

Clopidogrel or Aspirin to Prevent Recurrent Cardiovascular Events?

Schleinitz MD, Weiss JP, Owens DK. Clopidogrel versus aspirin for secondary prophylaxis of vascular events: a cost-effectiveness analysis. Am J Med 2004;116:797–806.

Study Overview

Objective. To evaluate the cost-effectiveness of clopidogrel or aspirin to prevent cardiovascular events in patients with prior myocardial infarction (MI), stroke, or peripheral arterial disease (PAD).

Design. Markov models were used to model lifetime outcomes and costs for the base case of a 63-year-old patient. Probabilities for vascular outcomes were taken from the Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events (CAPRIE) study [1]. Clopidogrel was assumed to cost \$3.80 per day.

Main outcome measures. Costs (from a societal perspective), life expectancy in quality-adjusted life-years (QALYs), incremental cost-effectiveness ratios, and number of vascular events averted.

Main results. For the base case, in patients with a prior MI, aspirin was less expensive and more efficacious than clopidogrel (–0.26 QALYs for a patient treated with clopidogrel versus aspirin). For patients with prior stroke, clopidogrel was more effective than aspirin (0.17 QALYs at \$31,200 per QALY). Patients with PAD benefitted the most using clopidogrel versus aspirin (0.55 QALYs gained with the use of clopidogrel at \$25,100 per QALY).

Conclusion. Compared with aspirin, clopidogrel increased quality-adjusted life expectancy for patients with PAD or recent stroke at an acceptable cost, but this is not true for post-MI patients.

Commentary

This study consists of 3 cost-effectiveness analyses of the use of aspirin compared with clopidogrel for the secondary prevention of cardiovascular events. By performing a separate analysis for each of the 3 groups of eligible patients (those enrolled following an MI, following a stroke, or with symptomatic PAD), this study extends the work of an earlier cost-effectiveness analysis comparing aspirin, clopidogrel, or

both for the secondary prevention of recurrent events, which found that increased life expectancy with the addition of clopidogrel came at a cost that was essentially prohibitive [2]. By focusing on the apparent cost-effectiveness for patients with PAD or prior stroke, the study by Schleinitz et al reaches different conclusions.

Does clopidogrel effect patients with PAD differently than it does persons with other forms of atherosclerosis, such as MI, as this subgroup analysis suggests? Probably not. Although there may be some statistical variation, there is overlap in the confidence intervals around the primary treatment effect for the 3 groups studied in the CAPRIE trial. Furthermore, in CAPRIE, patients treated with aspirin in the PAD group had a vascular death rate that was higher than the rate observed in the stroke or MI groups [1]. It is possible that reductions in the rate of vascular death with clopidogrel are similar in various groups of atherosclerosis patients but that CAPRIE had insufficient power to detect this effect for the stroke and MI groups because the absolute vascular death rate was lower.

Another potential problem with the Schleinitz et al study is that the most relevant question for consideration may be whether or not clopidogrel should be used long-term in addition to aspirin rather than as a substitute for aspirin. Two recent clinical trials demonstrated a 20% to 27% relative risk reduction in cardiovascular events when clopidogrel was used in addition to aspirin for up to 1 year following an acute coronary syndrome or percutaneous revascularization [3,4]. This was a larger improvement than the overall 8.7% benefit seen in the CAPRIE study. However, the benefit of combination therapy comes at the expense of an increase in bleeding [3,4], and future decision analyses will need to examine this risk and its associated expenses.

Medication cost and its impact on a patient's willingness to adhere to therapy is an issue that cost-effectiveness analyses do not address. For patients who have to pay \$1387 per year out-of-pocket for clopidogrel, aspirin may appear as an acceptable alternative. Physicians should explore individual patient preferences around this issue when making treatment recommendations.

Applications for Clinical Practice

Despite its high cost, clopidogrel probably improves quality-adjusted life expectancy in patients at high risk of cardiovascular death (ie, the PAD group of the CAPRIE trial). This benefit comes at a cost that may be similar to other accepted health care expenses. However, determining which patients are most likely to benefit from clopidogrel long-term is not entirely clear. At the moment, the selection of the appropriate high-risk patients for antithrombotic treatment other than aspirin alone (eg, clopidogrel instead of or in addition to aspirin, or aspirin plus oral anticoagulation) is an area where consensus is lacking.

—Review by Stephen D. Persell, MD, MPH

References

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