# An Overview of the Randomized Trials of Carotid Endarterectomy versus Carotid Angioplasty



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**The Leicester Trial**

The Leicester Trial aimed to randomize 300 patients (without preliminary angiography) with a symptomatic 70 to 99% stenosis (Table 1). All CAS patients were stented primarily, employing predilatation as appropriate. Cerebral protection devices (CPD) were not available. The Data Monitoring Committee (DMC) suspended the trial after 23 patients had been randomized. By that time, 10 had undergone an uneventful CEA, but 5 of 7 patients suffered a stroke following CAS.

**Table 1. Overview of the Randomized Trials of Carotid Endarterectomy versus Carotid Angioplasty**

| Trial | Year | Patients | Stent | CPD | Suspended |
|---|---|---|---|---|---|
| Leicester Trial | 1998 | Symp (70-99%) | Yes | No | Yes |
| CAVATAS | 2001 | Symp (50-99%) | Some | No | No |
| WALLSTENT | 2001 | Symp (60-99%) | Yes | No | Yes |
| Lexington I | 2001 | Symp (70-99%) | Yes | No | No |
| EVA-3S | 2004 | Symp (70-99%) | Yes | Some | Yes |
| Lexington II | 2004 | Asymp (80-99%) | Yes | No | No |
| SAPPHIRE | 2004 | Asymp (80-99%) | Yes | All | No |
| | | Symp (50-99%) | Yes | All | No |

Asymp = asymptomatic; CPD = cerebral protection devices; Symp = symptomatic.

Comment

Although the numbers remain too small to influence clinical practice, one conclusion from this study was that you could not simply assume that patients who would otherwise undergo CEA can also undergo CAS without additional selection criteria.

**CAVATAS**

CAVATAS randomized 504 symptomatic patients with > 50% stenosis (the majority had stenosis > 70%). Stents were only used in 26% of patients, usually if there was a problem achieving a technically satisfactory result. No CPDs were available. The 30-day death/stroke rates were approximately 10% in each group. The restenosis and late stroke rates are summarized in Table 2.

**Table 2. Restenosis and Late Stroke Rates**

| | 30-Day Death/Stroke | | Restenosis | | Late Stroke* | |
|---|---|---|---|---|---|---|
| Trial | CEA | CAS | CEA | CAS | CEA | CAS |
| Leicester Trial | All 0/10 | 5/7 | n/a | n/a | n/a | n/a |
| CAVATAS | All 9.9% | 10.0% | 4.0% | 14% (1 yr) | 14% | 14% (3 yr) |
| WALLSTENT | All 4.5% | 12.1% | n/a | n/a | n/a | n/a |
| Lexington I | All 2.0% | 0.0% | 2.0% | 0.0% | | |
| EVA-3S | All n/a | 15% | n/a | n/a | n/a | n/a |
| | No CPD n/a | 26.7% | n/a | n/a | n/a | n/a |
| | CPD used n/a | 10.3% | n/a | n/a | n/a | n/a |
| Lexington II | All 0.0% | 0.0% | 0.0% | 0.0% (4 yr) | 0.0% | 0.0% (4 yr) |
| SAPPHIRE | All 7.3% | 4.8%† | n/a | n/a | 8.4% | 5.5% (1 yr) |
| | Asymp 6.1% | 5.8%† | n/a | n/a | n/a | n/a |

Asymp = asymptomatic; CPD = cerebral protection devices; n/a = not available.
*Includes operative death/stroke.
†Derived from national/international presentations as this data was not presented in the article.

Comment

This trial has been heavily criticized for the excessively high perioperative death/stroke rate. The investigators (but not many others!) concluded that this was because their randomized patients had more comorbidity than in ECST or NASCET. However, CAVATAS was the first trial to indicate that following successful CAS, the long-term results were no different than CEA despite a much higher rate of restenosis.

**WALLSTENT**

WALLSTENT randomized 219 symptomatic patients with a symptomatic 60 to 99% stenosis. All were stented primarily, but CPDs were not available. The trial was suspended when it was observed that the 30-day death/stroke rate was significantly higher in CAS patients (12.1% vs 4.5%). One-year death/any stroke (including the operative risk) was not published. One-year death/ipsilateral stroke rates were 12.1% for CAS vs 3.6% for CEA.

Comment

This is the third largest trial undertaken to date. Notwithstanding commercial pressures, it remains extremely disappointing that the results have only been published as an abstract.

**EVA-3S**

This is the French national trial in symptomatic patients with > 70% stenosis. All patients were stented primarily by experienced or proctored interventionalists, though there was no uniform policy on the use of CPDs. The DMC suspended this trial after 80 patients had been randomized and issued a clinical alert. The outcomes following CEA were not published. Overall, the 30-day death/stroke rate following CAS was 15%. Unprotected CAS incurred a 26.7% risk, and the DMC advised restarting the trial with the recommendation that all CAS procedures should use a CPD.

Comment

Notwithstanding the fact that the trial was never powered to make this type of decision, the observed differences between protected and unprotected CAS were not statistically significant and the lower limits of the confidence intervals were compatible with an absence of difference! Finally, and lost amid the statistical debate, is the inevitable observation that if CPDs are so good, why were they still associated with a 10% death/stroke rate in this trial?

**Lexington I and II**

Lexington I randomized 104 symptomatic patients with > 70% stenosis, whereas Lexington II randomized 85 asymptomatic patients with > 80% stenoses. All were stented primarily, but none involved CPDs. The early and late outcomes in these studies are quite unusual. In Lexington I, there was one non-stroke death following CEA. Otherwise (in both Lexington I and II), no strokes

were reported either within 30 days or during follow-up. Accordingly the 2-year rate of death/stroke (including the operative risk) was 2% for CEA versus 0.0% for CAS. In Lexington II, the parallel 4-year figures were 0.0% versus 0.0%, and no patient suffered restenosis at any time.

Comment
Notwithstanding how one derived a power calculation that concluded that only 85 asymptomatic patients needed to be recruited in Lexington II, it is very difficult to know how these trials can be assessed.

**SAPPHIRE**
The hypothesis underlying SAPPHIRE was that protected CAS would be equivalent or not inferior to CEA in patients "deemed high-risk for CEA." Seven hundred forty-seven patients were registered, but only 334 were randomized. Readers of the article will find it extremely hard to ascertain procedural and late outcomes (in the format presented above), so these have been documented to presentations from international and national meetings. Overall, the 30-day death/stroke rate for all randomized patients was 4.8% (CAS) versus 7.3% (CEA). One-year death/ipsilateral stroke (including the operative risk) was 8.4% (CEA) versus 5.5% (CAS). Neither was statistically significant. However, 78% of the randomized cohort was asymptomatic, including many with recurrent stenosis after CEA. In this asymptomatic subgroup, the 30-day death/stroke rate was 5.8% for CAS versus 6.1% for CEA. SAPPHIRE was, however, unique in having a primary end point, which also included myocardial infarction (MI). A diagnosis of MI was made on the basis of enzyme assay. In the study overall, CAS was associated with a significantly lower 30-day risk of death/stroke/MI (5.8% vs 12.1%).

Comment
Many surgeons have "cried foul" at the inclusion of MI in the primary end point. However, if this is a real observation, it is clearly important as evidence suggests that non-Q wave infarction may be associated with increased cardiac morbidity during follow-up. However, although much of the debate has been focused on the definition of procedural morbidity, few have commented on the death/stroke rates observed in these so-called high-risk asymptomatic patients. To-date, neither ACST nor ACAS have shown that the benefits of CEA (or CAS) can be sustained with a procedural risk of 6%. An alternative conclusion from SAPPHIRE might therefore be that where no treatment is warranted, CAS is safer than CEA.

**References**

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**NOTES**