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Acute and long term results of unprotected left main stenting using drug eluting stents

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Abstract

Background: *Most available data indicates that stenting for unprotected left main coronary artery disease (ULMCA) with drug-eluting stents (DES) is safe and effective. At present, surgery is considered the gold standard for optimal revascularization. The aim of this study was to evaluate the immediate and long term outcome of patients with ULMCA stenosis who underwent percutaneous coronary intervention (PCI) with DES implantation in a single center.*

Methods: *Coronary stents were implanted into ULMCA in 72 patients. Patients with a* de novo *≥ 50% diameter stenosis, or ≤ 4.0 mm² on intravascular ultrasound measurement of left main coronary artery were treated using 1.6 ± 1.2 DES per patient. ULM stenting was performed when coronary artery bypass grafting was considered at high surgical risk (mean EuroSCORE 7.1) and/or surgery was refused despite their physician's recommendation. Patients enrolled in the study underwent clinical evaluation one, six and 12 months after the procedure, and then annually. Coronary angiography was routinely performed at nine to 12 months from the index procedure and/or was clinically driven at any time. Acute and long term main adverse cardiac events (MACE) were assessed: cardiac death, myocardial infarction and additional target lesion or non-target lesion revascularization (TLR).*

Results: *Angiographic and clinical success of PCI was 100%. Complete revascularization was performed in all patients. Mean follow-up duration was 2.5 years ± 10 months with 3% mortality in the first 12 months and total MACEs in 30.6%. During follow-up, death occurred in four (5.5%) patients. Angiographic follow-up was performed in 59 (82%) patients and TLR occurred in 18.05% of treated lesions. One possible stent thrombosis was documented.*

Conclusions: *Considering the high surgical risk present in most of our patients, ULM stenting is feasible and safe with excellent immediate and mid-term results. Long term results seem to be encouraging, showing limited mortality and the total absence of definite or probable thrombosis.* (Cardiol J 2011; 18, 2: 165–170).

Key words: coronary artery disease, left main coronary disease, percutaneous transluminal coronary angioplasty

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Introduction

Significant unprotected left main disease (ULM) occurs in around 5% of patients with coronary artery disease [1, 2], with significant prognostic and therapeutic implications, as only coronary revascularization can provide long-term freedom from myocardial ischemia and is thus recommended in all suitable patients. Coronary artery bypass surgery (CABG) has been considered the standard therapy for patients with unprotected left main coronary disease (ULMD) in recent decades. However, several studies have demonstrated low in-hospital complications with elective left main stenting [3, 4]. Reduced periprocedural risks such as the need for emergency CABG, restenosis, and target lesion failure with bare metal stents compared to simple balloon angioplasty and afterwards with drug-eluting stents (DES) have raised the possibility of their use in more complex lesion subsets such as ULMD. DESs have been introduced into clinical practice in the last few years and have proved able to reduce the risk of restenosis; but the long-term outcome of these patients remains uncertain [5]. Follow-up data is particularly important in view of the potential consequences of either stent thrombosis or restenosis. At present, there is controversy as to whether these patients can be managed using an interventional strategy with an efficacy equal to that of surgery. Thus, the purpose of the present study was to review a single center experience on left main stenting. We evaluated procedural outcomes, techniques used, and clinical and angiographic follow-up.

Methods

Seventy two consecutive (3.9% of the total volume) stable or unstable (acute coronary syndrome — ACS) patients with ULMD treated with DES from July 2004 to September 2009 at our institution, were considered for analysis. EuroSCORE was used in order to identify high preoperative risk patients with symptomatic left main disease. ULMD was defined as a greater than 50% stenosis within the left main coronary artery without distal protection from previous bypass surgery. According to lesion location within the left main segment, patients were classified into groups. In Group A, the lesion was confined to the ostium or body of the left main, with at least 5 mm of angiographic insignificant disease between the distal lesion margin and the bifurcation. In Group B, the disease involved the bifurcation of the left main.

The types of stents used were: paclitaxel-eluting Taxus stents (Boston Scientific, Natick, Massachusetts, USA), sirolimus-eluting Cypher stents (Cordis, Miami Lakes, Florida, USA), zotarolimus-eluting Endeavor stents (Medtronic, Inc. NYSE: MDT, Minneapolis, Minnesota, USA) and everolimus-eluting Promus stents (Boston Scientific Corporation, Natick, Massachusetts, USA). Stent selection was based solely on availability or operator preference. Heparin, bivalirudin or a glycoprotein IIb/IIIa inhibitor were administered at the discretion of the operator. Prior to the procedure, all patients were loaded with either 300 or 600 mg clopidogrel and remained on a 75 mg dosage daily for at least 12 months. Aspirin 100 mg daily was also co-administered indefinitely.

Deaths were classified as either cardiac or non-cardiac. All deaths were considered to be of cardiac origin unless a clinical diagnosis or an autopsy proved the origin to be non-cardiac. Myocardial infarction (MI) was diagnosed by an elevation of creatine kinase two times the upper limit of normal, together with an increased MB fraction, in either the absence or presence of Q-waves. We appraised the incidence of stroke and heart transplantation, as well as stent thrombosis according to the Academic Research Consortium definitions. Functionally complete revascularization was defined as complete and successful treatment of all diseased vessels with reference diameter > 2.0 mm, serving a portion of viable myocardium. Procedural success was defined as residual stenosis of less than 25% associated with thrombosis in myocardial infarction (TIMI) flow grade III without death, MI or emergency bypass surgery prior to hospital discharge.

All patients gave written informed consent before participation in the study, and the protocol has been approved by our Institutional Ethics Committee.

Follow-up data was obtained by clinical evaluation at one month, six months, 12 months and subsequently once a year including control angiography between nine and 12 months, from index procedure. The study end-points were death, post-procedure MI, and target vessel revascularization (TVR) including target and non-target lesion revascularization. MI was defined as a CPK-MB elevation of three times the upper limit of normal during the initial hospitalization or follow-up. Stent thrombosis was defined according to established criteria [16]. Death included both cardiac and non-cardiac causes. QCA analysis was performed by the experienced and certified technicians of our cath lab, using Philips Integris BH 5000 (Philips, Eindhoven, The Netherlands) with updated software. Continu-

Table 1. Clinical characteristics.

Variable	72 pts
Age (years)	70 ± 12
Male	56 (73.6%)
Smoker	17 (23.6%)
Cholesterol	33 (45.8%)
Diabetes	10 (13.8%)
Family history	39 (54%)
Hypertension	39 (54%)
Chronic renal failure	4 (5.5%)
Previous CABG	16 (22%)
Previous PCI	14 (23.6%)
Previous myocardial infarction	25 (34.7%)
History of valve replacement	3 (4%)
LVEF (%)	51.6 ± 13.2
EuroSCORE	7.1 ± 4.5
EuroSCORE > 6	47 (65.2%)
Congestive heart failure	6 (8.3%)

CABG — coronary artery bypass grafting; LVEF — left ventricular ejection fraction; PCI — percutaneous coronary intervention

Table 2. Clinical presentation.

Variable	72 pts
Asymptomatic	2 (2.8%)
Stable angina	17 (23.6%)
Unstable angina and non-STEMI	51 (70.0%)
STEMI	1 (1.4%)
Cardiogenic shock	1 (1.4%)

STEMI — ST elevation myocardial infarction

ous variables were expressed as mean ± standard deviation of the mean, or as percentages. The Kaplan-Meier method was used for survival analysis, and computations were performed with SPSS 11.0 (SPSS, Chicago, Illinois, USA).

Results

Demographics and clinical presentation of the study population are shown in Table 1. The mean age was 70 ± 12 years; 56 (73.6%) patients were male. Ten (13%) patients were diabetic, and 14 (23.6%) had a previous percutaneous intervention. The mean ejection fraction was 51.6 ± 13.2. The mean EuroSCORE was 7.1 ± 4.5 and 47 (65.2%) patients had a EuroSCORE > 6. One patient had a diagnosis of cancer at the time of the index procedure. The most frequent clinical presentations were unstable angina or non-ST elevation myocardial infarction (NSTEMI), and the next most frequent was stable angina. Procedural characteristics are shown in Table 2. ULMD was limited to the ostium or shaft in 32 (44%) patients and involved predivisional segment or bifurcation in 40 (56%) patients. Femoral access was utilized in the majority of patients. An intra-aortic balloon pump was utilized in seven (9.7%) patients. Heparin anticoagulation was used in all patients. Glycoprotein IIb/IIIa inhibitor was used quite frequently in 41 (56.9%) patients. Procedures were intravascular ultrasound -guided in 18 (25.8%) patients. Most patients presented with a three vessel disease associated with LMD (40 pts, 55.5%). LM lesions were moderately calcified in 29 (40.0%) patients, eccentric in 42 (58.3%) patients, with TIMI III in the majority of patients (70 pts, 97.2%) (Table 3). ULMD was treated with 1.6 ± 1.2 stents per LM for a total of 126 DES. Cutting balloon was required in 18 (25.8%) patients. A total of 40 bifurcations (including 27 true bifurcations) was treated using the following techniques: mini crush, 15 (37.5%), T stenting, two (5%) and provisional stenting, 23 (57.5%). QCA results are shown in Table 4. Mean reference diameter, minimal lumen diameter and acute gain were respectively 3.58 ± 0.66 mm, 3.53 ± 0.35 mm and 2.09 ± 0.54 mm. Procedural success was achieved in all (100%) patients while clinical success occurred in 70 (96%) patients. Two patients had a NSTEMI during recovery, while no other complication occurred in hospital. A clinical evaluation was achieved in all patients, while an angiographic follow-up was performed on 59 (82%) patients (Table 5). Mean follow-up

Table 3. Angiographic findings.

Variable	72 pts
LM	3 (4.1%)
LM + 1 VD	4 (5.6%)
LM + 2 VD	25 (34.7%)
LM + 3 VD	40 (55.5%)
A	3 (4%)
B	3 (4%)
B_2	31 (43.0%)
C	35 (48.6%)
Ca^{++}	29 (40.0%)
Eccentric	42 (58.3%)
TIMI 3	70 (97.2%)
TIMI 2	1 (1.4%)
TIMI 1	1 (1.4%)

LM — left main; VD — vessel disease; Ca^{++} — calcification; TIMI — thrombolysis in myocardial infarction

Table 4. QCA analysis after percutaneous coronary intervention.

	Main vessel	Side branch
Mean reference diameter [mm]	3.58 ± 0.66	2.97 ± 0.50
Minimal lumen diameter [mm]	3.53 ± 0.35	2.74 ± 0.53
Acute gain [mm]	2.09 ± 0.54	0.42 ± 0.71
Stent length [mm]	23.5 ± 18.8	16.4 ± 4.3
Stenosis (%)	9.7 ± 5.5	12.2 ± 4.7

Table 5. QCA analysis at follow-up. Angiographic follow-up in 59 (82%) patients

	Main vessel	Side branch
Mean reference diameter [mm]	3.38 ± 0.66	2.64 ± 0.58
Minimal lumen diameter [mm]	3.36 ± 0.63	2.30 ± 0.54
Stenosis (%)	19.4 ± 11.7	34.2 ± 23.0
Late loss [mm]	0.39 ± 0.56	0.44 ± 0.58
Restenosis	5 (6.9%)	10 (13.8%)

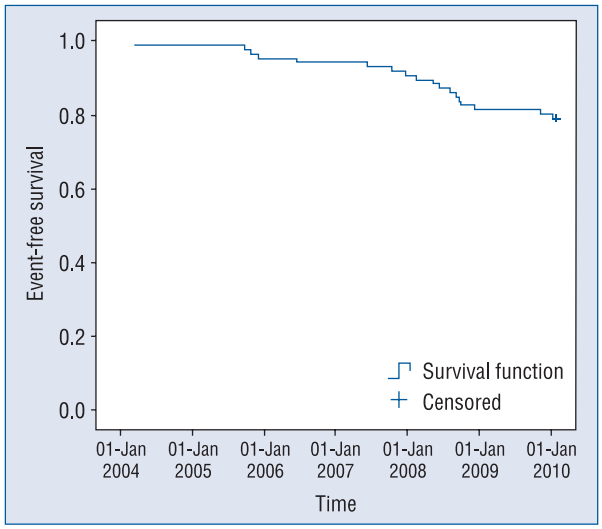

Figure 1. Kaplan-Meier analysis depicting event-free survival.

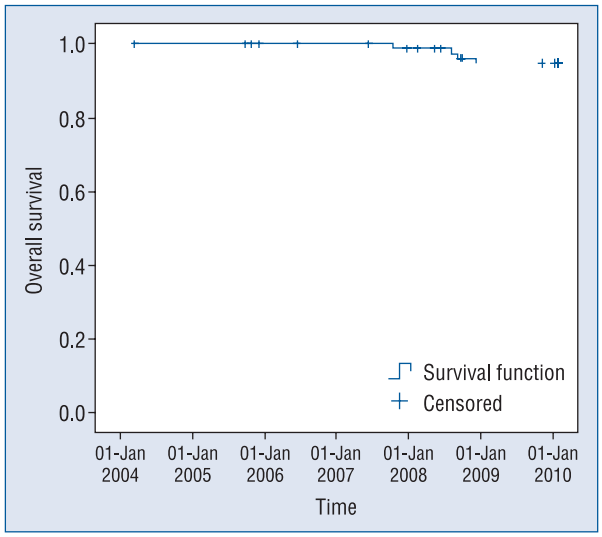

Figure 2. Kaplan-Meier analysis depicting overall survival.

was 2.5 years ± 10 months. Total major adverse cardiac events (MACE) occurred in 22 (30.5%) patients. Overall event-free survival (69.5%) is shown in Figure 1. During the first 12 months after index procedure, free of death survival reached 97%, shaped by two non-cardiac deaths. Overall cardiac and non-cardiac death occurred in four (5.5%) patients (Fig. 2). One patient died of throat cancer, a second patient had a post-traumatic cerebral hemorrhage and secondary exitus, and a third died of progressively deteriorated end stage renal failure. Finally, a fourth patient died suddenly 24 months after the index procedure. This was considered as a possible stent thrombosis. Five (6.9%) patients had a NSTEMI without further complication (Fig. 3). Overall TVR, including target lesion revascularization, was 14.2%. No CABG was required during follow-up. Furthermore, quantitative coronary angiographic (QCA) analysis during angiographic follow-up showed no significant variation of MLD (3.36 ± ± 0.63 mm) with a mean late loss of 0.39 ± 0.56 mm.

Discussion

The salient finding of our study is that PCI of ULMD using DES in patients not eligible for CABG is a safe and effective option. This message concords with that of previous large studies [1, 3, 4], indicating that PCI could be considered as a sound alternative to CABG with respect to ULMD, in carefully selected patients. In fact, there are voices calling for reconsideration of the current indications regarding PCI for ULMD with favorable characteristics, possibly altering the standard clinical practice.

Moreover, most clinical follow-up is to date still limited at the mid-term threshold; thus, results from randomized trials comparing percutaneous versus surgical revascularization are still needed to establish the role of percutaneous DES implantation in the evi-

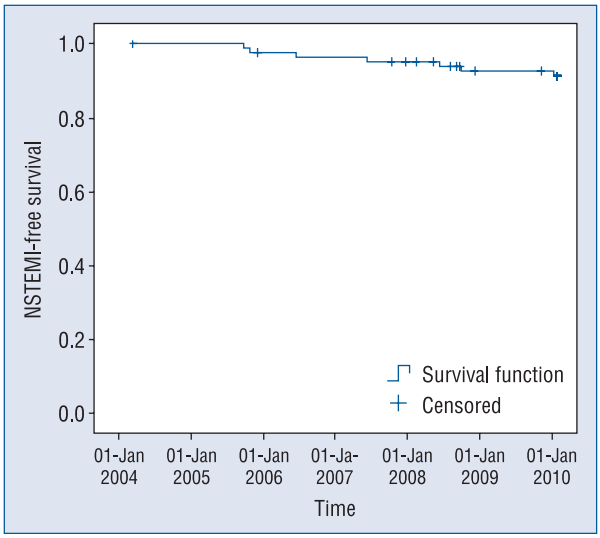

Figure 3. Kaplan-Meier analysis depicting NSTEMI-free survival.

dence-based medicine hierarchy, in comparison with the reference treatment, i.e. surgery, especially given recent concerns about late stent thrombosis.

ULMD is present in 5% of patients undergoing coronary angiography [6] and has been, for decades, a strict indication for CABG. Since DES approval [5], their use has been not only limited in patients with ULM at very high surgical risk, but also expanded in those with more favorable lesion characteristics [7]. Although most reports represented small, single-center experiences, with obvious limitations in external validity, the available evidence on patient selection and risk stratification in patients undergoing PCI with DES for ULM has already established that non-bifurcational ULMD is associated with a more favorable prognosis than distal ULM. However, whether surgery should be the first-line treatment even for non-bifurcational ULMD remains a topic for debate [8]. Recent studies have led to an overall reappraisal of the long-term safety of DES [9] given the likely increase in stent thrombosis, and this has had even greater implications on DES-based PCI for ULM. The beneficial impact of DES over BMS in these lesions is clearly shown in the available controlled studies. Indeed, in-stent restenosis has been called into question as a potential cause of acute coronary syndromes in unspecified lesions, but in ULM restenosis, it is recognized as a potential cause of sudden cardiac death or MI. Thus, the antiproliferative action of DES is of paramount importance in ULM lesions, and to date, DES should probably be recommended whenever PCI for ULMD is planned.

This is a single-center study regarding ULMD stenting. Events were both cardiac and secondary to comorbid conditions in these patients with increased surgical risk. The 4% incidence of in-hospital complications with two NSTEMI is consistent with other reports demonstrating that ULM stenting can be performed with few periprocedural complications [10–18]. However, there was a substantial incidence of late adverse events in the present study, and overall event-free survival was 70% at a mean period of 2.5 years. Overall mortality at 30 months was 6.1% with three non-cardiac deaths. No definite or probable stent thrombosis was documented. It should be emphasized that the study population did have increased surgical risk. Sixty-two percent had a EuroSCORE > 6, which corresponds to an expected 30-day operative mortality of between 10% and 12%, and the mean EuroSCORE was 7.1 ± 4.5 for the entire cohort [19, 20]. Surgical risk was increased primarily due to comorbid conditions, as opposed to left ventricular dysfunction, since resting mean ejection fraction was 51.6 ± 13.2%. Thus, the overall event-free survival was at least in part caused by comorbid conditions. The final results of this study will ultimately be necessary to answer questions regarding the efficacy of left main stenting. In the meantime, most experts recommend a cautious approach. ULMD remains a Class I indication for CABG, and stenting should be performed only in patients with definitely increased surgical risk, or serious comorbid illnesses limiting life expectancy [21]. The most important limitation of the present study is that it is a single-center, retrospective, observational work, performed on a somewhat selected population. Thus, the results and conclusions must be interpreted with caution, and not generalized from.

Conclusions

Despite a high in-hospital procedural success rate with ULM stenting using DES, a substantial number of adverse events occurred during the follow-up period in our study. Events occurred with greater frequency in bifurcation groups as compared to ostial or mid-shaft lesions. Pending definitive data from randomized ULMD trials in broader cohorts, ULM stenting should be reserved for patients who are not appropriate surgical candidates.

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