Cost-effectiveness of coronary stenting and abciximab for patients with acute myocardial infarction: results from the CADILLAC (Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications) 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 study examined coronary stenting and abciximab, a glycoprotein IIb/IIIa inhibitor, for patients undergoing primary balloon angioplasty (PTCA) for acute myocardial infarction (AMI). Abciximab was administered as a 0.25mg/kg bolus followed by a 12-hour infusion of 0.125 micrograms per kilogram per minute (no more than 10 micrograms per minute).

Type of intervention
Secondary prevention.

Economic study type
Cost-utility analysis.

Study population
The study sample consisted of patients presenting within 12 hours of a suspected AMI who were deemed suitable for PTCA following an emergency coronary angiography. The average age was 59, and 73% were male. Fifteen percent had experienced a prior myocardial infarction, and 13% were diabetic. Forty-three percent were current smokers and 48% had hypertension. (see 'Other Publications of Related Interest' below for further detail about the study).

Setting
The setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness evidence relate to 2002 and the cost data to 2001, which was also the price year.

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

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

Study sample
The study sample consisted of a subset of 1,703 patients enrolled in the US centres of a multinational randomised trial. The authors did not report any power calculations. For more details of study protocol, readers are referred to 'Other Publications of Related Interest' below. Of the 1,703 patients, 425 were randomised to PTCA alone, 432 to PTCA with
abciximab, 417 to stenting alone and 429 to stenting with abciximab. The protocol allowed for treatment crossovers from PTCA to stenting (severe dissection or unacceptable PTCA result), and from no abciximab to abciximab (persistent angiographic thrombus or inability to re-establish flow in the absence of a mechanical obstruction).

**Study design**
The study was a 2 by 2 factorial design, multinational, randomised, controlled trial. The number of centres and method of randomisation were not reported. The study was unblinded. The duration of follow-up was 1 year. No loss to follow-up was reported.

**Analysis of effectiveness**
The analysis of effectiveness was based on intention to treat. The analysis appears to have been based on an assumption of no interaction between stenting and abciximab, and so the comparators were stent (n=846) versus PTCA (n=857), and abciximab (n=861) versus no abciximab (n=842). The primary health outcomes used in the analysis were quality of life (based on utilities of 1 year with or without revascularisation) and repeat revascularisations. Treatment groups were shown to be well matched for socio-demographic and clinical characteristics.

**Effectiveness results**
There was no significant difference in mortality at one-year between the PTCA and stent group, and the abciximab and the no abciximab group.

The number of patients with repeat revascularisations was 23.9% in the PTCA group, and 17.7% in the stent group, (p<0.01).

The difference in number of repeat revascularisations was not significant with abciximab (no abciximab 19.4%, abciximab 22.3%, p=0.14).

**Clinical conclusions**
Stenting was associated with fewer repeat hospitalisations and fewer repeat revascularisation procedures than PTCA alone. Abciximab was not associated with significant favourable outcomes compared to the no abciximab group.

**Modelling**
A simple mathematical model was used to extend the results of the study to a lifetime perspective. This was achieved by estimating the quality-adjusted life expectancy and medical care costs beyond 1-year for any survivors, based on a previously published study and assuming an average age of 60 years.

**Measure of benefits used in the economic analysis**
The study estimated quality-adjusted life-years (QALYs). The utility estimates were based on a previously published study of patients with AMI, and the instrument used was not specified (see 'Other Publications of Related Interest' below).

**Direct costs**
The study included the direct hospital costs. The costs included the overhead costs, based on procedure duration, the costs of equipment including catheters, guidewires, balloons, stents and abciximab, and the costs of hospital stays and nursing care. The cost of the procedures was calculated using 'bottom-up' accounting methods on data recorded in the study. The other hospitalisation costs were based on each hospital's Medicare Cost Report. Procedures and hospitalisations deemed not to be 'clinically driven' were excluded from the analysis. The authors did not provide a description or definition of what was meant by 'clinically driven' and so the implications of this are unclear. Costs were extrapolated using an estimated annual medical care cost from another published study. Resource use quantities and unit
costs were reported separately. All costs were adjusted to 2001 levels using the medical Consumer Price Index. The study reported average costs.

Statistical analysis of costs
Costs were treated in a stochastic manner. The authors provided the mean, median and standard error of the individual components. The lifetime cost was reported as incremental cost with a 95% confidence interval. The difference in mean costs was assessed using a 2-tailed Student's t test, and p values less than 0.05 were considered statistically significant. The cost data were typically right skewed, with median values below the mean. A Student's t test was based on the assumption that the data approximated a Normal distribution (although with heavier tails), and so this test may have been inappropriate. However, the sample size was large and this may mean that the results were robust to this misspecification. The confidence interval for the incremental costs was based on a non-parametric bootstrap, which would be suitable if the true distribution were not too extreme. The study did not report power calculations with respect to cost data. However, the sample sizes indicated by a power calculation for economic data were typically very large and may be unachievable.

Indirect Costs
Indirect costs were not included in the analysis.

Currency
US dollars ($)

Sensitivity analysis
The base case analysis excluded long-term mortality effects, as the difference in mortality rates at the end of the trial was not statistically significant. The non-significant absolute risk reductions with stenting and abciximab were included in a secondary analysis. This sensitivity analysis addressed assumptions used in extrapolating the data beyond the clinical trial. The model itself was fully probabilistic and so a probabilistic sensitivity analysis was carried out in both the primary and secondary analyses.

Estimated benefits used in the economic analysis
In the primary analysis, the incremental utility of stenting was estimated to be 0.015 (95% CI: 0.011 to 0.019) QALYs compared to PTCA alone.

The incremental utility of abciximab was estimated to be -0.002 (95% CI: -0.006 to 0.002) QALYs compared to no abciximab.

QALYs were discounted at a rate of 3% per annum.

The analysis considered the lifetime of the cohort by extrapolating beyond the end of the 1-year clinical trial.

In the primary analysis, the effects of each treatment on long-term mortality were not included, and this was addressed in a secondary analysis.

The analysis assumed that QALYs would be equal for all survivors post 1-year, regardless of treatment.

Cost results
In the primary analysis, the incremental cost of stenting was estimated to be $169 (95% CI: -$821 to $1177) compared to PTCA alone.

The incremental cost of abciximab was estimated to be $1,244 (95% CI: $289 to $2,288) compared to no abciximab.
Costs were discounted at a rate of 3% per annum.

The analysis excluded costs that were deemed not to be ‘clinically driven’ although no definition of this was provided. The analysis considered the lifetime of the cohort by extrapolating beyond the end of the 1-year clinical trial. The analysis assumed that costs would be equal for all survivors post year-1, regardless of treatment.

**Synthesis of costs and benefits**

Costs and QALYs were combined to provide incremental cost-effectiveness ratios. Stenting was estimated to cost $11,237 per QALY gained compared to PTCA alone in the primary analysis. In 1000 bootstrap simulations of trial results, the incremental cost-effectiveness ratio was below $50,000 per QALY in 86.4%. Abciximab was dominated by no abciximab in the primary analysis, and the incremental cost-effectiveness ratio was below $50,000 per QALY in only 0.1% of simulations. Costs and benefits were both discounted at a rate of 3% per annum. When the non-significant absolute risk reductions in mortality at 1-year were incorporated in the model, the incremental cost-effectiveness ratio of stenting compared to PTCA fell to $7,067 per QALY gained, and the incremental cost-effectiveness ratio of abciximab compared to no abciximab became $25,136 per QALY, and remained below $50,000 per QALY in 64% of bootstrap simulations. The authors stated that the cost-effectiveness of abciximab was highly sensitive to the inclusion of long-term mortality effects, which the clinical trial was not adequately powered to detect.

**Authors’ conclusions**

The authors concluded that stenting is a cost-effective adjunctive therapy for patients undergoing primary percutaneous coronary intervention for AMI. They also concluded that the inclusion of long-term mortality effects is probably justified, and so there is a possibility that treatment with abciximab is cost-effective, but the results are less clear cut.

**CRD COMMENTARY - Selection of comparators**

The study compared adjunctive therapies for patients undergoing PTCA for AMI with PTCA alone, thus the choice of comparator was appropriate. However, the study was based on a clinical trial with a factorial design. The analysis compared all patients with PTCA only (with and without abciximab) and all patients with stenting (with and without abciximab), and similarily for the abciximab comparison, which would be valid only if there were no interaction effect between stenting and abciximab. There was little discussion of this in the present study, and so readers may wish to refer to the original trial analysis details of which are given in ‘Other Publications of Interest' below.

**Validity of estimate of measure of effectiveness**

The study design was an unblinded, 2 by 2 factorial design randomised trial, which would be appropriate as long as there is no reason to expect an interaction effect between stenting and abciximab. The study sample appeared representative of the study population, and patient groups were shown to be comparable at analysis. The analysis of effectiveness was based on intention to treat, which preserved the randomisation. However, the study protocol allowed for treatment crossovers (18% of patients in the PTCA alone group required stenting) and so the estimate of effectiveness based on intention to treat analysis will have been diluted.

**Validity of estimate of measure of benefit**

The authors acknowledged that the estimate of utilities used in the economic analysis was taken from a different sample from that used for the cost and effectiveness analysis, but it appeared to be from a similar patient group. The instrument used to derive the utilities was not specified. The validity of the estimate of benefits was dependent on there being no difference in utility between 1-year survivors from any treatment group.

**Validity of estimate of costs**

The authors reported that the study was carried out from the perspective of a US health care payer. However, the cost analysis did not include all health care costs incurred during the trial, as costs deemed not to be clinically driven were excluded. The validity of the estimate of trial costs therefore depended on the assumption that the excluded costs did
not differ systematically between treatment groups. Costs and quantities were reported separately for the trial period, and a statistical analysis was performed. The prices used were, in part, obtained from hospital charges, which is appropriate given the study perspective, and also from 'bottom-up' accounting methodology, which may less accurately reflect the final cost of these procedures to a health care payer, who may not bear the exact accounting cost. Sensitivity analysis of prices was not conducted. The projected lifetime costs of the patients were based on a separate, previously published study that appears to have used a similar patient group. The validity of the estimate of long-term costs depended on the assumption that costs would not differ between 1-year survivors from any treatment group. Since the lifetime costs occurred over a period greater than 1-year, discounting was used appropriately.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. The issue of generalisability to other settings was not addressed. The authors do not appear to have presented their results selectively, although more discussion of the validity of the factorial design would have been useful. The study enrolled patients presenting with AMI who were suitable for PTCA, although further inclusion or exclusion criteria were not reported here. The conclusions reflected the scope of the analysis. The authors stated that the clinical study had little power to detect small differences in mortality, and this was a sensitive parameter in the model for abciximab. They also acknowledged that they did not explore any differences between treatment groups beyond 1 year.

Implications of the study
The authors recommend that further studies with longer follow-up should be undertaken to determine the cost-effectiveness of abciximab as an adjunct to PTCA in patients with AMI.

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Other publications of related interest


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