International Journal of Cardiology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Provisional versus elective two-stent strategy for unprotected true left main bifurcation lesions: Insights from a FAILS-2 sub-study

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ARTICLE INFO

Article history:
Received 14 May 2017
Received in revised form 26 August 2017
Accepted 18 September 2017
Available online xxxx

Keywords:
Unprotected left main coronary artery
True bifurcation lesions
Drug-eluting stent
Percutaneous coronary intervention

ABSTRACT

Background: This study sought to investigate the optimal percutaneous coronary intervention (PCI) strategy for true unprotected left main coronary artery (ULMCA) bifurcations.
Methods: The FAILS-2 was a retrospective multi-center study including patients with ULMCA disease treated with second-generation drug-eluting stents. Of these, we compared clinical outcomes of a provisional strategy (PS; n = 216) versus an elective two-stent strategy (E2S; n = 161) for true ULMCA bifurcations. The primary endpoint was the incidence of major adverse cardiac events (MACEs) at 3-years. We further performed propensity-score adjustment for clinical outcomes.
Results: There were no significant differences between the groups in terms of patient and lesion characteristics. 9.7% of patients in the PS group crossed over to a provisional two-stent strategy. MACEs were not significantly different between groups (MACE at 3-year; PS 28.1% vs. E2S 28.9%, adjusted p = 0.99). The rates of target lesion revascularization (TLR) on the circumflex artery (LCX) were numerically high in the E2S group (LCX-TLR at 3-years; PS 11.8% vs. E2S 16.6%, adjusted p = 0.51).
Conclusions: E2S was associated with a comparable MACE rate to PS for true ULMCA bifurcations. The rates of LCX-TLR tended to be higher in the E2S group although there was no statistical significance.
Condensed abstract: This study sought to compare the clinical outcomes of a provisional strategy (PS) with an elective two-stent strategy (E2S) for the treatment of true unprotected left main coronary artery bifurcations. 377 Patients (PS 216 vs. E2S 161 patients) were evaluated, and 9.7% in the PS group crossed over to a two-stent strategy. E2S was associated with a similar major adverse cardiac event rate at 3-years when compared to the PS strategy (PS 28.1% vs. E2S 28.9%, p = 0.99). However, the left circumflex artery TLR rate at 3-year tended to be higher in the E2S group (PS 11.8% vs. E2S 16.6%, p = 0.51).

1. Introduction

Percutaneous coronary intervention (PCI) using drug-eluting stents (DES) has become an alternative for unprotected left main coronary artery (ULMCA) disease in patients with low-to-intermediate SYNTAX scores [1]. Previous studies have shown that PCI for ostial and/or mid-shaft lesions in ULMCA disease is associated with comparable clinical outcomes to coronary artery bypass grafting (CABG) [2,3]. However, the majority of stenoses involve distal ULMCA bifurcations, which are

Abbreviations: ULMCA, unprotected left main coronary artery; PS, provisional stenting strategy; E2S, elective two-stent strategy; MACEs, major adverse cardiac events; TLR, target lesion revascularization.

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https://doi.org/10.1016/j.ijcard.2017.09.207
0167-5273/

associated with an increase in procedural complexity when compared to ostial and/or mid-shaft lesions [4,5]. In addition, true bifurcations of the distal ULMCA are associated with higher rates of target lesion revascularization (TLR) [6].

Although a provisional strategy is currently recommended for most ULMCA bifurcation lesions [7–11], a systematic two-stent strategy remains a treatment option when treating complex bifurcations (e.g. true bifurcation lesions) to reduce the risk of acute left circumflex artery (LCX) occlusion. Recently, the EBC TWO (European Bifurcation Coronary TWO) randomized study, which compared provisional versus systematic culotte stenting for non-ULMCA true bifurcations reported comparable outcomes at 1-year [12]. However, little is known regarding the optimal strategy and clinical outcomes following different PCI strategies for true ULMCA bifurcations [13]. EBC MAIN study (European Bifurcation Club Left Main Study; ClinicalTrials.gov NCT02497014) is currently on going and will be the first randomized clinical trial to evaluate the optimal stenting strategy in true ULMCA bifurcation lesions [14]. Therefore, the aim of this study was to investigate mid-term outcomes of a provisional strategy (PS) versus an elective two-stent strategy (E2S) for true ULMCA bifurcations treated with second-generation DES from a multi-center registry.

2. Methods

2.1. Study population

The FAILS 2 (Failure in Left Main Study with the second generation stents) study is a multi-center registry retrospectively including all consecutive patients with ULMCA stenoses treated with second-generation DES between July 2006 and March 2015. This study initially aimed to evaluate the incidence, clinical presentation and prognosis of restenosis after treatment of ULMCA disease with second-generation DES [15]. Of these, we compared clinical outcomes between a PS and an E2S for true ULMCA bifurcations. Five European centers and one Japanese center were involved. The indication to perform PCI rather than CABG was decided at each individual center. The decision to opt for a provisional or elective two-stent strategy was at the operators' discretion. In general, an E2S was employed when there was severe stenosis at the ostium of LCX or diffuse disease extending from the LCX ostium. Using the provisional strategy, stenting to the LCX was indicated by major dissections or compromised flow following side branch dilatation or kissing balloon inflation. All clinical or procedural data were site-reported. Clinical data during follow-up were obtained from hospital visits or telephonic contacts.

Exclusion criteria for this sub-study included PCI for ostial/body lesions, non-true ULMCA bifurcations, acute myocardial infarction (MI), cardiogenic shock or unreviewable techniques for ULMCA bifurcations. We compared PS with E2S by intention-to-treat for true ULMCA bifurcations.

2.2. Study definitions

ULMCA lesions were classified by visual assessment at each center according to the Medina classification [16]. A true bifurcation lesion was defined as Medina class 1-1-1, 1-0-1, or 0-1-1 [16]. MACEs were defined as a composite of all-cause death, MI, and overall target lesion revascularization (TLR). Overall TLR was defined as either repeat PCI or CABG for the ULMCA lesion stented previously including the proximal and distal edge segments of the stent, or at the ostium of the side branches (SBs). Furthermore, TLR of the left main stem (LM-TLR), LAD (LAD-TLR), and LCX (LCX-TLR) were separately evaluated. Death was considered cardiac in origin unless obvious non-cardiac causes were identified. The definition of MI was according to the Third Universal Definition of Myocardial Infarction [17]. Stent thrombosis (ST) was classified according to the Academic Research Consortium (ARC) definitions [18].

2.3. Study endpoints

The primary endpoint was the rate of MACE at 3-years. The secondary endpoints were each component of MACE, cardiac death, LM-TLR, LAD-TLR, LCX-TLR, and definite or probable ST.

2.4. Statistical analysis

Continuous variables are presented as the mean ± standard deviation (SD). Differences in continuous variables between the groups were calculated with the Student *t*-test. Categorical data were compared using the chi-square or Fisher's exact tests. The cumulative clinical events were generated with Kaplan–Meier method, and reported as hazard ratios (HR; elective two-stent vs. provisional strategy) and 95% confidence interval (CI) using Cox regression analysis. Follow-up was censored at the date of the last follow-up or at 3 years. Because of the nonrandomized nature of this study, clinical outcomes were evaluated between unadjusted groups and again following propensity-score adjustment. Adjusted ratios were calculated using Cox regression analysis with elective two-stent strategy (vs. provisional strategy) as a fixed dummy covariate and propensity score as the stratification variable [19,20]. Propensity score were calculated using covariates as following; stent-drug, Medina classification, LCX proximal disease, male, age, hypertension, diabetes mellitus, insulin-dependent diabetes mellitus, current smoking, dyslipidemia, previous myocardial infarction, previous PCI, chronic obstructive pulmonary disease, previous stroke, low ejection fraction (<35%), low estimated glomerular filtration rate (GFR) <60 ml/min/1.73 m^2, acute coronary syndrome, SYNTAX score, radial access, IVUS use, three vessel disease, and treated vessel. The C-statistic was 0.66, and the Hosmer–Lemeshow p-value was 0.28, indicating good discrimination and calibration of the propensity-matching model, respectively.

We performed multivariable Cox regression analysis to identify the independent risk factors of MACE during follow-up period. Variables used in the Cox regression model were all variables with values of $p < 0.10$ at univariate analysis and those judged to be clinically important. To avoid over-fitting, the number of independent variables entered into the final multivariable logistic regression model was limited to 1 for every 8–10 events. Analyses were performed using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA). All reported p values were 2-sided, and values of $p < 0.05$ regarded as statistically significant.

Table 1
Baseline clinical and lesion characteristics.

	Provisional (n = 216)	Elective two-stent (n = 161)	p Value
Clinical characteristics			
Male	170 (78.7)	128 (79.5)	0.85
Age (years)	70.8 ± 9.9	70.4 ± 10.4	0.74
Hypertension	181 (83.8)	126 (78.3)	0.17
Dyslipidemia	150 (69.8)	104 (66.2)	0.47
Current smoker	24 (12.3)	25 (18.2)	0.13
Diabetes	98 (46.7)	59 (38.6)	0.12
Insulin-dependent	30 (14.3)	15 (9.9)	0.21
Chronic kidney disease			
eGFR, ml/min/1.73 m^2	63.6 ± 29.4	60.4 ± 25.3	0.31
eGFR < 60 ml/min/1.73 m^2	91 (48.7)	63 (47.4)	0.82
Previous PCI	114 (53.0)	79 (51.0)	0.7
Previous MI	80 (37.4)	43 (28.1)	0.06
COPD	17 (8.5)	6 (4.5)	0.16
Previous stroke	13 (6.3)	12 (8.3)	0.47
Clinical presentation			0.81
Stable angina	164 (75.9)	124 (77.0)	
Unstable angina	52 (24.1)	37 (23.0)	
LVEF (%)	55.0 ± 12.5	55.6 ± 9.9	0.65
Lesion characteristics			
LAD disease	190 (88.0)	134 (84.3)	0.3
LCX disease	187 (86.6)	135 (84.9)	0.65
RCA disease	165 (76.4)	132 (82.5)	0.15
3VD	136 (63.0)	106 (66.3)	0.51
SYNTAX score	29.0 ± 10.0	29.9 ± 10.0	0.4
Low SYNTAX score	53 (26.8)	36 (23.5)	0.79
Intermediate SYNTAX score	70 (35.4)	57 (37.3)	
High SYNTAX score (>33)	75 (37.9)	60 (39.2)	
IVUS	48 (22.2)	44 (27.3)	0.25
Trans radial approach	24 (11.2)	21 (13.1)	0.57
Stent type			0.07
Biolimus-eluting stent	25 (11.6)	30 (18.6)	
Everolimus-eluting stent	171 (79.2)	108 (67.1)	
Zotarolimus-eluting stent	17 (7.9)	18 (11.2)	
Others	3 (1.4)	4 (2.5)	
Stent techniques			
Provisional two stent	21 (9.7)		
Crush		12 (7.5)	
Culotte		53 (32.9)	
Mini-crush		64 (39.8)	
T		23 (14.3)	
V		9 (5.6)	
Medina classification			0.36
0,1,1	23 (10.6)	24 (14.9)	
1,0,1	34 (15.7)	20 (12.4)	
1,1,1	159 (73.6)	117 (72.7)	
LCX proximal disease (non-ostial)	131 (60.6)	95 (59.7)	0.86

Data are presented as absolute numbers and percentages or mean ± standard deviation. eGFR = estimated glomerular filtration rate; PCI = percutaneous coronary intervention; MI = myocardial infarction; COPD = chronic obstructive pulmonary disease; LVEF = left ventricular ejection fraction; LAD = left anterior descending artery; LCX = left circumflex coronary artery; RCA = right coronary artery; VD = vessel disease; IVUS = intravascular ultrasound.

Please cite this article as: H. Kawamoto, et al., Provisional versus elective two-stent strategy for unprotected true left main bifurcation lesions: Insights from a FAILS-2 sub-study, Int J Cardiol (2017), https://doi.org/10.1016/j.ijcard.2017.09.207