

Clopidogrel reduced recurrent ischaemic events in patients with previous cardiac surgery more than aspirin

Bhatt DL, Chew DP, Hirsch AT, et al. *Superiority of clopidogrel versus aspirin in patients with prior cardiac surgery. Circulation* 2001 Jan 23;103:363–8.

QUESTION: In patients with recent ischaemic stroke, recent myocardial infarction (MI), or peripheral arterial disease and previous cardiac surgery, is clopidogrel more effective than aspirin in reducing recurrent ischaemic events?

Design

Subgroup analysis of a randomised [allocation concealed*]†, blinded [patients, clinicians, outcome assessors, and statisticians]‡,* placebo controlled trial with 1–3 year follow up (mean 1.6 y) (Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events [CAPRIE] study).

Setting

{384 clinical centres in 16 countries}†.

Patients

1480 patients (mean age 64 y, 84% men, 96% white) with recent stroke or MI or peripheral arterial disease who had also had cardiac surgery. Exclusion criteria were a history of bleeding disorders, uncontrolled hypertension, or severe renal or hepatic dysfunction. Follow up was 99.9%.

Intervention

775 patients were allocated to clopidogrel, 75 mg/day, and 705 to aspirin, 325 mg/day.

Main outcome measures

Combined end point of vascular mortality, MI, and ischaemic stroke. Individual end points were also assessed.

Main results

Clopidogrel was associated with decreased annual rates of the primary end point (combined vascular death, MI, and stroke) ($p=0.004$), vascular death, MI, all cause hospitalisation (table), admission to hospital for ischaemia or bleeding ($p=0.02$), and 3 other combined end points. The groups did not differ for annual rates of all cause mortality (3.4% for aspirin *v* 2.6% for clopidogrel, $p=0.2$) or stroke (3.5% *v* 2.6%, $p=0.2$).

Conclusion

Clopidogrel was more effective than aspirin for reducing recurrent ischaemic events in patients with recent stroke, recent myocardial infarction, or peripheral arterial disease who had also had previous cardiac surgery.

*See glossary.

†CAPRIE Steering Committee. *Lancet* 1996;348:1329–39.

Clopidogrel v aspirin for stroke, myocardial infarction, or peripheral arterial disease and previous cardiac surgery‡

Outcomes/year	Clopidogrel	Aspirin	RRR (95% CI)	NNT (CI)
Primary combined end point§	5.8%	9.1%	36% (13 to 53)	30 (21 to 82)
Vascular death	2.0%	3.3%	43% (5 to 66)	71 (46 to 659)
Myocardial infarction	2.4%	3.9%	39% (2 to 62)	66 (41 to 1070)
Admission to hospital	36%	48%	22% (9 to 33)	10 (6 to 24)

‡Abbreviations defined in glossary; RRR, NNT, and CI provided by author.

§Primary combined end point = vascular death, myocardial infarction, and stroke.

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COMMENTARY

Platelet thrombi on ruptured plaques provoke many of the complications of atherosclerosis. Antiplatelet treatment with aspirin has been shown in numerous randomised trials to reduce the rate of MI, stroke, and death among patients with clinically evident atherosclerosis. Nevertheless, high risk patients receiving aspirin treatment have a substantial incidence of adverse ischaemic events. Better therapeutic options would be welcome.

Clopidogrel reduced the rate of vascular events more than aspirin in the CAPRIE trial (an absolute risk reduction of 0.51% for the combined end points).¹ Bhatt *et al* show in post-hoc analysis that this benefit was magnified in the subgroup of patients with previous cardiac surgery (absolute risk reduction of 3.3%). The observation that clopidogrel improved patient outcomes after coronary stenting enhances the plausibility of this result.² However, the apparent benefit of clopidogrel must be weighed against its higher cost and risk for adverse effects. Clopidogrel costs substantially more than aspirin and has been associated with a small, but definite incidence of haematological complications.³ Thus, pending confirmatory evaluation and a thorough assessment of cost effectiveness, we would reserve clopidogrel for patients in the first weeks after coronary stenting or for those in whom aspirin is ineffective or contraindicated.

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1 CAPRIE Steering Committee. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). *Lancet* 1996;348:1329–39.

2 Mishkel GJ, Aguirre FV, Ligon RW, *et al*. Clopidogrel as adjunctive antiplatelet therapy during coronary stenting. *J Am Coll Cardiol* 1999;34:1884–90

3 Bennett CL, Connors JM, Carwile JM, *et al*. Thrombotic thrombocytopenic purpura associated with clopidogrel. *N Engl J Med* 1999;342:1773–7.