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


**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.
‡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.1 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.2 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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