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CLINICAL RESEARCH

CORONARY

Angiographic and Clinical Outcomes After Everolimus-Eluting Stenting for Unprotected Left Main Disease and High Anatomic Coronary Complexity

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ABSTRACT

OBJECTIVES This study determined angiographic and clinical outcomes after everolimus-eluting stent (EES)–supported percutaneous coronary intervention for unprotected left main disease (ULMD) and high SYNTAX (SYNergy between PCI with TAXus and Cardiac Surgery) trial score (≥33).

BACKGROUND The SYNTAX trial has shown the superiority of coronary surgery over percutaneous coronary intervention (PCI) in patients with ULMD and complex coronary anatomy. It has been hypothesized that, if newer generation drug-eluting stents had been used in the SYNTAX trial, there would have been a significant reduction in clinical events.

METHODS Patients had angiograms scored according to the SYNTAX score algorithm and were divided into 2 groups: those with SYNTAX score of ≥33 and those with <33. The main endpoints were ULMD restenosis and 3-year cardiac mortality.

RESULTS From May 2008 to July 2014, 393 patients underwent EES implantation for ULMD (181 patients had a SYNTAX score ≥33, whereas 212 patients had a SYNTAX score <33). Overall, the restenosis rate was 4.9% (6% in SYNTAX patients scoring ≥33 and 4.1% in SYNTAX patients scoring <33; $p = 0.399$). On multivariate analysis, the only variable related to restenosis was stent length (odds ratio [OR]: 1.06; 95% confidence interval [CI]: 1.02 to 1.09; $p = 0.002$). Three-year cardiac survival rates were 99 ± 1% and 98 ± 2% in patients with European system for cardiac operative risk evaluation (EuroSCORE) <6 and SYNTAX <33 and ≥33, respectively, and 90 ± 3% and 87 ± 3% in patients with a EuroSCORE >6 and SYNTAX score <33 and ≥33, respectively. EuroSCORE was strongly related to cardiac mortality, while the SYNTAX score ≥33 was not both in patients with a EuroSCORE <6 or ≥6, and there were no interactions between EuroSCORE and SYNTAX score ≥33.

CONCLUSIONS For ULMD patients, high anatomical complexity as defined by a SYNTAX score ≥33 is not predictive of clinical outcome after PCI. (TAXUS Drug-Eluting Stent Versus Coronary Artery Bypass Surgery for the Treatment of Narrowed Arteries [SYNTAX]; NCT00114972) (J Am Coll Cardiol Intv 2016;9:1001–7) © 2016 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass graft

CTO = chronic total occlusion

DES = drug-eluting stent(s)

EES = everolimus-eluting stent(s)

EuroSCORE = European system for cardiac operative risk evaluation

MACCE = major adverse cardiac and cerebrovascular event(s)

PCI = percutaneous coronary intervention

TVR = target vessel revascularization

ULMD = unprotected left main disease

Randomized comparison of percutaneous coronary intervention (PCI) with coronary artery bypass graft (CABG) for unprotected left main disease (ULMD) has shown the superiority of CABG in patients with complex coronary anatomy, and guidelines do not recommend PCI in patients with complex coronary anatomy (1–5). The SYNTAX (SYNergy between PCI with TAXus and Cardiac Surgery) trial introduced an anatomic complexity score and showed that patients with ULMD and high SYNTAX score had a higher major adverse cardiac and cerebrovascular event (MACCE) rate if treated with PCI than those treated with CABG, that is, at 5-year follow-up, MACCE rates were 46.5% and 29.7%, respectively ($p < 0.0001$) (3). It has been hypothesized that if newer generation drug-eluting stents (DES) had been used in the SYNTAX trial, there would have been a significant reduction in clinical events. This hypothesis is supported by registry studies (6,7), and 2 ongoing trials will compare PCI with surgery by using everolimus-eluting stents (EES).

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No study of EES has focused on ULMD in patients with complex coronary anatomy. The aim of this study was to describe the angiographic and clinical outcomes after EES-supported PCI for ULMD and high SYNTAX score (≥33).

METHODS

PATIENTS AND TREATMENT. The Florence ULMD PCI registry is a prospective single-center registry that started in 2003 and includes consecutive patients treated with DES supported PCI for ULMD.

Details of this registry have been published previously (6,8,9). From the database, we identified all patients with ULMD who received exclusively EES (either XIENCE; Abbott Vascular, Santa Clara, California; or Promus, Boston Scientific Corp., Natick, Massachusetts) and complex coronary anatomy (SYNTAX score ≥33). Patients underwent PCI instead of coronary surgery because of either the patient's preference or the high risk associated with surgery. High surgical risk was defined as a logistic European system for cardiac operative risk evaluation (EuroSCORE) ≥6 (10). All angiograms were scored according to the SYNTAX scoring algorithm (11).

PCI was performed using standard techniques. For distal left main disease, a single-stent technique was preferred in patients with a normal or diminutive appearing side branch, whereas a double-stent technique was considered in patients with disease of both ostia and proximal segments of left anterior descending artery and circumflex artery. Whatever the stenting technique used, routine final kissing balloon post-dilation with noncompliant balloons had to be performed in all cases. Intravascular ultrasonographic guidance was used at the discretion of the operator. Multivessel disease was defined as stenosis >70% of 1, 2, or 3 major coronary arteries on visual assessment at baseline angiography, other than the LM lesion. Disease of left anterior descending artery and of the circumflex artery included lesions beyond 10 mm from the ostia. Chronic total occlusion (CTO) was defined as a complete occlusion (Thrombolysis In Myocardial Infarction [TIMI] flow grade 0) lasting >3 months. Completeness of revascularization was defined as successful revascularization of all vessels with a stenotic diameter >70% and a diameter >2 mm on visual assessment achieved either during index hospitalization or at any time within 30 days after the first ULMD PCI.

Procedural adjunctive antithrombotic therapy included unfractionated heparin (an initial bolus of 70 U per kg, and additional boluses during the procedure to achieve an activated clotting time of 200 to 250 s), whereas glycoprotein IIb/IIIa inhibitors were prescribed at the discretion of the operator. Chronic antithrombotic treatment included aspirin (300 mg/day, indefinitely) and clopidogrel, 75 mg daily, or prasugrel, 10 mg daily for at least 1 year.

Treatment protocol included routine 6- to 9-month angiographic follow-up. All patients were considered eligible for angiographic follow-up, except for asymptomatic patients with severe renal insufficiency. Unscheduled angiography was allowed on the basis of clinical indication.

ENDPOINTS. The angiographic endpoint of the study was angiographic restenosis, defined as left main binary angiographic in-segment restenosis >50% at the scheduled or unscheduled angiographic follow-up. Left main restenosis was defined as >50% luminal narrowing at the segment site, including the stent and 5-mm proximal and distal to the stent edges of the target vessel on follow-up angiography. Angiographic parameters were assessed using an automated edge-contour detection computer analysis system (Innova 2100IQ, General Electric Healthcare Technologies, Little Chalfont, Buckinghamshire, United Kingdom). Clinical endpoints were 1- and 3-year cardiac mortality rates. Other clinical exploratory endpoints were 1-year MACCE that included cardiac death, nonfatal myocardial infarction, target vessel revascularization (TVR), and stroke; 1-year TVR was defined as repeat

percutaneous or surgical revascularization of the left main. All deaths were considered cardiac-related, unless an unequivocal noncardiac cause could be documented. Diagnosis of non-Q-wave myocardial infarction was based on an increase of creatine kinase myocardial band isoenzyme or troponin I >3 times the upper limit of normal or, for patients with elevated values on admission, as a re-elevation of creatine kinase-MB or troponin I values. A Q-wave myocardial infarction was defined as the development of new Q waves in 2 or more electrocardiographic leads and in addition to creatine kinase-MB or troponin I elevation. Stroke was defined as an acute neurological defect lasting more than 24 h. All patients were scheduled for clinical follow-up at 1, 6, and 12 months and yearly thereafter. All other possible information derived from hospital readmission or by the referring physician, relatives, or municipality live registries were entered into the prospective database. The study was approved by the institutional review committee, and all patients gave informed written consent to intervention and the study.

STATISTICAL ANALYSIS. Discrete data were summarized as frequencies, and continuous data were expressed as mean ± SD or median (interquartile range), as appropriate. The chi-square test was used for comparison of categorical variables, and the unpaired 2-tailed Student *t* test or Mann-Whitney rank sum test was used to test differences among continuous variables. Survival curves were generated by use of the Kaplan-Meier method, and the differences between groups were assessed by log-rank test. The multivariate analysis to evaluate the independent contribution of clinical, angiographic, and procedural variables to left main binary in-segment restenosis was performed by forward stepwise logistic regression analysis. Variables tested were age, sex, diabetes mellitus, previous PCI, acute coronary syndrome on admission, 3-vessel disease, EuroSCORE, total stent length, and intravascular ultrasound guidance. Multivariate analyses were performed to evaluate the independent contribution associated with cardiac mortality, by using Cox regression analyses, using EuroSCORE and completeness of revascularization for clinical risk and SYNTAX score for extension of coronary artery disease; no other covariates were entered into the multivariate model in order to avoid collinearity and overfitting. The proportional hazard assumption was assessed and satisfied graphically by plotting log (-log) survival curves against log survival time for each predictor category and verifying whether curves were parallel. Interaction between EuroSCORE and SYNTAX score was tested with Cox regression model. In addition Cox regression analysis was used to test SYNTAX score ≥33 in the subset of patients with EuroSCORE <6 and >6. A p value of <0.05 was considered significant. Analyses were performed using SPSS version 11.5 software (SPSS Inc., Chicago, Illinois).

RESULTS

Between May 2008 and July 2014, 393 patients underwent EES implantation for ULMD. Of these, 181 patients had a SYNTAX score ≥33, whereas 212 had a SYNTAX score <33.

Table 1 summarizes baseline clinical and angiographic characteristics of the 2 patient groups. Patients with high SYNTAX score had higher EuroSCOREs on admission than patients with SYNTAX score <33 (14.0 ± 13.6 and 8.8 ± 11.5, respectively; p <0.001). EuroSCORE >6 was revealed more frequently in the high SYNTAX score group than in the low and intermediate SYNTAX score group (65% and 42%, respectively; p < 0.001). Again, the high SYNTAX score group had a higher incidence of severe left ventricular dysfunction, ST-segment elevation acute myocardial infarction, and renal insufficiency on admission. As expected, 3-vessel disease and CTO of the right coronary artery were more frequent in

TABLE 1 Baseline Clinical and Angiographic Characteristics

	Overall (N = 393)	SYNTAX <33 (n = 212)	SYNTAX ≥33 (n = 181)	p Value
Age, yrs	72 ± 11	70 ± 11	72 ± 11	0.082
Males, %	307 (78)	167 (70)	140 (77)	0.733
Current smokers, %	66 (17)	38 (18)	28 (15)	0.516
Arterial hypertension, %	266 (68)	140 (66)	126 (70)	0.450
Diabetes mellitus, %	96 (24)	48 (23)	48 (26)	0.372
Hypercholesterolemia, %	215 (55)	110 (52)	105 (58)	0.224
Peripheral vascular disease, %	76 (19)	36 (17)	40 (22)	0.778
Previous MI, %	85 (22)	47 (22)	38 (21)	0.778
Previous PCI, %	157 (40)	98 (46)	59 (33)	0.006
Acute coronary syndrome, %	200 (51)	103 (49)	97 (54)	0.322
STEMI, %	30 (10)	13 (6)	26 (14)	0.007
Creatinine >150 μmol/l, %	48 (12)	15 (7)	33 (18)	<0.001
LVEF ≤30%, %	64 (16)	25 (12)	39 (21)	0.007
Logistic EuroSCORE				
Mean ± SD	11.2 ± 12.7	8.8 ± 11.5	14.0 ± 13.6	<0.001
Median (IQR)	12.7 (2.8–14.6)	4.6 (2.4–9.7)	13.6 (3.6–20.2)	<0.001
Logistic EuroSCORE ≥6, %	208 (53)	90 (42)	118 (65)	<0.001
LM plus 2-vessel disease, %	154 (39)	86 (41)	68 (38)	0.544
LM plus 3-vessel disease, %	132 (34)	40 (19)	92 (51)	<0.001
Distal LM location, %	368 (94)	196 (93)	172 (95)	0.297
RCA disease, %	220 (56)	94 (44)	126 (70)	<0.001
RCA total occlusion, %	83 (21)	17 (8)	66 (36)	<0.001

Values are mean ± SD or n (%).

IQR = interquartile range; LM = left main; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction; RCA = right coronary artery.

TABLE 2 Procedural Characteristics

	Overall (N = 393)	SYNTAX <33 (n = 212)	SYNTAX ≥33 (n = 181)	p Value
Ostial/shaft LM stenting only, %	25 (6)	16 (7)	9 (5)	0.297
Distal LM, %	368 (94)	196 (93)	172 (95)	0.297
Single stent, %	205 (62)	118 (60)	87 (51)	0.063
Stenting of both branches, %	163 (44)	78 (40)	85 (49)	0.063
T-stenting	54	26	28	
Crush stenting	109	52	57	
Total LM stent length, mm	24.4 ± 11.1	23.6 ± 10.7	25.3 ± 11.5	0.120
Stent length of ≥24 mm	179 (46)	86 (41)	93 (51)	0.032
Rotational atherectomy, %	15 (4)	4 (2)	11 (6)	0.031
IVUS guidance, %	267 (68)	154 (73)	113 (62)	0.031
Abciximab, %	187 (48)	114 (54)	73 (40)	0.008
IABP, %	32 (8)	6 (3)	26 (14)	<0.001
Maximum pressure inflation, atm	21 ± 3	21 ± 2	21 ± 2	0.715
RVD pre-PCI, mm	3.83 ± 0.33	3.83 ± 0.31	3.82 ± 0.35	0.795
MLD pre-PCI, mm	1.18 ± 0.81	1.21 ± 0.81	1.14 ± 0.82	0.395
MLD post-PCI, mm	3.81 ± 0.42	3.86 ± 0.28	3.84 ± 0.38	0.386
Multivessel PCI, %	248 (63)	108 (51)	140 (77)	<0.001
Complete revascularization, %	319 (81)	194 (91)	125 (70)	<0.001
CTO vessel, %	130 (33)	27 (13)	103 (56)	<0.001
Successful CTO PCI, %	78/90 (87)	18/21 (86)	60/69 (87)	0.883

Values are n (%) or mean ± SD or n/N (%).

CTO = chronic total occlusion; IABP = intra-aortic balloon counterpulsation; IVUS = intravascular ultrasound; LM = left main; MLD = minimum luminal diameter; PCI = percutaneous coronary intervention; RVD = reference vessel diameter.

patients with high SYNTAX score. Conversely, a history of PCI was more frequent in patients with a SYNTAX score <33.

Table 2 summarizes the procedural characteristics. Intraaortic balloon counterpulsation was used more frequently in patients with high SYNTAX score (14% vs. 3%; p < 0.001), while abciximab use and intravascular ultrasound guidance were more frequent in patients with SYNTAX score <33. Most patients had distal left main disease, and a single stent implantation was performed more frequently in patients with low or intermediate anatomic complexity (60%) than high anatomic complexity (51%; p = 0.063). As a consequence total stent length of left main bifurcation >24 mm was more frequent in patients with SYNTAX score ≥33. Left main lesion preparation by rotational atherectomy before stenting was more frequent in high SYNTAX score patients. Multivessel PCI, including CTO PCI were performed more frequently in patients with high coronary anatomy complexity (77% vs. 51%; p < 0.001) and a complete revascularization was achieved more frequently in low or intermediate complex coronary anatomy (91% vs. 70%, respectively; p < 0.001).

ANGIOGRAPHIC OUTCOME. Overall, 365 patients were eligible for angiographic follow-up. The follow-up rate was 95%. Overall binary in-segment left main restenosis rate was 4.9%. Restenosis rates were similar in patients with high anatomic complexity and intermediate or low complexity anatomy (6% and 4.1%, respectively; p = 0.399). On multivariate analysis, the only variable related to restenosis was stent length (odds ratio [OR]: 1.06; 95% confidence interval [CI]: 1.02 to 1.09; p = 0.002).

CLINICAL OUTCOME. The 1-year clinical follow-up rate was 100%. The median follow-up length was 785 days (interquartile range [IQR]: 415 to 1,110 days). Table 3 summarizes the clinical outcome. At 1 year, all-cause death and cardiac death rates were very low in patients with a EuroSCORE <6 whatever the SYNTAX score, from 0.8% to 1.6%. Conversely, a EuroSCORE ≥6 was associated with 1-year high cardiac mortality rates: 4.4% in patients with SYNTAX score <33 and 10.2% in those with SYNTAX score >33. No differences were revealed among groups in the incidence of myocardial infarction and stroke, whereas TVR was more frequent in patients with high EuroSCORE and SYNTAX score ≥33 (9.3%) than in those with EuroSCORE <6 and SYNTAX ≥33 (1.6%; p = 0.046). The median time from index procedure to TVR was 187 days (IQR: 180 to 222 days).

The highest 1-year MACCE rate was revealed in the 118 patients with high EuroSCORE and SYNTAX ≥33 (25%), although MACCE rates ranged from 4.8% to 11% in the other 3 patient groups.

Figure 1 show 3-year cardiac survival curves. Cardiac survival rates were 99 ± 1% and 98 ± 2% in patients with EuroSCORE <6 and SYNTAX <33 and ≥33, respectively (p = 0.630), and 90 ± 3%

TABLE 3 1-Year Clinical Outcome

Outcome	EuroSCORE <6	EuroSCORE ≥6	p Value
SYNTAX score <33	n = 122	n = 90	
All-cause death (%)	1 (0.8)	7 (7.8)	0.009
Cardiac death	1 (0.8)	4 (4.4)	0.086
Myocardial infarction	1 (0.8)	2 (2.2)	0.399
TVR	5 (4.1)	3 (3.3)	0.773
Stroke	0 (0)	1 (1.1)	0.243
MACCE	7 (5.7)	10 (11)	0.154
SYNTAX score ≥33	n = 63	n = 118	
All-cause death	1 (1.6)	23 (19.5)	0.001
Cardiac death	1 (1.6)	12 (10.2)	0.033
Myocardial infarction	0 (0)	4 (3.4)	0.139
TVR	1 (1.6)	11 (9.3)	0.046
Stroke	1 (1.6)	2 (1.7)	0.958
MACCE	3 (4.8)	29 (25)	<0.001

Values are n (%).

MACCE = major adverse cardiac and cerebrovascular event(s); TVR = target vessel revascularization.

and 87 ± 3% in patients with a EuroSCORE ≥6 and SYNTAX score <33 and ≥33, respectively (p = 0.211).

Table 4 shows the results of multivariate analyses for 3-year cardiac mortality. EuroSCORE was strongly related to cardiac mortality, whereas SYNTAX score ≥33 was not, either in patients with a EuroSCORE <6 or those with ≥6, and there were no interactions between EuroSCORE ≥6 and SYNTAX score ≥33.

Table 5 compares the Florence Registry and the SYNTAX Trial left main PCI patient cohorts with high complex anatomical complexity.

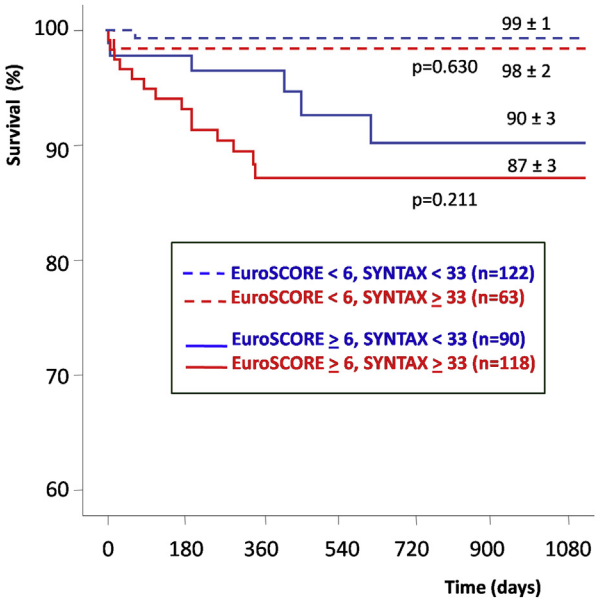
DISCUSSION

The main findings of this study can be summarized as follows: 1) EES-supported LM PCI is associated with a very low rate of restenosis whatever the anatomic complexity; 2) as a consequence, repeat revascularization of LM is lower than that reported in previous studies using first-generation generation DES; 3) the strongest variable after LM EES-supported PCI related to clinical outcome was EuroSCORE, and a EuroSCORE ≥6 identified patients at high risk of death; and 4) the SYNTAX score is not predictive of cardiac mortality, and there was no interaction between EuroSCORE and SYNTAX score.

There are few data for angiographic restenosis after DES implantation for ULMD. The SYNTAX-LE MANS angiographic left main substudy that included 156 patient treated with first-generation paclitaxel-eluting stent reported a restenosis rate of 7% (12). The Florence ULMD PCI registry showed the superiority of EES over that of first-generation drug-eluting stents: the restenosis rates were 5.2% and 15.6%, respectively (p = 0.002; follow-up rate was 98%) (6). The current study showed a restenosis rate of 4.9%, without significant differences between patients with SYNTAX score ≥33 and those with <33. The SYNTAX trial reported the 1-year repeat revascularization rate of 12% in the PCI arm (n = 357) and 6.7% in the surgery arm (348 patients) (3). More importantly, the repeat revascularization rate was very high, 17.2%, in PCI patients with a SYNTAX score ≥33 (n = 135). The last finding drove differences in MACCE between PCI and surgery in left main high anatomic complexity and supports a class III recommendation of current guidelines (4,5).

In this study, the highest TVR rate occurred in the subgroup of patients, 9.3%, with EuroSCORE ≥6 and SYNTAX score ≥33. In the other patient subgroups, the TVR rate was very low, ranging from 1.6% in patients with EuroSCORE <6 and SYNTAX score ≥33 to 4.1%, in patients with EuroSCORE <6 and SYNTAX score <33 (p = NS). Most TVR procedures were

FIGURE 1 3-Year Cardiac Survival Curves



EuroSCORE <6, SYNTAX < 33	122	120	92	71	46	37	22
EuroSCORE <6, SYNTAX ≥ 33	63	61	46	38	24	18	12
EuroSCORE ≥ 6, SYNTAX < 33	90	83	70	44	36	22	10
EuroSCORE ≥ 6, SYNTAX ≥ 33	118	108	95	62	45	28	20

Three-year cardiac survival curves according to EuroSCORE ≥6 or <6 and to SYNTAX score ≥33 or <33. EuroSCORE = European system for cardiac operative risk evaluation; SYNTAX = SYNergy between Percutaneous Coronary Intervention with TAXus and Cardiac Surgery trial.

TABLE 4 Multivariate Analyses for 3-Year Cardiac Mortality

	HR	95% CI	p Value
SYNTAX score ≥33	1.81	0.73–4.48	0.198
EuroSCORE ≥6	8.46	1.95–36.72	0.004
Complete revascularization	0.63	0.253–1.57	0.323
SYNTAX score ≥33	1.97	0.12–31.4	0.632
EuroSCORE ≥6	8.87	1.07–73.7	0.043
SYNTAX score/EuroSCORE interaction	0.91	0.05–17.3	0.951
EuroSCORE <6 subgroup (n = 185)			
SYNTAX score ≥33	1.95	0.12–31.2	0.636
EuroSCORE >6 subgroup (n = 208)			
SYNTAX score ≥33	1.80	0.69–4.67	0.230

CI = confidence interval; EuroSCORE = European system for cardiac operative risk evaluation; HR = hazard ratio; SYNTAX = SYNergy between Percutaneous Coronary Intervention with TAXus and Cardiac Surgery trial.

TABLE 5 Comparison of Florence Registry Patient Cohort and SYNTAX Trial Percutaneous Coronary Intervention Cohort With High Anatomical Complexity

	Florence Registry (n = 181)	SYNTAX PCI Randomized (n = 135)
EuroSCORE	14.0 ± 13.6	3.9 ± 2.8*
Complete revascularization	70.0	46.2*
1-year mortality		
Death	13.3	9.7
Cardiac death	7.2	NA
3-year outcome†		
Death	18.8	13.4
Cardiac death	8.5	NA
MI	2.4	10.9
Stroke	2.1	1.6

Values are n (%) or mean ± SD. *Overall left main PCI cohort. †Kaplan-Meier event rate.
MI = myocardial infarction; NA = not available; PCI = percutaneous coronary intervention; SYNTAX = SYNergy between Percutaneous Coronary Intervention with TAXus and Cardiac Surgery.

performed in asymptomatic patients at the scheduled angiographic follow-up, as revealed by the time from the index procedure to TVR.

In the current study, a EuroSCORE ≥6 is a strong predictor of 3-year cardiac mortality whereas a SYNTAX score ≥33 was not, and there were no interactions between EuroSCORE and SYNTAX scores. This finding, in part, is consistent with the results of the SYNTAX trial that showed EuroSCORE having a strong impact on clinical outcome in surgical and PCI patients. In the SYNTAX trial PCI patients, the EuroSCORE had a predictive ability superior to the SYNTAX score. A major limitation of the SYNTAX score is the lack of clinical variables that have a strong impact on clinical outcome in the scoring algorithm. Capodanno et al. (13) developed a global risk classification that included SYNTAX score and EuroSCORE to improve the predictive ability of cardiac mortality, with a net reclassification improvement of 26% for patients with ULMD. The results of this study were confirmed by Serruys et al. (14) from the SYNTAX trial, who showed the combination of clinical and anatomical variable increases the predictive ability of EuroSCORE in ULMD PCI patients. More recently, the SYNTAX trial investigators have proposed a new risk score that includes the anatomical characteristics of the SYNTAX score and clinical variables, referred to as SYNTAX score II (15). Most of the clinical variables included in the SYNTAX score II are the same for the EuroSCORE, and this may explain the validation in clinical cohorts of the SYNTAX score II as a predictor of 3-year mortality.

In the current study, SYNTAX score ≥33 is not predictive of cardiac mortality and other adverse events but TVR in the subgroup of patients with EuroSCORE ≥6, and there was no interaction between EuroSCORE and SYNTAX score for cardiac mortality. This findings may be explained, at least in part, by major differences in baseline and procedural characteristics of the population of the present study compared with the SYNTAX trial. The Florence registry includes a real-world "all comers" population with high EuroSCORE (53% of patients had a EuroSCORE ≥6), and the routine treatment of complex lesions, including CTO, resulted in high rates of complete revascularization. Completeness of revascularization was achieved in 81% of treated patients, and CTO PCI success rate was 87%. These findings compare favorably with the SYNTAX-randomized PCI patients: in this study only 52.8% of patients received a complete revascularization, and the success rate of CTO PCI was 49%. The SYNTAX investigators have shown that incomplete percutaneous or surgical revascularization have a strong impact on clinical outcome including cardiac mortality and that CTO is the strongest predictor of incomplete revascularization after PCI (16). The high procedural success rate of complex lesions reduces or even cancel the prognostic impact of coronary anatomy complexity and calls the SYNTAX score into question. For left main disease patients, a SYNTAX score ≥33 should be no more considered to determine the optimal revascularization modality agreed that a complete revascularization can be achieved by PCI supported by new generation DES.

STUDY LIMITATIONS. This was a nonrandomized study. Despite the shortcomings inherent in all registries, the study provides original insights into the clinical and angiographic outcomes after EES implantation for ULMD in patients with high anatomic complexity. Moreover, the population of the present study could be considered more representative than the selected population of concluded and ongoing randomized trials such as Left Main/NOBLE (NCT01496651) and EXCEL (NCT01205776) trials, focused in low surgical risk and low anatomic coronary complexity. Although multivariate adjustments were performed for significant confounders the possibility of other unmeasured confounders having affected the results cannot be excluded.

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PERSPECTIVES

WHAT IS KNOWN? Randomized comparison of PCI with CABG for ULMD has shown the superiority of CABG in patients with complex coronary anatomy and guidelines do not recommend PCI in patients with complex coronary anatomy.

WHAT IS NEW? The availability of new generation DES that are more effective and safe than 1st generation DES, and of new techniques and devices for the treatment of complex coronary lesions, including CTO, reduces the prognostic impact of complex coronary anatomy on clinical outcome in patients with ULMD. SYNTAX score ≥33 should be no more considered to determine the optimal revascularization modality agreed that a complete revascularization can be achieved by PCI supported by use of new generation DES.

WHAT IS NEXT? More clinical trials focused on high EuroSCORE and/or SYNTAX ≥33 are needed to verify whether completeness revascularization achieved by PCI in ULMD with complex coronary anatomy is equivalent or superior to coronary surgery.

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