Essential Update: Carotid Disease 2019

Piotr Musiałek

Jagiellonian University Dept. of Cardiac & Vascular Diseases
John Paul II Hospital, Kraków, Poland

Disclosures

Proctoring/Speaker Bureau/Advisory Boards - Abbott, InspireMD, Medtronic

Research Support - Abbott (IIS)

This presentation is to my best personal knowledge, without any external bias

Q1

These days, <u>asymptomatic</u> carotid stenosis is a benign pathology:

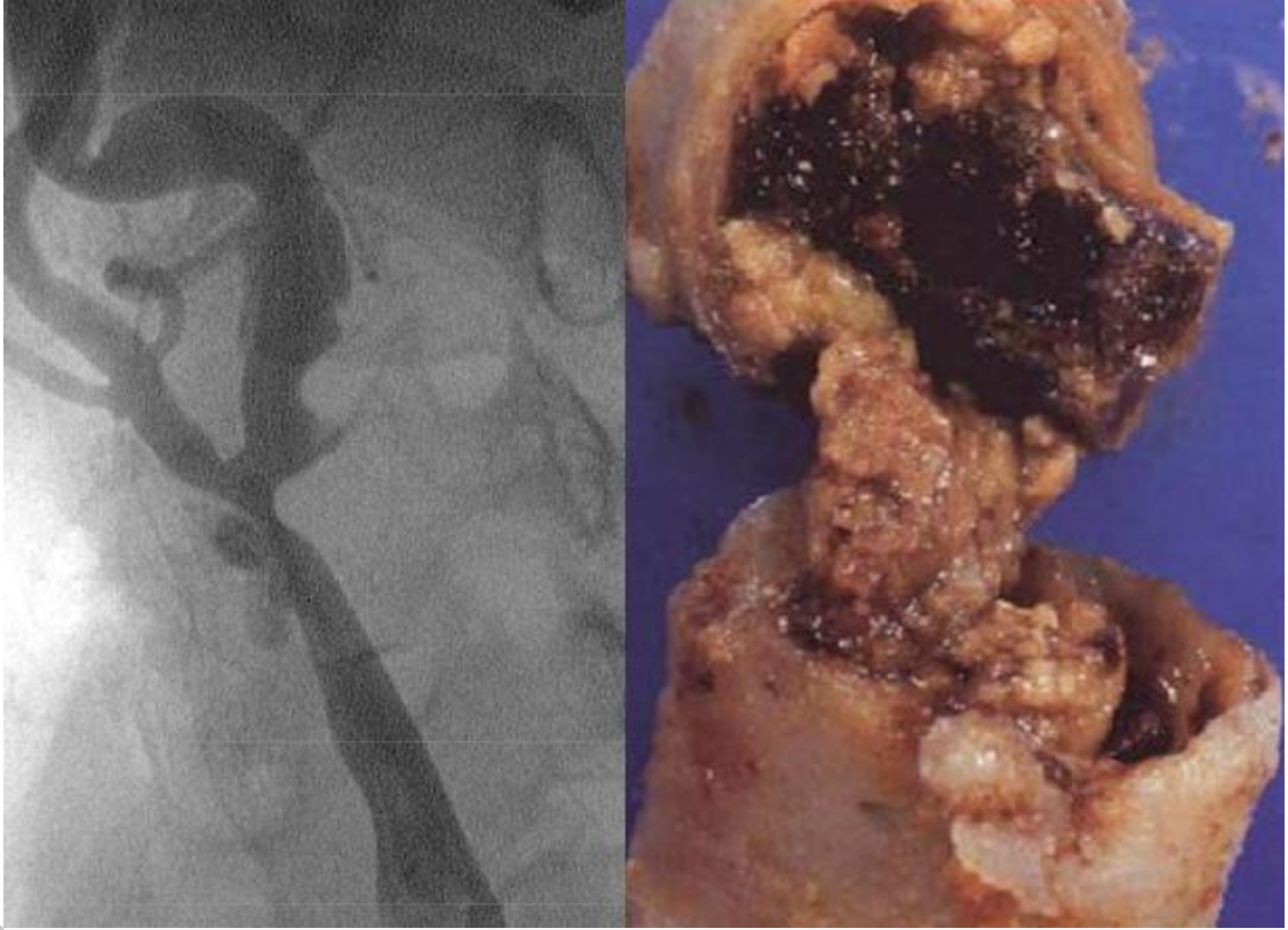
Q1 Please vote

These days, asymptomatic carotid stenosis is a benign pathology:

A. Yes

B. No

C. Don't know



Every ***symptomatic*** carotid plaque

– causing cerebral infarct/stroke –

starts as an *asymptomatic* plaque

Point to remember #1

Every ***symptomatic*** carotid plaque

– causing cerebral infarct/stroke –

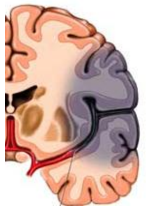
starts as an *asymptomatic* plaque

(aka. ”Where are the symptomatic patients coming from?”)

Essential Update: Carotid Disease 2019

- The disease
- Who to treat?
- How to treat? (medical therapy, surgery, stents, novel technologies)
- 2017 ESC/ESVS Guidelines: strengths and gaps

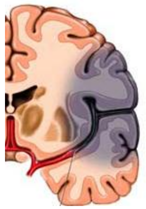
Q2



Prevalence of CS -in relation to prevalence of AFib- is

Q2

Please vote



Prevalence of CS -in relation to prevalence of AFib- is

A. ≈ 3 : 1 (*more* CS)

B. ≈ 1 : 1 (*similar* prevalence)

C. ≈ 1 : 3 (more Afib)

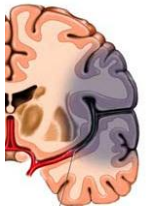


Table 14-2. Modifiable Stroke Risk Factors

Factor	Prevalence, %	PAR, %*	RR
Cigarette smoking			
Overall	19.8	12–14†	1.9
Men	22.3		
Women	17.4		
Hypertension		‡	8
Ages 20–34 y			
Men	13.4	99	
Women	6.2	98	
Ages 35–44 y			
Men	23.2	99	
Women	16.5	106	
Ages 45–54 y			
Men	36.2	100	
Women	35.9	103	
Ages 55–64 y			
Men	53.7	100	
Women	55.8	102	
Ages 65–74 y			
Men	64.7	100	
Women	69.6	101	
Ages ≥75 y			
Men	64.1	100	
Women	76.4	101	
Diabetes mellitus	7.3	5–27	1.8–6.0
High total cholesterol	Data calculated for highest quintile (20%) vs lowest quintile	9.1 (5.7–13.8)	1.5 (95% CI, 1.3–1.8)
	Continuous risk for ischemic stroke	…	1.25 per 1-mmol/L (38.7 mg/dL) increase
AF (nonvalvular)			
50–59	0.5	1.5	4.0
60–69	1.8	2.8	2.6
70–79	4.8	9.9	3.3
80–89	8.8	23.5	4.5
Asymptomatic carotid stenosis	2–8	2–7§	2.0

European Heart Journal (2015) 36, 281–287
doi:10.1093/eurheartj/ehu307

CLINICAL RESEARCH
Atrial fibrillation

Risk of ischaemic stroke according to pattern of atrial fibrillation: analysis of 6563 aspirin-treated patients in ACTIVE-A and AVERROES

Thomas Vanassche[1]*, Mandy N. Lauw[1], John W. Eikelboom[1], Jeff S. Healey[1], Robert G. Hart[1], Marco Alings[2], Alvaro Avezum[3], Rafael Díaz[4], Stefan H. Hohnloser[5], Basil S. Lewis[6], Olga Shestakovska[1], Jia Wang[1], and Stuart J. Connolly[1]

[1]Population Health Research Institute, McMaster University and Hamilton Health Sciences, 237 Barton St. E, Hamilton, ON, Canada L8L 2X2; [2]Amphia Ziekenhuis, Breda, The Netherlands; [3]Instituto Dante Pazzanese de Cardiologia, São Paulo, Brazil; [4]Estudios Clínicos Latinoamérica, Rosario, Argentina; [5]Department of Cardiology, Johann-Wolfgang-Goethe-Universität, Frankfurt, Germany; and [6]Cardiovascular Clinical Research Institute, Lady Davis Carmel Medical Center and the Ruth and Bruce Rappaport School of Medicine, Technion-IIT, Haifa, Israel

Aims

The pattern of atrial fibrillation (AF) occurrence—paroxysmal, persistent, or permanent—is associated with progressive stages of atrial dysfunction and structural changes and may therefore be associated with progressively higher stroke risk. However, previous studies have not consistently shown AF pattern to predict stroke but have been hampered by methodological shortcomings of low power, variable event ascertainment, and variable anticoagulant use.

Methods and results

We analysed the rates of stroke and systemic embolism in 6563 aspirin-treated patients with AF from the ACTIVE-A/AVERROES databases. There was thorough searching for events and adjudication. Multivariable analyses were performed with the adjustment for known risk factors for stroke. Mean age of patients with paroxysmal, persistent, and permanent AF was 69.0 ± 9.9, 68.6 ± 10.2, and 71.9 ± 9.8 years ($P < 0.001$). The CHA_2DS_2-VASc score was similar in patients with paroxysmal and persistent AF (3.1 ± 1.4), but was higher in patients with permanent AF (3.6 ± 1.5, $P < 0.001$). Yearly ischaemic stroke rates were 2.1, 3.0, and 4.2% for paroxysmal, persistent, and permanent AF, respectively, with adjusted hazard ratio of 1.83 ($P < 0.001$) for permanent vs. paroxysmal and 1.44 ($P = 0.02$) for persistent vs. paroxysmal. Multivariable analysis identified age ≥ 75 year, sex, history of stroke or TIA, and AF pattern as independent predictors of stroke, with AF pattern being the second strongest predictor after prior stroke or TIA.

Conclusion

In a large population of non-anticoagulated AF patients, pattern of AF was a strong independent predictor of stroke risk and may be helpful to assess the risk/benefit for anticoagulant therapy, especially in lower risk patients.

Keywords Atrial fibrillation • Paroxysmal • Permanent • Stroke

’asymptomatic’

A Fib

Pressure to

! ”GO” for PREVENTION !

(incl. Intervention)

’asymptomatic’

CAROTID STENOSIS

Pressure to

! ”WAIT” for **S T R O K E** !

(”symptoms”)

logic ???

'asymptomatic'
A Fib

Pressure to

! "GO" for PREVENTION !
(incl. Intervention)

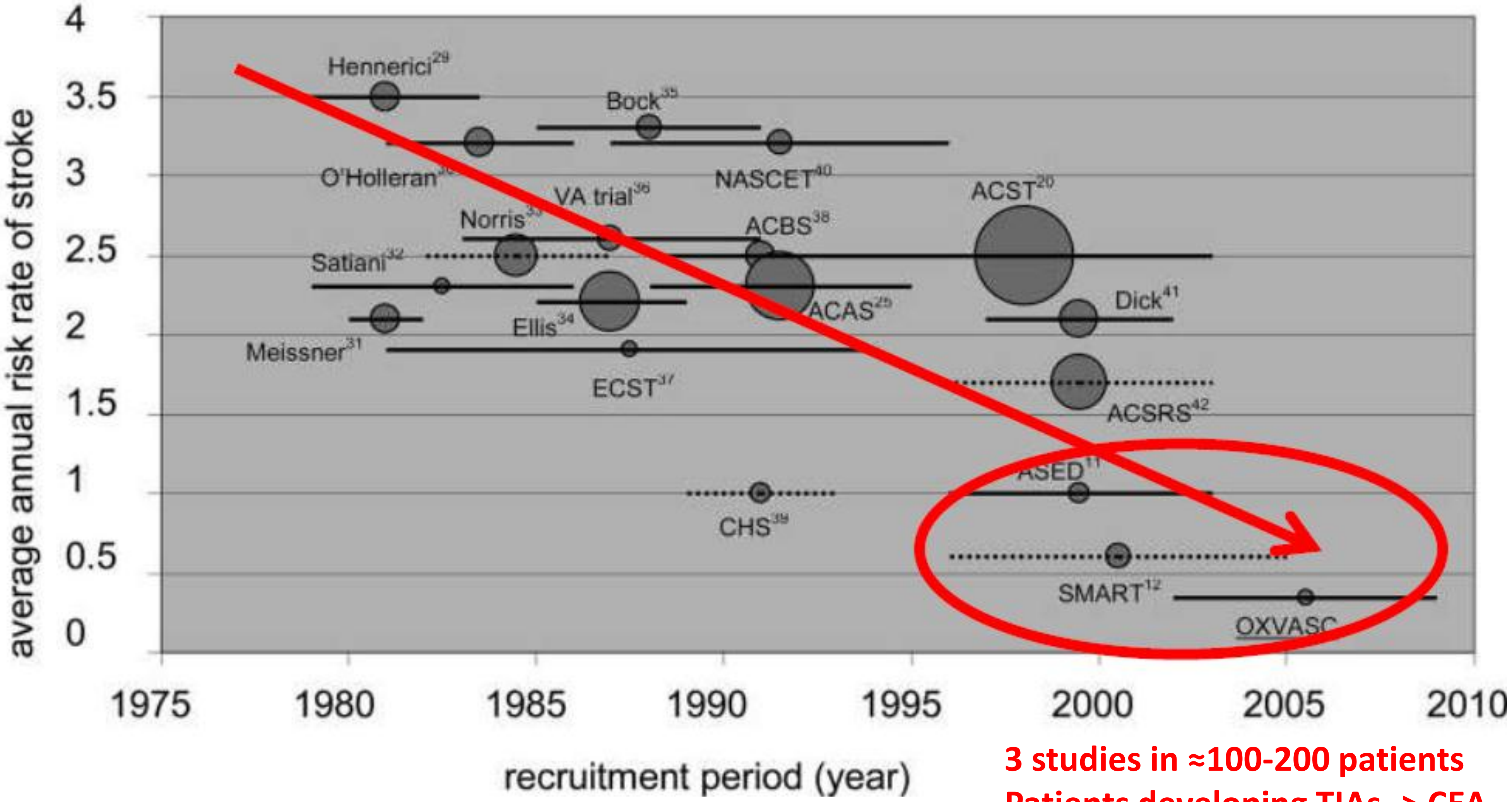
'asymptomatic'
CAROTID STENOSIS

Pressure to

! "WAIT" for S T R O K E !
("symptoms")

Why the management of asymptomatic Carotid Stenosis continues to be so controversial ?

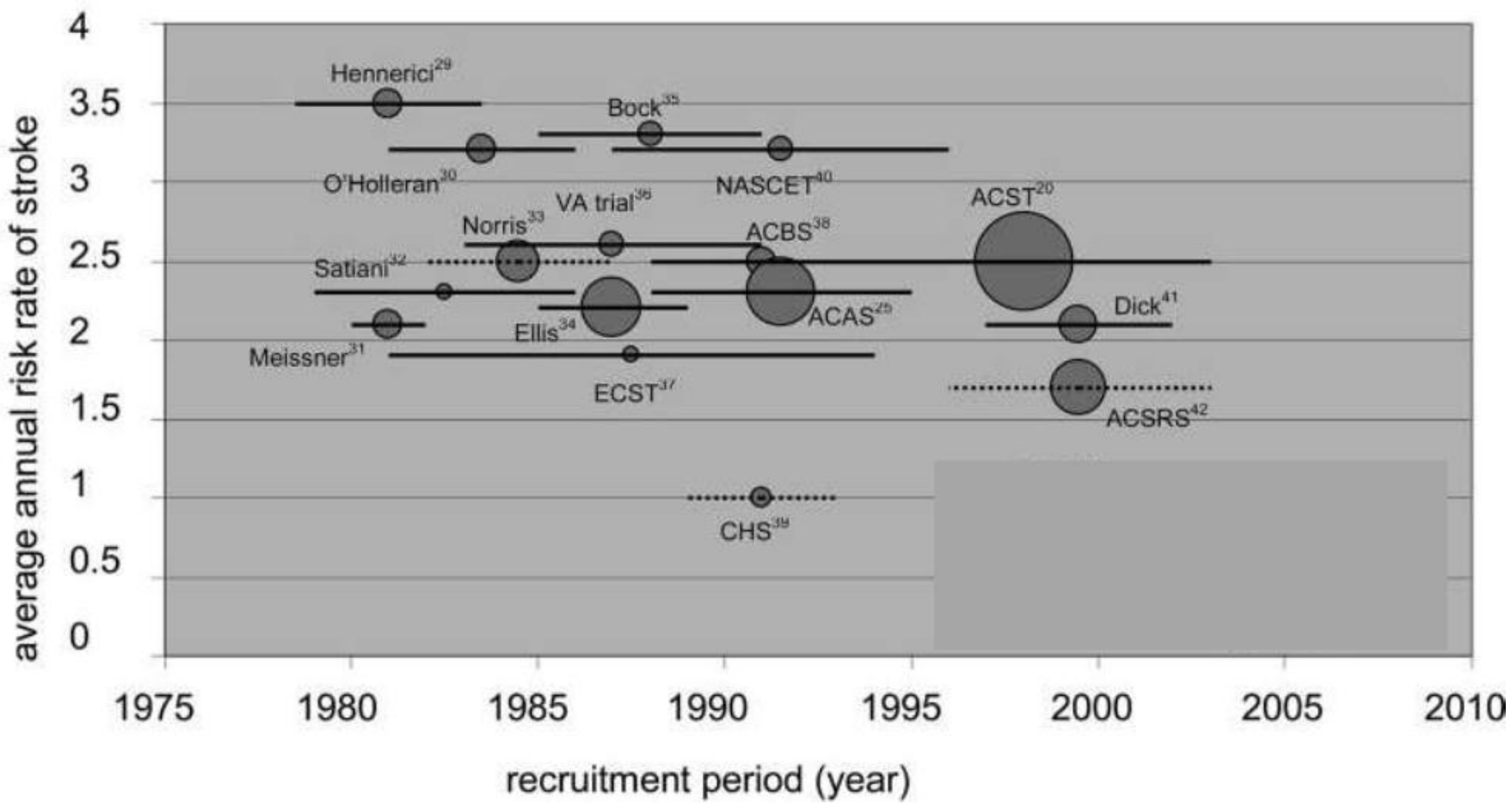
Annual stroke risk with asymptomatic carotid stenosis



P Schneider LINC 2018; modified

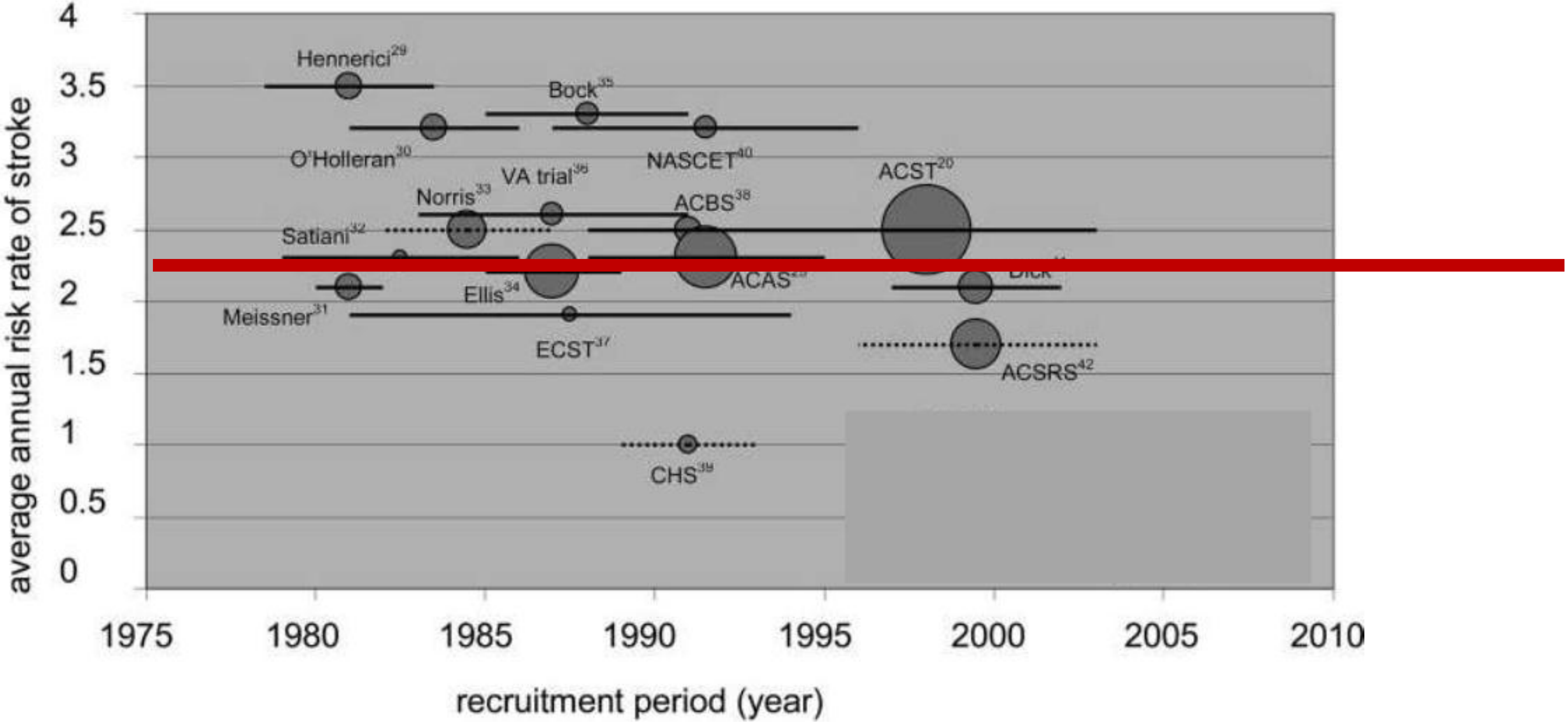
3 studies in ≈100-200 patients
Patients developing TIAs -> CEA

Annual stroke risk with asymptomatic carotid stenosis



P Schneider LINC 2018; modified

Annual stroke risk with asymptomatic carotid stenosis



P Schneider LINC 2018; modified

Annual stroke rate with asymptomatic carotid stenosis:

Contemporary cardiovascular clinic patients on OMT

2.4% per year (Conrad MF et al. *J Vasc Surg* 2013)

2.9% per year (Kakkos SK et al. *J Vasc Surg* 2014)

Annual stroke rate with asymptomatic carotid stenosis:

Contemporary cardiovascular clinic patients on OMT

2.4% per year (Conrad MF et al. *J Vasc Surg* 2013)… 5 years… 10 years

2.9% per year (Kakkos SK et al. *J Vasc Surg* 2014)… 5 years… 10 years

Fundamental Issue

”People” with Carotid Stenosis

Vascular Clinic Referral Patient	≠	General Popu- -lation Subject
annual ipsilateral stroke risk 2.5-3.0%		annual ipsilateral stroke risk ≈0.5%

Point to remember #2

Fundamental Issue

”People” with Carotid Stenosis

Vascular Clinic Referral Patient ≠ **General Popu- -lation Subject**

annual ipsilateral stroke risk 2.5-3.0%

annual ipsilateral stroke risk ≈0.5%

Q3 **There is large-scale Level 1 evidence (Randomized Controlled Trial) that patients with asymptomatic CS benefit from intervention:**

Please vote

Q3 **There is large-scale Level 1 evidence (Randomized Controlled Trial) that patients with asymptomatic CS benefit from intervention:**

A. Yes

B. No

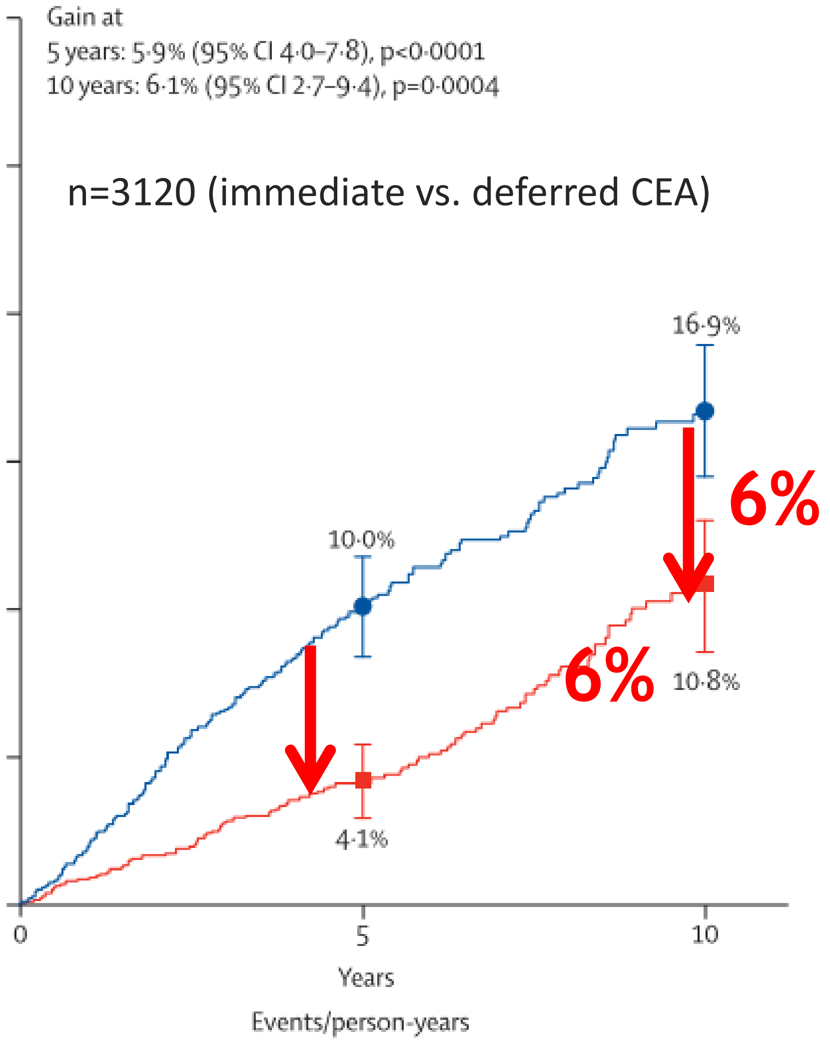
C. Don't know

ACST-1

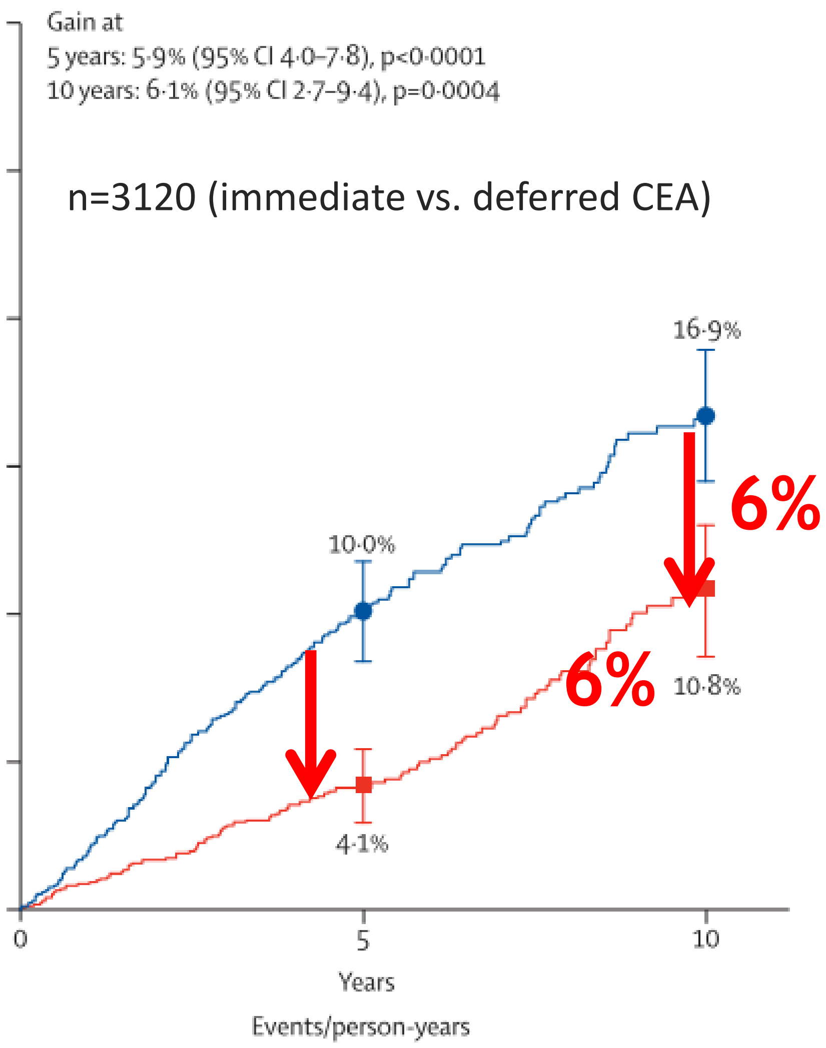
3120 asymptomatic CS patients randomised to CEA vs. deferred CEA

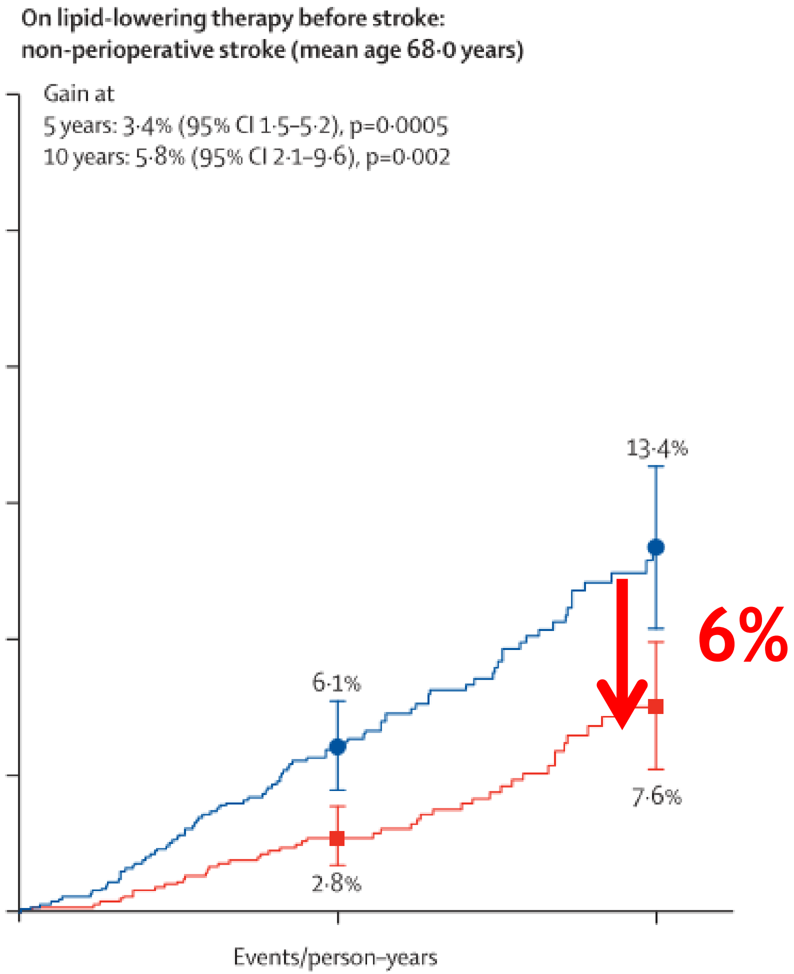
Result: successful CEA reduces 10-year stroke risk.

Stroke reduction with revascularization in asymptomatic carotid stenosis

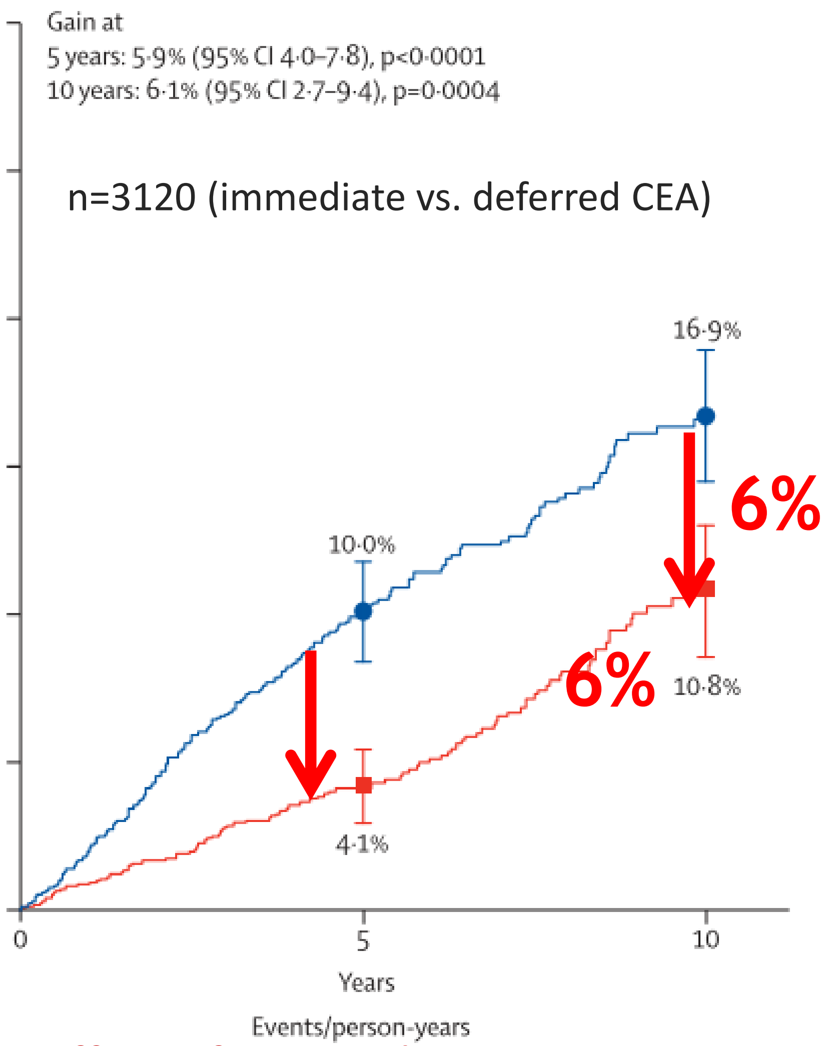


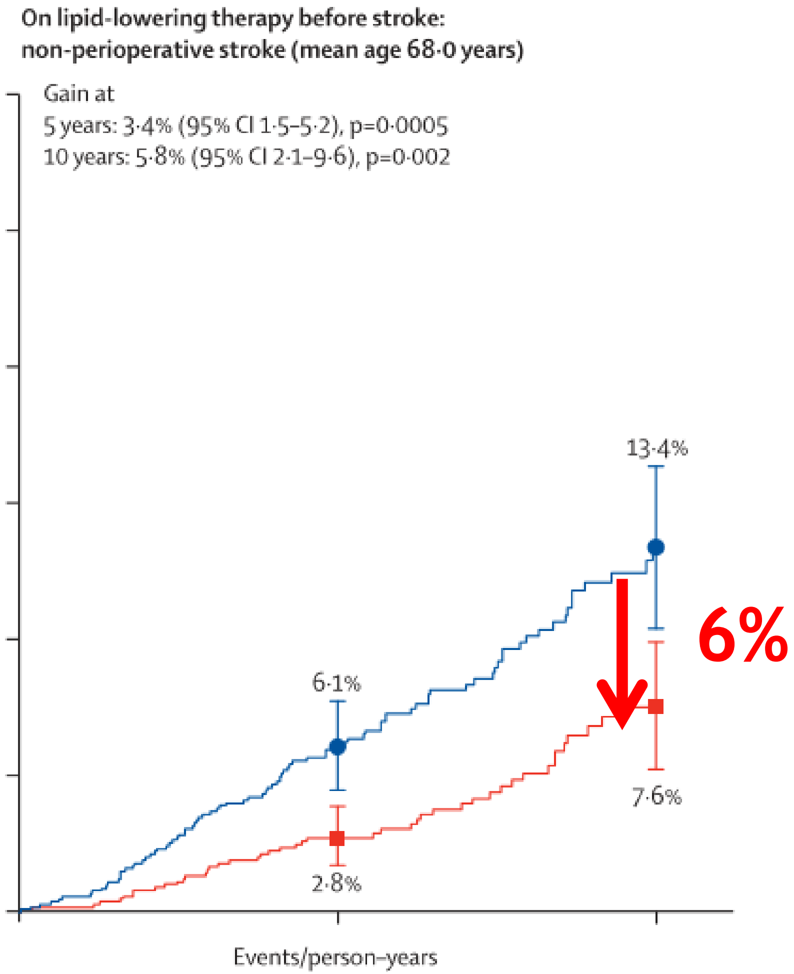
Stroke reduction with revascularization in asymptomatic carotid stenosis





Stroke reduction with revascularization in asymptomatic carotid stenosis





NB. Effect of revascularization maintained at 15 years, and also in patients on triple medical therapy

5%

> 60 years of age

5% > 60 years of age

... in 10 years (2029)

5% > 60 years of age

in 10 years (2029)

in 10 years (2029)

Point to remember #3

Stroke: "Systematic Review and Analysis"…

Table 1. Average Annual Stroke +/−TIA Rates of Patients With Asymptomatic Severe (>50%) Carotid Stenosis Managed With Medical Intervention Alone (%)*

		Ipsilateral Stroke		Ipsilateral Stroke/TIA		Any Territory Stroke		Any Territory Stroke/TIA	
Study	Sample Size	Raw Data	KM Estimates	Raw Data	KM Estimates	Raw Data	KM Estimates	Raw Data	KM Estimates
Johnson, 1985[76]	121	3.3	. . .	19.0	. . .	. . .	. . .	. . .	. . .
Toronto, 1986[2]	113	0	. . .	7.9 (all TIA)	. . .	1.9	. . .	10.7	11.0
VACS, 1993[10]	233	2.4	. . .	5.2	. . .	3.0	. . .	6.1	. . .
ACAS, 1995[11]	834	2.3	2.2	4.5	3.8	3.8	3.5	. . .	. . .
ECST, 1995[77]	127	2.3	1.9	. . .	. . .	. . .	. . .	. . .	. . .
ACBS, 1997[78]	357	1.2	1.4	3.4	4.2	2.1	2.5	5.8	. . .
CHS, 1998[82]	185	1.3	1.0	. . .	. . .	2.6	2.3	. . .	. . .
NASCET, 2000[3]	216	. . .	3.2	. . .	. . .	. . .	. . .	. . .	. . .
ACSRS, 2005[79]	1115	1.3	1.7	3.1	3.4	. . .	2.1	. . .	4.1
ASED, 2005[80]	202	1.2	1.0	3.2	3.1	2.4	2.2	5.6	5.1
SMART, 2007[81]	221	0.6	. . .	. . .	. . .	0.7	. . .	. . .	. . .

*ACAS indicates Asymptomatic Carotid Atherosclerosis Study; ECST, European Carotid Surgery Trial; ACBS, Asymptomatic Cervical Bruit Study; NASCET, North American Symptomatic Carotid Endarterectomy Trial; ACSRS, Asymptomatic Carotid Stenosis and Risk of Stroke Study; ASED, Asymptomatic Stenosis Embolus Detection Study; SMART, Second Manifestations of ARTerial disease Study.

Stroke: "Systematic Review and Analysis"…

Table 1. Average Annual Stroke +/−TIA Rates of Patients With Asymptomatic Severe (>50%) Carotid Stenosis Managed With Medical Intervention Alone (%)*

		Ipsilateral Stroke		Ipsilateral Stroke/TIA		Any Territory Stroke		Any Territory Stroke/TIA	
Study	Sample Size	Raw Data	KM Estimates	Raw Data	KM Estimates	Raw Data	KM Estimates	Raw Data	KM Estimates
Johnson, 1985[76]	121	3.3	...	19.0	...	...	...	...	...
Toronto, 1986[2]	113	0	...	7.9 (all TIA)	...	[illegible]	...	10.7	11.0
VACS, 1993[10]	233	2.4	...	5.2	...	[illegible]	...	6.1	...
ACAS, 1995[11]	834	2.3	2.2	4.5	[illegible]	3.8	3.5	...	...
ECST, 1995[77]	127	2.3	1.9	...	...	...	...	...	...
ACBS, 1997[78]	357	1.2	1.4	[illegible]	4.2	2.1	2.5	5.8	...
CHS, 1998[82]	185	1.3	1.0	...	...	2.6	2.3	...	...
NASCET, 2000[3]	216	...	[illegible]	...	...	...	...	...	...
ACSRS, 2005[79]	1115	1.3	[illegible]	3.1	3.4	...	2.1	...	4.1
ASED, 2005[80]	202	[illegible]	1.0	3.2	3.1	2.4	2.2	5.6	5.1
SMART, 2007[81]	221	0.6	...	...	...	0.7	...	...	...

*ACAS indicates Asymptomatic Carotid Atherosclerosis Study; ECST, European Carotid Surgery Trial; ACBS, Asymptomatic Cervical Bruit Study; NASCET, North American Symptomatic Carotid Endarterectomy Trial; ACSRS, Asymptomatic Carotid Stenosis and Risk of Stroke Study; ASED, Asymptomatic Stenosis Embolus Detection Study; SMART, Second Manifestations of ARTerial disease Study.

where is ACST ? (n=3120)

Stroke: "Systematic Review and Analysis"…

Point to remember #4

where is ACST ? (n=3120)

Table 1. Average Annual Stroke +/−TIA Rates of Patients With Asymptomatic Severe (>50%) Carotid Stenosis Managed With Medical Intervention Alone (%)*

		Ipsilateral Stroke		Ipsilateral Stroke/TIA		Any Territory Stroke		Any Territory Stroke/TIA	
Study	Sample Size	Raw Data	KM Estimates	Raw Data	KM Estimates	Raw Data	KM Estimates	Raw Data	KM Estimates
Johnson, 1985[76]	121	3.3	...	19.0	...	...	...	...	...
Toronto, 1986[2]	113	0	...	7.9 (all TIA)	...	1.9	...	10.7	11.0
VACS, 1993[10]	233	2.4	...	5.2	...	[illegible]	...	6.1	...
ACAS, 1995[11]	834	2.3	2.2	4.5	[illegible]	3.8	3.5	...	...
ECST, 1995[77]	127	2.3	1.9	...	...	...	...	...	...
ACBS, 1997[78]	357	1.2	1.4	[illegible]	4.2	2.1	2.5	5.8	...
CHS, 1998[82]	185	1.3	1.0	...	...	2.6	2.3	...	...
NASCET, 2000[3]	216	...	[illegible]	...	...	...	...	...	...
ACSRS, 2005[79]	1115	1.3	1.7	3.1	3.4	...	2.1	...	4.1
ASED, 2005[80]	202	[illegible]	1.0	3.2	3.1	2.4	2.2	5.6	5.1
SMART, 2007[81]	221	0.6	...	...	...	0.7	...	...	...

*ACAS indicates Asymptomatic Carotid Atherosclerosis Study; ECST, European Carotid Surgery Trial; ACBS, Asymptomatic Cervical Bruit Study; NASCET, North American Symptomatic Carotid Endarterectomy Trial; ACSRS, Asymptomatic Carotid Stenosis and Risk of Stroke Study; ASED, Asymptomatic Stenosis Embolus Detection Study; SMART, Second Manifestations of ARTerial disease Study.

Even if a "good" journal – READ critically !

Assumptions

are not powered to dismiss

Large-scale level 1 evidence

(ACST, >3100 pts)

Determining ”Symptomatic” CS…

Symptoms vs. Signs

Determining ”Symptomatic” CS…

Point to remember #5

Symptoms vs. Signs

stroke

cerebral infarct

How asymptomatic is "asymptomatic" carotid stenosis?

Resolving fundamental confusion(s)—and confusions yet to be resolved

Piotr Musiałek[1], Iris Q. Grunwald[2,3]

1 Department of Cardiac and Vascular Diseases, Jagiellonian University Medical College, John Paul II Hospital, Kraków, Poland
2 Neuroscience and Vascular Simulation, Anglia Ruskin University, Chelmsford, United Kingdom
3 Southend University Hospital NHS Foundation Trust, Westcliff-on-Sea, United Kingdom

Atherosclerotic stenosis of the internal carotid artery of 50% or more is a relatively common pathology (about 2% to 8% of the general population aged 60 to 80 years), with the prevalence similar to that of nonvalvular atrial fibrillation.[1] However, patients with manifest atherosclerosis in other vascular beds show a significantly greater prevalence of carotid stenosis (CS) and a greater risk of cerebral symptoms that occur through the thromboembolic or hemodynamic mechanisms.[2]

The ACST-1 trial[3] in 3120 patients with asymptomatic CS followed for 10 years demonstrated, with an elective (rather than deferred) CS revascularization, a profound absolute risk reduction in nonperioperative stroke by 5.9% at 5 years (risk reduction from 11.0% to 5.1%) and 6.1% at 10 years (risk reduction from 16.9% to 10.8%, with the magnitude of the effect maintained in patients on lipid-lowering therapy).[3] Surprisingly, in the absence of any new randomized data, there have been vocal calls recently to disregard the level-1 evidence from the ACST-1 trial through either ignoring the trial completely in some meta-analyses[4] or attempting to construct an alternative body of "new evidence." Such "new-evidence" observational studies, performed not infrequently in as few as 100 subjects[5] (rather than the usually referenced 1153 subjects)[5] followed for a relatively short time[5] (and with most transient ischemic attacks [TIAs] leading—rightly—to carotid revascularization to pre- with asymptomatic CS on optimized medical therapy (OMT). As the risk is cumulative, the annual risk level of about 2.5% to 3.0% indicates—for instance for a 50-year-old man with an asymptomatic CS on contemporary OMT—a statistical stroke risk of about 25% to 30% by the age of 60 and 50% to 60% by the age of 70 (the actual risk can be still higher when additional risk factors, such as diabetes, are present).[2] As 85% of strokes occur without a warning sign, and of those who survive stroke (about 40% at 5 years) about half are disabled,[2] many families and physicians find it difficult to ignore such a risk.[4] This is particularly relevant because contemporary CS revascularization studies continue to enroll patients with CS strokes despite OMT; this provdes circumstantial evidence that OMT, at least in some patients, does not sufficiently protect against stroke.[4]

So why is the management of asymptomatic CS (to some at least) controversial today? Principal reasons seem to stem from: 1) definition problems ("asymptomatic" vs "symptomatic" CS; "stroke" vs "cerebral infarct"); 2) fundamental differences between the low-risk general population and higher-risk populations with atherosclerotic disease manifestations; 3) poor appreciation of increased stroke risk characteristics in CS; 4) risk of intervention (until recently) of about 3%[8]; and 5) lack of randomized data (OMT vs OMT + intervention) in current populations with asymptomatic CS across the whole risk spectrum.

Q4 The CREST Randomized Controlled Trial,

(conducted in 2502 pts, 53% symptomatic)

showed, in primary endpoint and long-term follow-up, EQUIVALENCE of CEA and first-generation CAS:

Please vote

Q4 The CREST Randomized Controlled Trial,
(conducted in 2502 pts, 53% symptomatic)
showed, in primary endpoint and long-term follow-up, EQUIVALENCE of CEA and first-generation CAS:

A. Yes

B. No

C. Don’t know

CREST

N Engl J Med 2010;363:11-23.

	Periprocedural Period				
	CAS (N=1262)	CEA (N=1240)	Absolute Treatment Effect of CAS vs. CEA (95% CI)	Hazard Ratio for CAS vs. CEA (95% CI)	P Value
	no. of patients (% ±SE)		*percentage points*		
Death	9 (0.7±0.2)	4 (0.3±0.2)	0.4 (−0.2 to 1.0)	2.25 (0.69 to 7.30)†	0.18†
Stroke					
Any	52 (4.1±0.6)	29 (2.3±0.4)	1.8 (0.4 to 3.2)	1.79 (1.14 to 2.82)	0.01
Major ipsilateral	11 (0.9±0.3)	4 (0.3±0.2)	0.5 (−0.1 to 1.2)	2.67 (0.85 to 8.40)	0.09
Major nonipsilateral‡	0	4 (0.3±0.2)	NA	NA	NA
Minor ipsilateral	37 (2.9±0.5)	17 (1.4±0.3)	1.6 (0.4 to 2.7)	2.16 (1.22 to 3.83)	0.009
Minor nonipsilateral	4 (0.3±0.2)	4 (0.3±0.2)	0.0 (−0.4 to 0.4)	1.02 (0.25 to 4.07)	0.98†
Myocardial infarction	14 (1.1±0.3)	28 (2.3±0.4)	−1.1 (−2.2 to −0.1)	0.50 (0.26 to 0.94)	0.03
Any periprocedural stroke or postprocedural ipsilateral stroke	52 (4.1±0.6)	29 (2.3±0.4)	1.8 (0.4 to 3.2)	1.79 (1.14 to 2.82)	0.01
Major stroke	11 (0.9±0.3)	8 (0.6±0.2)	0.2 (−0.5 to 0.9)	1.35 (0.54 to 3.36)	0.52
Minor stroke	41 (3.2±0.5)	21 (1.7±0.4)	1.6 (0.3 to 2.8)	1.95 (1.15 to 3.30)	0.01
Any periprocedural stroke or death or post-procedural ipsilateral stroke	55 (4.4±0.6)	29 (2.3±0.4)	2.0 (0.6 to 3.4)	1.90 (1.21 to 2.98)	0.005
Primary end point (any periprocedural stroke, myocardial infarction, or death or postprocedural ipsilateral stroke)	66 (5.2±0.6)	56 (4.5±0.6)	0.7 (−1.0 to 2.4)	1.18 (0.82 to 1.68)	0.38

CREST

N Engl J Med 2010;363:11-23.

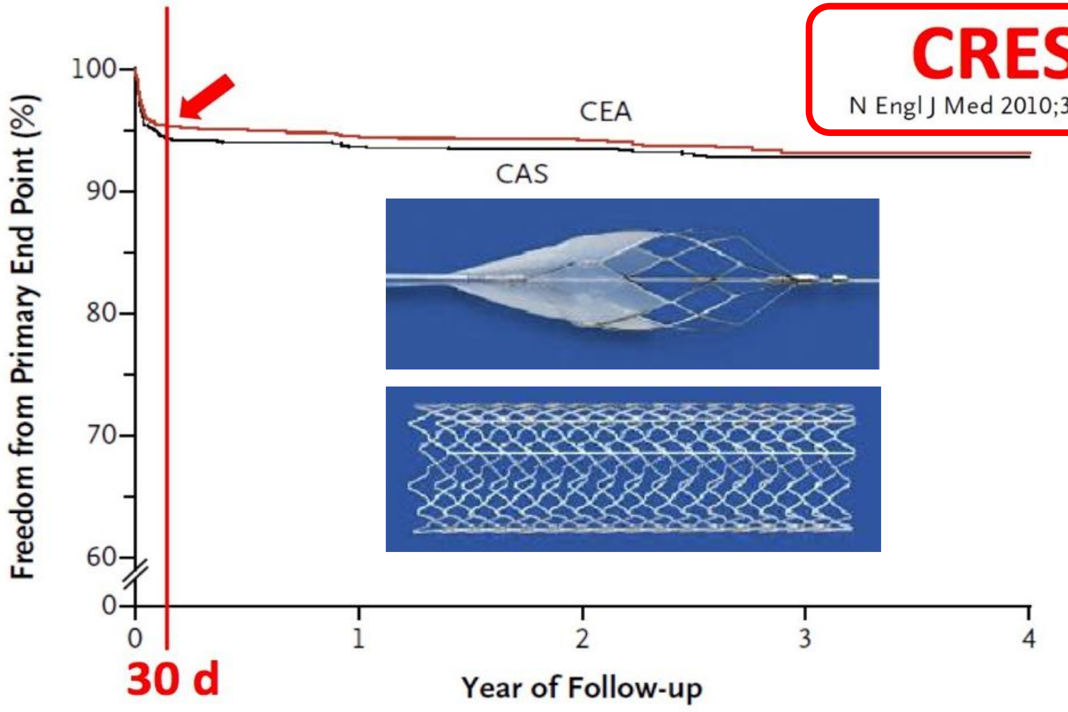
	CAS (N=1262)	CEA (N=1240)	Periprocedural Period Absolute Treatment Effect of CAS vs. CEA (95% CI)	Hazard Ratio for CAS vs. CEA (95% CI)	P Value
	no. of patients (% ±SE)		*percentage points*		
Death	9 (0.7±0.2)	4 (0.3±0.2)	0.4 (−0.2 to 1.0)	2.25 (0.69 to 7.30)†	0.18†
Stroke					
Any	52 (4.1±0.6)	29 (2.3±0.4)	1.8 (0.4 to 3.2)	1.79 (1.14 to 2.82)	0.01
Major ipsilateral	11 (0.9±0.3)	4 (0.3±0.2)	0.5 (−0.1 to 1.2)	2.67 (0.85 to 8.40)	0.09
Major nonipsilateral‡	0	4 (0.3±0.2)	NA	NA	NA
Minor ipsilateral	37 (2.9±0.5)	17 (1.4±0.3)	1.6 (0.4 to 2.7)	2.16 (1.22 to 3.83)	0.009
Minor nonipsilateral	4 (0.3±0.2)	4 (0.3±0.2)	0.0 (−0.4 to 0.4)	1.02 (0.25 to 4.07)	0.98†
Myocardial infarction	14 (1.1±0.3)	28 (2.3±0.4)	−1.1 (−2.2 to −0.1)	0.50 (0.26 to 0.94)	0.03
Any periprocedural stroke or postprocedural ipsilateral stroke	52 (4.1±0.6)	29 (2.3±0.4)	1.8 (0.4 to 3.2)	1.79 (1.14 to 2.82)	0.01
Major stroke	11 (0.9±0.3)	8 (0.6±0.2)	0.2 (−0.5 to 0.9)	1.35 (0.54 to 3.36)	0.52
Minor stroke	41 (3.2±0.5)	21 (1.7±0.4)	1.6 (0.3 to 2.8)	1.95 (1.15 to 3.30)	0.01
Any periprocedural stroke or death or post-procedural ipsilateral stroke	55 (4.4±0.6)	29 (2.3±0.4)	2.0 (0.6 to 3.4)	1.90 (1.21 to 2.98)	0.005
Primary end point (any periprocedural stroke, myocardial infarction, or death or postprocedural ipsilateral stroke)	66 (5.2±0.6)	56 (4.5±0.6)	0.7 (−1.0 to 2.4)	1.18 (0.82 to 1.68)	0.38

CREST

N Engl J Med 2010;363:11-23.

	CAS (N=1262)	CEA (N=1240)	Periprocedural Period: Absolute Treatment Effect of CAS vs. CEA (95% CI)	Hazard Ratio for CAS vs. CEA (95% CI)	P Value
	no. of patients (% ±SE)		*percentage points*		
Death	9 (0.7±0.2)	4 (0.3±0.2)	0.4 (−0.2 to 1.0)	2.25 (0.69 to 7.30)†	0.18†
Stroke					
Any	52 (4.1±0.6)	29 (2.3±0.4)	1.8 (0.4 to 3.2)	1.79 (1.14 to 2.82)	0.01
Major ipsilateral	11 (0.9±0.3)	4 (0.3±0.2)	0.5 (−0.1 to 1.2)	2.67 (0.85 to 8.40)	0.09
Major nonipsilateral‡	0	4 (0.3±0.2)	NA	NA	NA
Minor ipsilateral	37 (2.9±0.5)	17 (1.4±0.3)	1.6 (0.4 to 2.7)	2.16 (1.22 to 3.83)	0.009
Minor nonipsilateral	4 (0.3±0.2)	4 (0.3±0.2)	0.0 (−0.4 to 0.4)	1.02 (0.25 to 4.07)	0.98†
Myocardial infarction	14 (1.1±0.3)	28 (2.3±0.4)	−1.1 (−2.2 to −0.1)	0.50 (0.26 to 0.94)	0.03
Any periprocedural stroke or postprocedural ipsilateral stroke	52 (4.1±0.6)	29 (2.3±0.4)	1.8 (0.4 to 3.2)	1.79 (1.14 to 2.82)	0.01
Major stroke	11 (0.9±0.3)	8 (0.6±0.2)	0.2 (−0.5 to 0.9)	1.35 (0.54 to 3.36)	0.52
Minor stroke	41 (3.2±0.5)	21 (1.7±0.4)	1.6 (0.3 to 2.8)	1.95 (1.15 to 3.30)	0.01
Any periprocedural stroke or death or post-procedural ipsilateral stroke	55 (4.4±0.6)	29 (2.3±0.4)	2.0 (0.6 to 3.4)	1.90 (1.21 to 2.98)	0.005
Primary end point (any periprocedural stroke, myocardial infarction, or death or postprocedural ipsilateral stroke)	66 (5.2±0.6)	56 (4.5±0.6)	0.7 (−1.0 to 2.4)	1.18 (0.82 to 1.68)	0.38

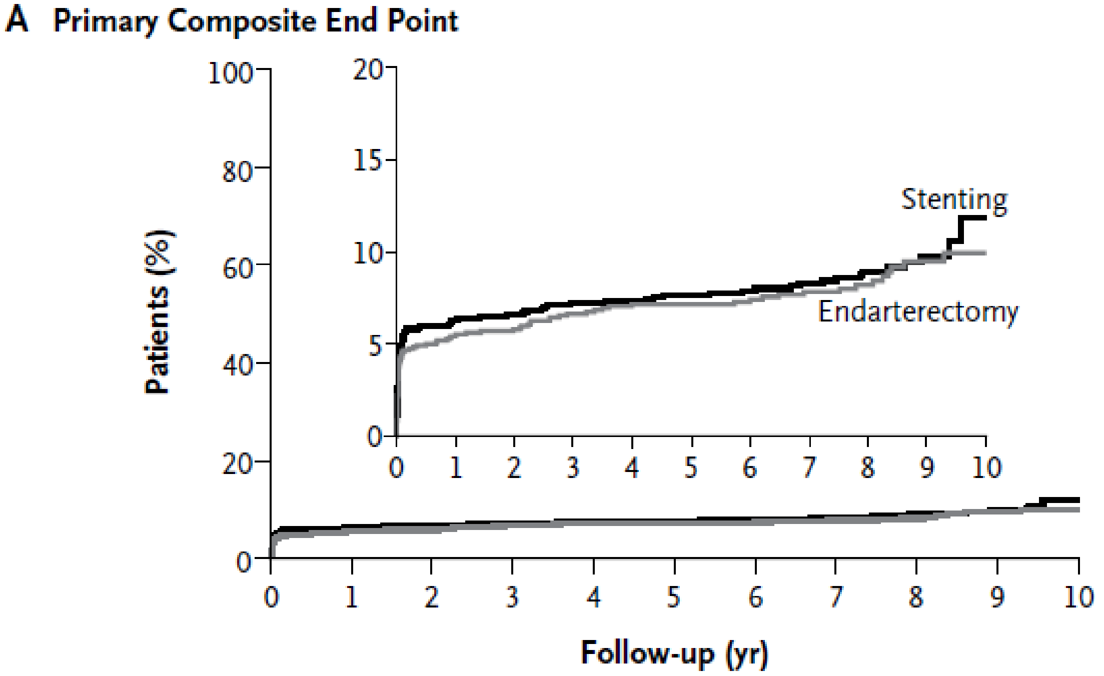
The first 30 days make the difference:
CEA vs conventional-stent CAS



No. at Risk					
CAS	1262	1100	787	460	162
CEA	1240	1099	770	430	145

19/48 strokes ≤30d after CAS were POST-procedural

CREST
N Engl J Med 2010;363:11-23.

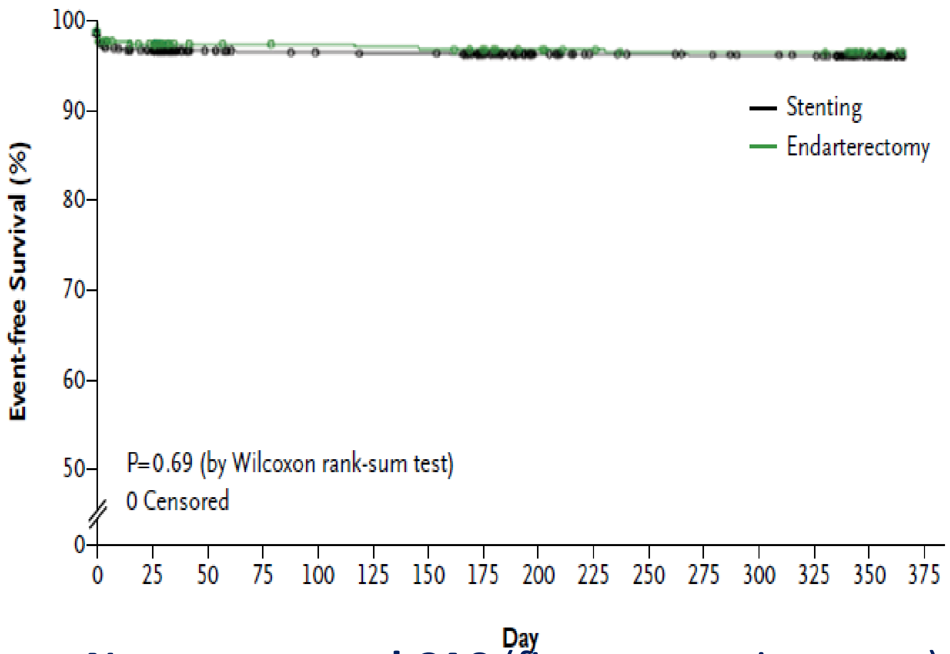


No. at Risk											
Endarterectomy	1240	1104	1036	949	833	736	695	620	438	243	66
Stenting	1262	1103	1041	972	884	774	738	676	477	264	68

Brott et al, NEJM 2016

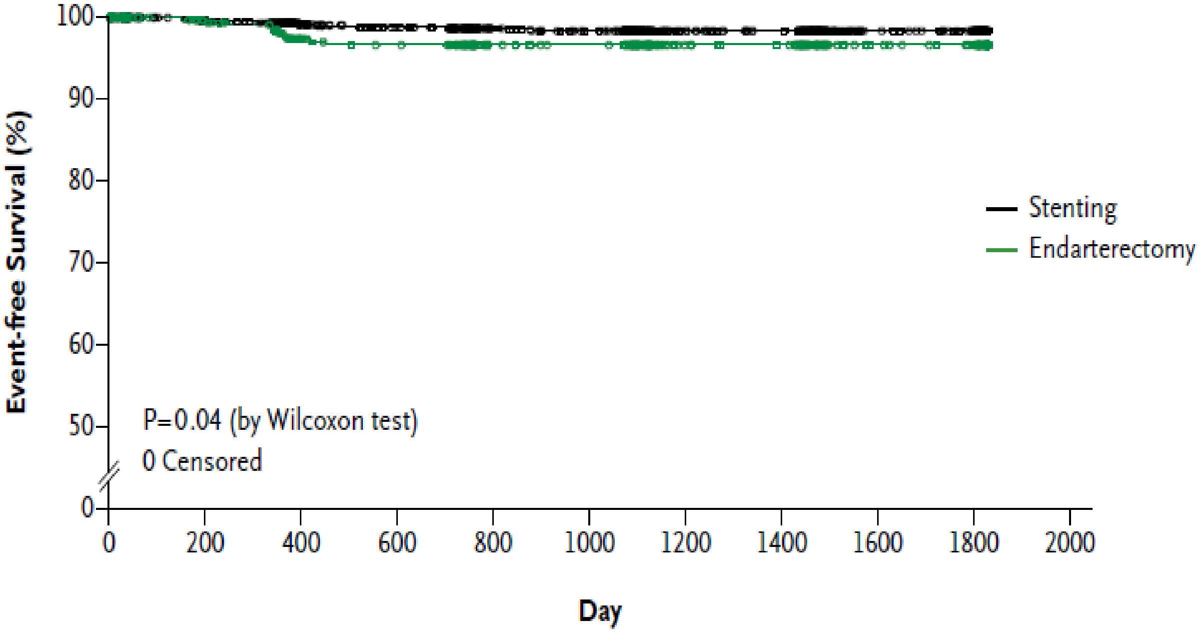
ACT-1 RCT: **Neuroprotected CAS** (first-generation stent) vs . **CEA** in 1453 average surgical risk patients

Primary endpoint: Freedom from death, stroke, MI by 30 days and from ipsilateral stroke by 365 days



Neuroprotected CAS (first-generation stent)
NON-INFERIOR to **CEA**

Freedom from clinically-driven target lesion revascularization by 5 years



Rosenfield et al, NEJM 2016

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 69, NO. 18, 2017

ISSN 0735-1097/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jacc.2017.02.053

Carotid Artery Stenting Versus Endarterectomy for Stroke Prevention

A Meta-Analysis of Clinical Trials

Partha Sardar, MD,[a] Saurav Chatterjee, MD,[b] Herbert D. Aronow, MD,[c] Amartya Kundu, MD,[d] Preethi Ramchand, MD,[e] Debabrata Mukherjee, MD,[f] Ramez Nairooz, MD,[g] William A. Gray, MD,[h] Christopher J. White, MD,[i] Michael R. Jaff, DO,[j] Kenneth Rosenfield, MD,[j] Jay Giri, MD[k,l]

RESULTS We analyzed 6,526 patients from 5 trials with a mean follow-up of 5.3 years. The composite outcome of periprocedural death, stroke, myocardial infarction (MI), or nonperiprocedural ipsilateral stroke was not significantly different between therapies (OR: 1.22; 95% CI: 0.94 to 1.59). The risk of any periprocedural stroke plus nonperiprocedural ipsilateral stroke was higher with CAS (OR: 1.50; 95% CI: 1.22 to 1.84). The risk of higher stroke with CAS was mostly attributed to periprocedural minor stroke (OR: 2.43; 95% CI: 1.71 to 3.46). CAS was associated with significantly lower risk of periprocedural MI (OR: 0.45; 95% CI: 0.27 to 0.75); cranial nerve palsy (OR: 0.07; 95% CI: 0.04 to 0.14); and the composite outcome of death, stroke, MI, or cranial nerve palsy during the periprocedural period (OR: 0.75; 95% CI: 0.60 to 0.93).

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 69, NO. 18, 2017

ISSN 0735-1097/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jacc.2017.02.053

Carotid Artery Stenting Versus Endarterectomy for Stroke Prevention

A Meta-Analysis of Clinical Trials

Partha Sardar, MD,[a] Saurav Chatterjee, MD,[b] Herbert D. Aronow, MD,[c] Amartya Kundu, MD,[d] Preethi Ramchand, MD,[e] Debabrata Mukherjee, MD,[f] Ramez Nairooz, MD,[g] William A. Gray, MD,[h] Christopher J. White, MD,[i] Michael R. Jaff, DO,[j] Kenneth Rosenfield, MD,[j] Jay Giri, MD[k,l]

RESULTS We analyzed 6,526 patients from 5 trials with a mean follow-up of 5.3 years. The composite outcome of periprocedural death, stroke, myocardial infarction (MI), or nonperiprocedural ipsilateral stroke was not significantly different between therapies (OR: 1.22; 95% CI: 0.94 to 1.59). The risk of any periprocedural stroke plus nonperiprocedural ipsilateral stroke was higher with CAS (OR: 1.50; 95% CI: 1.22 to 1.84). The risk of higher stroke with CAS was mostly attributed to periprocedural minor stroke (OR: 2.43; 95% CI: 1.71 to 3.46). CAS was associated with significantly lower risk of periprocedural MI (OR: 0.45; 95% CI: 0.27 to 0.75); cranial nerve palsy (OR: 0.07; 95% CI: 0.04 to 0.14); and the composite outcome of death, stroke, MI, or cranial nerve palsy during the periprocedural period (OR: 0.75; 95% CI: 0.60 to 0.93).

Table 4 Features associated with increased risk of stroke in patients with asymptomatic carotid stenosis treated medically (for details see Web Table 5

Clinical[a]	• Contralateral TIA/stroke[121]
Cerebral imaging	• Ipsilateral silent infarction[122]
Ultrasound imaging	• Stenosis progression (> 20%)[123] • Spontaneous embolization on transcranial Doppler (HITS)[124] • Impaired cerebral vascular reserve[125] • Large plaques[b126] • Echolucent plaques[96] • Increased juxta-luminal black (hypoechogenic) area[127]
MRA	• Intraplaque haemorrhage[128] • Lipid-rich necrotic core

HITS = high intensity transient signal; MRA = magnetic resonance angiography; TIA = transient ischaemic attack.

[a]Age is not a predictor of poorer outcome.

[b]More than 40 mm^2 on digital analysis.

– thrombus-containing
– documented progressive
– irregular and/or ulcerated
– contralateral ICA occlusion/stroke
– asymptomatic ipsilateral brain infarct

AbuRahma A et al. *Ann Surg*. 2003;238:551-562.
Ballotta E et al. *J Vasc Surg* 2007;45:516-522.
Kakkos SK et al. (ACSRS) *J Vasc Surg*. 2009;49:902-909.
Lovett JK et al. *Circulation* 2004;110:2190-97
Nicolaides AN et al. *J Vasc Surg* 2010;52:1486-96.
Tausskу P et al. *Neurosurg Focus* 2011;31:6-17.

Point to remember #6

Table 4 Features associated with increased risk of stroke in patients with asymptomatic carotid stenosis treated medically (for details see Web Table 5

Clinical[a]	• Contralateral TIA/stroke[121]
Cerebral imaging	• Ipsilateral silent infarction[122]
Ultrasound imaging	• Stenosis progression (> 20%)[123] • Spontaneous embolization on transcranial Doppler (HITS)[124] • Impaired cerebral vascular reserve[125] • Large plaques[b126] • Echolucent plaques[96] • Increased juxta-luminal black (hypoechogenic) area[127]
MRA	• Intraplaque haemorrhage[128] • Lipid-rich necrotic core

HITS = high intensity transient signal; MRA = magnetic resonance angiography; TIA = transient ischaemic attack.

[a]Age is not a predictor of poorer outcome.

[b]More than 40 mm^2 on digital analysis.

– thrombus-containing
– documented progressive
– irregular and/or ulcerated
– contralateral ICA occlusion/stroke
– asymptomatic ipsilateral brain infarct

AbuRahma A et al. *Ann Surg*. 2003;238:551-562.
Ballotta E et al. *J Vasc Surg* 2007;45:516-522.
Kakkos SK et al. (ACSRS) *J Vasc Surg*. 2009;49:902-909.
Lovett JK et al. *Circulation* 2004;110:2190-97
Nicolaides AN et al. *J Vasc Surg* 2010;52:1486-96.
Tausskу P et al. *Neurosurg Focus* 2011;31:6-17.

Spontaneous embolization (TCD) in **Symptomatic** patients admitted for CEA

results (ii)

spontaneous embolisation on pre-operative TCD

30 minutes TCD monitoring	current audit	preceding audits
accessible TCD window	83/100	189/212
embolus positive embolus negative	5 (6%) 78 (94%)	39 (21%) 150 (79%)

OR 4.1 (95%CI 1.5-10.7); p=0.0047

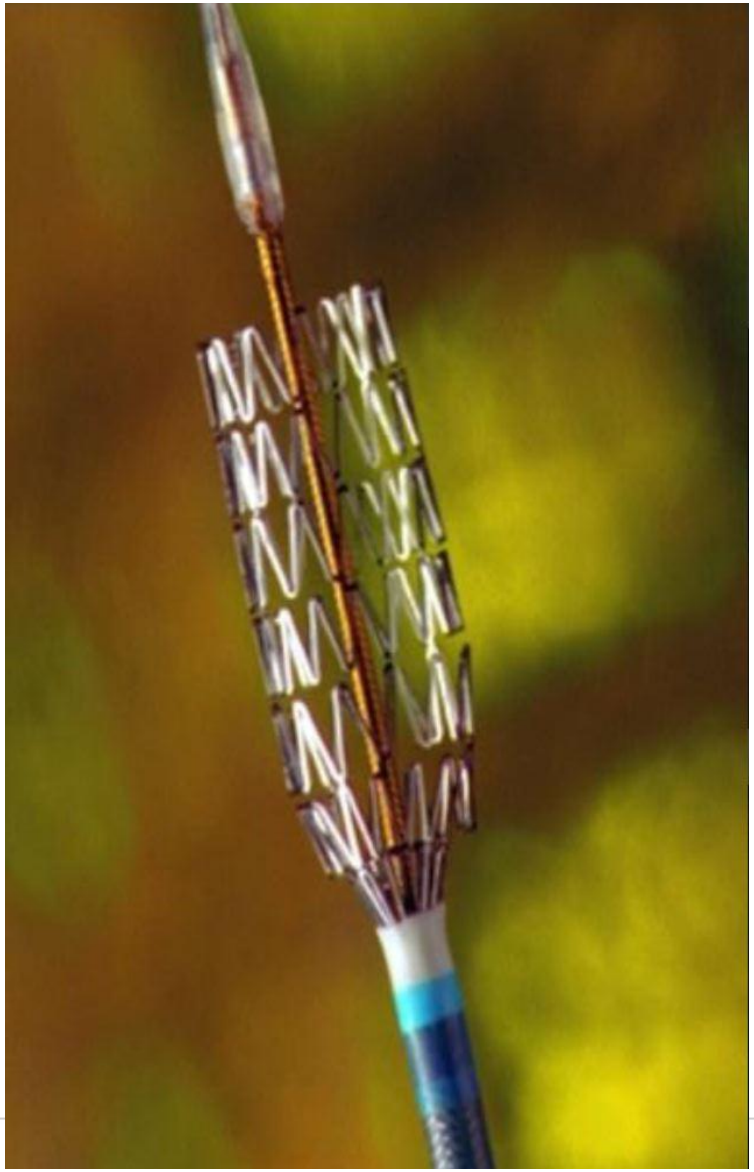
R Naylor, Charing Cross 2016

plus…

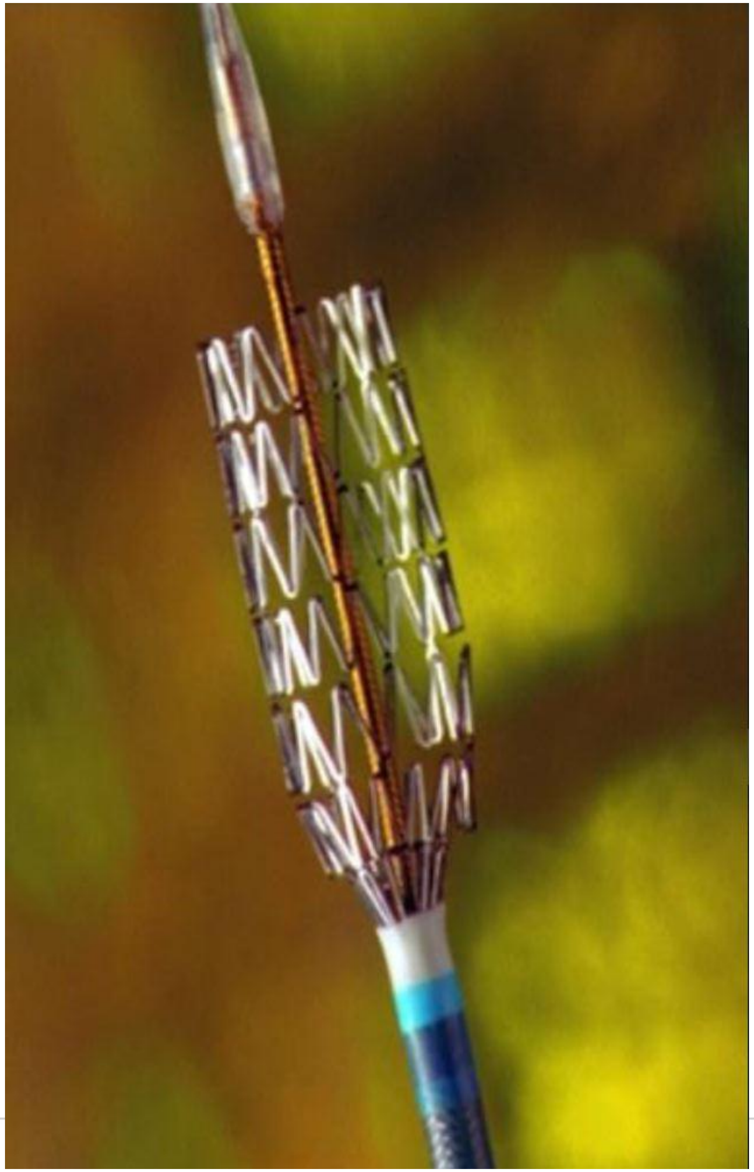
- **cumbersome**
- **poorly standardized**
- **poorly reproducible**

any practical value today in risk-stratification of Asymptomatic CS ?

Conventional Carotid Stents



Conventional Carotid Stents
Do Have A Problem

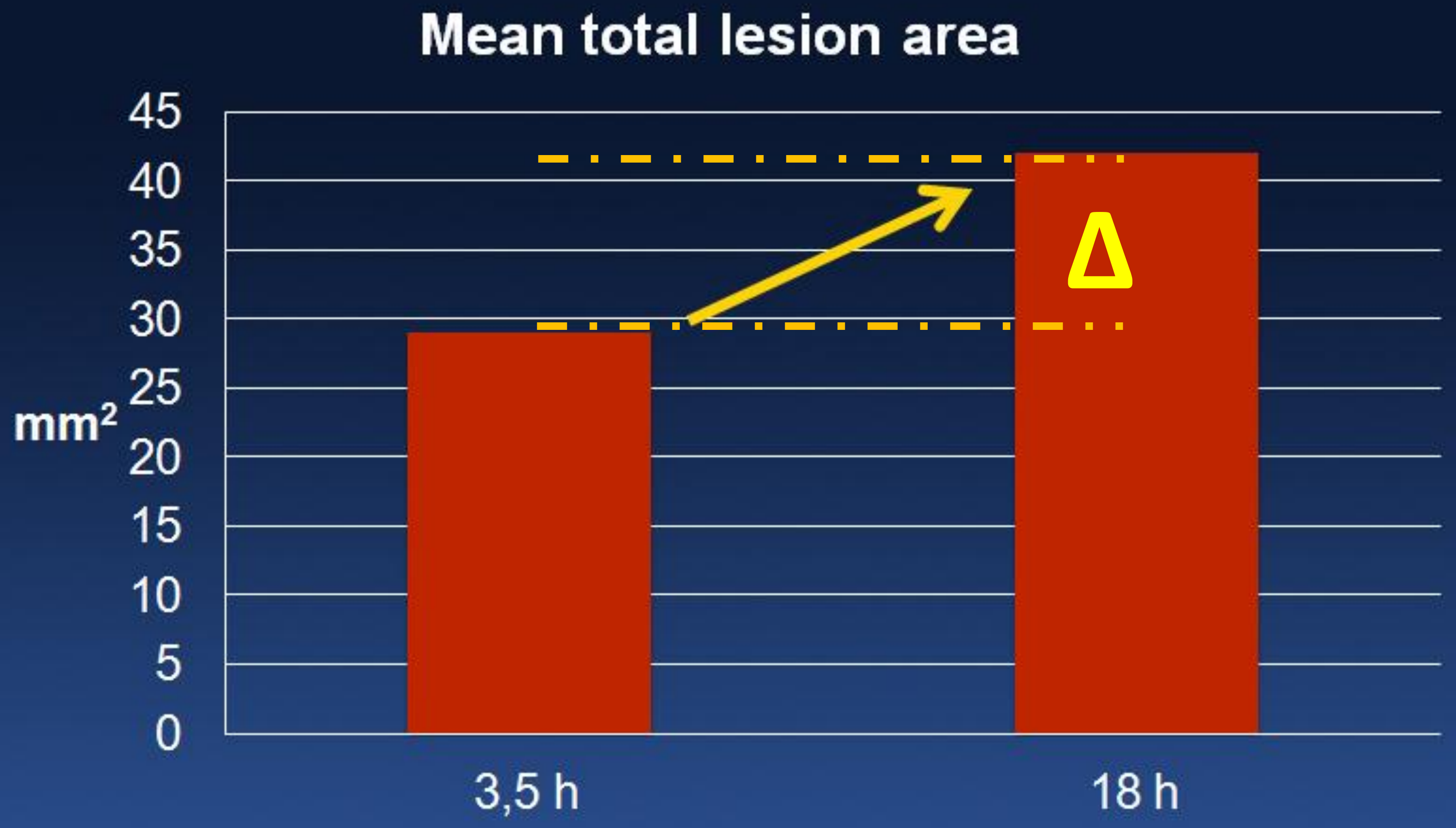


Human carotid artery treated using a conventional stent; OCT

Image courtesy Joan Rigla, MD PhD; Perceptual Imaging Lab, Univerity of Barcelona

Post-procedural Embolization with conventional carotid stents

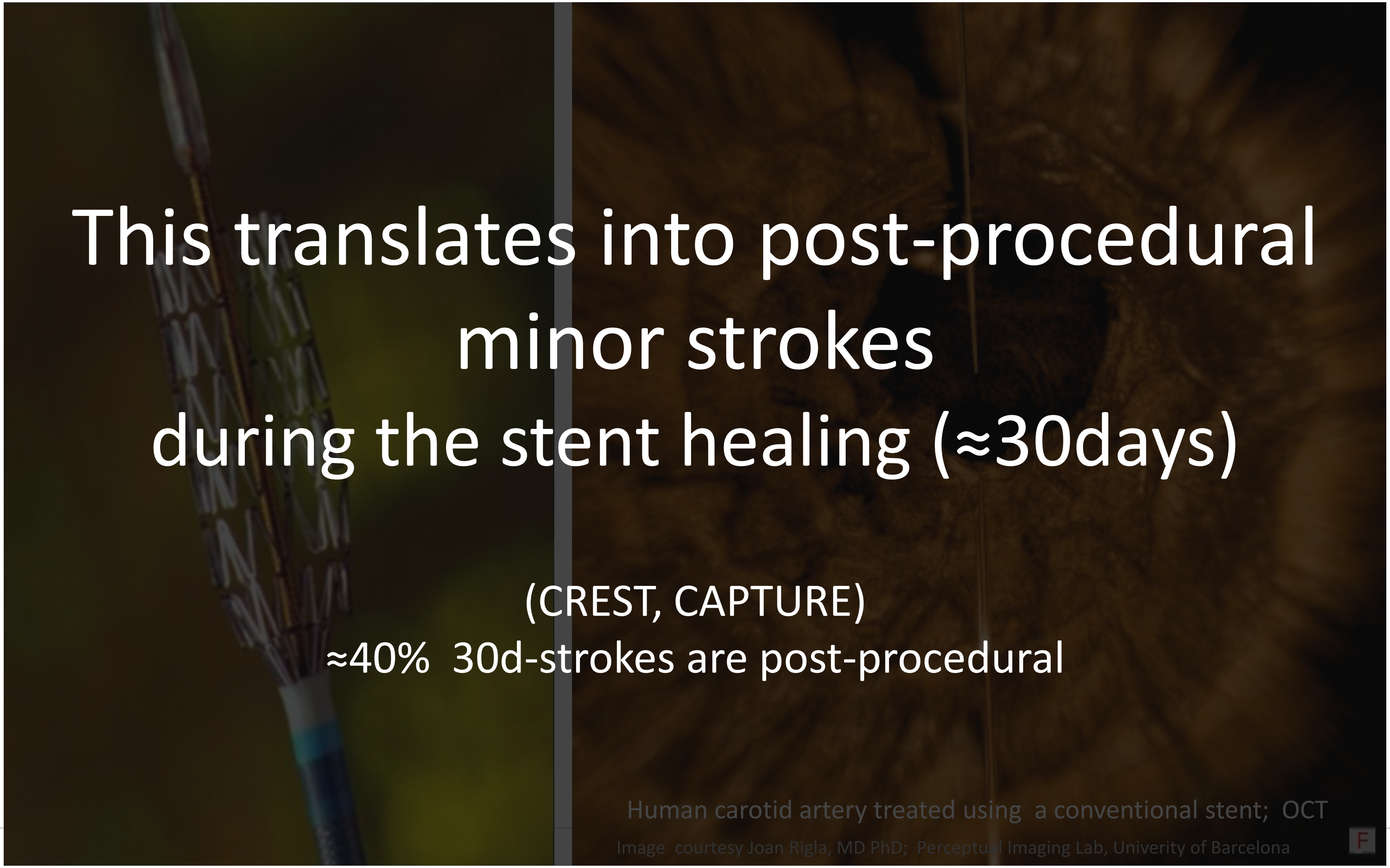
DW-MRI post CAS



Schofer J et al, JACC Cardiovasc interv 2008

Conventional Carotid Stents

Do Have A Problem



This translates into post-procedural minor strokes
during the stent healing (≈30days)

(CREST, CAPTURE)

≈40% 30d-strokes are post-procedural

Human carotid artery treated using a conventional stent; OCT

Image courtesy Joan Rigla, MD PhD; Perceptual Imaging Lab, Univerity of Barcelona

JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 10, NO. 8, 2017

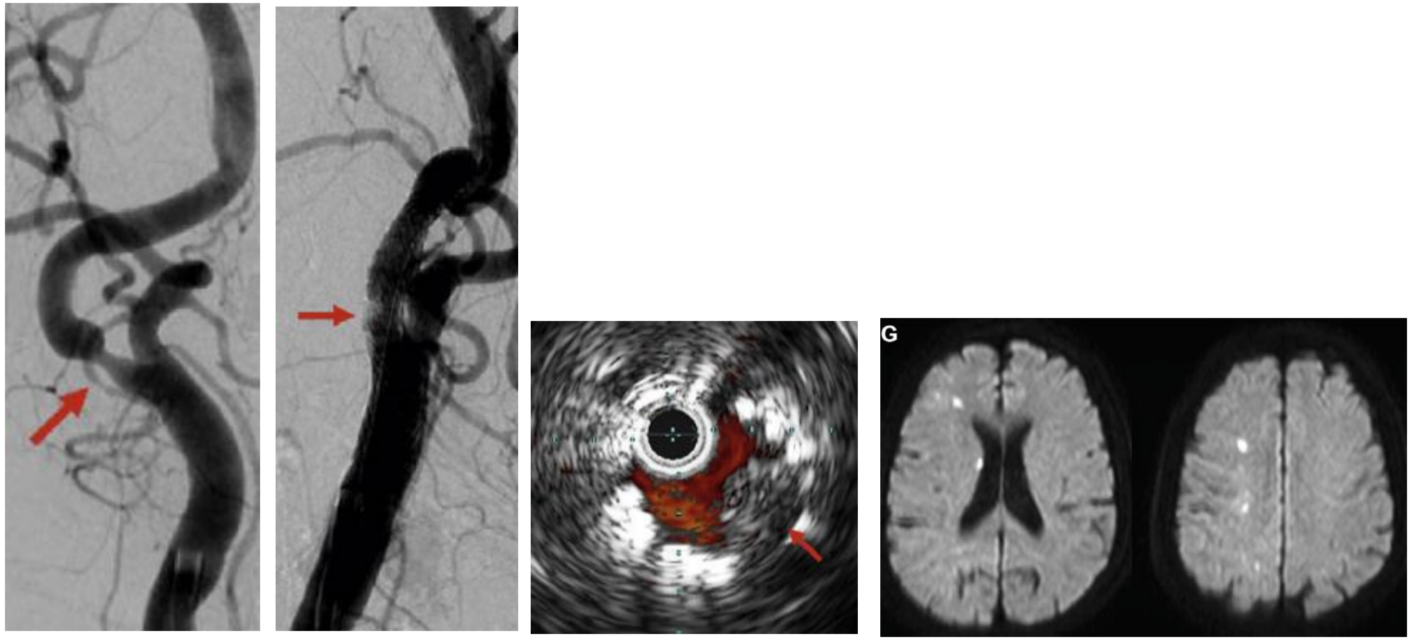
ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcin.2017.01.029

PERIPHERAL

Carotid Artery Stenting

Investigation of Plaque Protrusion Incidence and Prognosis

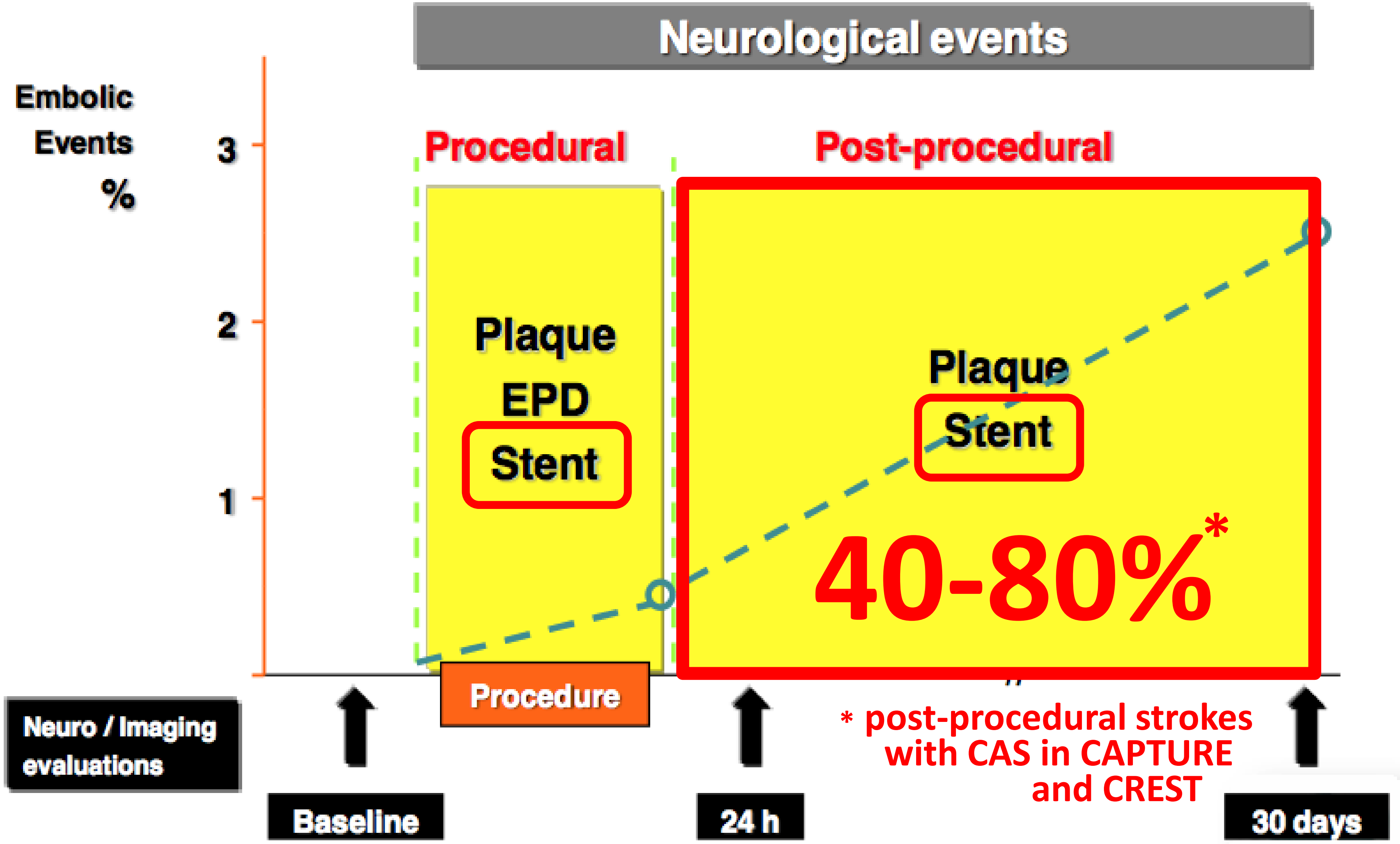
Masashi Kotsugi, MD,[a] Katsutoshi Takayama, MD,[b] Kaoru Myouchin, MD,[b] Takeshi Wada, MD,[c] Ichiro Nakagawa, MD,[d] Hiroyuki Nakagawa, MD,[c] Toshiaki Taoka, MD,[c] Shinichiro Kurokawa, MD,[a] Hiroyuki Nakase, MD,[d] Kimihiko Kichikawa, MD[c]



RESULTS PP was observed in 9 cases (2.6%). Ischemic stroke occurred in 6 of 9 PP cases (66.7%; 1 major, 5 minor). Ischemic lesions were observed on diffusion-weighted imaging in 8 of 9 cases (88.9%). PP was strongly associated with perioperative ischemic stroke. A significant increase in PP susceptibility was observed with open-cell stent use and unstable plaque.

CONCLUSIONS The incidence of PP in CAS was 2.6%, with a high risk of ischemic complications if PP was observed. The present findings indicate the necessity of appropriate device selection to avoid PP.

Timing of neuro-embolic events after CAS

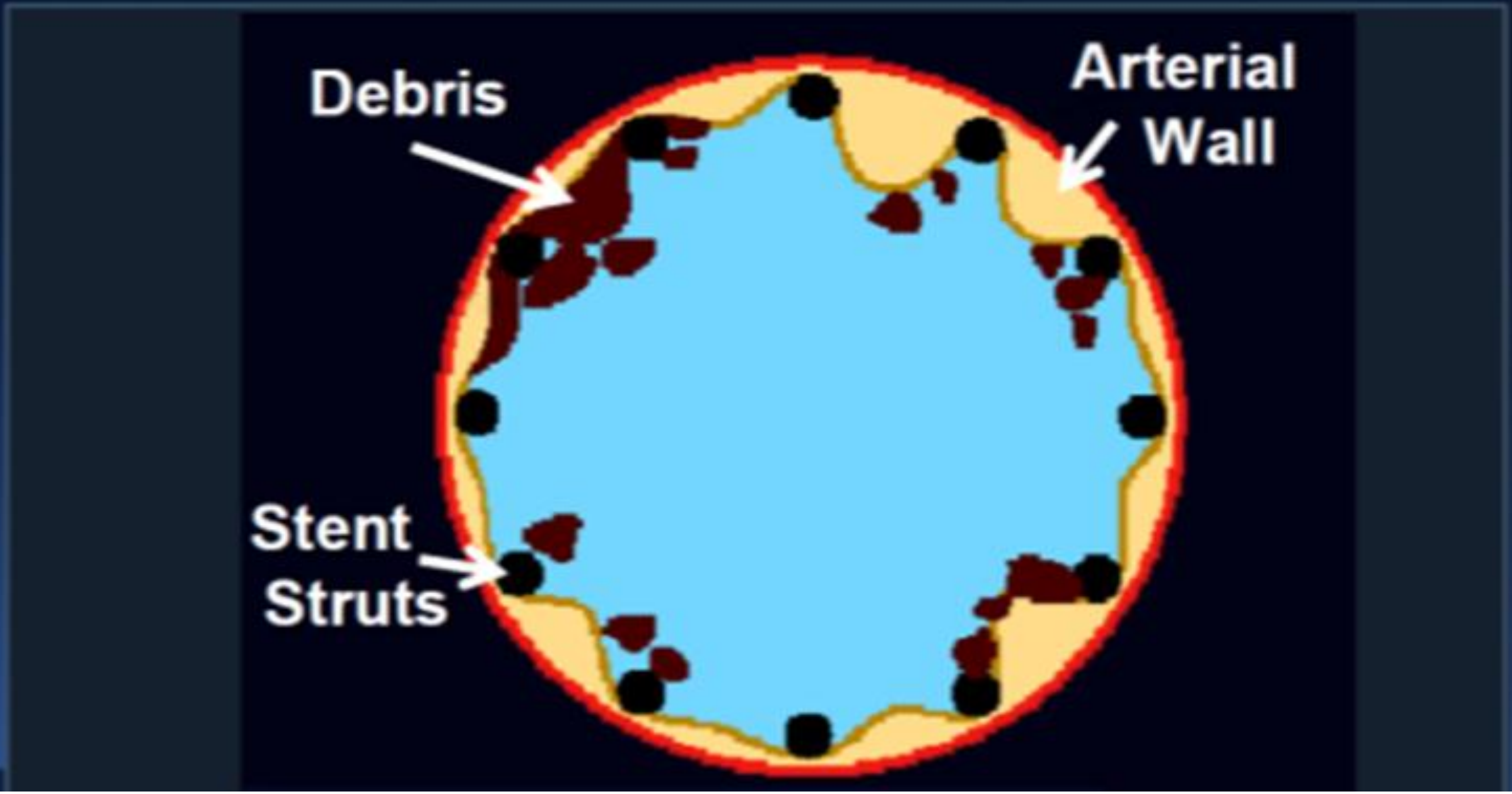


* post-procedural strokes with CAS in CAPTURE and CREST

D. McCormick TCT 2012, modified

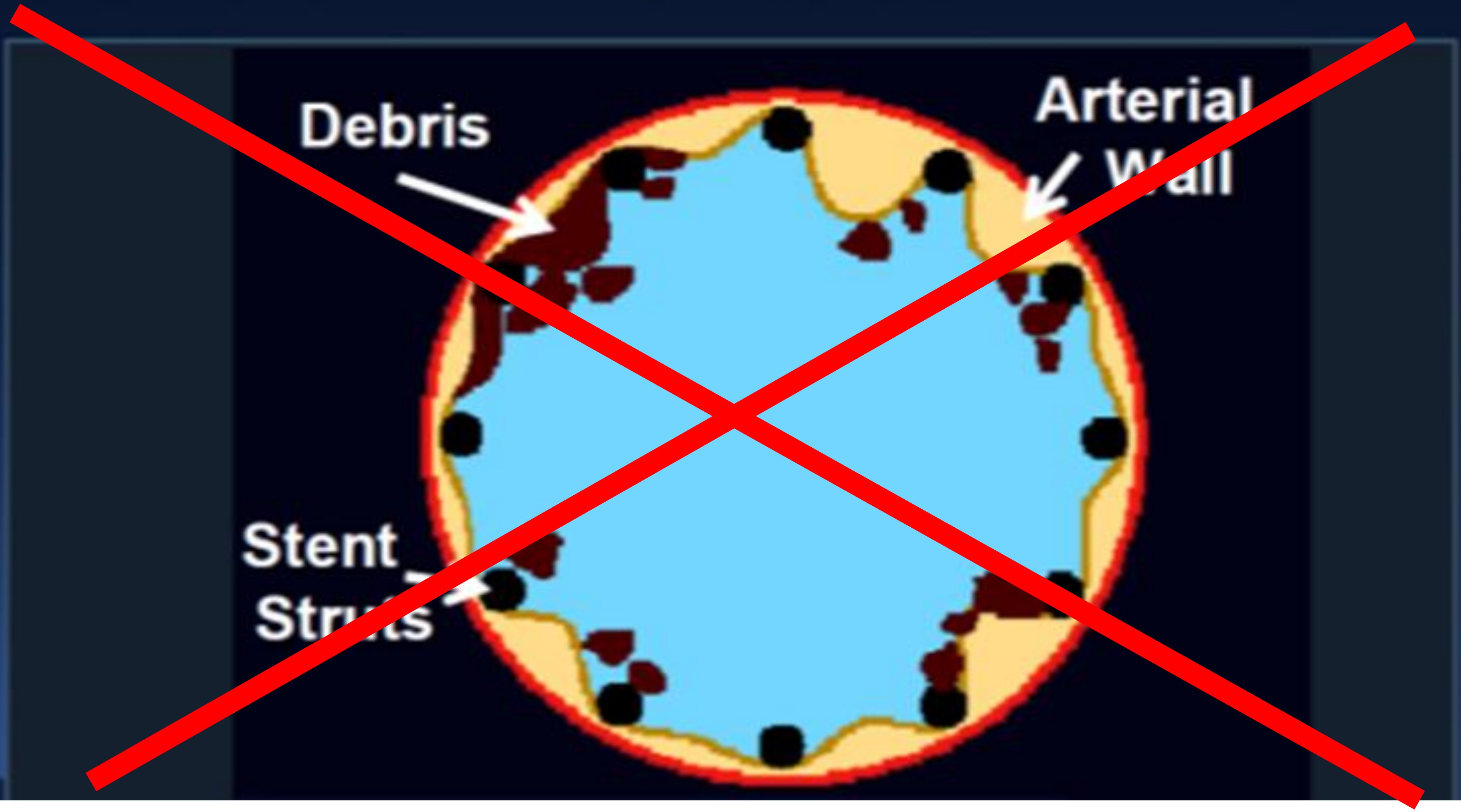
Conventional Carotid Stent

Plaque protrusion may lead to early and late distal embolization



Conventional Carotid Stent

Plaque protrusion may lead to early and late distal embolization



FUNDAMENTAL

- **CEA, by excluding the plaque, excludes the post-procedural problem of the plaque**

FUNDAMENTAL

- CEA, by excluding the plaque, excludes the post-procedural problem of the plaque

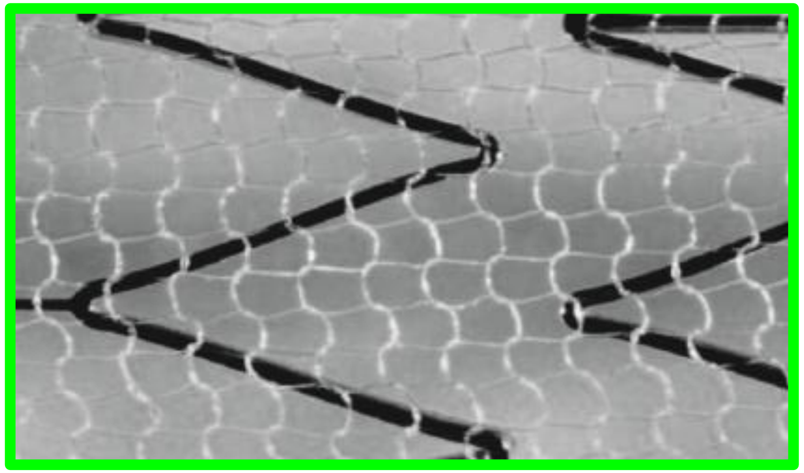
- In CAS, the stent needs to exclude the plaque too

FUNDAMENTAL

Point to remember #7

- CEA, by excluding the plaque, excludes the post-procedural problem of the plaque

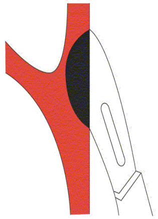
- In CAS, the **stent needs to exclude the plaque too**



- <u>Periprocedural embolization</u> *may be protected with EPD* (mesh stent, once implanted, may inhibit the plaque embolic potential)

- <u>Post-procedural</u> embolization *may not be protected with EPD but it may be protected with improved stent design - Mesh Stents*

Stenting vs. Surgery

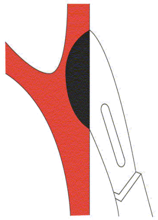


ACST-2

Collaborators are free to use their usual techniques

GA or LA; Primary or patch closure…

Any CE marked stent. EPD not mandated



ACST-2

Collaborators are free to use their usual techniques

GA or LA; Primary or patch closure…

Any CE marked stent. EPD <u>not mandated</u>

ACST-2 Recruitment target = 3600

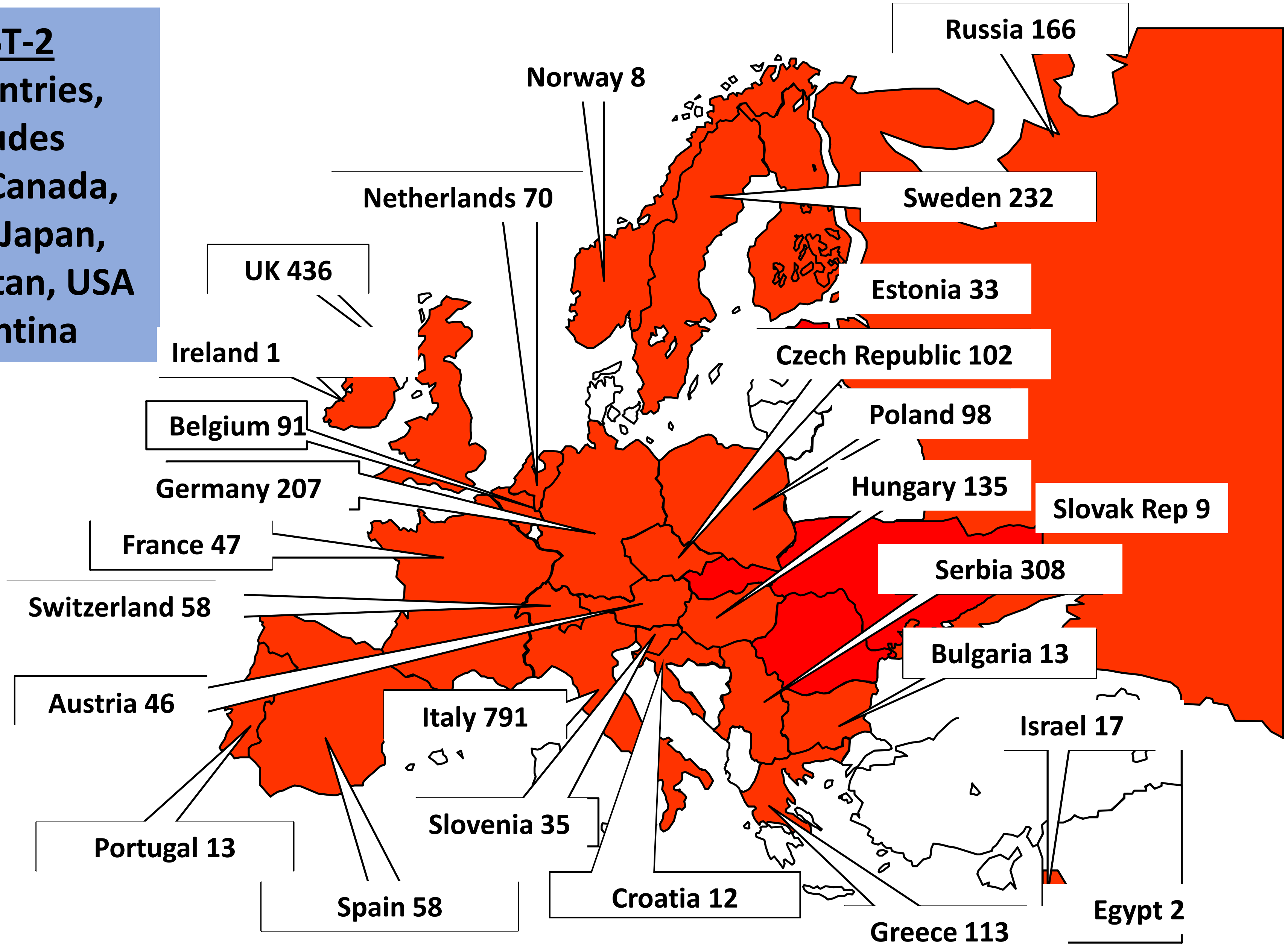
3400 (95% total)

Mean follow-up 2019
CEA: 4.0 person-years CAS: 4.0 person-years

Overall peri-procedural Death/Major Stroke

≈1%

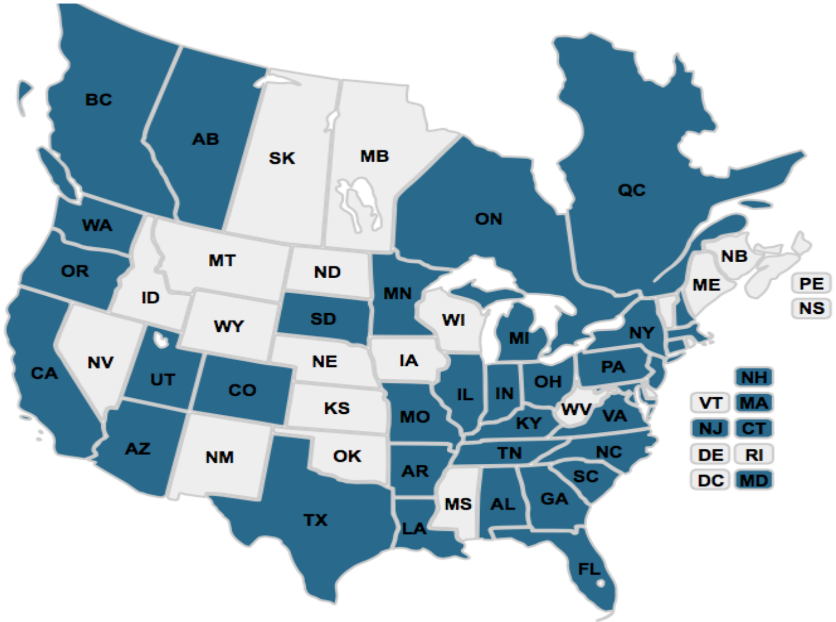
ACST-2
33 countries, includes Brazil, Canada, China, Japan, Kazakhstan, USA Argentina



The Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Study

CREST-2

Health and Hope for Patients at Risk for Stroke



Enrollment >> half-way
(119 Centers;
1479 of 2480 Participants)

vs 2 CEA or 3 CAS

The success of CREST-2…
(OMT + Intervention in asympt. CS vs OMT only)

will critically depend on

1. Effective recruitment (inclusion) of HIGH-risk asympt. CS pts

2. Safe intervention (CEA arm, CAS arm)

HIGH-risk asympt. CS pts naturally gravitate towards Intervention

(RCT patient selection bias)

Eur J Vasc Endovasc Surg (2016) 51, 761—765

SPACE-2: A Missed Opportunity to Compare Carotid Endarterectomy, Carotid Stenting, and Best Medical Treatment in Patients with Asymptomatic Carotid Stenoses

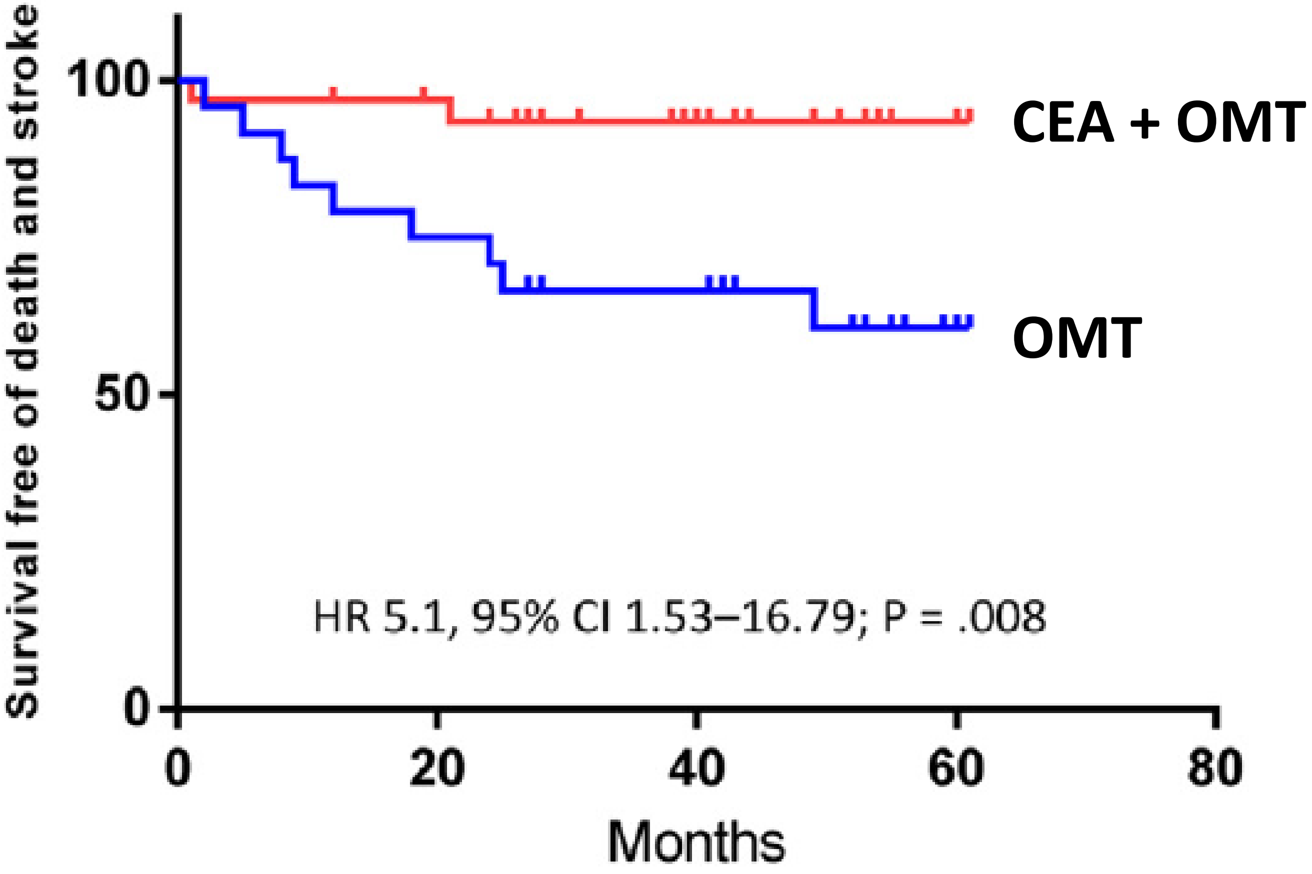
H.-H. Eckstein [a], T. Reiff [b], P. Ringleb [b], O. Jansen [c], U. Mansmann [d], W. Hacke [b,*], on behalf of the SPACE 2 Investigators

[a] Department of Vascular and Endovascular Surgery, Technical University of Munich, Munich, Germany
[b] Department of Neurology, University of Heidelberg, Heidelberg, Germany
[c] Department of Radiology and Neuroradiology, UKSH Campus Kiel, Kiel, Germany
[d] Institute of Medical Informatics, Biometry and Epidemiology, Ludwig Maximilian University Munich, Munich, Germany

WHAT THIS PAPER ADDS

Despite being considered to be a very important study, the SPACE-2 randomized trial had to be abandoned after recruiting only 513 patients. Reasons for the poor recruitment rates were multifactorial and included patient unwillingness to accept medical therapy alone (having originally been referred for an intervention), the availability of reimbursement for CEA and CAS outwith the trial despite a lack of high-quality evidence justifying any intervention, and financial 'penalties' to hospitals/clinicians because patients randomized to BMT did not attract additional reimbursement. There are important lessons to be learned for future RCTs.

AMTEC RCT in Asymptomatic CS: Trial **STOPPED** by DSMB



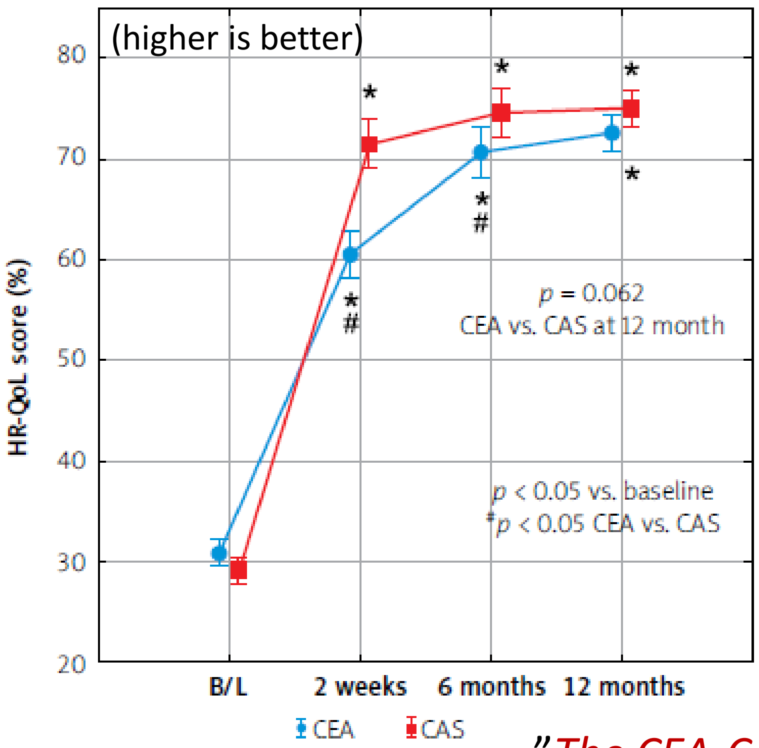
Kolos et al. *J Vasc Surg* 2015

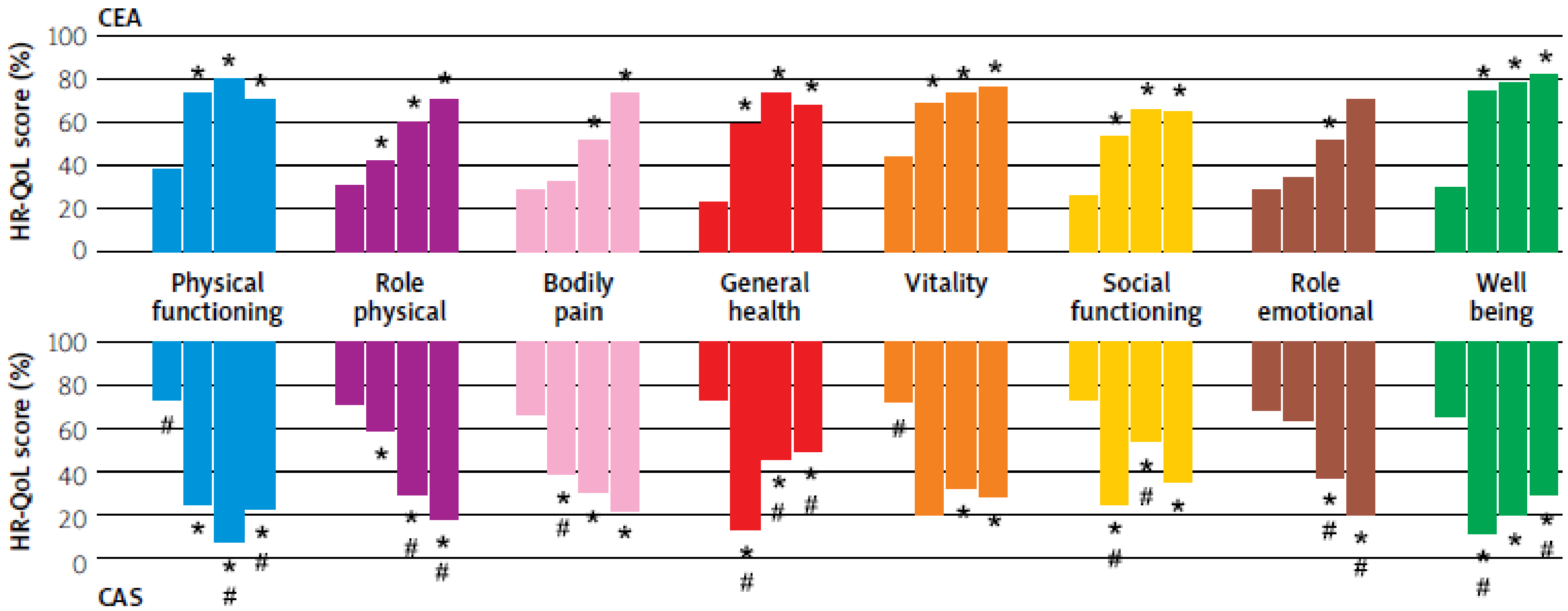
Given the lack of significant differences in baseline parameters between groups and a significant increase in the number of primary composite end point in the group of MMT (6.5% and 37.5%, *P* = .008), 10 of the 12 committee members decided to stop patient recruitment at the second meeting.

Impact of the Tx mode on the QoL

Health-related quality of life in ischaemic stroke survivors after carotid endarterectomy (CEA) and carotid artery stenting (CAS): confounder-controlled analysis

Adv Interv Cardiol
DOI: https://doi.org/10.5114/aic.2019.84441





*p < 0.05 vs. baseline, #p < 0.05 CEA vs. CAS for each of the 8 SF-36 domains, the 4 bars show sequentially the mean score at baseline, 2 weeks, 6 months and 12 months.

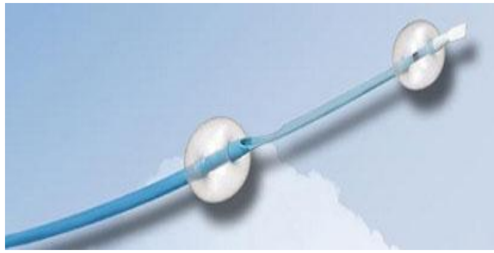
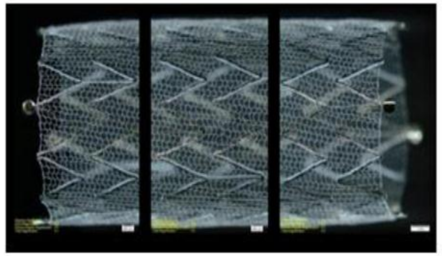
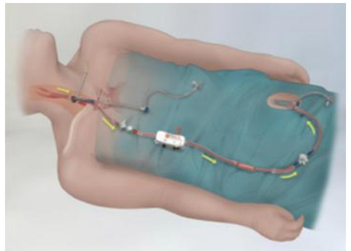
"The CEA-CAS difference was driven by less bodily pain and better physical functioning/role-physical plus better role-emotional and higher general well-being scores in CAS (p < 0.05)"

Modern CAS therapy

Statins and DAPT lower peri-procedural risk and ...

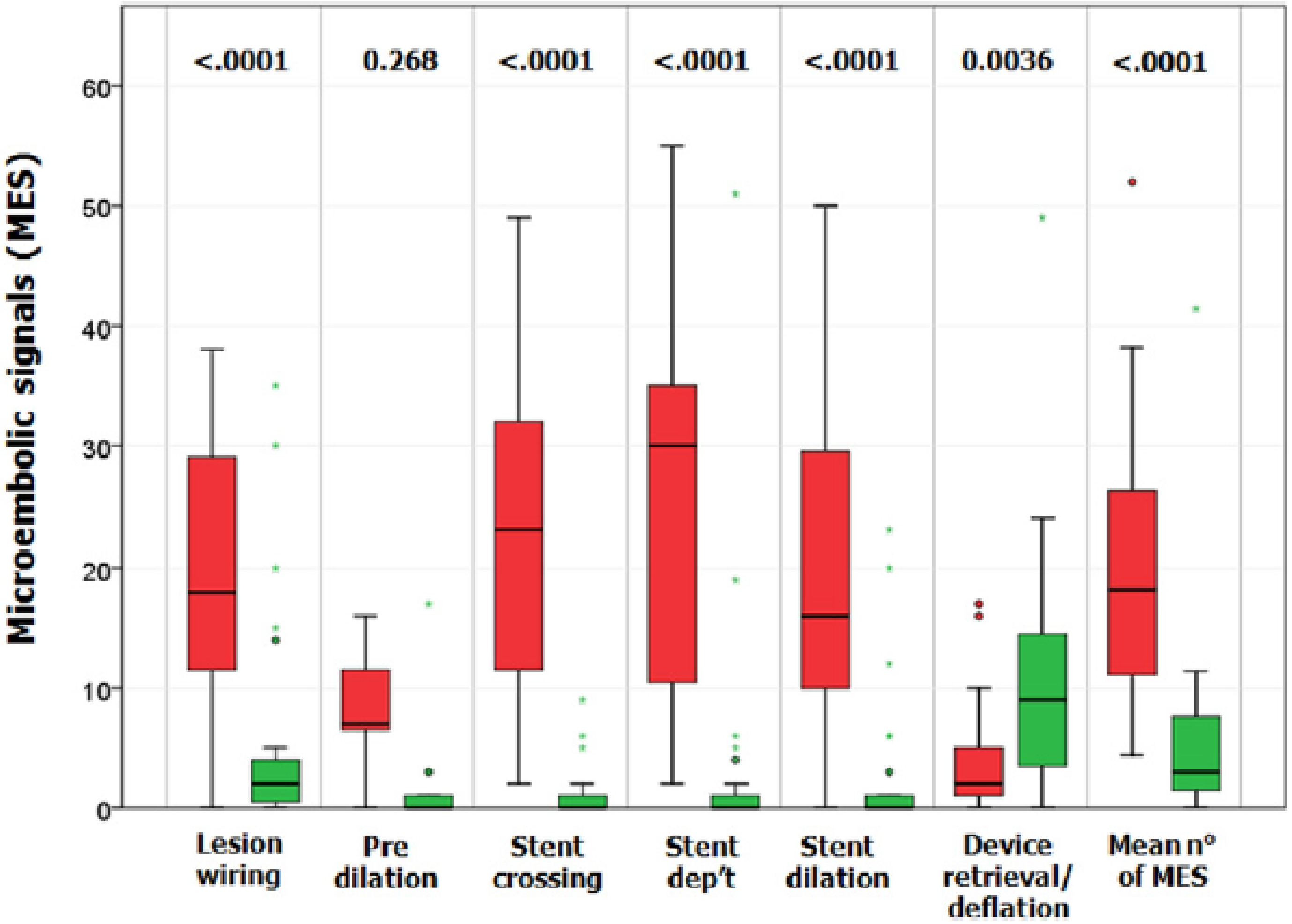
- Newer stent designs
- Flow reversal (MOMA)
- Direct cervical access (TCAR)
- Greater experience

Can reduce risk further

Microembolization During Carotid Artery Stenting

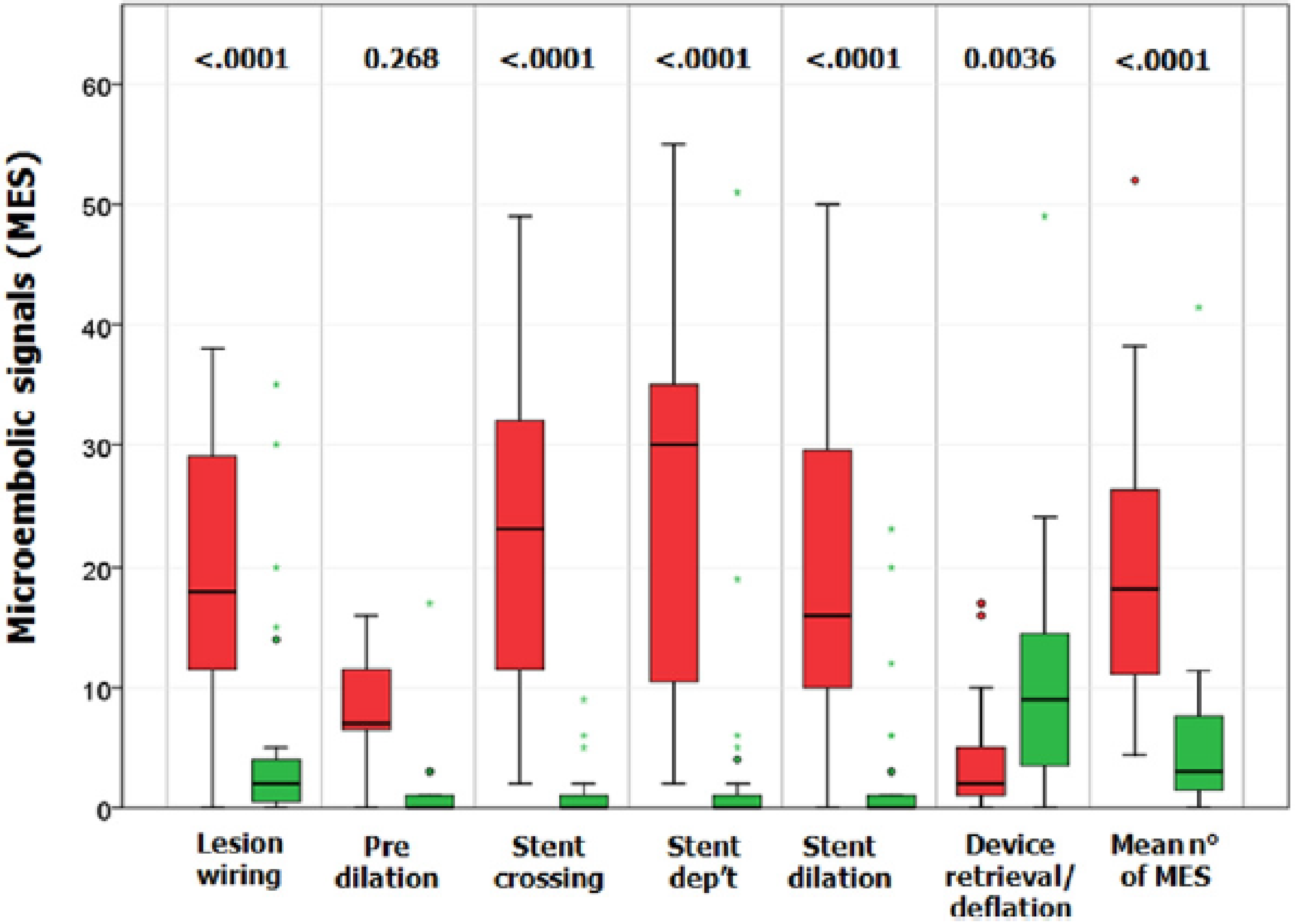
A Randomized Trial of Proximal Versus Distal Cerebral Protection



Montorsi P et al. JACC

Microembolization During Carotid Artery Stenting

A Randomized Trial of Proximal Versus Distal Cerebral Protection

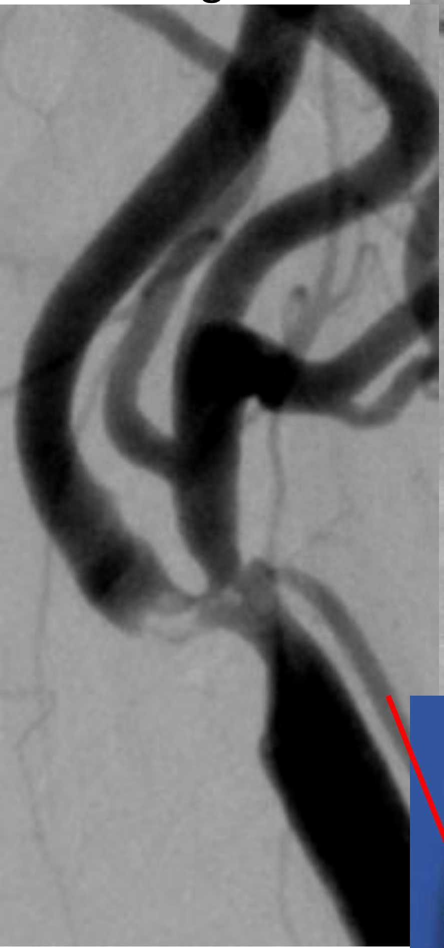


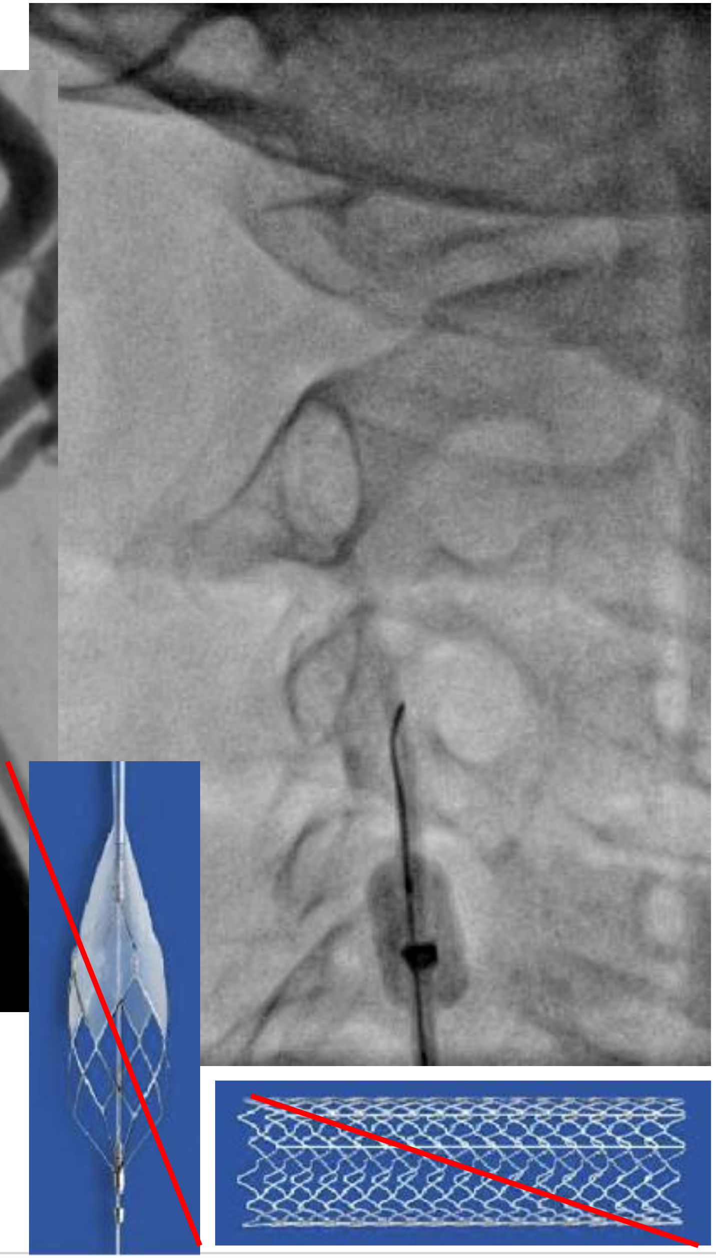
Montorsi P et al. JACC

63-yo woman
recurrent TIAs
Stroke-in-evolution

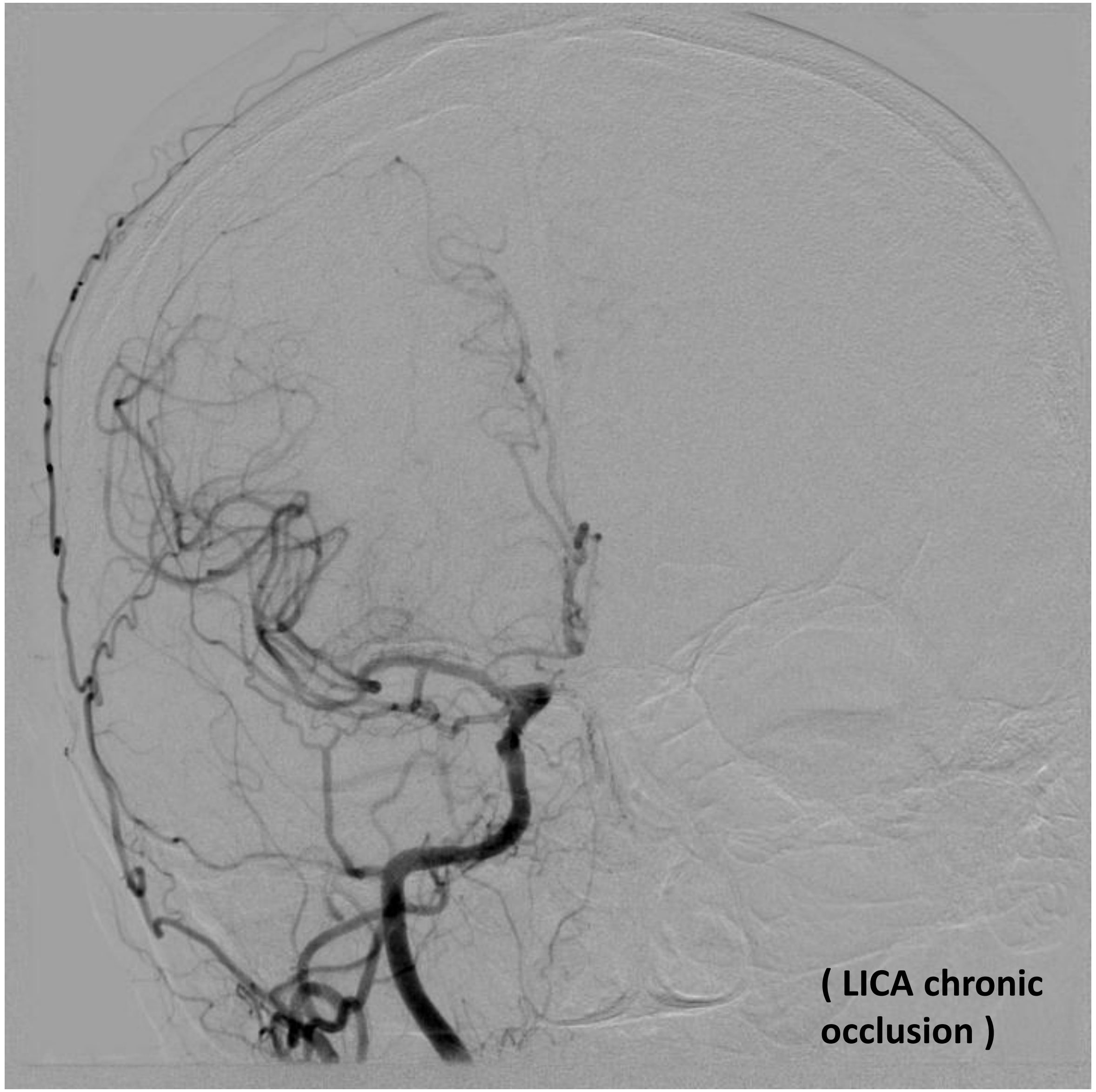
63-yo woman
recurrent TIAs
Evolving Stroke

Severe HF + severe COPD

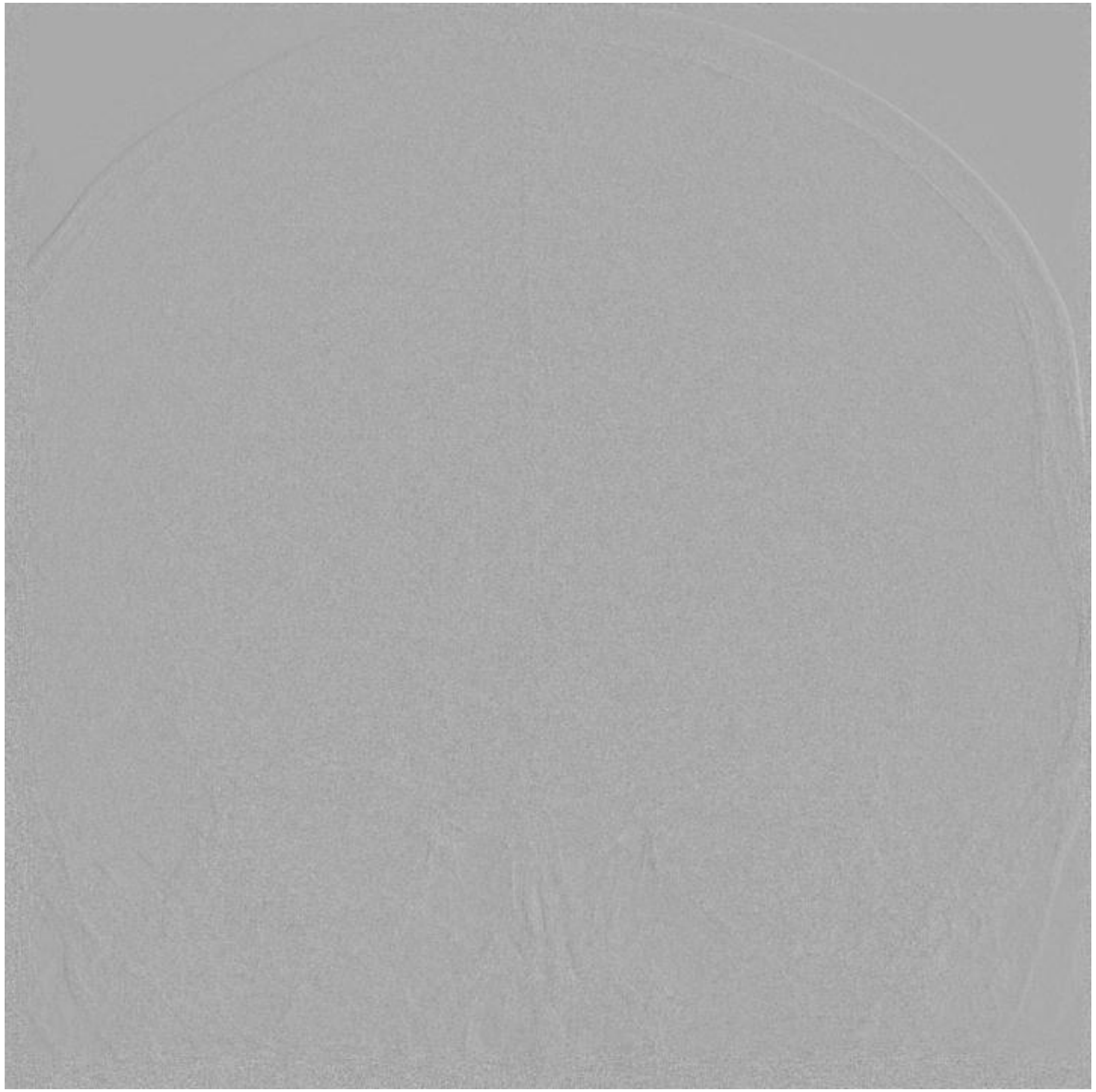




Evolving Stroke

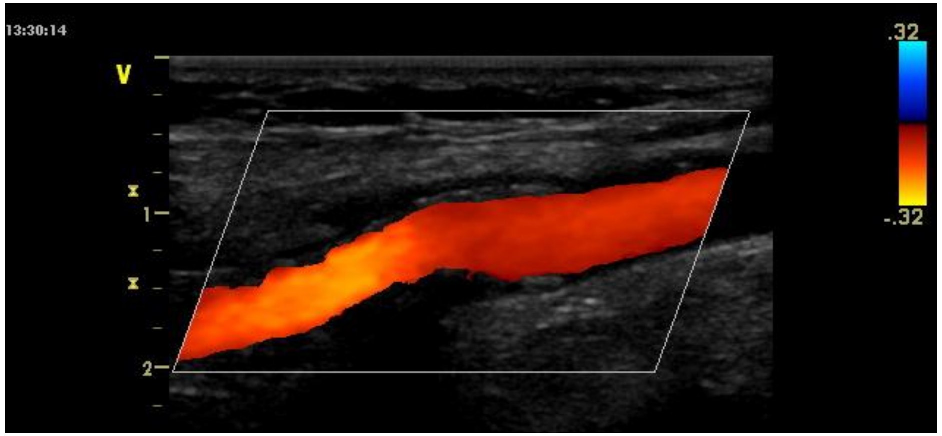


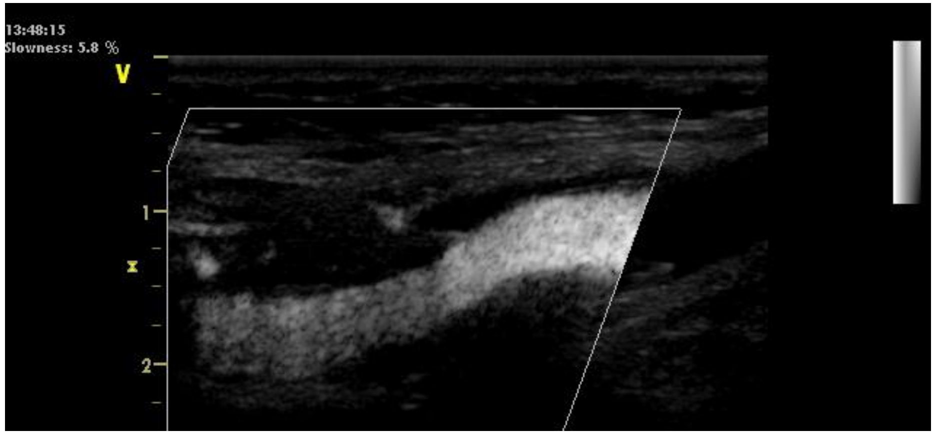
Safe, effective, minimally-invasive therapeutic procedure



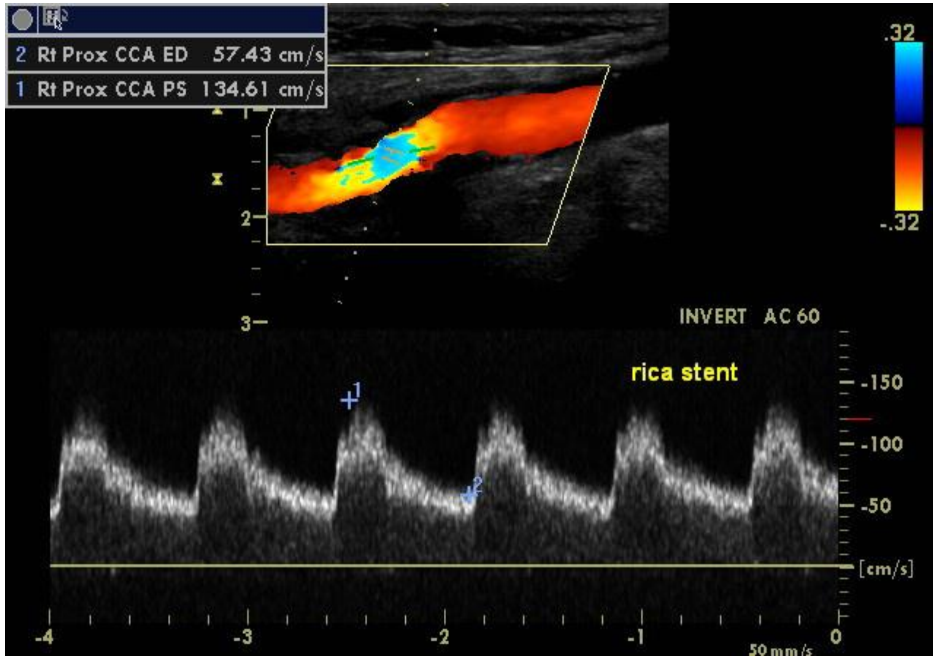
Point to remember #8

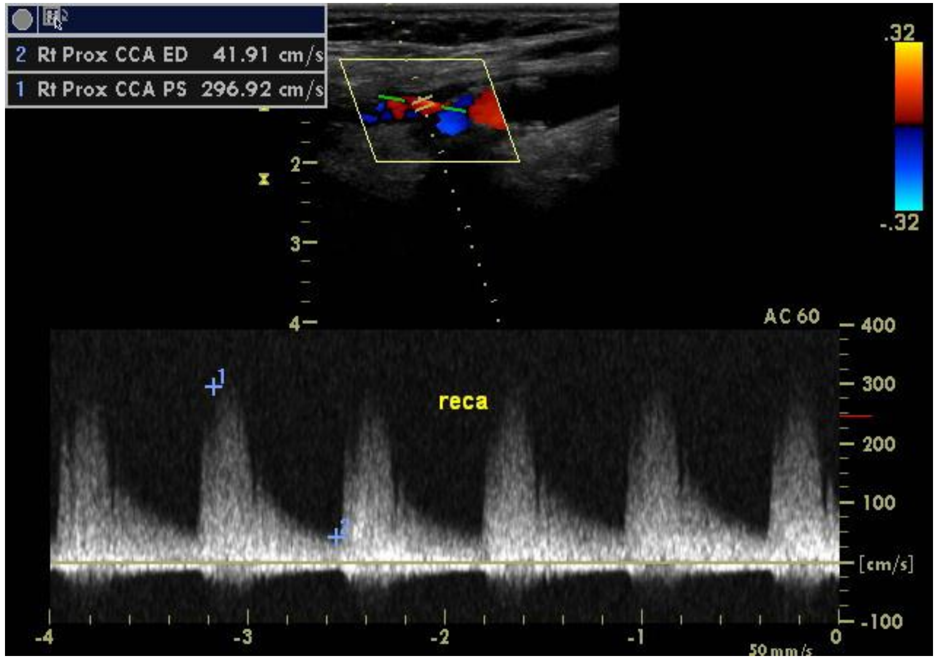
Patient A/S, discharged home @ Day2 post procedure





Normal stent image





Normal velocities

ECA patent

Study ID	ES	95% CI	N
Bijuklic K. et al. 2012	-1.05	-1.58 , -0.52	62
Cano N.M. et al. 2013	-0.54	-1.06 , -0.03	60
Castro-Afonso LH. et al. 2013	0.64	0.00 , 1.28	40
El-Koussy M. et al. 2007	-0.61	-1.22 , -0.00	44
Flach Z.H. et al. 2007	0.37	-0.38 , 1.11	33
Leal I. et al. 2012	-0.60	-1.10 , -0.10	64
Montorsi P. et al. 2011	-0.52	-1.21 , 0.17	35
Taha M.M. et al. 2009	-1.25	-2.42 , -0.08	19
Overall (random-effects model)	-0.43	-0.84 , -0.02	357

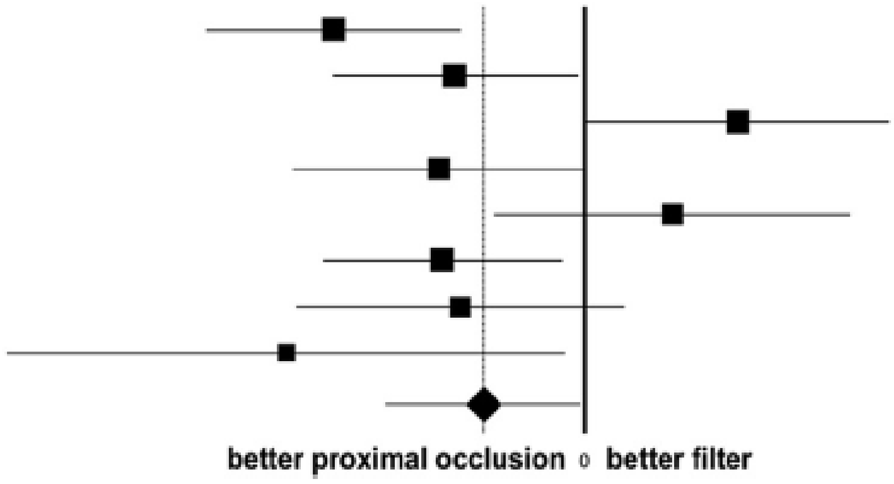
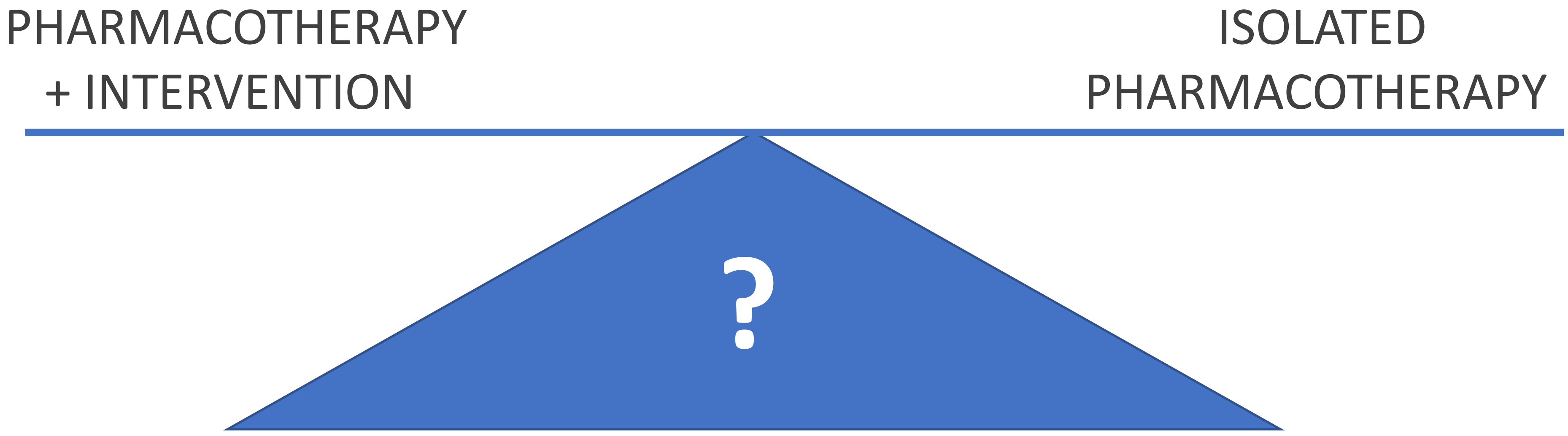


FIGURE 2 **Incidence of New Ischemic Lesions/Patient at DW-MRI**

Forrest plot representing the pooled estimate analysis for overall incidence of new ischemic lesions/patient detected at diffusion-weighted magnetic resonance imaging (DW-MRI). CI = confidence interval; ES = effect size.

Why the management of asymptomatic Carotid Stenosis continues to be so controversial ?

A/S Carotid Stenosis
Decision-making



A/S Carotid Stenosis
Decision-making

PHARMACOTHERAPY
+ INTERVENTION

ISOLATED
PHARMACOTHERAPY

Point to remember #9

A/S Carotid Stenosis Decision-making

PHARMACOTHERAPY + INTERVENTION

ISOLATED PHARMACOTHERAPY

RISK OF PROCEDURE

Effective Cerebral Protection, Effective Stent, Operator Skills

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 11, NO. 23, 2018

PUBLISHED BY ELSEVIER

Use of Dual-Layered Stents in Endovascular Treatment of Extracranial Stenosis of the Internal Carotid Artery

Results of a Patient-Based Meta-Analysis of 4 Clinical Studies

Eugenio Stabile, MD, PhD,[a] Gianmarco de Donato, MD, PhD,[b] Piotr Musialek, MD, PhD,[c] Koen De Loose, MD,[d] Roberto Nerla, MD,[e] Pasqualino Sirignano, MD,[f] Salvatore Chianese, MD,[a] Adam Mazurek, MD,[c] Tullio Tesorio, MD,[g] Marc Bosiers, MD,[d] Carlo Setacci, MD,[b] Francesco Speziale, MD,[f] Antonio Micari, MD,[d] Giovanni Esposito, MD, PhD[a]

TABLE 2 Incidence of Adverse Clinical Events up to 30 Days of Follow-Up

	Peri-Procedural (in Hospital)	Discharge to 30 Days	Total 30 Days
Minor stroke	1.07 (6)	0.17 (1)	1.25 (7)
Major stroke	0 (0)	0 (0)	0 (0)
Death	0 (0)	0.17 (1)	0.17 (1)
Any stroke and death	% 1.07 (6)	0.36 (2)	% 1.44 (8)

Patient-level meta-analysis

30-day

4 clinical trials

556 patients

(both symptomatic and asymptomatic)

Stabile et al. 2018

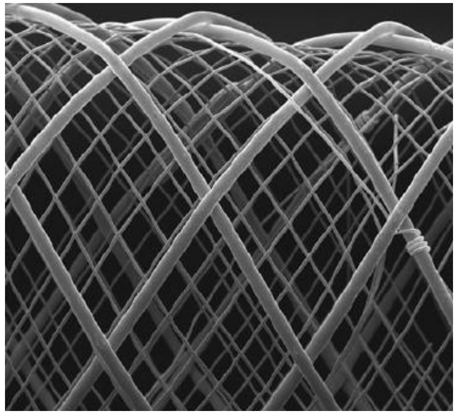
JACC: CARDIOVASCULAR INTERVENTIONS VOL. 11, NO. 23, 2018

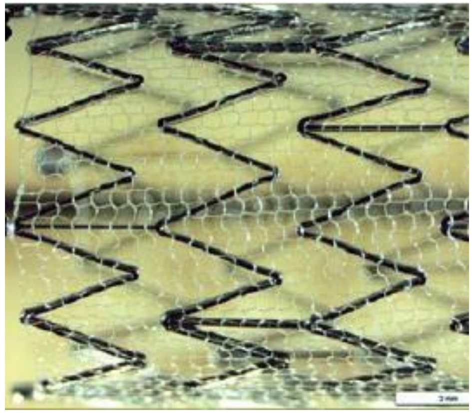
PUBLISHED BY ELSEVIER

Use of Dual-Layered Stents in Endovascular Treatment of Extracranial Stenosis of the Internal Carotid Artery

Results of a Patient-Based Meta-Analysis of 4 Clinical Studies

Eugenio Stabile, MD, PhD,[a] Gianmarco de Donato, MD, PhD,[b] Piotr Musialek, MD, PhD,[c] Koen De Loose, MD,[d] Roberto Nerla, MD,[e] Pasqualino Sirignano, MD,[f] Salvatore Chianese, MD,[a] Adam Mazurek, MD,[c] Tullio Tesorio, MD,[g] Marc Bosiers, MD,[d] Carlo Setacci, MD,[b] Francesco Speziale, MD,[f] Antonio Micari, MD,[d] Giovanni Esposito, MD, PhD[a]





"This meta-analysis suggests that DLS can be *safely* used for CAS, and their use minimizes the incremental risk related to symptomatic status and other risk factors".

TABLE 3 Clinical and Procedural Characteristics Affecting the Occurrence of In-Hospital Stroke

	Incidence in Patients With the Characteristic	Incidence in Patients Without the Characteristic	Relative Risk	Odds Ratio (95% CI)	p Value
Octogenarians	0	1.3 (6)	0	0	0.63
Smoking	1.4 (5)	0.4 (1)	3.22	3.25 (0.37-27.79)	0.73
Hypertension	2.2 (5)	0.2 (1)	7.57	7.73 (0.10-7.65)	0.18
Diabetes	1.1 (2)	1.0 (4)	1.1	1.10 (0.20-6.07)	0.99
Dyslipidemia	1.2 (5)	0.7 (1)	1.71	1.72 (0.20-14.75)	0.96
Symptomatic status	1.0 (1)	1 (5)	0.95	0.95 (0.11-8.23)	0.99
Use of protection system	1.1 (6)	0			0.91
Use of proximal protection	0	1.6 (6)	0	0	0.52
Pre-dilatation	1.0 (2)	1.1 (4)	0.94	0.93 (0.17-5.15)	0.99
Roadsaver stent	0	1.9 (6)	0	0	0.17
Post-dilatation	0.9 (5)	2.9 (1)	0.32	0.31 (0.03-2.80)	0.75

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 11, NO. 23, 2018

PUBLISHED BY ELSEVIER

Use of Dual-Layered Stents in Endovascular Treatment of Extracranial Stenosis of the Internal Carotid Artery

Results of a Patient-Based Meta-Analysis of 4 Clinical Studies

Eugenio Stabile, MD, PhD,[a] Gianmarco de Donato, MD, PhD,[b] Piotr Musialek, MD, PhD,[c] Koen De Loose, MD,[d] Roberto Nerla, MD,[e] Pasqualino Sirignano, MD,[f] Salvatore Chianese, MD,[a] Adam Mazurek, MD,[c] Tullio Tesorio, MD,[g] Marc Bosiers, MD,[d] Carlo Setacci, MD,[b] Francesco Speziale, MD,[f] Antonio Micari, MD,[d] Giovanni Esposito, MD, PhD[a]

"This meta-analysis suggests that DLS can be *safely* used for CAS, and their use minimizes the incremental risk related to symptomatic status and other risk factors".

TABLE 3 Clinical and Procedural Characteristics Affecting the Occurrence of In-Hospital Stroke

	Incidence in Patients With the Characteristic	Incidence in Patients Without the Characteristic	Relative Risk	Odds Ratio (95% CI)	p Value
Octogenarians	0	1.3 (6)	0	0	0.63
Smoking	1.4 (5)	0.4 (1)	3.22	3.25 (0.37–27.79)	0.73
Hypertension	2.2 (5)	0.2 (1)	7.57	7.73 (0.10–7.65)	0.18
Diabetes	1.1 (2)	1.0 (4)	1.1	1.10 (0.20–6.07)	0.99
Dyslipidemia	1.2 (5)	0.7 (1)	1.71	1.72 (0.20–14.75)	0.96
Symptomatic status	1.0 (1)	1 (5)	0.95	0.95 (0.11–8.23)	0.99
Use of protection system	1.1 (6)	0			0.91
Use of proximal protection	0	1.6 (6)	0	0	0.52
Pre-dilatation	1.0 (2)	1.1 (4)	0.94	0.93 (0.17–5.15)	0.99
Roadsaver stent	0	1.9 (6)	0	0	0.17
Post-dilatation	0.9 (5)	2.9 (1)	0.32	0.31 (0.03–2.80)	0.75

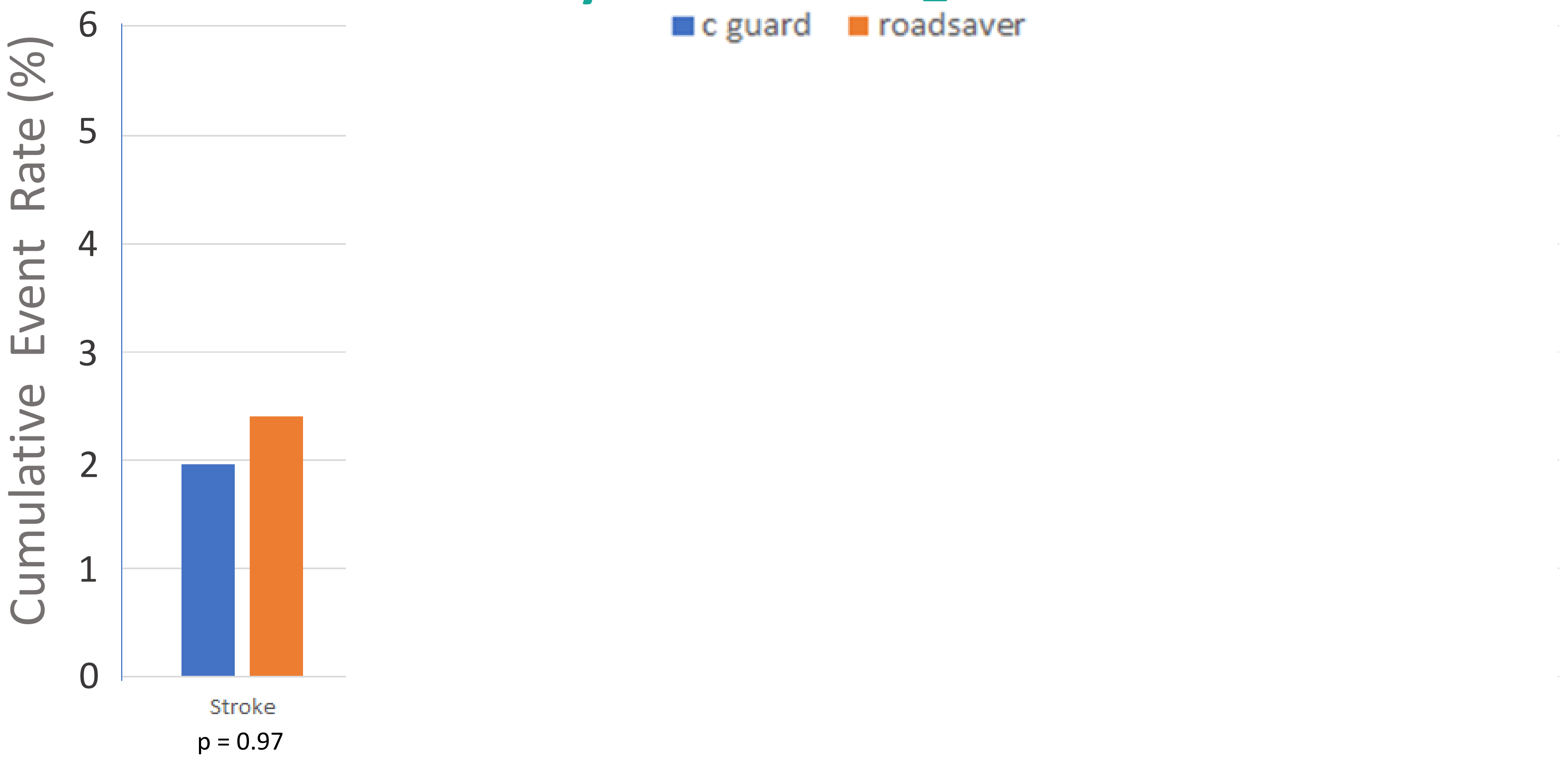
Patient-level meta-analysis

556 patients / 4 trials

(both symptomatic and asymptomatic)

Dual-layer stents
1-year data

Results at one year according to Stent Platform



ESC Congress Paris 2019

Stabile et al. 2019 (at review)

Patient-level meta-analysis

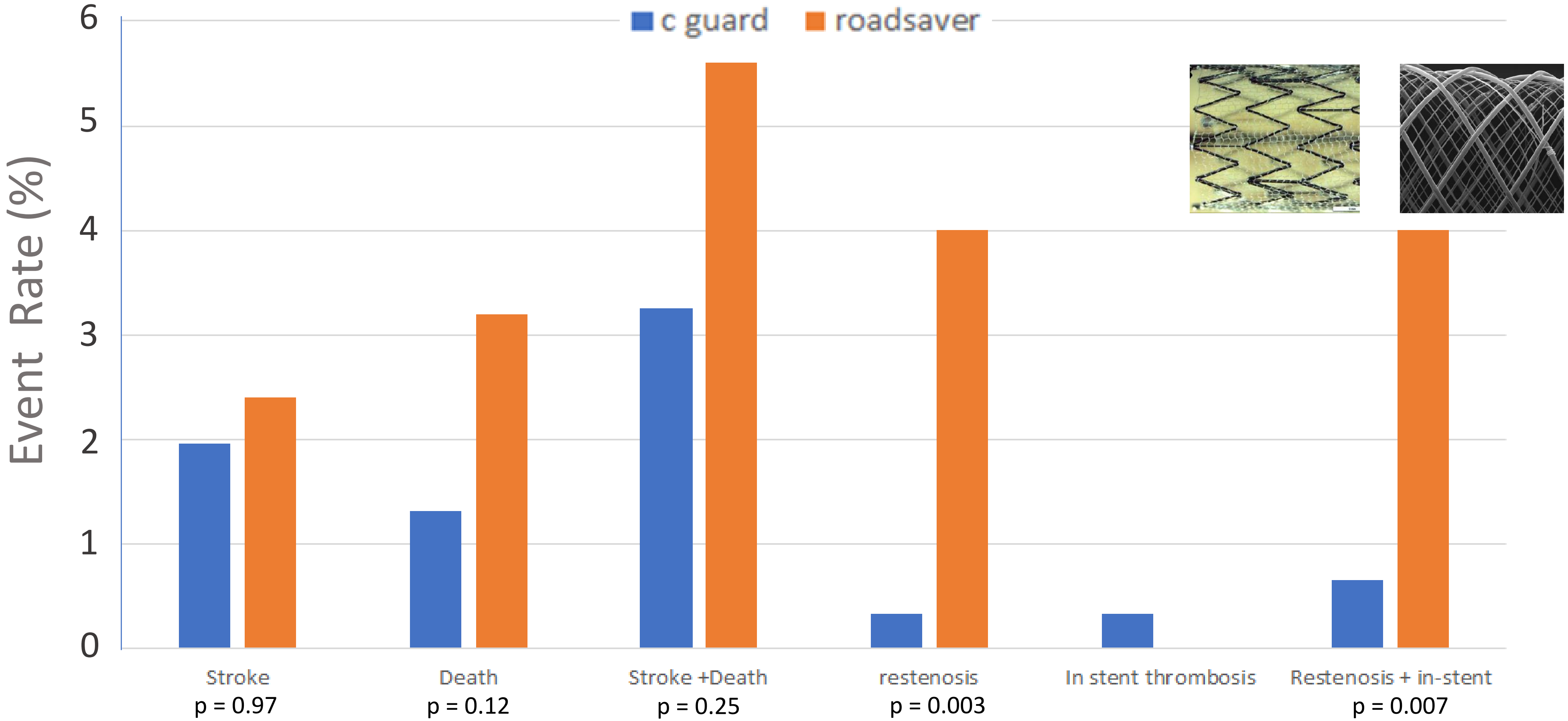
556 patients / 4 trials

(both symptomatic and asymptomatic)

Dual-layer stents

1-year data

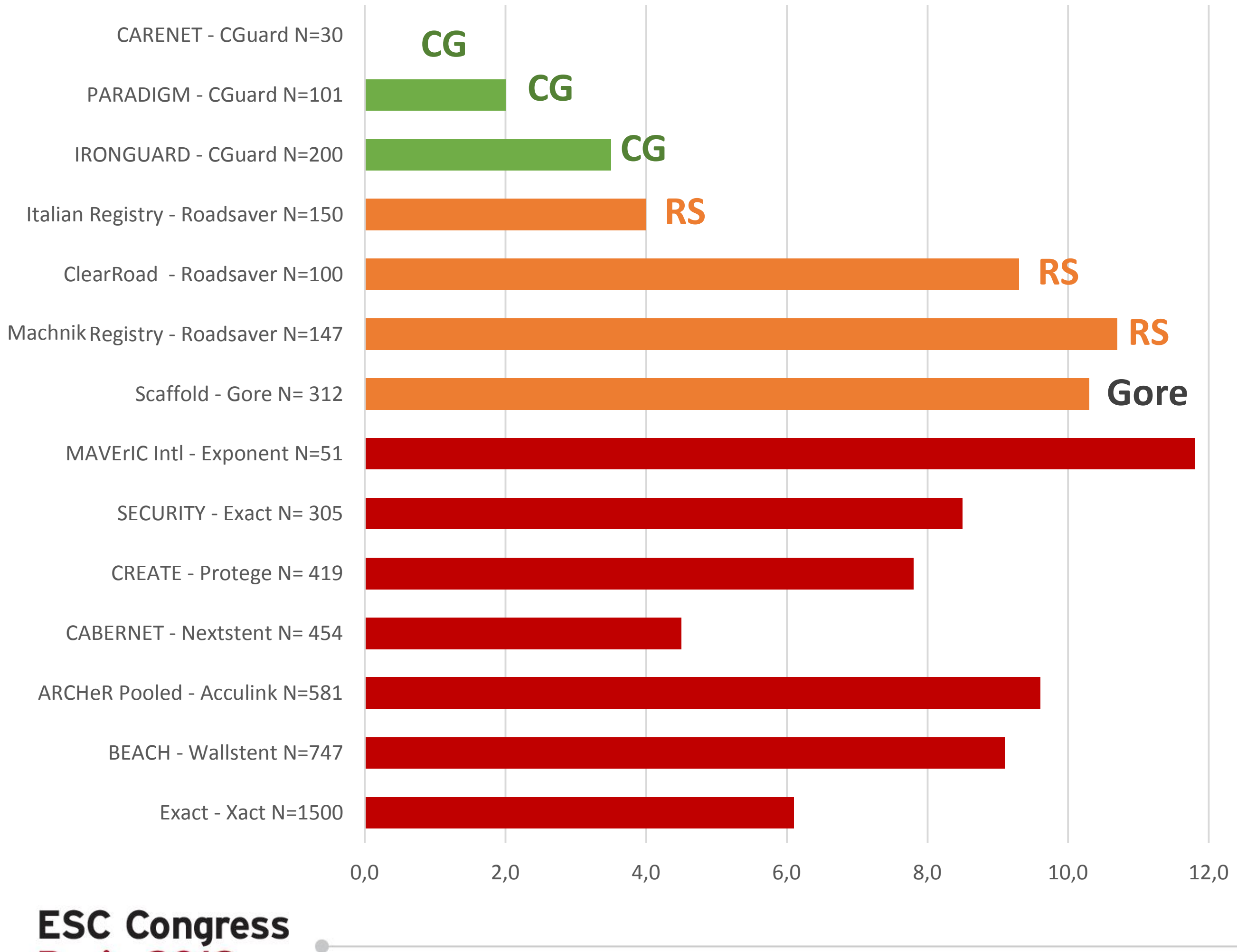
Cumulative results at one year according to Stent Platform



Stabile et al. 2019 (at review)

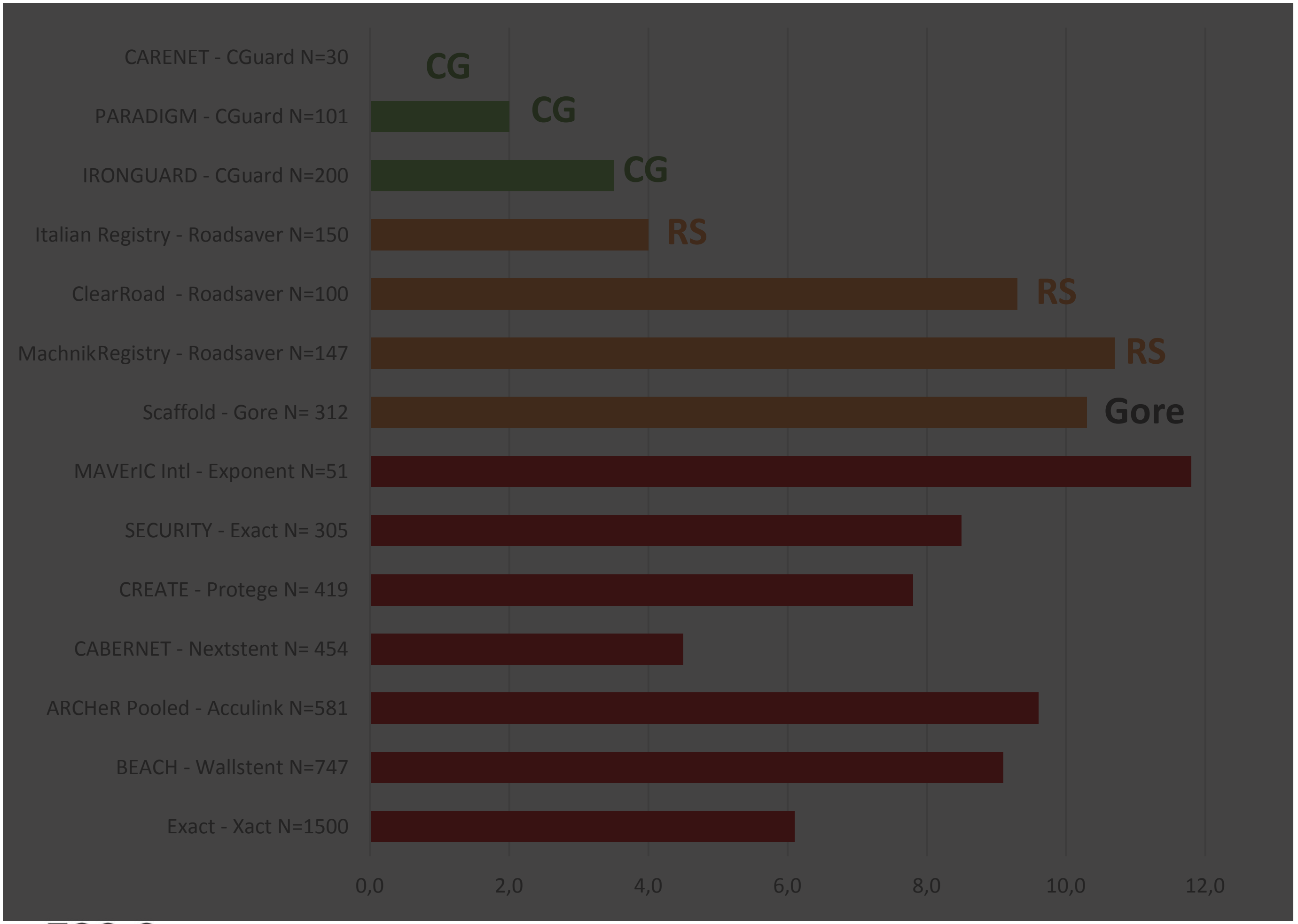
Comparative analysis of the carotid stent data available in public domains by 07.2019 (journal publications plus congress presentations published on-line)

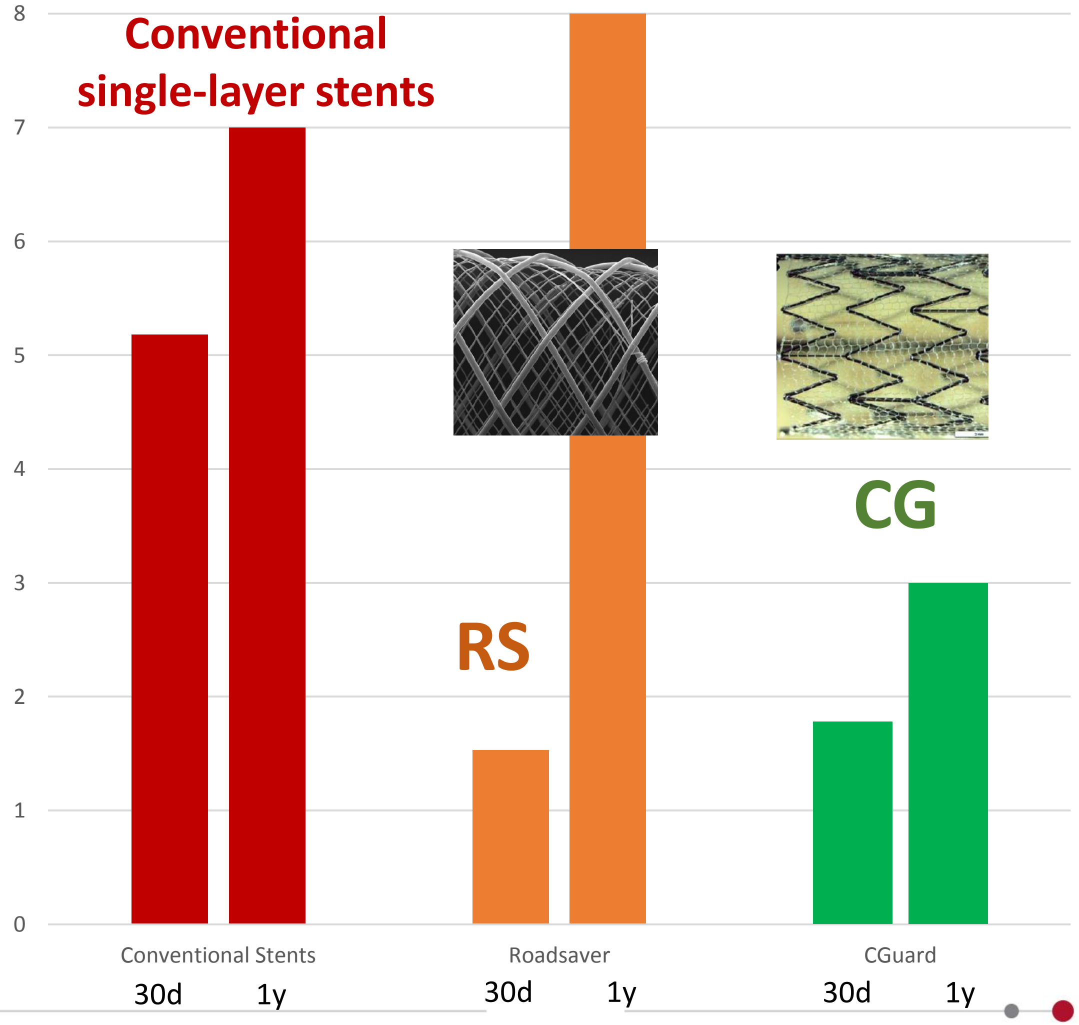
Cumulative Incidence of Death/Stroke/MI @ 30 days *plus* 1-year ipislateral stroke rate



Combined data from different studies/populations; confounders may contribute => compare with caution !

Cumulative Incidence of Death/Stroke/MI @ 30 days *plus* 1-year ipislateral stroke rate



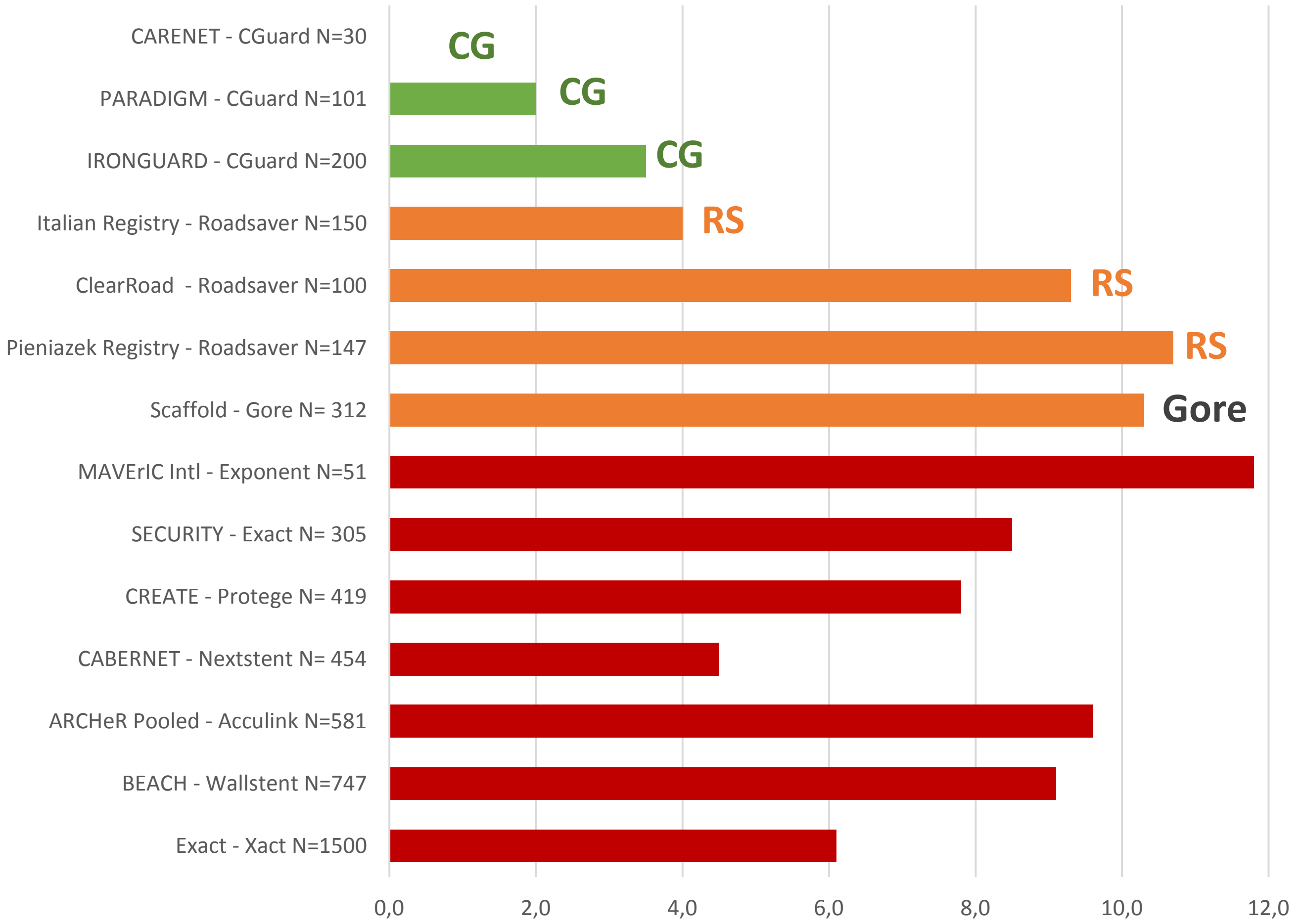


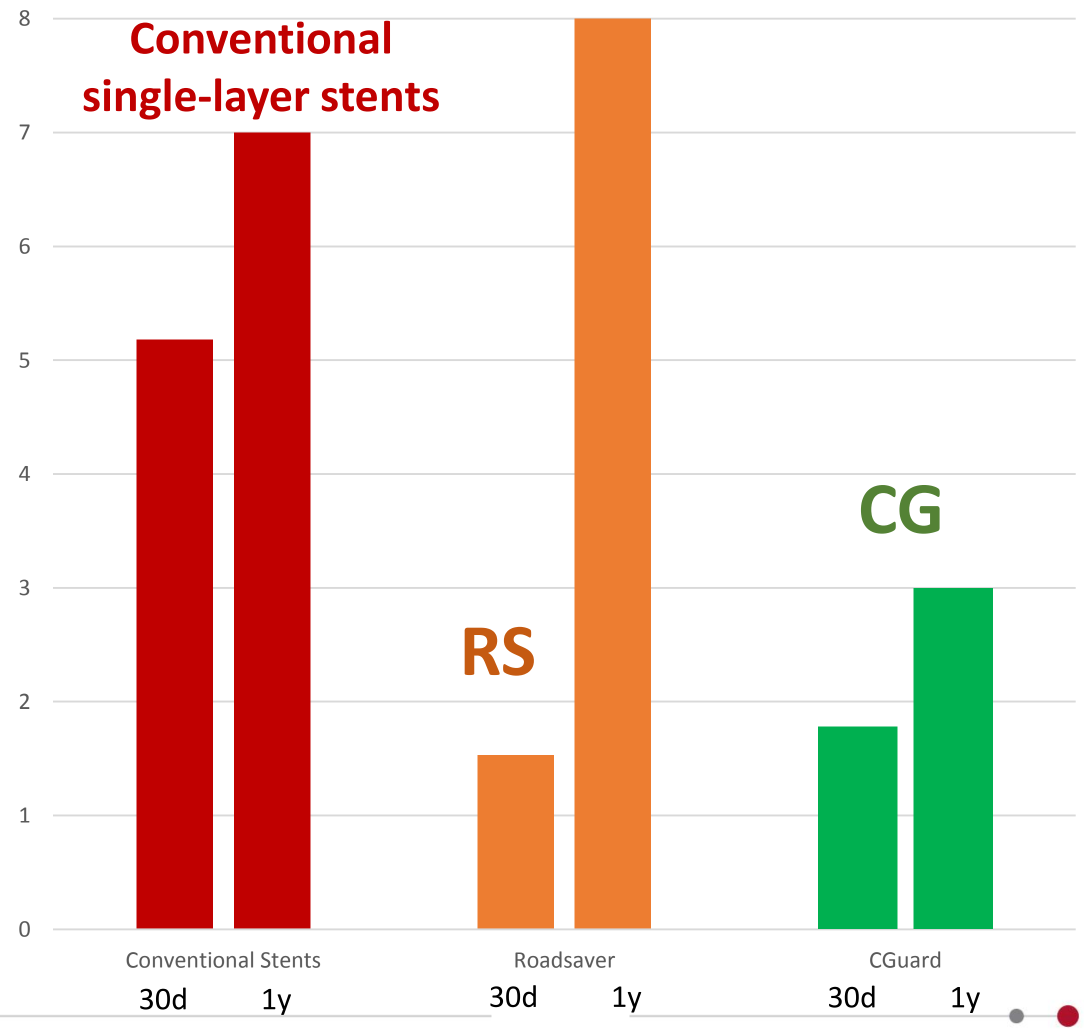
Combined data from different studies/populations; confounders may contribute => compare with caution !

Comparative analysis of the carotid stent data available in public domains

(journal publications plus congress presentations published on-line)

Cumulative Incidence of Death/Stroke/MI @ 30 days *plus* 1-year ipislateral stroke rate





Combined data from different studies/populations confounders may contribute => compare with caution

Determining the type of intervention…

Endo: If one can safely treat high-risk patients/lesions *why not* average-risk ones?

Point to remember #10

Q5 Please vote

For your 70 yo Mother/Father, with a clearly increasing asymptomatic CS carotid stenosis
You suggest (NB. you have access to a skilled operator):

A. OMT + Surgery (CEA)

B. OMT + Neuroprotected CAS with plaque sequestration

C. OMT + Wait for symptoms of cerebral damage (TIA or )

CONCLUSIONS

- The prevalence of asymptomatic carotid stenosis is similar to that of Atrial Fibrillation
- ”Asymptomatic” carotid stenosis is not (at least: not universally) a benign disease
- Most strokes do not give a warning
- There is no evidence that Optimized Medical Therapy is sufficient to protect against CS-related stroke (it may *reduce* or *delay* – but not abolish - the stroke risk)
- Limiting interventional treatment (CEA or CAS) to symptomatic patients is – for those with a stroke – treating TOO LATE
- Novel endovascular technologies (proximal neuroprotection, micro-net covered stents) allow safe endovascular plaque sequestration and may constitute a game-changer

Stroke Risk Stratification tools - 2019

AFib

Carotid Stenosis

Stroke Risk Stratification tools - 2019

$CHADS_2$ Calculator for Atrial Fibrillation

Evaluates ischemic stroke risk in patients with atrial fibrillation

AFib

Carotid Stenosis

Criteria		Poss. Point
Congestive heart failure Signs/symptoms of heart failure confirmed with objective evidence of cardiac dysfunction	Yes No	+1
Hypertension Resting BP > 140/90 mmHg on at least 2 occasions or current antihypertensive pharmacologic treatment	Yes No	+1
Age 75 years or older	Yes No	+2
Diabetes mellitus Fasting glucose > 125 mg/dL or treatment with oral hypoglycemic agent and/or insulin	Yes No	+1
Stroke, TIA, or TE Includes any history of cerebral ischemia	Yes No	+2
Vascular disease Prior MI, peripheral arterial disease, or aortic plaque	Yes No	+1
Age 65 to 74 years	Yes No	+1
Sex **C**ategory (female) Female gender confers higher risk	Yes No	+1

Results:

Total Criteria Point Count: **0**

Reset Form

Stroke Risk per 100 Person Years/Warfarin Rx Interpretation

0 Points:	0.25 ON Rx; 0.49 NO Rx
1 Point:	0.72 ON Rx; 1.52 NO Rx
2 Points:	1.27 ON Rx; 2.50 No Rx
3 Points:	2.20 ON Rx; 5.27 NO Rx
4 Points:	2.35 ON Rx; 6.02 NO Rx
5-6 Points:	4.60 ON Rx; 6.88 NO Rx

The ABC (age, biomarkers, clinical history)-stroke risk score[2]

- Age
- NT-proBNP and cTn-hs
- Prior stroke/TIA

Stroke Risk Stratification tools - 2019

$CHADS_2$ Calculator for Atrial Fibrillation

Evaluates ischemic stroke risk in patients with atrial fibrillation

Criteria		Poss. Point
Congestive heart failure Signs/symptoms of heart failure confirmed with objective evidence of cardiac dysfunction	Yes No	+1
Hypertension Resting BP > 140/90 mmHg on at least 2 occasions or current antihypertensive pharmacologic treatment	Yes No	+1
Age 75 years or older	Yes No	+2
Diabetes mellitus Fasting glucose > 125 mg/dL or treatment with oral hypoglycemic agent and/or insulin	Yes No	+1
Stroke, TIA, or TE Includes any history of cerebral ischemia	Yes No	+2
Vascular disease Prior MI, peripheral arterial disease, or aortic plaque	Yes No	+1
Age 65 to 74 years	Yes No	+1
Sex **C**ategory (female) Female gender confers higher risk	Yes No	+1

Results:

Total Criteria Point Count: 0

Reset Form

Stroke Risk per 100 Person Years/Warfarin Rx Interpretation

0 Points:	0.25 ON Rx; 0.49 NO Rx
1 Point:	0.72 ON Rx; 1.52 NO Rx
2 Points:	1.27 ON Rx; 2.50 No Rx
3 Points:	2.20 ON Rx; 5.27 NO Rx
4 Points:	2.35 ON Rx; 6.02 NO Rx
5-6 Points:	4.60 ON Rx; 6.88 NO Rx

The ABC (age, biomarkers, clinical history)-stroke risk score[2]

- Age
- NT-proBNP and cTn-hs
- Prior stroke/TIA

AFib

Carotid Stenosis

Ø

Take-home messages

- CS-related Strokes should be PREVENTED rather than experienced
- IMPLEMENT the evidence we have today
- STRIVE for improved risk-stratification tools in carotid stenosis
- All-comer patient registries will guide real-life decision-making
- ↓↓ Invasiveness of Intervention

Double-Layer Carotid Stents: From the Clinical Need, through a Stent-in-Stent Strategy, to Effective Plaque Isolation… the Journey Toward Safe Carotid Revascularization Using the Endovascular Route

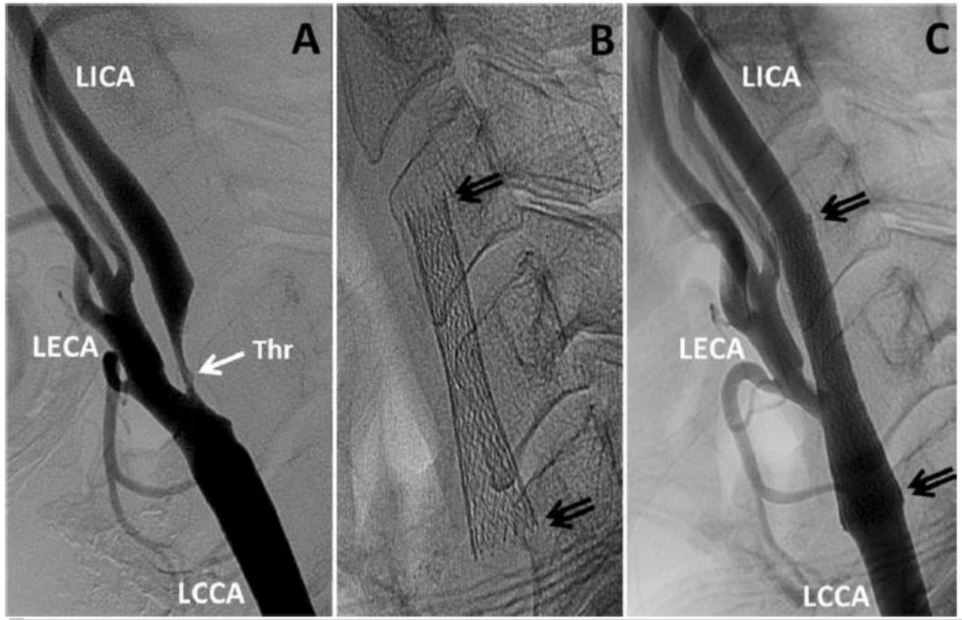
Journal of Endovascular Therapy
2019, Vol. 26(4) 572–577

DOI: 10.1177/1526602819861546
www.jevt.org
SAGE

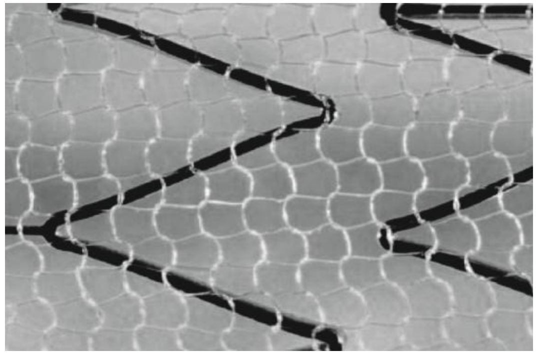
Piotr Musiałek, MD, DPhil[1] and Gary S. Roubin, MD, PhD[2]

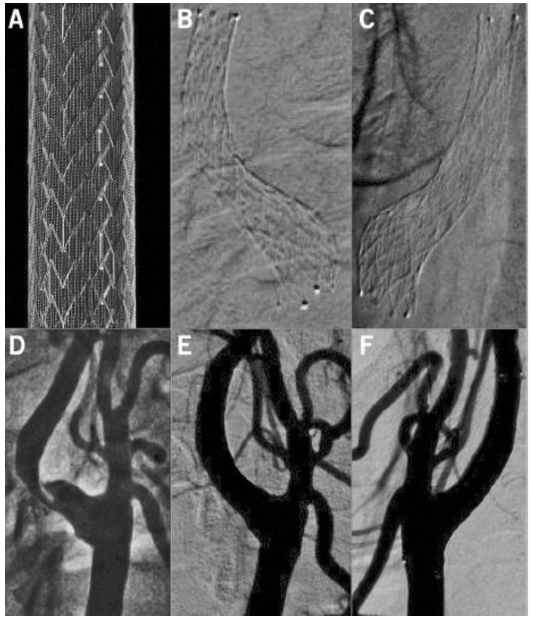
Keywords
carotid artery stenosis, carotid artery stenting, carotid endarterectomy, closed-cell stent, MicroNET, open-cell stent, plaque protrusion, stent-graft, restenosis, double-layer stent, unstable plaque

Both surgical and endovascular routes of carotid revascularization are associated with the risk of symptomatic and asymptomatic cerebral embolism.[1-3] Optimized pharmacotherapy, the mainstay of atherosclerosis management, can reduce or delay but not abolish the risk of stroke from atherosclerotic carotid artery stenosis.[4-7] Interventional elimination or sequestration of the thromboembolic carotid plaque[8-10] remains an important consideration in a significant proportion of patients if carotid stenosis–related strokes are to be prevented rather than experienced. This is the focus and the stent free-cell area also affect the risk of embolism after stent placement. Thus, while optimized neuroprotection during CAS may minimize intraprocedural cerebral embolism,[18-20,23,24] the problem of early or delayed post-procedural embolism remains.[3,25-27] With optimal patient selection technique and antiplatelet therapy, post-stent embolic phenomena are largely related to intrastent plaque prolapse, balloon trauma, and subsequent embolization. This may occur after the period of intraprocedural cerebral protection using flow reversal techniques and/or filters.



Stent-in-stent technique for unstable plaque (G. Roubin , J Vitek 1999)





Endovasc. reconstruction with Plaque sequestration