Comparative 30-day economic and clinical outcomes of platelet glycoprotein IIb/IIIa inhibitor use during elective percutaneous coronary intervention: Prairie ReoPro Versus Integrilin Cost Evaluation (PRICE) 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 two parenteral glycoprotein (GP) IIb/IIIa inhibitors, abciximab and eptifibatide, for patients undergoing elective percutaneous coronary intervention (PCI). The patients received either abciximab (0.25 mg/kg bolus plus 0.125 microg/kg per minute infusion for 12 hours) or eptifibatide (180 microg/kg plus 2.0 microg/kg per minute continuous infusion for 18 to 24 hours).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged older than 21 years, who were undergoing elective, non-urgent coronary balloon angiography or stent implantation. Patients were excluded for any of the following reasons:

- acute myocardial infarction (MI), less than 48 hours;
- unstable angina with new or presumably new concomitant ST-segment or T-wave abnormalities, or haemodynamic instability, less than 12 hours;
- degenerated saphenous vein graft lesions;
- type C lesions, according to the American College of Cardiology or American Heart Association classification system;
- a history of haemorrhagic diathesis or major surgery or trauma less than 6 weeks before randomisation;
- a known baseline platelet count of less than 100,000 mm3;
- planned rotational atherectomy;
- a baseline serum creatinine level of greater than 3 mg/dL;
- administration of abciximab or eptifibatide within 7 days of randomisation;
- a planned staged interventional procedure during index hospitalisation; and
- participation in other clinical research studies within 30 days of randomisation.
Setting
The setting was tertiary care (university-affiliated community hospital). The economic study was carried out at the Heart Center (Memorial Medical Center) and at the Prairie Heart Institute (St. John's Hospital) in Springfield (IL), USA.

Dates to which data relate
The effectiveness evidence and resource use data were gathered from 4 April 1999 to 28 January 2000. No price year was reported.

Source of effectiveness data
The effectiveness evidence was 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 analysis.

Study sample
Power calculations were performed retrospectively to determine the sample size. These indicated that with a 30-day "event rate" of about 6.0%, a total sample size of 16,000 patients would be required to demonstrate a 1% absolute difference in the "event rate" between the study groups, with a power of 80%. Of the 1,881 PCIs performed at the two study centres, 655 were eligible and 320 (49%) were enrolled in the study. There were 163 patients in the abciximab group and 157 in the eptifibatide group. The mean age of the patients in the abciximab group was 63 years (range: 55 - 71) and 67% were men. The mean age in the eptifibatide group was 63 years (range: 52 - 72) and 68% were men. No patient was excluded from the initial sample. A total of 155 patients were involved in the substudy, 74 in the abciximab group and 81 in the eptifibatide group. The baseline characteristics were presented.

Study design
This was a randomised, double-blind clinical trial, carried out at two centres (the Heart Center and the Prairie Heart Institute in Illinois). The patients were randomly assigned using sealed envelopes and stratified on the basis of the type of PCI (balloon angioplasty or intracoronary stenting). Both the patients and physicians were blinded to the treatment received. The patients were followed for 30 days after the operation. The loss to follow-up was not reported.

Analysis of effectiveness
The basis for the clinical analysis was intention to treat. The primary health outcomes were in-hospital outcomes and 30-day outcomes. The in-hospital outcomes included death, nonfatal MI (Q-wave or no Q-wave), urgent coronary artery bypass grafting (CABG), urgent repeat PCI, serious bleeding and blood transfusions. The 30-day outcomes outcomes included death, nonfatal MI and urgent repeat PCI or CABG. A composite outcome measure, including death, nonfatal MI and urgent target vessel revascularisation, was also assessed for both in-hospital and 30-day outcomes.

In the substudy, four blood samples were obtained for each patient. These were taken at baseline, 5 to 10 minutes after the initiation of the GP IIb/IIIa inhibitor therapy, the end of the procedure, and less than 30 minutes before the cessation of the GP IIb/IIIa inhibitor infusion. The main outcome measure was the degree of platelet inhibition at each time point. This was expressed as a percentage of the baseline platelet aggregation.

The study groups were shown to be comparable at baseline in terms of their demographics and clinical characteristics.

Effectiveness results
Among the in-hospital outcomes:
death occurred in 1 patient (0.6%) in the abciximab group and in no patient in the eptifibatide group;

nonfatal MI (Q-wave or no Q-wave) occurred in 6 patients (3.7%) in the abciximab group and in 7 patients (4.4%) in the eptifibatide group;

urgent CABG occurred in no patient in the abciximab group and in 1 patient (0.6%) in the eptifibatide group;

urgent repeat PCI occurred in 1 patient (0.6%) in the abciximab group and in no patient in the eptifibatide group;

serious bleeding episodes occurred in 5 patients (3.1%) in the abciximab group and in 3 patients (1.9%) in the eptifibatide group;

blood transfusions were reported in 5 patients (3.1%) in the abciximab group and in 2 patients (1.3%) in the eptifibatide group;

composite events occurred in 8 patients (4.9%) in the abciximab group and in 8 patients (5.1%) in the eptifibatide group.

All the above comparisons had p-values greater than or equal to 0.45.

In terms of 30-day outcomes:

deaths were reported in 1 patient (0.6%) in the abciximab group and in 1 patient (0.6%) in the eptifibatide group, (p<0.00001);

nonfatal MI occurred in 7 patients (4.3%) in the abciximab group and in 8 patients (5.1%) in the eptifibatide group;

urgent repeat PCI or CABG occurred in 2 patients (1.2%) in the abciximab group and in 2 patients (1.3%) in the eptifibatide group;

composite events occurred in 9 patients (5.6%) in the abciximab group and in 10 patients (6.3%) in the eptifibatide group.

For the substudy:

effective platelet inhibition was obtained within 10 minutes after the initiation of the GP IIb/IIIa therapy, and immediately after PCI, in both groups;

29% of the abciximab patients had less than 80% platelet inhibition within 30 minutes before the cessation of the drug, compared with 4% of patients in the eptifibatide group;

the degree of platelet inhibition remained consistent among eptifibatide patients, while marked late variability of platelet inhibition was observed among the abciximab patients.

Clinical conclusions
The effectiveness analysis showed that the two drugs were similar in terms of the main outcome measures. However, the substudy indicated that eptifibatide was associated with better outcomes in terms of platelet inhibition.

Measure of benefits used in the economic analysis
The health outcomes were left disaggregated and no summary benefit measure was used. A cost-consequences analysis was therefore carried out.

Direct costs
The main analysis focused on the total in-hospital costs. The secondary analyses assessed in-hospital charges and 30-day
total costs and total charges. Discounting was not carried out since the costs per patient were incurred over a short period of time. The unit costs and the quantities of resources were not reported separately. The costs included in the analysis referred to:

cardiac catheterisation costs, such as cardiac catheterisation supplies, guidewires, balloons and stents;

laboratory costs, such as blood chemistries, haematologic studies and transfusion costs;

cardiology costs, such as noninvasive cardiac services, electrocardiograms and echocardiograms; and

pharmacy costs, that is, the cost and administration of the drugs.

Physician fees were not included in the analysis. The cost/resource boundary adopted appears to have been that of the hospital. The unit costs were assessed at the cost centre level at the two participating hospitals. The quantities of resources were estimated using actual data derived from the trial, and measured between 4 April 1999 and 28 January 2000. No price year was reported.

Statistical analysis of costs
Power calculations indicated that a sample size of 320 patients was required to identify a 10% difference in in-hospital costs between the two groups, assuming an estimated procedural cost of $8,900 (alpha=0.05; power 80%). Statistical analyses of the total costs were carried out to test for statistical significance of the results. A bootstrap analysis of in-hospital and 30-day costs was performed in which the data were resampled 1,000 times.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not carried out.

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

Cost results
The median in-hospital total costs were $8,268 (95% confidence interval, CI: 7,715 - 8,666) in the abciximab group and $7,207 (95% CI: 6,588 - 7,729) in the eptifibatide group. There was a statistically significant difference of $1,061 in favour of eptifibatide, (p=0.009). The difference was attributed to the pharmacy costs, which were higher in the abciximab group ($1,561) than in the eptifibatide group ($511), (p<0.0001). The remaining cost components were similar in the study groups.

The median in-hospital total charges were higher in the abciximab group ($20,639) than the eptifibatide group ($18,310), (p=0.002).

The 30-day total costs and 30-day total charges were also higher in the abciximab group than the eptifibatide group. The 30-day total costs were $8,336 versus $7,207, (p=0.009), while the 30-day total charges were $20,650 versus $18,380, (p=0.003).

The bootstrap analysis resulted in an average in-hospital cost difference of $723 (95% CI: 15 - 1,427), and a 30-day
cost difference of $749 (95% CI: 10 - 1,465), between the abciximab and eptifibatide groups.

Synthesis of costs and benefits
Not relevant.

Authors' conclusions
Eptifibatide achieved more durable platelet inhibition than abciximab throughout infusion. In addition, it reported lower in-hospital and 30-day costs in patients undergoing elective percutaneous coronary intervention (PCI).

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear. The two GP IIb/IIIa inhibitors were selected as they are currently approved by the Food and Drug Administration (USA) for use during elective PCI. The exclusion of placebo appears to have been justified, as both drugs had been demonstrated to be more effective than placebo. However, although eptifibatide might be preferred to abciximab on the grounds of its lower cost and greater effectiveness, its cost would still need to be compared with that of no treatment. You should assess whether these represent widely used health interventions in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness analysis used a randomised, double-blind, double-centre clinical trial. The method used to randomise the patients was stated clearly and the study groups were shown to be comparable at baseline. The baseline characteristics were presented to check whether the study sample was representative of the study population. The authors noted that the major threat to the internal validity of the study was the small sample size, and the fact that retrospectively performed power calculations indicated that the sample size was insufficient.

Validity of estimate of measure of benefit
No summary benefit measure was used in the economic analysis. The health outcomes were left disaggregated, due to the cost-consequences design. The use of a composite outcome measure appears to be fairly common in studies concerning patients undergoing PCIs.

Validity of estimate of costs
The perspective of the study was not explicitly stated, but appears to have been that of the hospital. The physician costs were not included in the analysis. Both the costs and the charges were reported. Statistical analyses were carried out on the costs. In addition, power calculations were performed in the planning phase of the study to detect statistically significant differences in the total costs. The unit costs and the quantities of resources were not reported separately, thus reducing transparency and hindering generalisability. The price year was not reported, thus making any reflation exercises to other settings difficult.

Other issues
The authors compared their findings with those from other studies. Sensitivity analyses were not carried out, thus reducing the external validity of the analysis. In terms of the generalisability to all patients undergoing PCI procedures, the authors stated that the study population included in the analysis was likely to reflect low-risk patients, and it is unclear whether the study results could be extrapolated to high-risk PCI patients. A further limitation of the study, as noted by the authors, was the small sample size. The authors reported the effectiveness results in detail.

Implications of the study
According to the study results, the use of eptifibatide should be recommended as a platelet GP IIb/IIIa inhibitor among patients undergoing PCIs. Assuming that the data reported in the study may be generalisable to a population of 245,000
(low-risk) patients in the USA, the use of eptifibatide over abciximab would result in an estimated annual reduction of $171.5 million in the drug acquisition costs.

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