The cost-effectiveness analysis of using Drug Eluting Stents (DES) and Bare Metal Stents (BMS)

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ABSTRACT

A stent is a small, flexible, coil-like device used to support artery walls during a balloon surgery and can treat artery blockages in different parts of the body. Special stents called Drug Eluting Stents (DES) are the newest treatment for coronary artery narrowing. These stents are coated with a tiny dose of a drug that slowly dissolves. The costly DES are now being vigorously tested worldwide and are becoming substantial with the economic impact of these devices. We wish to perform a cost-effectiven ess analysis of the more expensive DES compared with the standard Bare Metal Stent (BMS) approach by careful follow-ups and comparing the outcomes using data from Dunedin Hospital.

Keywords

Drug Eluting Stents, Bare Metal Stents, cost-effectiveness analysis, strategy cost, NZ data

INTRODUCTION AND RATIONALE

Stents are small coil-like tubes made of various types of metal. They are designed to keep blockages in the coronary arteries open increasing the arterial lumen by scaffolding the arterial vessel wall, hence improving blood flow. Coronary artery stents have emerged as the preferred tool for percutaneous coronary interventions (PCI) during the past two decades. Their popularity results from the ease and speed of applicability and the improved safety by elimination of abrupt closure and the need for urgent coronary artery bypass grafting (CABG).

About 500 patients have stents placed in Dunedin Hospital each year. Since it is a University based research center, approximately 200 patients have joined Drug Eluting Stent (DES) trials over the last four years in Dunedin. The success of this endovascular metallic scaffolding is largely owing to significant improvements in technique and advancements in equipment. However, these procedures still have a number of limitations. In-stent restenosis (ISR) emerged as an iatrogenic adverse event in 10 to 30 per cent of patients, resulting in the need for another PCI within six months.[1] In addition, when ISR does occur repeat angioplasty is not effective in preventing its recurrence in 30 to 60 per cent of patients.[2]

This problem is growing as more Bare Metal Stents (BMS) are being used. A number of therapeutic strategies emerged from these insights into the pathophysiology of vascular repair following stent implantation. These include the DES which has a drug coating on its surface to attenuate the vasculoproliferative repair cascade. Two drugs, sirolimus and paclitaxel, were the first available on these new stents. Sirolimus is an inhibitor of the G1-phase of the cell cycle, whereas paclitaxel inhibits microtubule formation, both of which are necessary for cell division. Thus they inhibit intimal hyperplasia that would result in restenosis.

Various studies[3, 4, 5, 6] suggest that DES have offered promise by reducing the rates of restenosis and target lesion revascularisation. Unfortunately these stents come at a huge increase in economic cost and their use in NZ public hospitals poses a new and formidable financial challenge. As a result, the benefits of this cost need to be critically analysed.

Background Research

There is no prospective trial-based data on incremental cost-effectiveness of DES versus BMS in unselected patients as treated in everyday practice.[7] Up until now, there have been no studies regarding this topic undertaken in New Zealand. The most recent systematic review in our neighbourhood was done at the University of Sydney.[8] The cost per revascularisation avoided by using DES was $AUS3,750 - 6,100, with an estimated cost per Quality Adjusted Life Year (QALY) gained of $AUS46,829 - 76,467. The authors suggest that decisions to limit DES only to patients at the highest risk of restenosis may improve their cost-effectiveness but this would need to be reassessed when evidence is available to compare absolute benefits between patient groups.

In Quebec selective use of DES in high-risk patients is the most acceptable strategy in terms of cost-effectiveness. Sensitivity analyses suggest little additional health benefits but escalating cost-effectiveness ratios once DES have been used in 40 per cent of the patients.[9] This study is an excellent example of how to evaluate the cost-effectiveness of selective use of a new technology in high-risk patients.

In Switzerland the prospective, randomised, controlled Basel stent cost effectiveness trial (BAsel Stent Kosten Effektivitäts Trial, BASKET)[7] gives answers as to whether it is rational to withhold DES for economic reasons. BASKET was conducted independently from the device business industry, therefore these findings may reflect true impact on the use of DES in daily practice. They show that incremental cost-effectiveness ratio of DES compared with BMS to avoid one major adverse cardiac event (MACE) was €8018,031 and subgroup analyses showed that DES were

more cost-effective for elderly patients in specific high-risk groups.

METHODS

Study Population / Protocol

Patients eligible for enrolment were those who had successfully had a stent put in place under major international trials within Dunedin Public Hospital. Patients were not randomised or double-blinded but were recruited retrospectively under trials including TAXUS ATLAS, DESTINY I, Endeavor I and II and those under private settings in Dunedin. We gathered 80 stents during the last four years (DES: n=40 and BMS: n=40). Patients were selected under the following general selection criteria:

Key Inclusion Criteria: eligible for PCI or CABG; documented stable/unstable angina pectoris.

Key Exclusion Criteria: hypersensitivity to paclitaxel, sirolimus, clopidogrel and ticlopidine; allergy to stainless steel or contrast agents; MI within 72 hours before index procedure; CVA within six months; cardiogenic shock; life expectancy of less than 24 months due to other medical conditions; co-morbid condition.

Angiographic Exclusion Criteria: bifurcation (side branch >2mm); total occlusion; thrombus; three or more lesions in target vessel; calcification in proximal region; tortuous anatomy; severe angulation (75°).

Baseline characteristics in each group were noted: age, gender, presence of diabetes, hypertension, dyslipidaemia, obesity, smoking, previous MI, and lesion characteristics such as location, length, and diameter.

Data Collection

Data were collected from case report forms that had already documented baseline characteristics, angiographic features, procedural details, clinical outcomes, and associated procedural costs during the initial hospitalisation and one-year follow-up period in Dunedin. All end points were reviewed by hospital consultant cardiologists. Only clinically indicated repeated revascularisation procedures (and their associated costs) were included in the economic analysis.

Determination Of Costs

Initial equipment costs were retail prices given by the manufacturers and any subsequent hospitalisations during the one-year follow-up period were obtained from the CardioBase® programme used in this hospital. Complete baseline and follow-up economic data were available for 80 out of 80 patients (100 per cent). Hospital admissions that were purely for the purpose of protocol-mandated cardiac catheterisation (compulsory six-month angiographic follow-up) were excluded from the economic analysis unless clinically indicated coronary revascularisation was performed at the time of angiographic follow-up. Private physician's visits costs not related to the intervention and other medications and rehabilitation services were excluded since they followed usual standard care practices, therefore they can be assumed to be equally distributed in all patient groups.

The cost of each cardiac catheterisation laboratory procedure was determined by standard accounting methods. Detailed resource utilisation and its costs including the number of angioplasty balloons, stents, other devices, guiding catheters, guide wires, and contrast volume were recorded in lab books but not presented in this report. Overhead costs for catheterisation laboratory maintenance and personnel were estimated on the basis of the average cost per procedure at Dunedin Public Hospital.

Follow-Up

Patients were prospectively seen on an outpatient basis after six, nine and 12 months for primary endpoint assessment and for the effectiveness of the intervention. Patients not seen personally were contacted by telephone.

The primary endpoints were MACE which include cardiac death, non-fatal myocardial infarction (MI), and target vessel revascularisation (TVR). TVR was defined as PCI or CABG driven by a lesion in the same vessel as initially treated. The cost-effectiveness after one year was expressed in cost per MACE avoided. Episodes of angina were also recorded but not considered as part of MACE.

Statistical Methods

Discrete data have been reported as percentages and continuous data have been reported as mean ±standard deviation. Normally distributed continuous variables were compared by Student's t test. Cost data were reported as means and were compared by t tests with an α-level of 0.05 and a power of 80 per cent. The primary end point for the cost-effectiveness analysis was the cumulative cost per MACE avoided by DES compared with conventional BMS.

RESULTS

Table 1 suggests that all key baseline clinical and angiographic characteristics between the BMS and DES groups are not significantly different.

Table 1. Baseline Clinical and Angiographic Characteristics

	BMS Group, n=40	DES Group, n=40
Age, y	60±19	61±110
Male, %	71	67
Diabetes mellitus, %	13	12
Current smoker, %	8	10
Hypertension, %	37	35
Dyslipidaemia, %	65	61
BMI > 30, %	29	25
Previous myocardial infarction, %	46	41
Left Dominance, %	21	18
Multivessel disease, %	41	39
Lesion location, %		
Left anterior descending (LAD)	41	39
Circumflex (Cx)	29	28
Right coronary artery (RCA)	32	32
Number of stents per patient	1.4	1.5
Lesion length, mm	14.1±15.4	15.8±16.3
Reference diameter, mm	2.85±10.32	2.96±10.43
p>0.05 or NS for all comparisons		

Table 2 summarises resource costs for the index revascularisation procedures. Not surprisingly, apart from the cost of the stents themselves, the use of procedural resources was not significantly different for the two treatment groups. The times taken for each treatment were not different from each other. An average of 1.4 -1.5 stents per patient were implanted in both treatment groups. The difference in initial procedural costs was $2933 per patient (95% CI was 1306, 4560; p-value<0.01) and was driven entirely by the higher cost for DES compared with BMS.

MACE consisted of cardiac death, MI and TVR as shown in Table 3. Since this was a small study the dominant factor in MACE was the TVR portion which was not shown to be significantly different between the two groups. Mean medical care costs over a one-year period were also shown to be $885 (p<0.05) per patient lower in the DES group compared with the BMS group. Although these cost savings were substantial, they did not fully offset the higher cost of the initial stents. As seen by the total aggregate one-year medical care costs between the two groups which remained $2048 per patient higher for the DES group compared with the control group which accounted for true clinical difference (p<0.05).

Data for costs were collected periodically after the initial intervention at six, nine and 12 month periods and shown as cumulative costs in Graph 1. This illustrates clearly the significant difference in the costs of stents themselves at the time of intervention which gradually converge to its competitor's but still could not outcompete after the 12-month period.

Table 2. Initial Treatment Costs

	BMS Group n=40	DES Group n=40	Difference (95% CI)	*p-value*
Procedure duration, min	77±139	76±135	–1 (–6,4)	0.76
No. of Stents per patient	1.4±10.6	1.5±10.8	0.1 (–0.1,0.3)	0.54
Overhead	1237±1529	1222±1313	–15 (–60,30)	0.79
Devices	**2653±1982**	**5601±12514**	**2948 (1366,4530)**	**<0.01**
Total procedural cost, $	**3890±11511**	**6823±11527**	**2933 (1306,4560)**	**<0.01**

Table 3. Follow-Up Events and Costs

	BMS Group	DES Group	Difference (95% CI)	p-value
Death, %	0	0	0.0 (–0.2,0.2)	0.99
MI, %	0	0	0.0 (–0.2,0.2)	0.99
TVR, %	22.8	17.3	–5.5 (–7.8, –2.3)	0.78
Angina, %	14.5	18.4	3.9 (–1.3,9.1)	0.72
Follow-up costs, $				
Repeat procedures	**2240**	**1768**	**–472 (–780, –236)**	**<0.05**
Hospital costs	**3249**	**1836**	**–1413 (–2745, –80)**	**<0.05**
Total follow-up costs	**4489**	**3604**	**–885 (–1109, –661)**	**<0.05**
Aggregate 1-year costs, $	**8379**	**10427**	**2048 (1518, 2578)**	**<0.05**

Graph 1. Cumulative costs for BMS and DES groups

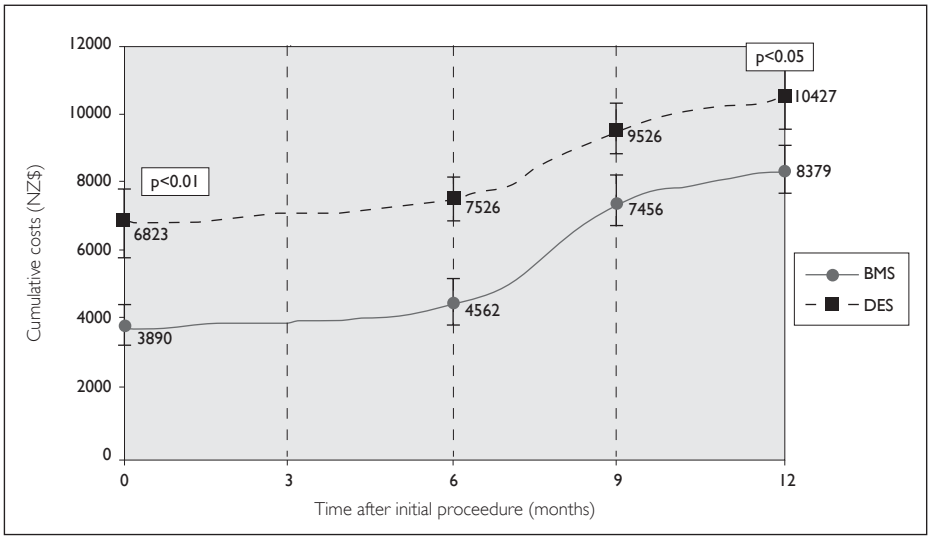

Table 4. Cost-Effectiveness of DES Stents

Scenario	Mean Cost (95% CI), $	MACE	C/E Ratio, $/MACE Avoided	>$1000 per MACE Avoided, %
C/E Analysis	-2048 (1518, 2578)	2	20 480 (15939,25780)	s98.2

However the ranges of costs between the two interventional groups remained substantially different

Cost-effectiveness was calculated in Table 4 by considering the absolute MACE reduction in conjunction with absolute cost reduction. This showed that to avoid one MACE $20480 would have to be spent on average per person. Also calculated here was the percentage of patients who were able to avoid one MACE by spending more than $1000. This accounted for about 98 per cent of the population who used DES.

DISCUSSION

Careful selection of patients in the BMS group to match the ones in the DES group was to ensure that the baseline characteristics of patients in each group were not dissimilar. All characteristics recorded in this study, including major risk factors of ischaemic heart disease, were also featured in other major literature regarding the same topic.[3,4,7] These were compared statistically to be non-significant at baseline.

There are two types of parameters that can be used as primary endpoints. These are non-clinical or angiographic (such as diameter of stenosis or in-stent late lumen loss) and clinical (TVR and MACE) parameters. In this study we chose clinical parameters since major limitations can result from choosing an angiographic parameter as the primary endpoint.[10]

Our results showed repeat revascularisation (which also represented MACE) in the DES group reduced 5.5 per cent ($p < 0.05$). So far three trials with a primary clinical endpoint have also shown a significantly positive impact on patient outcome: the SIRIUS trial[3] (Cypher stent) with its reduction of primary endpoint TVF (21.0 per cent vs 8.6 per cent), the TAXUS-IV trial (12.0 per cent vs 4.7 per cent) and TAXUS-VI[4] in long lesions (19.4 per cent vs 9.1 per cent).

It was drawn to attention that the high upfront costs of DES shown in Table 2 were mainly due to their initial cost difference of $2933 per patient (95% CI was 1306, 4560; $p<0.01$). Furthermore within this given time frame of 12 months, the follow-up costs for BMS tended to converge towards the overall cost for DES but it still resulted in a significant distinction ($2048; 95%CI 1518, 2578; p-value <0.05). This proved DES to not be cost-effective up to this point, but if the extrapolation was allowed the trend seemed to be that the two lines would meet at some point in the future. A longer term cost-effectiveness analysis would give more insight into the real outcome.

The cost-effectiveness ratio illustrated that to avoid one MACE, $20480 on average per person would need to be spent. This high cost per TVR avoided should be considered in conjunction with the smaller than expected difference in TVR between the two groups. The question came down to whether it was justifiable for this amount of money to be spent within this community setting given 98.2 per cent of patients would have to spend more than $1000 to avoid one MACE anyway.

This study had a number of limitations. Its sample size of 40 patients in each group was relatively small in comparison with the other studies mentioned earlier which indeed affected the end clinical outcomes. Nevertheless, this intended to model our real local population based only in the Dunedin setting and we made sure that the power be retained at 80 per cent for the internal strength of this study.

Cost per Quality Adjusted Life Year (QALY), which was another clinical predictor used in many studies, was not possible to obtain here due to the retrospective nature of this study and the fact that data had not been collected during the trials.

Shrive and colleagues from the APPROACH[6] group performed the cost-effectiveness of DES by taking into account the restenosis reduction and the quality of life. They reported a cost-utility ratio of $58721 per QALY gained with the use of sirolimus-eluting stents. Not astoundingly, when the risk of restenosis is higher (in elderly patients and in those with diabetes) the cost-effectiveness ratio falls. This study at least supported our local data. The authors concluded that the use of sirolimus-eluting stents has a cost-effectiveness profile similar to that of other accepted technologies, however, this was limited to sirolimus-eluting stents and could not be applied to other DES.

Previous studies have suggested that hospital charges do not necessarily reflect true economic costs and that their use may provide misleading

data with regard to cost-effectiveness. It is suggested that there are still discrepancies between cost-based and charge-based methodologies and may have important implications for future studies evaluating the relative cost-effectiveness of drug-eluting stents.[11]

Another limitation was that all costs were not converted to recent values of dollars on the basis of the medical care component of the Consumer Price Index, which may in turn overestimate the costs for more recently-admitted patients due to national inflation. However, we assume that this effect would be minimal.

CONCLUSION

Drug Eluting Stents (DES) have entered the area of interventional cardiology with high expectations and intensive research. A cost-effectiveness analysis was needed to evaluate its economic impact. This local retrospective cohort study conducted in Dunedin showed some reduction in repeat revascularisation rate in the DES group compared with the BMS group. Yet the high upfront cost of DES was not shown to be translated into a lower overall strategy cost within a one-year time frame in comparison with BMS. A larger and longer term analysis would extend our understanding of their usefulness in the future.

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ETHICAL CONSIDERATIONS

The study protocol was an audit of approved trial patients approved by the University of Otago Ethics Committee.

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