

Alma Mater Studiorum Università di Bologna

Vascula Surgery - Ospedale Maggiore Hospital - Italy



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Nothing to disclose

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CEA is Superior to CAS

an EBM conclusion

Prof. Andrea Stella





CEA vs. CAS

From the introduction of carotid artery stenting (CAS) many trials have been performed to compare this procedure with the carotid endarterectomy (CEA) that represented the gold standard in carotid revascularization.

Despite the high number of studies made on this subject, the results are inconsistent.

The most important vascular societies presently recommend CAS only for symptomatic carotid stenosis in patients with high surgical risk due to anatomical or clinical factors



CEA vs. CAS: the RCTs

The first randomized controlled trial (RCT) on CEA vs. CAS was performed by Naylor et al. in 1998¹. Since then many other trials have been conducted.

The studies differed for number of patients included, case selection and in the percentage cerebral protection devices used for CAS.



CEA vs. CAS: the RCTs

Randomized Clinical Trials

- CAVATAS 2001
- SAPPHIRE 2004
- EVA-3S 2006
- SPACE 2006
- ICSS 2010
- CREST 2010

Most studies have focused mainly on **symptomatic** patients

Study	Centres	N pts (CAS/CEA)	Pts risk	Asympt	Filters	Stent	Outcome
CAVATAS 2001	22 centres in Europe, Australia, and Canada	505 (252/253)	normal	10%	0%	26%	Stroke/death
SAPPHIRE 2004	29 centres, USA	334 (167/167)	high	29%	100%	100%	Stroke/death/MI
EVA-3S 2006	30 centers in France	527 (265/262)	normal	0	92%	100%	Stroke/death
SPACE 2007	35 centres in Germany, Austria and Switzerland	1214 (613/601)	normal	0	27%	100%	Stroke/death
ICSS 2009	50 academic centers in Europe, Australia, New Zealand, and Canada	1713 (855/858)	normal	0	80%	100%	Stroke/death/MI
CREST 2010	108 centers in the USA and 9 centers in Canada	2522 (1271/1251)	normal	47%	96%	100%	Stroke/death/MI

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Cavatas and Sapphire are weak

CEA vs CAS – 30 day outcomes

Cea superior to Cas in most studies

Study	Death, Stroke	p
EVA3S 2006	4.1% vs. 10.1%	0.01
SPACE 2007	6.6 % vs. 7.4 %	0.51
ICSS 2009	3.9 % vs. 7.6 %	0.001
CREST 2010	2.3 % vs. 4.4 %	0.005

CEA vs CAS – 30 day outcomes

Cea superior to Cas in most studies also considering Myocardial Infarction

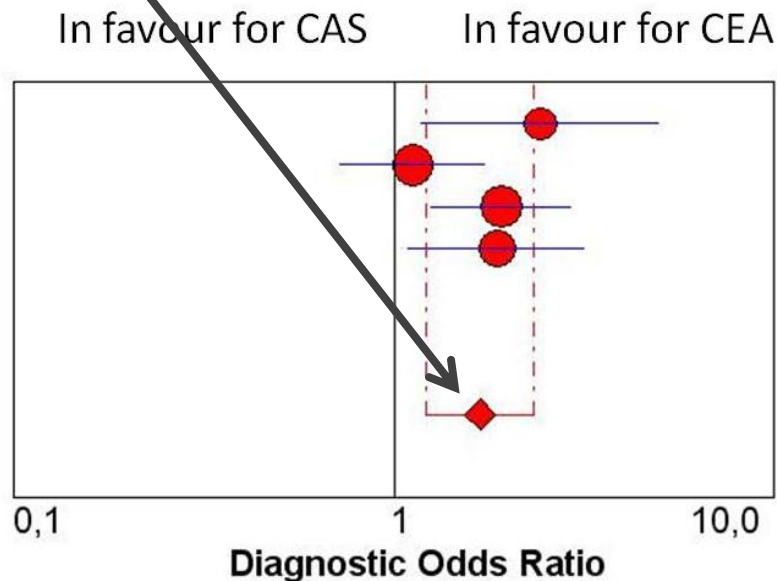
Study	Death, Stroke	p	Death, Stroke, or MI	p
EVA3S 2006	4.1% vs. 10.1%	0.01	4.6% vs. 10.5%	0.02
SPACE 2007	6.6 % vs. 7.4 %	0.51	6.6 % vs. 7.4 %	0.65
ICSS 2009	3.9 % vs. 7.6 %	0.001	4.5 % vs. 7.6 %	0.006
CREST 2010	2.3 % vs. 4.4 %	0.005	4.5 % vs. 5.2 %	0.38



30-day outcomes – **symptomatic** patients

A Recent Methanalysis study confirms this superiority

Any stroke or death

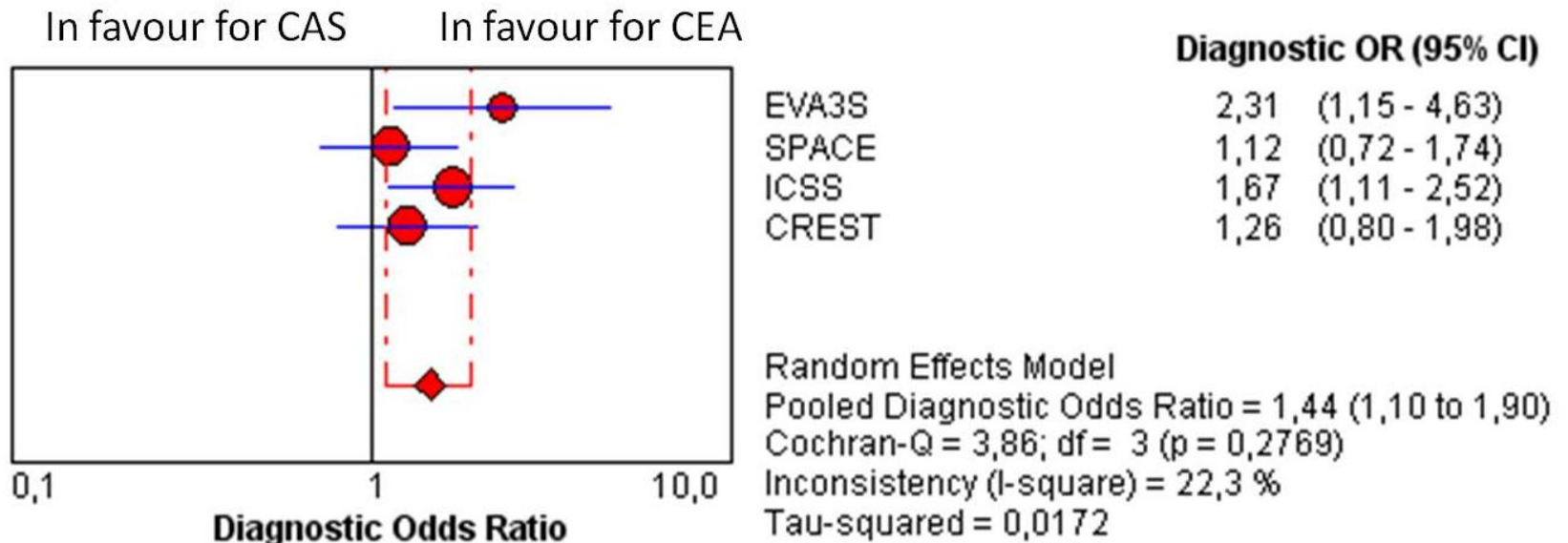


OR 1.68 (CI 95%: 1.22-2.32)



30-day outcomes – **symptomatic** patients

Any stroke or death or **Myocardial Infarction**



OR 1.44 (CI 95%: 1.10-1.90)

The timing of intervention appears to be an important factor because
the Risk of Carotid Artery Stenting compared with
Carotid EndArterectomy is greatest in patients treated
within 7 days
independently from the severity of symptoms

Stroke or Death	CEA	CAS	Adjusted RR (95% IC)	p
0-7 day	2.8%	9.4%	4.0 (1.2-13.8)	0.03
8-14 days	3.4%	8.1%	2.3 (1.0-5.3)	0.06
> 14 days	4.0%	7.3%	1.9 (1.3-2.7)	0.001

EVA-3S, SPACE, ICSS

Carotid Stenting Trialist' Collaboration,
J Vasc Surg, in press



The Issue of Myocardial Infarction

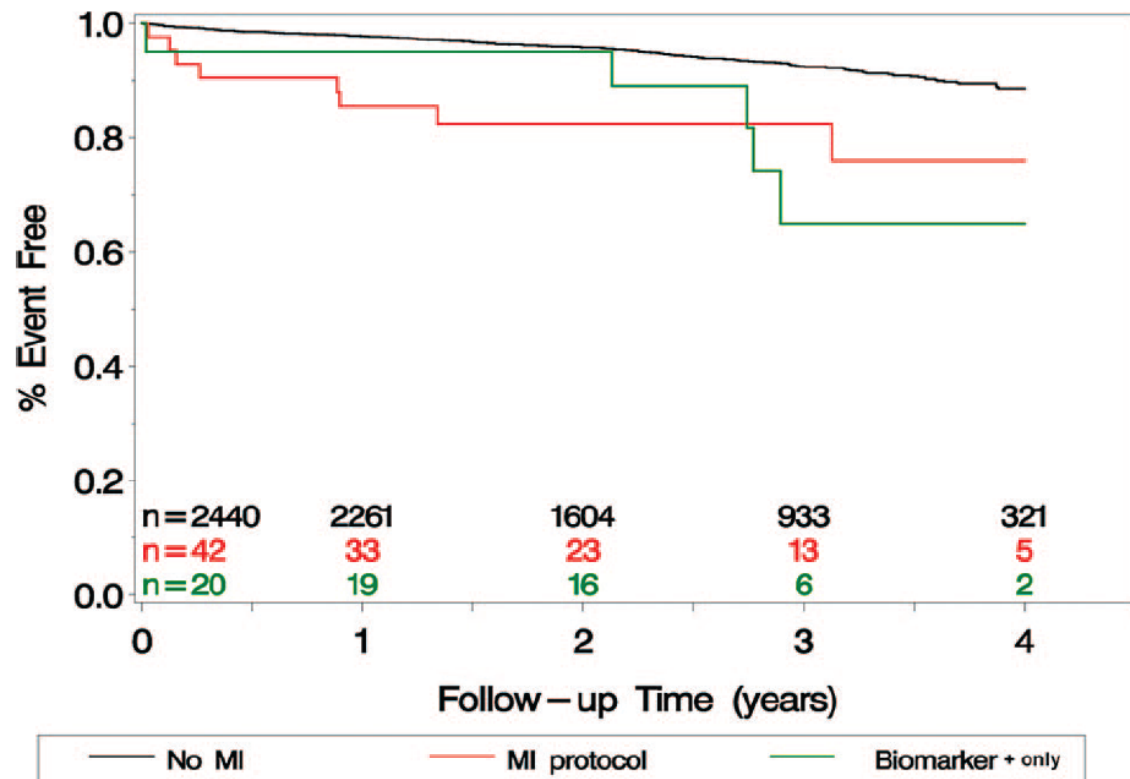
The inclusion of MI as a **Primary Outcome** in CREST is a matter of debate

- Many Authors emphasize the long term effects of any type of MI
- Other Authors believe that the primary goal of carotid revascularization is the prevention from neurological events and death, considering MI a secondary event



CREST : Myocardial Infarction

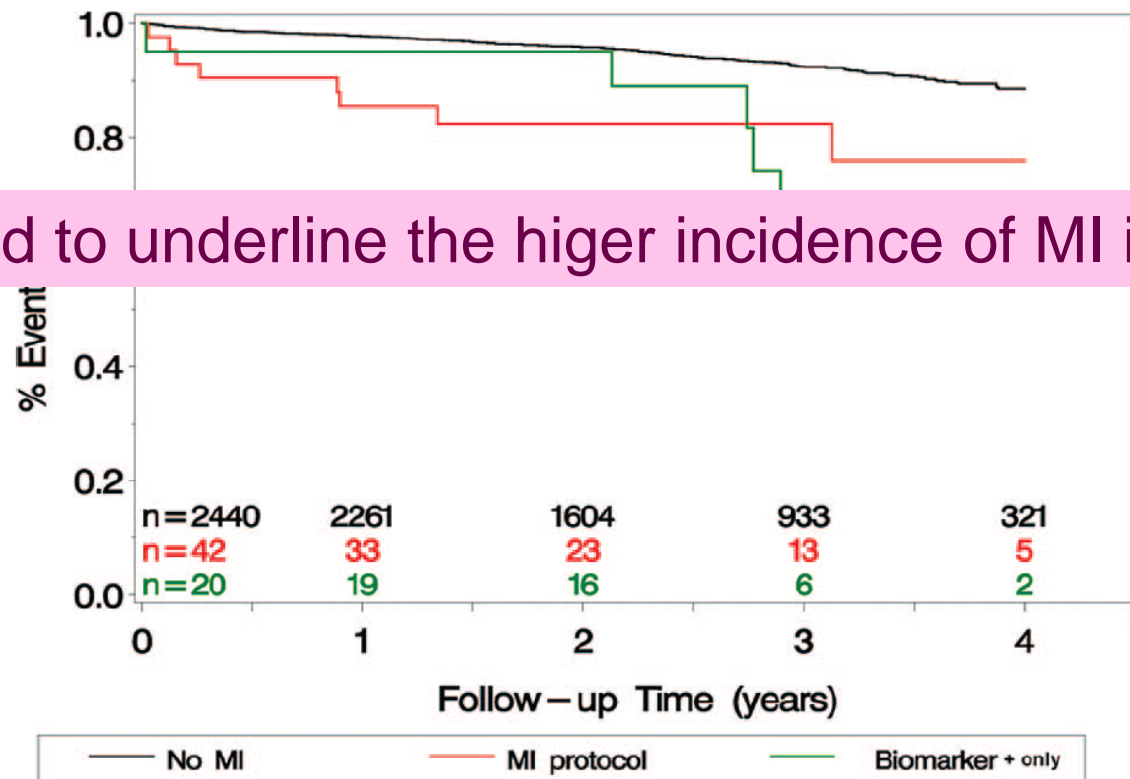
- CEA has higher incidence of MI
- MI or elevation of biomarker only leads to higher future mortality





CREST : Myocardial Infarction

- CEA has higher incidence of MI
- MI or elevation of biomarker only leads to higher future mortality



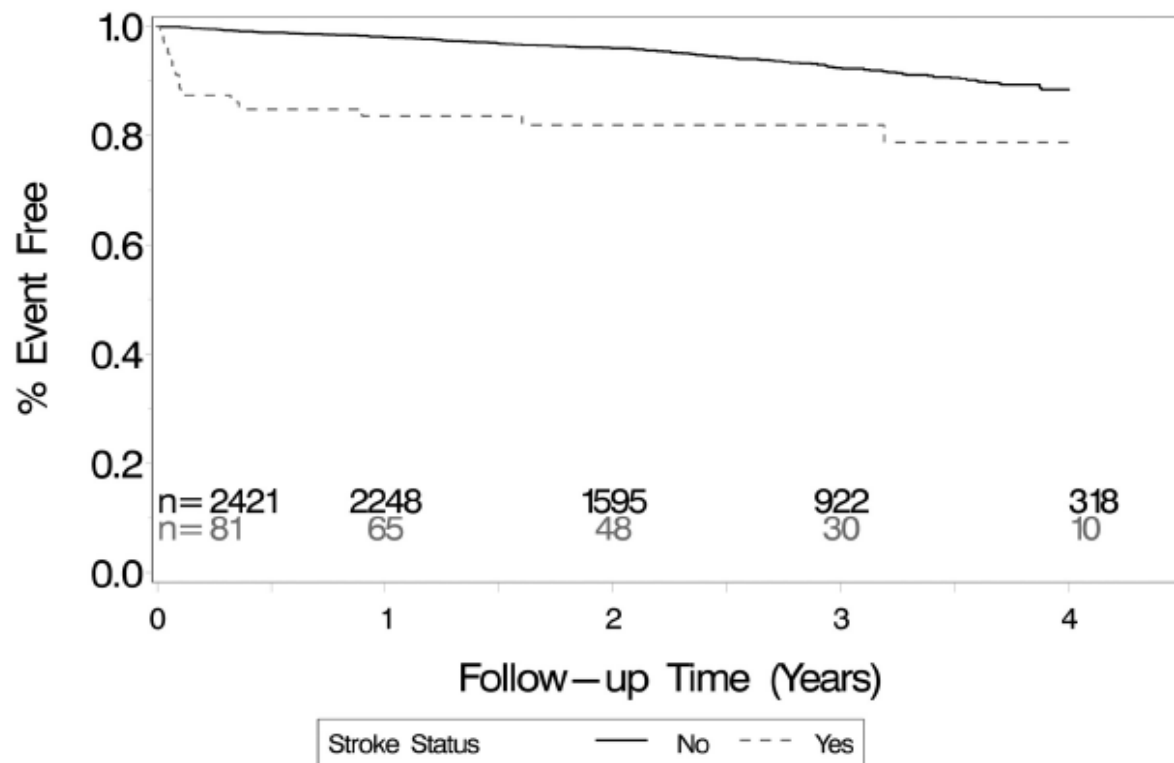
CREST : Stroke

4-year mortality

More recent data enforce the importance of Stroke

Stroke: mortality 21.1%

No-stroke: mortality 11.6%





“Clinical Debates with the European Society for Vascular Surgery and the SVS Vascular Chairs Committee”

We have now many published data from CREST,
but CAS is not still the preferred solution for
Asymptomatic Disease

The Long Awaited CREST Results Have Now Been Published, So Why Is
Carotid Artery Stenting (CAS) For Asymptomatic Disease Languishing?

Andrea Stella - SVS Annual Meeting
Washington D.C. June 7-9, 2012



Asymptomatic Patients

CREST

Secondary End points	CAS	CEA	P
Perioperative myocardial infarction	1.2%	2.2%	0.20
Any periprocedural stroke or death or postprocedural (4yrs FU) ipsilateral stroke	4.5%	2.7%	0.07
Any periprocedural stroke, MI, or death or postprocedural (4yrs FU) ipsilateral stroke	5.6%	4.9%	0.56

Considering just the asymptomatic patients

there was a trend in favour of Open Surgery for the periprocedural stroke or death



CREST

1. Asymptomatic patients included in the trial afterwards
2. Risk factors
3. Medical therapy
4. Myocardial infarction


Asymptomatic patients included in the trial afterwards (1)

CREST Investigational Plan:

- The study initially intended to include **only symptomatic** patients, but, due to the slow enrollment pace, also asymptomatic patients were added
- Adding asymptomatic patients to the study diluted the power and prevented significance

Risk factors (2)

Risk factors	CAS	CEA	P
Hypertension %	85.8	86.1	Ns
Diabetes %	30.6	30.4	Ns
Dyslipidemia %	82.9	85.8	0.05
Current smoker %	26.4	26.1	Ns
Previous cardiovascular disease %	42.4	45.0	Ns
Previous coronary-artery bypass %	19.9	21.5	Ns



There was a statistical difference in the two groups based on dyslipidemia, probably significant factor considering postprocedural complication as Myocardial Infarction



Risk factors (2)

CREST Investigational Plan: **anatomic exclusion criteria**

- Severe vascular tortuosity or anatomy that would preclude the safe introduction of a guiding catheter, guiding sheath or stent placement
- Presence of extensive or diffuse atherosclerotic disease involving the aortic arch and proximal common carotid artery...

Subjective criteria

10% of patients did **not** undergo CAS in the stenting arm



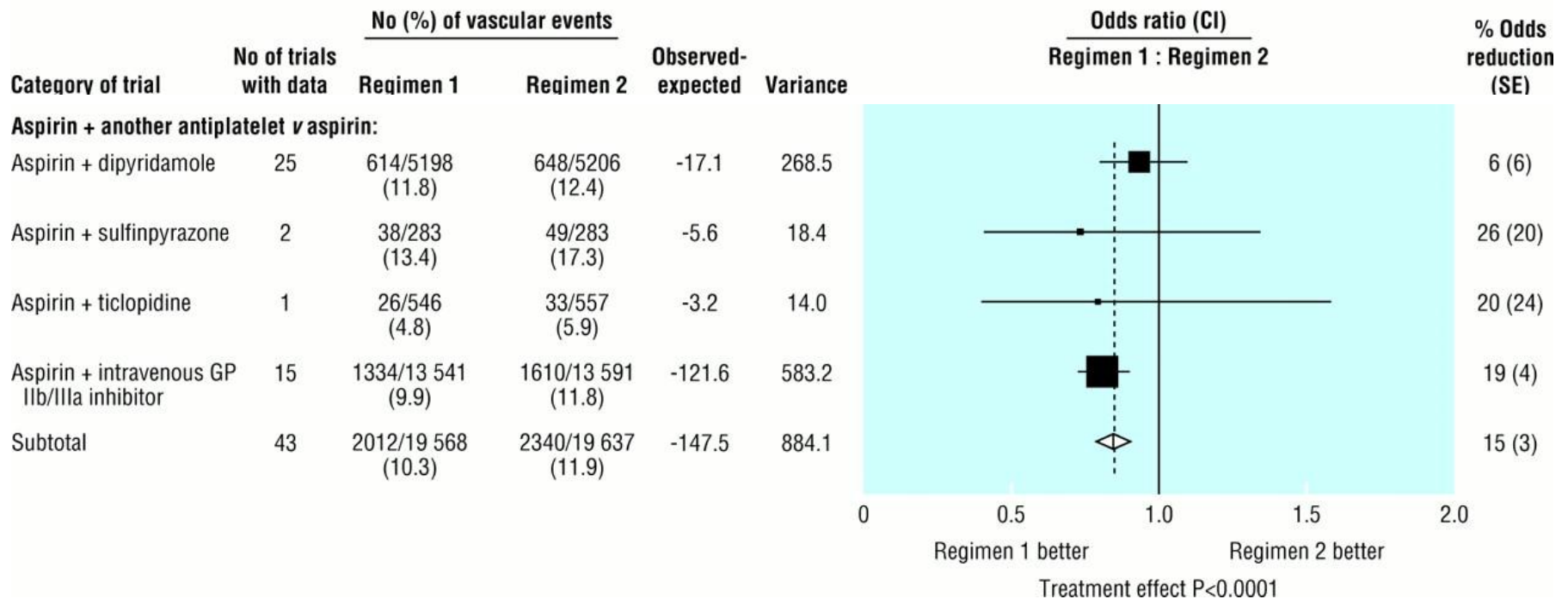
Medical therapy (3)

- Double antiplatelet therapy in CAS
Single antiplatelet therapy in CEA
- Some patients did not receive any antiplatelet therapy at all



Medical therapy

Direct comparisons of proportional effects of different antiplatelet regimens on vascular events in high risk patients





Medical therapy (3)

- Double antiplatelet therapy in CAS
Single antiplatelet therapy in CEA
- Some patients did not receive any antiplatelet therapy at all



CREST: Antiplatelet therapy

Post-operative medical treatment
in asymptomatic patients

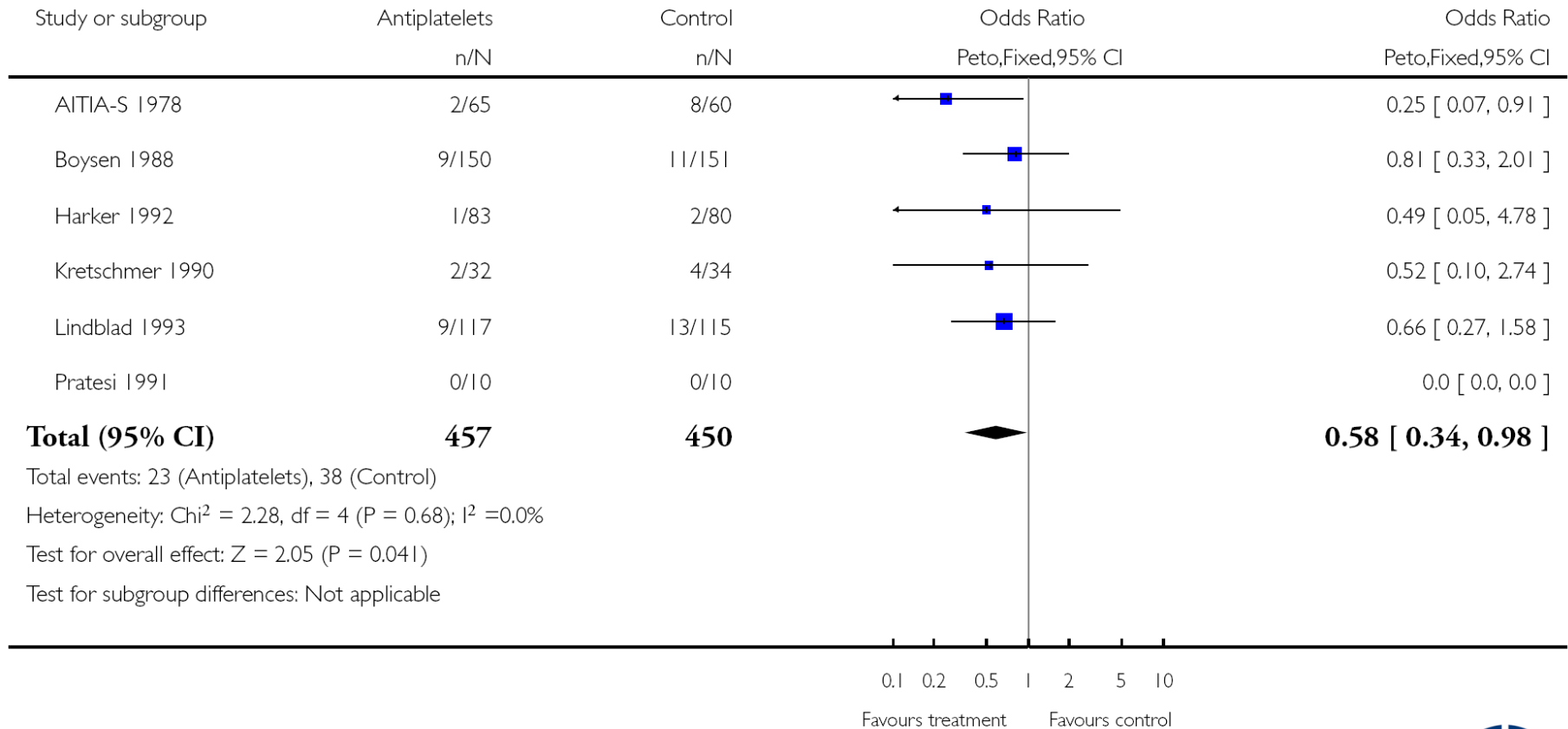
	CAS	CEA	p
No antiplatelet therapy at all	0.2 %	3.1 %	<0.001

Data reported only in the CREST supplementary appendix
with no direct comparison



Antiplatelet therapy

Antiplatelet therapy reduces the risk of stroke after CEA





CREST : Myocardial Infarction (4)

Despite:

- Higher incidence of MI
- Different medical therapy
- Different post-operative doses



Perioperative and Post-op Mortality were quite similar

	Perioperative			4-year FU		
	CAS	CEA	p	CAS	CEA	p
Death	0.7%	0.3%	0.18	11.3%	12.6%	0.45



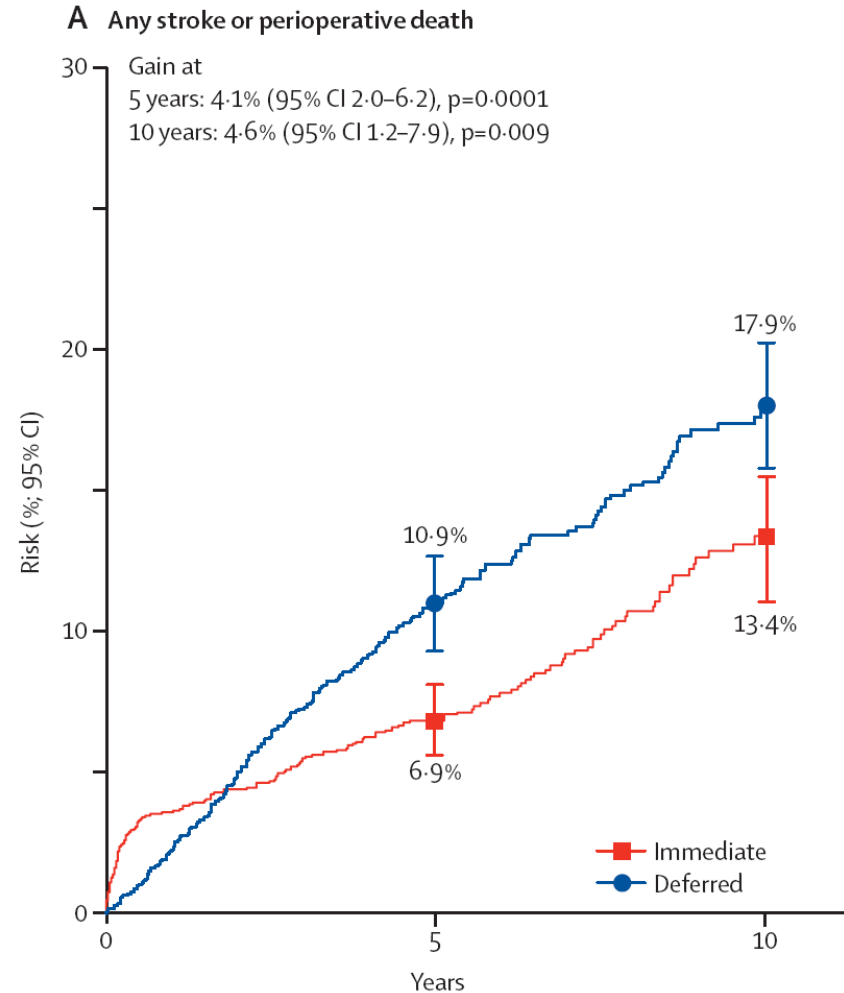
CREST: Asymptomatic Patients

Endpoints	CAS	CEA	P
Perioperative myocardial infarction	1.2%	2.2%	0.20
Any periprocedural stroke or death or postprocedural (4yrs FU) ipsilateral stroke	4.5%	2.7%	0.07

We **cannot** affirm that CAS is **not-inferior** to CEA
in **asymptomatic** patients

Comments

- ACAS and ACST demonstrated **the benefit of CEA** in asymptomatic patients
- But no study demonstrated the benefit of CAS for asymptomatic patients





Conclusions

- Considerations about the Guidelines
- CEA is superior to CAS with low rate of stroke/death/MI in symptomatic patients (EVA-3S, SPACE, ICSS, CREST)
- For asymptomatic patients, CAS is not demonstrated superior or equivalent to CEA



Guidelines from Vascular Surgery Societies

SVS - ESVES

Vascular Surgeons

Symptomatic patients

In most patients with carotid stenosis who are candidates for intervention, **CEA is preferred to CAS** for reduction of all-cause and periprocedural death [grade I; level of evidence, B].

Asymptomatic patients

There are insufficient data to recommend CAS as primary therapy for neurologically asymptomatic patients with 70% to 99% diameter stenosis. In properly selected asymptomatic patients, CAS is equivalent to CEA in the hands of experienced interventionalists with a combined stroke and death rate <3% [grade II; level of evidence, B].



Guidelines from **Cardiologist Societies**

ACC/AHA

Cardiologist

Symptomatic patients

CAS is indicated **as an alternative to CEA for symptomatic** patients at average or low risk of complications associated with endovascular intervention **[grade I; level of evidence, B]**

Asymptomatic patients

Prophylactic **CAS might be considered** in highly selected patients with asymptomatic carotid stenosis (..), but its effectiveness compared with medical therapy alone in this situation is not well established **[class IIb; level of evidence, B]**.



Conclusions

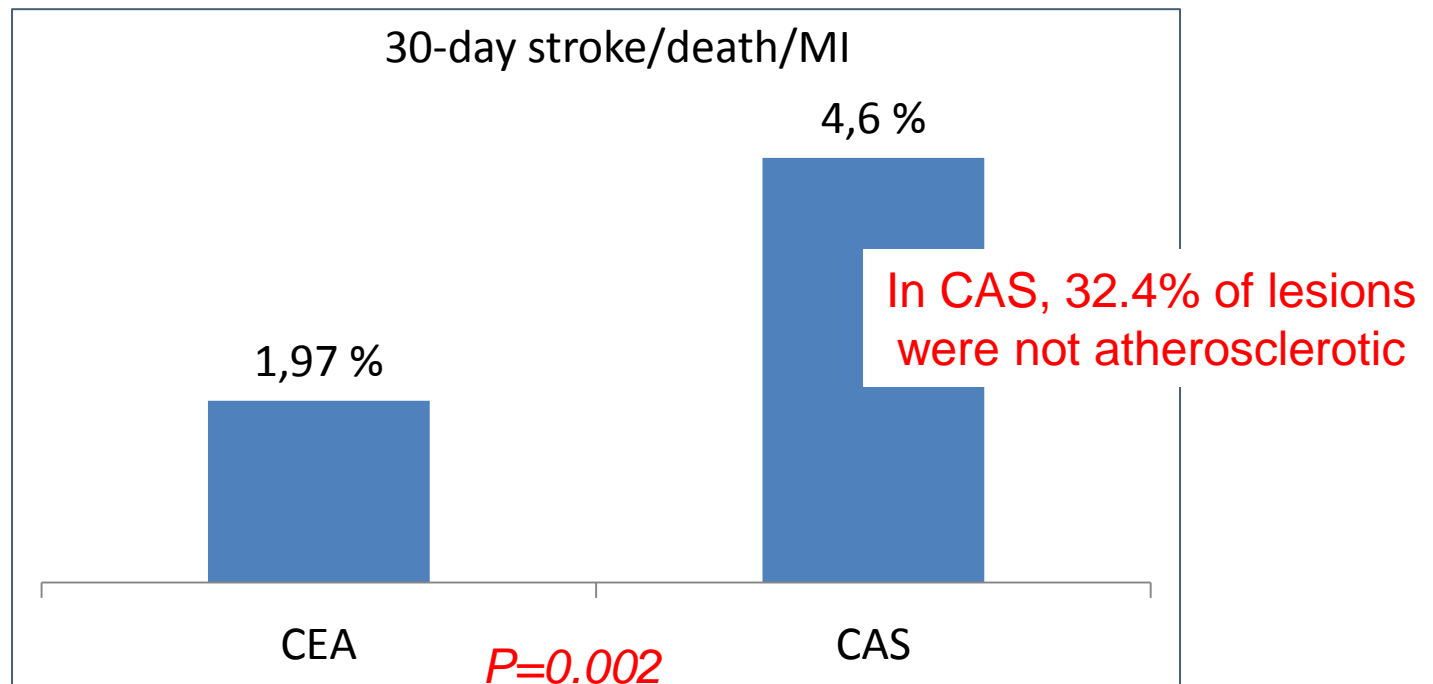
- Considerations about the Guidelines
- CEA is superior to CAS with low rate of stroke/death/MI in symptomatic patients (EVA-3S, SPACE, ICSS, CREST)
- For asymptomatic patients, CAS is not demonstrated superior or equivalent to CEA

Risk-adjusted 30-day outcomes of carotid stenting and endarterectomy: Results from the SVS Vascular Registry

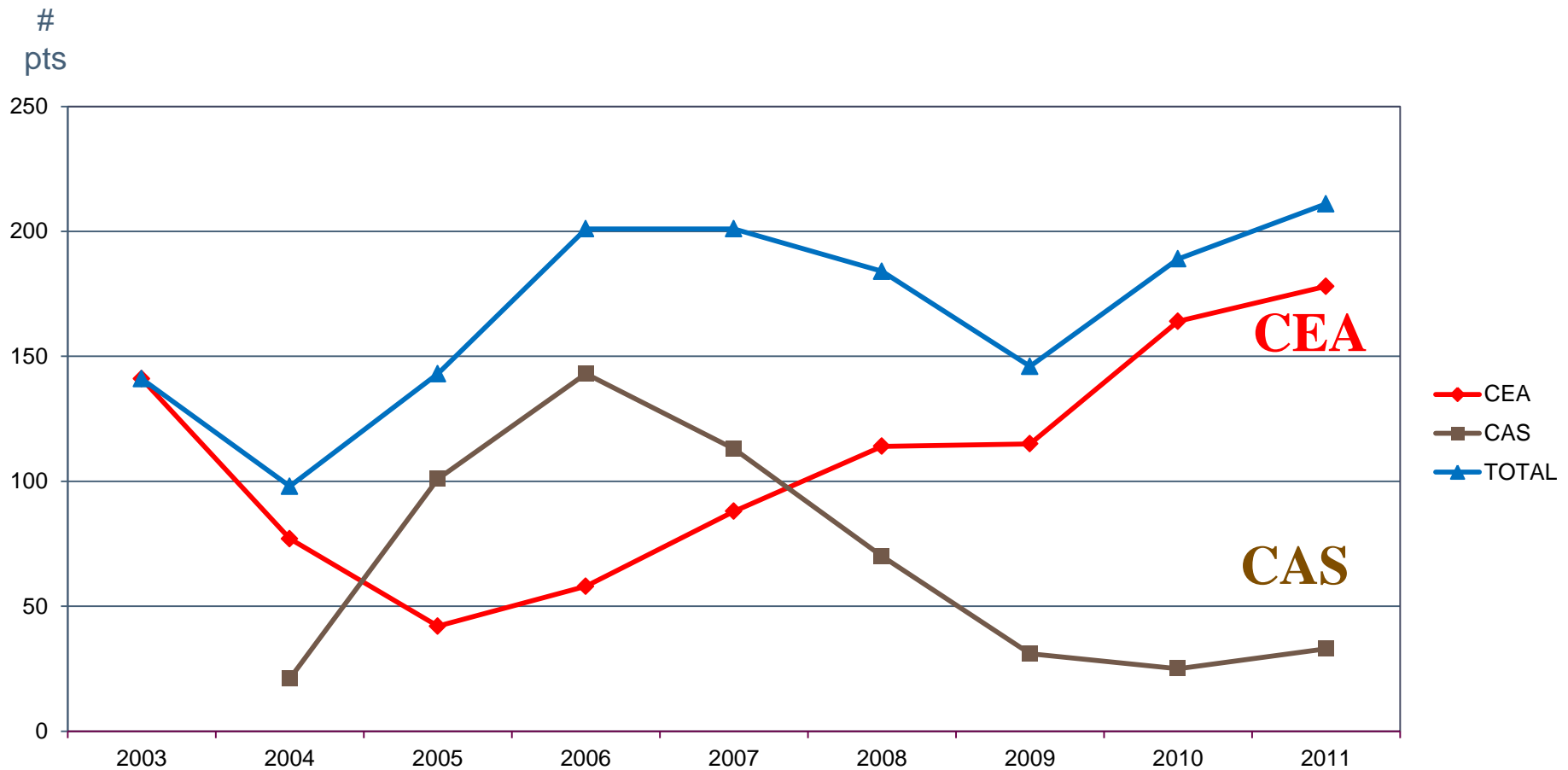
Sidawy et al., J Vasc Surg 2009

CAS vs CEA in the real world

- Asymptomatic: CEA 862, CAS 805



Carotid revascularization procedures at the Vascular Surgery Unit, University of Bologna



- **Probably we need a different stent's design**
To reduce the periprocedural complication

