Unprotected left main percutaneous coronary intervention: prognostic value of SYNTAX score II

Angioplastie du tronc commun gauche non protégé : valeur pronostique du SYNTAX score II

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RÉSUMÉ

Introduction : Les sténoses du tronc commun gauche (TCG) représentent des lésions complexes mettant en jeu le pronostic vital.

But : Evaluer les résultats ainsi que les facteurs pronostiques à long terme des patients traités par intervention coronarienne percutanée (ICP) du TCG non protégé.

Méthodes : Nous avons réalisé une étude prospective entre 2012 et 2017 incluant tous les patients ayant bénéficié d'une ICP du TCG non protégé.

Résultats : Entre janvier 2012 et décembre 2017, nous avons retenu 150 patients consécutifs. L'âge moyen était 64±12 ans et 85% des patients étaient de sexe masculin. Le diabète était présent dans 50.7% des cas. Une revascularisation dans contexte de sauvetage a été notée chez 20,7% des patients avec 3,3% de chocs cardiogéniques. L'atteinte distale du TCG était prédominante (76.7%). 94.0% des patients avaient un SYNTAX score I bas ou intermédiaire (≤32). Le SYNTAX score II médian était de 31.1. Les stents actifs ont été utilisés dans 78,7% des cas. Dans le contexte de sauvetage, seuls les stents nus étaient disponibles. Parmi les atteintes distales, une approche à un stent était préférée (81,7%). Au terme d'un suivi médian de 13,4 mois, le taux d'événements cardiaques majeurs était de 23,3%, avec une estimation de 37,9% à 5 ans. Les facteurs prédictifs en étaient le choc cardiogénique, l'utilisation de stent nu, l'antécédent d'ICP et le SYNTAX score II ≥30.

Conclusion : L'ICP du TCG présente des résultats encourageants à court et à long terme. Le SYNTAX score II permettrait de prévoir la survenue de MACE à long terme.

Mots-clés

Tronc commun non protégé, angioplastie, pronostic, SYNTAX score II.

SUMMARY

Background : Unprotected left main (LM) coronary artery disease (CAD) represents a challenging lesion with a major prognostic impact.

Aim: Evaluate the clinical outcome and major adverse cardiac events (MACE) predictors of unprotected LM percutaneous coronary intervention (PCI) in an «all-comers» population.

Methods: We performed a prospective observational study of patients with unprotected LM stenosis treated by PCI. MACE were defined as the composite endpoint of all-cause death, myocardial infarction and target lesion revascularization.

Results: From January 2012 to December 2017, 150 consecutive patients who underwent unprotected LM PCI were included. The mean age was 64±12 years and 75.3% were males. Diabetes was noted in 50.7%. Emergent revascularization was performed in 20.7% of cases, including 3.3% patients with cardiogenic shock. Distal LM was involved in 76.7% of cases. A majority of patients (94.0%) had low or intermediate SYNTAX Score I (≤32). The median SYNTAX score II was 31.1. Drug-eluting stents were used in 78.7% and bare metal stents in 21.3% of patients, mainly in emergent setting where the former were unavailable. In distal LM PCI, provisional approach was mostly used (81.7%). The median follow-up was 13.4 months. MACE occurred in 23.3% with an estimate of 37.9% at 5 years. Significant predictors of MACE were cardiogenic shock, bare metal stents use, previous PCI, and SYNTAX score II ≥30.

Conclusion: Unprotected LM PCI presents encouraging short and long term outcomes. SYNTAX score II might represent a predictor for long-term outcome in this particular lesion subset.

Key-words

Unprotected left main, percutaneous coronary intervention, outcome, SYNTAX score II.

INTRODUCTION

Left main (LM) coronary artery disease is observed in 5 to 7% of patients undergoing coronary angiography (1–3). This lesion subset has an important prognostic impact as it may jeopardize more than 75% of myocardial blood flow (4). Mortality under medical treatment alone is as high as 50% at three years (5).

For many decades, coronary artery bypass grafting (CABG) was considered as the gold standard treatment of unprotected LM disease because of the high prevalence of distal LM involvement (more than 80% of cases) and the frequent association with multivessel disease (6). However, nowadays, this dogma has tended to change in favor of percutaneous coronary intervention (PCI) in selected patients with unprotected LM coronary artery disease (CAD) owing to the recent major technological developments of PCI techniques, supported by the recent published data of large scale randomized clinical trials (7–11).

The current guidelines are still relying on SYNTAX score I tertiles indicating that PCI is an appropriate alternative to CABG in LM disease and low-to-intermediate anatomical complexity (12). However, more and more evidence is supporting the added value and even the superiority of SYNTAX score II in this particular lesion subset (13).

In Tunisia, outcome data regarding unprotected LM-PCI are scarcely reported. Therefore, we sought to assess the long-term of PCI in all-comers population with LM disease, focusing on the predictive value of the SYNTAX scores I and II in this particular subset of lesions.

METHODS

Study design

From January 2012 to December 2017, all consecutive patients with unprotected LM-CAD treated by PCI were prospectively analyzed in this, “all-comers”, monocentric registry.

All in-hospital data were recorded. The latest clinical follow-up status were collected by the mean of clinical visits, telephone interviews or referring physicians. Dual-antiplatelet therapy was administered according to current guidelines. Angiographic controls and subsequent revascularizations were ischemia-driven (ie: noninvasive evaluation or clinical symptoms suggesting ischemia).

Definitions

In this study, events were analysed cumulatively at latest clinical follow-up available: all- cause and cardiac deaths, myocardial infarction (MI), cerebrovascular accident, target lesion revascularization (TLR), and target vessel revascularization (TVR). The occurrence of stent thrombosis (ST) was classified on the basis of the Academic Research Consortium definitions. Major adverse cardiac and event was defined as a composite endpoint of all-cause death, MI, and ischemia driven-TLR (14).

The European System for Cardiac Operative Risk Evaluation (EuroSCORE) and the Society of Thoracic Surgery (STS) risk score were used to stratify the risk of death at 30 days.

Distal LM lesions were classified using the Medina classification. A true bifurcation was defined as a significant involvement of the side branch (Medina classification of 1.1.1, 1.0.1 or 0.1.1).

Coronary angiograms were scored according to the SYNTAX score I calculator. Patients were divided into low score (0−22), intermediate score (23−32) and high score (>32) groups (7,8).

SYNTAX score II was evaluated in all patients to predict 4-year mortality after revascularization with PCI or CABG (15).

Study endpoints

The primary study endpoint was the incidence of MACE, all-cause and cardiac deaths, MI and ischemia-driven TLR at long-term follow-up. The secondary endpoints were to evaluate the predictive value of SYNTAX score I and SYNTAX score II for MACE occurrence.

Statistical analysis

Individual patient data were pooled and analyzed. Baseline characteristics were reported as number (percentage), mean ± standard deviation, or median (interquartile range). Event rates with 95% confidence intervals at follow-up were estimated by the Kaplan-Meier method as time to first event. Predictors for endpoint events were estimated by multivariate Cox regression analysis including variables with p values <0.10 in univariate analysis and using a rule of 1:10 covariates per number of events to avoid overfitting.

RESULTS

From January 2012 to December 2017, 150 consecutive patients undergoing unprotected LM-PCI were

prospectively included, which represented 3.8% of all PCI procedures performed in our catheterization laboratory during the study period. As shown in Figure 1, and compared with CABG, a considerable increase in percutaneous unprotected LM revascularization was noted (from 21.7% in 2012 to 56.9% in 2017), becoming the main management strategy for this lesion subset.

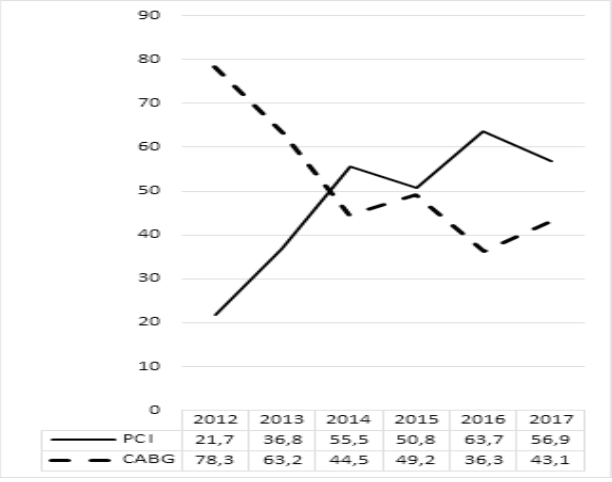

Figure 1: Evolution of percutaneous and surgical revascularization strategies rates for unprotected left main coronary artery disease between 2012 and 2017.
CABG: coronary artery bypass grafting, PCI: percutaneous coronary intervention.

Clinical and angiographic characteristics of the study population

Table 1 summarized the clinical characteristics of the study population. The mean age was 64.4 ± 12.1 years and 75.3% were males. Diabetes was prevalent in 50.7% of cases. In this report, acute coronary syndromes were the most reviling presentation of unprotected LM-CAD (66.6%) whereas stable angina or silent ischemia were observed in the 33.3% of cases. Cardiogenic shock was noted in 3.3% of patients. The mean left ventricular ejection fraction (LVEF) was 45.6 ± 13.1% and 20.7% of patients had reduced LVEF ≤30%.

Angiographic characteristics of unprotected LM-CAD are presented in Table 1. LM lesions were mainly located at its distal bifurcation (N=115, 76.7%). True bifurcations were noted in 26.0% of cases. LM lesions were associated with two or three-vessel-CAD in 58.7% of cases. Anatomic SYNTAX score I was ≤22 in 72.7%; between 23 and 32 in 21.3% and >32 in 6.0% of patients.

The median SYNTAX score II for PCI was 31.1 [22.2−39.8] with a predicted 4-years mortality of 7.5% [3.6−14.8%]. If the same population was assigned to CABG, the median SYNTAX score II was 30.1 [22.5−39.2] with an estimated 4-years mortality of 6.8% [3.7−13.2%]. A high risk surgical mortality (>5%) was found in 14.0% and 5.3% as estimated by EUROSCORE II and STS Risk Score respectively.

Table 1: Baseline clinical and angiographic characteristics.

	N=150
Age (years)	64.4 ± 12.1
Patients > 75 years old	35 (23.3)
Male	113 (75.3)
Smoking history (current or former)	94 (62.7)
Diabetes	76 (50.7)
Hypertension	69 (46.0)
Dyslipidemia	47 (31.3)
Family history of CAD	9 (6.0)
Previous MI	31 (20.7)
Previous PCI	34 (22.7)
Previous CABG	7 (4.7)
Clinical presentation*	
- Stable angina / silent ischemia	50 (33.3)
- Unstable angina	6 (4.0)
- Non ST elevation MI	56 (37.3)
- ST elevation MI	38 (25.3)
- Cardiogenic shock	5 (3.3)
LVEF (%)	45.6 ± 13.1
Euroscore II	1.8 [1.1−3.4]
STS risk score	0.9 [1.1−1.6]
Left dominance	14 (9.3)
Lesion localisation	
- Ostial/shaft	35 (23.3)
- Distal	115 (76..7)
True bifurcation	39 (26.0)
Total occlusion	1 (0,6%)
Calcifications	39 (26.0)
Thrombus	9 (6.0)
Associated CAD	
- Isolated LM CAD	14 (9.3)
- LM + single vessel CAD	48 (32.0)
- LM + two-vessel CAD	58 (38.7)
- LM + three-vessel CAD	30 (20.0)
SYNTAX score I	16.5 [12.0−24.0]
- ≤22	109 (72.7)
- 23-32	32 (21.3)
- >32	9 (6.0)
SYNTAX score II (PCI)	31.1 [22.2−39.8]

Values are mean ± SD, n (%), or median (interquartile range).
*Clinical presentation refers to initial diagnosis revealing left main coronary artery disease which was not the culprit lesion in all acute coronary syndrome presentations.
CABG: coronary artery bypass grafting, CAD: coronary artery disease, LM: left main, LVEF: left ventricular ejection fraction, MI: myocardial infarction, PCI: percutaneous coronary intervention.

Procedural characteristics

Procedural features of unprotected LM-PCI are summarized in Table 2. Radial approach was used in 63.3% while femoral route was preferred in 36.7% of cases. Of note, 20.7% of PCI were performed in emergent setting in front of sub-occlusive stenosis (10 patients), bail-out for iatrogenic dissections (8 patients), very high risk non ST elevation MI (8 patients) or ST segment elevation MI (5 patients). New-generation drug eluting stents were implanted in 78.7% of cases and bare metal stents in 21.3% of patients mainly in previously described emergent indications where the former were unavailable. Intravascular ultrasound guidance was used only in 2.7% of cases. No circulatory support in hemodynamically stable patients with reduced LVEF was planned in our experience and only one case of intra-aortic balloon pump insertion was reported after PCI in a cardiogenic shock presentation. Rotational atherectomy for heavy calcified LM lesions was used in 8.7% of patients.

Table 2: Procedural characteristics of unprotected left main percutaneous coronary interventions.

	N=150
Emergent procedure	31 (20.7)
Radial approach	95 (63.3)
Guiding catheter	
- 6F	144 (96.0)
- 7F	6 (4.0)
GPIIbIIIa antagonists	9 (6.0)
Intra-aortic balloon pump	1 (0.7)
Intravascular ultrasound	4 (2.7)
Rotational atherectomy	13 (8.7)
Stent type	
- Drug eluting stent	118 (78.7)
Zotarolimus eluting stent	64 (42.7)
Everolimus eluting stent	54 (36,0)
- Bare metal stent	32 (21.3)
Number of stents for LM lesion	1.1 ± 0.3
LM stent diameter (mm)	3.6 ± 0.4
LM stent length (mm)	23.9 ± 9.1
Two stents approach*	21/115 (18.3)
T and protrusion*	16/115 (13.9)
T stenting*	3/115 (2.6)
Mini-crush*	1/115 (0.9)
Double kissing Double crush*	1/115 (0.9)
Proximal optimisation technique*	106/115 (92.2)
Side branch optimization or Kissing balloon*	60/115 (52.2)

Values are mean ± SD, n (%), or median (interquartile range).
*Applicable only for patients with distal left main coronary artery percutaneous coronary interventions, N=115. LM: left main.

For distal LM-PCI (N=115), the provisional stenting technique was the rule and two-stent techniques were needed in 18.3%. Only one case of cross-over from planned provisional technique to T and protrusion bail-out technique was necessary owing to left circumflex coronary artery occlusion after LM to left anterior descending coronary artery stenting. When managing LM bifurcation lesions, proximal optimization technique (POT) was performed in the majority of cases (92.2%) and side branch optimization (by the POT-side branch inflation-RePOT or kissing balloon techniques) was performed in 52.2% of patients. When a two-stent technique was adopted, kissing balloon was carried out in 95.2%.
Angiographic success was obtained in all patients.

In-hospital and follow-up outcomes.

In-hospital MACE rate was 3.3%. Adverse outcomes consisted of four deaths (3 for cardiogenic shocks and one for major femoral access site bleeding) and one non-fatal MI due to a definite subacute stent thrombosis.
After a median follow-up of 13.4 months with an interquartile range of 5.1 to 24.1 months (clinical follow-up rate: 94.7%), MACE occurred in 35 patients (23.3%) of cases: all-cause death (N=16; 10.7%) among them 12 (8.0%) were adjudicated as cardiac deaths, MI (N=5; 3.3%) and TLR (N=14; 9.3%). In-stent restenosis was observed in 13 patients (8.7%) and a total of 4 patients (2.6%) experienced definite or probable stent thrombosis. TVR was reported in 19 (12.7%). Cerebrovascular accident complicated follow-up in 2 patients (1.2%). As illustrated in Kaplan-Meier curve in Figure 2, five years MACE free survival was estimated to 62.1% while five years global survival was 81.5%.
Multivariate Cox regression performed for MACE predictors analysis identified the following factors: cardiogenic shock (HR=4.1; 95%CI=1.17−14.65; p=0.028), bare metal stent implantation (HR=2.6; 95%CI=1.03−6.39; p=0.042), prior PCI (HR=2.5; 95%CI=1.11−5.77; p=0.027) and SYNTAX score II ≥30 (HR=2.3; 95%CI=1.02−5.33; p=0.045) (Figure 3). It is important to mention that in univariate analysis, both SYNTAX score I tertiles and SYNTAX score II ≥30 were associated to long-term cardiac death (p=0.001 and p=0.003 respectively) but multivariate analysis was not possible for this end-point with respect to the rule of 1:10 covariates per number of events.

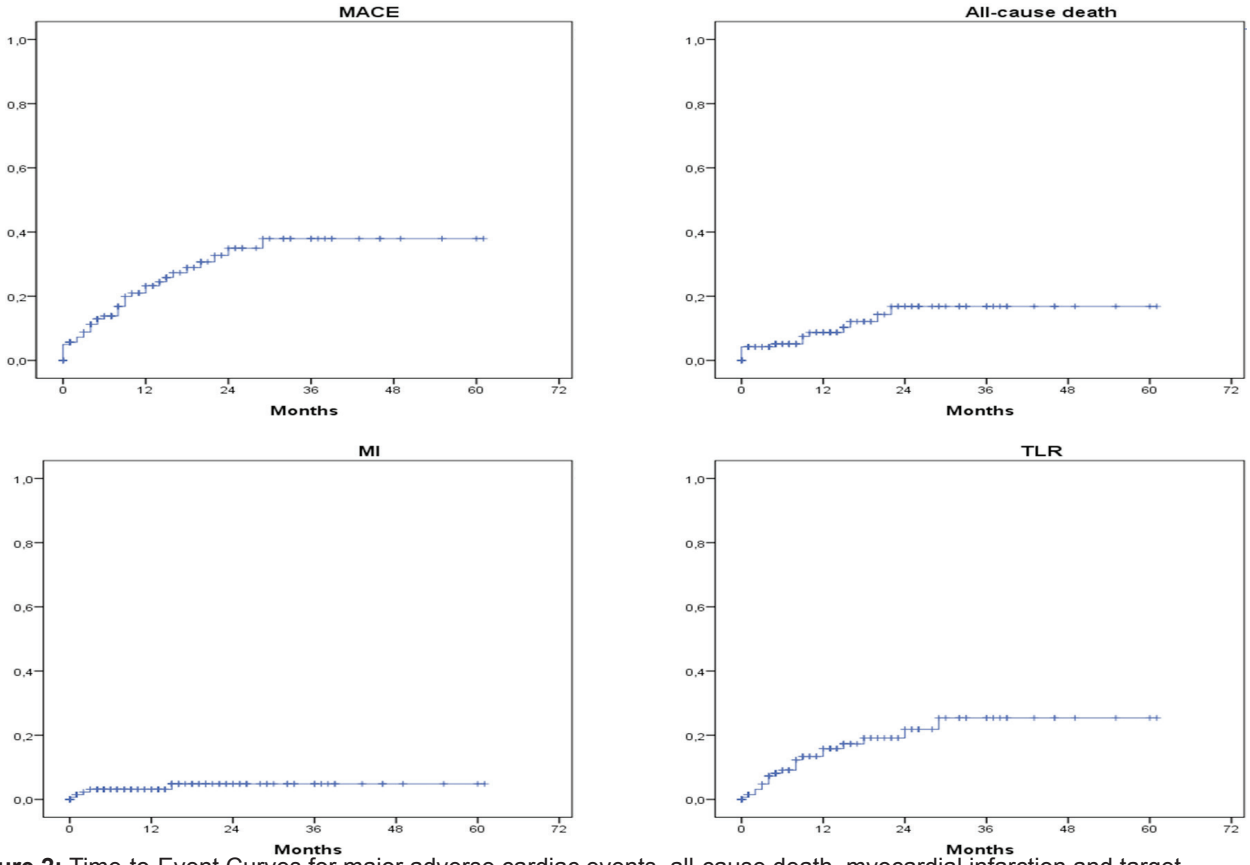

Figure 2: Time-to-Event Curves for major adverse cardiac events, all-cause death, myocardial infarction and target vessel revascularization.
MACE: Major adverse cardiac event, MI: Myocardial infarction, TLR: Target lesion revascularization.

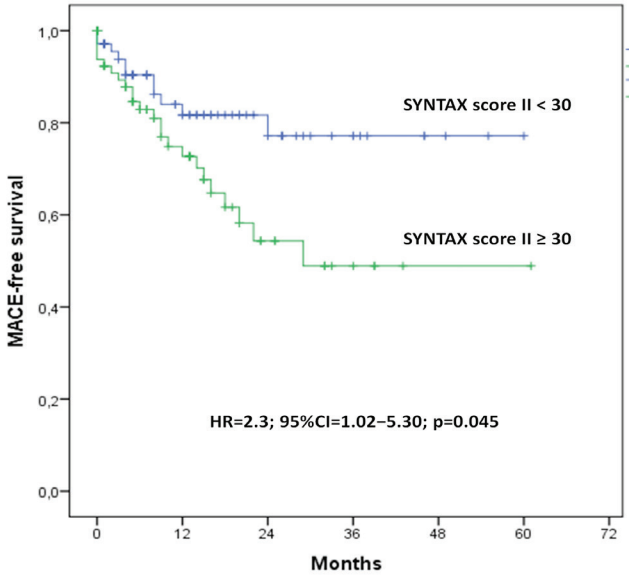

Figure 3: Major adverse cardiac events free survival according to SYNTAX score II.

DISCUSSION

To our knowledge, this study represented the largest Tunisian prospective registry evaluating unprotected LM-PCI (16). Our main findings can be summarized as follows: a) In our last six-year experience, PCI has become, since 2014, the most performed revascularization strategy for unprotected LM lesion subset with the cumulative evidence about its efficacy and security in selected patients, as well as the operators' expertise. b) In our series, with an "all-comers" design, more than the half patients presented with acute coronary syndromes, were diabetic and had multivessel disease. Furthermore, 3.3% of patients had cardiogenic shock, underlying the high risk profile of our population. c) After a median follow-up of 13.4 months, MACE, all-cause mortality and TLR rates were 23.3%, 10.7% and 9.3% respectively. d) Predictors of MACE were cardiogenic shock, bare metal stent implantation, prior PCI and SYNTAX score II ≥30.

Recent MI and cardiogenic shock presentations were exclusion criteria in most relevant SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) (7), EXCEL (Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) (9) and NOBLE (Percutaneous coronary angioplasty versus coronary artery bypass grafting in treatment of unprotected left main stenosis) randomized clinical trials led on unprotected LM revascularization strategies (10) and in PRECOMBAT 2 registry (Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease) (17). Two large registries (DELFT (18) and DELTA-2 (19) had an "all-comers" design concordant to our study. In order to compare our outcomes data to literature, we focused on the most contemporary DELTA-2 large-scale international multicenter registry that has involved high-volume centers and included 3986 patients treated with second generation drug eluting stents. This registry included 3.1% patients in cardiogenic shock vs. 3.3% in our study. After a median follow-up of 13.4 months in our series and 17 months in the DELTA-2 registry, our results were nearly comparable in terms of MACE (23.3% vs 21.2%), all-cause mortality (10.7% vs 8.3%), cardiac deaths (8.0% vs. 5.3%); TLR (9.3% vs. 7.8%) and stent thrombosis (1.3% vs. 0.7%).

Percutaneous revascularization in our experience was roughly conform to current practice and last guidelines (20–24), with low to intermediate SYNTAX score I in 94% of cases, predominant use of radial approach and new-generation drug-eluting stents. In distal LM-PCI, mainly one-stent technique was performed with quasi-systematic POT. When two-stent technique was required, final kissing balloon was carried out in the vast majority of cases.

According 2018 revascularization guidelines of the European society of cardiology (22), in the setting of unprotected LM disease, the decision to perform PCI or CABG is still dependent on SYNTAX score I. PCI is indicated if the SYNTAX score I is less than 33 (class IIa recommendation) and at best less than 23 (class I recommendation) (22). This is due to the large evidence of the prognostic impact of this score demonstrated in SYNTAX trial showing similar cardiac and cerebrovascular events of PCI versus CABG in patients with SYNTAX score I ≤32 (7,8).

In our report, beyond the angiographic SYNTAX score I, SYNTAX score II ≥30 was a predictor of MACE (in multivariate analysis) and was associated to long term cardiac death (in univariate analysis). The latter score was derived from the SYNTAX cohort retrospectively and was composed of two anatomical variables (SYNTAX score I and unprotected LM stenosis) and of six clinical items (age, sex, creatinine clearance, LVEF, chronic obstructive pulmonary disease, and peripheral artery disease) (15). SYNTAX score II was validated externally in DELTA registry as a PCI and CABG related 4-years mortality independent predictive factor (25). Its prognostic value was confirmed in four further trials (13,26–28), two of them included patients with LM and multivessel disease (26,28) while the two others only included patients with unprotected LM stenosis (13,27). Xu and al. included 1528 patients undergoing LM-PCI and followed for 4.4 years. They confirmed the superiority of SYNTAX score II over SYNTAX score I as a mortality independent predictive factor (13). Despite these encouraging results, last European guidelines noted that more evidence is needed before recommending SYNTAX score II in daily practice because of concerns raised by EXCEL trial that failed to demonstrate its impact for assigning patients to PCI or CABG, this score predicting an equipoise for mortality between the 2 strategies in patients with low to intermediate SYNTAX score I included in this trial (29).

Study limitations

The main limitations of this study were its monocentric design, the use of bare metal stents in emergent unprotected LM-PCI because of unavailability of drug eluting stents in these situations in our center and the lack of systematic functional or morphologic approach for LM lesions assessment and PCI guidance for economic reasons (ie: intravascular ultrasound was used only in 2.7% in this series vs. nearly 75% in EXCEL and NOBLE trials, >90% in PRECOMBAT 2 and in 36% in DELTA 2 registry).

CONCLUSION

In this "all-comers" registry, unprotected LM-PCI presented as reasonable revascularization strategy with encouraging short and long term outcomes comparable to large scale registries with a similar "real-life" design. If SYNTAX score I tertiles remain the basis of current revascularization guidelines, this report emphasized the interest of SYNTAX score II to predict occurrence of long-term MACE in this setting.

Conducting a Tunisian national multicenter unprotected LM-PCI registry comprising larger sample size and surgical arm could support the results of our study.

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