



# Bitesize RESEARCH

## Asymptomatic Carotid Disease

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**ACAS** working group (1995) Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. JAMA Vol 273, Issue 18, pp 1421-8

### SUMMARY

The Asymptomatic Carotid Atherosclerosis Study (ACAS) found that asymptomatic patients in generally good health, with carotid stenosis of >60% NASCET will have a 5-year reduced risk of ipsilateral stroke after CEA, maintaining that there is <3% perioperative morbidity and mortality and aggressive management of modifiable risk factors.

### PROS

Multicentre prospective trial with large sample size of 1662 patients recruited. The results of the study were reproduced in ACST-1.

### CONS

Aggressive management in 1995 involved only daily aspirin administration for all patients. In 2023 patients are given statins, blood pressure control, aspirin and clopidogrel or modified release dipyridamole, so the ACAS results may be outdated.

### IMPACT ON PRACTICE

At the time, ACAS increased the number of asymptomatic patients with >60% carotid stenosis undergoing CEA.

**ACST-1** working group (2004) Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. The Lancet, Vol 363, Issue 9420, pp 1491-1502

**ACST-2** working group (2021) Second asymptomatic carotid surgery trial (ACST-2): a randomised comparison of carotid artery stenting versus carotid endarterectomy. The Lancet, Vol 398, Issue 10305, pp 1065-1073

### SUMMARY

ASCT1&2 recommended immediate intervention for asymptomatic patients had beneficial outcomes, where in patients <75 y/o and stenosis >70% NASCET intervention reduced stroke risk by half. They also identified similar risk reduction between stenting and CEA for disabling and fatal events. However, stenting did have a higher rate of non-disabling stroke.

### PROS

Large multicentre randomized trials with big sample size (2000-3000 patients)

### CONS

Medical therapy was not standardised in ACST1 and both studies do not address whether or when intervention is needed. Patients who had asymptomatic plaque below surgical threshold were not included but could have a future risk of stroke.

### IMPACT ON PRACTICE

CEA or stenting for asymptomatic carotid plaque is safe. Further follow-up of ACST-2 is needed to determine to procedural durability and longer-term protective effects.

Markus, H. et al (2010) Asymptomatic embolisation for prediction of stroke in the Asymptomatic Carotid Emboli Study (ACES): a prospective observational study. The Lancet Neurology, Vol 9, Issue 7, pp 663-71

### SUMMARY

This study utilised transcranial doppler (TCD) to identify patients with asymptomatic carotid stenosis at higher risk of stroke and determined that presence of embolic signals on TCD may aid selection of patients for whom CEA might prove beneficial.

### PROS

Multicentre worldwide study with a sample size of 482 patients. Embolic signals were recorded and reviewed by a second observer to ensure consistency.

### CONS

Bias could have occurred in the cases of asymptomatic carotid stenosis where the surgeon was unwilling to enrol the patient, excluding the higher risk patients.

### IMPACT ON PRACTICE

TCD could help to determine which asymptomatic patients would benefit most from CEA but a large proportion of the national workforce would need training and organisations would need to invest in specialist equipment.



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## Asymptomatic Carotid Disease Cont.

Howard, D. P. J. et al (2021) Risk of stroke in relation to degree of asymptomatic carotid stenosis: a population-based cohort study, systematic review, and meta-analysis. **Oxford Vascular Study**. The Lancet Neurology, Vol 20, Issue 3, pp 193-202.

### SUMMARY

The role of surgical intervention in asymptomatic patients with carotid stenosis remains controversial. Research by Howard et al (2021) found that the risk of stroke has declined over decades and suggest that stroke risk in this patient cohort is highly dependent on the severity of stenosis. Howard et al reaffirmed there is benefit from CEA for severe disease (>70% NASCET). However, they found that for patients with moderate stenosis (50-69% NASCET) the 5-year stroke risk was low when given best medial therapy, therefore questioning the need for revascularisation in this cohort.

### PROS

The Oxford Vascular Study (OxVasc) database including 92748 patients was used for this review; some 2178 had carotid imaging. Additionally, there was substantial analysis of association of risk factors, stenosis severity and stroke risk.

### CONS

The asymptomatic patients included were patients that had experienced previous cerebrovascular events in other territories.

### IMPACT ON PRACTICE

These findings promote the use of carotid screening programmes and the benefit of CEA in severe (>70%) stenosis but question the need for CEA with moderate disease.

Reiff, T et al. (2022) Carotid endarterectomy or stenting or best medical treatment alone for moderate-to-severe asymptomatic carotid artery stenosis: 5-year results of a multicentre, randomised controlled trial (SPACE-2). The Lancet Neurology, Vol 21, Issue 10, pp 877-888.

### SUMMARY

SPACE-2 compared three treatments in patients with 70% ECST stenosis (equates to 50% NASCET): CEA with BMT, carotid artery stenting with BMT, and BMT alone. However, as a result of slow recruitment this was amended. SPACE-2a compared CEA and BMT with BMT alone. SPACE-2b compared stenting and BMT with BMT alone. They found that CEA or stenting along with BMT was not superior to BMT alone regarding risk of stroke or death within 30 days or ipsilateral stroke during 5-year observation period.

### PROS

Good follow up of patients, for a mean of 60 months.

### CONS

Due to difficulties with patient recruitment and other financial issues, only 513 patients were included, forming a relatively small sample size, so results must be interpreted with caution.

### IMPACT ON PRACTICE

CEA or stenting for patients with 70% ECST (equates to 50% NASCET) stenosis may not be superior to modern best medical therapy (see ACAS cons for outline). Rates of surgical intervention for stroke prevention in asymptomatic carotid disease may reduce with improved evidence.

### WHAT'S ON THE HORIZON

#### ECST-2

The 2nd European Carotid Surgery Trial (ECST-2) continues to recruit both asymp/symptomatic patients with >50% NASCET stenosis. Similarly to SPACE-2, interim analysis indicates at 2-years, the rate of a composite of periprocedural death, stroke, or MI in those receiving CEA was similar to BMT alone (10.3% with 10.0%), again questioning the need for carotid revascularization.

#### CREST-2

The Carotid Revascularization Endarterectomy Versus Stenting Trial 2 (CREST-2) is a USA based trial designed like the original SPACE-2 study (CEA vs stent vs BMT) but is also interested in improvement of cognitive function. Results are not yet available, but many experts anticipate similar results to SPACE-2 and ECST-2.

#### CONCLUSION

The number of carotid interventions to prevent future stroke may reduce in coming years because of reduced benefit in those with moderate stenosis and significant improvements in best medical therapy. Data is clear that intervention for severe disease is important and protective. However, the large proportion of research has not explored the importance of sub-surgical threshold disease (<50%) and its risk for future stroke nor for other cardiovascular events such as MI. There are works being carried out in both Oxford and Manchester exploring novel techniques such as artificial intelligence on those with mild, moderate and severe carotid stenosis to establish their predictive ability for all types of major adverse cardiovascular event. Data from both groups will be presented in November at the SVT ASM in Dublin.