The impact of severe distal left main disease on target lesion revascularization in patients with trifurcating coronary artery disease receiving the paclitaxel drug-eluting stent

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BACKGROUND: The presence of severe left main (LM) disease has been shown to adversely influence the outcome of patients undergoing percutaneous treatment of bifurcating LM disease. LM trifurcating coronary artery disease (LMTCAD) is even more complex and challenging to treat. The present article reports on the immediate and midterm outcomes of patients with severe LM disease treated with the paclitaxel drug-eluting stent for LMTCAD.

METHODS: Consecutive patients (n=52) who underwent LM trifurcating stenting with the paclitaxel drug-eluting stent at the Genesis Medical Center (Iowa, USA) over a two-year period were divided into two groups: type A (with severe [50% or greater] LM involvement including trifurcating branches) and type B (with no LM involvement but involving the trifurcating branches). Demographic, clinical, procedural and midterm clinical outcomes were reviewed. Angiograms

were analyzed by an operator who was blinded to patient histories. The primary end point of the study was target lesion revascularization (TLR) on follow-up. Descriptive and univariate analyses were performed, and survival curves were plotted to compare the two groups.

RESULTS: Demographic and clinical variables were identical in both groups. Type A lesions required significantly more stents to treat than type B lesions (4.13 ± 1.78 versus 2.33 ± 1.22 ; $P=0.001$). The techniques to treat both lesions were considerably different, with more V stenting in type B and more Y stenting in type A. The TLR rate was 64.3% in type A versus 18.2% in type B ($P=0.005$). On follow-up, one patient with type B disease had sudden death, possibly related to stent thrombosis.

CONCLUSION: Severe LM disease has a significant adverse impact on TLR in patients with LMTCAD. Given the high TLR rate, bypass surgery needs to be considered as first-line therapy in patients with type A trifurcating coronary artery disease.

Key Words: Left main; Paclitaxel drug-eluting stent; Thrombosis; Trifurcating stent

Severe left main (LM) disease has been shown to negatively influence the outcome of patients undergoing LM bifurcating stenting, leading to higher target lesion revascularization (TLR) rates and adverse outcomes. Trifurcating coronary stenting is an even more complex percutaneous procedure that has been reported in a small series (1-6), with good acute procedural outcomes. However, a high need for repeat revascularization was reported on midterm follow-up. In one series by Shammass et al (3), in which 20 patients were treated with the paclitaxel drug-eluting stent (DES), the combined end point of death, acute stent thrombosis and TLR rate was 29.4%. Furuichi et al (5) noted a TLR rate of 20% in 15 trifurcating LM patients also receiving DESs. A previous classification of trifurcating LM disease (7) separated patients with severe LM disease (type A) versus those with trifurcating branch disease but no LM involvement (type B). It is unclear how the TLR is influenced by type A versus type B LM trifurcating disease.

In the present study, we report on our experience with 52 patients treated with the paclitaxel DES, who were analyzed based on the type of coronary artery disease present – type A versus type B (Figures 1A and 1B). To our knowledge, this is the first study to systematically examine the impact of LM involvement on the outcome of patients with LM trifurcating disease.

METHODS

Fifty-two consecutive patients who underwent LM trifurcating stenting with the paclitaxel DES at the Genesis Medical Center (Iowa, USA) from January 1, 2006, to December 31, 2007, were divided into type A and B groups based on LM involvement (Figure 1). A retrospective review of prospectively collected demographic, clinical and procedural data in the cardiac catheterization laboratory and a retrospective review of data from medical records were performed on all these patients. Follow-up was performed by telephone interviews. The Institutional Review Board approved the study.

A qualitative evaluation by an independent, experienced interventional cardiologist was performed for vessel size, the number of diseased vessels, the presence of calcium, the number of stents deployed, stenting technique (T, V, Y and single-vessel stenting as described in a previous study [7]; Figure 2), the use of double- or triple-kissing balloons, pre- and post-treatment lesion severity, the presence of embolization or dissection and thrombolysis in myocardial infarction (MI) flow. Procedural success was defined as a residual narrowing of less than 30% in all treated branches.

The definition of MI by The Joint European Society of Cardiology/American College of Cardiology Committee (8)

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Figure 1) Classification of trifurcating left main disease into type A (left main involved with the origin of trifurcating branches) (A) and type B (only the origin of the trifurcating branches involved) (B). MB Middle branch; MT Main trunk; SB Side branch. Reproduced with permission from reference 7

was used to diagnose ST elevation MI on preprocedure and follow-up. The primary end point of the study was TLR on follow-up. Secondary end points included target vessel revascularization, and acute stent thrombosis in hospital and on follow-up; the secondary end points were characterized as per the Academic Research Consortium definition (9) – total death, cardiac death and nonfatal MI. All events were adjudicated by an independent, experienced cardiologist.

Descriptive analysis was performed on all variables. Univariate analysis was performed to compare the angiographic, clinical and procedural variables between patients with type A versus type B lesions. SPSS software (SPSS Inc, USA) was used for analysis.

RESULTS

Demographic, procedural and clinical variables were identical in both groups (Tables 1 and 2). Using univariate analysis, the results showed that type A lesions required significantly more stents to treat than type B lesions (4.13 ± 1.78 versus 2.33 ± 1.22 ; $P=0.001$). The techniques to treat both lesions were also considerably different, with more V stenting in type B and more Y stenting in type A. The LM was angiographically larger in type B lesions than

Figure 2) Various techniques to treat left main trifurcating disease. Illustrated are T (A), Y (B) and V (C and D) techniques. MB Middle branch; MT Main trunk; SB Side branch. Reproduced with permission from reference 7

TABLE 1
Demographics and clinical variables

	Type A lesion (n=16)	Type B lesion (n=36)	P
Age (years), mean $\pm$ SD	67.63 $\pm$ 10.76	67.67 $\pm$ 13.62	NS
Male sex	87.5	69.4	NS
Body mass index, mean $\pm$ SD	30.4 $\pm$ 2.03	30.83 $\pm$ 5.21	NS
Previous bypass surgery	31.3	11.1	NS
Protected left main	18.8	8.3	NS
Previous myocardial infarction	6.3	27.8	NS
Family history of coronary artery disease	68.8	55.2	NS
Congestive heart failure	6.3	19.4	NS
Chronic lung disease	25	19.4	NS
Peripheral vascular disease	18.8	13.9	NS
Hypertension	75	80.6	NS
Cerebrovascular disease	12.5	13.9	NS
Diabetes mellitus	25	36.1	NS
Hyperlipidemia	93.8	83.3	NS
Past or current smoker	53.3	61.8	NS
Procedure status – elective	75	74.3	NS
Presentation – elective	71.4	55.9	NS

P < 0.05 is considered significant. Data are presented as % unless otherwise indicated. NS Not significant

type A lesions (4.29 ± 0.42 versus 4.0 ± 0.18 ; $P=0.01$). Simultaneous double- or triple-kissing balloons were used in all patients. Intravascular ultrasound was not used to guide stenting, and all patients received heparin as an anticoagulant.

Follow-up (Table 3) was longer in patients with type B lesions. Despite this, type A lesions showed an overall TLR rate of 64.3% versus 18.2% in type B lesions ($P=0.005$) on follow-up. Also, the target vessel revascularization rate was significantly higher in type A lesions (64.3% versus 30.3%; $P=0.05$). Overall, in-hospital outcomes were favourable. One patient, 89 years of age, died of acute renal failure. Another patient had definite acute stent thrombosis. One cardiac death

TABLE 2
Summary of procedural and angiographic variables

	Type A lesion (n=16)	Type B lesion (n=36)	P
Ejection fraction	60±17.8	54.44±14.88	NS
IVUS-guided procedure, %	0	0	NA
Stenting techniques, %			
V	12.5	77.8	0.001
Y	75	2.8	0.001
T	6.3	0	NS
S	6.3	19.4	NS
Simultaneous kissing balloons			
Triple-kissing balloons, %	60	27.6	NS
Double-kissing balloons, %	40	72.4	NS
Mean number of stents used per case	4.13±1.78	2.33±1.22	0.001
Embolization or slow flow, %	0	0	NA
Drug-eluting stents – paclitaxel, %	100	100	NA
On chronic Plavix* use preprocedure, %	56.3	77.8	NS
Anticoagulant during procedure – heparin, %	100	100	NA
Glycoprotein IIb/IIIa inhibitor use, %	0	2.8	NA
Side branch 1 (SB1) treatment variables			NS
SB1 size, mm	2.84±0.24	2.74±0.38	NS
SB1 restenotic lesions, %	0	21.7	NS
SB1 calcified lesion, %	62.5	47.2	NS
SB1 pretreatment lesion severity, %	68.85±17.58	59.81±29.03	NS
SB1 post-treatment lesion severity, %	0±0	3.2±11.08	NS
SB1 pressure dilation, mmHg	14±0.0	15.04±2.76	0.083
SB1 stent number used	1.46±0.78	1.33±0.87	NS
SB1 stent size used, mm	3.06±0.21	2.96±0.33	NS
SB1 stented length, mm	26.15±20.50	27.68±19.12	NS
Side branch 2 (SB2) treatment variables			
SB2 size, mm	2.78±0.41	2.79±0.38	NS
SB2 restenotic lesions, %	0	12	NS
SB2 calcified lesions, %	56.3	38.9	NS
SB2 pretreatment lesion severity, %	70.00±19.64	61.4±24.00	NS
SB2 post-treatment lesion severity, %	0±0	1.3±4.6	NS
SB2 pressure dilation, mmHg	14.71±2.67	15.52±3.66	NS
SB2 stent number used	1.53±0.83	0.96±0.48	0.024
SB2 stent size used, mm	3.0±0.4	3.1±0.4	NS
SB2 stented length, mm	28.29±16.66	16.63±10.85	0.072
Middle branch (MB) treatment variables			
MB size, mm	2.22±0.31	2.31±0.28	NS
MB restenotic lesions, %	0	0	NS
MB calcified lesions, %	50	33.3	NS
MB pretreatment lesion severity, %	71.33±15.52	70.52±22.85	NS
MB post-treatment lesion severity, %	2.14±5.79	0.37±1.92	NS
MB pressure dilation, mmHg	14.29±1.07	15.08±2.73	NS
MB stent number used	0.79±0.43	1.04±0.43	0.0825
MB stent size used, mm	2.59±0.30	2.66±0.23	NS
MB stented length, mm	13.45±6.01	17.74±11.04	NS
Main trunk (MT) treatment variables			
MT size, mm	4.0±0.18	4.29±0.42	0.011
MT restenotic lesions, %	0±0	0±0	NA
MT calcified lesions, %	56.3	25	NA
MT pretreatment lesion severity, %	71.88±20.07	–	NA
MT post-treatment lesion severity, %	0±0	–	NA
MT pressure dilation, mmHg	20.71±2.89	–	NA
MT stent number used	2.34±0.88	–	NA
MT stented length, mm	14.00±2.6	–	NA

P<0.05 is considered significant. *Bristol-Myers Squibb/Sanofi Pharmaceuticals, USA. LM is left main, SB1 is left anterior descending artery, SB2 is left circumflex, MB is ramus intermedius, MT is left main trunk. All continuous variables are expressed as mean ± SD. IVUS Intravascular ultrasound; NA Not applicable; NS Not significant

TABLE 3
In-hospital and outpatient outcomes

	Type A lesions	Type B lesions	P
In-hospital outcome (n=16 for type A, n=36 for type B)			
Renal failure	0	2.8	NS
Acute closure of successfully treated vessel	0	0	NS
Distal embolization	0	0	NS
Vascular access site complication	0	0	NS
ST elevation myocardial infarction (STEMI)	0	0	NS
Death*	0	2.8	NS
Definite stent thrombosis (ARC definition)	0	2.8	NS
Major bleeding	0	0	NS
Outcome on follow-up postdischarge (n=14 for type A, n=33 for type B)			
Follow-up rate	87.5	91.7	NS
Follow-up, days, mean ± SD	238.0±118.7	316.1±90.1	0.04
Target lesion revascularization	64.3	18.2	0.005
Target vessel revascularization	64.3	30.3	0.05
Probable cardiac death†	0	3	NS
Death	0	6.1	NS
Possible stent thrombosis (ARC definition)	0	3	NS
Non-STEMI nonfatal	0	0	NS
STEMI nonfatal	0	3	NS

P<0.05 is considered significant. Data are presented as % unless otherwise indicated. *An 89-year-old patient died of acute renal failure; †Unexplained sudden death after one month (same patient, with possible stent thrombosis – Academic Research Consortium [ARC] definition). NS Not significant

occurred out of hospital, presumably related to possible acute stent thrombosis (Academic Research Consortium definition).

Survival curves for the combined end point of TLR, cardiac death and nonfatal MI for type A and B lesions are shown in Figure 3. Type A lesions resulted in an overall higher combined end point of TLR, cardiac death and nonfatal MI than type B lesions (nine of 16 [56.3%] versus seven of 36 [19.4%]; *P*=0.02).

DISCUSSION

In the present study, we have shown that severe LM disease is a significant risk factor for TLR rate in patients undergoing trifurcating LM stenting with the paclitaxel DES. In our study, the location of LM type A disease was distal and extended into the ostium of the trifurcating branches. Distal LM involvement was shown to have a high rate of revascularization compared with ostial or mid-LM disease. Pavei et al (10) have shown that the presence of unprotected distal LM disease has an OR of 8.5 (95% CI 1.1 to 15; *P*=0.041) for TLR compared with nondistal bifurcating disease. In the Drug-Eluting Stent for the Treatment of Left Main Disease (DISTAL) study (11), distal bifurcating LM lesion was shown to be an independent predictor of major adverse events (HR=3.42, 95% CI 1.34 to 5.61; *P*=0.001) mostly driven by repeat TLR. Finally, Vecchio et al (12) reported a higher percentage of nonstent LM stenting in patients who died on follow-up after LM stenting (92.3% versus 66.3%; *P*=0.05, respectively). Our data support and extend the observation that type A distal trifurcating LM disease carries a higher rate of TLR compared with when the distal LM is not involved. No conclusions, however, can be made in patients with trifurcating branch disease because they were not represented in our cohort.

Figure 3) Survival curves showing freedom from the combined events of cardiac death, nonfatal myocardial infarction and target lesion revascularization in patients with type A (solid line) and type B (interrupted line) left main trifurcating disease undergoing percutaneous intervention with the paclitaxel drug-eluting stent

Similar to our previous report on trifurcating LM stenting (3) and that of Furuichi et al (5), trifurcating disease continues to have a high rate of TLR despite DES use. It is unknown how the TLR rate would be different with a nonpaclitaxel DES. Also, intravascular ultrasound was not used in our cohort, and its role remains unknown in treating trifurcating LM disease. At this time and based on our findings, type A trifurcating LM lesions are best treated with bypass surgery if this option is available to the patient.

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