Randomised Data in Carotid Artery Stenting: Current Evidence and Future Perspectives

Marco Roffi

Division of Cardiology

University Hospital

Geneva, Switzerland

HUG
Hôpitaux Universitaires de Genève

Disclosure

Speaker name:

.....Marco Roffi.....

I have the following potential conflicts of interest to report:

Unrestricted institutional research grants from Biotronik, Abbott Vascular, Medtronic, Boston Scientific, Terumo

We could be talking about the limitations of the CAS vs. CEA RCTs, but let's talk about evidence-based data

→ the primary endpoints of the RCTs

Primary Endpoints in CEA vs CAS RCTs Enrolling >300 patients

Trial	Begin of Enrolment	N	Symptomatic Patients	Primary Endpoint
CAVATAS	1992	504	100%	*No difference* in 30-d death or stroke.
SAPPHIRE	2000	334	29%	*No difference* in death, stroke, MI within 30 d or death or ipsilateral stroke at 1 y
EVA-3S	2000	527	100%	*CEA superior* in any stroke or death at 30 d.
CREST	2000	2502	53%	*No difference* in periprocedural stroke, MI, or death or ipsilateral stroke within 4 y.
SPACE	2001	1200	100%	*No difference* in ipsilateral stroke or death at 30 d
ICSS	2001	1713	100%	*No difference* in fatal or disabling stroke at 5 y
ACT-1	2005	1453 (3:1)	0%	*No difference* in death, stroke, MI within 30 d or death or ipsilateral stroke at 1 y

Adapted from Roffi M et al. Heart 2016;102:1059-69

2017 Meta-Analysis of RCT CEA vs. CAS

Pre-specified criteria for trial inclusion

- >50 patients
- Trials had to mandate embolic-protection devices (EPDs) use (defined as use in >50% cases)

Trials	Total Patients (CAS/CEA)*	Follow-Up Duration (Median yrs)	Recruitment Period	Use of EPD (%)	Asymptomatic Patients (%)
ACT I 2016	1,089/364	5.0	2005-2013	Yes (97.8)	100.0
CREST 2010 and 2016†	1,262/1,240	7.4	2000-2008	Yes (96.1)	47.2
EVA-3S 2006 and 2014	265/262	7.1	2000-2005	Yes (91.9)	0.0
ICSS 2010 and 2015‡	853/857	4.2	2001-2008	Yes (70.7)	0.0
SAPPHIRE 2004 and 2008	167/167	3.0	2000-2002	Yes (95.6)	72.3

Sardar P et al. J Am Coll Cardiol 2017;69:2266–75

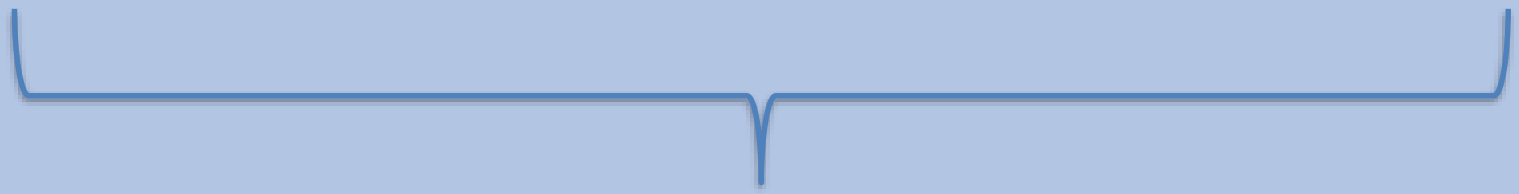
EVA-3S: EPDs initially not mandatory…

First 80 patients treated with CAS in EVA-3S

→ Protected group: stroke or death 10.3%

→ Unprotected group: stroke or death 26.7%

→ Procedure could not be performed in 7.5% of cases



Clinical Alert:

→ Stopped the unprotected CAS arm

→ Mandated the use of EPDs

Stroke 2004;35:e18-e21

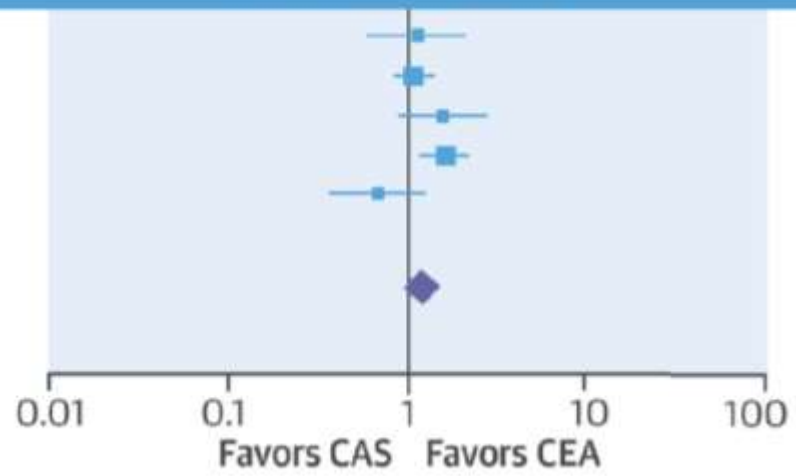
2017 Meta-Analysis Primary Outcome Measure: periprocedural death, stroke, or MI and ipsilateral stroke during long-term follow-up

→ No difference between CAS and CEA

Study or Subgroup	CAS Events	CAS Total	CEA Events	CEA Total	Weight
ACT I 2016	41	1,089	12	364	12.4%
CREST 2016	108	1,262	97	1,240	31.9%
EVA-3S 2014	33	265	22	262	15.2%
ICSS 2015	95	853	62	857	28.0%
SAPPHIRE 2008	18	167	25	167	12.6%
Total (95% CI)		**3,636**		**2,890**	**100.0%**
Total Events	295		218		

Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 6.80$, df = 4 (P = 0.15); $I^2 = 41\%$

Test for Overall Effect: Z = 1.48 (P = 0.14)



Sardar P et al. J Am Coll Cardiol 2017;69:2266–75

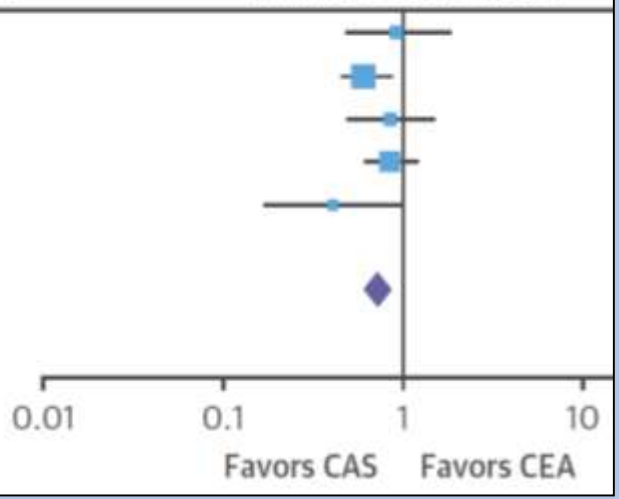
Periprocedural Adverse Events: composite of death, stroke, MI, or cranial nerve palsy

→ Advantage for CAS

Study or Subgroup	CAS Events	CAS Total	CEA Events	CEA Total	Weight	Odds Ratio M-H, Random, 95% CI
ACT I 2016	37	1089	13	364	10.5%	0.95 [0.50, 1.81]
CREST 2010	79	1262	119	1240	37.4%	0.63 [0.47, 0.85]
EVA-3S 2006	29	265	32	262	14.6%	0.88 [0.52, 1.51]
ICSS 2010	71	853	81	857	31.5%	0.87 [0.62, 1.21]
SAPPHIRE 2004	8	167	18	167	6.1%	0.42 [0.18, 0.99]
Total (95% CI)		**3636**		**2890**	**100.0%**	**0.75 [0.60, 0.93]**
Total events	224		263			

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 4.76$, df = 4 (P = 0.31); $I^2 = 16\%$

Test for overall effect: Z = 2.64 (P = 0.008)



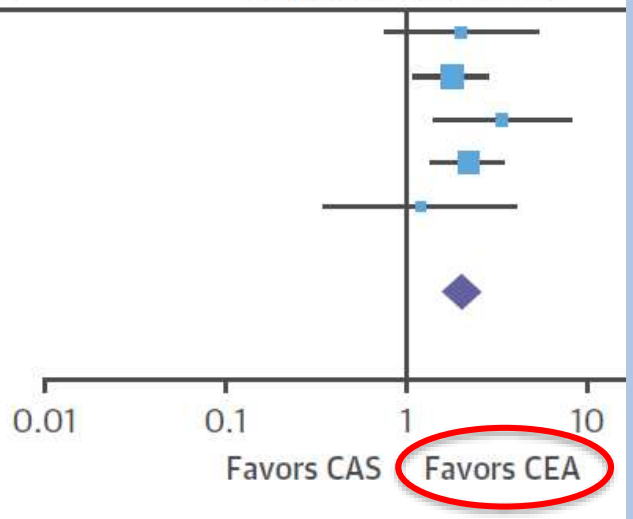
Sardar P et al. J Am Coll Cardiol 2017;69:2266–75

Periprocedural stroke

Study or Subgroup	CAS Events	CAS Total	CEA Events	CEA Total	Weight	Odds Ratio M-H, Random, 95% CI
ACT I 2016	30	1089	5	364	8.8%	2.03 [0.78, 5.28]
CREST 2010	52	1262	29	1240	37.9%	1.79 [1.13, 2.85]
EVA-3S 2006	23	265	7	262	10.8%	3.46 [1.46, 8.22]
ICSS 2010	58	853	27	857	37.0%	2.24 [1.41, 3.58]
SAPPHIRE 2004	6	167	5	167	5.5%	1.21 [0.36, 4.04]
Total (95% CI)		3636		2890	100.0%	2.07 [1.56, 2.75]
Total events	169		73			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.61$, df = 4 (P = 0.62); $I^2 = 0\%$

Test for overall effect: Z = 5.02 (P < 0.00001)

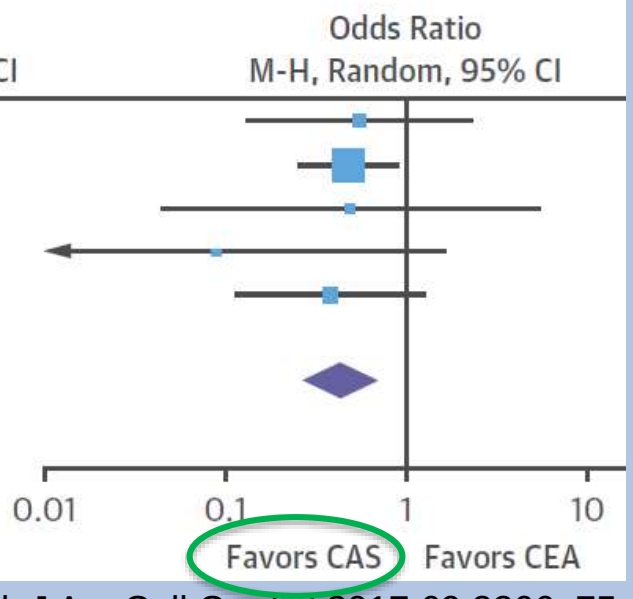


Periprocedural MI

Study or Subgroup	CAS Events	CAS Total	CEA Events	CEA Total	Weight	Odds Ratio M-H, Random, 95% CI
ACT I 2016	5	1089	3	364	12.5%	0.56 [0.13, 2.33]
CREST 2010	14	1262	28	1240	61.6%	0.49 [0.25, 0.93]
EVA-3S 2006	1	265	2	262	4.4%	0.49 [0.04, 5.46]
ICSS 2010	0	853	5	857	3.1%	0.09 [0.01, 1.64]
SAPPHIRE 2004	4	167	10	167	18.5%	0.39 [0.12, 1.25]
Total (95% CI)		3636		2890	100.0%	0.45 [0.27, 0.75]
Total events	24		48			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.41$, df = 4 (P = 0.84); $I^2 = 0\%$

Test for overall effect: Z = 3.09 (P = 0.002)



Sardar P et al. J Am Coll Cardiol 2017;69:2266–75

Absolute Risk Metrics of Outcomes of Major Interest

Outcome of Interest	NNT/NNH for CAS
Aggregate efficacy/safety outcome*	–
Periprocedural any stroke + nonperiprocedural ipsilateral stroke	50 (NNH)
Periprocedural any stroke	47 (NNH)
What are the implications for YOUR patients treated at YOUR institution?	
Periprocedural MI	99 (NNT)
Periprocedural CN palsy	22 (NNT)
Periprocedural neurological injury	43 (NNT)
Periprocedural neck hematoma	73 (NNT)
Composite periprocedural safety outcome†	34 (NNT)
Long-term stroke in any territory (includes periprocedural stroke)	68 (NNH)
Long-term death	–

Sardar P et al. J Am Coll Cardiol 2017;69:2266–75

Conclusions From the RCT

- **Asymptomatic patients**: SAPPHIRE, CREST-asympt, ACT-1
  - No difference in the primary endpoint
  - No difference in the composite or individual endpoints at 30 d
  - Results of ECST-2 eagerly awaited

- **Symptomatic patients**: despite equivalence in the primary endpoint in all but one trial (EVA-3S), RCT (with all their limitations) showed an increase in (minor) strokes and this has primed the skeptics, in particular the neurology community.

- **For all patients :** comparable long-term efficacy in terms of ipsilateral stroke prevention, restenosis or repeat revascularization.

Future/Perspective

- **CAS has to further reduce peri-procedureal embolic events** through improved skills, appropriate patient selection, and technical innovations (surgery is also getting better over the years!).

- **Symptomatic patients:** CAS has in the near future no chance to change the data landscape as no major trial directly comparing CEA and CAS is ongoing.

- **Asymptomatic patients:** let's wait for ACST-2, the only large-scale CAS vs. CEA RCT currently recruiting.

Randomised Data in Carotid Artery Stenting: Current Evidence and Future Perspectives

Marco Roffi

Division of Cardiology

University Hospital

Geneva, Switzerland

HUG
Hôpitaux Universitaires de Genève