ORIGINAL RESEARCH

Proximal Left Anterior Descending Artery Treatment Using a Bioresorbable Polymer Coating Sirolimus-Eluting Stent: Real-World Outcomes From the Multicenter Prospective e-Ultimaster Registry

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***Background*—**Guidelines recommend heart team discussion and coronary artery bypass graft consideration in patients with proximal left anterior descending (LAD) artery stenosis. Evidence suggests that outcomes of proximal LAD angioplasty might not differ from treatment of nonproximal LAD locations. We aim to determine clinical outcomes of patients undergoing percutaneous coronary intervention in the proximal LAD segment in comparison with nonproximal LAD angioplasty, using a thin-strut drug-eluting stent.

***Methods and Results*—**In this analysis of the e-Ultimaster registry, patients undergoing angioplasty in the proximal LAD territory were compared with those treated in nonproximal LAD locations. Multivariate analysis and propensity score were used to adjust for differences among the groups. The primary outcome was target lesion failure: a composite of cardiac death, target-lesion–related myocardial infarction, and/or clinically driven target lesion revascularization at 1-year follow-up. Of the 17 805 patients (mean age, 64.2±11; 76% male), 5452 (30.6%) underwent proximal LAD and 12 353 (69.4%) nonproximal LAD percutaneous coronary intervention. Patients in the proximal LAD group had more multivessel disease (48.7% versus 43.5%; $P<0.001$) and 2-fold more bifurcations lesions (18.8% versus 9.2%; $P<0.0001$). After propensity-weighted adjustment, target lesion failure did not differ between the groups (3.3% versus 2.9%; $P=0.17$ for proximal LAD versus nonproximal LAD angioplasty, respectively). In multivariate analysis, proximal LAD treatment was not an independent predictor of target lesion failure (odds ratio, 1.07; 95% CI, 0.88–1.31; $P=0.48$).

***Conclusions*—**At 1-year follow-up, patients had similar clinical outcomes independent of stenting location, questioning whether proximal LAD treatment should be regarded differently from stenting in any other coronary artery territory. **(*J Am Heart Assoc.* 2019;8:e013786. DOI: 10.1161/JAHA.119.013786.)**

Key Words: catheterization outcomes • proximal left anterior descending angioplasty • stenting

Proximal left anterior descending (LAD) coronary artery disease is considered as a high-risk feature in interventional cardiology attributable to the large area of myocardium it supplies. Patients with stable coronary artery disease and isolated proximal LAD disease have similar survival rates whether treated with coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI).[1–3]

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Accompanying Tables S1 through S4 and Figures S1 through S3 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.013786

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Clinical Perspective

What Is New?

- From the analysis of this large all-comer stent registry, clinical outcomes of patients with coronary artery disease in the proximal left anterior descending segment did not differ from those with coronary obstruction elsewhere in the coronary tree.

What Are the Clinical Implications?

- The study contributes to the growing evidence that the proximal left anterior descending segment should not be considered differently than other coronary arteries or segments at the time of with current available techniques, devices and medications.

Current revascularization guidelines recommend a "heart team" discussion in patients with stable coronary artery disease and proximal LAD disease and confer a class I indication level of evidence A to both, percutaneous and surgical, treatment strategies.[4] Yet, this is not the case when isolated lesions in the right coronary artery or left circumflex are planned for treatment.

Whether PCI of the proximal LAD segment is associated with higher rates of adverse events in comparison with nonproximal LAD PCI has been of interest. Several subgroup analyses of randomized and registry trials found no major differences in mortality or in the composite rate of major adverse cardiac events (MACE).[5–8] We aimed to compare outcomes of a large cohort of patients enrolled in the e-Ultimaster prospective and multinational registry study undergoing drug-eluting stent (DES) implantation and stratified according to lesion location within or outside the proximal LAD artery.[9]

Methods

Study Design

The large e-Ultimaster is an all-comer, single-arm, prospective, and multicenter registry. The study was conducted worldwide across Europe, Asia, South America, and Africa to further evaluate the safety and performance of the Ultimaster DES system (Terumo Corporation, Tokyo, Japan) in an all-comer clinical setting.[9]

Inclusion and exclusion criteria were described previously.[9] Briefly, patients with coronary artery disease (reference vessel diameters between 2.5 and 3.5 mm) eligible for PCI using DES according to local hospital practice and who were treated using the Ultimaster stent were enrolled in the registry. Local institutional review board approval was obtained at each institution while subjects included in the registry were waived to provide informed consent.

Inclusion Criteria for the Current Analysis

The present study analyzed clinical outcomes of patients enrolled in the e-Ultimaster registry divided according to whether stents were implanted in a proximal LAD versus a nonproximal LAD segment. In cases where stents were implanted in the proximal LAD as well as in another location, they were grouped into the proximal LAD group. Patients with left main segment involvement and treatment and those with previous CABG surgery were excluded. All other patients from the e-Ultimaster registry with a follow-up at 3 months and 1 year were included.

In this interim analysis, proximal LAD was defined according to the CASS (Coronary Artery Surgery Study) classification[11]: end of left main to the first large septal or first diagonal, whichever is more proximal. The current interim analysis assessed data of 19 842 patients enrolled between October 2014 and May 2017 who had complete 3-month and 1-year follow-up data or had died on the date of census (May 31, 2018; Figure 1).

Renal impairment was defined as estimated glomerular filtration rate <60 mL/min/1.73 m^2. Lesion complexity was defined by the American College of Cardiology/American Heart Association classification.[12]

Study Device

The Ultimaster coronary stent system is a new-generation, open-cell, cobalt-chromium, thin-strut (80-μm) sirolimus-eluting stent with an abluminal bioresorbable polymer coating (poly-D,L-lactic acid polycaprolactone).[10] Sirolimus is released over a 3- to 4-month period, after which the polymer coating is fully degraded.

Outcomes and Definitions

The primary outcome was target lesion failure (TLF) defined as a composite of cardiac death, target vessel–related myocardial infarction (MI), and for clinically driven target lesion revascularization (TLR) at 1-year follow-up.

Secondary outcomes included any death, cardiac death, MI, rate of TLR, rate of target vessel revascularization (TVR), target vessel failure (a composite of cardiac death, target-vessel–related MI, and TVR), and major vascular and bleeding complications. Stent thrombosis was defined according to the Academic Research Consortium definitions at 3-month and 1-year follow-up. Patient-oriented composite end point (POCE) was defined as a composite of any death, any MI, and any coronary revascularization. All end-point–related serious adverse events were reviewed and adjudicated by an independent clinical event committee.

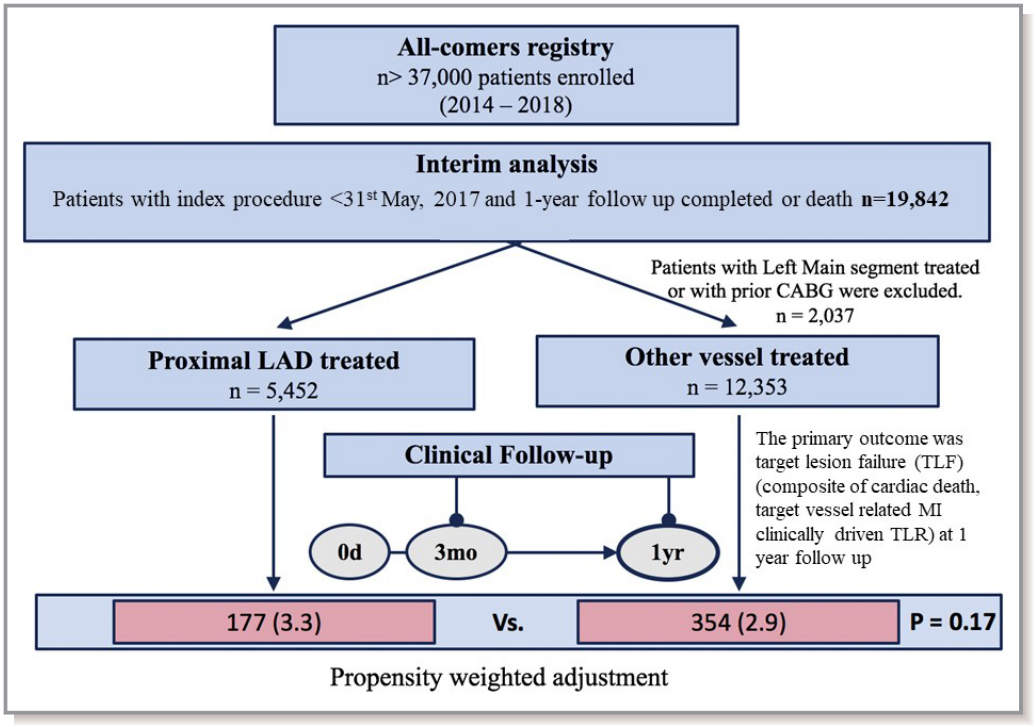

Figure 1. Study flow chart and primary outcome results. CABG indicates coronary artery bypass graft; LAD, left anterior descending; d, days; mo, months; yr, year.

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Statistical Analysis

Baseline characteristics were reported as mean and SDs for continuous variables and number and percentages for categorical variables. Statistical differences between baseline characteristics were reported using a *t* test for continuous variables and chi-squared test for categorical variables while the outcomes of interest were reported at 3 months and 1 year.

To reduce the effect of baseline differences between the 2 groups, a propensity-score analysis was performed using separate models for lesion location. Propensity scores were calculated using a logistic regression model, with the subgroup (proximal LAD or nonproximal LAD) as outcome and the variables which needed to be matched for as independent variables. The probability of belonging to 1 of the 2 groups was used as a propensity score. Variables to be entered into the model were predefined based on any possible impact on the outcomes and included: age, sex, body mass index, smoking, hypertension, hypercholesterolemia, history of MI, previous PCI, ST-segment–elevation myocardial infarction, multivessel disease, number of lesions treated, number of stents implanted, length of implanted stents, type B2 and C lesions, bifurcation, moderate to severe calcification, ostial lesions, long lesions (≥25 mm), small vessels (1 stent ≤2.75 mm), radial access, postdilatation, and thrombus aspiration. The inverse probability of treatment weights methodology was used to perform a matched analysis. This methodology uses the inverse of the propensity score of its own subgroup (ie, the probability of the subject of belonging to the subgroup it is in) as a weight that can be used in the analyses. Using these weights, analyses were balanced for the covariates in the logistic regression model. The balance after matching can be tested by calculating weighted standardized difference for the inverse probability of treatment weights analysis using the calculated weights. Generally, standardized difference for all variables below 0.20 are considered well balanced, whereas standardized difference for all variables below 0.10 can be considered extremely well balanced (Figure S1). Weighted chi-square tests were used for binary or categorical data; weighted Wilcoxon rank-sum tests were used for continuous data.

Multivariate analyses on the proximal LAD subgroups included logistic regression models to assess the odds ratio of events. For primary outcome target lesion failure, a stepwise selected model was used, where all variables are entered 1 by 1 if their *P* value is <0.25 ("entry *P* value") and retains the variables in next steps when the *P* value remains below 0.15 ("stay *P* value"). This gives a model with only a set of important, predictive variables and also avoiding multicollinearity. The variables entered were age, sex, body mass index, diabetes mellitus, hypertension, hypercholesterolemia,

Table 1. Baseline Patients Characteristics

	Unadjusted			Propensity Weighted		
	Proximal LAD n=5452 (%)	Nonproximal LAD n=12 353 (%)	*P* Value	Proximal LAD n=5452 (%)	Nonproximal LAD n=12 353 (%)	*P* Value
Age, y	64.1±11.3	64.3±11.0	0.28	64.1±11.3	64.1±11.1	0.99
Male sex	4180/5452 (76.7)	9400/12 353 (76.1)	0.41	4156/5420 (76.2)	9333/12 353 (76.2)	0.99
Current smoker	1117/5050 (22.1)	2895/11 446 (25.3)	<0.001	1177/5055 (23.3)	2668/11 418 (23.4)	0.92
Diabetes mellitus	1457/5452 (26.7)	3400/12 353 (27.5)	0.27	1475/5452 (27.1)	3295/12 352 (26.7)	0.59
Hypertension	3148/5195 (60.6)	7532/11 815 (63.8)	<0.001	3196/5194 (61.5)	7242/11 791 (61.4)	0.89
Hypercholesterolemia	2755/5204 (52.9)	6680/11 777 (56.7)	<0.001	2797/5204 (53.7)	6337/11 747 (53.9)	0.81
Renal impairment	387/5450 (7.1)	836/12 349 (6.8)	0.42	387/5450 (7.1)	831/12 349 (6.7)	0.35
Previous MI	900/5261 (17.1)	2499/11 992 (20.8)	<0.001	950/5264 (18.0)	2152/11 987 (18.0)	0.89
Previous PCI	997/5260 (19.0)	3101/12 001 (25.8)	<0.001	1087/5263 (20.6)	2464/11 988 (20.6)	0.87
ACS	3113/5446 (57.2)	7025/12 345 (56.9)	0.75	3125/5446 (57.4)	7121/12 344 (57.7)	0.70
STEMI	1201/5446 (22.1)	2567/12 345 (20.8)	0.06	1211/5446 (22.2)	2743/12 344 (22.2)	0.99
Multivessel disease	2656/5452 (48.7)	5372/12 352 (43.5)	<0.001	2546/5452 (46.7)	5768/12 353 (46.7)	0.99

Values are mean±SD or percentage (number). ACS indicates acute coronary syndrome; LAD, left anterior descending artery; MI, myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction.

smoking, previous MI, previous PCI, renal impairment, acute coronary syndrome, multivessel disease, number of lesions identified, number of lesions treated, number of stents implanted, length of stents implanted, in-stent restenosis, chronic total occlusion, bifurcation, long lesions, small vessels, moderate-to-severe calcification, lesions type according to the American College of Cardiology/American Heart Association classification, and radial access. Proximal LAD lesion, age, and sex were forced into the logistic regression model.

P<0.05 was considered significant. Statistical analyses were performed using SAS software (version 9.4; SAS Institute Inc., Cary, NC).

Results

Study Patients

The e-Ultimaster registry recruited 37 000 patients in 413 sites over 50 countries. Enrollment ended in May 2018. The current

Table 2. Baseline Lesion and Procedural Characteristics

	Unadjusted			Propensity Weighted		
	Proximal LAD n=5452 (%)	Nonproximal LAD n=12 353 (%)	*P* Value	Proximal LAD n=5452 (%)	Nonproximal LAD n=12 353 (%)	*P* Value
No. of lesions detected, n	1.92±1.06	1.79±1.05	<0.001	1.87±1.04	1.87±1.08	0.94
No. of lesions treated, n	1.44±0.70	1.29±0.57	<0.001	1.38±0.64	1.38±0.67	0.99
Type C lesions (ACC/AHA classification)	1407/4569 (30.8)	2868/10 321 (27.8)	<0.001	1358/4529 (30.0)	3076/10 412 (29.5)	0.59
Ostial lesion	472/5420 (8.7)	625/12 241 (5.1)	<0.001	382/5417 (7.1)	866/12 263 (7.1)	0.99
Moderate-to-severe calcification	1113/5420 (20.5)	2102/12 241 (17.2)	<0.001	1049/5417 (19.4)	2376/12 263 (19.4)	0.98
Bifurcation	1020/5420 (18.8)	1130/12 241 (9.2)	<0.001	785/5417 (14.5)	1778/12 263 (14.5)	0.98
Long lesion (≥25 mm)	2618/5436 (48.2)	5020/12 305 (40.8)	<0.001	2492/5436 (45.8)	5647/12 305 (44.9)	0.96
Small vessels (≤2.75 mm)	2124/5436 (39.1)	5770/12 305 (46.9)	<0.001	2199/5436 (40.5)	4982/12 305 (40.5)	0.97
Radial access	4373/5356 (81.7)	10 269/12 118 (84.7)	<0.001	4432/5363 (82.6)	10 041/12 095 (83.0)	0.53
No. of implanted study stents, n	1.59±0.95	1.39±0.75	<0.001	1.51±0.86	1.51±0.88	0.99
Total length of implanted study stents, mm	35.8±24.1	30.6±19.8	<0.001	33.9±22.1	33.9±22.9	0.99
Postdilatation	2794/5452 (51.3)	5181/12 352 (41.9)	<0.001	2624/5452 (48.1)	5945/12 353 (48.1)	0.99

Values are mean±SD or percentage (number). ACC/AHA indicates American College of Cardiology/American Heart Association; LAD, left anterior descending artery.

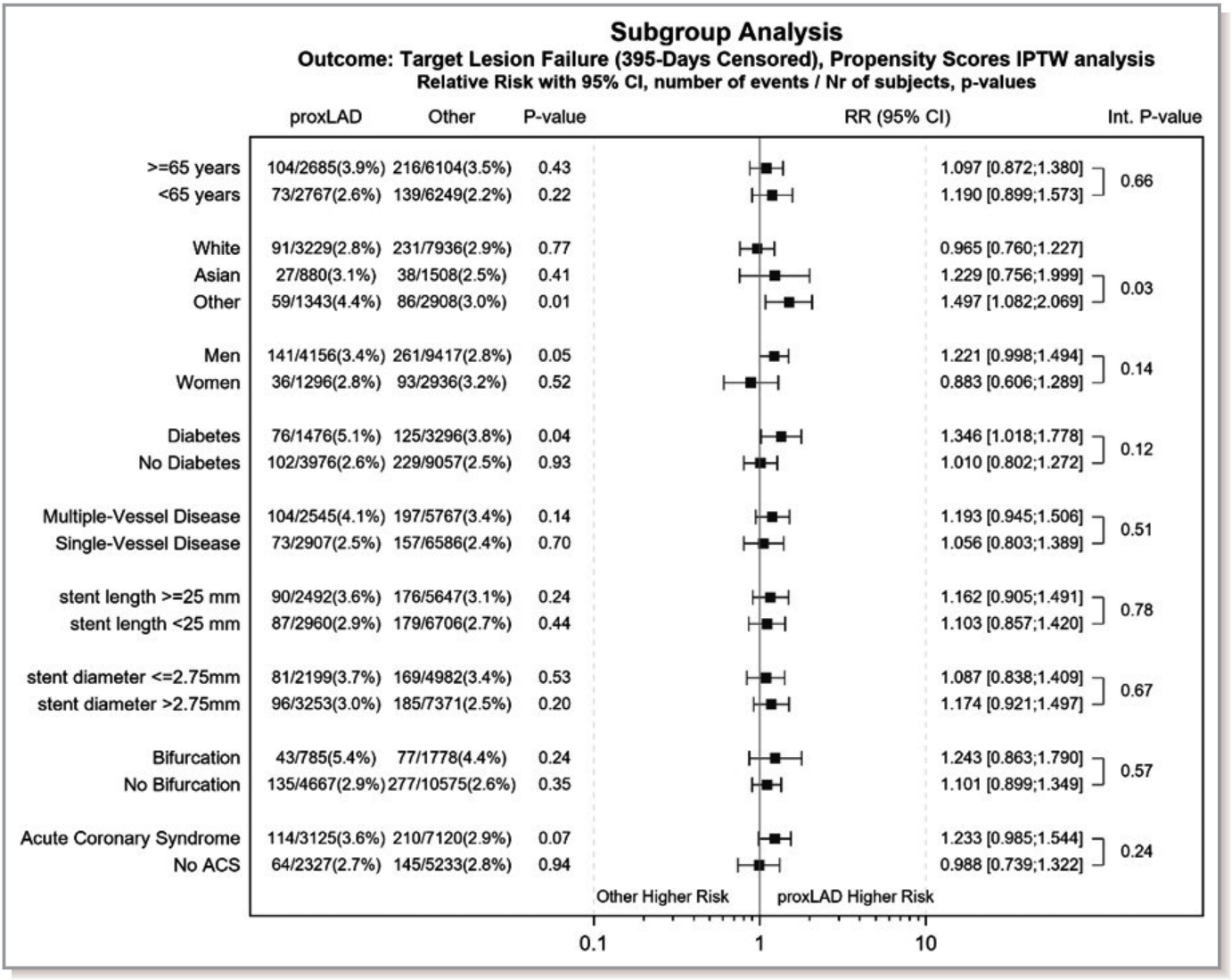

Figure 2. Subgroup analysis (logistic regression) showing propensity-adjusted relative risk (RR) with 95% CI. ACS indicates acute coronary syndrome; IPTW, inverse probability of treatment weights; proxLAD, proximal left anterior descending; RR, relative risk.

interim analysis includes 19 842 patients with complete 1-year follow-up data by May 2018, of which 2037 were excluded because of previous CABG and/or left main disease involvement. Patients (n=17 805) treated with stent implantation within the proximal LAD segment (N=5452) were compared with those treated in a nonproximal LAD (N=12 353) territory. To adjust for differences in baseline characteristics, a propensity-score analysis was done (see flowchart, Figure 1).

Baseline Demographics

Patients' (N=17 805; 23.7% women) mean age was 64.2±11.1. Baseline characteristics (unadjusted and propensity-score adjusted) comparing the 2 groups are presented in Table 1. Patients in the proximal LAD group had lower-incidence hypertension, hypercholesterolemia, current smoking, and previous MI than their counterparts (Table 1). Stable angina was the reason for PCI in 1885 (34.6%) patients in the proximal LAD versus 4215 (34.1%) in the nonproximal group (P=0.55).

Procedural and Lesion Characteristics

Procedural details and angiographic information (unadjusted and propensity adjusted) are presented in Table 2. Multivessel disease incidence was higher in patients treated in the proximal LAD segment (48.7% versus 43.5%; P<0.001) and had 2-fold more bifurcation than those treated in other locations (18.8% versus 9.2%; P<0.0001). Rates of long (>25 mm) and moderate-to-severe calcified lesions were higher in the proximal LAD group, and lesion complexity (according to the American College of Cardiology/American

Heart Association classification)[12] was, in general, more severe in these patients as well (Table 2). Patients in the proximal LAD group had, on average, more lesions treated and more stents implanted and hence an overall longer stent length. The complete distribution of the lesions in both groups is detailed in Table S1.

Clinical Outcomes

All patients included in the current analysis completed 3-month and 1-year follow-up. Table S2 details the nonadjusted event rates. After propensity weighing (Figure S1), the primary end point of TLF was similar among treatment groups (76 [1.4%] versus 179 [1.5%]; *P*=0.76 and 177 [3.3%] versus 354 [2.9%]; *P*=0.17, for proximal LAD versus nonproximal LAD at 3-month and 1-year follow up, respectively).

Subgroup analysis (logistic regression) showing propensity-adjusted relative risk with 95% CI are presented in Figure 2. Separate subanalyses and event rates of proximal LAD lesions with 1-, 2-, and 3-vessel disease and for diabetes mellitus appear in Tables S3 and S4 and Figures S2 and S3. Diabetes mellitus or multivessel disease were not a significant effect modifier for the risk of TLF between proximal LAD and nonproximal LAD group (no significant interaction effect).

Propensity-weighted–adjusted rates of all-cause mortality, cardiac death, and any MI and the composite end points of target vessel failure and patient-oriented composite end point were not different within studied groups at 3-month or 1-year follow-up (Table 3). Propensity-weighted target lesion and vessel revascularizations were similar at 3-month follow-up (TLR [0.46% versus 0.49%; *P*=0.83] and TVR [0.6% versus 0.73%; *P*=0.32]), but higher at 1-year follow-up in the proximal LAD group (TLR [1.8% versus 1.3%; *P*=0.008] and TVR [2.4% versus 1.9%; *P*=0.06]). Relief from angina symptoms was similar at 3 months (angina-free rate, 91.8% versus 91.6%; *P*=0.68) and at 1 year (angina-free rate, 92.1% versus 91.3%; *P*=0.12) in proximal LAD compared with nonproximal-LAD–treated patients, respectively. Definite and probable stent thrombosis rates at 1 year were low and similar (0.67% versus 0.64%; *P*=0.77). Both groups received similar duration of dual antiplatelet therapy at discharge (97.9% versus 97.5%; *P*=0.15) and at 3 months (94.6% versus 94.7%; *P*=0.83), with slightly higher dual antiplatelet therapy at 1-year follow-up in the proximal LAD group (67.6% versus 65.9%; *P*=0.03).

Multivariate Analysis

We also performed a multivariate logistic regression analysis; proximal LAD stenting was not identified as an independent predictor for the primary outcome measure of TLF (odds ratio, 1.07; 95% CI, 0.88–1.31; *P*=0.48; Table 4). The following variables were predictors of TLF: age, diabetes mellitus, renal impairment, previous PCI, acute coronary syndrome, and angiographic complexity of the lesion.

Table 3. Propensity-Adjusted Clinical Outcomes

	3-month			1-year		
	Proximal LAD n=5452 (%)	Nonproximal LAD n=12 353 (%)	*P* Value	Proximal LAD n=5452 (%)	Nonproximal LAD n=12 353 (%)	*P* Value
All-cause death	55/5452 (1.0)	106/12 353 (0.9)	0.27	117/5452 (2.1)	246/12 353 (2.0)	0.53
Cardiac death	45/5452 (0.8)	76/12 353 (0.6)	0.10	73/5452 (1.3)	147/12 353 (1.2)	0.44
Any MI	26/5452 (0.5)	96/12 353 (0.8)	0.03	51/5452 (0.9)	145/12 353 (1.2)	0.16
Target-vessel MI	24/5452 (0.4)	81/12 353 (0.7)	0.08	40/5452 (0.7)	117/12 353 (1.0)	0.16
All TLR	27/5452 (0.5)	61/12 353 (0.5)	0.99	101/5452 (1.9)	167/12 353 (1.4)	0.01
Clinically driven TLR	25/5452 (0.5)	60/12 353 (0.5)	0.83	97/5452 (1.8)	158/12 353 (1.3)	0.008
All TVR	35/5452 (0.6)	93/12 353 (0.8)	0.41	134/5452 (2.5)	250/12 353 (2.0)	0.06
Clinically driven TVR	33/5452 (0.6)	91/12 353 (0.7)	0.32	128/5452 (2.4)	237/12 353 (1.9)	0.06
TLF	76/5452 (1.4)	179/12 353 (1.5)	0.76	177/5452 (3.3)	354/12 353 (2.9)	0.17
TVF	82/5452 (1.5)	201/12 353 (1.6)	0.55	204/5452 (3.7)	419/12 353 (3.4)	0.25
POCE	124/5452 (2.3)	304/12 353 (2.5)	0.47	321/5452 (5.9)	717/12 353 (5.8)	0.82
Definite or probable ST	28/5452 (0.5)	69/12 353 (0.6)	0.71	37/5452 (0.7)	79/12 353 (0.6)	0.77
Bleeding (BARC 1–5)	68/5452 (1.3)	164/12 353 (1.3)	0.67	120/5452 (2.2)	276/12 353 (2.2)	0.89

Values are percentage (number). BARC indicates Bleeding Academic Research Consortium; LAD, left anterior descending artery; MI, myocardial infarction; POCE, patient-oriented composite end point, a composite of all-cause death, any MI, and any coronary revascularization; TLF, target lesion failure, a composite of cardiac death, target-vessel MI, and clinically driven TLR; TLR, target lesion revascularization; TV, target vessel; TVF, target vessel failure, a composite of cardiac death, target-vessel MI, and clinically driven TVR; TVR, target vessel revascularization; ST, stent thrombosis.

Discussion

In this large, real-world analysis of all-comer stent practice from a prospective, multicenter large registry, we report comparable clinical and procedural outcomes in patients treated for proximal LAD lesions compared with nonproximal LAD lesion at both 3-month and 1-year follow-up. The dogma that patients with proximal LAD lesions treated with PCI are thought to have greater risks of future cardiac events compared with patients with lesions in other coronary segments was found not to be true in our large study.

The optimal treatment of proximal LAD stenosis remains a matter of debate. Data derived from the current study and other contemporary data question whether the proximal LAD segment should be considered and treated differently than other proximal lesions elsewhere in the coronary vasculature in contemporary coronary revascularization guidelines.[5–8]

The LAD supplies a large portion of the left ventricular myocardium; hence, compromise of this artery can have adverse consequences for left ventricular function and prognosis. Randomized controlled trials have shown similar mortality and MACE after treatment of single proximal LAD lesions with a DES or CABG.[13,14]

The present registry includes only stented patients and therefore has an inherited selection bias. It does not contain any comparison with CABG patients. The choice of revascularization was done before entering into the registry. It is difficult to know why those patients were referred to surgery and how they would have fared if they underwent PCI. The 1-year repeat revascularization was higher in the proximal LAD group (TLR 1.8% versus 1.3%; *P*=0.008 and TVR 2.4% versus 1.9%; *P*=0.06). The incidence is small, but may suggest another potential reason why CABG may be preferred and emphasizing the need for such a study. Therefore, while the point of similar outcomes of proximal LAD patients to those with other lesions is well taken, it is not the same as the comparison with those who were referred to surgery. Obviously, if that was available, there will be a host of selection biases that will be difficult to account for as well.

In the SORT OUT (Scandinavian Organization for Randomized Trials With Clinical Outcome) II trial,[8] there was a 12% TLR rate 10 years after treatment of a proximal LAD lesion with first-generation DES. This result is fairly similar to the one expected after CABG using the left internal mammary artery to the LAD. The reported long-term patency rates for this bypass graft vary slightly according to whether patients with multivessel disease are also included (85–90% patency rates)[14–16] or whether patients have only single proximal LAD lesions (89–100% patency rates).[17,18] Contemporary studies have reported similar outcomes in the medium and longer term in proximal LAD lesions compared with other lesions treated with PCI. The NOBORI-2 trial found no differences in outcomes between patients who underwent PCI of the proximal LAD (N=834) and those treated in a nonproximal LAD territory (N=2203), using the NOBORI Bioliomus A9 DES.[5] In another study, Roguin et al analyzed 4-year outcomes of 8709 patients undergoing PCI with either the Endeavor zotarolimus-eluting stent or the Cypher sirolimus-eluting stent enrolled in the PROTECT (Prophylaxis for Thromboembolism in Critical Care Trial) trial. Patients were stratified according to lesion location within or outside the proximal LAD. At 4-year follow-up, mortality rates, target vessel failure, stent thrombosis, and MACE were the same, although patients in the proximal LAD group had higher rates of MI.[6]

Ten-year clinical outcomes expressed as all-cause mortality and MACE were determined for 1479 patients with a single non-left-main coronary stenosis treated with a first-generation DES in the SORT OUT II trial.[8] Patients treated with a DES in the proximal LAD were found to have similar, if not better, long-term clinical outcomes compared with patients stented in other coronary artery segments. Follow-up was 99.3%

Table 4. Multivariate Logistic Regression: Odds Ratio for Risk of 1-Year Target Lesion Failure

	Odds Ratio	95% CI	*P* Value
Proximal LAD, yes	1.07	0.88–1.31	0.48
Age, +10 y	1.25	1.15–1.37	<0.001
Male sex	1.09	0.88–1.35	0.42
Body mass index, +1 kg/m^2	0.98	0.961–1.004	0.12
Diabetes mellitus, yes	1.71	1.42–2.06	<0.001
Hypercholesterolemia, yes	0.84	0.70–1.01	0.07
Renal impairment, yes	1.81	1.40–2.34	<0.001
Previous PCI, yes	1.57	1.29–1.91	<0.001
Acute coronary syndrome, yes	1.39	1.15–1.67	0.001
Right coronary artery treated, yes	0.81	0.65–0.99	0.04
Graft treated, yes	3.75	0.81–17.4	0.09
No. of lesions identified, +1	1.23	1.13–1.34	<0.001
No. of lesions treated, +1	0.88	0.75–1.03	0.11
No. of implanted stents, +1	1.39	1.14–1.69	0.001
Length of implanted stent, +1 mm	0.99	0.985–1.001	0.08
Bifurcation, yes	1.56	1.24–1.96	<0.001
Type A lesion (ACC/AHA classification), yes	0.57	0.37–0.88	0.01
Type C lesion (ACC/AHA classification), yes	1.31	1.07–1.61	0.009

ACC/AHA indicates American College of Cardiology/American Heart Association; LAD, left anterior descending artery; PCI, percutaneous coronary intervention.

complete. All-cause mortality was 24.9% in the proximal LAD group (n=365) versus 26.3% in the nonproximal LAD group (n=1114; *P*=0.60). MACE occurred less frequently in the proximal LAD group: 24.6% versus 31.0% with a hazard ratio of 0.77 (95% CI, 0.61–0.97; *P*=0.024). After multivariate analysis, which included baseline characteristics that were unevenly distributed between the groups, the hazard ratio for MACE was 0.82 (95% CI, 0.65–1.03; *P*=0.09). As also noted in the NOBLE (Nordic-Baltic-British Left Main Revascularization Study) left main trial, a difference in outcomes may be driven not by the lesion of interest (eg, left main or proximal LAD), but by other de novo lesions.[19]

Limitations

The current study is a subgroup analysis of a prospective, single-arm, multicenter observations Ultimaster DES registry (e-Ultimaster), which was a postmarketing study aimed to assess rates of TLF in all-comer patients treated with the thin-strut, cobalt chromium, biodegradable-polymer, sirolimus-eluting coronary stent Ultimaster in real-world situations.[9] Our findings are subject to certain limitations. First, our study is observational in nature, and the stent strategy, stenting technique, and use of adjuvant procedural techniques were based on operator choice, rather than randomized as per in randomized controlled trials. Second, only 1 type of stent was used. Our findings may therefore not be applicable to other stent platforms. Third, patients in the proximal LAD group had worse baseline procedural and lesion characteristics, and although we used a robust statistical method to account for all the differences, the possibility of unmeasured confounders cannot be ruled out. Fourth, the study outcomes were clinically driven with data around angiographic follow-up not captured. Finally, while we observed similar outcomes at 1 year, we cannot rule out significant differences in clinically relevant end points in the longer term.

Conclusions

In this real-world analysis, we report good clinical safety and procedural efficacy of a newer-generation thin-strut DES (Ultimaster stent) in treating proximal LAD lesions compared with other coronary lesions. Patients had comparable clinical outcomes independent of stenting location and strategy. Treatment of the proximal LAD with PCI did not confer a different prognosis to lesion in different anatomical sites, therefore questioning whether disease in the proximal LAD should be regarded differently from that in other anatomical sites within the coronary artery vasculature.

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Disclosures

None.

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Supplemental Material

Table S1. Segment information (per patient).

	Proximal LAD n=5452	Non-proximal LAD n=12353	p-value
1 RCA proximal	6.7 (366/5452)	17.5 (2164/12353)	<0.001
2 RCA mid	8.0 (434/5452)	22.2 (2739/12353)	<0.001
3 RCA distal	3.3 (182/5452)	10.2 (1257/12353)	<0.001
4 Posterior descending artery	0.9 (51/5452)	2.2 (270/12353)	<0.001
16 Posterolateral branch from RCA	0.8 (41/5452)	2.2 (265/12353)	<0.001
5 Left Main	0 (0/5452)	0% (0/12353)	-
6 LAD proximal	100 (5452/5452)	0% (0/12353)	<0.001
7 LAD mid	10.7 (585/5452)	32.2 (3973/12353)	<0.001
8 LAD apical	2.5 (136/5452)	3.0 (369/12353)	0.07
9 First diagonal	4.3 (234/5452)	4.7 (581/12353)	0.24
10 Second diagonal	0.2 (10/5452)	0.3 (31/12353)	0.50
11 Proximal circumflex artery	7.4 (401/5452)	11.6 (1438/12353)	<0.001
12 Intermediate/anterolateral artery	2.4 (132/5452)	4.2 (516/12353)	<0.001
12a Obtuse marginal a	2.6 (144/5452)	5.8 (716/12353)	<0.001
12b Obtuse marginal b	0.4 (24/5452)	1.4 (169/12353)	<0.001
13 Distal circumflex artery	5.9 (323/5452)	12.6 (1556/12353)	<0.001
14 Left posterolateral	1.0 (52/5452)	2.2 (267/12353)	<0.001
15 Posterior descending	0.6 (30/5452)	1.4 (168/12353)	<0.001

LAD: left anterior descending artery; RCA: right coronary artery

Table S2. Unadjusted clinical outcomes.

	3-months			1-year		
	Proximal LAD n=5452	Non-proximal LAD n=12353	p-value	Proximal LAD n=5425	Non-proximal LAD n=12353	p-value
All-cause death	1.1 (58/5452)	0.8 (103/12353)	0.14	2.2 (120/5452)	2.0 (247/12353)	0.38
Cardiac death	0.9 (47/5452)	0.6 (74/12353)	0.05	1.4 (74/5452)	1.2 (145/12353)	0.31
Any MI	0.6 (30/5452)	0.7 (80/12353)	0.44	1.1 (57/5452)	1.1 (132/12353)	0.89
Target-vessel MI	0.5 (27/5452)	0.5 (65/12353)	0.79	0.8 (45/5452)	0.8 (104/12353)	0.91
All TLR	0.5 (27/5452)	0.4 (52/12353)	0.49	1.9 (104/5452)	1.3 (162/12353)	0.003
Clinically driven TLR	0.5 (27/5452)	0.4 (52/12353)	0.67	1.8 (100/5452)	1.2 (153/12353)	0.002
All TVR	0.6 (35/5452)	0.7 (80/12353)	0.97	2.5 (137/5452)	1.9 (239/12353)	0.01
Clinically driven TVR	0.6 (32/5452)	0.6 (78/12353)	0.73	2.4 (130/5452)	1.8 (227/12353)	0.02
TLF	1.5 (79/5452)	1.3 (155/12353)	0.29	3.4 (184/5452)	2.7 (337/12353)	0.02
TVF	1.6 (85/5452)	1.4 (175/12353)	0.47	3.9 (210/5452)	3.2 (397/12353)	0.03
POCE	2.4 (129/5452)	2.2 (277/12353)	0.61	6.1 (330/5452)	5.7 (704/12353)	0.35
Definite or probable ST	0.5 (29/5452)	0.5 (61/12353)	0.74	0.7 (38/5452)	0.6 (71/12353)	0.34
Bleeding (BARC 1-5)	1.3 (68/5452)	1.3 (155/12353)	0.97	2.2 (119/5452)	2.2 (266/12353)	0.90

Values are percentage (number)

BARC: Bleeding Academic Research Consortium; MI: myocardial infarction; LAD: left anterior descending artery; POCE: patient-oriented composite endpoint, a composite of all-cause death, any MI and any coronary revascularization; TLF: target lesion failure, a composite of cardiac death, target-vessel MI and clinically driven TLR; TLR: target lesion revascularization; TV: target vessel; TVF: target vessel failure, a composite of cardiac death, target-vessel MI and clinically driven TVR; TVR: target vessel revascularization; ST: stent thrombosis

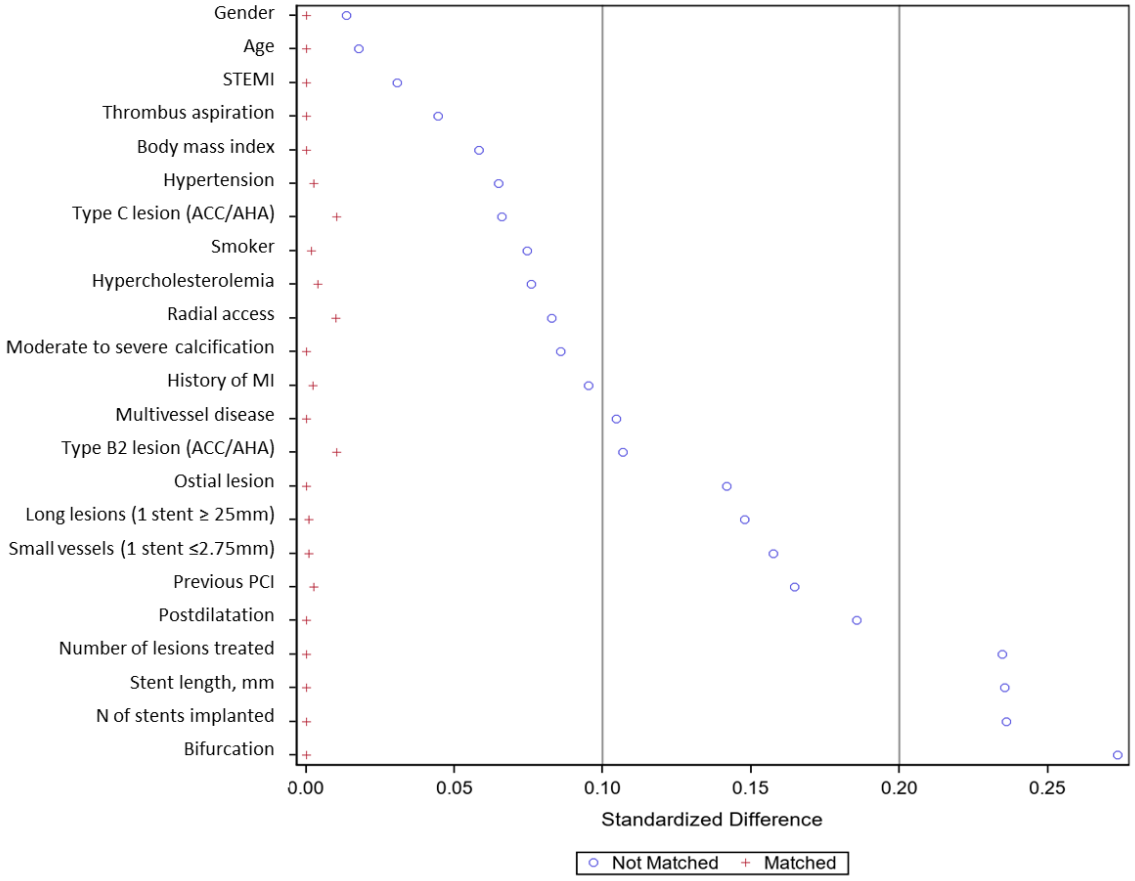
Table S3. Clinical outcomes according to number of vessel diseased.

	1-year			
	Proximal LAD – 1 vessel disease n=2776 (%)	Proximal LAD – 2 vessels diseased n=1772 (%)	Proximal LAD – 3 vessels diseased n=874 (%)	Overall p-value
All-cause death	1.69% (47/2,776)	1.92% (34/1,772)	4.24% (37/872)	<0.001
Cardiac death	0.94% (26/2,776)	1.19% (21/1,772)	2.87% (25/872)	<0.001
Any MI	0.58% (16/2,776)	0.96% (17/1,772)	2.64% (23/872)	<0.001
Target-vessel MI	0.50% (14/2,776)	0.73% (13/1,772)	2.06% (18/872)	<0.001
All TLR	1.59% (44/2,776)	1.75% (31/1,772)	3.33% (29/872)	0.004
Clinically driven TLR	1.51% (42/2,776)	1.64% (29/1,772)	3.33% (29/872)	0.002
All TVR	1.95% (54/2,776)	2.77% (49/1,772)	3.90% (34/872)	0.004
Clinically driven TVR	1.87% (52/2,776)	2.48% (44/1,772)	3.90% (34/872)	0.003
TLF	2.52% (70/2,776)	3.27% (58/1,772)	6.19% (54/872)	<0.001
TVF	2.85% (79/2,776)	4.01% (71/1,772)	6.65% (58/872)	<0.001
POCE	4.32% (120/2,776)	6.43% (114/1,772)	10.78% (94/872)	<0.001
Definite or probable ST	0.58% (16/2,776)	0.51% (9/1,772)	1.49% (13/872)	0.009
Bleeding (BARC 1-5)	1.98% (55/2,776)	2.60% (46/1,772)	1.95% (17/872)	0.34

Table S4. Clinical outcomes according to diabetes.

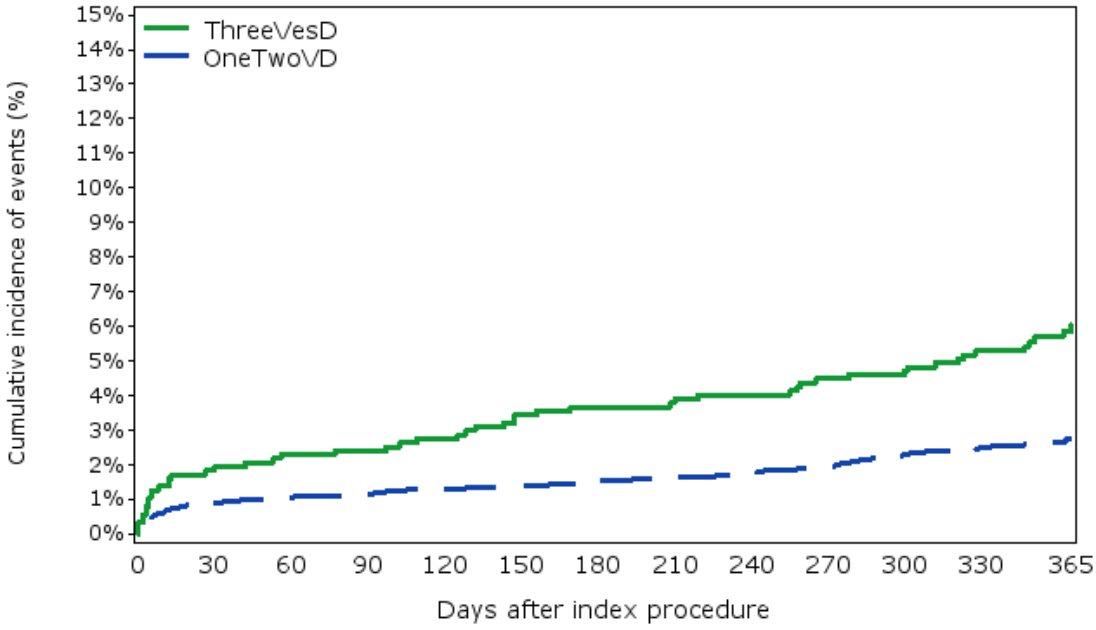
	1-year outcomes		
	Proximal LAD – Diabetes n=1457	Proximal LAD – No diabetes n=3995	p-value
All-cause death	3.16% (46/1,457)	1.85% (74/3,995)	0.004
Cardiac death	2.13% (31/1,457)	1.08% (43/3,995)	0.003
Any MI	1.37% (20/1,457)	0.93% (37/3,995)	0.15
Target-vessel MI	1.17% (17/1,457)	0.70% (28/3,995)	0.09
All TLR	2.95% (43/1,457)	1.53% (61/3,995)	<0.001
Clinically driven TLR	2.95% (43/1,457)	1.43% (57/3,995)	<0.001
All TVR	3.71% (54/1,457)	2.08% (83/3,995)	<0.001
Clinically driven TVR	3.71% (54/1,457)	1.90% (76/3,995)	<0.001
TLF	5.35% (78/1,457)	2.65% (106/3,995)	<0.001
TVF	5.97% (87/1,457)	3.08% (123/3,995)	<0.001
POCE	8.30% (121/1,457)	5.23% (209/3,995)	<0.001
Definite or probable ST	0.82% (12/1,457)	0.65% (26/3,995)	0.50
Bleeding (BARC 1-5)	1.99% (29/1,457)	2.25% (90/3,995)	0.56

Figure S1. Standardized differences in variables included in the propensity score between proximal LAD versus non-proximal LAD group.



Standardized difference for all variables below 0.20 are considered well balanced, while standardized difference for all variables below 0.10 can be considered extremely well balanced (STEMI: ST-elevation myocardial infarction; PCI: percutaneous Coronary intervention.

Figure S2. Comparison between 1 or 2 vessel disease vs 3 vessels diseased.



Multivessel disease was not a significant effect modifier for the risk of TLF between proximal LAD and non-proximal LAD group (no significant interaction effect)

Figure S3. Comparison between diabetes and non-diabetes in Proximal LAD group.