Cost-effectiveness of distal embolic protection for patients undergoing percutaneous intervention of saphenous vein bypass grafts: results from the SAFER 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 distal embolic protection using a balloon-occlusion device (PercuSurge GuardWire, Medtronic) was investigated. Patients assigned to this intervention, underwent percutaneous coronary intervention (PCI) using the GuardWire to occlude the distal vessel during balloon angioplasty and stent deployment, followed by aspiration of atherosclerotic debris from the saphenous vein bypass graft (SVG) using the Export aspiration catheter, before the occlusion balloon was deflated and antegrade flow was restored. This intervention was compared with conventional PCI performed over a standard angioplasty guidewire using balloon expandable or self-expanding coronary stents.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing PCI for a stenotic SVG. Patients were eligible if they were undergoing planned PCI to an SVG with a reference diameter between 3 and 6 mm. Patients with ongoing myocardial infarction (MI) were excluded, as were those with an ejection fraction of less than 25% and a serum creatinine level greater than 2.5 mg/d. Patients requiring multi-vessel PCI were also excluded.

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

Dates to which data relate
The patients from which the resource use and effectiveness data were derived were enrolled in the study between January 1999 and August 2000. The price year was 2001.

Source of effectiveness data
The effectiveness data were derived from a single study, further details of which can be found elsewhere (Baim et al., see Other Publications of Related Interest).

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

Study sample
The authors did not report whether the sample size was determined in the planning phase of the study. They also did not report any retrospective power calculations. During the enrolment period, a total of 801 patients undergoing PCI for a SVG were enrolled in the Saphenous Vein Graft Angioplasty Free of Emboli Randomised (SAFER) trial. Out of the 801 patients, 406 were allocated to the GuardWire group and 395 were allocated to the conventional PCI group. The patients in the GuardWire group had a mean age of 68 (+/- 10) years and 82% were male. The patients in the conventional PCI group had a mean age of 69 (+/- 9) years and 84% were male.

**Study design**
The study was a randomised controlled trial (RCT) that was undertaken in multiple sites. The patients were randomised to any of the two groups, stratified by clinical site and by whether the operator planned to use a glycoprotein IIb/IIIa receptor antagonist. An independent clinical events committee who were blinded to the treatment assignment reviewed all end points. The patients were followed up for 30 days. The authors reported no loss to follow-up.

**Analysis of effectiveness**
The analysis of the clinical study was conducted on an intention to treat basis. The health outcomes were MI, haemorrhagic complications, any repeat revascularisation and death. MI was defined as an elevation of creatinine kinase-MB (CKMB) greater than three times the upper limit of normal at any time during the follow-up period. Large MI was defined prospectively as any MI with a peak CKMB greater than 5 times the upper limit of normal, or any Q-wave MI. The authors assumed that only large MIs would adversely affect long-term prognosis after PCI. Haemorrhagic complications included the need for vascular surgical repair, ultrasound-guided compression, or bleeding requiring transfusion. The baseline characteristics of the two treatment groups were well-matched, with patients shown to be comparable in terms of age, gender and prognostic features.

**Effectiveness results**
There was no difference in in-hospital mortality between the GuardWire and control groups (0.7% versus 1.0%; p=0.72).

Patients randomised to the GuardWire group had a significantly lower incidence of periprocedural MI during the index hospitalisation (8.4% versus 13.9%; p=0.01). In addition, the GuardWire group was associated with a modest reduction in the incidence of bleeding complications compared with conventional treatment (5.4% versus 7.1%; p=0.38).

Between hospital discharge and 30-day follow-up, there were trends toward reduced rates of death (0.3% versus 1.6%; p=0.06) and nonfatal MI (0.5% versus 1.6%; p=0.17) in the GuardWire group.

When these results were combined with the observed in-hospital outcomes, use of the GuardWire was associated with a 42% reduction in the 30-day risk of death or any MI (95% confidence interval, CI: 17 - 65) and a 44% reduction in the risk of death or large MI (95% CI: 10 - 68). There were no significant differences in the rates of repeat revascularisation procedures.

**Clinical conclusions**
The GuardWire balloon occlusion device was effective in reducing mortality and MI in comparison with conventional PCI.

**Modelling**
As the empiric outcomes data were only collected for the 30-day follow-up period, the authors developed a probabilistic model to project long-term survival beyond the study observation period, contingent on the observed 30-day outcomes.

**Measure of benefits used in the economic analysis**
The measures of benefits used were combined deaths and MIs avoided during the 30-day trial period, and the lifetime life-years gained. The life expectancy was derived from a long-term survival model (probabilistic model). The life expectancy was discounted at a rate of 3% per year.

**Direct costs**

The total costs and resource use were reported separately. The direct costs included in the analysis were those to the health care system. These were the costs of initial and repeat procedures, hospitalisation, doctors' fees and follow-up costs. The cost of the GuardWire device was based on its current sales price. The costs of additional disposable equipment, overheads and depreciation for the cardiac catheterisation laboratory were estimated on the basis of the average cost per procedure in the authors' setting, and adjusted for actual procedure duration. All of the other hospital costs were determined using a top-down accounting method based on each hospital's Medicare cost report. Billing data were obtained for 776 admissions during the 30-day study period. The hospital costs were determined by multiplying itemised hospital charges by the cost-centre-specific cost-to-charge ratio. For those admissions for which billing data were not available (n=123), non-procedural hospital costs were imputed on the basis of a linear regression model, which was developed using the hospital admissions for which complete billing information was available. Other costs such as physician office visits, emergency department visits, echocardiograms and stress tests, were estimated by patient self-report and were calculated on the basis of 2001 Medicare reimbursement rates. Physician's fees were based on the 2001 Medicare fee schedule. Discounting was irrelevant, as all the costs were incurred during a short time, and was therefore not performed. All the costs were converted to 2001 dollars using the medical care component of the Consumer Price Index. The study reported the average costs.

**Statistical analysis of costs**

The costs and the resource use data were treated stochastically. Data were compared using the Wilcoxon rank-sum test. To define the factors that contributed to the net cost of GuardWire treatment more precisely, the authors used multivariable linear regression to determine the impact of clinical outcomes, complications and other factors on the initial hospital costs.

**Indirect Costs**

The indirect costs were not included.

**Currency**

US dollars ($).

**Sensitivity analysis**

The CIs for the cost-effectiveness ratios were estimated by the bootstrap method, using 1,000 re-samples of the study population. In addition, although future costs beyond the 30-day trial period were not included in the primary analysis, these additional costs were considered in sensitivity analyses. The authors also carried out sensitivity analyses by varying the assumptions concerning the long-term outcomes, and by varying the relative risk of death or MI. Lastly, the authors conducted sub-group analyses according to angiographic, clinical and treatment-specific factors.

**Estimated benefits used in the economic analysis**

Use of the GuardWire was associated with a 42% reduction in the 30-day risk of death or any MI (95% CI: 17 - 65) and a 44% reduction in the risk of death or large MI (95% CI: 10 - 68).

The mean life expectancy (undiscounted) was 11.38 years for the GuardWire group and 11.16 years for the conventional therapy group, a difference of 0.22 years. After discounting, the life expectancy difference was reduced to 0.17 years (95% CI: 0.04 - 0.29).
Cost results
The 30-day mean costs were $14,399 (+/- 6,731) in the GuardWire group and $13,774 (+/- 7,016) in the conventional PCI group, (p=0.006).

The multivariable linear regression model of initial hospital costs identified both procedure-related complications (i.e. death, large MI, haemorrhagic complications) and the need for unplanned bypass surgery as the principal determinants of the hospital costs.

Synthesis of costs and benefits
The costs and benefits were combined as the incremental cost-effectiveness ratio (ICER) per year of life gained for PCI using the GuardWire, compared with conventional PCI. This ICER was calculated by dividing the difference in mean 30-day medical care costs for the two groups by the difference in life expectancy. The authors also calculated a "within-trial" cost-effectiveness analysis in which the ICER was expressed as the cost per death or MI avoided.

The within-trial cost-effectiveness ratio for GuardWire-based PCI compared with conventional PCI was $9,342 per death or MI avoided.

The lifetime ICER for GuardWire-based PCI compared with conventional PCI was $3,718 per life-year gained (95% CI: 0 - 43,079).

A bootstrap simulation demonstrated that the ICER for embolic protection remained less than $40,000 per life-year gained in 97.3% of samples. The authors reported that the results were relatively stable over a broad range of alternative assumptions concerning long-term outcomes. The authors also reported that varying the relative risk of death or large MI demonstrated that the ICER remained below $40,000 per life-year gained over a broad range of assumptions.

Stratified analyses according to selected baseline patient characteristics showed that there were no significant interactions between 30-day outcomes or costs and treatment assignment for each sub-group.

Authors' conclusions
Distal embolic protection in patients undergoing percutaneous coronary interventions (PCIs) of diseased saphenous vein bypass graft (SVG) was highly cost-effective in comparison with conventional treatment. The cost-effectiveness of the GuardWire was highly favourable when compared with accepted medical interventions, and it remained reasonable over a wide range of alternative modelling assumptions and patient sub-groups.

CRD COMMENTARY - Selection of comparators
A justification was given for the use of conventional PCI as the comparator. It represented current practice in the authors' settings. You should decide if this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a blinded RCT. This was appropriate for the study question as well-conducted RCTs, such as this one, are considered the 'gold' standard when comparing different health interventions. The study sample appears to have been representative of the study population. The patient groups were shown to be comparable in terms of age, gender and prognostic features. The clinical analysis was undertaken on an intention to treat basis, and appropriate statistical techniques were used to test for statistically significant differences between the two groups.

Validity of estimate of measure of benefit
The benefits were derived from a probabilistic model to project long-term survival beyond the study observation period, contingent on the observed 30-day outcomes. As no details of the probabilistic model were provided in the present study, it was unclear whether the model was appropriately undertaken to project long-term survival. The future benefits were appropriately discounted at an annual rate of 3%.
Validity of estimate of costs
The perspective of the analysis was not explicitly stated, but was consistent with that of the health care system. All the cost categories relevant to the perspective adopted were included in the analysis, and all the relevant costs appear to have been included. The costs and the quantities were reported separately, which will increase the generalisability of the authors' results to other settings. Resource use was derived from the single study, with appropriate statistical techniques being used to test for any significant differences between the two groups. The unit costs were derived from several sources, with the majority being derived from Medicare charges. Although charges were used, the authors adjusted charges to the specific cost-to-charge ratio, so that these costs would more accurately depict the actual cost of providing an intervention. The authors performed a multiple linear regression to identify the predictors of initial hospital costs. Discounting was not relevant, as all the costs were incurred during a short time, and was not performed. The price year was appropriately reported, which will aid any possible inflation exercises.

Other issues
The authors did not compare their findings with those from other studies. It would appear that this is the first economic evaluation of GuardWire. The issue of generalisability to other settings was addressed in the sensitivity and statistical analyses. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The clinical study enrolled patients undergoing PCI for a stenotic SVG and this was reflected in the authors' conclusions.

The authors reported a number of further limitations to their study. First, their cost-effectiveness model could have biased their results against GuardWire, based on conservative assumptions of MI affecting long-term prognosis. Second, the lack of empiric data beyond the 30-day trial period meant that extensive modelling was required to develop a meaningful cost-effectiveness analysis. Finally, the results should only apply to their study population and should not be extrapolated to other populations at high risk of distal embolisation, such as thrombotic native coronary lesions or patients undergoing PCI for acute MI, or to other embolic devices.

Implications of the study
The authors reported that for patients undergoing PCIs of diseased SVG, distal protection using the GuardWire system was an attractive use of limited health care resources. However, they also noted that further studies are needed to demonstrate the cost-effectiveness of alternative embolic protection devices for SVG PCI, and to extend the results of this study to other PCI populations at high risk of embolic complications.

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