5-year results of ACST-2

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23rd June 2022
Vascular Symposium 9
Auditorium
11.07-11.14

ACST-2: trial of carotid stenting (CAS) vs endarterectomy (CEA)

Background on asymptomatic patients
with severe carotid stenosis

Trials have shown CEA restores patency and ~halves later stroke rates, and that modern medical therapy also ~halves long-term stroke rates.

CAS can also restore patency, and in recent nationwide registry data CAS and CEA each has ~1% risk of causing disabling stroke or death.

in-hospital* CAS/CEA risks, asymptomatic patients

	18,000 CAS	86,000 CEA
Disabling stroke or death:	0.7%	0.7%
Any stroke or death:	1.8%	1.4%

NB In-hospital stroke risks not affected by gender or age.

* Median 4-5 days to discharge; 30-day risks would be higher.

Source: https://iqtig.org/qs-verfahren/qs-karotis

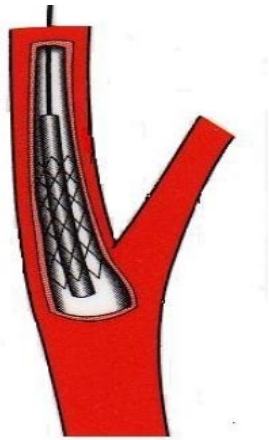
ACST-2: carotid stenting (CAS) vs endarterectomy (CEA)

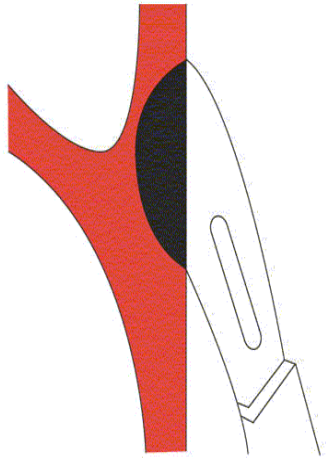
CAS vs CEA: why do we need randomised evidence?

Large, representative registries can assess procedural hazards, and determine reliably whether they depend on gender or age.

But, registries cannot reliably compare long-term non-procedural stroke rates; for this, *large-scale randomised evidence* is required.

ACST-2: trial in 3625 patients of carotid artery stenting (CAS) vs carotid artery surgery (CEA: “endarterectomy”)





ACST-2: carotid stenting (CAS) vs surgery (CEA)

- Severe carotid artery stenosis (≥60% on ultrasound), with no recent ipsilateral stroke or other symptoms from it

- Thought to need a carotid procedure (stenting or surgery), but substantially uncertain whether to prefer CAS or CEA

ACST-2: carotid stenting (CAS) vs surgery (CEA)

- Randomised trial in 130 hospitals (mostly European), each with a collaborating vascular surgeon, interventionist, and stroke doctor

- Collaborators used their normal procedures, with, for stenting, any CE-approved devices and double anti-platelet therapy.

ACST-2 compares the
long-term durability
of protection against stroke
of CEA vs CAS

ACST-2: carotid stenting (CAS) vs surgery (CEA)

- 3625 patients randomised, half to stenting and half to surgery (70% male, 30% diabetic, mean age 70, mean follow-up 5 years)

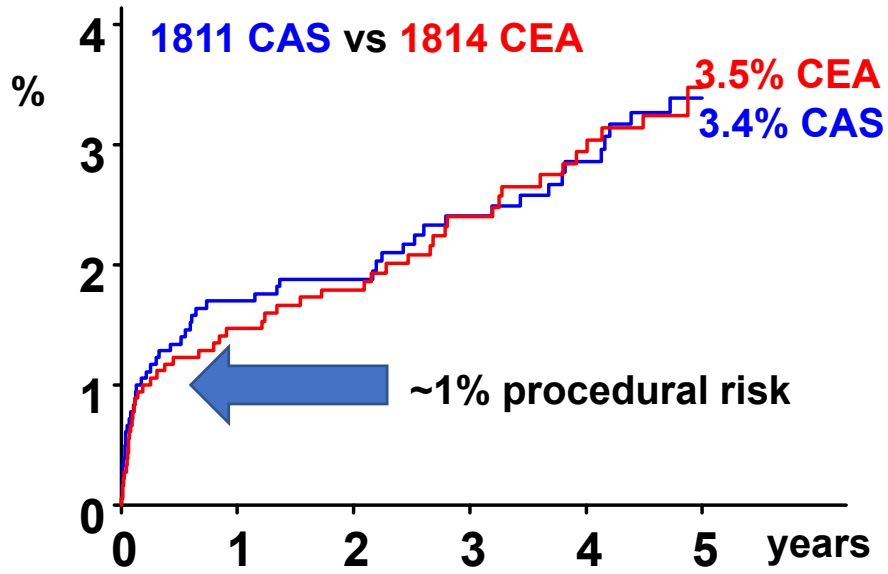
- Both groups got good long-term medical treatment, 80-90% with lipid-lowering, anti-thrombotic and anti-hypertensive therapy.

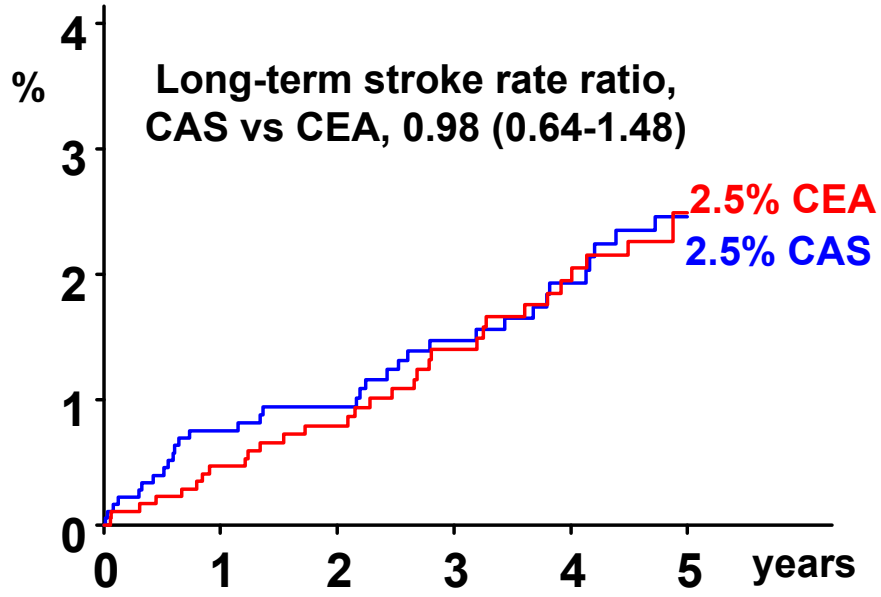
- Strokes were classified by residual disability 6 months afterwards (defining a “disabling” stroke as modified Rankin Score [mRS] 3-5).

ACST-2: carotid stenting (CAS) vs surgery (CEA)

5-year risk of procedural death, or of disabling or fatal stroke

Left: Including procedural risks, **Right:** Excluding procedural risks





ACST-2: carotid stenting (CAS) vs surgery (CEA)

Any procedural death or any stroke at any time, by severity

	Allocated CAS n=1811	Allocated CEA n=1814
mRS >1: Fatal, disabling, or unable to carry out some previously usual activities	77	77
mRS 0-1: Non-disabling, and still able to carry out all previously usual activities	77 (4.2%)	49 (2.7%)

ACST-2: carotid stenting (CAS) vs surgery (CEA)

3625 patients with severe stenosis but no recent ipsilateral symptoms, half allocated CAS, half CEA; good compliance, good medical therapy.

Summary of results

1% 30-day risk, in each group, of *procedural death or disabling stroke*; 2.5% 5-year risk, in each group, of *non-procedural disabling/fatal stroke*.

But, with stenting, there was a 1-2% excess risk of *non-disabling stroke* that left patients still able to carry out all their previously usual activities.

CAS vs CEA: ACST-2 results plus other evidence

Procedural strokes: An excess of non-disabling procedural strokes with CAS is consistent with large, recent, nationally representative registry data.

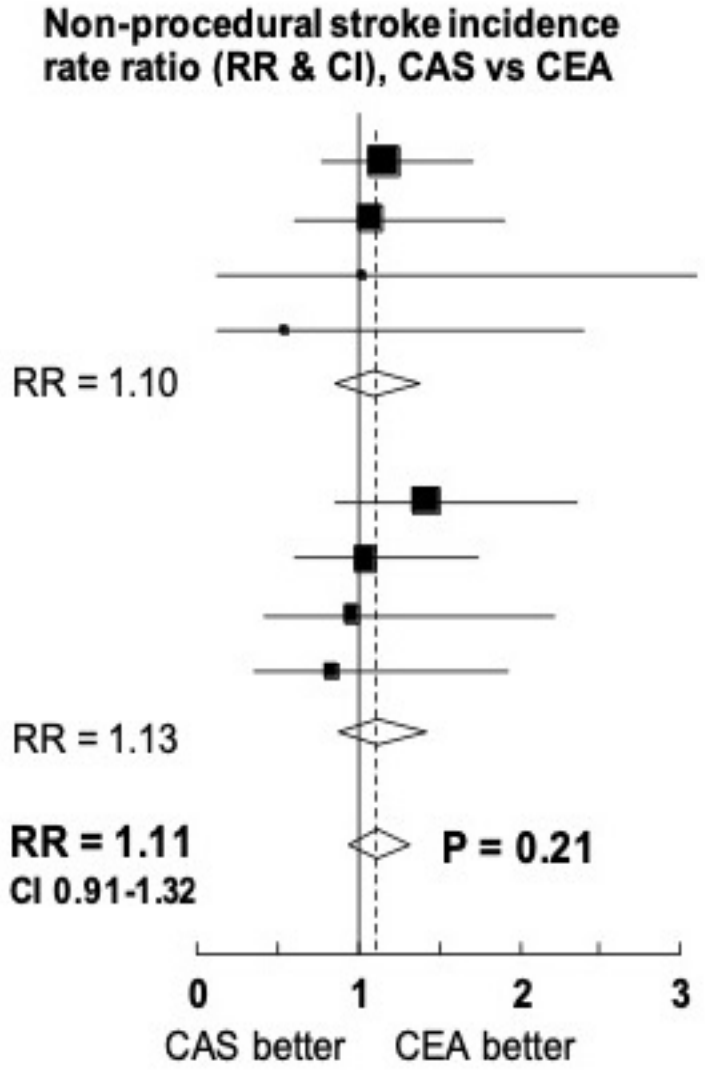
Non-procedural strokes: To compare the effects of CAS vs CEA, ACST-2 should be considered along with all other major trials.

8 major trials of CAS vs CEA, 4 in asymptomatic and 4 in symptomatic patients, have been reported. A formal meta-analysis can combine their findings.

Non-procedural stroke incidence in the 8 major trials of CAS vs CEA

Trial, and mean follow-up reported		Allocated CAS	Allocated CEA
a. No symptoms in past 6 months			
ACST-2	5 years	91 /1811	79 /1814
CREST	6 years	47 /594	43 /587
SPACE-2 ACT-1	each only 1 year		
Subtotal (a)		145 /3116	133 /3150
b. Symptoms in past 6 months			
ICSS	4 years	65 /842	47 /853
CREST	6 years	55 /661	52 /651
SPACE	2 years	20 /601	20 /584
EVA3S	7 years	19 /263	22 /259
Subtotal (b)		159 /2367	141 /2347
Total (a + b)		**304 /5483 5.6%**	**274 /5497 5.0%**

99% or 95% confidence interval (CI)



For the Total, RR is similar for ipsilateral strokes (131 vs 119) and for other strokes (173 vs 155)

Conclusions from ACST-2 and the other major trials of CAS vs CEA

Competent CAS and CEA involve ~1% procedural death or disabling stroke, then have similar effects on long-term rates of fatal or disabling stroke.

For asymptomatic patients with severe stenosis, previous trials showed that, even if good medical treatment is given, CEA ~halves long-term stroke rate.

If so, then in ACST-2, where 0.5%/year had a fatal or disabling stroke with either CAS or CEA, with neither procedure ~1% per year would have done so.

ACST-2 was published online in *The Lancet* on 29 Aug 2021 with immediate open access

The chief acknowledgements are to the patients who agreed to participate; the collaborating doctors at 130 hospitals in 33 countries who randomised them from 2008-20 and are continuing follow-up until 2026, and trial staff.

ACST-2 is currently hosted and funded by
Oxford University's Nuffield Department of Population Health
Current funding is from the MRC/BHF/CRUK core support for the NDPH.
Until 2013, funding was from the UK NIHR HTA and BUPA Foundation.