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


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

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

**Setting**
[384 clinical centers 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/d, and 705 to aspirin, 325 mg/d.

**Main outcome measures**
Combined end point of vascular mortality, MI, and ischemic 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 hospitalization (Table), hospitalization for ischemia 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 vs 2.6% for clopidogrel, $P = 0.2$) or stroke (3.5% vs 2.6%, $P = 0.2$).

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

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For correspondence: Dr. E.J. Topol, Department of Cardiology, F25, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, USA. FAX 216-445-9595.

*See Glossary.

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

Clopidogrel reduced the rate of vascular events more than did aspirin in the CAPRIE trial (an absolute risk reduction of 0.51% for the combined end points) (1). Bhatt and colleagues show in posthoc 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 hematologic 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.

Peter W. Groeneveld, MD
Mark A. Hlatky, MD
Stanford University School of Medicine
Palo Alto, California, USA

**References**