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MID-TERM CLINICAL OUTCOMES OF ZOTAROLIMUS-ELUTING STENT IN PATIENTS WITH STABLE ANGINA PECTORIS

Yasir Adnan[1], Shahab Ud Din[2], Lubna Noor[3], Farooq Ahmad[4], Syed Tahir Shah[5], Adnan Mahmood Gul[6], Mohammad Hafizullah[7]

[1,3-7]Lady Reading Hospital & Khyber Medical University, Peshawar - Pakistan

[2]Medical A unit, Ayub Teaching Hospital, Abbottabad"

Address for Correspondence:
Dr. Yasir Adnan,
Department of Cardiology,
Lady Reading Hospital, Peshawar-Pakistan

E-mail:
yasiradnan1982@hotmail.com

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ABSTRACT

Objectives: The study was designed to evaluate the safety and effectiveness of the Endeavor zotarolimus-eluting stent (ZES) for the treatment of stable coronary artery disease.

Methodology: This was a cross sectional descriptive study. Patients who were admitted to Cardiology Unit of Lady Reading Hospital, Peshawar, through OPD or casualty department, fulfilling the inclusion criteria were enrolled in the study. This study included all the patients with stable coronary artery disease who had received Endeavor stents from January 2010, to March 2011. Total study duration was 15 months. The primary end point was the rate of major adverse cardiac events (MACE) at 12 months. All patients who underwent PCI with Endeavor stent implant for stable angina pectoris were followed up and reassessed after 12 months from the index procedure.

Results: A total of 128 patients were included in the study. Mean age was 54 ±2.4years. Male were 91 (71.1 %) while females were 37 (28.9). Of these 49.2% were hypertensive, 28.9% diabetic, 19.5% smokers, and 39.8% dyslipidemics. Overall 12-month outcome rates were: MACE 5.5%; cardiac death 0.8%; STEMI 0.8%; NSTEMI 1.6% and revascularization 2.3%.

Conclusion: This study provides important information regarding the mid-term safety and efficacy of the Endeavor zotarolimus-eluting stent. Frequency of clinical outcomes including cardiac death, myocardial infarction, and revascularization were low and consistent with pooled results of other major trials.

Key Words: Coronary artery disease, Drug eluting stents, Myocardial infarction, Unstable angina, Stable angina.

INTRODUCTION

Results from multiple randomized trials have demonstrated that drug-eluting stents (DES) significantly reduce rates of restenosis and target lesion revascularization (TLR) in patients with symptomatic coronary artery disease when compared with bare-metal stents (BMS).[1-4] Although concerns have been raised about the safety of DES due to apparent increases in late stent thrombosis, the clinical benefits seem to outweigh the risks.[5]

First-generation drug-eluting stents have reduced angiographic and clinical restenosis, but long-term safety remains controversial. A second-generation drug-eluting stent, which delivers zotarolimus, a potent antiproliferative agent, has shown promising experimental and early clinical results.[6-9] Recent data on endothelial function after stent placement in porcine coronaries showed a normally functioning endothelium 1 and 3 months after zotarolimus-eluting stent implantation, whereas a dysfunctional endothelium was observed after both Cypher and Taxus implantation.[10]

In the ENDEAVOR I and II trials, the phosphorylcholine polymer-based cobalt-alloy Driver coronary stent (Medtronic Vascular, Santa Rosa, Calif), loaded with zotarolimus, proved to be superior to BMS in both angiographic and clinical end points.[4,11]

The ENDEAVOR III trial was a prospective randomized comparison of the Endeavor zotarolimus-eluting stent and the Sirolimus-eluting stents. At 8 months, the Endeavor stent failed to meet its non-inferiority end point in terms of late lumen loss. Of note, the rates of death, myocardial infarction, and target vessel revascularization were equal in both groups.[12] A possible explanation for the lack of non-inferiority of the Endeavor stent might be the rate of elution. The Cypher stent elutes 75% of its drug within the first 10 days; in the Endeavor stent this took only 2 days.[13] Therefore, we took up this study with the aim to know the frequency of mid-term clinical outcomes of Zotarolimus Eluting Stents in patients with stable angina pectoris, as seen in our daily real-world practice.

METHODOLOGY

This was a cross sectional descriptive, non-randomized open label study based on our real-world clinical practice. It involved a single centre but multiple operators. Patients who were admitted to the Cardiology Unit of Lady Reading Hospital, Peshawar through OPD or casualty department meeting the inclusion criteria were included in the study. Written informed consent was obtained from all patients. Our study included all the patients with stable coronary artery disease who had received Endeavor stents from January 1, 2010, to March 31, 2011. The total study duration was 15 months.

All patients of stable angina pectoris of any age and gender who were treated with Zotarolimus Eluting Stents irrespective of the lesion length were included in the study. Patients with previous history of revascularization whether percutaneous coronary intervention or Coronary artery bypass graft and primary percutaneous coronary intervention were excluded from the study. Patients with Left main stem disease or triple vessel disease on coronary angiography were also excluded from the study.

The primary end point was the frequency of major adverse cardiac events (MACE) at 12 months, which included cardiac death, STEMI, NSTEMI, and revascularization in the form of PCI or CABG. All patients who underwent PCI with an Endeavor stent implant for stable angina pectoris were called for follow-up after 12 months from the index procedure, and reassessed. History was taken regarding the occurrence of unstable angina, myocardial infarction and hospitalization for any of these events over the last 12 months. Data analysis was done using SPSS version 16. Mean $\pm$ standard deviation was calculated for continuous variables like age, stent length and stent diameter. Frequency and Percentages were calculated for categorical variables like gender, vessels stented, unstable angina, revascularization, death and myocardial infarction. Mid-term clinical outcomes were stratified among the length of stent, stent diameter, vessel stented, age and gender to see the effect.

RESULTS

A total of 128 patients were included in the study. Mean age was 54$\pm$9.27 years. Male were 91 (71.1 %) while females were 37 (28.9%). Of these, 49.2% were hypertensive patients, 28.9% were diabetic, and 19.5% were having a positive smoking history. About 39.8% were having hyperlipidemia (Table 1). The angiographic characteristics of the study patients are shown in Table 2.

Major adverse cardiac events included composite of death, STEMI, NSTEMI, and revascularization. At 12 months overall MACE were 5.5%. As shown in Table 3, out of a total of 128 patients, one patient died during 12 months follow up. Two patients suffered from non ST-elevation myocardial infarction and only one patient suffered from ST-elevation myocardial infarction. Three patients underwent revascularization in the form of PCI. When the 12 months clinical outcomes were stratified among male and female patients, the event rate for the individual outcome of STEMI and death was higher in female patients (2.7%) as compared to male patients (0%). However, the event rate of NSTEMI was slightly lower in the male group 1.1%% versus female group 2.7%%. Frequency of revascularization was higher in male patients (3.29%) as compared to female patients (0%), as shown in Table 3.

Table: 1 Patients Characteristics and Demographic Data

Variables	Overall (n=128)
Age (years)	54±9.27
Male	71.1 %(91)
Diabetes	28.9% (37)
Hypertension	49.2% (63)
Hyperlipidemia	39.8% (51)
History of smoking	19.5% (25)

Table 2: Angiographic characteristics

Target vessel	Percentage % (n)
Left anterior descending	58.6% (75)
Left circumflex	31.2% (40)
Right coronary	10.2% (13)
Number of diseased, native, major epicardial coronary vessels (50% stenosed)	
Single	60.93% (78)
Double	39.05% (50)

Table 3: MACE at 12 months

Variables	Overall (n=128)	Male (n=91)	Female (n=37)
Death	0.8% (1)	0% (0)	2.7% (1)
STEMI	0.8% (1)	0% (0)	2.7% (1)
NSTEMI	1.6% (2)	1.1%(1)	2.7% (1)
Revascularization	2.3% (3)	3.29%(3)	0%(0)

DISCUSSION

Before the availability of DES, the major limitation of PCI was restenosis, which necessitated repeat intervention in 20% to 30% of cases after BMS implantation.[14] In contrast, currently approved DES are notable for much lower rates of clinical and angiographic restenosis in the mostly non-complex lesion types enrolled in the pivotal randomized trials and, as a result, DES have been widely adopted for the majority of patients undergoing PCI. With the passage of time, we have come to realize that the undoubted efficacy of first-generation DES in preventing coronary restenosis has been achieved at the expense of a delay in healing of the stented arterial segment. Although multifactorial in origin, pathological and pre-clinical research data strongly implicate polymer residue as a key etiological factor.[15,16] This concern has focused attention on the development of newer DES providing high anti-restenotic efficacy with lesser impact on arterial healing. The second-generation Endeavor ZES has attempted to address the issue of impaired vascular healing by utilizing a thin-strut (91-_m) cobalt chromium backbone—which causes less acute arterial injury—and an enhanced biocompatibility polymer system—which is hypothesized to reduce medium- to long-term inflammatory response.

Our report describes 12-months frequency data of clinical outcomes of the Endeavor ZES. These results, obtained from 128 patients, provide compelling evidence for the safe and effective use of the Endeavor ZES in patients with stable angina. The results are similar to those reported in randomized clinical trials in the past. All reported events were adjudicated. The overall 12-month MACE rate was 5.5%. The MACE included cardiac death which was 0.8%,

STEMI which was 0.8%, NSTEMI which was 1.60% and revascularization in the form of PCI which was 2.30%. The rates were slightly lower in our study as compared to the previous randomized trials.[4,17,18] However, it is worth noting that in our study we excluded patients with TVD and those with complex lesions which might be the reason for slightly better outcomes. Overall outcomes reported for the sirolimus-eluting stent (SES) and paclitaxel-eluting stent (PES) in recent registry reports suggest that the Endeavor ZES performs similarly as the other DES.[19,20] The overall rate of MACE at 12 months was reported to be 5.8% for the SES in the e-Cypher registry[21] and at 9 months was 8.0% and 7.5% for the SES and PES groups, respectively, in the STENT registry report.[22] The REWARDS registry, which compared outcomes with everolimus-eluting stent and PES placement in over 2,700 consecutive patients treated at a single site, reported no difference in the rate of MACE at 12 months (hazard ratio: 1.06, 95% confidence interval: 0.85 to 1.33), although the actual rates were not reported.[23]

We also found that the rate of clinical outcomes were slightly lower in male as compared to female patients except for revascularization which was more in male patients. Clinical outcome of women after PCI has been challenging. Historically, female gender has been associated with increased complications during and after PCI.[24,25] Women undergoing PCI usually present with more comorbid conditions, including hypertension, older age, elevated cholesterol, more complex and diffuse coronary disease, and longer referral time as compared to men.[26,27] This makes the comparison between men and women nearly impossible. However, with the significant improvements in angioplasty techniques, the introduction of drug-eluting stents (DES), and the availability of small-size stents, the previously noted gender gap in outcomes is expected to narrow down in near future.

LIMITATIONS

An important limitation of this study is the potential of under-reporting of adverse events. The patient inclusion criteria for this study IS somewhat restrictive. Thus, the reported findings can only be applied to the patients with stable angina with SVD or DVD. Another limitation of this study is the subjective nature of the lesion length data, which were reported by visual estimation or by local quantitative angiographic methods. Another limitation is the lack of information about the duration of clopidogrel treatment in individual patients.

CONCLUSIONS

Mid-term follow-up results from our study show that ZES Endeavor is safe and effective. The 12-months frequency of MACE was comparable to other major clinical trials of ZES in reducing cardiac death, MI and revascularization.

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