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Cost effectiveness of coronary revascularisation

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Coronary artery bypass graft surgery (CABG) is a relative expensive treatment for coronary artery disease (CAD). However, it provides a successful management for this disease as it improves quality of life (QoL), restores general well being, and alleviates symptoms, particularly angina, in more than 90% of patients[1].

Percutaneous treatment of CAD has evolved over the last few decades, especially with the advent of percutaneous coronary intervention (PCI). Coronary stenting has revolutionised the current treatment of CAD. Despite the high cost, CABG however has been the gold standard for treating multivessel and left main coronary artery disease, mainly because of its higher rate of complete revascularisation and lower need for repeat revascularisations compared to PCI with bare-metal stents (BMS). The difference in QoL favouring CABG driven by the lower need for repeat revascularisation, makes CABG more cost effective compared with PCI with BMS.

To improve the outcome of PCI and narrow the gap between PCI and CABG, drug-eluting stents (DES) have been developed. DES represents one of the most innovative developments in interventional cardiology today. Despite a benefit of DES compared with BMS in reducing in-stent restenosis and thrombosis and thus repeat revascularisations in simple and complex coronary disease[2], stenting remains limited by a restenosis rate in 20% to 30% of "ideal" lesions, with rates approaching 50% in more complex clinical and anatomical subsets[3]. Furthermore, costs of DES are higher compared to BMS[4] and so far no significant effect on either mortality or rates of non-fatal myocardial infarction has been proven[5]. In addition, the initial euphoria, which led to an unrestricted use of DES, was somewhat tempered by concerns relating to a possible late in-stent thrombosis of DES due to delayed intimal healing and related clinical events[6].

New medical products and technologies, such as DES, are an important driver of increased healthcare costs[7]. As a result, government officials, stakeholders, and health policy makers would rightly question the economic value of recent technological advances in medicine and would try to estimate as precisely as possible the actual price the society is to pay for a particular new treatment.

Cost effectiveness analysis is a method of comparing the expected benefits of a medical technology with the net cost of the technology. The relationship is expressed in terms of an incremental cost effectiveness ratio (ICER), which is calculated by dividing the net cost of the treatment being evaluated (relative to the standard of care) by its net benefits (also compared with standard of care). The standard approach is to assess long-term healthcare outcomes in terms of quality-adjusted life years (QALY). The QALY concept uses years of life in perfect health as a common metric to value both life expectancy and QoL. In the USA, an ICER of <$50,000 per QALY gained is deemed economically favourable, an ICER of $50,000 to $100,000 per QALY gained is considered to be in the "grey zone", and an ICER of >$100,000 per QALY gained is not attractive[8]. In Europe, an ICER of <£30,000 per QALY gained is deemed economically favourable[9].

Regarding single-vessel disease, Bahkai et al[10] examined the cost effectiveness of DES versus BMS for patients undergoing PCI for single vessel disease as part of the randomised TAXUS-IV trial over a 1-year follow-up period. They reported an incremental cost effectiveness ratio of $47,798 per QALY gained.

Regarding multivessel revascularisation, cost effectiveness of DES in the USA was examined alongside the SIRIUS trial[11]. In this study, initial hospital cost were $2,800 higher with the sirolimus-eluting stent compared with the BMS ($11,345 versus $8,464, $p < 0.001$).

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However, much of this difference in initial costs was offset by lower follow-up costs ($5,468 versus $8,040, p < 0.001), mainly due to a reduced requirement for repeat revascularisation procedures. Thus, at 12 months, the sirolimus-eluting stent compared to BMS was associated with a net 1-year cost of $309 per patient and a reduction of 19 revascularisation events per 100 patients treated, yielding $27,540 per QALY gained.

However, the SIRIUS and TAXUS-IV trials are randomised clinical trials with highly selected patient populations. To evaluate the cost effectiveness of DES versus BMS in unselected patients, as treated in everyday clinical practice, the BASKET trial[4] was conducted. Despite the reduced rate of major adverse cardiac events by 44% with DES at six months follow-up, total costs were higher with DES compared with BMS, €10.544 versus €9.639 (p < 0.0001), respectively. Incremental cost effectiveness ratio of DES per QALY gained was €73.283, indicating DES to be less cost effective compared with BMS over a 6-month period in a real-world setting. Similarly, the Swedish study of Ekman et al[12] distinguished results for the overall population and a high-risk subgroup, defined as patients with medically treated diabetes, small vessels (<2.5 mm), and long lesions (>20 mm). Paclitaxel-eluting stents were considered cost effective in high-risk patients, particularly at 24 months, and less cost effective for the general population. In a recent review comparing the cost effectiveness of DES with BMS in day-to-day practice conditions, Neyt and colleagues[13] emphasised that the combination of a higher cost (>€700) of DES versus BMS, no life-years gained, a relative small absolute reduction in repeat revascularisations, and a small improvement in QoL results in unfavourable cost effectiveness ratios for DES. These results are probably the effect of treatment of patients with more complex lesions than those enrolled in trials. The claimed reduction in repeat revascularisation only resulted in minor and uncertain utility gains, while the use of DES certainly caused substantial additional net treatment costs.

Recent studies examining the effectiveness of DES have reported that the use of DES is associated with a significant increase in the incidence of late in-stent thrombosis and very late in-stent thrombosis[14], occurring at a constant rate of 0.6% per year during a follow-up period of three years[15]. Late in-stent thrombosis is responsible for a small but important increase in death (30%) and myocardial infarction (> 60%) in DES recipients, and this increase may negate the reported benefits associated with the use of DES[15]. Previous studies on DES have been limited by an average follow-up period of only one year and thus have not incorporated the costs associated with the occurrence of late in-stent thrombosis and its relative adverse events. In addition, these studies also have not considered the cost of extended dual-antiplatelet therapy (aspirin and clopidogrel), which has been recommended due to the occurrence of late in-stent thrombosis[16]. Filion and colleagues[17] examined the effect of late in-stent thrombosis on the cost effectiveness of DES extrapolating the results of the SIRIUS and TAXUS-IV trials by incorporating the anticipated costs of adverse events due to late in-stent thrombosis. Late in-stent thrombosis associated costs increased the cost per QALY gained from $27,500 to $250,935 in the SIRIUS trial and from $47,798 to $257,591 in the TAXUS-IV trial. Consequently, when late in-stent thrombosis associated costs were incorporated, DES exceeds the accepted thresholds of $100,000 per QALY gained, and thus, DES is not cost effective.

The use of DES increases initial hospital costs compared to conventional BMS, in particular due to the significantly higher cost of DES. However, DES is associated with a substantial reduction in morbid events, including repeat revascularisation, re-hospitalisation, and CABG[11], with similar rates of death and myocardial infarction[18]. This has led to an associated reduction in follow-up medical care costs. These cost savings, however, are insufficient to fully offset the higher initial cost of DES in the real-world setting. Despite the higher cost of DES, several lines of reasoning suggest that DES may be viewed as reasonably attractive, at least within some subgroups of patients with a high risk of requiring reintervention. However, a perception exists among cardiologists that the early evidence of DES is so compelling that there should be a widespread implementation of the use of DES. As a consequence, this has led to expanded use of DES in patients with complex coronary anatomical features, though most randomised clinical trials comparing DES with BMS excluded such patients. As a consequence, off-label use is associated with increased risk of both early and late in-stent thrombosis, as well as death or myocardial infarction.

PCI is unlikely to become more cost effective compared with CABG with the use of DES, which have not been shown to improve survival or freedom from myocardial infarction in any situation compared with BMS and with which uncertainties persist with regard to the precise risk of in-stent thrombosis. Most studies indicate that DES are not cost effective compared with BMS for the overall PCI population. For high-risk subgroups such as diabetics and patients with small vessel disease and/or long lesions, results appear more favourable.

The SYNTAX trial[19], in which CABG was compared with DES PCI, recently failed to show that PCI with the Taxus stent was non-inferior to CABG and the conclusion was that CABG remained the standard of care in patient with left main and three vessel disease. The cost effectiveness data at one-year follow-up of the SYNTAX trial has been presented at the American College of Cardiology meeting and at EuroPCR. The results showed that total medical costs at one year were lower with PCI compared with CABG[20]. However, no significance difference was observed between CABG and PCI for patients within the highest SYNTAX score (SYNTAX score ≥33). No significant differences were observed between the two treatments at six or 12 months in terms of QoL. The 5-year cost effectiveness outcome of the SYNTAX trial is essential and might provide new insights into the comparison of cost effectiveness between CABG and DES PCI.

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