Outcomes at 1 year and economic implications of platelet glycoprotein IIb/IIIa blockade in patients undergoing coronary stenting: results from a multicentre randomised 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
Platelet glycoprotein IIb/IIIa inhibitor (abciximab) given at the time of coronary stenting.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness study.

Study population
Patients undergoing elective or urgent percutaneous coronary revascularisation.

Setting
The study setting was a hospital. The economic study was performed in the USA.

Dates to which data relate
The dates of the effectiveness and resource data were not mentioned, but the methods of the study were reported in 1998 and 1999. 1997 prices were used.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness study.

Study sample
The study sample comprised patients undergoing elective or urgent percutaneous coronary revascularisation. 2,399 patients were randomised as follows:

- stent plus placebo (809 patients);
- stent plus abciximab (794 patients);
- balloon angioplasty plus abciximab (796 patients).
25 of the 2,399 patients (1%) were lost to follow-up. 1,438 patients were from the USA.

**Study design**
The study was a randomised controlled trial containing patients from 63 centres in the USA and Canada. Randomisation to one of three treatment groups was carried out by telephone, but the study drug allocation was concealed from patients and investigators in the groups assigned to stenting. The masking of the study drug allocation was maintained throughout the 1 year follow-up. The heparin dose was concealed from the investigator by designating a heparin coordinator to take measurements of activated clotting time and to direct the administration according to a predefined algorithm. The major outcomes assessed were death, myocardial infarction and revascularisation at 1 year. However, the trial was not adequately powered to detect whether improved survival was concentrated in particular clinical subgroups (including age, sex and diabetes), although these factors were prespecified so as to allow observation of possible important trends in outcome.

**Analysis of effectiveness**
All analyses were based on intention to treat. Kaplan-Meier methods were used to estimate the event rates for each treatment group and pairwise comparisons between any two groups were carried out with log-rank tests. A multivariate Cox's proportional-hazard model was developed to investigate the independent association of demographic and procedural factors with survival. After identification of the significant risk factors, the effect of treatment was evaluated in the model. Subgroup analysis was prospectively planned for patients with diabetes since the condition was associated with a particularly high risk. Hazard ratios, 95% confidence intervals (95% CI) and Wald chi square p values were presented based on the model containing treatment and significant risk factors. The p values were two-sided.

**Effectiveness results**
By 1 year, 8 of the 794 patients in the stenting plus abciximab group had died (1.0%), 19 of the 809 patients in the stenting plus placebo group (2.4%) had died and 17 of the 796 patients in the balloon angioplasty plus abciximab group (2.1%) had died.

The combined endpoint of death or large myocardial infarction occurred in 42 patients in the stenting plus abciximab group (5.3%), 89 patients in the stenting plus placebo group (11.0%), and 64 patients in the balloon angioplasty plus abciximab group (8.1%).

Through multivariate modelling, independent factors associated with improved survival were found to be assignment to stenting with abciximab, (p=0.027) and greater preprocedural stenosis, (p=0.002).

Independent factors associated with worse survival included age greater than 70 years (p<0.001), previous heart failure (p=0.001), diabetes treated with insulin (p=0.02), and postprocedural occlusion (p<0.001).

**Clinical conclusions**
Coronary stenting with abciximab, compared with stenting alone or balloon angioplasty with abciximab, is associated with improved survival rates.

**Modelling**
A resource-based linear regression model was used to determine costs up to 1 year. This had been developed from empirical follow-up costs data collected in the Evaluation of PTCA to Improve Long-term Outcome by e7E3 GP IIb/IIIa receptor blockade (EPILOG) trial.

**Measure of benefits used in the economic analysis**
Survival was the measure of benefit used.
Direct costs
The economic analysis comprised two parts:

- a prospective comparison by intention to treat of medical costs up to 1 year for the US patients;
- a lifetime cost-effectiveness model based on the empirical US cost data and the overall 1-year survival data from the trial.

Hospital costs were calculated from hospital bills (US92 form) and hospital department-specific ratios of cost to charge. During the design phase, hospital bills for the index hospital stay were collected to obtain an accurate estimate of any potential cost offset from abciximab. For follow-up costs to 1 year, the resource use data from the case report form and a resource-based linear regression model (developed from empirical follow-up cost data collected in the EPILOG trial) were used. Physician fees were estimated from the Medicare Fee Schedule. The cost of abciximab was calculated to be $450 per vial and the cost of a Palmaz-Schatz stent to be $1,600 (undiscounted price).

Statistical analysis of costs
Log-rank tests were performed to compare costs.

Indirect Costs
Indirect costs were not considered. Earlier work suggested that employment status was not significantly affected by different revascularisation strategies.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was carried out on the price of the Palmaz-Schatz stent.

Estimated benefits used in the economic analysis
Compared with the stent plus placebo group, the stent plus abciximab group had an incremental life expectancy of 11 years per survivor (expected duration of life for a survivor) or 0.15 years per patient treated (discounted at 3%). Compared with the balloon angioplasty plus abciximab group, the stent plus abciximab group had an incremental life expectancy of 0.11 years (discounted at 3%).

Cost results
The cost for baseline hospital stay was $11,923 for stent plus placebo, $13,228 for stent plus abciximab, and $11,357 for balloon angioplasty plus abciximab, (p=0.0001).

Follow-up costs at one year were $5,096 for stent plus placebo, $4,723 for stent plus abciximab and $6,013 for balloon angioplasty plus abciximab.

Therefore at 1 year, the cumulative costs for the stent plus abciximab group exceeded those for the stent plus placebo group by $932 and those for the balloon angioplasty plus abciximab group by $581, (p=0.0008).

Synthesis of costs and benefits
Compared with the stent plus placebo group, the stent plus abciximab group gave a cost-effectiveness ratio of $6,213 per added life year.
Compared with the balloon angioplasty plus abciximab group, the stent plus abciximab group gave a cost-effectiveness ratio of $5,291 per added life year.

Use of a discounted cost for stents ($1,400) did not significantly affect the results.

**Authors’ conclusions**
The authors stated that, in terms of cost-effectiveness, stenting with abciximab compares favourably with other widely used therapies such as coronary bypass surgery for left mainstream disease (about $7,000 per added life year), the treatment of acute myocardial infarction with tissue plasminogen activator rather than streptokinase ($33,000 per added life year), and haemodialysis for chronic renal failure (about $35,000 per added life year). For every 1,000 patients undergoing percutaneous coronary revascularisation treated by the new combination strategy (stent plus abciximab) rather than one of the two previous standard care strategies (stent alone, balloon angioplasty plus abciximab), healthcare costs would increase by $600,000-900,000 and would allow 14 extra patients to survive on average for longer than 10 years.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of comparators was clear. The authors chose a placebo as one of the comparators. This allowed the active value of the treatment to be evaluated.

**Validity of estimate of measure of benefit**
The analysis was based on a randomised trial, which was appropriate for the study question. The study sample was representative of the study population and the patient groups were shown to be comparable at analysis. Appropriate statistical analyses were undertaken to take account of potential biases and confounding factors. The authors noted that their analysis might be conservative in that it did not consider the long-term (beyond 1 year) prognostic benefit of the myocardial infarctions prevented by abciximab. It was assumed that there would be no amplification of the survival benefit evident at 1 year, which may or may not be correct.

**Validity of estimate of costs**
Although the authors reported that the study was undertaken from the societal perspective, indirect costs, non-medical costs and outpatient costs (apart from invasive cardiac procedures) were not included.

**Other issues**
The authors made appropriate comparisons of their findings with those from other studies. However, the issue of generalisability to other settings was not addressed nor were the implications for Canadian patients in the study discussed. The authors, however, do not appear to have presented their results selectively.

**Implications of the study**
The results of the trial stimulate the search for even cheaper future strategies yielding similar or better clinical outcomes. With lower device and drug costs, the combination of stenting and abciximab could potentially be an economically dominant strategy by lowering the cost of acute care and extending life expectancy.

**Bibliographic details**

**PubMedID**
10636365
Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Aged; Angioplasty, Balloon, Coronary /economics; Antibodies, Monoclonal /administration & dosage /adverse effects /economics; Coronary Disease /blood /economics /mortality /therapy; Cost-Benefit Analysis; Death, Sudden, Cardiac /prevention & control; Female; Follow-Up Studies; Humans; Immunoglobulin Fab Fragments /administration & dosage /adverse effects /economics; Male; Middle Aged; Platelet Aggregation Inhibitors /administration & dosage /adverse effects /economics; Platelet Glycoprotein GPIIb-IIIa Complex /antagonists & inhibitors; Stents /economics; Survival Rate; Treatment Outcome

AccessionNumber
21999008347

Date bibliographic record published
31/01/2002

Date abstract record published
31/01/2002