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Pharmacoeconomical comparison of bare metal stent and drug eluting stent

Hiren R. Patel*[1], M. A. Patel[1], I. S. Anand[1], C. N. Patel[1], K. H. Parikh[2] and P. A. Bhatt [3]

[1]Department of Clinical Pharmacy, Shri Sarvajanik Pharmacy College, Mehsana
[2]The Heart Care Clinic, Ahmedabad
[3]L. M. College of Pharmacy, Ahmedabad, Gujarat, India

Abstract

Coronary artery disease (CAD) is the leading cause of death and disability world over. To achieve PCI; either bare metal stent (BMS) or drug eluting stent (DES) are used. The objective of the present retrospective study was to evaluate pharmacoeconomics between BMS (Driver ^{TM}) and DES (Endeavor ^{TM}) in patients who underwent coronary angioplasty. 20 patients underwent PCI between December 2007 and June 2009 at The Heart Care Clinic, Ahmedabad, out of which 10 patients were implanted with Zotarolimus Eluting Stent (ZES) and 10 were implanted with BMS. Both groups had similar demographics and risks factors. Follow-up was conducted. In pharmacoeconomics cost and effectiveness in terms of quality of life (Seattle Angina Questionnaires) and quality adjusted life years (QALY) was analyzed. Cost (in Indian Rupees) of BMS and DES was 96225±34732 and 152967±39086 ($p<0.0001$*), respectively. Effectiveness in term of QALY (Quality adjusted Life Year gained) was 1.58±0.33 in BMS group patients and 2.05±0.38 in DES group patients ($p<0.0001$*). The Pharmacoeconomical prospective show DES was a better compared to BMS which was statistically significant.

Key words: PCI, Stent, BMS, DES, QALY.

Introduction

Cardiovascular disease (CVD) is the leading cause of death and disability in the world [1]. Although the burden appears to be decreasing in developed countries, estimates suggest a sharp

rise in developing countries [2]. Between 1990 and 2020 Cerebrovascular related mortality is predicted to increase by 78% in women and by 95% in men. This overall increase is similar to that expected for coronary heart disease (CHD) [80% in women and 100% in men]. CVD is expected to account for 14.7 % of the disability adjusted life years [DALY's] lost and by 2020 will consume about 6 billion DALYs. The burden of CVD has decreased in developed countries as effective strategies to prevent and treat the conditions were implemented. Between 1965 and 1996 CVD related mortality fell by about 50% in Australia, Canada, France and the US and by 60% in Japan [3]. This was due to a decline in both stroke and CHD mortality. By contrast, over this period the CVD burden increased substantially in developing countries. In 1990, CVD deaths in developed countries were 5.3 million, whereas it was 8-9 million in developing countries [4]. In addition, deaths in developing countries occurred at a younger age. In the same year, the proportion of CVD deaths in those less than 70 years in developed countries was 26.5%, while in developing countries it was 46.7%. It was estimated that the DALY's lost in developing countries was about three times greater than that in the developed countries [5]. Unstable angina (UA) and non-ST segment elevation myocardial infarction (NSTEMI) are most commonly caused by rupture of an atherosclerotic plaque leading to thrombin generation, platelet activation, and thrombus formation1.These patients are at high risk of ischemic events, both early during the initial hospitalization and long term [2]. An early invasive strategy has been shown to improve major cardiovascular outcomes in higher risk patients [3-4]. The benefits of this strategy are observed mainly over the long term, with an early hazard associated with this strategy during the initial hospitalization [2]. Future advances in the acute management of ACS should therefore focus on minimizing the early hazard, thereby enhancing the overall benefit of an invasive strategy. Treatment with ASA, heparin and glycoprotein IIb/IIIa inhibitors have been shown to improve outcomes in ACS.

Coronary artery is the blood vessels that supplies blood and oxygen to heart muscle. Coronary Artery Disease is disease occurring in coronary artery in which fatty deposits build up in blood vessel walls and narrow the passageway for the movement of blood. This condition leads to eventual blockage of the coronary arteries and a "Heart attack". CAD can be treated by either of these methods Percutaneous Transluminal Coronary Angioplasty (PTCA), Coronary Artery Bypass Graft surgery (CABG), Percutaneous Coronary Intervention (PCI). PCI refers to both nonstenting procedures and stent interventions. The introduction of Percutaneous Transluminal coronary angioplasty (PTCA) in the 1970s provided a revascularization alternative to coronary artery bypass graft surgery (CABG). However, angiographic restenosis occurred in approximately 40 percent of patients at percutaneous coronary intervention (PCI) refers to both nonstenting procedures and stent interventions. Six months after PTCA, 50 to 75 percent of whom had recurrent ischemic symptoms, most often progressive effort angina. The absence of recurrent symptoms in the remaining patients can be related to a variety of factors including lesion severity, collateral blood supply, and a lower level of exertion, silent ischemia, and prior MI. Thus, 20 to 30 percent of patients required clinically driven repeat target lesion revascularization within the first year after PTCA. Later restenosis is uncommon as recurrent ischemia after a year is most often due to a new or progressive lesion; still after the restenosis period, the target lesion remained stable or regressed [7-9]. The introduction of bare metal stents (BMS) produced a significant improvement in the durability of balloon angioplasty as the rate of angiographic restenosis fell to 20 to 30 percent and the rate of target lesion revascularization to

10 to 15 percent [10-12]. BMS also produced better short-term results such as less residual stenosis, elimination of dissection, and lower rates of in-hospital CABG and myocardial infarction [13-14]. As a result, BMS replaced nonstent interventions (PTCA and Atherectomy) for most patients. Drug-eluting stents (DES) were developed in an effort to further reduce the rate of restenosis and, accordingly, target lesion revascularization. DES consist of a standard metallic stent, a polymer coating, and an anti-restenotic drug (e.g., sirolimus or paclitaxel) that is mixed within the polymer and is released over a period as short as days to as long as one year after implantation to reduce the local proliferative healing response. After years of unsuccessful attempts to prevent post-PCI restenosis by the systemic delivery of anti-proliferative drugs, coronary brachytherapy, in the late 1990s, became the first effective treatment of in-stent restenosis. However, it is associated with considerable logistic challenges, requires collaboration among several scientific disciplines in the catheterization laboratory, and is ineffective for indications other than in stent restenosis. Most importantly, it became rapidly apparent that irradiated coronary artery segments are at high risk of acute, sub-acute or late stent thrombosis, since the irradiation hampers subsequent re-endothelialization.

With the introduction of the CYPHER (Sirolimus-eluting Coronary Stent) in April 2002, a more powerful prevention of restenosis became commercially available in Europe and soon thereafter, in the United States and Japan. This device revolutionized PCI since it outperformed coronary brachytherapy in all aspects. Consequently, brachytherapy became rapidly obsolete, other drug-eluting stents were developed and introduced clinically, and the use of bare-metal stents decreased in many countries. The success of the CYPHER stent was based on a series of feasibility and prospectively randomized clinical landmark trials impressively documenting the superior efficacy and safety of this new device. In brief, the CYPHER stent was significantly more effective than bar-metal stents in lowering the rates of angiographic and clinical restenosis, without observation of safety concerns. Besides the large program of randomized clinical trials, the “e-Cypher” worldwide post-market surveillance registry was conducted to evaluate the efficacy and safety of SES in “real-life” clinical practice. While there is consensus that drug-eluting stents in general, and SES in particular, reduces the need for repeat PCI significantly, there is debate regarding whether this superior efficacy might be at the cost of long-term adverse events, late development of stent thrombosis in particular, with its serious, sometimes fatal, consequences. Just recently, a meta-analysis of four randomized trials comparing the Sirolimus-eluting stent with its bare-metal equivalent found no statistically significant differences in the rates of acute, sub-acute and late stent thrombosis, up to 3 years of follow-up. Since late stent thrombosis is a rare event, the sample sizes of the clinical trials were insufficient to draw definitive conclusions regarding this clinically important issue.

Restenosis after Percutaneous Coronary Intervention (PCI) reduces the quality of life and increases the morbidity of patients with this complication it may even increase the risk of death. [15]

Pharmacoeconomics

Pharmacoeconomics refers to the scientific discipline that compares the value of one pharmaceutical drug or drug therapy to another. A pharmacoeconomic study evaluates the cost (expressed in monetary terms) and effects (expressed in terms of monetary value, efficacy or

enhanced quality of life) of a pharmaceutical product. We can distinguish several types of pharmacoeconomic evaluation: cost-minimization analysis, cost-benefit analysis, cost-effectiveness analysis, and cost-utility analysis. Pharmacoeconomic studies serve to guide optimal healthcare resource allocation, in a standardized and scientifically grounded manner.

Cost-effectiveness analysis (CEA) is a form of economic analysis that compares the relative expenditure (costs) and outcomes (effects) of two or more courses of action. Cost-effectiveness analysis is often used where a full cost-benefit analysis is inappropriate e.g. the problem is to determine how best to comply with a legal requirement. Cost-effectiveness is typically expressed as an incremental cost-effectiveness ratio (ICER), the ratio of change in costs to the change in effects. The CEA is expressed in terms of a ratio where the denominator is a gain in health from a measure (years of life, premature births averted, and sight-years gained) and the numerator is the cost of the health gain [16]. The most commonly used outcome measure is quality-adjusted life years (QALY) [17].

Material and Methods

It was a retrospective observational study including 20 patients had undergone surgery of Percutaneous Coronary Intervention (PCI) during December 2007 to June 2009 were being taken as a study population. These patients were stented by different types of stent: Drug Eluting Stent or Bare Metal Stent. Application of antiplatelet medication and any other medical therapy was provided according to local usual practice. In this study pharmacoeconomical (Cost Effective Ratio) comparison were being performed.

Group of Patients:

Group I: Patients implanted with Drug Eluting Stents

Group II: Patients implanted with Bare Metal Stents

Methodology for Pharmacoeconomical Study:

$$ICER = \frac{\text{(Cost of therapy A - Cost of therapy B)}}{\text{(Effectiveness of therapy A - Effectiveness of therapy B)}}$$

Where,

ICER = Incremental Cost Effectiveness Ratio

Therapy A: Patients were stented with DES

Therapy B: Patient were stented with BMS

What was measured in Cost

Net Costs = cost of therapy + costs of intervention + costs of treatment side effects (if any) + other health sector costs – exclusion of associated drugs cost.

What was measured in Effectiveness

Net Effectiveness = Quality Adjusted Life Years (QALY) + improvements in health state, and take into account treatment to other side effects.

Eligibility Criteria

Inclusion Criteria:

1. Patients were >18 years old.
2. Male & Female patients had angina or acute coronary syndrome.
3. All lesions requiring intervention in one or more native coronary artery/coronary artery by-pass graft were amendable for implantation of drug-eluting stents only or bare-metal stents only.

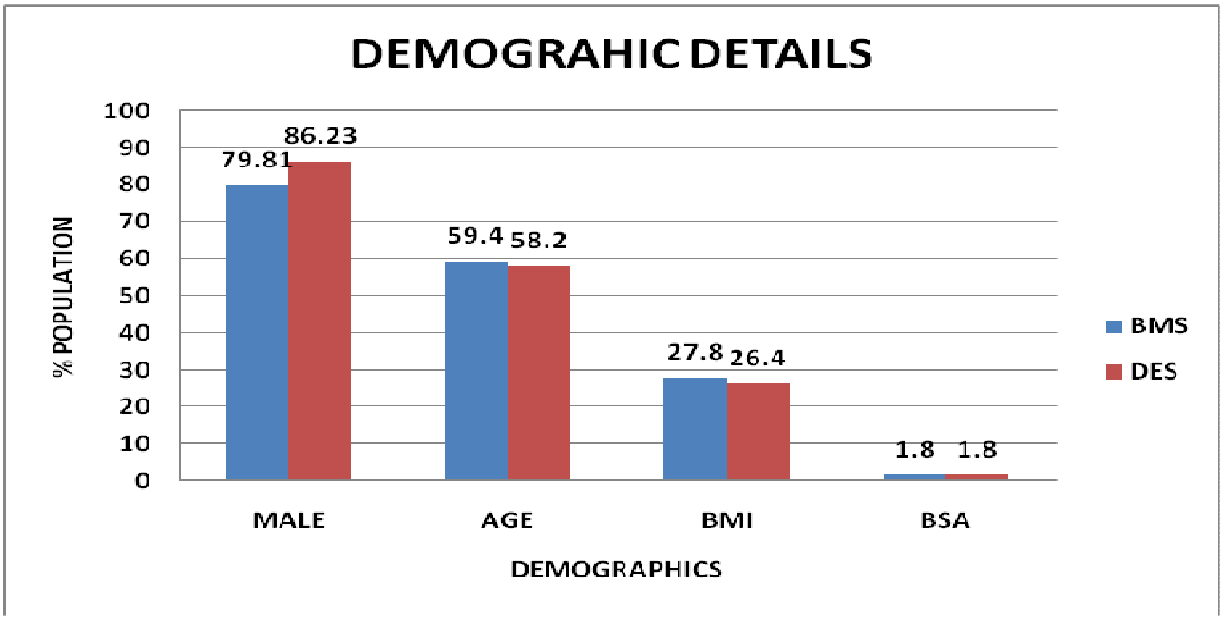
Exclusion Criteria:

1. Previous implantation of a coronary bare metal stent or coronary drug eluting stent.
2. Planned intervention of a bifurcation lesion with overlapping 2-stent technique.
3. The patient had a serious medical condition (with other Comorbidity) that may affect survival directly or indirectly with a life expectancy less than 5 years.
4. Currently participating in another randomized trial that clinically interferes with the present trial, or requires coronary angiography or other coronary artery imaging procedures.
5. Hypersensitivity or allergies to drugs or components in use with percutaneous coronary intervention.
6. Contraindications for treatment with Clopidogrel/Ticlid for 9-12 months
7. Patient is receiving chronic anticoagulation therapy (e.g., Warfarin, Heparin)

Statistics

All associated data were analyzed in its group including risk-benefit ratio. All process variables were summarized using Mean & Standard Deviation. By applying t-test significant difference between both groups were estimated.

Graph – 1: Demograpic Details of Patients

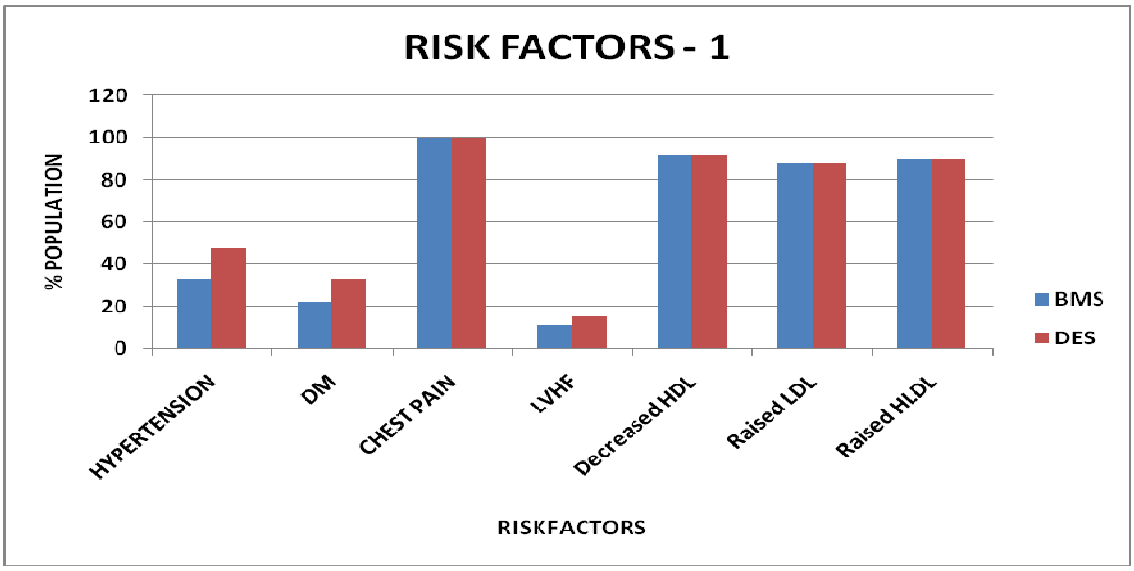


Result and Discussion

20 patients underwent PCI between December 2007 and June 2009 at The Heart Care Clinic, Ahmedabad. The demographic details of two groups are shown in table - 1.

As shown in graph - 1, among all patients male were reported by 79.81% patients in BMS received groups, while 86.23% patients were in DES received groups (p=0.281). Among all patients, mean age of patients in BMS group was 59.4 ±11.0 and in DES group was 58.2±10.3 (p=0.406). Body Mass Index (BMI) among patients of BMS group was 27.8±18.3 and 26.4±4.0 in another group (p=0.436). Body Surface Area (BSA) in BMS group patients was 1.8±0.2 and in DES group patients was 1.8±0.2 (p=1). Statistically it was found that the kind of gender, mean age, BMI and BSA were similar in both groups.

Graph – 2: Risk Factors



Graph – 2 and 3 shows, risk of hypertension in BMS group patients was 33.02% (36) and in DES patients was 47.70% (52) (p=0.038) and Diabetes Mellitus was reported 22.02% (24) in BMS group patients and 33.02% (36) were reported in DES group patients (p=0.096). All patients of both groups had chest pain. Left ventricular hypertrophy was 11.01 % (12) and 15.60 % (17) in BMS group patients and DES group patients, respectively (p=0.423). 91.74% (100) patients were hyperlipidemic in both groups. History of Early Onset CVD was 12.84% (14) Vs 14.68% (16), (p=0.843) and Family History of CVD was 12.84% (14) Vs 15.60% (17), p=0.690 reported in patients of BMS inserted and DES inserted group, respectively. It was also found among each group of patients smokers were 26.60% (29) Vs 28.44% (31), (p=0.884); tobacco chewer were 11.01 % (12) Vs 15.60 % (17), (p=0.423); alcoholic were 9.17% (10) Vs 10.09% (11), (p=0.997) and renal failure patients were 9.17% (10) Vs 10.09% (11), (p=0.997) in BMS group patients and DES group patients, respectively. Risk factors were found similar statistically in both groups of patients.

Graph – 3: Risk Factors and History

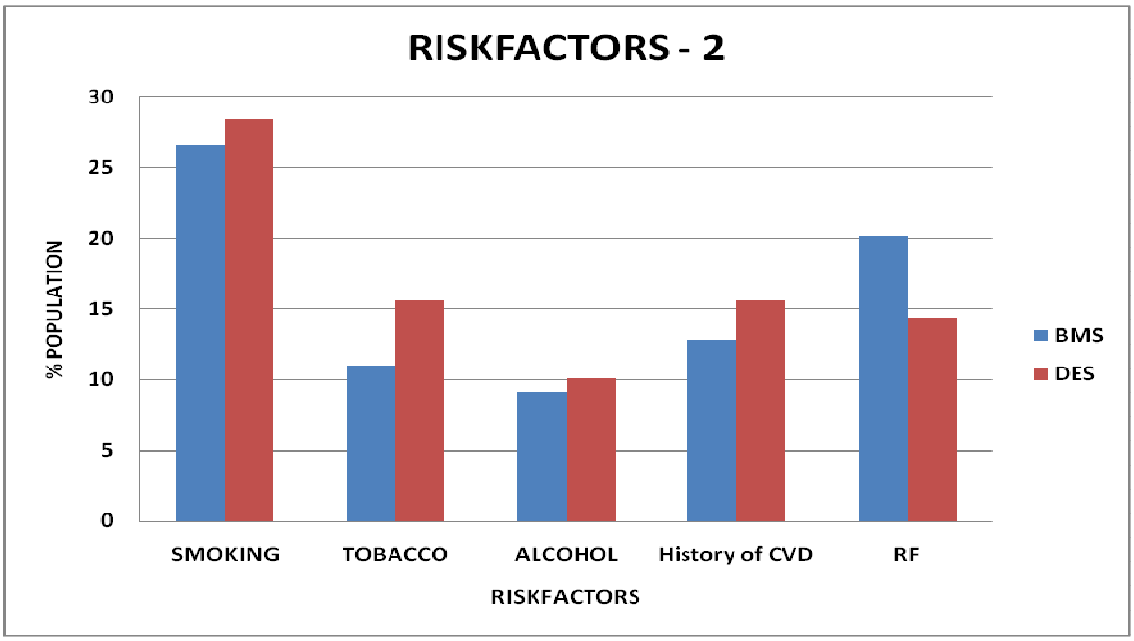


Table- 1: Pharmacoeconomical comparison between Bare Metal Coronary Stent (Driver) and Drug Eluting Coronary Stent (Endeavor)

Parameters	Patient with BMS (Driver) (n=109)	Patient with DES (Endeavor) (n=109)	p-value
Net Cost (INR)	**96225±34732**	**152967±39086**	**<0.0001***
Quality of Life (Utility)	**0.65±0.07**	**0.74±0.07**	**0.0001***
Life Years Gained	**2.45±0.59**	**2.78±0.33**	**0.393**
QALY	**1.58±0.33**	**2.05±0.38**	**<0.0001***

(Data expressed as mean ± Standard Deviation)
(* Significantly difference)

$$\text{ICER} = \frac{\text{(Cost of therapy A - Cost of therapy B)}}{\text{(Effectiveness of therapy A - Effectiveness of therapy B)}} = 115948.9144$$

Figure – 4: Comparison of Cost between BMS and DES

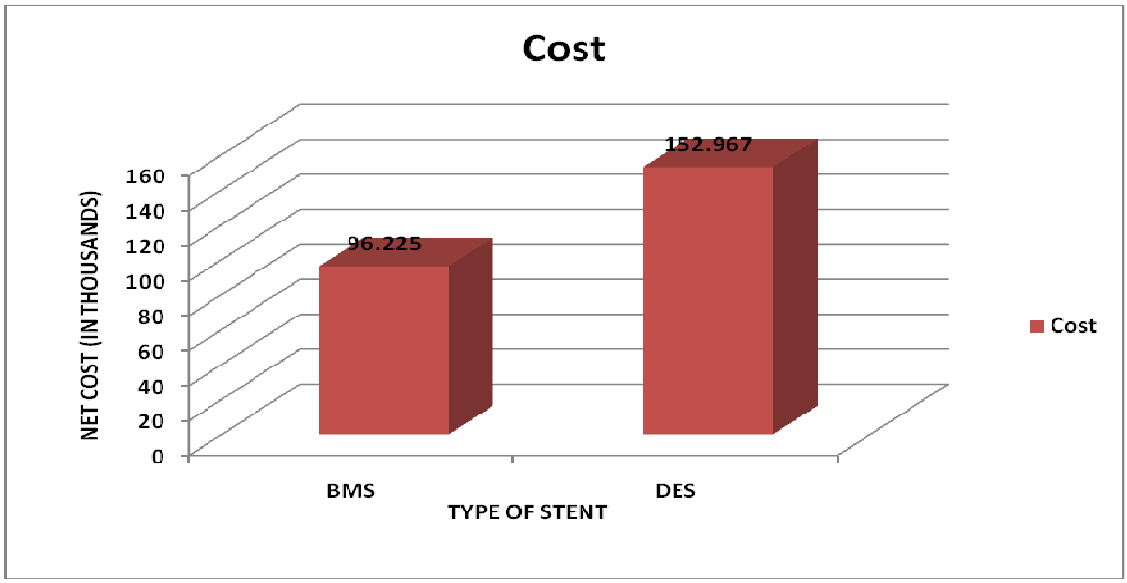


Figure – 5: Comparison of Effectiveness between BMS and DES

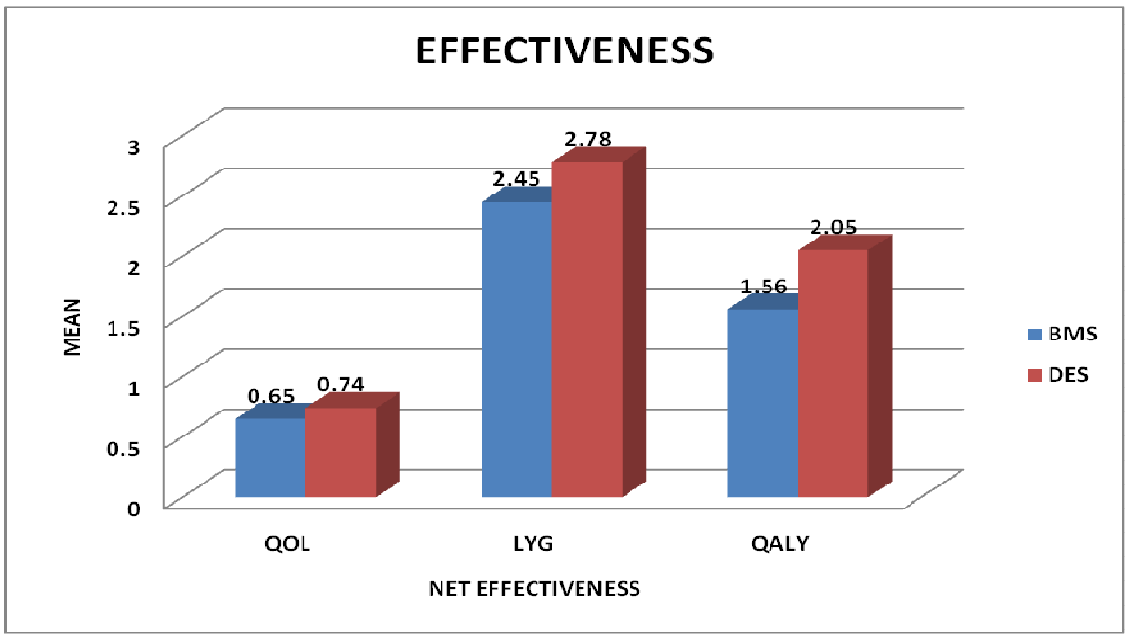


Fig- 4 shows Pharmacoeconomical comparison between Bare Metal Coronary Stent (Driver) and Drug Eluting Coronary Stent (Endeavor). Net Cost (in Indian Rupees) of BMS and DES was 96225±34732 and 152967±39086 ($p<0.0001$*), respectively. Quality of Life in BMS group patients was 0.65±0.07 while in DES group patients it was 0.74±0.07 ($p=0.0001$*) BMS group patients gained 2.45±0.59 life years while DES group patients gained 2.78±0.33 life years ($p=0.393$). Effectiveness in term of QALY (Quality adjusted Life Year gained) was 1.58±0.33 in

BMS group patients and 2.05±0.38 in DES group patients ($p<0.0001$*). Statistically, there were significant difference found in Cost, Quality of life and QALY between BMS and DES. So, there were statistically significant differences between the two arms with respect to Pharmacoeconomical comparison.

Conclusion

Higher costs with drug-eluting stents occurred despite the study using one of the most expensive bare metal stents, the Driver stent, which should have narrowed the cost gap between the two stent types however, the Pharmacoeconomical prospective in terms of Cost and QALY show DES was a better compared to BMS which was statistically significant. These study results justify with cost-effectiveness study of the BASKET trial. The Endeavor stent can be recommended as a valuable new tool for the Percutaneous treatment of coronary artery stenosis. The device is highly deliverable, has significant antirestenosis properties, and has a favorable economical and safety profile. Further long term study is required to get more viable results with larger population.

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