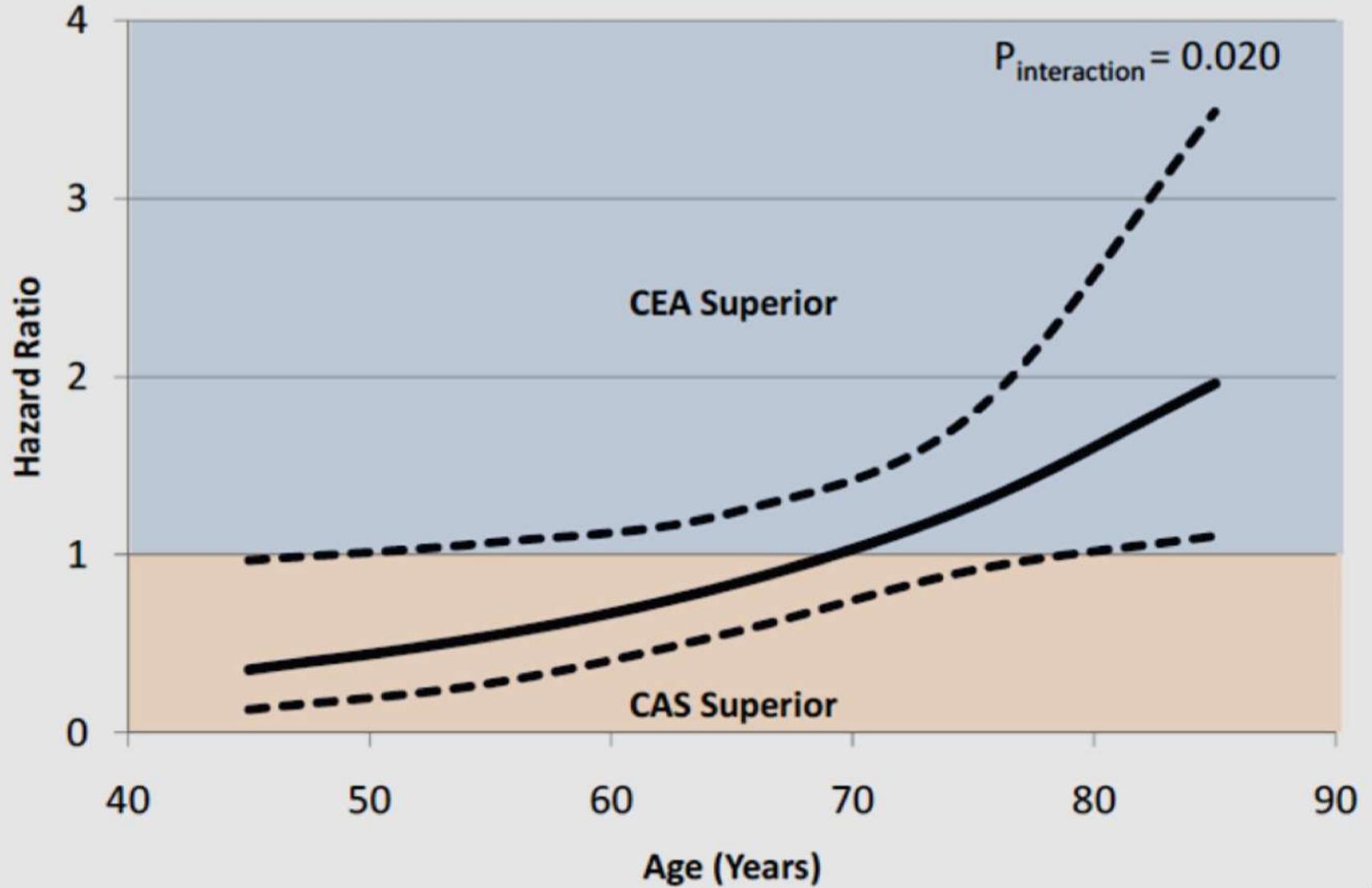
CREST Endpoint Components

	CAS	CEA	HR	95% CI	P value
Peri-procedural CVA	4.1%	2.3%	1.79	1.14-2.82	0.01
Peri-procedural MI	1.1%	2.3%	0.50	0.26-0.94	0.03
Peri-procedural Major CVA	0.9%	0.7%	1.35	0.54-3.36	0.52
Peri-procedural CN palsies	0.3%	4.8%	0.07	0.02-0.18	<0.0001
Periprocedural					
Death/stroke asympt	2.5%	1.4%	1.88	0.79-4.42	0.15
Death/stroke symptom	6.0%	3.2%	1.89	1.11-3.21	0.02
Ipsilateral CVA after peri-procedural period ≤4 years	2.0%	2.4%	0.94	0.50-1.76	0.85

Periprocedural Outcomes Comparison

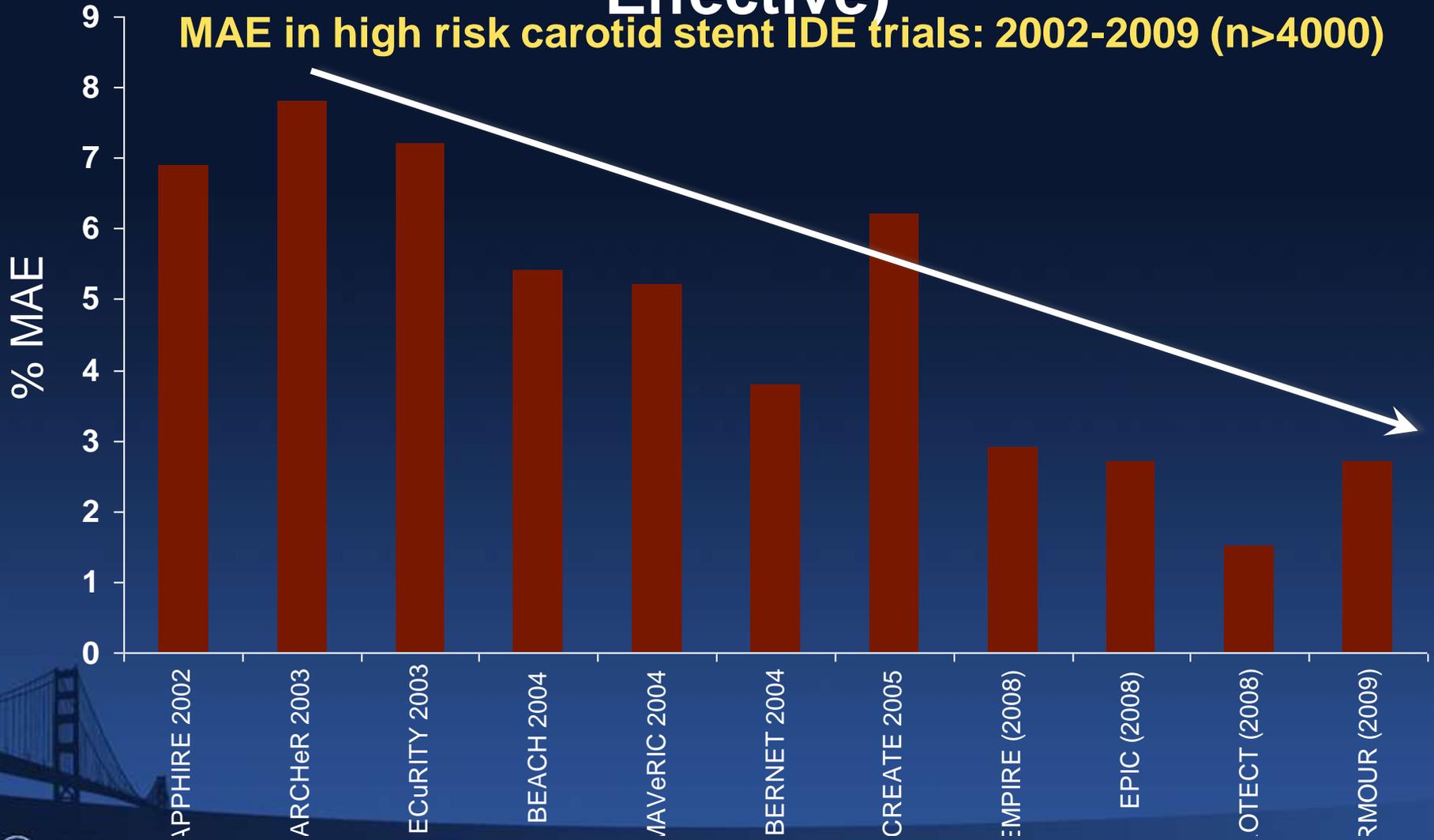
	CAS - a	CEA - a	CAS - s	CEA -s
NASCET 70-99%				5.8%
ECST				6.8%
ACAS		2.3%		
ACST		3.1%		
SPACE			6.8%	6.3%
EVA 3S			9.6%	3.9%
ICSS			7.4%	3.4%
CREST	2.5%	1.4%	6.0%	3.2%

Primary outcome – 4 year



11 US FDA Approval Trials with Improving Outcomes (all Approved as Safe and Effective)

MAE in high risk carotid stent IDE trials: 2002-2009 (n>4000)



2011 Stroke Guidelines

Table 7. Recommendations for Interventional Approaches to Patients With Stroke Caused by Large-Artery Atherosclerotic Disease

Risk Factor	Recommendations	Class/Level of Evidence*
Symptomatic extracranial carotid disease	For patients with recent TIA or ischemic stroke within the past 6 months and ipsilateral severe (70% to 99%) carotid artery stenosis, CEA is recommended if the perioperative morbidity and mortality risk is estimated to be <6% (<i>Class I; Level of Evidence A</i>).	<u>Class I; Level A</u>
	For patients with recent TIA or ischemic stroke and ipsilateral moderate (50% to 69%) carotid stenosis, CEA is recommended depending on patient-specific factors such as age, sex, and comorbidities if the perioperative morbidity and mortality risk is estimated to be <6% (<i>Class I; Level of Evidence B</i>).	Class I; Level B
	When the degree of stenosis is <50%, there is no indication for carotid revascularization by either CEA or CAS (<i>Class III; Level of Evidence A</i>).	Class III; Level A
	When CEA is indicated for patients with TIA or stroke, surgery within 2 weeks is reasonable rather than delaying surgery if there are no contraindications to early revascularization (<i>Class IIa; Level of Evidence B</i>).	Class IIa; Level B
Symptomatic extracranial carotid disease	CAS is indicated as an alternative to CEA for symptomatic patients at average or low risk of complications associated with endovascular intervention when the diameter of the lumen of the internal carotid artery is reduced by >70% by noninvasive imaging or >50% by catheter angiography (<i>Class I; Level of Evidence B</i>).	<u>Class I; Level B</u>
	Among patients with symptomatic severe stenosis (>70%) in whom the stenosis is difficult to access surgically, medical conditions are present that greatly increase the risk for surgery, or when other specific circumstances exist, such as radiation-induced stenosis or restenosis after CEA, CAS may be considered (<i>Class IIb; Level of Evidence B</i>).	Class IIb; Level B
	CAS in the above setting is reasonable when performed by operators with established periprocedural morbidity and mortality rates of 4% to 6%, similar to those observed in trials of CEA and CAS (<i>Class IIa; Level of Evidence B</i>).	Class IIa; Level B
	For patients with symptomatic extracranial carotid occlusion, EC/IC bypass surgery is not routinely recommended (<i>Class III; Level of Evidence A</i>).	Class III; Level A
	Optimal medical therapy, which should include antiplatelet therapy, statin therapy, and risk factor modification, is recommended for all patients with carotid artery stenosis and a TIA or stroke as outlined elsewhere in this guideline (<i>Class I; Level of Evidence B</i>). (New recommendation)	Class I; Level B

CEA

CAS

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Extracranial Large Vessel Disease: Causes

1. Atherosclerosis
2. Dissection
3. Takayasu arteritis
4. Giant cell arteritis
5. Fibromuscular dysplasia



Cerebrovascular FMD I

Table 1. Arterial Involvement in Fibromuscular Dysplasia.*

Arteries Involved	Frequency of Involvement (%)
Renal arteries	60–75
Bilateral	35
Extracranial cerebrovascular circulation (carotid or vertebral arteries)	25–30
Associated intracranial aneurysm	7–50
Multiple vascular beds	28
Other arterial beds (iliac, popliteal, splanchnic, hepatic, coronary, sub- clavian, brachial, aorta, superficial femoral, tibial, or peroneal)	Uncommon, exact frequency unknown

* Fibromuscular dysplasia may be a generalized process; in rare cases, it has also been identified in the venous system.



Cerebrovascular FMD III

**Intracranial MRA
recommended in
all pts with
cerebrovascular
FMD**

**Intracranial aneurysm
in 7-50%**



Carotid Dissection I

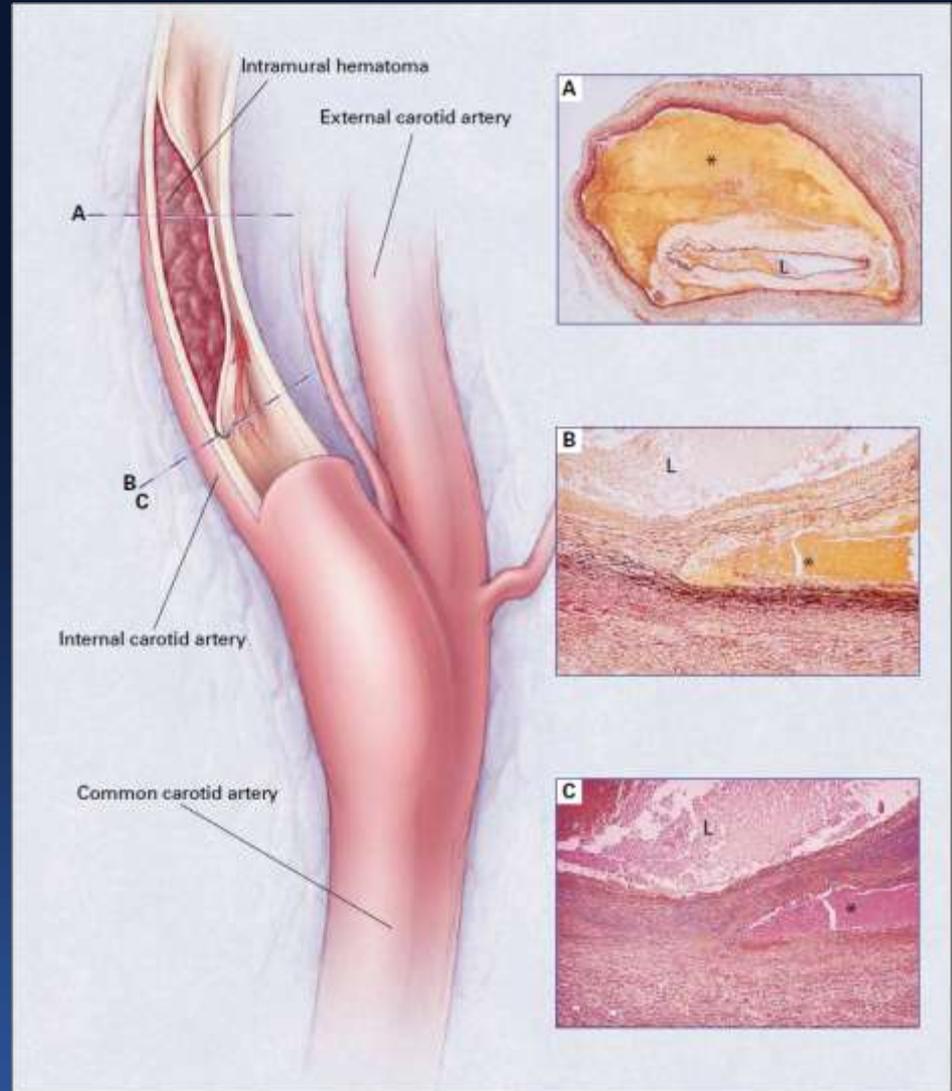
Causes

- FMD
- cystic medial necrosis
- trauma
- Neck hyperextension
rotation (yoga,
chiropractors...)

Presentation

“classic triad”

- Neck pain
- Partial Horner’s
- Cerebral/retina
ischemia



QUESTIONS



Question 1

Which of the following is appropriate for patients with carotid fibromuscular dysplasia?

A. Primary carotid stenting

B. Intracranial magnetic resonance angiography

C. Cyclosporin

D. Warfarin



Question 1

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Question 2

How many patients with asymptomatic carotid stenosis $\geq 60\%$ need to be treated with CEA to prevent 1 stroke per year?

A.10

B.100

C.1,000

D.10,000



Question 2

How many patients with asymptomatic carotid stenosis $\geq 60\%$ need to be treated with CEA to prevent 1 stroke per year?

A.10

B.100

C.1,000

D.10,000

ACAS: 5.9% ARR in 5 yrs

ACST: 5.4% ARR in 5 yrs

~ 1% ARR per year

Question 3

The CREST trial compared carotid endarterectomy and stenting in 2,502 pts. Which of the following statements is wrong:

A. CREST enrolled both symptomatic and asymptomatic pts

B. The incidence of stroke was higher in the CAS group

C. The incidence of MI was higher in the CAE group

D. CAS was better for pts >70-year-old

Question 3

The CREST trial compared carotid endarterectomy and stenting in 2,502 pts. Which of the following statements is wrong:

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C. The incidence of MI was higher in the CAE group

D. CAS was better for pts >70-year-old

Question 4

The presence of a cervical bruit suggests:

A. >90% likelihood for severe carotid stenosis

B. A recent TIA or stroke

C. Higher risk for cardiovascular death

D. 90-99% carotid stenosis



Question 4

The presence of a cervical bruit suggests:

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D. 90-99% carotid stenosis



Question 5

Carotid endarterectomy offers the most benefits in symptomatic patients with which degree of carotid stenosis:

A. Near occlusion

B. 70-99%

C. 50-69%

D. <50%



Question 5

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C. 50-69%

D. <50%



Question 6

In the SAPPHIRE trial of high-risk patients compared to carotid endarterectomy (CEA), carotid artery stenting:

A. was superior to CEA at 1 year

B. was superior to CEA at 3 years

C. Had lower incidence of cranial nerve palsy

D. Was associated with lower mortality



Question 6

In the SAPPHIRE trial of high-risk patients compared to carotid endarterectomy (CEA), carotid artery stenting:

A. was superior to CEA at 1 year

B. was superior to CEA at 3 years

C. Had lower incidence of cranial nerve palsy

D. Was associated with lower mortality



Question 7

Carotid artery stenting is reimbursed by CMS for pts with:

A. High risk for CEA and symptomatic stenosis $\geq 70\%$

B. High-risk for CEA and symptomatic stenosis 50-69% not enrolled in a trial

C. High-risk for CEA and asymptomatic stenosis $\geq 80\%$ not enrolled in a trial

D. Low risk for CEA



Question 7

Carotid artery stenting is reimbursed by CMS for pts with:

A. High risk for CEA and symptomatic stenosis $\geq 70\%$

B. High-risk for CEA and symptomatic stenosis 50-69% not enrolled in a trial

C. High-risk for CEA and asymptomatic stenosis $\geq 80\%$ not enrolled in a trial

D. Low risk for CEA



Question 8

All of the following are acceptable options for secondary stroke prevention, EXCEPT:

A. Aspirin 81 mg daily

B. Clopidogrel 75 mg daily

C. ASA 81 mg and Clopidogrel 75 mg daily

D. ASA and extended-release dipyridamole



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