

Low-dose aspirin reduced combined 3-month risk for stroke, MI, and death after carotid endarterectomy

Taylor DW, Barnett HJ, Haynes RB, et al., for the ASA and Carotid Endarterectomy (ACE) Trial Collaborators. Low-dose and high-dose acetylsalicylic acid for patients undergoing carotid endarterectomy: a randomised controlled trial. *Lancet*. 1999 Jun 26;353:2179-84.

QUESTION

In patients scheduled for carotid endarterectomy (CE), is low-dose aspirin as effective as high-dose aspirin for reducing perioperative stroke, myocardial infarction (MI), and death after CE?

DESIGN

Randomized (allocation concealed*), blinded (patients, clinicians, and outcome assessors)*, placebo-controlled trial with 3-month follow-up (ASA [Carotid Endarterectomy [ACE] trial).

SETTING

48 clinical centers in the United States, 19 in Canada, 4 in Australia, and 1 each in Italy, Argentina, and Finland.

PATIENTS

2849 patients (mean age 69 y, 70% men, 95% white) scheduled for CE who could tolerate aspirin at 1300 mg/d. Exclusion criteria were essential aspirin or anti-platelet therapy, recent disabling stroke, or recent or planned cardiac surgery. Follow-up was > 99%.

INTERVENTION

Patients were allocated to aspirin, 81 mg/d ($n = 709$), 325 mg/d ($n = 708$), 650 mg/d

($n = 715$), or 1300 mg/d ($n = 717$), starting before surgery and continuing for 3 months.

MAIN OUTCOME MEASURES

Morbidity and mortality at 30 days and at 3 months after surgery. Composite end points were any stroke, MI, or death; any stroke or death; and ipsilateral stroke or death with comparisons between the 2 low-dose and 2 high-dose groups.

MAIN RESULTS

Surgery was canceled in 45 patients. Intention-to-treat analysis showed that the patients in the low-dose aspirin groups had a lower rate of combined stroke, MI, or death at 3 months than those in the high-dose groups ($P = 0.03$) but did not differ for the other combined end points (Table). A predefined efficacy analysis of

1116 patients who had been taking aspirin < 656 mg/d and were randomized > 1 day before surgery showed even stronger findings favoring low-dose aspirin at 30 days and 3 months.

CONCLUSION

Low-dose aspirin reduced the combined end point of stroke, myocardial infarction, or death at 3 months for patients scheduled for carotid endarterectomy more than did high-dose aspirin.

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*See Glossary.

Low- vs high-dose aspirin with carotid endarterectomy†

Outcomes at 3 mo	Low-dose aspirin	High-dose aspirin	RRR (95% CI)	NNT (CI)
Any stroke, MI, or death	6.2%	8.4%	25.5% (3 to 43)	47 (24 to 471)
Any stroke or death	5.7%	7.1%	20.2% (-6 to 40)	Not significant
Ipsilateral stroke or death	4.9%	6.5%	24.5% (-2 to 44)	Not significant

†MI = myocardial infarction. Other abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

The U.S. Food and Drug Administration recently ruled that low-dose aspirin may be used to prevent stroke in patients with a previous stroke or transient ischemic attack. The ACE trial is likely to fuel the move toward this use of low-dose aspirin. Unlike other aspirin studies, the ACE trial is restricted to the period after CE and shows that low-dose aspirin should now be used at the time of CE.

Should low-dose aspirin be used for all stroke prevention? The ACE trial data do not directly answer this question. However, support for high-dose aspirin is mainly based on greater reductions in stroke risk in studies using higher aspirin doses than in studies using lower doses (1) or on secondary analyses (2) and not on randomized controlled trials. The ACE trial is the first randomized study to show a differential effect among aspirin doses and suggests that low-dose aspirin may be superior to high-dose aspirin. Other randomized studies (3, 4) and a meta-analysis (1) have shown no difference between aspirin doses, a finding that makes it unlikely that high-dose aspirin is better. A higher rate of gastrointestinal and serious hemorrhage may occur with high-dose aspirin (5). Low-dose (≤ 325 mg/d) aspirin should probably be used for all stroke

prevention. 75 mg or even 30 mg may be just as effective as somewhat higher doses, but further studies are needed to confirm this.

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References

1. Barnett HJ, Eliasziw M, Meldrum HE. Drugs and surgery in the prevention of ischemic stroke. *N Engl J Med*. 1995;332:238-48.
2. Barnett HJ, Taylor DW, Eliasziw M, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. *N Engl J Med*. 1998;339:1415-25.
3. Farrell B, Godwin J, Richards S, Warlow C. The United Kingdom transient ischaemic attack (UK-TIA) aspirin trial: final results. *J Neurol Neurosurg Psychiatry*. 1991;54:1044-54.
4. The Dutch TIA Trial Study Group. A comparison of two doses of aspirin (30 mg vs. 283 mg a day) in patients after a transient ischemic attack or minor ischemic stroke. *N Engl J Med*. 1991;325:1261-6.
5. Hart RG, Harrison MJ. Aspirin wars: the optimal dose of aspirin prevents stroke. *Stroke*. 1996;27:585-7.