Intermediate term outcomes with bifurcation coronary stenting using the paclitaxel drug-eluting stent: A single centre experience

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BACKGROUND: Percutaneous treatment of bifurcation coronary artery disease (BCD) is complex and, in the era of bare metal stents (BMS), was reported to have a high rate of repeat target lesion revascularization (TLR). Paclitaxel drug-eluting stents (PES) have been used in the treatment of BCD, with better overall outcomes than BMS. Also, acute stent thrombosis (AST), with an incidence ranging from 2.7% to 4.3%, has been reported with the use of bifurcation PES, and remains a concern in treating these patients. In the present report, intermediate term outcomes with BCD stenting using TAXUS Express (Boston Scientific, USA) PES are presented from the Genesis Medical Center.

METHODS: In the present retrospective study, 518 consecutive de novo bifurcation stenting procedures are reported. They were performed in 2005 at the present institution using the TAXUS Express PES. Follow-up data on 312 patients (60.2%) was achieved through telephone interviews and reviews of medical records after a mean of 6.7 months. The primary end point of the present study was the

combined end points of cardiac death, nonfatal myocardial infarction (MI) and TLR. Secondary outcomes included the individual end points of death, cardiac death, AST, target vessel revascularization (TVR), TLR, ST elevation MI and non-ST elevation MI on intermediate term follow-up.

RESULTS: The mean ($\pm$ SD) age of the patients was 66 ± 12 years. Acute procedural success was 95% (main branch, 99%; side branch, 95.9%). The following intermediate term outcomes with bifurcation drug-eluting stents were: TLR, 6.7%; TVR, 12.2%; definite and probable AST, 1.6%; death, 6.7%; cardiac death, 2.9%; non-ST elevation MI, 0.7%; ST elevation MI, 2.0%; and the combined primary end point, 9.9%. The outcomes for patients who underwent main branch stenting were not statistically different from those with bifurcation stenting, with an overall combined end point favouring main branch stenting alone (5.8% versus 10.8%, *P* not significant).

CONCLUSION: The TAXUS Express PES carry acceptable intermediate term outcomes in the treatment of BCD compared with historic controls with BMS, with low TLR, TVR and overall primary combined end point. Main branch stenting alone is safe, with a trend toward fewer adverse events than bifurcation stenting.

Key Words: Bifurcation lesions; Outcome; Paclitaxel; Registry

The TAXUS Express (Boston Scientific, USA) paclitaxel drug-eluting stent (PES) is Food and Drug Administration-approved for the treatment of coronary artery disease in non-complex coronary lesions. However, the PES has been widely used off-label in complex lesions, including bifurcation disease, chronic total occlusions, long lesions, small vessels and left main stenting, with overall acceptable outcomes (1-4). Randomized trials and 'real world' registries of drug-eluting stents (DES) (4-9), including PES, have shown that they yield superior results to bare metal stents (BMS), with less restenosis and target lesion revascularization (TLR), and no increase in myocardial infarction (MI) or death rates. Late stent thrombosis seems to be a problem with both DES and BMS, although in DES it occurs later than BMS and appears as a primary thrombosis (10).

In the present registry, we investigated the procedural success and intermediate outcomes of patients who received bifurcation PES at the Genesis Medical Center for de novo lesions, and assessed acute stent thrombosis (AST) as defined by the Academic Research Consortium (ARC) (10). The present study was approved by the Institutional Review Board at the Genesis Medical Center.

METHODS

In-hospital demographic, angiographic and clinical data on patients in the present study were obtained from a prospectively collected database at the Genesis Medical Center. Data were entered by the operator at the end of the procedure, and were audited by a monitoring coordinator. The database defines bifurcation coronary artery disease (BCD) as a 50% or greater angiographic stenosis at a bifurcation in the main vessel and/or a side branch. Patients were included if they received a PES (the only DES in the present cardiac catheterization laboratory in 2005) in a de novo bifurcation lesion. Patients were excluded if they received a stent other than a PES, had treated vessels other than the index vessel, had a restenotic lesion or if the side branch was less than 2 mm in diameter. Out-of-hospital follow-up was retrospectively performed by reviewing medical records and by telephone interviews with the patients and their families. A standardized script of follow-up questions was approved by the Institutional Review Board at the Genesis Medical Center.

The primary end point of the present study was the combined end points of cardiac death, nonfatal MI (ST elevation MI [STEMI] and non-ST elevation MI [NSTEMI]) and TLR.

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TABLE 1
Demographics and clinical presentation of all patients

Demographic or clinical presentation	Value (%)
Men	68.9
Tobacco use	
Never	35.9
Yes, past	41.9
Yes, current	22.2
Age, years	66.03±12.01*
Body mass index, kg/m ²	29.51±6.20*
Previous percutaneous coronary intervention	63.9
Previous CABG	17.8
Previous myocardial infarction	38.6
Family history of premature CAD	18.5
Congestive heart failure	12.4
Renal failure	5.2
Peripheral vascular disease	14.3
Hypertension	80.1
Hyperlipidemia	71.8
Diabetes	31.9
Cerebrovascular disease	13.9
Presentation	
Non-ST elevation myocardial infarction	10.8
ST elevation myocardial infarction	6.8
Unstable angina	25.5
Stable angina	35.6
Atypical chest pain	1
Asymptomatic	20.3
Status of procedure	
Elective	65.4
Urgent	24.9
Emergent	9.7

*Results presented as mean ± SD. CABG Coronary artery bypass graft surgery; CAD Coronary artery disease

Secondary outcomes included the individual end points of death, cardiac death, AST, target vessel revascularization (TVR), TLR, STEMI and NSTEMI on intermediate term follow-up. AST was considered if its occurrence was definite or probable, according to the ARC definition [10]. Acute procedural success was defined as achieving a residual stenosis of 30% or lower in both main and side branches.

Descriptive analysis was performed on all variables (displayed in Tables 1 and 2). Continuous variables were expressed as mean ± SD and dichotomous variables as percentages. Univariate analysis was conducted to compare the differences in variables between patients who met the primary combined end point versus those who did not. Also, univariate analysis was performed to compare patients who underwent bifurcation stenting versus main branch stenting.

RESULTS

Five hundred eighteen consecutive de novo bifurcation coronary stenting procedures were performed in 2005 at the Genesis Medical Center using a PES. Follow-up data on 312 patients (60.2%) were collected using telephone interviews and by reviewing medical records after a mean of 6.7 months. Patients who died were classified as cardiac (due to AST,

TABLE 2
Angiographic variables of all patients

Variable	Value (%)
Stenting technique	
T	43.9
Crush	0.4
V	30.1
Y	3.9
Culotte	0.2
Main branch only	16.7
Final kissing balloon	76
Success, side branch	95.9
Success, main branch	99
Type C lesion	29.4
Angiographic thrombus	6.1
Residual stenosis in main branch, mm	0.89±4.31*
Residual stenosis in side branch, mm	2.4±8.44*
Lesion length, mm	16.8±9.63*
Intraprocedural complications	
Dissection	2.9
Perforation	0.8
Acute closure	1.7
Slow flow	1.2
Distal embolization	0.4

*Results presented as mean ± SD

according to the ARC definition [10], or non-AST due to another heart-related reason), noncardiac or death from indeterminate reasons. Demographic and clinical characteristics of patients included in the present study are shown in Table 1.

The following bifurcation stenting techniques were used (Table 2): T stenting, 43.9%; V stenting, 30.1%; crush stenting, 0.4%; culotte stenting, 0.2%; Y stenting, 3.9%; and main branch stenting with no stenting of the side branch, 16.7%. Kissing balloon stenting was performed in 76% of patients. The mean age of the patients was 66±12 years. The procedure was elective, urgent and emergent in 65.4%, 24.9% and 9.7% of cases, respectively (Table 1). The bifurcation lesions were located in the left anterior descending or diagonal artery, 50.7%; left circumflex or obtuse marginal artery, 26.7%; left anterior descending or left circumflex artery, 13.5%; postero-lateral branch or posterior descending artery, 6.6%; others, 2.5%.

The acute procedural success was 95% (main branch, 99%; side branch, 95.9%). The following intermediate term outcomes were seen: TLR, 6.7%; TVR, 12.2%; definite and probable AST, 1.6%; total death, 6.7%; cardiac death, 2.9%; NSTEMI, 0.7%; STEMI, 2.0%. The combined primary end point of cardiac death, nonfatal MI and TLR was met in 9.9% of patients.

Univariate analysis (Table 3) showed no differences in the demographic, clinical and angiographic variables between patients who met the primary end point versus those who did not, with the exception of main branch residual stenosis that was slightly, but significantly, lower in the group that met the primary end point. The distribution of stenting methods was similar between the two groups. Furthermore, the outcomes for patients who underwent main branch stenting were not statistically different from those who underwent two-branch

TABLE 3
Univariate analysis between subjects with posthospital follow-up data

	Met primary end point		P
	No (%)	Yes (%)	
Men	65.2	72.7	NS
Tobacco use			NS
Never	36.2	45.5	
Yes, past	40.9	39.4	
Yes, current	22.9	15.2	
Age, years	68.9±11.1*	64.5±13.3*	NS
Body mass index, kg/m ²	29.2±5.7*	30.9±5.9*	NS
Previous PCI	64.2	60.6	NS
Previous CABG	14.3	27.3	NS
Previous myocardial infarction	38.4	36.4	NS
Family history of premature CAD	19.7	15.2	NS
Congestive heart failure	13.6	3	NS
Renal failure	4.7	9.1	NS
Peripheral vascular disease	16.8	18.2	NS
Hypertension	83.5	78.8	NS
Hyperlipidemia	68.5	60.6	NS
Diabetes	32.3	39.4	NS
Cerebrovascular disease	11.8	21.2	NS
Presentation			NS
NSTEMI	12.5	12.1	
STEMI	6.5	6.1	
Unstable angina	21.5	36.4	
Stable angina	39.8	24.2	
Atypical chest pain	0.4	0	
Asymptomatic	19	21.2	
Status of procedure			NS
Elective	64.9	72.7	
Urgent	25.4	18.2	
Emergent	9.7	9.1	
Stenting technique			NS
T	43.1	45.5	
Crush	0.4	0	
V	30.7	18.2	
Y	3.6	3	
Culotte	0.4	0	
Main branch only	16.8	15.2	
Final kissing balloon	75.6	81.8	NS
Success, side branch	95.4	88.5	NS
Success, main branch	98.1	100	NS
Type C lesion	29.1	27.3	NS
Angiographic thrombus	4.1	7.4	NS
Residual stenosis in main branch, mm	1.14±4.97*	0±0*	0.001
Residual stenosis in side branch, mm	3.1±10.47*	1.22±4.44*	NS
Lesion length, mm	17.01±8.84*	14.88±5.52*	NS
Intraprocedural complications			NS
Dissection	2.2	3	
Perforation	0.7	3	
Acute closure	1.8	3	
Slow flow	1.4	3	
Distal embolization	0.4	3.1	

*Results presented as mean ± SD. CABG Coronary artery bypass graft surgery; CAD Coronary artery disease; NS Not significant; NSTEMI Non-ST elevation myocardial infarction; PCI Percutaneous coronary intervention; STEMI ST elevation myocardial infarction

stenting (Table 4), with an overall combined primary end point favouring main branch stenting (5.8% versus 10.8%, respectively, P not significant).

DISCUSSION

Bifurcation stenting is a complex procedure that carries a higher rate of major adverse events than noncomplex bifurcation stenting, including a higher rate of restenosis and TLR (11). Multiple techniques have been used, with no convincing superiority of one over the other. DES have recently been shown to have a better overall outcome in treating off-label complex coronary lesions, including BCD, with outcomes superior to historic BMS data (4-9). However, late and very late stent thromboses have raised significant concerns over the off-label use of DES, including BCD. Nonetheless, this concern seems to be shared for both DES and BMS, as recently published (10).

In the present single centre registry, 518 patients were treated for BCD using a PES in one year. Follow-up was achieved in 60.2% of these patients. The overall outcome of this 'real world' cohort of patients appears favourable and consistent with published results from studies on bifurcation DES. In the present study, TLR and TVR occurred in 6.7% and 12.2% of cases, respectively, with definite and probable AST in 1.6% of cases. Di Mario et al (12) reported a 2.7% occurrence of stent thrombosis in their consecutive series of 150 bifurcation lesions treated with PES. In addition, data from the ARRIVE I registry (13) showed an AST rate of 4.3% in PES-treated bifurcation lesions at two years follow-up. ARRIVE I also showed that bifurcation lesions treated with PES resulted in the following: major cardiac events (death, MI and reintervention), 13.2%; cardiac death, 2.1%; and reinterventions, 11.8% (13); these were well within the limits of our registry results. Finally, in a randomized trial (14) between sirolimus-eluting stents and PES for bifurcation lesions, TLR was reported to occur in 13% of cases with PES at a mean of 24 months.

Procedural complexity

Main branch stenting was safe and had statistically similar outcomes to bifurcation stenting, similar to multiple reports that specifically addressed this issue (15-19). Main branch stenting with provisional stenting of the side branch is a simpler strategy that has been shown to reduce fluoroscopy and procedure times, and lower rates of procedure-related biomarker elevation. Although main branch stenting, with provisional stenting of the side branch, was based on operator preference and therefore inherently biased by selection, our data remain in line with published series showing the feasibility and safety of this approach.

Predictors of the primary outcome

In the present study, demographic, clinical and angiographic variables were not predictive of the occurrence of major adverse events in patients undergoing BCD stenting with PES. Di Mario et al (12) have shown that postprocedural main branch minimal luminal diameter was the only variable predictive of TLR and TVR in 150 consecutive patients who underwent BCD stenting with a PES. In the present study, minimum lumen diameter was not among the variables collected, and was therefore not included in the analysis. Similar to the study of Di Mario et al (12), however, none of the other

variables were predictors of adverse events in our large series. In our registry, residual percentage narrowing in the main branch was the only variable that was slightly, but significantly, lower in patients that met the primary end point; however, the difference was too small to be clinically significant and was likely due to chance.

Clinical implications

The TAXUS Express PES carries acceptable intermediate term outcomes in the treatment of BCD compared with historic controls with BMS; it has an overall low primary combined end point of cardiac death, nonfatal MI and TLR. Stenting of bifurcation lesions using the TAXUS Express PES appears to be a feasible strategy for treating this complex coronary anatomy.

Limitations

The present study was limited by the retrospective nature of its follow-up. Also, only 61% of patients were followed after their index procedure, which could have lead to an underestimation of clinical outcomes and AST. The number of patients who were followed, however, was substantially large and the overall data on these patients remained consistent with other published series.

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TABLE 4
Univariate analysis between subjects with posthospital follow-up data

	Two-branch stenting (%)	One-branch stenting (%)	P
Men	67.3	59.6	NS
Tobacco use			NS
Never	37.7	34.6	
Yes, past	40.8	40.4	
Yes, current	21.5	25	
Age, years	68.8±11.2*	66.7±12.4*	NS
Body mass index, kg/m ²	29.1±5.5*	30.7±6.9*	NS
Previous PCI	65	57.7	NS
Previous CABG	14.6	21.2	NS
Previous myocardial infarction	39.6	30.8	NS
Family history of premature CAD	17.7	26.9	NS
Congestive heart failure	13.1	9.6	NS
Renal failure	5	5.8	NS
Peripheral vascular disease	18.1	11.5	NS
Hypertension	83.8	78.8	NS
Hyperlipidemia	67.7	67.3	NS
Diabetes	34.2	26.9	NS
Cerebrovascular disease	13.8	7.7	NS
Presentation			NS
NSTEMI	13.1	9.6	
STEMI	6.2	7.7	
Unstable angina	23.1	23.1	
Stable angina	37.7	40.4	
Atypical chest pain	0.4	1.9	
Asymptomatic	19.6	17.3	
Status of procedure			NS
Elective	65.8	65.4	
Urgent	25	23.1	
Emergent	9.2	11.5	
Success, side branch	94.8	94.4	NS
Success, main branch	98	100	NS
Type C lesion	27.4	36.5	NS
Angiographic thrombus	4.9	2.3	NS
Residual stenosis in main branch, mm	1.06±4.84*	0.83±4.04*	NS
Residual stenosis in side branch, mm	2.63±9.73*	6.5±13.39*	NS
Lesion length, mm	16.78±8.72*	16.83±7.79*	NS
Intraprocedural complications			NS
Dissection	3	2.3	
Perforation	0.5	2.3	
Acute closure	1.4	3.5	
Slow flow	0.9	2.3	
Distal embolization	0.5	0	
Outcomes on follow-up			
Target lesion revascularization	7.3	3.8	NS
Target vessel revascularization	13.5	5.8	NS
Acute stent thrombosis	1.2	1.9	NS
Death	6.5	3.8	NS

*Results presented as mean ± SD. CABG Coronary artery bypass graft surgery; CAD Coronary artery disease; NS Nonsignificant; NSTEMI Non-ST elevation myocardial infarction; PCI Percutaneous coronary intervention; STEMI ST elevation myocardial infarction

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