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Original Article

Comparison of Bare metal Vs Drug eluting stents for in-stent Restenosis among Diabetics

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ABSTRACT:
Background: Diabetes mellitus is associated with an increased risk of restenosis, stent thrombosis, and death after percutaneous coronary interventions. Little is known about the late outcome of patients with diabetes mellitus who receive drug-eluting stents (DES) or bare metal stents (BMS).
Methods: From January 2008 to January 2010, six patients with DES and 20 with BMS, ISR were identified at our institution.
Results: The median age of our diabetic cohort was 63 years, and 87 of the patients were male. For two years, rates of repeat target-vessel revascularization were significantly lower among diabetic patients treated with DES compared with those treated with BMS (5.8% vs. 17.0%, p=0.003).
Conclusions: DES is effective among diabetic patients in substantially reducing the need for repeat TVR.

Keywords: Diabetics; Bare metal stents (BMS); Drug eluting stents (DES); In-stent restenosis (ISR); Target Vessel Revascularization (TVR).

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1. INTRODUCTION

Cardiovascular disease is a major cause of morbidity and mortality among patients with diabetes (1, 2). It is currently estimated that 25 to 30 percent of all percutaneous coronary interventions (PCI) are performed among patients with diabetes (3, 4). Although ISR was once a feared consequence of PCI among diabetic patients, recent studies have demonstrated DES to be highly effective in reducing restenosis and thereby minimizing the need for future coronary revascularization (5-9). Several trials are underway to evaluate whether PCI with DES would be superior to coronary bypass grafting surgery among diabetic patients with multivessel coronary artery disease (10). Recently, the enthusiasm for DES has been dampened by some data showing higher rates of late-stent thrombosis and possibly higher rates of myocardial infarction and death (11, 12). Although our group has demonstrated the safety of DES in a large population-based cohort, the safety of diabetic patients was not assessed specifically (13). Indeed, the safety concerns of DES are perhaps even greater among diabetic patients with a recent study showing a three-fold increase in the hazard of death compared with BMS (14). However, several limitations of the study led the authors to urge cautious interpretation of their findings (14).

Addressing this important gap in knowledge could have a substantial impact on the choice of coronary revascularization for diabetic patients with

coronary artery disease. Accordingly, the main objective of our study was to evaluate the long-term safety and effectiveness of diabetic patients who received DES and BMS using a population-based PCI in Tbilisi, Georgia.

2. MATERIAL AND METHODS

Between January 2008 and January 2010, 113 patients with acute coronary syndrome underwent PCI, with either a BMS or DES implantation (sirolimus or paclitaxel) in native coronary arteries at our center. All patients were asked to return for follow-up angiography at six months after the procedure. Diabetes was defined as active treatment with insulin or an oral antidiabetic agent or if the patient had an abnormal blood glucose level after an overnight fasting or abnormal glucose tolerance test results according to the WHO criteria (15).

Data Sources: The Cardiological Clinic "GULI" maintains a medical record section, hence prospective clinical data was collected with the help of the medical record section for relevant data collection when needed. This study was approved by the board at Cardiological Clinic "GULI."

Study Sample: We initially identified a cohort who received PCI with either DES or BMS in Cardiological Clinic "GULI" from January 1, 2008, to January 31, 2010. This time frame was chosen to allow adequate follow-up to examine the long-term outcomes of DES and BMS. We excluded patients without diabetes, who had stenting of the left main artery, and patients who had PCI within the past year (possibly indicative of ISR) because these patients were likely to have received a DES, and thus, it would be difficult to identify a suitably matched BMS patient. We also excluded patients who had placement of both BMS and DES during PCI.

Outcomes: TVR due to in-stent restenosis was defined as repeat PCI with new stent placement in the same vessel, repeat PCI without stent, or subsequent coronary artery bypass graft surgery or subsequent repeat angina.

Statistical Analysis: We compared the demographics and clinical and procedure characteristics between the DES and BMS groups stratified by diabetes status using student tests for continuous variables, and Microsoft Excel 2007 was utilized for the graphic representations and graphs. All analyses were performed using Microsoft Excel 2007. A P value $< .05$ was considered to indicate statistical significance.

Intervention and Adjunct Drug Therapy: All patients received a loading dose of 300 mg of clopidogrel at least two hours before undergoing coronary angiography (16). The same type of DES was implanted if the patient needed >1 stent. Aspirin and unfractionated heparin were administered according to standard practice. After the intervention, the patients received aspirin 200 mg indefinitely and clopidogrel 150 mg for the first three days and 75 mg for ≥ six months. BMS patients received aspirin 200 mg and Clopidogrel 150mg indefinitely. Follow-up Evaluation: Baseline, post-procedural, and follow-up coronary angiograms or exercise stress test by experienced interventionists. Measurements were performed on cineangiogram recorded after the intracoronary administration of nitroglycerin. Binary angiographic restenosis was defined as a diameter stenosis ≥50 percent at angiographic follow-up at six months measured at any point within the stented segment or in the 5-mm proximal or distal segments adjacent to the stent or positive exercise stress test with significant angina.

Study End Points and Follow-Up Criteria: Target lesion revascularization (clinical restenosis), clinical angina symptoms and mortality at two years of follow-up were the primary end points of the study. Binary angiographic restenosis, stent thrombosis, and the composite of death or myocardial infarction were selected as the secondary end points. Adverse cardiac events were monitored throughout the follow-up period by a telephone interview at 30 days, a clinical visit at six to eight months, and telephone interviews at one-year intervals after procedure. If patients reported cardiac symptoms during the telephone interview, at least one clinical, exercise stress test and electrocardiographic follow-up visit was performed at the outpatient clinic. Relevant data were collected and entered into a computer database. The criteria for target lesion revascularization included the presence of angiographic restenosis accompanied by symptoms and/or positive exercise test results.

3. RESULTS

Baseline Patient Characteristics: The median age was 63 ± 10 years, 77% were male. Procedural Characteristics: DES were used in 25.66% of cases, BMS were used in 74.33% of cases, and the mean stent length per case was 18.99 mm and a mean stent diameter of 3.05 mm. Clinical Characteristics: The mean time from PCI to follow up was six, 12, and 18 months. 76.99% were asymptomatic and 23.01% presented with angina pectoris. The overall incidence of angiographic stent thrombosis in the 113 patients was 23%. The 76.99% asymptomatic patients underwent coronary angiography because ischemia was detected on stress testing. Out of the 23.01% patients who presented with angina pectoris, 31 patients underwent repeat PCI.

Definition and classification: ISR was defined as >50% diameter stenosis (DS) by quantitative coronary angiography (QCA) within a previously (at least four months) stented vessel segment. ISR was classified as focal (<10 mm long), diffuse (>10 mm long), proliferative (>10 mm long and extending outside the stent edges), or totally occluded. The pathophysiology of restenosis involves a complex cascade of the effects of various growth factors and cytokines, each of which contributes to the progressive loss of luminal diameter due to smooth muscle cell proliferation.

4. DISCUSSIONS

Our study evaluated the long-term safety and efficacy of diabetic patients treated with DES and BMS using a small population-based PCI. We found that DES was highly efficacious among diabetic patients in reducing the need for TVR.

Previous studies evaluating the risk of diabetic patients treated with DES and BMS have been mixed, with some studies showing similar safety between DES and BMS and others showing higher risk of adverse outcomes associated with DES (17-20). Most of these studies, however, have limited power to detect a difference in outcomes because relatively few events were observed at follow-up. It is noteworthy that patients in Ontario ≥65 years old are eligible to receive a one-year supply of clopidogrel after DES placement and most of the younger patients have private insurance coverage for prescribed medications (21).

We urge caution in interpreting these findings because randomized studies have not shown a mortality benefit (22-24). With regard to the efficacy of DES among diabetic patients, we found that future TVR was reduced by approximately one half compared with BMS. Furthermore, the absolute rate reduction in TVR continued to diverge in our study period favoring diabetic patients treated with DES. One of the reasons for the discrepancy in TVR rates between clinical trials and registry data may relate to the performance of routine angiographic follow-up in clinical trials that may have overestimated the true absolute benefits of DES relative to BMS (25). Because the impact of any therapy in the population is dependent on baseline risk, decisions regarding the type stent placement should incorporate the anticipated risk of TVR (26, 28).

Limitations of study: Stent thrombosis is currently defined by the Academic Research Consortium to require the presence of an acute coronary syndrome with angiographic or autopsy evidence of thrombus or occlusion (29). Because this information was not available from our databases, we used myocardial infarction after PCI and exercise stress test as a measurement of safety. This liberal definition for safety assessment would tend to introduce a large number of events and tend to diminish the ability to find significant differences between DES and BMS.

5. CONCLUSION

Diabetic patients treated with DES have lower risk of future need for TVR. The overall rates of angina did not differ significantly between DES and BMS-treated patients. Most importantly, our data suggest diabetic patients treated with DES are at decreased risk ISR compared to diabetic patients treated with BMS. New and better strategies for improving clinical and angiographic outcomes following PCI with DES in diabetic patients are required. Drug-eluting stents with improved designs or drug elution systems that further decrease the incidence of ISR are needed.

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