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Research Paper

Efficacy of Sirolimus-Eluting Stents Compared With Paclitaxel-Eluting Stents in an Unselected Population With Coronary Artery Disease: 24-Month Outcomes of Patients in a Prospective Non-randomized Registry in Southern Turkey

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Abstract

Background: The efficacy of drug-eluting stents has been shown in randomized trials, but some controversy exists regarding which stent sirolimus-eluting or paclitaxel-eluting is more effective in unselected Turkish patients. Therefore, we investigated the clinical outcomes of patients who were treated with one type of these drug-eluting stents in the real world.

Methods: We created a registry and prospectively analyzed data on a consecutive series of all patients who presented to our institution with symptomatic coronary artery disease between February 2005 and March 2007 and who were treated with the sirolimus- or the paclitaxel-eluting stent. The follow-up period after stent implantation was approximately 24 months. The primary end point was a major cardiac event, and the secondary end point was stent thrombosis. Informed consent was obtained from all subjects, and the study protocol was approved by the local ethical committee.

Results: In total, 204 patients were treated with either the sirolimus-eluting stent (n = 103) or the paclitaxel-eluting stent (n = 101). The lesions in the 2 arms of the study were treated similarly by conventional technique. At 24-month follow-up, patients who received the paclitaxel-eluting stent showed significantly higher rates of non–Q-wave myocardial infarction (1.9% vs 5.9%; *P*: .002), target vessel revascularization (1.9% vs 4.9%; *P*: .002), coronary artery bypass graft surgery (1.9% vs 6.9%; *P*: .001), and late stent thrombosis (1.9% vs 3.9%, *P*: .002).

Conclusions: Patients who received the sirolimus-eluting stent showed better clinical outcomes compared with those who had the paclitaxel-eluting-stent.

Key words: coronary artery disease, drug-eluting stent, major adverse cardiac event, stent thrombosis.

INTRODUCTION

Because of their association with decreased incidents of restenosis and repeat intervention, the sirolimus-eluting stent (SES)[1] and the paclitaxel-eluting stent (PES)[2] have been shown to be superior to the bare-metal stent. Along with the accumulation of clinical experiences, drug-eluting stents increasingly have been used for more complex lesions involving the left main coronary artery,[3] in-stent restenosis,[4]

chronic total occlusion,[5] and acute myocardial infarction.[6] Although several head-to-head analyses of the SES and the PES have been published in the medical literature, uncertainty remains regarding whether a true difference in clinical outcomes exists. The randomized, multicenter REALITY trial[7] did not demonstrate a difference in clinical outcomes between patients who received the SES and those who received the PES. This finding has been supported by large registries.[8,9] In contrast, a number of smaller randomized studies have shown differences in end points, confirmed both angiographically and clinically, in favor of the SES.[10-13] Furthermore, in meta-analyses of studies comparing the 2 stent types, authors have confirmed a clinical advantage for those who receive the SES.[14–17] However, the long-term safety of drug-eluting stents has been questioned.[17-19] Despite the results of meta-analyses of randomized studies that refute these concerns,[20] the possible association of the stents with late stent thrombosis remains a limitation of this new technology. The long-term outcomes of Turkish patients treated with the SES vs the PES in real-world practice are not well reported. Therefore, we report the 24-month outcomes of unselected patients in southern Turkey who had coronary artery disease that was treated with either the SES or the PES.

METHODS

Patient Population

The study population consisted of 204 consecutive series of all patients who had undergone coronary stent implantation for coronary artery disease between February 2005 and March 2007; 103 of the patients received the SES (CYPHER; Cordis Corporation, Johnson and Johnson, Miami Lakes, Florida), and the other 101 patients received the PES (TAXUS, Boston Scientific, Natick, Massachusetts). Patients were eligible for enrollment if there was symptomatic coronary artery disease or positive functional testing, and angiographic evidence of a target lesion stenosis of ≥ 70% in a ≥ 2-mm vessel. Patients with a contraindication to antithrombotic therapy were excluded from the study. The coronary angiograms were obtained when there was evidence of ischemia. The follow-up period was approximately 24 months. Informed consent was obtained from all subjects, and the study protocol was approved by the local ethical committee.

Medications and Percutaneous Coronary Intervention Procedure

All patients were pretreated with aspirin and clopidogrel. A loading dose of 300 mg of clopidogrel was administered before the procedure for those who were not pretreated. During the procedure, a bolus dose of unfractionated heparin (100 U/kg) was injected through a femoral or radial artery sheath, with a bolus repeated as needed to maintain an activated clotting time of 250 to 300 seconds. Patients received intracoronary nitroglycerin (0.1 to 0.2 mg) before initial and final angiograms to achieve maximal vasodilatation. The use of glycoprotein IIb/IIIa inhibitor (Tirofiban) was at the operator's discretion. All patients maintained antiplatelet therapy after the procedure (aspirin 300 mg/d for 3 months, then 100 mg/d infinitely; clopidogrel 75 mg/d for 6 to 12 months). The percutaneous coronary intervention procedure and stent implantation were performed using standard methods, through a femoral or radial approach. The operators were free to use the stent approach and the stent (ie, SES or PES) that they considered better.

Study End Points and Definitions

The primary clinical end points were major adverse cardiac events (MACE), including cardiac death, myocardial infarction (MI), and target vessel revascularization (TVR). MI was defined as the elevation of creatine kinase (CK) > 2 times above the upper limit of normal with any associated elevation in the CK myocardial band or the development of new pathologic Q waves in 2 contiguous electrocardiographic leads. TVR was defined as either percutaneous or surgical revascularization (CABG) of the stented epicardial vessel. The secondary end point was stent thrombosis (ST) (ie, acute, < 1 day; subacute, 1 to 30 days; late, ≥ 30 days; and very late, ≥1 year). For the assigned study stent, device success was defined as ≤ 50% diameter stenosis of the target lesion, and procedure success was defined as device success with no in-hospital MACE. The definitions of MI and ST used in this study were consistent with the newest consensus of the Academic Research Consortium.[21] All primary and secondary clinical end points were adjudicated by an independent clinical events committee blinded to the patient's treatment assignment.

Follow-up

Clinical follow-up was performed at 1, 6, 12, and 24 months by telephone contact or office visit. Relevant data were collected and entered into a computerized database by specialized personnel at the cardiovascular interventional heart center.

Statistical Analysis

All statistical analyses were performed with SPSS for Windows (version 10.0, Chicago, USA). Continuous variables were described as mean (SD),

and categorical variables were reported as percentages or proportions. Comparison of continuous variables was performed with unpaired *t* tests (normal distribution) and the nonparametric Mann-Whitney test (skew distribution). Analysis of categorical variables was made with Fisher's exact test and χ^2 test. We used Kaplan-Meier time-to-event estimates for the primary events at 24-month follow-up. With the Kaplan-Meier method and log-rank test, we compared the difference between the SES and PES cohorts. A *P* value < 0.05 was considered statistically significant.

RESULTS

Baseline clinical, angiographic, and lesion characteristics are shown in Tables 1 and 2. The baseline clinical or demographic characteristics indicated no statistically significant differences between patients who received the SES vs those who received the PES. Baseline angiographic characteristics were also similar according to the modified ACC/AHA (American College of Cardiology/American Heart Association) classification.[22] Overall, most lesions were located in the left anterior descending artery and were types B1 or C. The mean stent diameter was 30 (SD, 4) mm among those who received the SES and 31 (SD, 5) mm (*P*:.4) among those who received the PES (Table 2). The mean stent length was 26 (SD, 7) mm in the SES cohort and 28 (SD, 8) mm (*P*:0.3) in the PES cohort.

In-Hospital Outcomes

In-hospital outcomes were similar between the 2 cohorts. In-hospital incidence of MACE was 1.9% for patients receiving the SES and 1.9% in patients receiving the PES (*P*: .8).

Long-term Clinical Outcomes

Complete clinical follow-up at 24 months was accomplished for 199 patients. The outcomes are reported in Table 3. At 24 months, the incidence of MACE was 9.7% in the SES cohort and 17.8% in the PES cohort (*P*:.04). The incidence of coronary artery bypass graft procedures (1.9% vs 6.9%; *P*:.001), TVR (1.9% vs 4.9%; *P*: .002), and non–Q-wave MI (1.9% vs 5.9%; *P*:.002) was significantly higher in the PES cohort. There were no major differences in the rates of death (1.9% vs 0.9%; *P*: .307), Q-wave MI (3.8% vs 5.9%; *P*: .326), and non–TVR (1.9% vs 3.9%; *P*: .3). As reported in Table 4, the incidence of late ST at 24 months was significantly higher in the PES cohort (1.9% vs 3.9%; *P*:.002). Between the SES and PES cohorts, no major differences existed in the incidence of acute (0.9% vs 0.9%; *P*:1.1) and subacute (0.9% vs 3.9%; *P*:.08) ST.

Table 1. Age and Baseline Clinical Characteristics of Patients by Treatment Cohort

Characteristic	Sirolimus[a] (n = 103)	Paclitaxel[b] (n = 101)	*P* Value[c]
Age, mean (SD), y[c]	57 (10.9)	58 (10.2)	.9
History, No. (%)			
Diabetes mellitus	40 (39)	36 (36)	.5
Hypertension	62 (60)	64 (63)	.5
History of smoking	72 (70)	55 (54)	.08
Hyperlipidemia	67 (65)	69 (68)	.8
Prior MI	11 (11)	7 (7)	.1
Prior PTCA	9 (9)	6 (6)	.6
Prior CABG	8 (8)	3 (3)	.2
SAP	29 (28)	34 (34)	.2
USAP	59 (57)	47 (47)	.08
MI	15 (15)	20 (20)	.3
Serum concentrations, mean (SD), mg/dL			
Total cholesterol	214.5 (63.6)	233.8 (57.4)	.7
LDL	145.5 (52.3)	150.3 (48.4)	.5
HDL	38.4 (6.2)	39.4 (8.3)	.7
Triglyceride	161.1 (95.4)	158.6 (101.2)	.6
Glucose	141.3 (67.3)	114.7 (46.4)	.06

Abbreviations: CABG, coronary artery bypass graft; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MI, myocardial infarction; SAP, stable angina pectoris; USAP, unstable angina pectoris.

[a]Indicates patients who received sirolimus-eluting stents. Numbers in the column do not total 100% because some patients had more than one condition.

[b]Indicates patients who received paclitaxel-eluting stents. Numbers in the column do not total 100% because some patients had more than one condition.

[c]*P* < 0.05 defined as statistically significant.

Table 2. Baseline Angiographic Characteristics

Characteristic	Sirolimus[a] (n = 103)	Paclitaxel[b] (n = 101)	*P* Value[c]
Site of Lesion Treated, No. (%)			
LAD	74 (72)	76 (75)	.7
Cx	12 (12)	9 (9)	.5
RCA	17 (17)	16 (16)	.9
LVEF[d,e]	68.3 (6.1)	67.4 (7.3)	.9
Stent diameter, mm[e]	30 (4)	31 (5)	.4
Stent length, mm[e]	26 (7)	28 (8)	.3
Lesion length, mm[e]	21 (6)	22 (7)	.4
Type of lesion, No. (%)			
A	0 (0)	2 (1.9)	.3
B1	46 (45)	47 (47)	.9
B2	15 (14)	11 (11)	.6
C	42 (41)	41 (41)	.8

Abbreviations: Cx, left circumflex coronary artery; LAD, left anterior descending coronary artery; LVEF, left ventricular ejection fraction; RCA, right coronary artery.

[a]Indicates patients who received sirolimus-eluting stents.

[b]Indicates patients who received paclitaxel-eluting stents.

[c]$P < 0.05$ defined as statistically significant.

[d]Reported as percentage.

[e]Data expressed as mean (SD).

Table 3. Clinical Outcomes at 24-Month Follow-up

Outcome	Sirolimus[a] [No. (%)]	Paclitaxel[b] [No. (%)]	*P* Value[c]
MACE	10 (9.7)[d]	18 (17.8)	**.04**
Death	2 (1.9)	1 (0.9)	.307
Myocardial infarction			
Q-wave	4 (3.8)	6 (5.9)	.326
Non–Q-wave	2 (1.9)	6 (5.9)	**.002**
Revascularization			
Target vessel	2 (1.9)	5 (4.9)	**.002**
Non–target vessel	2 (1.9)	4 (3.9)	.3
CABG surgery	2 (1.9)	7 (6.9)	**.001**

Abbreviations: CABG, Coronary artery bypass graft; MACE, Major adverse cardiac event (ie, death, myocardial infarction, and target vessel revascularization.

[a]Indicates patients who received sirolimus-eluting stents. Percentages in this column are based on a cohort of 103 patients.

[b]Indicates patients who received paclitaxel-eluting stents. Percentages in this column are based on a cohort of 101 patients.

[c]$P < 0.05$ defined as statistically significant.

Table 4. Comparison of Secondary End Points by Cohort

Type of Stent Thrombosis	Sirolimus[a] [No. (%)]	Paclitaxel[b] [No. (%)]	P Value[c]
Acute	1 (0.9)	1 (0.9)	1.1
Subacute	1 (0.9)	4 (3.9)	.08
Late	2 (1.9)	4 (3.9)	**.002**
Very late	0 (0)	1 (0.9)	.09

[a]Indicates patients who received sirolimus-eluting stents. Percentages in this column are based on a cohort of 103 patients.

[b]Indicates patients who received paclitaxel-eluting stents. Percentages in this column are based on a cohort of 101 patients.

[c]$P < 0.05$ defined as statistically significant.

Discussion

The major finding in the present study is that the SES was associated with better long-term safety and efficacy than the PES in unselected Turkish patients with coronary artery disease. However, despite our study and several others in which the SES and the PES have been compared, uncertainty still remains regarding whether any real difference in clinical outcomes exists. Ong and colleagues[8] recently compared the results of 2 registries SES-based RESEARCH (Rapamycin-Eluting Stent Evaluated at Rotterdam Cardiology Hospital) and PES-based T-SEARCH (Taxus-Stent Evaluated at Rotterdam Cardiology Hospital) and showed similar adjusted clinical outcomes for patients who received the PES compared with those who received the SES. The authors suggested that the inferior trend in crude outcome observed for PES recipients in other studies can be attributed to the higher risk profiles of these patients. Two randomized trials comparing the SES and the PES head to head have been published recently.[7,10] Each trial equally showed better angiographic parameters for patients who received the SES vs those who received the PES, but regarding clinical outcomes and binary restenosis rates, they showed controversial results. In the REALITY trial, [7] patients who had MI, ostial lesions, in-stent restenosis, or chronic total occlusion lesions were excluded, and there was no significant difference between the 2 types of stents in clinical outcomes and binary restenosis. However, in the SIRTAX trial,[10] all comers were enrolled and over 9 months, patients treated with the PES showed higher rates of MACE and binary restenosis rates than those treated with the SES. The superiority of the SES over the PES in clinical outcomes resulted mainly from differences in rates of target lesion revascularization; SES use did not decrease death and MI rates. Moreover, meta-analysis results showed that patients receiving the SES had a significantly lower risk of restenosis and TVR compared with those receiving the PES and suggested that SES use may result in better outcomes in relatively complex lesions and high-risk patients.[14]

In our study, no differences existed in baseline clinical and angiographic characteristics between those who received the SES and those who received the PES. The SES was associated with better clinical outcomes compared with the PES; rates of MACE were 9.7% vs 17.8% (*P*:.04). The superiority of the SES over the PES in clinical outcomes resulted mainly from differences in rates of late ST and target lesion revascularization. The incidence of late ST was significantly higher at 24 months for PES recipients. No major differences existed in the incidence of acute and subacute ST between SES recipients and PES recipients. In the PES cohort, the incidence of TVR was significantly higher due to ST. Seven patients in the PES cohort and 4 patients in SES cohort were prematurely taken off klopidogrel therapy, and this change likely played a role in the MACE events observed in the PES and SES cohort. Of those continuing dual antiplatelet therapy, 96% were in the SES cohort, and 93% were in the PES cohort. And the difference between PES and SES groups seems to be associated with much number of patients prematurely taken off klopidogrel in PES group.

PES treatment still was associated with poor overall clinical outcomes compared with outcomes associated with SES treatment. Also, in the multivariate analysis, after adjusting for clinical variables, we found that PES use was a predictor of MACE within 24 months. Given that our patients tend to have high-risk profiles (eg, type C lesions, 41%; type B1 lesions, 45%; mean [SD] lesion length, 21 [6] mm; hypertension, 62%; diabetes mellitus, 37%; hyperlipidemia, 67%; and acute MI, 17%), our results correspond with those of previous randomized studies in which relatively high-risk patients showed better clinical outcomes after SES use.[10, 14, 21]

Study Limitations

The study has several limitations—mainly, the small number of patients, lack of direct randomization, and relatively low compliance with angiographic follow-up.

CONCLUSIONS

On the basis of the clinical results of this 24-month study, one might reasonably conclude that treating with a sirolimus-eluting stent is more effective than treating with a paclitaxel-eluting stent in Turkish patients.

Acknowledgments

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Abbreviations

ACC: American College of Cardiology; AHA: American Heart Association; CABG: coronary artery binding graft; CK: creatine kinase; MACE: major adverse cardiac events; MI: myocardial infarction; PES: paclitaxel-eluting stent; RESEARCH: Rapamycin-Eluting Stent Evaluated at Rotterdam Cardiology Hospital; SES: sirolimus-eluting stent; ST: stent thrombosis; T-SEARCH: Taxus-Stent Evaluated at Rotterdam Cardiology Hospital; TVR: target vessel revascularization.

Conflict of Interest

None declared.

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