The economics of adjunctive therapies in coronary angioplasty: drugs, devices, or both?

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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 study examined a combination of abciximab and stenting for the treatment of patients undergoing angioplasty. Bolus and infusion of abciximab consisted of a dose of 0.25 mg/kg bodyweight up to 60 minute before intervention, followed by an infusion of 0.125 microg/kg per minute to a maximum of 10 microg per minute for 12 hours post angioplasty.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients undergoing angioplasty.

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

Dates to which data relate
The effectiveness data and some resource use data were derived from studies published between 1994 and 2002. The price year was 1998.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies.

Modelling
A decision tree model was constructed to assess the cost-effectiveness of the combined strategy, compared with stenting alone, in a hypothetical cohort of patients undergoing percutaneous transluminal coronary angioplasty (PTCA). After surgery, patients could or could not develop a major bleed and then experience no event or several alternative events at 30 days or at 1-year follow-up, such as myocardial infarction (MI) or death. Alternatively, they could undergo either urgent PTCA or coronary artery bypass grafting (CABG). Survival was extended beyond the 1-year horizon of the EPISTENT study using three approaches. These were a Markov model based on death rate assumptions, extrapolations of 1-year survival from the EPISTENT study using the Duke cardiac registry, and pooled survival data from three clinical trials. A graphical representation of the decision tree was reported.

Outcomes assessed in the review
The outcomes estimated from the literature were:

- a primary composite end point (death, MI and urgent revascularisation) at 30 days and 1 year;
- the rate of death and any MI at 30 days and 1 year;
- the rate of any revascularisation at 30 days;
- the rate of target vessel revascularisation at 1 year;
- the death rate at 1 year; and
- the rate of any MI over a 1-year time horizon.

Long-term survival was calculated using published data on background mortality for those patients without a repeat procedure or a complication, late mortality associated with peri-procedural MIs following an angioplasty, or excess mortality following cardiac procedures.

Study designs and other criteria for inclusion in the review
Most of the clinical data were derived from the EPISTENT study. This was a randomised, prospective, double-blind multi-centre study that evaluated the effect of abciximab and stents, alone or in combination, in 2,399 patients undergoing PCI in 63 hospitals in the USA and Canada over a 1-year time horizon. Other data came from Canadian statistics and other clinical trials. Information on the design was provided for most studies. The primary studies appear to have been identified selectively.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
The use of data from a large clinical trial ensured a high internal validity.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Eight primary studies provided the clinical data used in the short- and long-term model.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The primary composite end point was 5.3% in the combination group and 10.8% in the stenting group at 30 days, and 20.1% and 24.0%, respectively, at 1 year.

The rate of death and any MI was 3.0% in the combination group and 7.8% in the stenting group at 30 days, and 6.8%
and 13.1%, respectively, at 1 year.

At 30 days, the rate of any revascularisation was 6.4% in the combination group and 12.7% in the stenting group.

At 1 year, the rate of target vessel revascularisation was 15.2% in the combination group and 15.6% in the stenting group.

At 1 year, the death rate was 1.0% in the combination group and 2.4% in the stenting group.

At 1 year, the rate of any MI was 5.9% in the combination group and 11.3% in the stenting group.

Measure of benefits used in the economic analysis
Two summary benefit measures were used in the economic analysis, depending on the model time horizon. Over the 1-year timeframe, the benefit measure was the composite end point of death or large MI. In the lifetime analysis, the benefit measure was the expected survival. This was calculated using the three approaches mentioned already (see 'Modelling' for details). Future life-years were discounted at an annual rate of 3%.

Direct costs
The analysis of the costs was carried out from the perspective of the Canadian health care system. It included the costs of abciximab, (uncomplicated and complicated) PTCA, CABG, MI and death. The unit costs and the quantities of resources used were not presented separately, except for abciximab. The costs were estimated from Ontario hospital data (the Ontario Case Costing Initiative that included financial data from 13 teaching and community hospitals in the Province of Ontario) and the manufacturer of abciximab. The source of the resource use data was unclear, but it might have been the hospital databases and published studies. Discounting was not relevant since the costs were incurred during a short timeframe. The price year was 1998.

Statistical analysis of costs
The costs were treated deterministically. However, Monte Carlo simulations were performed to generate confidence intervals (CIs) around the costs.

Indirect Costs
The indirect costs were not considered.

Currency
Canadian dollars (CAD).

Sensitivity analysis
Univariate sensitivity analyses were carried out to assess the robustness of the cost-effectiveness estimates to variations in relative risk reductions, bleeding rates and expected survival. Published ranges of values were used. A Monte Carlo simulation was also performed, using 10,000 individual patient trials to generate CIs around the costs and incremental cost-effectiveness ratios.

Estimated benefits used in the economic analysis
The rate of patients experiencing the composite end point over the 1-year time horizon was 5.3% with the combination strategy and 11.0% with the stenting approach.

When using the Markov approach, the survival estimate was 11.57 years with the combination strategy and 11.19 years with the stenting approach (difference 0.38 years).
When using the Duke database, the expected survival gain with the combined strategy over stenting was 0.15 years. The use of pooled survival data led to a survival estimate of 11.77 years with the combination strategy and 11.53 years with the stenting approach (difference 0.24 years).

**Cost results**
The 1-year costs were CAD 8,617 with the combined approach and CAD 7,541 with the stenting strategy (difference CAD 1,076).

One-third of the additional cost of abciximab was offset by reductions in expenditures on hospitalisations for ischaemic events and interventional procedures.

**Synthesis of costs and benefits**
Several incremental cost-effectiveness ratios (ICERs) were calculated in order to combine the costs and benefits of the alternative strategies.

Over the 1-year time horizon, the incremental cost per death or large MI avoided with the combination strategy in comparison with stenting alone was CAD 18,874 (95% CI: 14,559 to 30,657).

The incremental cost per life-year gained with the combination strategy in comparison with stenting alone was CAD 2,832 with the Markov approach, CAD 7,173 with the Duke database, and CAD 4,483 with the pooled survival data.

The deterministic sensitivity analysis showed that the incremental cost per life-year gained ranged from CAD 4,615 to CAD 45,167, with changes in the 30-day outcomes and mortality post-MI having the greatest impact.

The Monte Carlo simulation suggested that the 95% CI for the cost-difference was CAD 601 to CAD 1,536, while the 95% CI for the ICER based on Duke mortality data was CAD 4,007 to CAD 10,240.

**Authors’ conclusions**
The combination of abciximab plus stenting for the treatment of patients undergoing angioplasty was cost-effective in Canada.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparators was clear. The selection of a combination of abciximab and stenting versus stenting alone was consistent with the objective of the study. Dosages of abciximab were reported. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness evidence might have been derived from selectively identified studies, as details of the methods and conduct of a systematic review of the literature were not reported. However, most of the evidence came from a single large clinical trial, which should ensure a high internal validity for the clinical data. Other clinical data also appear to have been taken from clinical trials, although there was limited information on the design and other characteristics of these studies. The methods used to extract and combine the primary estimates were not described, and the issue of heterogeneity across the primary studies was not addressed. Three different approaches were used appropriately to extrapolate the short-term results to a lifetime horizon, in order to take the different possible future scenarios into consideration. The impact of variations in clinical estimates on the results of the analysis was investigated in the sensitivity analysis, which identified key model inputs.

**Validity of estimate of measure of benefit**
Both a disease-specific and a more generalisable benefit measure were used. Life-years represent an appropriate benefit
measure because they are usually employed to assess the impact of health care interventions on patients undergoing angioplasty. They can also be compared with the benefits of other health care interventions. Discounting was applied, as recommended by guidelines for the economic evaluation of long-term interventions.

Validity of estimate of costs
The costs included were consistent with the perspective considered in the analysis. A detailed breakdown of the cost items was not given and neither was information on the unit costs and quantities of resources used, most costs being presented as macro-categories. This limits the possibility of replicating the analysis in other settings. Few details of resource consumption were provided. The cost estimates were specific to the Canadian setting and sensitivity analyses were not performed. However, the impact of using alternative sources of costs was investigated. The price year was reported, which will facilitate reflaction exercises in other time periods.

Other issues
The authors reported the findings from other economic evaluations of the combined strategy, which corroborated the results of the current study. The authors stated that similar findings could be expected from a strategy that combines eptifibatide and stenting, as clinical trials have shown that eptifibatide is an effective therapy for patients undergoing angioplasty. It was pointed out that the current study has the same limitations as all modelling studies (e.g. mixed sources of data, use of assumptions), but sensitivity analyses were carried out to deal with the issue of uncertainty in the clinical estimates. However, since the economic data were not varied, caution will be required if extrapolating the results of the analysis to other countries.

Implications of the study
The study results support the use of a combined strategy (abciximab and stenting) for the treatment of patients undergoing angioplasty.

Source of funding
Supported by a research grant from Eli Lilly Canada Inc.

Bibliographic details

PubMedID
15520474

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Angioplasty, Balloon, Coronary /economics /methods; Antibodies, Monoclonal /economics /therapeutic use; Chemotherapy, Adjuvant /economics; Combined Modality Therapy /economics; Coronary Disease /economics /therapy; Cost-Benefit Analysis; Decision Trees; Follow-Up Studies; Humans; Immunoglobulin Fab Fragments /economics /therapeutic use; Models, Economic; Platelet Aggregation Inhibitors /economics /therapeutic use; Platelet Glycoprotein GPIIb-IIIa Complex /antagonists & inhibitors; Randomized Controlled Trials as Topic; Reoperation /economics; Stents /economics; Survival Analysis

AccessionNumber
22006006343

Date bibliographic record published
31/12/2006

Date abstract record published
31/12/2006