Optimum percutaneous transluminal coronary angioplasty compared with routine stent strategy trial (OPUS-1): a 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
Initial balloon angioplasty with provisional stenting for suboptimum results (optimum angioplasty plus provisional stenting) in the treatment of patients requiring percutaneous coronary interventions.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients between the ages of 21 and 81 years with stable or unstable angina, a positive functional test for ischaemia, or who were undergoing angioplasty after recent myocardial infarction (> 24 h). Angiographic inclusion criteria included at least 70% stenosis in native coronary arteries, a single lesion of length no more than 20 mm, and a coronary artery reference diameter of at least 3.0 mm. Eligible target-vessel lesions had to be potentially treatable by balloon angioplasty or a stent. The clinical exclusion criteria were as follows: a known requirement for treatment of more than one coronary vessel, more than one previous intervention at the target-vessel site, allergy or contraindication to aspirin, or a concurrent illness that was believed to limit life expectancy to less than 1 year. The angiographic exclusion criteria were as follows: more than 45 degree angulation of the lesion, moderate to severe calcification, and ostial stenosis.

Setting
Hospital. The economic analysis was carried out in the USA and Canada.

Dates to which data relate
Effectiveness and resource use data corresponded to patients admitted to the study institutions during a 19-month study period up to January 1998. The price year was 1997.

Source of effectiveness data
The evidence for the final outcomes was based on a single study.

Link between effectiveness and cost data
Costing was conducted prospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were used to determine the sample size, but the study enrolment was terminated prematurely.
because of a low recruitment rate and the unavailability of funds to extend or expand the study. The required sample size was 2,184 patients based on the rates of primary endpoint of 20% in the control group and 25% in the intervention group, and a restenosis rate of 15% in the control group with beta of 0.80 and alpha of 0.05; recruitment was terminated after the recruitment of 479 patients. A total of 479 patients were randomly assigned to receive either optimum percutaneous transluminal coronary angioplasty (PTCA) with provisional stents for suboptimal cases (n=249, mean age of 51 years) or routine stent implantation (n=230, mean age 51 years).

Study design
This was a multi-centre, randomised controlled clinical trial, carried out in 44 centres in the USA and Canada. The duration of the follow-up was 6 months after the index procedure. Loss to follow-up was 1 patient in each treatment group. A central computer interactive voice-recognition system was used to collect initial data and randomise patients to the study groups. The randomisation scheme was sequential and stratified by site. Balloon angioplasty and stent implantation were carried out according to standard clinical practice. Participating clinicians were encouraged to use the Palmaz-Schatz stent but were allowed to use any approved stents at their discretion. Recommendations for treatment with aspirin, ticlopidine, and heparin were identical in both groups. All patients' data were prospectively recorded on case report forms, which were sent to the co-ordinating centre for data entry and analysis.

Analysis of effectiveness
The principle used in the analysis of effectiveness was claimed to be intention-to-treat but appears to have been treatment completers only. The primary end point was a composite of myocardial infarction, cardiac surgery, target-vessel revascularisation, or death in the 6 months after randomisation. The Seattle angina questionnaire was sent to all participants at 6 months after their index procedure to assess disease-specific quality of life. The total number of re-admissions was also reported. The study groups were comparable in terms of baseline demographics and cardiovascular risk factors. Adjustments were made for any differences in patients' baseline characteristics.

Effectiveness results
At 6 months the composite endpoint was significantly lower in the routine stent strategy (14 events, 6.1%) than with the strategy of balloon angioplasty with provisional stenting (37 events, 14.9%, hazard ratio 2.53 (95% CI: 1.38 - 4.71; p=0.003).

Functional status was similar, with no differences in physical limitation, frequency of angina, treatment satisfaction, or overall Seattle angina questionnaire scores (85 versus 86) between groups.

The total number of re-admissions was 17 in the routine stent group versus 39 in the PTCA group.

Clinical conclusions
This study demonstrates that routine stent strategy is better in terms of reducing clinical events.

Measure of benefits used in the economic analysis
No summary benefit measure was identified in the economic analysis, and only separate clinical outcomes were reported.

Direct costs
Costs were not discounted due to the short time frame of the cost analysis. Some quantities were reported separately from the costs. Some cost items were reported separately. The cost analysis covered the hospital-related elements of procedure-related costs, including the costs of equipment (guide catheters, perfusion balloons, and stents), use of the catheterisation laboratory (overheads, disposables, and standard staff costs) and non-procedure-related costs such as routine laboratory testing and radiology services. The perspective adopted in the cost analysis appears to have been that of the hospital. Resource consumption after randomisation was recorded and costs assigned to each item. The sources
of cost data were two previous trials, the results of which were published in 1995 and 1998. Hospital charges were adjusted to true costs using Medicare cost-to-charge ratios for each centre. The price year was 1997.

**Statistical analysis of costs**
A log-linear model was used to adjust for the underlying non-normally distributed costs. A bootstrap simulation of mean 6-month cost differences was used.

**Indirect Costs**
Not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
Not conducted.

**Estimated benefits used in the economic analysis**
Not applicable.

**Cost results**
The cost of the initial revascularisation procedure was higher than when a routine stent strategy was used ($389 versus $339, (p<0.001)) but at 6 months, average per-patient hospital costs did not differ ($10,206 routine stent group versus $10,490 PTCA group). Bootstrap replication of 6-month cost data showed continued economic benefit of the routine stent strategy.

**Synthesis of costs and benefits**
Costs and benefits were not combined since the intervention (the use of PTCA with provisional stenting) was the weakly dominated strategy (worse clinical outcomes with statistically comparable costs).

**Authors' conclusions**
Routine stent implantation leads to better acute and long-term clinical outcomes at a cost similar to that of initial balloon angioplasty with provisional stenting.

**CRD COMMENTARY - Selection of comparators**
The strategy of using routine stenting, as the predominant treatment in the context in question, was regarded as the comparator. You, as a database user, should consider whether this is a widely used health technology in your own setting.

**Validity of estimate of measure of effectiveness**
Although the study unable to reach its pre-specified target sample size, the effectiveness results are likely to be internally valid given the randomised nature of the study design. However, it was reported that the substantial differences between the authors’ pre-specified estimates and the observed endpoint rates provided the statistical power to find a difference. Good features were that the study groups were comparable in terms of baseline demographic characteristics and cardiovascular risk factors, and adjustments were made for any differences in patients’ baseline characteristics. The study sample also appears to have been representative of the study population (a population with
clinically stable conditions whose coronary arteries were suitable for stent or balloon angioplasty).

**Validity of estimate of measure of benefit**
The authors did not derive a summary measure of health benefit. The study was therefore a cost-consequences analysis.

**Validity of estimate of costs**
Good aspects of the cost analysis were that some quantities were reported separately from the costs; adequate details of methods of cost estimation were given; the use of cost-to-charge ratios (which strengthens the validity of the cost analysis); and the statistical analyses that were performed on some resource consumption and cost data. However, the perspective adopted in the cost analysis was not explicitly specified and the effects of alternative procedures on indirect costs were not addressed. The reader should also note that the cost results may not be generalisable outside the study setting.

**Other issues**
The authors' conclusions appear to be justified given the uncertainties in the data. The issue of generalisability to other settings or countries was partially addressed by acknowledging that the study results could not be extrapolated to patients undergoing emergency procedures. Appropriate comparisons were made with other studies. The degree to which the study sample was representative of the study population was discussed, the authors noting that the study sample represented a population with clinically stable conditions whose coronary arteries were suitable for stent or balloon angioplasty. It was noted that this study was designed as an effectiveness trial and deliberately allowed clinical judgement to be used; investigators were free to choose on-line quantitative coronary angioplasty, intravascular ultrasound, or Doppler flow wire to help in decisions about crossover to stent. It was reported that in fact, most (95%) did not use these adjunctive methods, relying instead on visual assessment of residual stenosis, which is typical of contemporary North American practice. It was also acknowledged that this trial did not fully address the complication of in-stent restenosis, which might have required follow-up of a year or longer.

**Implications of the study**
These results suggest that routine coronary stent implantation in suitable vessels should be viewed as a superior approach to the strategy of initial balloon angioplasty and provisional stenting.

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