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# Early and Long-Term Results of Unprotected Left Main Coronary Artery Stenting

## The LE MANS (Left Main Coronary Artery Stenting) Registry

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**Objectives** The aim of the study was to evaluate early and late outcomes after percutaneous coronary intervention (PCI) of unprotected left main coronary artery disease (ULMCA) and to compare bare-metal stent (BMS) and drug-eluting stent (DES) subgroups.

**Background** PCI is an increasingly utilized method of revascularization in patients with ULMCA.

**Methods** This multicenter prospective registry included 252 patients after ULMCA stenting enrolled between March 1997 and February 2008. Non–ST-segment elevation acute coronary syndrome was diagnosed in 58% of patients; ST-segment elevation myocardial infarction cases were excluded. Drug-eluting stents were implanted in 36.2% of patients.

**Results** Major adverse cardiovascular and cerebral events (MACCE) occurred in 12 (4.8%) patients during the 30-day period, which included 4 (1.5%) deaths. After 12 months there were 17 (12.1%) angiographically confirmed cases of restenosis. During long-term follow-up (1 to 11 years, mean 3.8 years) there were 64 (25.4%) MACCE and 35 (13.9%) deaths. The 5- and 10-year survival rates were 78.1% and 68.9%, respectively. Despite differences in demographical and clinical data in favor of BMS patients, unmatched analysis showed a significantly lower MACCE rate in DES patients (25.9% vs. 14.9%, $p = 0.039$). This difference was strengthened after propensity score matching. The DES lowered both mortality and MACCE for distal ULMCA lesions when compared with BMS. Ejection fraction <50% was the only independent risk factor influencing long-term survival.

**Conclusions** Stenting of ULMCA is feasible and offers good long-term outcome. Implantation of DES for ULMCA decreased the risk of long-term MACCE, and particularly improved survival in patients with distal ULMCA disease. (J Am Coll Cardiol 2009;54:1500–11) © 2009 by the American College of Cardiology Foundation

Unprotected left main coronary artery (ULMCA) disease occurs in 3% to 5% of patients with coronary artery disease and is the subject of intense investigation. Present guidelines consider this finding a major indication for coronary artery bypass grafting (CABG) (1) based mostly on the CASS (Coronary Artery Surgery Study) (2) and ECSS (European Coronary Surgery Study) trials (3). These trials showed that in comparison with medical therapy, CABG improves survival in patients with ULMCA during a 5-year follow-up period. However, these benefits diminish after 10- and 15-year follow-up with a mortality rate of over 50% with both treatment strategies (4–6).

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On the other hand, recent studies suggest that percutaneous coronary intervention (PCI) in this lesion subset is a feasible alternative offering similar results when compared with surgical revascularization (7,8). The use of bare-metal stents (BMS) in comparison to balloon angioplasty has lowered the incidence of

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abrupt vessel closure, whereas drug-eluting stents (DES) have significantly decreased the risk of restenosis and major adverse cardiovascular and cerebral events (MACCE) (7,9–11). As a result, after years of procedural improvements, left main coronary artery (LM) stenting has been proven to be safe and to offer a good midterm outcome. However, there are no data concerning longer (5- to 10-year) follow-up periods, especially with the use of DES.

Therefore, the aim of this study was to evaluate early and long-term results of ULMCA stenting with BMS and DES, as well as to indicate independent risk factors influencing mortality and incidence of MACCE.

## Methods

This is a prospective registry of 314 consecutive patients with significant stenosis (>50% diameter) of the LM treated with stent implantation between January 1997 and March 2008 at the Upper Silesian Heart Center, Katowice, and the 1st and 3rd Department of American Heart of Poland in Ustron and Dabrowa Gornicza, Poland.

We excluded patients with ST-segment elevation myocardial infarction (n = 20), completely occluded LM, and/or with at least 1 patent graft to the left anterior descending or circumflex artery (n = 42). Patients with both single and multiple lesions in 1 to 3 vessels were included. After meeting inclusion/exclusion criteria, 252 patients qualified for further analysis (Fig. 1).

The admission diagnosis was non–ST-segment acute coronary syndrome (NSTE-ACS) in 152 (60.3%) patients and stable angina in 100 (39.7%) patients. Within the NSTE-ACS group, 60 (39.4%) patients had non–ST-segment elevation myocardial infarction and 92 (60.5%) patients had unstable angina (Table 1).

The study population mean age was 68.5 ± 12 years. Diabetes mellitus was present in 61 (24.2%) patients. Mean cardiac surgery risk according to EuroSCORE (12) was 6 ± 2.8. Occurrence of distal LM stenosis was 59% (Table 1).

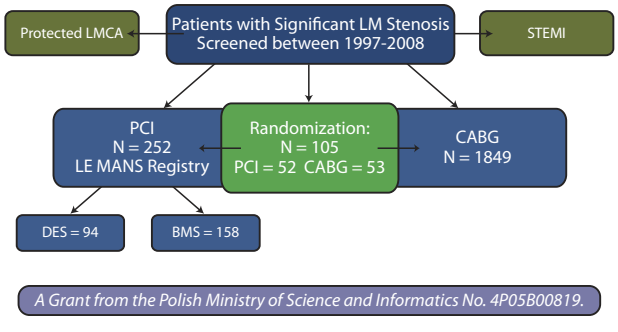


**Figure 1** The LE MANS Study Algorithm

The LE MANS algorithm is from Buszman et al. (24) but is based on new data. BMS = bare-metal stent(s); CABG = coronary artery bypass grafting; DES = drug-eluting stent(s); LMCA = left main coronary artery; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

PCI was a preferred strategy over CABG surgery because of anatomical suitability for PCI (n = 88; 34.9%), high surgical risk according to EuroSCORE of more than 6 (n = 132; 52.4%), or patient preference (n = 32; 12.7%). Anatomical suitability was defined as proximal and/or shaft noncalcified LM lesions with high vessel diameter (>3.5 mm). All decisions to withhold from CABG were based on consensus between the surgeon and interventionalist.

**Percutaneous revascularization.** In the majority of cases, direct stenting was the preferred technique, except in critical and calcified lesions, which were predilated with a small balloon (2.0 to 2.5 mm). For distal LM stenosis, stenting across the bifurcation toward the left anterior descending artery was performed first, followed by plain old balloon angioplasty and provisional stenting of the circumflex artery with T-stenting or a culotte technique per operator preference. Post-dilation with kissing balloon angioplasty was consistently used to complete the distal LM stenting procedure (Table 2). Between 1997 and 2001, exclusively BMS were used for all cases. After that time, DES were recommended for the LM with a reference diameter <3.8 mm, and BMS were implanted if the LM reference diameter was ≥3.8 mm. In

**Abbreviations and Acronyms**

**BMS** = bare-metal stent(s)
**CABG** = coronary artery bypass grafting
**CI** = confidence interval
**DES** = drug-eluting stent(s)
**LM** = left main coronary artery
**LVEF** = left ventricular ejection fraction
**MACCE** = major adverse cardiovascular and cerebral event
**NSTE-ACS** = non–ST-segment acute coronary syndrome
**OR** = odds ratio
**PCI** = percutaneous coronary intervention
**TLR** = target lesion revascularization
**ULMCA** = unprotected left main coronary artery

**Table 1** Demographic and Clinical Data, LE MANS PCI (n = 252)

| | |
|---|---|
| Male | 173 (68.6%) |
| Age (yrs) | 68.5 ± 12 |
| DM | 61 (24.2%) |
| Arterial hypertension | 193 (76.6%) |
| Hypercholesterolemia | 145 (57.5%) |
| Smoking | 105 (41.7%) |
| COPD | 24 (9.5%) |
| Peripheral artery disease | 63 (25%) |
| Previous MI | 113 (44.8%) |
| Previous PCI | 79 (31.3%) |
| Previous CABG | 18 (7.1%) |
| LVEF (%) | 48.6 ± 7 |
| NSTE-ACS | 152 (60.3%) |
| Unstable angina | 92 (60.5%) |
| NSTEMI | 60 (39.4%) |
| EuroSCORE | 6.0 ± 2.8 |

CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NSTE-ACS = non–ST-segment elevation acute coronary syndrome; NSTEMI = non–ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention.

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**Table 2** Angiographic and Procedural Data, LE MANS PCI (n = 252)

| | |
|---|---|
| Angiographic characteristics | |
| Isolated LM | 13 (5.6%) |
| LM with 1-vessel disease | 51 (20.2%) |
| LM with 2-vessel disease | 105 (41.6%) |
| LM with 3-vessel disease | 83 (33%) |
| Distal LM involvement | 149 (59%) |
| No. of diseased vessels | 2 ± 0.9 |
| PCI data | |
| Direct stenting of LM | 204 (81%) |
| Stent length in LM (mm) | 15.9 ± 5.7 |
| Stent diameter in LM (mm) | 3.7 ± 0.7 |
| Distal LM stenting | 149 |
| POBA side branch | 76 (51%) |
| T-stenting | 30 (20.1%) |
| Culotte technique | 43 (28.9%) |
| Kissing post-dilation of distal LM | 149 (59%) |
| DES for LM | 94 (37%) |
| PES | 60 (63.8%) |
| LES | 34 (36.2%) |
| BMS for LM | 158 (63%) |
| Total no. of implanted stents | 1.84 ± 0.8 |
| Complete revascularization | 196 (78%) |

BMS = bare-metal stent(s); DES = drug-eluting stent(s); LES = limus-eluting stent(s); LM = left main coronary vessel; PES = paclitaxel-eluting stent(s); POBA = plain old balloon angioplasty; other abbreviations as in Table 1.

total, BMS were used in 158 patients and DES in 94 (37.3%). Within the DES group, paclitaxel-eluting stents were used in 60 (63.8%) patients, whereas limus analogue-eluting stents were used in 34 (36.2%) patients (Table 2). The results of baseline and post-procedure quantitative coronary analysis are presented in Table 3.

An intra-aortic balloon pump was applied in 6.3% of patients with complex LM lesion and significantly depressed left ventricular function (left ventricular ejection fraction [LVEF] <30%). Intravenous glycoprotein IIb/IIIa blockers (abciximab or eptifibatide) were administered in 24% of the cases. Unfractionated heparin was used during the procedure to maintain an activated clotting time between 300 and 400 s or between 200 and 300 s for patients treated with glycoprotein IIb/IIIa blockers.

**Table 3** Quantitative Coronary Analysis

| | |
|---|---|
| Baseline | |
| Vessel reference (mm) | 3.63 ± 0.79 |
| Baseline MLD (mm) | 1.43 ± 0.63 |
| DS (%) | 60.82 ± 13.04 |
| Lesion length (mm) | 7.01 ± 3.57 |
| Post-procedure | |
| Reference (mm) | 3.92 ± 0.73 |
| MLD (mm) | 3.43 ± 0.86 |
| DS (%) | 9.22 ± 6.97 |

Values are mean ± SD.
DS = diameter stenosis; MLD = minimal lumen diameter.

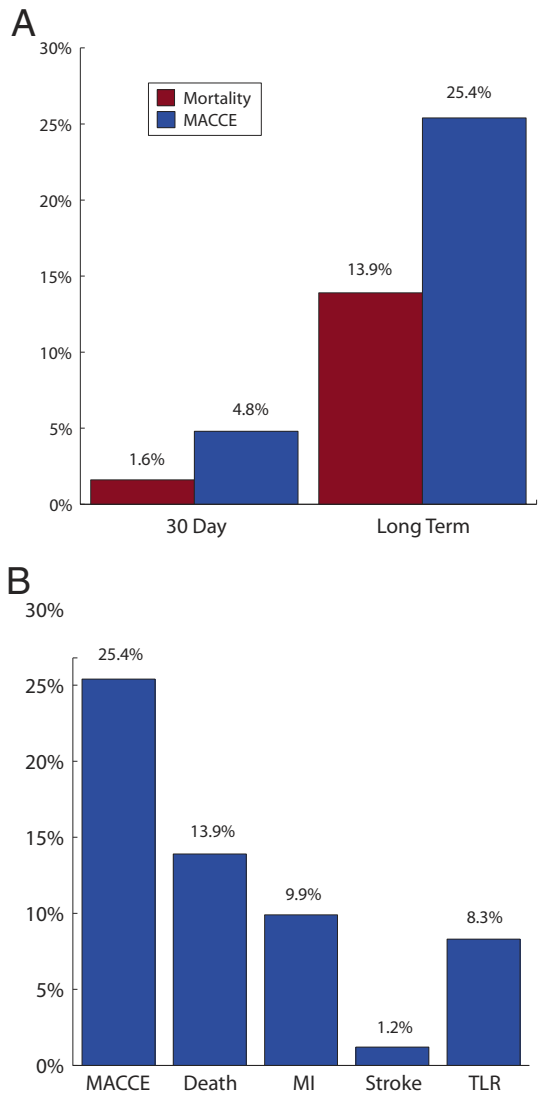


**Figure 2** Early and Long-Term Results for the Whole Study Group

**(A)** Mortality and major adverse cardiovascular and cerebral events (MACCE) at 30-day and long-term follow-up. **(B)** The incidence of MACCE, myocardial infarction (MI), stroke, and target lesion revascularization (TLR) at long-term follow-up.

Angiographic success was defined as LM residual stenosis <30%, minimal lumen diameter ≥3 mm, Thrombolysis In Myocardial Infarction flow grade 3, and no dissection. The definition of clinical success included angiographic success and death/myocardial infarct/stroke free in-hospital outcome.

**Antiplatelet regiment and concomitant pharmacological treatment.** Aspirin (300-mg initial dose, followed by 150 mg daily) was ordered in all patients indefinitely. In the first cohort of patients (treated between 1997 and 2001), ticlopidine was administered at least for 3 months, whereas in the later group clopidogrel (300- to 600-mg initial dose and 75 mg daily after completion of the procedure) was main-

tained for at least 12 months. The clopidogrel loading dose was given to all patients before the procedure, except in emergency cases, in which it was administered during or right after the intervention. After 1, 2, and beyond 2 years, 55.2%, 20.7%, and 16.6% of patients, respectively, were on double antiplatelet therapy.

Other pharmacological treatments (e.g., statins, angiotensin-converting enzyme inhibitors, beta-blockers) were recommended based on current practice and were left to the discretion of a supervising physician.

**Follow-up.** Six months after the index procedure, patients were scheduled for control coronary angiography. The long-term follow-up data (1 to 11 years, mean 3.8 years) were collected either by telephone through conversation with the patient or a relative, or during the ambulatory visits. Information on any adverse event (including cardiac and noncardiac death, myocardial infarction, stroke, or repeated revascularization) was confirmed with hospital discharge files where the adverse event took place and was analyzed by the Clinical Events Committee. The records of death were updated with the National Health System registry and Central Registry of Citizens. Eight patients were lost to follow-up.

**Study end points.** The primary end point of this study was the late incidence of any death in the whole study group; MACCE in the whole study group and within the subgroup

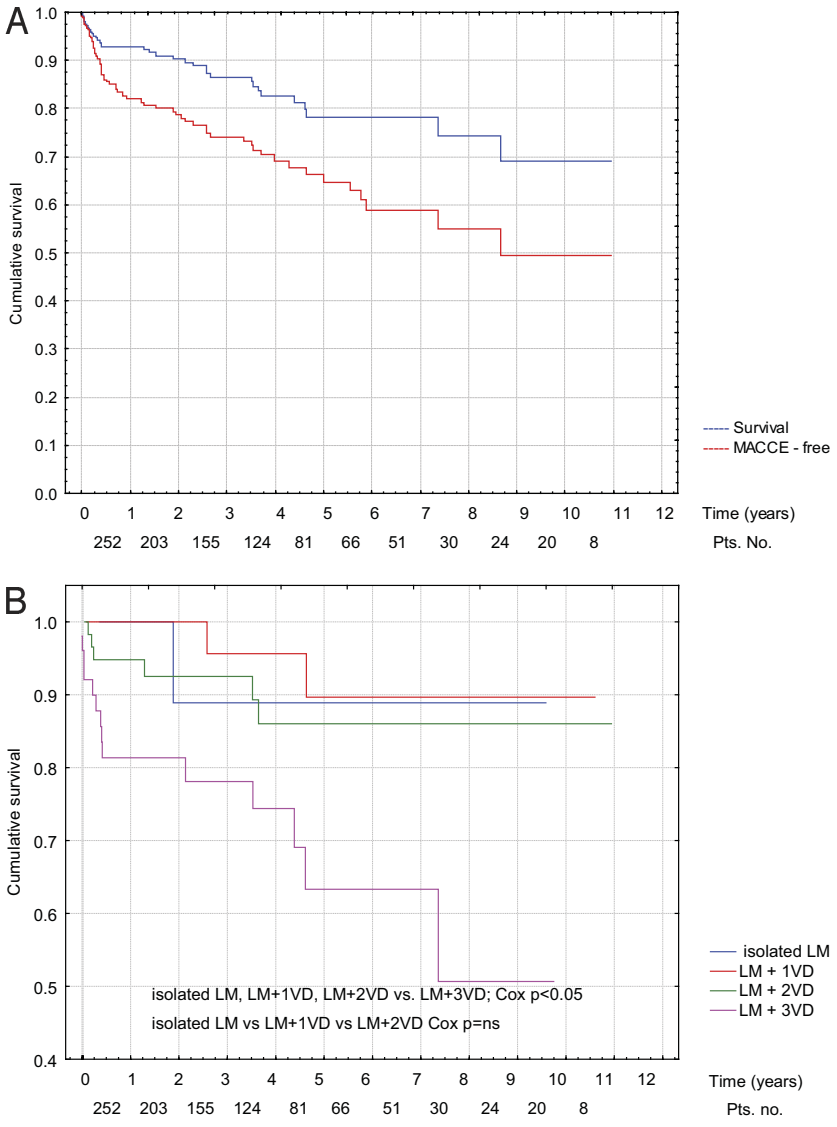


**Figure 3** Kaplan-Meier Survival Curves

**(A)** Survival and major adverse cardiovascular and cerebral event-free (MACCE) survival curves for the whole study group. **(B)** Survival in subgroups with isolated left main (LM) and LM with 1-, 2-, and 3-vessel disease (VD).

of patients with DES and BMS were considered secondary study objectives.

A MACCE was defined as death of any cause, myocardial infarction, stroke, target lesion revascularization (TLR), or acute stent thrombosis. Death was considered either cardiac or noncardiac. Deaths that could not be classified were considered cardiac. Myocardial infarction was defined as elevation of total creatine kinase 3 times above the upper limit of normal with a positive MB fraction. A TLR was defined as any revascularization in the treated segment within LM, or if distal LM was stented, in related proximal segments of left anterior descending and circumflex arteries. The incidence of stent thrombosis was evaluated in accordance with the Academic Research Consortium Dentitions of Stent Thrombosis (13).

**Safety and ethics.** The study protocol was approved by the Ethics Committee at the Medical University of Silesia. The PCI procedures were carried out by experienced interventional cardiology teams in high-volume centers (more than 1,000 PCIs per year in 1 center, with 300 interventions per operator) with cardiac surgery back-up on site or within 60 min of emergency transportation. All interventionalists underwent special training in LM stenting, based on the LE MANS protocol.

**Statistical analysis.** Parametric data were expressed as the mean ± SD, whereas nonparametric data were expressed as n (%). Group comparisons of parametric variables were performed using unpaired Student *t* tests. Nonparametric variables were compared using chi-square or Fisher exact tests. All tests were 2-sided. Survival curves were estimated using Kaplan-Meier analysis. Log-rank and Cox tests were performed for comparison of the survival curves between the treatment arms.

Because of the nonrandomized nature of the study, a propensity score analysis was performed to adjust for differences in demographical and procedural data in groups receiving DES and BMS. A multiple logistic regression model predicting DES assignment contained all covariate data categories. The resulting propensity scores were matched using the nearest available Mahalanobis metric matching within calipers (0.25 × propensity score mean). The resulting standardized difference was calculated for all baseline covariates. The single risk factors influencing early and long-term survival were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). The Cox proportional hazard model was used for multivariate analysis of independent risk factors**.** All statistical analyses were performed using SAS version 9.1 (SAS Institute Inc., Cary, North Carolina), Statistica version 6.0 (Statsoft Inc., Tulsa, Oklahoma) and Matlab using MATLAB (R2008a, The Mathworks, Natick, Massachusetts).

## Results

**Early outcomes.** Angiographic success was obtained in 98%, and clinical success was obtained in 95%. Within the 30-day period after the index procedure, MACCE were observed in 12 (4.8%) patients, including: 4 (1.6%) deaths, 9 (3.6%) myocardial infarcts, and 2 (0.8%) angiographically confirmed acute stent thromboses treated with balloon angioplasty (Fig. 2). Complete revascularization was obtained in 60% of patients during the index procedure and in an additional 18% in the second and third stage. The mean hospitalization period was 7 ± 5.8 days. The subacute stent thromboses occurred in 1 case (0.4%).

The univariate analysis showed that LVEF <30% (OR: 21.8, 95% CI: 2.19 to 216, p = 0.0002) and EuroSCORE >12 (OR: 30.8, 95% CI: 3.07 to 308) were the single risk factors influencing early survival.

**Mid-term and late outcomes.** Based on a 12-month observation, 1-year total and MACCE-free survival were 92.8% and 81.5%, respectively. One hundred forty-one patients (56%) underwent control coronary angiography 6 to 12 months after the index procedure, which detected 17 (12.1%) cases of

**Table 4** Demographic, Clinical, and Procedural Data in DES and BMS Subgroups

| | DES (n = 94) | BMS (n = 158) | p Value |
|---|---|---|---|
| Age (yrs) | 64.0 ± 10.3 | 65.1 ± 10.8 | 0.45 |
| Male | 59 (62.8) | 114 (72.2) | 0.10 |
| DM | 29 (30.9) | 32 (20.3) | 0.06 |
| Hypertension | 74 (78.7) | 119 (75.3) | 0.59 |
| Hypercholesterolemia | 56 (59.6) | 89 (56.3) | 0.70 |
| Smoking | 40 (42.6) | 65 (41.1) | 0.97 |
| EuroSCORE (additive) | 6.8 ± 3.9 | 5.6 ± 3.8 | 0.01 |
| CCS classification | 3.5 ± 0.9 | 3.3 ± 0.9 | 0.14 |
| NSTE-ACS | 65 (69.1) | 86 (54.4) | 0.04 |
| LVEF (%) | 49.3 ± 12.8 | 48.4 ± 12.9 | 0.61 |
| Distal LM involvement | 68 (72.3) | 81 (51.3) | 0.001 |
| Stent diameter (mm) | 3.4 ± 0.5 | 3.7 ± 1 | 0.01 |
| No. of diseased vessels | 2.1 ± 0.8 | 2.0 ± 0.9 | 0.43 |
| No. of lesions except LM stenosis | 1.5 ± 1 | 1.4 ± 1 | 0.4 |

Values are mean ± SD or n (%).
CCS = Canadian Cardiovascular Society; other abbreviations as in Table 2.

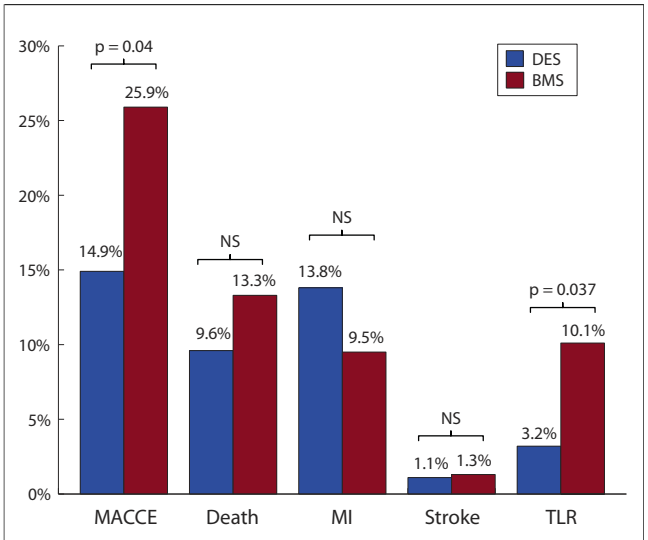


**Figure 4** **Long-Term Unadjusted DES Versus BMS Results**

Mortality and MACCE in DES and BMS groups.
Abbreviations as in Figures 1 and 2.

in-stent restenosis within the LM. For the vessels larger than 3.8 mm, the restenosis rate was only 6.1%.

The mean long-term follow-up was 3.8 years (range 1 to 11 years, median 38.6 months). There were 35 deaths (13.9%), of which 28 (11%) were considered cardiac. A MACCE occurred in 64 (25.4%) patients, which included 25 (9.9%) myocardial infarcts, 3 (1.2%) strokes, and 21 (8.3%) TLRs (Fig. 2). According to Kaplan-Meier analysis, the 5-year survival was 78.1% and the 10-year survival was 68.9% (Fig. 3A). According to the Academic Research Consortium definition, there was 1 event of definite very late in-stent thrombosis in a patient with a DES, 2.5 years after the index procedure, while not on double antiplatelet therapy. The rates of probable late and very late stent thromboses were 3 (1.2%) and 5 (2%), respectively.

Survival of patients with isolated LM and LM with accompanying 1- to 3-vessel disease is shown in Figure 3B. There was significantly better long-term survival in patients with isolated LM or LM with 1- and 2-vessel disease when compared with LM with 3-vessel disease (Cox $p = 0.02$, $p = 0.005$, $p = 0.008$, respectively).

The univariate predictors of death were: age >60 years ($p = 0.03$, OR: 2.48, 95% CI: 1.03 to 5.95), LVEF <50% ($p = 0.01$, OR: 3.25, 95% CI: 1.45 to 7.27) and EuroSCORE on admission >9 ($p = 0.04$, OR: 2.48, 95% CI: 1.1 to 4.56).

The Cox multivariate analysis for independent risk factors showed that LVEF <50% decreased survival rate, whereas DES implantation decreased and stent diameter <3.8 mm increased the risk of MACCE.

**DES versus BMS.** Baseline clinical, lesion, and angiographic data in DES and BMS subgroups are presented in Table 4. Patients receiving DES compared with BMS were more often diabetic (30.9% vs. 20.3%, $p = 0.06$) and more frequently diagnosed with NSTE-ACS (69.1% vs. 54.4%, $p = 0.04$). They had higher surgical risk according to EuroSCORE ($6.8 \pm 3.9$ vs. $5.6 \pm 3.8$, $p = 0.01$) and a higher incidence of distal LM stenosis (72.3% vs. 51.3%, $p = 0.001$). The mean DES diameter was lower than for BMS ($3.4 \pm 0.5$ mm vs. $3.7 \pm 1.0$ mm, $p = 0.01$).

Despite these differences in baseline characteristics, at 4-year follow-up the unadjusted occurrence of MACCE was significantly lower within the DES group (14.9% vs. 25.9%, $p = 0.039$). There was a nonsignificant difference favoring the DES group in mortality (DES vs. BMS: 9.6% vs. 13.3%) and BMS in the risk of myocardial infarction (DES vs. BMS: 13.8% vs. 9.5%). The TLR rate was significantly lower in the DES group (3.2% vs. 10.1%, $p = 0.04$) (Fig. 4).

**Table 5** **Demographic, Clinical, and Procedural Data in DES and BMS Subgroups After Adjustment**

| | DES (n = 78) | BMS (n = 78) | p Value | Standardized Difference (%) |
|---|---|---|---|---|
| Age (yrs) | 64.5 ± 10 | 64.1 ± 11.6 | 0.81 | 3.9 |
| Male | 53 (67.9) | 54 (69.2) | 0.86 | −2.8 |
| DM | 22 (28.2) | 20 (25.6) | 0.72 | 5.8 |
| Hypertension | 62 (79.5) | 64 (82.1) | 0.68 | −6.5 |
| Hypercholesterolemia | 43 (55.1) | 48 (61.1) | 0.45 | −12.1 |
| Smoking | 31 (39.8) | 33 (42.1) | 0.76 | −4.8 |
| EuroSCORE (additive) | 6.4 ± 3.7 | 6.6 ± 3.8 | 0.82 | −3.7 |
| CCS | 3.4 ± 0.9 | 3.4 ± 0.8 | 1.00 | 0.0 |
| NSTE-ACS | 51 (65.4) | 47 (60.3) | 0,7 | −10.6 |
| LVEF (%) | 49.0 ± 13 | 48.2 ± 13.2 | 0.70 | 6.2 |
| Distal LM involvement | 58 (74.1) | 57 (72.4) | 0.82 | 3.7 |
| Stent diameter (mm) | 3.4 ± 0.5 | 3.5 ± 0.8 | 0.82 | −3.7 |
| No. of diseased vessels | 2.1 ± 0.8 | 2.1 ± 0.7 | 0.89 | −2.2 |
| No. of lesions except LM stenosis | 1.6 ± 1 | 1.6 ± 1 | 0.84 | −3.2 |

Values are mean ± SD or n (%).
Abbreviations as in Table 4.

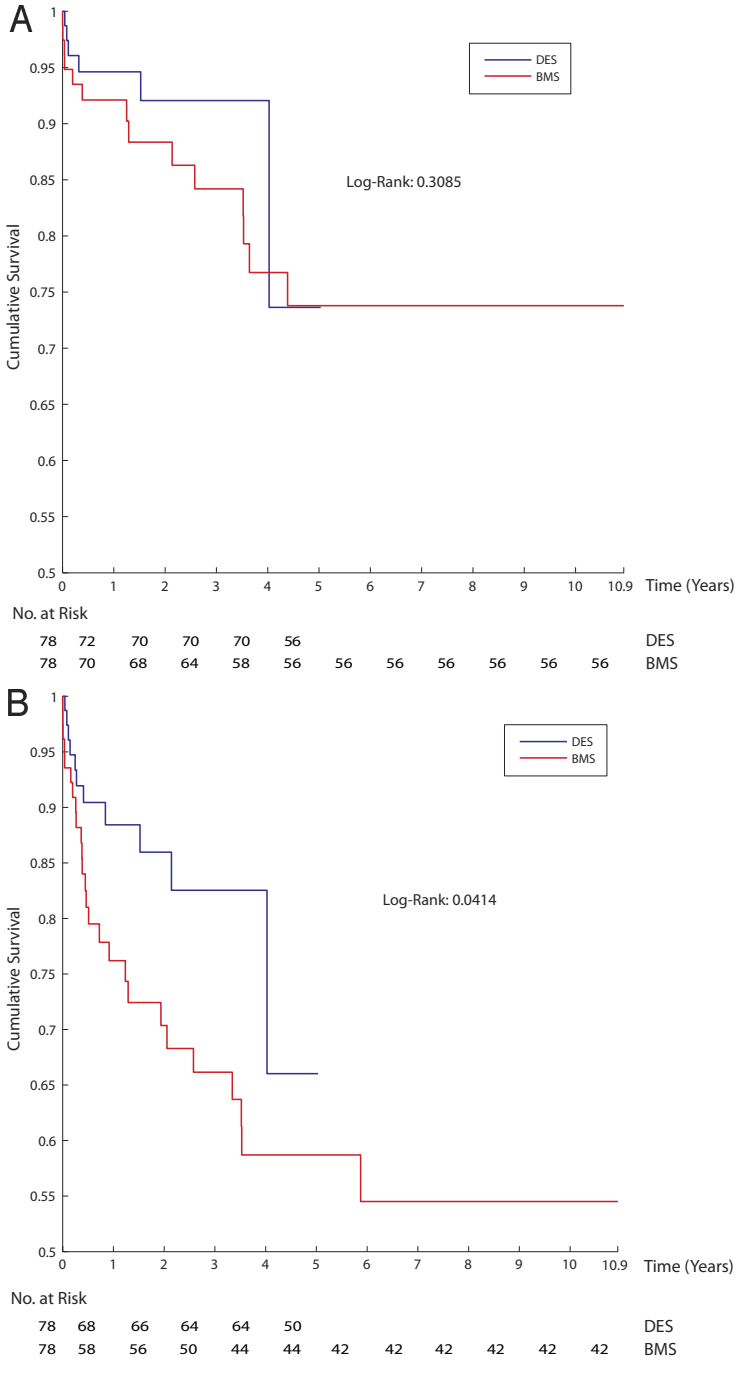


**Figure 5** **Long-Term Adjusted DES Versus BMS Results**

Survival **(A)** and MACCE-free survival **(B)** in BMS and DES cohorts. Abbreviations as in Figures 1 and 2.

Propensity score matching of the demographical, clinical, and procedural data resulted in a bias reduction in 13 of 14 of our parameters and a standardized difference of <10% in all but 2 parameters (Table 5). The results after propensity score adjustment were strengthened with higher significance in MACCE- and TLR-free survival, although there was no difference in mortality and incidence of myocardial infarction, as seen in Figures 5 and 6.

**Distal LM.** Comparison of the patient subsets with stenosis of distal (n = 149) versus proximal and/or medial LM showed no significant differences among demographical, clinical, and procedural data among those groups except a

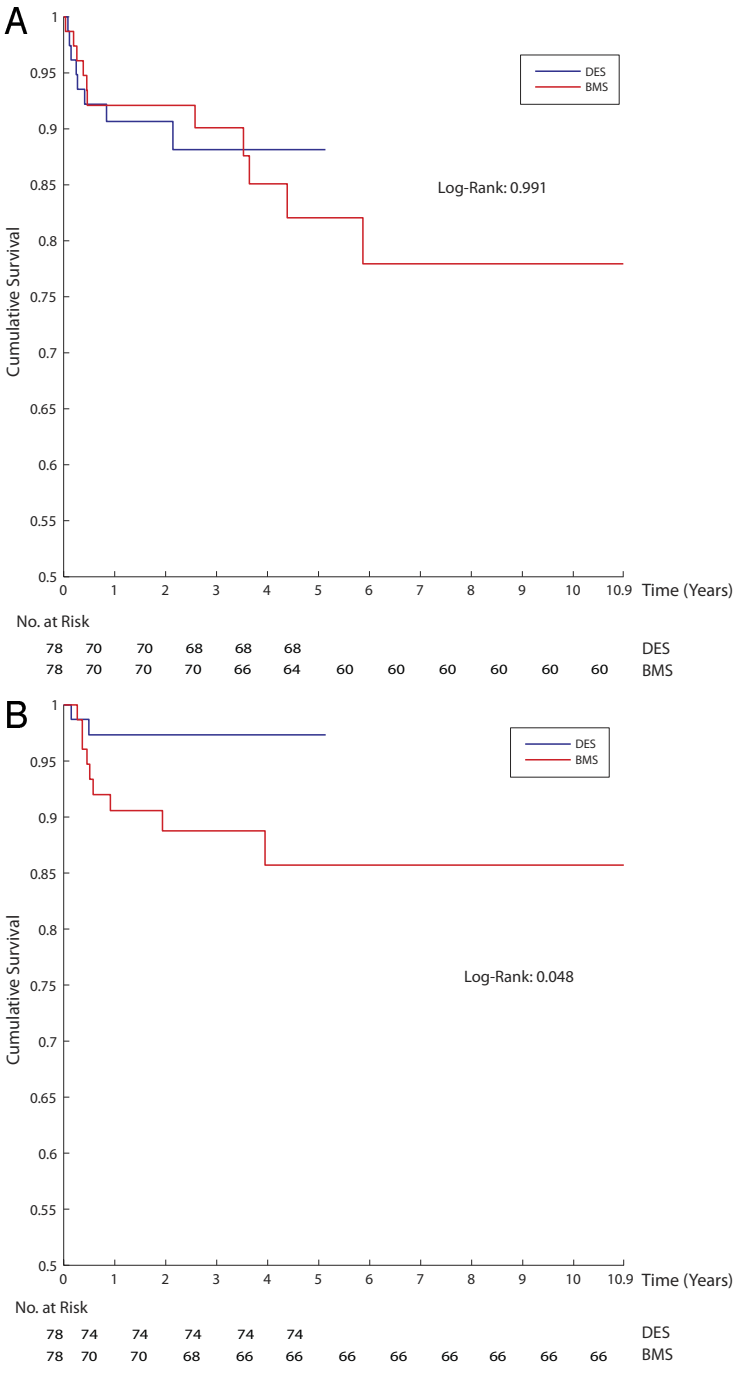


**Figure 6** **Long-Term Adjusted DES Versus BMS Results, Continued**

MI-free survival **(A)** and TLR-free survival **(B)** in BMS and DES cohorts. Abbreviations as in Figures 1 and 2.

higher number of implanted DES (45.6% vs. 24.3%, p = 0.001), a higher number of diseased vessels (2.2 ± 0.8 vs. 1.8 ± 1, p = 0.0002), and more lesions (1.6 ± 1 vs. 1.1 ± 0.9, p = 0.0006) in patients with distal LM disease. Kaplan-Meier analysis showed no difference in survival and MACCE-free survival (Fig. 7) among the subsets.

Further, we analyzed patients specifically with distal LM involvement and divided them into cohorts with regard to implanted DES (n = 68) or BMS (n = 81). Basic demographical, clinical, and procedural data were similar among those groups and no significant differences were noticed; however, there was a trend toward a higher

number of men than women (79.0% vs. 66.2%, p = 0.08) in the BMS group and a trend toward higher EuroSCORE (5.7 ± 3.3 vs. 6.67 ± 3.77, p = 0.09) in the DES cohort. In long-term follow-up, both survival and MACCE–free survival rates were higher in favor of DES for distal LM when compared with BMS (Fig. 8).

## Discussion

This is the first prospective study presenting long-term results (up to 11 years) of unprotected LM stenting (LE MANS registry). The early results of LM stenting with high procedural and clinical success (98% and 95%, respectively) and low periprocedural mortality (1.3%) and MACCE (4.8%) prove safety and feasibility of this procedure, despite the initial high risk profile of study population (EuroSCORE >6, NSTE-ACS in 60% of patients).

Long-term mortality of 13.9% at 4 years and the 5- and 10-year survival of 78.1% and 68.9% are very satisfactory and compare favorably with survival presented in long-term outcomes of coronary artery bypass surgery in the CASS (Coronary Artery Surgery Study) trial (2,15) and the Duke University database (15). Angiographically confirmed restenosis occurred in 12.1% of patients. This result is comparable with those of studies involving only DES patients

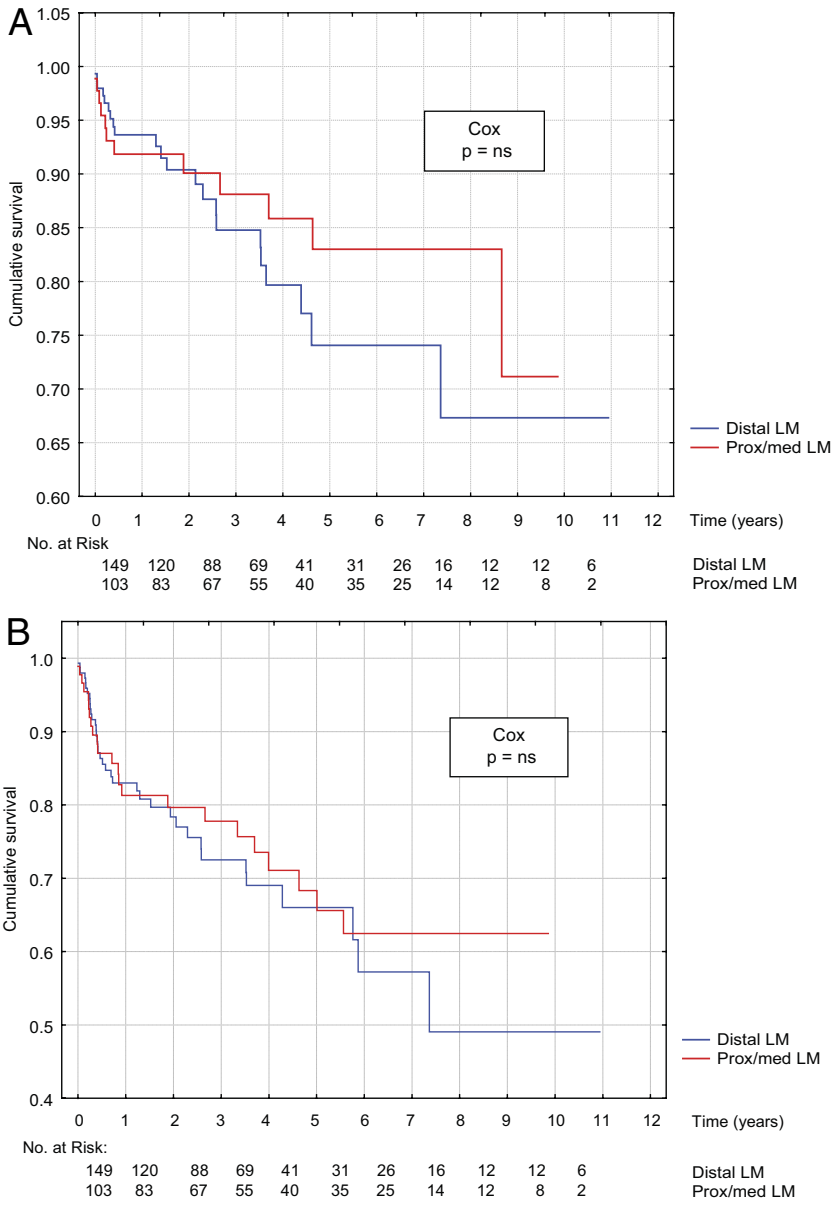


**Figure 7** **Patient Cohorts With Distal Versus Proximal/Medial LM Involvement**

**(A)** Survival and **(B)** MACCE-free survival. LM = left main coronary artery; med = medial; prox = proximal; other abbreviations as in Figures 1 and 2.

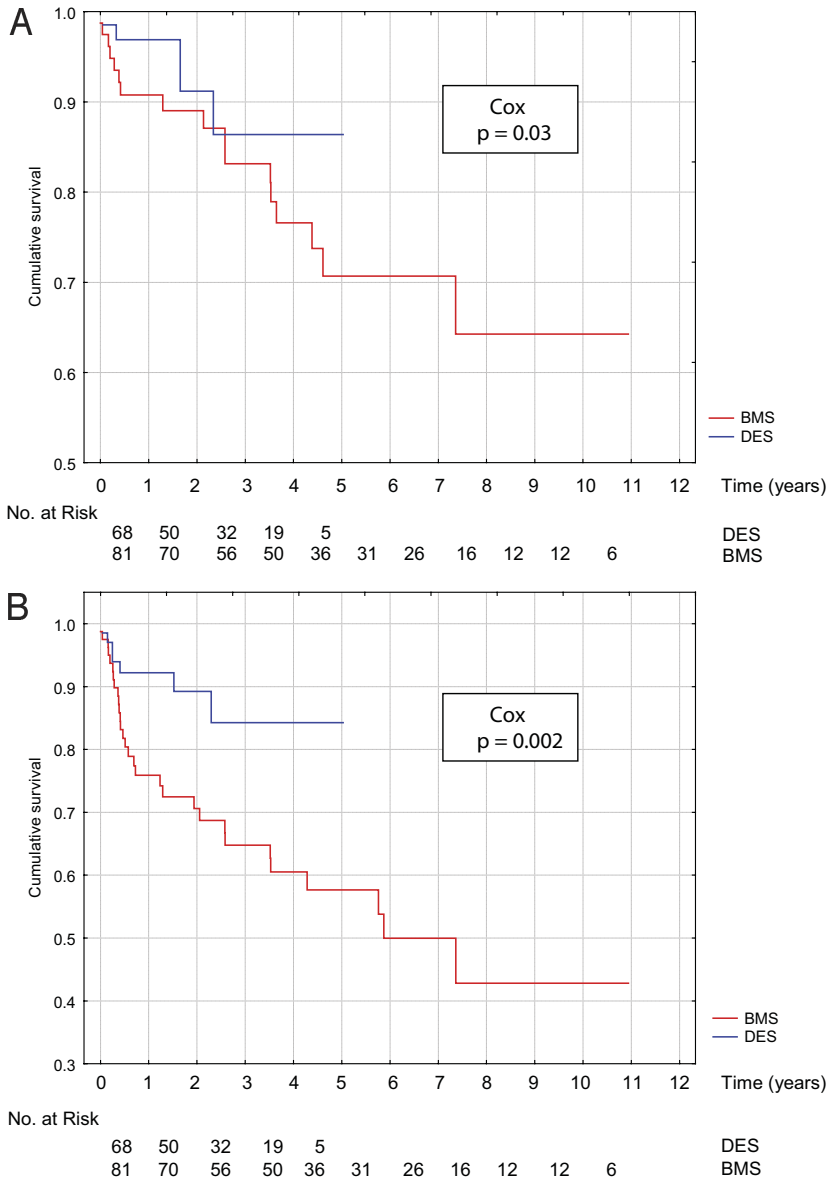


**Figure 8** **Distal Left Main Cohort**

**(A)** DES versus BMS survival. **(B)** The MACCE-free survival. Abbreviations as in Figures 1 and 2.

(16,17). Nevertheless, in our study, BMS were mostly implanted in vessels with reference diameter of 3.8 mm and above in which restenosis is relatively low (18), and in our study was found in 6.1% of cases. Additionally, most of the DES implanted in our study were paclitaxel-eluting stents, which in the ISAR LEFT MAIN (Intracoronary Stenting and Angiographic Results: Drug-Eluting Stents for Unprotected Coronary Left Main Lesions) study showed a numerically lower rate of restenosis and TLR when compared with sirolimus-eluting stents (16.0% vs. 19.4% and 13.6% vs. 15.8%, respectively) (17).

The analysis of the DES and BMS patient subgroups showed a higher clinical and lesion characteristic risk profile in patients treated with DES as evidenced by a higher incidence of diabetes mellitus and surgical risk according to EuroSCORE, higher number of patients with NSTE-ACS, and incidence of distal LM stenosis. Nonetheless, the long-term outcome was significantly better within the DES group, with lower MACCE (14.9% vs. 25.9%, $p = 0.04$) and lower TLR (10.1% vs. 3.2%, $p = 0.037$). Further propensity score matching and data adjustment confirmed and strengthened those findings.

The recorded difference in MACCE rate between DES and BMS is similar to the 6-month observation of Chieffo et al. (7) and the 17-month observation of Valgimigli et al. (19) in the same period. However, after longer follow-up we did not observe differences in mortality and incidence of myocardial infarction between DES and BMS. The incidence of adjusted TLR-free survival in both study groups is similar to that observed by Park et al. (10). There was 1 case (0.4% of the whole study group, 1% of the DES subgroup) of definite very late in-stent thrombosis that occurred 2.5 years after stent (DES) implantation. The incidence of this event is consistent with prior reports (20).

Contrary to reported data (21), there was no difference in the survival and MACCE-free survival of patients with involvement of distal LM, as opposed to proximal and/or medial LM. This may be because of the higher number of DES implanted within the distal LM compared with the proximal/medial LM (45.6% vs. 24.7%, $p = 0.001$). Hence, we analyzed the outcome of patients with only distal LM involvement. There was a significant decrease in mortality and MACCE in the patient subset who received DES when compared with BMS. This is the first study reporting improved survival after distal LM DES versus BMS. Consequently, based on these data, it is believed that the overall MACCE risk decrease in patients receiving DES for ULMCA is mainly attributable to their high efficacy in distal LM bifurcation. We believe that this should be the standard strategy for this lesion subset. On the other hand, we observed reasonable long-term follow-up data in patients who received BMS for large (>3.8 mm) LM vessels, especially in the ostial or shaft portion. Nevertheless, data from Chieffo et al. (22) after DES implantation in this lesion subset with a TLR rate of 1% remain superior. However, it must be stressed that there are no DES with a diameter larger than 4.5 mm. In these particular cases, implantation of BMS is acceptable.

Our 12-year experience with LM stenting reflects its continuous progress. First, we showed significant reduction of angina, significant improvement of the left ventricular systolic function, and preservation of exercise capacity in long-term follow-up (23). Second, we provided evidence for the superiority of ULMCA stenting over CABG in terms of restoring LVEF along with a trend for better survival (24). In the current study, we show the safety and feasibility of ULMCA stenting with longest follow-up over a decade, along with improved MACCE- and TLR-free survival with DES in comparison with BMS. These findings support and extend the recent results of the SYNTAX (SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery) study (25), in which the patient subset with LM disease treated with DES had a similar overall MACCE at 1-year follow-up to those treated with CABG. We showed excellent long-term results of ULMCA stenting, especially in patients with isolated LM disease or LM with 1- and 2-vessel coronary artery disease, in whom 10-year survival was nearly 90% and was significantly better than in patients with concomitant 3-vessel disease. In short follow-up, similar trends were observed in the SYNTAX study.

**Study limitations.** The rate of angiographic follow-up of <60% is relatively low, despite a recommendation for routine control. This was mainly related to more frequent use of DES and confidence in the method of LM stenting in later phase of the study. Another study limitation was not routinely using intravascular ultrasound to check the acute result of the stenting.

## Conclusions

Stenting of ULMCA is feasible and offers good late outcomes. Isolated LM lesions or LM with 1- and 2-vessel disease are associated with exceptional short- and long-term outcomes, with the longest observation up to 11 years. A DES implantation for ULMCA decreases the risk of long-term MACCE and particularly improves survival in patients with distal ULMCA disease. These findings are encouraging and support the need for long-term follow-up of patients with ULMCA randomized to DES or CABG in large trials.

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**Key Words:** unprotected left main coronary artery disease ■ percutaneous coronary intervention ■ drug-eluting stent ■ bare-metal stent.