Cost and effectiveness of glycoprotein IIb/IIIa-receptor inhibitors in patients with acute myocardial infarction undergoing percutaneous coronary intervention

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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 glycoprotein IIb/IIIa-receptor inhibitors to treat patients with acute myocardial infarction (AMI) during percutaneous coronary intervention (PCI). The three glycoprotein IIb/IIIa-receptor inhibitors examined were abciximab (ABC), eptifibatide (EPT) and tirofiban (TIR).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with AMI undergoing PCI.

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

Dates to which data relate
The effectiveness and resource use data were gathered from January 2000 to July 2001. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study and authors' assumptions.

Link between effectiveness and cost data
The costing was conducted retrospectively on the same sample of patients as that used in the effectiveness study.

Study sample
Power calculations do not appear to have been conducted. However, the large sample size should guarantee the ability to detect differences in the final outcomes. Patients with a diagnosis code for AMI and a primary procedure code for PCI were identified from a non-government database containing information from over 140 hospitals in the USA. No further details on the method of sample selection were provided. A final sample of 32,529 patients was included in the analysis. There were 11,816 patients in the ABC group, 10,093 patients in the EPT group, 3,700 patients in the TIR group, and 6,920 patients in the control group. The mean ages of the patients were 61.6 years (ABC), 62.3 years (EPT), 62.6 years (TIR) and 64.4 years (control), respectively. The proportion of men was 69.1% in the ABC group, 67.1%
men in the EPT group, 68.7% in the TIR group, and 63% in the control group.

**Study design**
This appears to have been a retrospective cohort study, with data derived from 99 hospitals. The length of and loss to follow-up were not reported. There were few details on the methods for assessing the outcomes. The data were obtained from the Solucient national all-payer database, which contained information on hospitalisations.

**Analysis of effectiveness**
It seems that all the patients included in the initial study sample have been accounted for in the effectiveness study. The primary health outcomes used were the complication rate and mortality rate. Both measures were risk-adjusted on the basis of patient and hospital characteristics. The complication index comprised over 40 variables but did not include deaths, which were analysed separately. The risk-adjustment was performed by logistic regression models and the model’s discrimination was evaluated using the C statistic. The authors did not discuss the baseline comparability of the four study groups, although patient demographics and health and hospital characteristics were provided. However, the authors did state that differences among the groups were possible, given the retrospective design of the study and the lack of randomisation.

**Effectiveness results**
The models demonstrated excellent discrimination.

The odds ratios (OR) and 95% confidence intervals (CIs) for the risk-adjusted mortality index relative to control patients were 0.74 (95% CI: 0.59 - 0.92; p=0.007) for ABC, 0.87 (95% CI: 0.68 - 1.10; p non significant) for EPT, and 0.99 (95% CI: 0.73 - 1.34; p non significant) for TIR.

The corresponding values of the risk-adjusted complications index were 0.92 (95% CI: 0.81 - 1.03; p non significant) for ABC, 0.86 (95% CI: 0.75 - 0.98; p=0.02) for EPT, and 0.94 (95% CI: 0.79 - 1.12; p non significant) for TIR.

**Clinical conclusions**
The effectiveness study showed that only ABC was effective in reducing mortality in comparison with no treatment. TIR and EPT had no statistically significant effect on the mortality rate. However, when the complications were considered, the index was neutral for ABC and TIR, while EPT significantly reduced the complication rate relative to the control patients.

**Methods used to derive estimates of effectiveness**
The authors made a critical assumption to calculate survival among patients with AMI.

**Estimates of effectiveness and key assumptions**
It was assumed that survival at discharge implied an additional life expectancy of 14 years. This was discounted at a rate of 3% per year to yield 11.6 discounted years.

**Measure of benefits used in the economic analysis**
The summary benefit measure used in the analysis was the number of life-years saved with the three study drugs in comparison with the control patients. The life-years gained with the three drug treatments were calculated assuming 11.6 discounted years gained after discharge.

**Direct costs**
Discounting was not performed because the costs per patient were incurred during a short time. The unit costs were not
analysed separately from the quantities of resources used. The hospital and drug costs were included, but a detailed breakdown of the costs was not provided. The cost/resource boundary adopted in the study was not explicitly reported, but it appears to have been that of the hospital. Both resource use and costs were estimated using actual data coming from the non-government database, which was used to derive the effectiveness evidence. The authors stated that wage-adjusted costs were used in the economic analysis. The price year was not reported.

**Statistical analysis of costs**
The hospital costs and length of stay were estimated using least-squares regression to fit general linear models. The adjusted costs and 95% CIs were reported.

**Indirect Costs**
The indirect costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were not conducted.

**Estimated benefits used in the economic analysis**
The number of life-years gained was not reported.

**Cost results**
The total costs associated with each study drug were not reported. However, the adjusted incremental costs relative to control patients were $1,807 (95% CI: 1,529 - 2,085; p<0.0001) with ABC, $1,147 (95% CI: 849 - 1,445; p<0.0001) with EPT, and $644 (95% CI: 252 - 1,036; p<0.0001) with TIR.

Compared with the control patients, only the ABC group showed significant reductions in length of stay (mean reduction: -0.21 days; 95% CI: -0.09 - -0.34; p=0.0013).

**Synthesis of costs and benefits**
An incremental cost-effectiveness ratio (ICER) was calculated to combine the costs and benefits.

The ICER of ABC relative to the control patients was $14,515 per life-year gained (point estimate), while it was $21,731 for EPT and $163,286 for TIR (although there was no statistically significant difference in term of mortality rate for either TIR or EPT in comparison with control patients).

**Authors' conclusions**
Abciximab (ABC) treatment had a significant impact on mortality reduction among patients with acute myocardial infarction (AMI), and was the most cost-effective therapy in comparison with no treatment. Eptifibatide (EPT) and tirofiban (TIR) did not improve survival versus no treatment, although their incremental costs (with respect to the control group) were lower than those observed with ABC.

**CRD COMMENTARY - Selection of comparators**
The authors did not explain the rationale for the choice of the comparators, but the three study drugs appear to have represented glycoprotein IIb/IIIa-receptor inhibitors widely used to treat patients with AMI. The basic comparator was
thus no treatment, which was selected to evaluate the active benefit or cost of the study drugs. You should decide whether the study drugs represented current treatment options for patients with AMI in your own setting.

**Validity of estimate of measure of effectiveness**

The effectiveness evidence came from a cohort study, which was appropriate for the study question. However, the retrospective nature of the study design, and the lack of random allocation of the patients to the study groups, were important limitations to the internal validity of the analysis. The authors stated that differences among the treatment groups were possible due to the lack of randomisation. Indeed, the baseline comparability of the groups was not discussed. The source of the data was stated. Logistic regression models were used to adjust the outcome data for risk factors.

The study sample was derived from a group of patients who received real-world treatments and who were not part of a hypothetical trial. In fact, the allocation of the patients to the study drugs reflected actual treatment patterns in the USA. Thus, the study sample was representative of the study population. The authors discussed the reasons for the beneficial effects observed in the abciximab group in terms of the significant reduction in mortality. They noted that potential coding biases may have weakened the use of complication rate as an outcome measure.

**Validity of estimate of measure of benefit**

The summary benefit measure used in the economic analysis was survival, which was appropriate for the study disease. In addition, it permitted the benefits of the present study treatments to be compared with the benefits of other interventions. The gain in survival was based on an assumption that was derived from some published studies.

**Validity of estimate of costs**

The perspective adopted in the economic analysis was not explicitly stated, but it should have been that of the hospital. A breakdown of the costs was not provided, although the authors stated that all hospital costs were included in the analysis. The unit costs and the quantities of resources used were not analysed separately and the price year was not reported. Thus, it may be difficult to reproduce the study in other settings. The source of the costs was reported, while it seems that resource use was estimated from individualised data. Statistical analyses were conducted on both the costs and quantities, but these estimates were specific to the study setting because sensitivity analyses were not performed.

**Other issues**

The authors compared some of the study findings with the results of other studies and found the conclusions were consistent. However, the authors did not address the issue of the generalisability of the study results to other settings and did not perform sensitivity analyses. Thus, the external validity of the analysis was low. The authors stressed that the study referred to patients with AMI who were undergoing PCI. The study results may not, therefore, be applicable to non-interventional medical therapy for AMI. The authors stated that this was the largest naturalistic study of glycoprotein IIb/IIIa-receptor inhibitors in AMI patients undergoing PCI to date. Finally, the authors discussed some limitations of their study, which have been highlighted already.

**Implications of the study**

The study results suggested that ABC is associated with a beneficial effect on mortality rate and length of hospital stay in patients with AMI who are undergoing PCI, although TIR and EPT present lower costs. The authors stated that further research should use data that differentiate between the degree of severity of the complications considered in the composite complication index used in the present study.

**Source of funding**

Supported by Eli Lilly & Co.
Bibliographic details

PubMedID
12845921

Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Angioplasty, Balloon, Coronary /statistics & numerical data; Antibodies, Monoclonal /economics /therapeutic use; Case-Control Studies; Drug Costs /statistics & numerical data; Female; Hospital Costs /statistics & numerical data; Hospital Mortality; Humans; Immunoglobulin Fab Fragments /economics /therapeutic use; Length of Stay /statistics & numerical data; Male; Middle Aged; Myocardial Infarction /drug therapy /mortality /surgery; Outcome and Process Assessment (Health Care); Peptides /economics /therapeutic use; Platelet Aggregation Inhibitors /economics /therapeutic use; Platelet Glycoprotein GPIIb-IIIa Complex /antagonists & inhibitors /economics; Treatment Outcome; Tyrosine /analogs & derivatives /economics /therapeutic use; United States /epidemiology

AccessionNumber
22003000945

Date bibliographic record published
31/03/2004

Date abstract record published
31/03/2004