Treatment of Left Main Coronary Trifurcation Lesions with the Paclitaxel Drug-Eluting Stent: Mid-Term Outcomes from a Tertiary Medical Center

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ABSTRACT: Background. Left main trifurcating coronary artery disease (LM T CAD) is a complex and challenging anatomy to treat percutaneously. We report on the immediate- and mid-term outcomes of 52 consecutive patients with LM T CAD treated with the Taxus® paclitaxel-eluting stent (PES) (Boston Scientific Corp., Natick, Mass.) in our center over a period of 2 years. Methods. All patients (n = 52) who underwent LM T CAD at our center in 2006–2007 and treated with the PES form the basis of this report. Demographic, clinical, procedural and in-hospital outcome variables were reviewed. Angiograms were analyzed by an operator blinded to the patients’ history. Mid-term follow up was achieved from medical records and/or phone calls. The primary endpoint of the study was either cardiac death, nonfatal myocardial infarction or target vessel revascularization (TVR) on follow up. Follow up was achieved in 47/51 patients (92.2%) at a mean of 292.8 ± 104.6 days. Patients were classified as Type A (30.8%) disease involving the LM and origin of branches, or Type B (69.2%) disease involving the origin of the trifurcation branches only, but not the LM artery. All patients were treated with kissing balloon after stenting. Descriptive analysis was performed on all variables with mean ± standard deviation for continuous variables and percentages describing dichotomous variables. Univariate and logistic regression analyses were performed to determine the predictors of the primary endpoint. Results. The mean patient age was 67.6 ± 12.7 years. The LM artery was unprotected in 88.5% of cases. On follow up, the primary endpoint was met in 34% of patients. TL R occurred in 31.9% of patients, and target vessel revascularization (TVR) in 40.4%. One patient had cardiac death (2.1%) 5 months after the index procedure, possibly related to acute stent thrombosis. By univariate analysis, Type A lesions (vs. type B; p = 0.02) and the placement of a greater number of stents (p = 0.044) correlated with a higher event rate. Logistic regression analysis showed that Type A lesions are the only independent predictors of the combined endpoint (p = 0.011). Conclusion. LM trifurcation stenting carries an overall high rate of adverse events, mostly driven by a high TL R rate. Type A lesions and the number of stents placed predicted a higher combined endpoint of death, nonfatal MI and TL R. By logistic regression analysis, Type A lesions are the only independent predictors of the primary outcome.

Key words: Trifurcation stent, left main, paclitaxel-eluting stent, thrombosis

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Left main (LM) trifurcation coronary stenting is a challenging and complex percutaneous procedure that has been reported in small series and case reports.1–9 A higher adverse event rate was described in these patients on long-term follow up. In a series of 20 patients treated with Taxus® paclitaxel-eluting stent (PES) (Boston Scientific Corp., Natick, Massachusetts), we previously reported a combined endpoint of death, acute stent thrombosis and target lesion revascularization (TLR) of 29.4%.6 Furuchi et al8 later reported a TLR rate of 20% in their series of 15 trifurcation LM lesions with drug-eluting stents (DES).8 We were able to identify approximately 50 patients reported in the literature who underwent percutaneous treatment for LM trifurcation coronary artery disease.1–9 LM trifurcation disease is typically treated surgically, particularly when the LM artery is involved, therefore its percutaneous treatment is generally reserved to high-volume centers performing complex coronary interventions.

In this study, we report our experience with an additional 52 patients treated with paclitaxel-eluting stents (PES) and present their mid-term outcomes. These were classified according to our previously published classification,10 allowing testing of the relevance of this classification in a larger series of patients. To our knowledge, this is currently the largest reported experience with LM trifurcation stenting using a PES in the literature with in-hospital and mid-term outcomes described.

Methods

Fifty-two consecutive patients who underwent LM trifurcation stenting with a PES at our institution from January 1, 2006 to December 31, 2007, were included. Two patients were treated with bare-metal stents during the same period and were excluded. These patients were prospectively identified from a database of patients undergoing cardiac angiography and percutaneous revascularization in the cardiac catheterization laboratory. This retrospective study was approved by the institutional review board at our center. All vessels were qualitatively evaluated by an independent, experienced interventional cardiologist for their size, presence of calcium, number of stents deployed, type of disease (Figure 1A or B), stenting technique used, use of double or triple kissing balloons, pre- and post-treatment lesion severity, and presence of dissection and embolization or thrombolysis in myocardial infarction...
(TIMI) flow. The classification of trifurcation disease and treatment methodology have been previously discussed in detail.\textsuperscript{10} Procedural success was defined as achieving a residual narrowing of < 30% in all branches treated. The Taxus PES was exclusively used in all patients.

Charts were all reviewed for clinical and demographic variables as well as the use of antiplatelet and anticoagulant agents periprocedurally. Dilatation pressures were recorded from the cardiac catheterization laboratory procedure log sheet. Patients with the admission diagnosis of myocardial infarction (MI) were diagnosed by serial cardiac enzymes prior to the procedure. A rapid rise and fall in creatinine kinase with abnormal MB fractions or a typical rise and gradual fall in troponin I with ischemic symptoms or electrocardiographic (ECG) changes was considered diagnostic for acute MI.\textsuperscript{11} Unfortunately, post-intervention CK and troponin I were not routinely ordered by the operators, thus the incidence of in-hospital non-Q wave MI post procedure cannot be accurately assessed. Only those patients with in-hospital acute ST-elevation MI (STEMI) secondary to acute stent thrombosis could be diagnosed using ECG and enzymatic criteria.

The primary endpoint of the study was the combined endpoint of cardiac death, nonfatal MI and target lesion revascularization (TLR) on follow up post hospital discharge. Follow-up data were obtained on 47/51 patients discharged alive (92.2%) from medical records and phone interviews (4 patients were alive and were reached, but refused to provide further information). Secondary endpoints included acute stent thrombosis in-hospital and on follow up and were characterized according to the Academic Research Consortium (ARC) definition:\textsuperscript{12} total death, cardiac death, STEMI and non-ST-elevation MI (NSTEMI). All events were adjudicated by an independent experienced cardiologist.

Descriptive analysis was performed on all variables included. Patients were divided into two groups: those who met the primary endpoint and those who did not. Using univariate analysis, these were compared for all angiographic, clinical and procedural variables. Logistic regression analysis with forward inclusion was also performed and included the following variables: age, gender, lesion type, lesion length, number of stents, pre- and post-treatment lesion severity, diabetes and vessel size. SPSS statistical software was utilized for analysis (SPSS, Inc., Chicago, Illinois).

Results

Patient demographics are included in Table 1. The procedure was performed urgently in 25.5% of patients. Patients had multiple comorbidities including hypertension (78.8%), diabetes mellitus (32.7%), past or current smoking history (59.2%), hyperlipidemia (86.5%) and prior bypass surgery (17.3%). The mean age was 67.6 ± 12.7 years. The majority of patients were male (75%). The LM artery was unprotected in 88.5% of cases. Approximately two-thirds (60.4%) of patients had stable symptoms on admission, and 39.6% had unstable angina or a NSTEMI. None of the patients admitted had STEMI. The procedure was performed urgently (within 24–48 hours of presentation) in 25.5% of patients.

A summary of angiographic and procedural variables are described in Table 2. Disease involving the trifurcation was classified into two main classes that have been previously published:\textsuperscript{10} Type A (30.8%), involving the main trunk with extension to one or more of the origin of the branches; Type B (69.2%), involving the origin of one or more of the main branches without extension to the main trunk (MT). LM trifurcation stenting was classified according to a previously published classification:\textsuperscript{10}

1. V-stenting (57.7%)
2. Y-stenting (25%)
3. T-stenting (1.9%)
4. Single-branch stenting (15.4%)

The acute procedural success was 100% in all vessels treated, including the main trunk (MT) and side branches (SB). Review of actual angiograms showed no distal embolization, slow-flow or dissections. In-hospital outcomes are described in Table 3. One patient had definite stent thrombosis (ARC definition) post procedure and was retreated successfully.

The follow-up duration was 292.8 ± 104.6 days. The primary endpoint was met in 16/47 (34%) patients. One out of

**Figure 1A.** Type A trifurcation disease.

**Figure 1B.** Type B trifurcation disease.
the 47 (2.1%) patients suffered sudden cardiac death 5 months after the procedure, with no autopsy performed. The same patient had a possible acute stent thrombosis (ARC definition). He was 47 years of age, hypertensive, nondiabetic, with dyslipidemia and a prior history of smoking. He had a history of MI, but no renal failure or known peripheral arterial disease. He presented with unstable angina and had Type B trifurcation LM disease. The patient was treated with the double V-stenting technique with simultaneous 3-balloon inflations in the trifurcation vessels. He received a total of 4 stents. His left anterior descending artery (LAD) and left circumflex artery (LCx) were treated with 3.5 mm stents and the ramus intermedius with a 2.5 mm stent. Kissing-balloon dilatation of all stents was performed simultaneously at 14 atm. He received heparin, but no glycoprotein (GP) IIb/IIIa inhibitor during the procedure. There was no intravascular ultrasound (IVUS) assessment of the lesions pre- or post treatment. The patient was on clopidogrel and aspirin chronically preprocedure and remained on oral clopidogrel 75 mg daily and oral aspirin 81 mg daily at follow up. It can be speculated that stenting of all trifurcation branches, the long cumulative lesion length (68 mm), and the lack of ultrasound guidance to verify stent apposition and full expansion might have contributed to the possible stent thrombosis.

A total of 15/47 (31.9%) patients underwent TLR. Target vessel revascularization (TVR) occurred in 19/47 (40.4%) patients, and no strokes occurred. Prior to the procedure, 83.8% of the patients were on maintenance clopidogrel (75 mg per day).
Table 3. In-hospital and out-patient outcomes.

<table>
<thead>
<tr>
<th>In-hospital outcome (n = 52)</th>
<th>1.9</th>
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<tbody>
<tr>
<td>Renal failure (n = 1)</td>
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<td>Acute closure of successfully treated vessel</td>
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<td>Distal embolization</td>
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<td>Vascular access site complication</td>
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<td>Periprocedural cardiac enzyme elevation meeting</td>
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<tr>
<td>ACC definition of Myocardial Infarction* (n = 7)</td>
<td>13.5</td>
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<tr>
<td>Death, noncardiac (n = 1)</td>
<td>1.9</td>
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<tr>
<td>Definite stent thrombosis (ARC definition)** (n = 1)</td>
<td>1.9</td>
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<tr>
<td>Major bleeding</td>
<td>0</td>
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<table>
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<tr>
<th>Outcome on follow up post discharge (n = 47)</th>
<th>292.8 ± 104.6</th>
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<tr>
<td>Follow-up rate; 1 hospital death censored (n = 47/51) (%)</td>
<td>92.2</td>
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<tr>
<td>Refused consent (n = 4/51) (%)</td>
<td>7.8</td>
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<tr>
<td>Mean follow up (n = 47) (days)</td>
<td>8.1</td>
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<tr>
<td>Target lesion revascularization (n = 15/47) (%)</td>
<td>31.9</td>
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<tr>
<td>Target vessel revascularization (n = 19/47) (%)</td>
<td>40.4</td>
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<tr>
<td>Cardiac death (n = 1/47) (%)</td>
<td>2.1</td>
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<tr>
<td>Death (n = 2/47) (%)</td>
<td>4.3</td>
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<tr>
<td>Acute stent thrombosis (%)</td>
<td>0</td>
</tr>
<tr>
<td>Possible (ARC definition) (n = 1/47)</td>
<td>2.1</td>
</tr>
<tr>
<td>N-STEMI – nonfatal (n = 0/47) (%)</td>
<td>0.0</td>
</tr>
<tr>
<td>STEMI – nonfatal (n = 1/47) (%)</td>
<td>2.1</td>
</tr>
<tr>
<td>Combined endpoint (cardiac death, nonfatal MI and TLR) (n = 16/47) (%)</td>
<td>34.0</td>
</tr>
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ARC = Academic Research Consortium; STEMI = ST-elevation myocardial infarction; TLR = target lesion revascularization; MI = myocardial infarction; ACC = American College of Cardiology

The remainder received their clopidogrel load of 600 mg on the day of the procedure. All patients received unfractionated heparin and < 2% of patients received GP IIb/IIIa inhibitors.

Univariate analysis showed that the combined endpoint occurred more in patients with type A lesions (56.2% vs. 19.4%; p = 0.02) and with patients who received more stents (3.6 ± 2.0 vs. 2.6 ± 1.4; p = 0.044). Logistic regression analysis with forward inclusion showed that type A lesion (OR 5.33, 95% CI 1.5–19.3; p = 0.011) was the only predictor of the occurrence of the primary endpoint. Type A lesion remained the same predictor when TLR was used as the only endpoint (OR 8.1, 95% CI 2.0–33.1; p = 0.004).

Discussion

LM trifurcation lesions are generally treated with bypass surgery. With the advent of DES, complex lesions including LM trifurcation disease, are now treated percutaneously, particularly in patients who refuse or at high risk for bypass. To our knowledge, this is the largest reported series of Taxus PES use in LM trifurcation stenting patients with long-term follow up.

In this retrospective series, the primary endpoint of cardiac death, nonfatal MI and TLR occurred in 34% of patients. This was mostly driven by a high TLR rate (31.9%). TVR was 40.4%, similar to a previously reported series, and indicates the rapid progression of native disease in these patients. One patient (1.9%) suffered sudden cardiac death possibly related to stent thrombosis. This is an overall favorable stent thrombosis rate considering that the average number of stents in these patients was 2.9 ± 1.6. This favorable thrombosis rate, despite the minimal use of GP IIb/IIIa inhibitors, is likely related to the use of a high-pressure (14.8 ± 3.2 mmHg) kissing-balloon technique in 84.6% of all patients and in 100% of patients who had > 1 vessel treated (13), as well as the high clopidogrel loading dose (600 mg) prior to the procedure in clopidogrel-naive patients.

In this study, the primary endpoint occurred in a greater number of patients with Type A lesions than Type B lesions (56.2% versus 19.4%; p = 0.02), and in patients who received more stents (3.6 ± 2.0 versus 2.6 ± 1.4; p = 0.044). Diabetes was not an independent predictor of the primary outcome. It is unclear whether this related to the overall small number of patients in the study or whether patients with diabetes have similar outcomes to nondiabetics with the use of the PES. Lesion length, number of stents used and stent length have also been reported to be predictors of major adverse events in high-risk coronary interventions with the use of DES. Furthermore, this study validates the previously published classification that separates trifurcation disease with (Type A) or without (Type B) LM disease. A higher adverse event rate is seen in Type A trifurcation lesions, leading one to conclude that a low threshold for surgical intervention rather than percutaneous treatment in these patients may be warranted. Unfortunately in this study, IVUS was not used to assess stent apposition and expansion, and therefore its impact on reducing TLR is unknown. Also, LM stenting was performed with the 3.5 mm Taxus stent that was available to us at the time and was postulated with a larger balloon. Whether the current 4 mm stent would have also reduced TLR remains unknown.

Conclusion

In conclusion, trifurcation stenting is technically feasible and offers a high procedural success rate. However, overall adverse events, particularly high rates of TLR and TVR with Type A lesions, are seen. At this time, we continue to recommend that PES stenting to treat trifurcation LM disease be reserved for patients who are at high risk for bypass surgery or refuse surgery.

Study limitations. This study is limited by its retrospective design. However, all patients with LM trifurcation disease were included and angiograms were independently reviewed by an experienced angiographer. The mid-term follow up on these patients also exceeded 90%. Also, angiographic restenosis cannot be determined from this study, as no systematic repeat angiography was performed on these patients. In addition, the incidence of patients with trifurcation LM disease who were sent for primary bypass surgery is unknown, and a comparative analysis between those who were treated with bypass versus the PES implantation cannot be made. We do expect, however, as recently seen in the
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the SYnergy between percutaneous coronary intervention with TAXus and cardiac surgery (SYNTAX) study\textsuperscript{19–20} that a higher TLR rate will be seen with DES treatment compared to bypass surgery. Although the overall rate of repeat revascularization (13.5\%) in SYNTAX appears significantly less than our TLR rate, SYNTAX included mostly bifurcation lesions and, to a lesser extent, trifurcation LMs. In our study, all patients had trifurcation lesions, more complex anatomy requiring more stents and longer overall treated lesion lengths. Finally, this study does not address the role of provisional stenting in trifurcation LM disease, an area that requires further study.

References

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20. Serruys P. SYNTAX trial end points in left main subset. TCT 2008; October 14, 2008; Washington, D.C.