Interventional Cardiology

Comparison between Exclusive and Selective Drug-Eluting Stent Strategies in Treating Patients with Multivessel Coronary Artery Disease

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***Background*:** The expanded usage of drug-eluting stents (DES) in treating patients with multivessel coronary artery disease (CAD) may sometimes be limited in real-world practice due to cost concerns. We compared the clinical outcomes of exclusive and selective DES use in treating patients with multivessel CAD.

Methods: From November 2004 to December 2011, 110 patients with multivessel CAD who received four or more stents were enrolled into this study, and divided into two groups according to the DES strategy employed: exclusive DES (n = 52), or selective DES (n = 58). In the selective DES group, DES was reserved for complex lesions only, such that the incidence and predictors of clinical events were assessed.

Results: At a mean follow-up of 41.4 ± 26.5 months, there were no significant differences between the two strategies in terms of baseline characteristics, all-cause mortality (exclusive vs. selective: 1.9% vs. 6.9%, p = 0.21), cardiac death (1.9% vs. 1.7%, p = 0.94) and nonfatal myocardial infarction (3.8% vs. 5.2%, p = 0.74). Despite the presence of more ostial lesions in the exclusive DES group, there was a trend such that major adverse cardiac events (MACE) and target lesion revascularization (TLR) rates were higher in the selective DES group (MACE: 17.3% vs. 31%, p = 0.16; TLR: 11.5% vs. 24.1%, p = 0.08). The higher MACE rate in the selective DES group was mainly driven by a higher target vessel revascularization (TVR) rate (15.4% vs. 29.3%, p = 0.08). In the exclusive DES group, SYNTAX score was an independent predictor of MACE [Haxard ratio (HR): 1.09, 95% confidence internal (CI): 1.02-1.16, p = 0.01] and TVR (HR 1.08, 95% CI 1.01-1.15, p = 0.04).

Conclusions: Compared to the exclusive DES strategy, the selective DES strategy with reservation of DES for complex lesions is associated with numerically higher, but not statistically significant, rates of MACE and all-cause mortality in this small group of patients with multivessel CAD receiving four or more stents.

Key Words: Bare metal stent • Drug-eluting stent • Multivessel coronary artery disease

INTRODUCTION

The development of drug-eluting stents (DES) has facilitated modern percutaneous coronary intervention (PCI) with a remarkable reduction in restenosis and consequent target lesion revascularization (TLR).[1-6] However, in patients with multivessel coronary artery disease (CAD), coronary artery bypass graft (CABG) has been considered the gold standard of therapy, mainly because of a higher rate of complete revascularization and fewer repeat revascularizations.[7-10] The SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) trial showed that in patients with multivessel disease and low lesion complexity (SYNTAX score ≦ 22), there was no significant difference in the rates of major

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adverse cardiac events (MACE) when treating patients with either PCI or CABG. In patients with intermediate or high lesion complexity (SYNTAX score 23-32 and ≧ 33, respectively), MACE rates were significantly higher in the PCI group.[11] However, regarding surgical risk, patients of advanced age and those with multiple comorbidities are not all surgical candidates. In this specific patient population, PCI using DES would be a reasonable alternative. However, the expanded use of DES in multivessel PCI is costly and typically subject to limited insurance reimbursement. In contrast to the strategy of exclusive use of DES for all lesions, selective use of DES for lesions of complex features in combination with bare metal stents (BMS) for simple lesions may be an alternative strategy in real-world practice. This study aimed to compare the clinical outcomes in patients treated with the selective DES strategy and those in patients treated with the exclusive DES strategy.

METHODS

Population and PCI strategies

Patients with multivessel coronary disease, defined as two or three vessel disease with or without left main (LM) involvement, who were treated with four or more stents between November 2004 and December 2011, were identified retrospectively from the cardiac catheterization database of the First Cardiovascular Division of Chang Gung Memorial Hospital. Patients with cardiogenic shock or who received PCI for bypass grafts were excluded. For patients presenting with ST elevation myocardial infarction (STEMI), the non-infarct related lesions were treated as separated procedures. The exclusive DES group consisted of patients in whom all the lesions were treated exclusively with DES. The selective group was composed of patients in whom the lesions were treated with a combination of DES and BMS. In this group, DES was reserved for complex lesions, including LM, bifurcation lesions, calcified lesions, long lesions, chronic total occlusion (CTO), ostium of left anterior descending (LAD), left circumflex (LCX) or right coronary artery (RCA). The remaining lesions were treated with BMS. The choice of exclusive or selective strategy was determined mainly by patient preference and physician discretion. Unfractionated heparin was administered as bolus doses to achieve an activated clotting time of longer than 300 seconds during the procedures. All patients were instructed to maintain a medication regimen of dual antiplatelet therapy with aspirin and clopidogrel for at least 1 year unless contraindicated.

Study definitions and clinical follow-up

Significant coronary lesions requiring PCI were defined as stenosis of ≧ 70% in a segment with a reference diameter of ≧ 2.0 mm. Angiographic success was defined as a residual stenosis < 20% after stent deployment and post-dilatation with Thrombolysis in Myocardial Infarction flow grade 3. Complete revascularization was defined as successful angiographic results for all significant lesions in major epicardial vessels (LAD, LCX and RCA) and their major branches (diagonal branches of LAD and obtuse marginal branches of LCX) with a reference diameter of ≧ 2.0 mm. Diffuse disease and small vessels were in accordance with the definition of the SYNTAX scoring system.[12] The study end-points were the major adverse cardiac events, including cardiac death, nonfatal myocardial infarction (MI), and target vessel revascularization (TVR). Follow-up coronary angiography was not routinely obtained but was at the discretion of the primary care physicians. Follow-up angiography was mainly performed for recurrent angina, suspected ischemia by non-invasive imaging or stress tests, or LM lesions. We obtained the clinical information by reviewing medical records. If the patients had regular follow-up visits in the outpatient clinic during the study period, we assumed that any MACE would have been recorded, had it occurred. For patients lost to follow-up, we contacted them and received the additional necessary clinical information by phone. Those who did not have regular follow-up visits and could not be contacted by phone were excluded from analysis. Unless documented otherwise, all deaths were considered to be cardiac-related. MI was defined as a rise of Troponin I with at least 1 value above the 99th percentile of the upper reference limit, together with any evidence of myocardial ischemia, such as symptoms of ischemia, electrocardiography changes indicative of new ischemia, development of pathological Q waves, or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality. TLR was defined as

any repeated PCI or surgical bypass to treat > 50% restenosis in the stent or within 5 mm of the stent edges. TVR was defined as any repeated PCI or surgical bypass of any segment of the treated vessel.

Statistical analysis

Comparisons were made between exclusive DES and selective DES groups. Categorical variables were expressed as percentages and continuous variables as mean ± SD. The chi-square test with Fisher's exact test was used to compare categorical variables and independent samples, and the t-test was used to compare continuous variables. A p value of < 0.05 was considered statistically significant. The cumulative incidence of MACE was estimated using the Kaplan-Meier method and survival curves were compared using the log-rank test. Univariate Cox regression analysis was used to assess the hazard ratio (HR) of variables. All variables with a probability value < 0.05 in the univariate Cox regression analysis were then entered into the multivariate Cox proportional hazard model to determine independently predictive factors for MACE, cardiac death, nonfatal MI and TVR. All analyses were performed using IBM SPSS Statistics 19 software.

RESULTS

A total of 110 patients who underwent multivessel PCI with four or more stents were included for analysis, with 52 patients in the exclusive DES group and 58 patients in the selective DES group. Table 1 summarizes the patient characteristics of the two groups. The majority of the overall population was male (85.5%), and the

Table 1. Patient characteristics

Characteristic	Total patients (N = 110) Number (%)	Exclusive DES (N = 52) Number (%)	Selective DES (N = 58) Number (%)	p value
Age (mean ± SD, years)	62.8 ± 11.3	62.1 ± 10.6	63.4 ± 12.0	0.54
Male gender (%)	93 (85.5%)	41 (78.8%)	52 (91.4%)	0.06
BMI (mean +/- SD, kg/m2)	26.43 ± 3.9	26.8 ± 3.5	26.1 ± 4.2	0.32
Current smoker	42 (38.2%)	23 (44.2%)	19 (32.8%)	0.22
Hypertension	74 (67.3%)	37 (71.2%)	37 (63.8%)	0.41
Diabetes mellitus	39 (35.5%)	19 (36.5%)	20 (34.5%)	0.82
Hypercholesterolemia	66 (60%)	36 (69.2%)	30 (51.7%)	0.62
ESRD	7 (6.4%)	4 (7.7%)	3 (5.2%)	0.59
Prior heart failure	16 (14.5%)	7 (13.5%)	9 (15.5%)	0.76
Prior MI	21 (19.1%)	11 (21.2%)	10 (17.2%)	0.60
Prior CABG	5 (4.5%)	4 (7.7%)	1 (1.7%)	0.13
Prior stenting	8 (7.3%)	3 (5.7%)	5 (8.6%)	0.57
Clinical presentation				
Stable angina	50 (45.5%)	25 (48.1%)	25 (43.1%)	0.61
Unstable angina	7 (6.4%)	2 (3.8%)	5 (8.6%)	0.30
NSTEMI	33 (30%)	16 (30.8%)	17 (29.3%)	0.87
STEMI	16 (14.5%)	6 (11.5%)	10 (17.2%)	0.40
CHF	4 (3.6%)	3 (5.8%)	1 (1.7%)	0.28
LV EF (mean ± SD, %)	57.5 ± 15.2	57.7 ± 15.3%	57.3 ± 15.2	0.92
Medication				
Aspirin	109 (99.1%)	51 (98%)	58 (100%)	0.32
Clopidogrel	110 (100%)	52 (100%)	58 (100%)	
ACEI/ARB	71 (64.5%)	34 (65.4%)	37 (63.8%)	0.86
Beta-blocker	95 (86.4%)	44 (84.6%)	50 (86.2%)	0.62
CCB	14 (12.7%)	10 (19.2%)	4 (6.8%)	0.06
Statin	86 (78.5%)	44 (84.6%)	42 (72%)	0.12

ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin II receptor blocker; BMI, body mass index; CABG, coronary artery bypass graft; CCB, calcium channel blocker; CHF, congestive heart failure; DES, drug-eluting stent; ESRD, end stage renal disease; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; SD, standard deviation; STEMI, ST elevation myocardial infarction.

prevalence of current smoker, hypertension, diabetes and hypercholesterolemia was 38.2%, 67.3%, 35.5%, and 60%, respectively. Seven patients (6.4%) had end stage renal disease and received maintenance hemodialysis. Fifty patients (45.5%) presented with stable angina. Among the 56 patients (51%) with acute coronary syndrome, seven (6.4%) had unstable angina, 33 (30%) had non-ST elevation MI, and 16 (14.5%) had ST elevation MI. Four patients (3.6%) presented with heart failure. There was no statistically significant difference in patient demographics between the two groups, although patients in the selective DES group were more often men and more often taking calcium channel blockers.

Angiographic and procedural characteristics are presented in Table 2. Among the study patients, 85 (77.3%) had three vessel disease, 25 (22.7%) had two vessel disease, and 21 (19.1%) had LM coronary disease. The mean SYNTAX score was 27.6 ± 8.7 in the exclusive DES group and 27.3 ± 10.2 in the selective DES group (p = 0.9). The distribution of lesion complexity, as indicated by low (34.6% vs. 24.1%, p = 0.73), intermediate (36.5% vs. 50%, p = 0.16), and high (28.8% vs. 35.9%, p = 0.23) SYNTAX scores, was comparable between the two groups.

Table 2. Angiographic and procedural characteristics

Characteristics	Total patients (N = 110) Number (%)	Exclusive DES (N = 52) Number (%)	Selective DES (N = 58) Number (%)	p value
No. of diseased vessels				
2 vessels ± LMCA	25 (22.7%)	11 (21.2%)	14 (24.1%)	0.71
2 vessels only	22 (20%)	8 (15.4%)	14 (24.1%)	0.25
2 vessels + LMCA	3 (2.7%)	3 (5.8%)	0 (0%)	0.25
3 vessels ± LMCA	85 (77.8%)	41 (78.8%)	44 (75.9%)	0.71
3 vessels only	67 (60.9%)	34 (65.4%)	33 (56.9%)	0.44
3 vessels + LMCA	18 (16.4%)	7 (13.5%)	11 (19.0%)	0.44
SYNTAX score, mean ± SD	27.5 ± 9.4	27.6 ± 8.7	27.3 ± 10.2	0.9
Low, ≦ 22	32 (29.1%)	18 (34.6%)	14 (24.1%)	0.73
Intermediate, 23-32	48 (43.6%)	19 (36.5%)	29 (50%)	0.16
High, ≧ 33	30 (27.3%)	15 (28.8%)	15 (35.9%)	0.23
No. of patients with CTO lesions	40 (36.4%)	21 (40.4%)	19 (32.8%)	0.39
1 CTO	27 (63.6%)	16 (30.8%)	11 (19%)	0.16
2 CTO	12 (24.5%)	4 (7.7%)	8 (13.8%)	0.30
3 CTO	1 (0.9%)	1 (1.9%)	0 (0%)	0.32
No. of patients with bifurcation lesions	47 (42.7%)	25 (48.1%)	22 (37.9%)	0.54
1 bifurcation lesion	41 (37.3%)	23 (44.2%)	18 (31%)	0.16
2 bifurcation lesions	6 (5.5%)	2 (3.8%)	4 (6.9%)	0.48
No. of patients with ostial lesions	32 (29.1%)	15 (28.8%)	17 (29.3%)	0.20
1 ostial lesion	18 (16.4%)	5 (9.6%)	14 (24.1%)	0.02*
2 ostial lesions	12 (10.9%)	8 (15.4%)	3 (5.2%)	0.04*
3 ostial lesions	2 (1.8%)	2 (3.8%)	0 (0%)	0.16
Diffuse small vessel < 2 mm	42 (38.2%)	23 (44.2%)	19 (32.8%)	0.22
No. of stents per patient (%)				
4 stents	69(62.7%)	37 (71.2%)	32 (55.2%)	0.09
5 stents	29 (26.4%)	11 (21.2%)	18 (31.0%)	0.24
6 stents	12 (10.9%)	4 (7.7%)	8 (13.8%)	0.30
Mean ± SD	4.48 ± 0.69	4.37 ± 0.63	4.59 ± 0.73	0.09
Total stent length, mean ± SD (mm)	110.14 ± 22.68	108.69 ± 20.10	111.43 ± 24.86	0.53
Complete revascularization	102 (92.7%)	48 (92.3%)	54 (93.1%)	0.87
Angiographic follow-up	42 (38.1%)	17 (32.7%)	25 (43.1%)	0.61

CTO, chronic total occlusion; DES, drug-eluting stent; LMCA, left main coronary artery; SD, standard deviation.
* p < 0.05.

The numbers of CTO, bifurcation, and ostial lesions were also comparable, although there were more patients with one ostial lesion in the selective DES group (exclusive vs. selective: 9.6% vs. 24.1%, p = 0.02) and more patients with two ostial lesions in the exclusive DES group (exclusive vs. selective: 15.4% vs. 5.2%, p = 0.04). The average number of stents per patient was 4.37 ± 0.63 in the exclusive DES group and 4.59 ± 0.73 in the selective DES group (p = 0.09). The total stent length was 108.69 ± 20.1 mm in the exclusive DES group and 111.43 ± 24.86 mm in the selective DES group (p = 0.53). DES and BMS comprised 55.6% (149/268) and 44.4% (119/268) of the total stents in the selective group. Complete revascularization rates were comparable between the two groups (92.3% vs. 93.1%, p = 0.87).

The follow-up periods were 35.56 ± 23.01 and 46.61 ± 28.38 months in the exclusive and selective DES groups, respectively (p = 0.03). Angiographic follow-up was performed in 42 patients (32.7% in the exclusive DES group and 43.1% in the selective DES group, p = 0.61). The clinical outcome was summarized in Table 3. There were no significant differences between the two strategies in terms of all-cause mortality, cardiac death and nonfatal MI (p = 0.21, 0.94, and 0.74, respectively). There was a trend that the MACE and TLR rates were higher in the selective DES group [(exclusive vs. selective) MACE: 17.3% vs. 31%, p = 0.16; TLR: 11.5% vs. 24.1%, p = 0.08]. In the selective DES group, 70.6% (12/17) of TLR was performed for in-stent restenosis after implantation of bare metal stents. One cardiac death occurred in each group, respectively. The causes of the three non-cardiac deaths in the selective DES groups were sepsis, intracerebral hemorrhage and death due to complication of therapeutic thoracentesis. Of note, one patient in the exclusive DES group presented with STEMI 25 months after the index procedure and was diagnosed as definite stent thrombosis. The Kaplan-Meier survival curves showed a trend towards a higher MACE rate in the selective DES group. The higher MACE rate in the selective DES group was driven by a higher TVR rate (log-rank p = 0.12 and 0.1 for MACE and TVR, respectively) (Figure 1).

Table 3. Clinical outcomes

Outcomes	Exclusive DES (N = 52) Number (%)	Selective DES (N = 58) Number (%)	p value
All-cause mortality	1 (1.9%)	4 (6.9%)	0.21
Cardiac death	1 (1.9%)	1 (1.7%)	0.94
Nonfatal MI	2 (3.8%)	3 (5.2%)	0.74
TLR	6 (11.5%)	14 (24.1%)	0.08
TVR	8 (15.4%)	17 (29.3%)	0.08
MACE	9 (17.3%)	18 (31%)	0.16
Stroke	1 (1.9%)	1 (1.7%)	0.94
Stent thrombosis	1 (1.9%)*	0 (0%)	0.32

* A definite stent thrombosis occurred in the exclusive DES group 25 months after the index procedure.
DES, drug-eluting stent; MACE, major adverse cardiac event; MI, myocardial infarction; TLR, target lesion revascularization; TVR, target vessel revascularization.

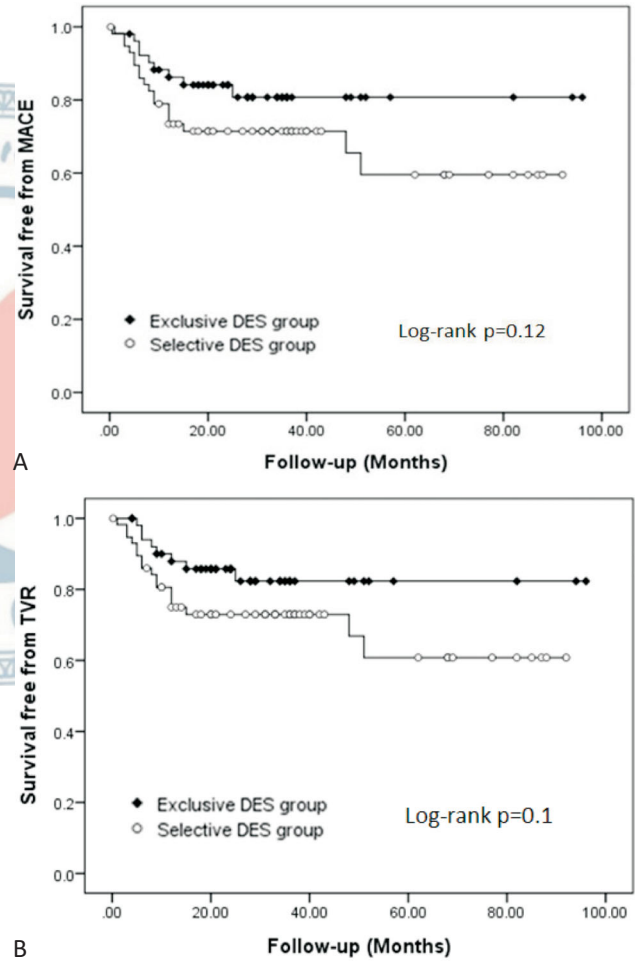

Figure 1. *Cumulative Survival According to Study Group. Kaplan-Meier survival curves are shown for the exclusive DES group and the selective DES group for MACE and TVR. There was a trend that MACE and TVR rates were higher in the selective DES group than those in the exclusive DES group. The higher MACE rate in the selective DES group was primarily driven by a higher TVR rate. DES, drug-eluting stent; MACE, major adverse cardiac event; TVR, target vessel revascularization.*

We used univariate and multivariate Cox regression analysis to determine the potential predictors of clinical events. In the exclusive DES group, univariate analysis showed that CKD was a predictor of MACE [harzard ratio (HR): 4.24, 95% confidence internal (CI): 1.13-15.98, p = 0.03] and that SYNTAX score was a predictor of MACE (HR: 1.08, 95% CI: 1.02-1.15, p = 0.01) and TVR (HR: 1.08, 95% CI: 1.01-1.15, p = 0.03) (Table 4). Multivariate analysis showed that CKD was an independent predictor of MACE (HR: 4.15, 95% CI: 1.07-16.11, p = 0.04) and that SYNTAX score independently affected MACE (HR: 1.09, 95% CI: 1.02-1.16, p = 0.01) and TVR (HR: 1.08, 95% CI: 1.01-1.15, p = 0.04; Table 5). In the selective DES group, univariate analysis showed both end stage renal disease (ESRD) and heart failure to be predictors of non-fatal MI (Table 6). However, neither ESRD nor heart failure remained significantly associated with non-fatal MI after adjustment for CAD risk factors (Table 7).

DISCUSSION

In this retrospective analysis, we compared the clinical outcome of patients with multivessel coronary disease treated by two different PCI strategies, the exclusive versus the selective use of DES. In the 110 patients with a mean SYNTAX score of 27.5 ± 9.4, we found no statistical difference in all-cause mortality, cardiac death, and nonfatal MI between the two groups. However, there was a trend towards increased MACE rate in the selective DES group, mainly driven by a higher rate of TVR.

When the lesion complexity of the patient population of the present study was compared with that of the PCI group of the SYNTAX trial, both groups are comparable (SYNTAX score 27.5 ± 9.4 vs. 28.4 ± 11.5).[11] The mean number of stents implanted per patient in both studies was also comparable (4.48 ± 0.69 vs. 4.3 ± 2.3).

Table 4. Predictors of events in the exclusive DES group (univariate Cox regression analysis)

	MACE HR (95% CI)	Cardiac death HR (95% CI)	Nonfatal MI HR (95% CI)	TVR HR (95% CI)
Age	1.02 (0.95-1.09)	1.56 (0.74-3.31)	1.07 (0.93-1.24)	0.99 (0.92-1.06)
Male gender	0.91 (0.19-4.37)	0.001 (0.00- > 100)	0.29 (0.02-4.68)	1.81 (0.22-14.69)
Smoking	1.46 (0.39-5.44)	1.16 (0.07-18.63)	1.16 (0.07-18.63)	1.93 (0.46-8.07)
Diabetes mellitus	0.21 (0.03-1.68)	0.02 (0.00- > 100)	0.03 (0.001- > 100)	0.24 (0.03-1.94)
Hypertension	3.59 (0.45-28.69)	34.40 (0.00- > 100)	35.34 (0.00- > 100)	3.18 (0.39-25.83)
LDL cholesterol level	1.0 (0.98-1.01)	0.97 (0.91-1.04)	0.97 (0.93-1.02)	1.0 (0.98-1.02)
CKD	4.24 (1.13-15.98)*	1382 (0.00- > 100)	5.12 (0.32-83.14)	3.26 (0.77-13.80)
ESRD	1.35 (0.7-10.80)	0.04 (0.00- > 100)	12.73 (0.80-203.73)	1.52 (0.19-12.39)
Heart failure	1.96 (0.39-8.95)	0.04 (0.00- > 100)	0.04 (0.00- > 100)	2.17 (0.44-10.77)
Presentation with ACS	1.49 (0.4-5.55)	76.96 (0.00- > 100)	73.47 (0.00- > 100)	1.19 (0.30-4.78)
No. of diseased vessel	31.08 (0.00- > 100)	29.06 (0.00- > 100)	31.42 (0.00- > 100)	31.31 (0.03- > 100)
LM disease	1.24 (0.26-5.96)	0.04 (0.00- > 100)	5.12 (0.32-83.04)	1.45 (0.29-7.19)
SYNTAX score	1.08 (1.02-1.15)*	1.15 (0.95-1.41)	1.11 (0.96-1.28)	1.08 (1.01-1.15)*

ACS, acute coronary syndrome; CI, confidence interval; CKD, chronic kidney disease; ESRD, end stage renal disease; HR, hazard ratio; LDL, low density cholesterol; LM, left main coronary artery; MACE, major adverse cardiac event; MI, myocardial infarction; TVR, target vessel revascularization.

* $p < 0.05$.

Table 5. Predictors of events in the exclusive DES group (multivariate Cox regression analysis)

	MACE HR (95% CI)	Cardiac death HR (95% CI)	Nonfatal MI HR (95% CI)	TVR HR (95% CI)
SYNTAX score	1.09 (1.02-1.16)*			1.08 (1.01-1.15)*
CKD	4.15 (1.07-16.11)#			

* Adjusted for chronic kidney disease; $p < 0.05$. # Adjusted for SYNTAX score; $p < 0.05$.

CI, confidence interval; CKD, chronic kidney disease; DES, drug-eluting stent; HR, hazard ratio; MACE, major adverse cardiac event; MI, myocardial infarction; TVR, target vessel revascularization.

Table 6. Predictors of events in the selective DES group (univariate Cox regression analysis)

	MACE HR (95% CI)	Cardiac death HR (95% CI)	Nonfatal MI HR (95% CI)	TVR HR (95% CI)
Age	0.98 (0.95-1.03)	0.94 (0.82-1.09)	1.09 (0.96-1.25)	0.98 (0.94-1.02)
Male gender	1.51 (0.20-11.32)	21.62 (0.00- > 100)	22.54 (0.00- > 100)	1.42 (0.19-10.69)
Smoking	1.67 (0.66-4.22)	72.10 (0.00- > 100)	0.97 (0.09-10.73)	1.84 (0.71-4.77)
Diabetes mellitus	2.01 (0.79-2.11)	2.01 (0.79-5.11)	4.37 (0.40-48.33)	1.76 (0.67-4.66)
Hypertension	1.91 (0.68-5.39)	50.52 (0.00- > 100)	1.21 (0.11-13.29)	1.77 (0.62-5.05)
LDL cholesterol level	1.0 (0.99-1.01)	1.04 (.96-1.12)	1.01 (0.98-1.03)	1.0 (0.99-1.02)
CKD	0.61 (0.18-2.11)	0.033 (0.00- > 100)	1.10 (0.14-17.80)	0.65 (0.19-2.27)
ESRD	2.95 (0.67-13.07)	0.05 (0.00- > 100)	60.05 (5.18-696.26)*	1.45 (0.19-11.14)
Heart failure	1.47 (0.48-4.49)	0.03 (0.00- > 100)	12.37 (1.12-136.40)*	1.10 (0.31-3.84)
Presentation with ACS	1.70 (0.66-4.41)	0.01 (0.00- > 100)	2.23 (0.20-24.64)	1.55 (0.59-4.09)
No. of diseased vessel	1.26 (0.41-3.85)	34.18 (0.00- > 100)	31.43 (0.00- > 100)	1.17 (0.38-3.60)
Left main disease	0.82 (0.24-2.85)	0.04 (0.00- > 100)	0.04 (0.00- > 100)	0.89 (0.25-3.08)
SYNTAX score	0.97 (0.91-1.03)	1.02 (0.79-1.31)	1.06 (0.95-1.18)	0.97 (0.91-1.03)
BMS number	1.18 (0.72-1.92)	0.73 (0.07-8.14)	1.05 (0.27-4.02)	1.26 (0.78-2.05)

ACS, acute coronary syndrome; BMS, bare metal stent; CI, confidence interval; CKD, chronic kidney disease; ESRD, end stage renal disease; HR, hazard ratio; LDL, low density cholesterol; MACE, major adverse cardiac event; MI, myocardial infarction; TVR, target vessel revascularization.

* $p < 0.05$.

Table 7. Predictors of events in the selective DES group (multivariate Cox regression analysis)

	MACE HR (95% CI)	Cardiac death HR (95% CI)	Nonfatal MI HR (95% CI)	TVR HR (95% CI)
ESRD			52.77 (3.27-851.56)*	
Heart failure			8.73 (0.61-124.86)	

* Adjusted for heart failure, $p < 0.05$.

CI, confidence interval; DES, drug-eluting stent; ESRD, end stage renal disease; HR, hazard ratio; MACE, major adverse cardiac event; MI, myocardial infarction; TVR, target vessel revascularization.

In addition, 35.5% of patients in the present study had diabetes, 77.8% had triple vessel disease and 44.5% presented with acute myocardial infarction. Given this high risk epidemiologic profile and high lesion complexity, the selective DES strategy resulted in a comparable outcome in terms of all-cause mortality, cardiac death and nonfatal MI when compared with the exclusive DES strategy ($p = 0.21$, 0.94, and 0.74, respectively). However, a clear trend towards higher rates of MACE and TLR in the selective DES group compared with the exclusive DES group was demonstrated. The small sample size may explain the lack of statistical difference while comparing MACE and TLR rates between the two strategies.

The SYNTAX score has been demonstrated to be an effective scoring system for outcome prediction in patients with stable angina, multivessel and LM coronary disease treated with PCI using exclusive DES.[12-16] Consistent with those studies, SYNTAX score was an independent predictor of MACE and TVR in the present study's exclusive DES group. However, in the selective DES group the SYNTAX score was not identified as an independent predictor for clinical outcomes. This finding suggests that in patients with multivessel disease treated with the combination of DES and BMS, SYNTAX score may not be applicable for outcome prediction. One potential explanation for this is that implantation of BMS, even in the less complex lesions, might result in a higher restenosis rate compared with DES. This may make lesion complexity less correlated with stenting effectiveness.

Several previous studies have compared the clinical outcomes between patients with multivessel CAD treated with the exclusive strategy and those treated with selective DES strategy. Bertrand et al. reported that no

significant difference was observed between the two groups in terms of death, MI and TLR.[17] Syed et al. analyzed the outcomes of 2065 patients receiving PCI with two different DES strategies and found no difference in MACE at one year follow-up.[18] In the REAL registry (Registro REgionale AngiopLastiche Emilia-Romagna), a prospective multicenter registry, Varani et al. reported that usage of DES in every lesion reduced the TVR risk by 37% and MACE by 39%.[19] Since the lesion complexity and the epidemiologic profiles differ among studies, it is difficult to compare the results between different studies. However, comparable rates of death and MI between patients treated with different strategies were constantly demonstrated among these studies.

STUDY LIMITATIONS

This single-center study was a retrospective and nonrandomized analysis with its inherent limitations. The initial strategy depended both on operator discretion and patient preference, which might lead to a bias. Different time periods at which PCI was performed and incomplete angiographic follow-up also introduced potential bias. The small patient number was the major limitation of the present study. It was the possible explanation for the lack of statistical difference in MACE and TLR rates between the two strategies, despite the fact that a clear trend was demonstrated towards higher rates of MACE and TLR in the selective DES group than in the exclusive DES group. Based on our results, and assuming a difference of 13.7% in MACE rate between the two strategies, the statistical power of our study, given the sample size and the 31% MACE rate in selective DES group, reaches only 50% at an alpha level of 0.05. Thus, a larger study population (an estimated 78 patients in each group) would provide enhanced statistical reliability (i.e. 80% of statistical power). Lastly, the cost-effectiveness of the two strategies remains to be estimated.

CONCLUSIONS

In conclusion, midterm follow-up in the present study showed that patients with multivessel CAD treated with the selective DES strategy had comparable rates of all-cause death, cardiac death and nonfatal MI when compared with those treated with exclusive DES strategy. However, the selective DES strategy was associated with a higher MACE rate driven by a higher TVR rate. These findings indicated that for patients with multivessel CAD with or without LM disease who are treated with PCI, the selective DES strategy with DES reserved for complex lesions might be a reasonable alternative when exclusive use of DES is not possible.

REFERENCES

1. Stettler C, Wandel S, Allemann S, et al. Outcomes associated with drug-eluting and bare-metal stents: a collaborative network meta-analysis. *The Lancet* 2007;370:937-48.
2. Schampaert E, Cohen EA, Schlüter M, et al. The Canadian study of the sirolimus-eluting stent in the treatment of patients with long de novo lesions in small native coronary arteries (C-SIRIUS). *Journal of the American College of Cardiology* 2004;43:1110-5.
3. Schofer J, Schlüter M, Gershlick AH, et al. Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries: double-blind, randomised controlled trial (E-SIRIUS). *The Lancet* 2003;362:1093-9.
4. Abbott JD, Voss MR, Nakamura M, et al. Unrestricted use of drug-eluting stents compared with bare-metal stents in routine clinical practice: findings from the National Heart, Lung, and Blood Institute Dynamic Registry. *J Am Coll Cardiol* 2007;50: 2029-36.
5. Kastrati A, Mehilli J, Pache J, et al. Analysis of 14 trials comparing sirolimus-eluting stents with bare-metal stents. *N Engl J Med* 2007;356:1030-9.
6. Marzocchi A, Piovaccari G, Manari A, et al. Comparison of effectiveness of sirolimus-eluting stents versus bare metal stents for percutaneous coronary intervention in patients at high risk for coronary restenosis or clinical adverse events. *Am J Cardiol* 2005;95:1409-14.
7. Booth J, Clayton T, Pepper J, et al. Randomized, controlled trial of coronary artery bypass surgery versus percutaneous coronary intervention in patients with multivessel coronary artery disease: six-year follow-up from the Stent or Surgery Trial (SoS). *Circulation* 2008;118:381-8.
8. Hoffman SN, TenBrook JA, Wolf MP, et al. A meta-analysis of randomized controlled trials comparing coronary artery bypass graft with percutaneous transluminal coronary angioplasty: one- to eight-year outcomes. *J Am Coll Cardiol* 2003;41:1293-304.
9. Rodriguez A, Bernardi V, Navia J, et al. Argentine randomized study: coronary angioplasty with stenting versus coronary bypass surgery in patients with multiple-vessel disease (ERACI II): 30-day and one-year follow-up results. *J Am Coll Cardiol* 2001; 37:51-8.

10. van den Brand MJ, Rensing BJ, Morel MA, et al. The effect of completeness of revascularization on event-free survival at one year in the ARTS trial. *J Am Coll Cardiol* 2002;39:559-64.
11. Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med* 2009;360:961-72.
12. Sianos G, Morel MA, Kappetein AP, et al. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. *EuroIntervention* 2005;1:219-27.
13. van Gaal WJ, Ponnuthurai FA, Selvanayagam J, et al. The Syntax score predicts peri-procedural myocardial necrosis during percutaneous coronary intervention. *Int J Cardiol* 2009;135:60-5.
14. Valgimigli M, Serruys PW, Tsuchida K, et al. Cyphering the complexity of coronary artery disease using the syntax score to predict clinical outcome in patients with three-vessel lumen obstruction undergoing percutaneous coronary intervention. *Am J Cardiol* 2007;99:1072.
15. Kim YH, Park DW, Kim WJ, et al. Validation of SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) score for prediction of outcomes after unprotected left main coronary revascularization. *JACC: Cardiovasc Interv* 2010;3:612-23.
16. Chen SL, Chen JP, Mintz G, et al. Comparison between the NERS (New Risk Stratification) score and the SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) score in outcome prediction for unprotected left main stenting. *JACC: Cardiovasc Interv* 2010;3:632-41.
17. Bertrand OF, Faurie B, Larose É, et al. Clinical outcomes after multilesion percutaneous coronary intervention: comparison between exclusive and selective use of drug-eluting stents. *J Invasive Cardiol* 2008;20:99-104.
18. Syed AI, Ben-Dor I, Li Y, et al. Hybrid strategy of a bare metal stent combined with a drug-eluting stent versus exclusive drug-eluting stent implantation for multivessel percutaneous coronary intervention. *EuroIntervention* 2011;6:1085-90.
19. Varani E, Saia F, Balducelli M, Guastaroba P. Percutaneous treatment of multivessel coronary disease in the drug eluting stent era: comparison of bare-metal stents, drug-eluting stents and a mixed approach in a large multicentre registry. *EuroIntervention* 2007;2:474-80.