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Original Research Article

Six-month clinical outcomes of drug eluting stents in patients with coronary artery disease: an experience in real-world Indian patients

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ABSTRACT

Background: Treatment of patients with coronary artery disease using drug eluting stents (DES) remains a challenge due to stent thrombosis and in-stent restenosis. The present study sought to investigate the safety and clinical performance of DES in real-world Indian patients with coronary artery disease.
Methods: This prospective, non-randomized, single-center study enrolled 114 patients with coronary artery disease who were implanted with DES from January-2005 to September-2007. Clinical and angiographic follow-up were performed at 6 months after the index procedure. The primary endpoints of the study were: (major adverse cardiac events (MACE) defined as a composite of any episode of rest angina, myocardial infarctions (MI), repeat percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG), or (angiographic restenosis defined as ≥50% diameter stenosis at the treated site at 6-month follow-up. The secondary endpoints of the study were occurrence of any MACE events and stent vessel occlusion during the first 30 postprocedural days.
Results: A total of 125 lesions were treated by implantation of 130 DES. Only one patient (0.9%) developed minor bleeding during hospitalization. At the 6-month follow-up, MACE was 10%, including 1 (1.3%) MI, 2 (2.5%) unstable angina, 3 (3.8%) stable angina, 1 (1.3%) repeat PCI, and 1 (1.3%) CABG. Angiographic restenosis was found in 7 (8.8%) patients. Comparison of characteristics between patients with and without angiographic restenosis revealed significant effects of presence of diabetes ($p<0.012$), hyperlipidaemia ($p<0.028$), and stent length>20 mm ($p<0.05$).
Conclusions: The study results demonstrated excellent safety and clinical performance of DES in real-world Indian patients with coronary artery disease.

Keywords: Coronary artery disease, Drug eluting stents, Myocardial infarction, Percutaneous coronary intervention, Restenosis

INTRODUCTION

Cardiovascular disease is one of the most important causes of death worldwide, representing 31% of all global death. Over the past three decades, the prevalence of mortality and morbidity due to coronary artery disease has doubled, making it a significant health concern in India.[1] Intracoronary stenting had become an established treatment, when compared to suboptimal results after conventional plain old balloon angioplasty (POBA), and it decreases the morbidity of acute vessel closure and reduces the restenosis rate in comparison with POBA.[2-9] However, clinical use of intracoronary stents impeded by the risk of stent thrombosis and augmented neointimal hyperplasia, leading to in-stent restenosis.[10-14] To address the problem of in-stent restenosis encountered with intracoronary stents, drug-eluting stents (DES) are developed not only to significantly attenuate the cellularity but also decrease the need for repeat revascularization.[15,16] Many large randomized clinical trials of DES

optimistically indicate that perhaps the "Achilles heel of angioplasty" has finally been conquered.[17,18] However, stent thrombosis, dependency on prolonged dual antiplatelet therapy, and continued restenosis remain issues for the use of DES.[19,20] Therefore, the aim of the present study is to evaluate the safety and clinical performance of DES in real-world Indian patients with coronary artery disease.

METHODS

Study design and population

This was a prospective, non-randomized, single-center study, which included 114 patients with coronary artery disease, who underwent elective percutaneous coronary intervention (PCI) through femoral approach at Seth Gordhandas Sunderdas Medical College (GSMC) and the King Edward Memorial (KEM) Hospital from January-2005 to September-2007 at a tertiary health care centre. The study population consisted of patients (aged ≥18 years) with the evidence of myocardial ischemia who were candidates for elective PCI. Additional eligibility criteria were the presence of 70% significant angiographic stenosis assessed by quantitative coronary angiography. Exclusion criteria were active bleeding, haemorrhagic diathesis, contraindication to anticoagulation or antiplatelet therapy, renal insufficiency with a serum creatinine of >2 mg/dl, leukocyte count <3500 per mm3, platelet count <1,00,000 per mm3, and coexisting morbidities that limited life expectancy (<24 months) or that could affect a patients' compliance with the protocol. The study was approved by Institutional Ethics Committee and adhered to the tenets of Declaration of Helsinki.

Interventional procedure and treatment

The coronary interventional procedure was done according to standard guidelines and local practice. All patients were administered a loading dose of aspirin (325 mg) and clopidogrel (600 mg). Intra-procedural anticoagulation was ensured using unfractionated heparin. Glycoprotein IIb/IIIa inhibitors were administered according to operator's discretion. All patients were implanted with either TAXUS paclitaxel-eluting stent, Infinnium paclitaxel-eluting stent, Cypher sirolimus-eluting stent, or Endeavor zotarolimus-eluting stent. Available stent diameters for this study were categorized into 3 groups (≤2.5, 2.7 to 3, >3 mm), and available stent lengths were grouped as lengths of <15, 15 to 20, and >20 mm. All patients were advised to receive dual antiplatelet therapy (aspirin 325 mg daily and clopidogrel 75 mg daily) for at least 12 months after the procedure, and complete blood count was monitored once in 15 days.

Study endpoints and definitions

The primary endpoints of the study were major adverse cardiac events (MACE) [composite of any episode of rest angina, myocardial infarctions (MI), repeat PCI, or coronary artery bypass grafting (CABG)], and angiographic restenosis [presence of ≥50% diameter stenosis at the treated site after follow-up] at 6 months. The secondary endpoints of the study were occurrence of any MACE and stent vessel occlusion during the first 30 postprocedural days.

Data collection and follow-up

Baseline demographics, clinical and procedural data, and in-hospital clinical outcomes were consecutively obtained from patients' medical records. Clinical and angiographic follow-up were performed at 6 months. A total of 80 patients (70.2%) were followed up, and 34 patients (29.9%) were lost to follow-up over the study period.

Statistical analysis

Data are presented as mean±SD for continuous variables and as number (percentage) for categorical variables. Student's t-test was used to compare continuous variables. Chi square test was used to compare categorical variables. A 2-tailed p value <0.05 was considered statistically significant. All analyses were performed using Statistical package for social sciences (SPSS) statistical software, version 15 (, Inc., Chicago, Illinois, USA).

RESULTS

Between January-2005 and September-2007, 114 patients with 125 lesions were treated with TAXUS paclitaxel-eluting stent (n=8), Infinnium paclitaxel-eluting stent (n=6), Cypher sirolimus-eluting stent (n=50), and Endeavor zotarolimus-eluting stent (n=66). The mean age of study population was 51.56±10.18 years, and majority of the patients (89.5%) were males. Of 114, 102 (89.5%) patients presented with acute coronary syndrome, 31 (27.2%) had diabetes mellitus and 40 (35.1%) had hypertension. The mean length and diameter of drug eluting stents were 18.91±5.92 mm and 2.91±0.34 mm, respectively. Among lesions treated, >90% of lesions were classified as B or A, and left anterior descending artery was the most frequent target vessel in study population. Baseline demographics, clinical and angiographic characteristics of the patients are depicted in Table 1.

In-hospital outcomes are illustrated in Table 2. No patient died or required emergent CABG. One patient developed minor bleeding. Procedural success was achieved in all patients. No cases of acute stent thrombosis, acute MI post-PCI, and major bleeding were reported.

Clinical and angiographic outcomes of 80 study patients at 6 months follow-up are presented in Table 3. No death was observed. Three patients had chronic stable angina with positive stress test at moderate to high workload. Of 80, seven patients presented with angiographic restenosis. The late lumen loss was 0.66 mm between post PCI minimal lumen diameter (2.94±0.26) and 6 months follow-up minimal lumen diameter (2.28±0.26 mm).

Table 1: Baseline demographics, clinical and angiographic characteristics.

Characteristics	Total (N= 114 patients)
Age (mean ± SD, years)	51.56±10.18
Male, n (%)	102 (89.5%)
History of MI, n (%)	58 (50.9%)
Risk factors, n (%)	
Diabetes	31 (27.2%)
Hypertension	40 (35.1%)
Hyperlipidemia	26 (22.8%)
Smoking	38 (33.3%)
Clinical presentation, n (%)	
Chronic stable angina	12 (10.5%)
Acute coronary syndrome	102 (89.5%)
Unstable angina	64 (62.7%)
STEMI	26 (25.5%)
NSTEMI	12 (11.8%)
Target coronary artery, n (%)	
Left circumflex artery	12 (9.6%)
Left main coronary artery	3 (2.4%)
Right coronary artery	20 (16%)
Left anterior descending artery	89 (71.2%)
Saphenous vein grafts	1 (0.8%)
ACC/AHA lesion classification, n (%)	
Type A	33 (26.4%)
Type B	83 (66.4%)
Type C	9 (7.2%)
GP IIb/IIIa inhibitors, n (%)	
Abciximab	2 (1.8%)
Eptifibatide	2 (1.8%)
Tirofiban	8 (7%)
Percentage stenosis (mean ± SD, %)	89.32±7.47
Reference vessel diameter (mean ± SD, mm)	2.91±0.34
Lesion length (mean ± SD, mm)	16.17±5.78
Stent diameter (mean ± SD, mm)	2.91±0.34
Stent length (mean ± SD, mm)	18.91±5.92
Stent diameter, n	
≤ 2.5 mm	12 (9.2%)
2.7-3 mm	93 (71.5%)
> 3 mm	25 (19.2%)
Stent length, n	
< 15 mm	36 (27.7%)
15-20 mm	86 (66.2%)
> 20 mm	8 (6.2%)
Stents used, n	
Endeavour (zotarolimus)	66 (50.8%)
Cypher (sirolimus)	50 (38.5%)
Taxus (paclitaxel)	8 (6.2%)
Infinnium (paclitaxel)	6 (4.6%)

§ MI-myocardial infarction; STEMI-ST-elevation myocardial infarction; NSTEMI-non-ST-elevation myocardial infarction; ACC/AHA-American college of cardiology/American heart association; GP-glycoprotein; SD-standard deviation

Comparison of characteristics between patients with and without angiographic restenosis are demonstrated in Table 4. There were no significant differences in demographics, clinical and angiographic parameters, except for diabetes ($p<0.012$), hyperlipidaemia ($p<0.028$), and stent length >20 mm ($p<0.05$).

Table 2: In-hospital outcomes.

Parameters	Total (N= 114 patients)
Death, n (%)	0
Acute stent thrombosis, n (%)	0
Emergent CABG, n (%)	0
Acute MI post-PCI, n (%)	0
Procedural success, n (%)	114 (100%)
Major bleeding, n (%)	0
Minor bleeding, n (%)	1 (0.9%)

§ CABG-Coronary artery bypass graft surgery; MI-myocardial infarction; PCI-percutaneous coronary intervention

Table 3: Clinical and angiographic outcomes at 6 months follow-up.

Outcomes	Total (N= 80 patients)
Major adverse cardiovascular events, n (%)	8 (10%)
Death, n (%)	0
Myocardial infarction, n (%)	1 (1.3%)
Unstable angina, n (%)	2 (2.5%)
Stable angina, n (%)	3 (3.8%)
Repeat PCI, n (%)	1 (1.3%)
CABG, n (%)	1 (1.3%)
Angiographic restenosis, n (%)	7 (8.8%)

§ PCI-percutaneous coronary intervention; CABG-Coronary artery bypass graft surgery

Table 4: Comparison of characteristics between patients with and without angiographic restenosis.

Characteristics	Patients with angiographic restenosis (n=7)	Patients without angiographic restenosis (n=73)	p value
Age	46.85	51.33	p>0.05
Male	7	67	p>0.05
Female	0	6	p>0.05
Risk factors			
Diabetes mellitus	5	17	p<0.012
Hypertension	3	26	p>0.05
Hyperlipidemia	4	24	p<0.028
Smoking	1	25	p>0.05
Clinical presentation			
Chronic stable angina	2	7	p>0.05
Acute coronary syndrome			
Unstable angina	3	43	p>0.05
STEMI	2	13	p>0.05
NSTEMI	0	10	p>0.05
Target coronary artery			
Left main coronary artery	0	3	p>0.05
Left anterior descending artery	4	52	p>0.05
Left circumflex artery	2	8	p>0.05
Diagonal	1	2	p>0.05
Right coronary artery	0	15	p>0.05
Saphenous vein grafts	0	2	p>0.05
ACC/AHA lesion classification			
Type A	2	20	p>0.05
Type B	5	53	p>0.05
Type C	0	9	p>0.05
Stent diameter			

Continued.

Characteristics	Patients with angiographic restenosis (n=7)	Patients without angiographic restenosis (n=73)	p value
≤ 2.5 mm or less	1	11	p>0.05
2.7-3 mm	5	60	p>0.05
> 3 mm	1	11	p>0.05
Stent length			
< 15 mm	2	17	p>0.05
15-20 mm	3	58	p>0.05
> 20 mm	2	7	p<0.05

§ STEMI-ST-elevation myocardial infarction; NSTEMI-non-ST-elevation myocardial infarction; ACC/AHA-American college of cardiology/American heart association

DISCUSSION

The introduction of coronary stenting became a remarkable landmark in the history of interventional cardiology worldwide.[2] The coronary stents remarkably decreased the occurrence of abrupt vessel occlusion after dissection and restenosis in comparison to POBA.[7,8] However, bare metal stents (BMS) raised the iatrogenic problem of acute stent thrombosis, while restenosis due to excessive neointimal formation still remains a cause for concern in up to 30–40% of cases.[21, 22]

Interestingly, DES were engineered specifically to provide local, site-specific, controlled release of antiproliferative drugs that can reduce the neointimal proliferation, thus resulting in lower rates of in-stent restenosis.[23] The success of initial large randomized controlled trials comparing both sirolimus and paclitaxel DES with BMS demonstrated the superiority of DES over BMS.[17,18] However, the initial enthusiasm was tempered following clinical reports of stent thrombosis in DES.[19,20] Concomitantly, autopsy studies indicate that vascular healing after DES is associated with delayed endothelialization, chronic inflammation, and neoatherosclerosis.[24,25] These drawbacks affiliated with DES have raised concerns regarding their safety.

The present study showed promising results of DES in Indian patients. This finding was associated with an improved outcome of low adverse clinical and angiographic events at 30-day follow-up. In our study, procedural success was achieved in all patients, and no cases of death, emergent CABG, acute stent thrombosis, acute MI post-PCI, and major bleeding were reported during hospitalization. At 6 months, the present study demonstrated 7.5% composite clinical events, comprising 1.3% MI, 2.5% unstable angina, 3.8% stable angina, 1.3% repeat PCI, and 1.3% CABG. The composite clinical events can be attributable to high-risk patients with complex lesion characteristics in our study (40% hypertensive patients, 31% diabetic patients, and 83% type B lesions).

In our study, we examined the 6-month angiographic restenosis rate after PCI for patients with coronary artery disease. Six-month angiographic follow-up was conducted in 70.2% (80/114) of cases, and the restenosis rate was 8.8% (7/80). Identification of predictors of 6-month angiographic restenosis by chi-square analysis revealed a significant association of angiographic restenosis in patients with diabetes mellitus and hyperlipidaemia, and >20 mm stents.

The study has certain limitations inherent to its design. First, this was a non-randomized study, bias in the selection of drug eluting stents could have affected the results. Second, this was a single-centre study with a small sample size, so our results may not be extrapolated to general population. Third, this also represents 6-month follow-up results; thus, in the future, further studies with long-term follow-up are warranted.

CONCLUSION

Herein, we demonstrate a favourable performance of DES in Indian patients, with low MACE rate and angiographic restenosis at 6-month follow-up.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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