Economic assessment of platelet glycoprotein IIb/IIIa receptor blockade with abciximab and low-dose heparin during percutaneous coronary revascularization: results from the EPILOG randomized trial


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of abciximab and low-dose heparin to inhibit the platelet glycoprotein IIb/IIIa receptor during percutaneous coronary revascularisation (PTCA). The comparator was justified on the basis that it was established practice not to use abciximab.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing urgent or elective PTCA. Patients with acute myocardial infection (MI) or unstable angina with associated electrocardiographic changes during the previous 24 hours were excluded.

Setting
The setting was a hospital. The economic analysis was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were collected between February and December 1995. The cost data were taken from hospital bills and from a 1994 source. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a single study (see Other Publications of Related Interest).

Link between effectiveness and cost data
The costing was carried out retrospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
The study sample comprised 2,792 patients undergoing elective or urgent PTCA. These received either abciximab with standard-dose weight-adjusted heparin (n=918), abciximab with low-dose weight-adjusted heparin (n=935), or placebo with standard-dose weight-adjusted heparin (n=939). The median age of the participants was 60 years. Seventy-two per cent of the participants were men, and 90% were white. Some of these patients also suffered from diabetes mellitus (23%), hypertension (59%) or peripheral vascular disease (9%), or used tobacco within the preceding year (33%).
The primary indications for revascularisation were unstable angina (48% of the patients), recent MI (21%), and stable ischaemia or a positive functional study (31%). Multivessel coronary artery disease was present in 47% of the patients, and median left ventricular ejection fraction was present in 55%. No power calculations were used to determine sample size.

**Study design**
The study was a prospective, double-blind randomised controlled trial carried out at 69 sites in the USA and Canada. The patients were followed-up for 6 months after hospital discharge. No patients were lost to follow-up.

**Analysis of effectiveness**
The data were analysed on an intention to treat basis. The primary health outcomes were a composite of death, MI, or urgent repeat revascularisation within 30 days and at 6 months. In addition, major and minor bleeding events were assessed. The three groups were stated to have been comparable in terms of age, body weight, gender, and primary indication for revascularisation; no statistical difference between the groups was reported in the original publication. Major and minor bleeding and MI were defined in the original publication (see Other Publications of Related Interest).

**Effectiveness results**
The incidence of the composite end point at 30 days was 11.7% in the placebo group, 5.2% in the abciximab with low-dose heparin group, and 5.4% in the abciximab with standard-dose heparin group. The relative risk reduction was 58% for the abciximab and low-dose heparin group, (p<0.0001), and 54% for the abciximab and standard-dose heparin group, (p<0.0001).

The incidence of MI was 8.7% in the placebo group, 3.7% in the abciximab with low-dose heparin group, and 3.8% in the abciximab with standard-dose heparin group.

The incidence of urgent CABG surgery was 1.7% in the placebo group, 0.4% in the abciximab with low-dose heparin group, and 0.9% in the abciximab with standard-dose heparin group.

The incidence of urgent repeat PTCA was 3.8% in the placebo group, 1.2% in the abciximab with low-dose heparin group, and 1.5% in the abciximab with standard-dose heparin group.

The rates of major bleeding unassociated with CABG surgery were 1.1% in the placebo group, 1.1% in the abciximab with low-dose heparin group, and 1.9% in the abciximab with standard-dose heparin group.

The differences among the treatment groups observed at 30 days, with regard to death, MI and urgent repeat revascularisation, were maintained during the 6-month follow-up.

The rates of death at 30 days were 0.8% for placebo, 0.3% for abciximab with low-dose heparin, and 0.4% for abciximab with standard-dose heparin, (p=0.39). At 6 months, the rates of death were more comparable (p=0.62).

The rates of MI at 6 months were still quite different from those at 30 days, (p<0.001).

The rates of repeat revascularisation at 6 months were 19.4% for placebo, 19.0% for abciximab with low-dose heparin, and 18.4% for abciximab with standard-dose heparin, (p=0.52).

Compared with the 30-day data, the incidence of the composite end point had switched at 6 months. The composite rates were 8.3% for abciximab with standard-dose heparin, 8.4% for abciximab with low-dose heparin, and 14.7% for placebo, (p<0.001).

**Clinical conclusions**
The use of abciximab with low-dose weight-adjusted heparin for the inhibition of the platelet glycoprotein IIb/IIIa receptor resulted in a marked reduction in the risk of acute ischaemic complications in patients undergoing PTCA.
without increasing the risk of haemorrhage. There was, however, no significant difference in mortality, although it was lowest with the abciximab and low-dose heparin combination. The composite risk of death, repeat revascularisation and MI was lowest at 6 months with the abciximab and standard-dose heparin combination.

Modelling
A multivariate linear regression analysis was conducted. This investigated the costs associated with the duration of hospital stay, catheterisation, PTCA, stent placement, coronary artery bypass graft (CABG) surgery, and major and minor bleeding not associated with coronary bypass surgery. This model was used to impute the costs for patients with incomplete data, and to identify the factors influencing the costs associated with abciximab therapy.

Measure of benefits used in the economic analysis
The authors did not derive a summary measure of health benefit. The analysis was therefore categorised as a cost-consequences analysis.

Direct costs
The direct costs were not discounted due to the short timeframe of the study (less than one year). The resource quantities and unit costs were reported separately for the duration of hospital stay and the procedures used (CABG, percutaneous coronary intervention, and catheterisation without percutaneous coronary intervention). The direct costs were for hospitalisation and the physicians’ fees. The quantity/cost boundary adopted was that of the hospital. The cost of hospitalisation was derived from hospital bills. The charges were converted into costs by use of department-specific cost-to-charge ratios. The physicians’ fees were taken from the 1994 Medicare Fee Schedule. The price year was not reported.

Statistical analysis of costs
A van der Waerden normal scores test was used for pairwise comparisons of the costs. The confidence intervals (CIs) for the differences between costs were computed using a bias-corrected bootstrap with 16,000 samples.

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analyses were reported.

Estimated benefits used in the economic analysis
See 'Effectiveness Results' section.

Cost results
The total, baseline hospitalisation costs were $9,632 (+/-6,434) in the placebo group, $10,215 (+/-5,173) in the abciximab with low-dose heparin group, (p<0.001), and $10,546 (+/-5,495) in the abciximab with standard-dose heparin group, (p<0.001).

The incremental, baseline hospitalisation costs, compared with placebo, were $583 (95% CI: 19 - 1079; p<0.001) in the abciximab with low-dose heparin group, and $914 (95% CI: 380 - 1458; p<0.001) in the abciximab with standard-dose
The follow-up hospitalisation costs were $3,568 (+/-8,813) in the placebo group, $4,221 (+/-10,270) in the abciximab with low-dose heparin group, (p=0.144), and $3,923 (+/-9,880) in the abciximab with standard-dose heparin group, (p=0.429).

The cumulative incremental costs over the 6-month period, compared with placebo, were $1,236 (95% CI: 209 - 2,345) in the abciximab with low-dose heparin group, and $1,268 (95% CI: 265 - 2,406) in the abciximab with standard-dose heparin group.

The baseline hospital saving in the abciximab with low-dose heparin group was $806. Of this, a saving of $603 was attributed to reductions in the CABG surgery rates, unplanned stenting, and the duration of hospital stay.

The baseline hospital saving in the abciximab with standard-dose heparin group was $489. Of this, a saving of $484 was attributed to reductions in the duration of hospital stay, and the rates of bypass surgery, repeat percutaneous coronary intervention and MI.

There were no excess costs associated with bleeding among patients who were randomised to abciximab with low-dose heparin. However, $40 in cost-savings was lost among patients treated with abciximab and standard-dose heparin, owing to the modest increase in major and minor bleeding events.

**Synthesis of costs and benefits**

Not applicable.

**Authors' conclusions**

Treatment with abciximab and low-dose, weight-adjusted heparin during PTCA reduced ischaemic events and associated costs, thereby offsetting some of the cost of the drug. In addition, by lowering the heparin dose the bleeding complications associated with abciximab were reduced. This further enhanced the economic attractiveness of this treatment strategy.

**CRD COMMENTARY - Selection of comparators**

The choice of a placebo for the comparator was justified. You should decide if these health technologies are relevant to your setting. A comparison with placebo plus low-dose heparin might also have been useful.

**Validity of estimate of measure of effectiveness**

The analysis was based on a prospective, double-blind randomised controlled trial, which was appropriate for the study question. The authors reported demographic and other baseline characteristics as evidence of the extent to which the participants studied were representative of the study population. The groups were shown to be comparable at analysis, and there was no loss to follow-up. The measures of effectiveness seem to have been appropriate as they covered both mortality and morbidity, as defined in the original paper. However there were three main limitations of the study.

1. The authors concluded that, overall, abciximab with low-dose heparin was the most effective therapy since it had comparable bleeding rates to placebo and standard-dose heparin, but with statistically significantly better 30-day outcomes in terms of death, MI or repeat revascularisation. The results became more ambiguous at 6 months. In fact, mortality rates were never statistically significantly different and abciximab plus standard-dose heparin was generally better than abciximab plus low-dose heparin, except for bleeding. Where one therapy offers inconsistent performance, an overall evaluation requires the weighting of the consequences in terms of, for example, individual preferences or quality of life.

2. The results were not reported in the economic evaluation paper, thus making a fully informed judgement of the study difficult.
3. The authors only reported the conclusions in terms of cost-savings (and not cost-effectiveness) although this was clearly due to improved effectiveness, justifying the study as one of cost-effectiveness.

**Validity of estimate of measure of benefit**
Since there was no summary measure of benefit, see comments in the 'Validity of estimate of measure of effectiveness' section.

**Validity of estimate of costs**
All the relevant hospital-related direct cost categories seem to have been included and statistical analyses were conducted. In addition, the quantities were reported separately for some components, and the hospital charges were converted into costs. However, no sensitivity analyses were reported on the quantities or costs, thus limiting the generalisability of the results. Also, the price year was not reported. A regression analysis was used to derive costs for patients with missing data. The authors acknowledged that they did not consider out-patient costs or the productivity costs relating to loss of employment. The authors used UB 92 bill forms to estimate costs; this approximation has been validated in selective instances, but not in all hospitals.

**Other issues**
The authors made appropriate comparisons of their findings with those from other studies, but did not address the issue of generalisability to other settings. The authors seem to have presented their results selectively in terms of mortality and at 6 months. The study considered patients undergoing urgent or elective PTCA and this was reflected in the authors' conclusions.

**Implications of the study**
The authors did not draw any further conclusions or make any recommendations. Their conclusions should be viewed with caution given the methodological concerns highlighted, such as the relative value of all the health consequences, the choice of the comparator, and their reporting of the outcome as merely cost-saving.

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**Other publications of related interest**

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