Cardiovascular Revascularization Medicine 15 (2014) 80–85

Contents lists available at ScienceDirect

Cardiovascular Revascularization Medicine

Calcification analysis by intravascular ultrasound to define a predictor of left circumflex narrowing after cross-over stenting for unprotected left main bifurcation lesions☆,☆☆

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ARTICLE INFO

Article history:
Received 3 December 2013
Received in revised form 27 January 2014
Accepted 31 January 2014

Keywords:
Plaque morphology
Left main coronary artery stenosis
Bifurcation
Intravascular ultrasound

ABSTRACT

Objectives: The aim of this study was to identify predictors of significant LCx-ostium compromise after distal unprotected left main coronary artery (ULMCA) stenting on the basis of baseline intravascular ultrasound (IVUS).
Background: Provisional single-stenting is considered as the default strategy for non-true bifurcation lesions in ULMCA. However, in certain cases, left circumflex artery (LCx)-ostium stenting is necessary.
Methods: A total of 77 patients underwent percutaneous coronary intervention with drug-eluting stents for non-true bifurcation lesions in ULMCA and had IVUS evaluation. Pre-procedural IVUS was performed to measure cross-sectional areas at the following segments: left main trunk, left anterior descending artery (LAD)-ostium. Post-stenting-narrowing at the circumflex ostium (PSN-LCx) was defined as the presence of more than 50% diameter stenosis at the LCx-ostium as determined by quantitative coronary angiography analysis.
Results: PSN-LCx occurred in 27 (35%) patients. The presence of calcified plaque at the culprit lesion as identified by IVUS was more frequently observed in the PSN-LCx group as compared to the non-PSN-LCx group (81.5% vs. 22.0%, $p < 0.001$). Calcium arc in the PSN-LCx group was significantly greater than that in the non-PSN-LCx group (118.1° ± 69.9° vs. 36.9° ± 63.0°, $p < 0.001$). On multivariable analysis, a calcium arc > 60° was an independent predictor of PSN-LCx (odds ratio: 5.12, 95% confidence interval: 1.21–25.01, $p = 0.03$).
Conclusions: The presence of calcified plaque at the culprit lesion appears to be one of the factors involved in LCx-ostial compromise in non-true bifurcation ULMCA lesions, especially when the calcium arc is >60°.

1. Introduction

Single cross-over stenting for unprotected left main coronary artery (ULMCA) has been demonstrated not only to be feasible but also to be associated with reasonable clinical outcomes [1–5]. Although technically this can be straightforward especially when the left circumflex (LCx) ostium is not diseased and therefore less likely to require treatment after stenting from the left main trunk (LMT) to the left anterior descending artery (LAD), significant LCx-ostium compromise can still occur converting the procedure in many occasions to a two-stenting strategy which inherently is more complex. Previous studies have identified side-branch diameter stenosis, side-branch minimal lumen area (MLA) and bifurcation angle as factors that adversely impact on the side-branch ostium.[6–10] However, there are no studies that have examined the impact of plaque morphology on side-branch ostial compromise. The aim of this study was to evaluate the impact of plaque morphology on LCx-ostium compromise in an ULMCA lesion cohort with no significant disease in the LCx-ostium (Medina classification [1, 0, 0], [1, 1, 0], [0, 1, 0]) [11] treated with a provisional strategy.

Abbreviations: ULMCA, unprotected left main coronary artery; LCx, left circumflex artery; IVUS, intravascular ultrasound; LAD, left anterior descending artery; PSN-LCx, post-stenting-narrowing at the circumflex ostium; CABG, coronary bypass surgery; PCI, percutaneous coronary intervention; DES, drug-eluting stent; LMT, left main trunk; DS, diameter stenosis; Non-PSN-LCx, non-post-stenting narrowing at the circumflex ostium; QCA, quantitative coronary angiography; MLD, Minimum lumen diameter; CSA, cross-sectional area; MLA, minimum lumen area; ROC, Receiver-operating curve; PPV, positive predictive value; NPV, negative predictive value.

☆ Sources of funding: None.
☆☆ Disclosures: None.
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http://dx.doi.org/10.1016/j.carrev.2014.01.014

2. Methods

Between March 2008 and June 2013, a total of 381 patients were treated with drug-eluting stents (DESs) for de novo distal bifurcation lesions of ULMCA at 2 centers (EMO-GVM Centro Cuore Columbus, Milan, Italy and Fukuyama Cardiovascular Hospital, Fukuyama, Japan). Among these 77 patients who had DES implantation for non-true bifurcation lesions (Medina classification [1, 0, 0], [1, 1, 0], [0, 1, 0]) in ULMCA were included in this study. Besides the described characteristics patients included had pre-procedural intravascular ultrasound (IVUS) evaluation. Performance of IVUS was operator's decision. Patients with in-stent restenosis, ST-elevation myocardial infarction requiring primary percutaneous coronary intervention (PCI) or previous history of coronary bypass graft (CABG) were excluded from this study. Other exclusion criteria included significant LCx disease including at the ostium (diameter stenosis [DS] >50%), diffuse severe LCx disease (>10 mm) extending from the ostium and LCx distal reference vessel diameter ≤2.00 mm.

In all patients, the provisional strategy was the default approach and involved cross-over stenting from the LMT to the LAD. Patients were retrospectively classified into two groups according to the angiographic results at the LCx-ostium after cross-over stent implantation: a post-stenting narrowing (PSN)-LCx group and a non-PSN-LCx group. PSN-LCx was defined as the presence of >50% DS at the LCx-ostium as determined by quantitative coronary angiography (QCA) analysis. Kappa (κ) test was used to assess the interobserver and intraobserver variability for PSN-LCx assessment by angiography. The reproducibility variability for PSN-LCx assessment by angiography was as follows; κ=0.89 for interobserver and κ = 0.94 for intraobserver. All patients signed specific informed consent for ULMCA interventions including IVUS evaluation prior to the procedure.

2.1. Angiographic analysis

All pre-procedural angiograms were analyzed before the introduction of the coronary guide wire by independent observers without the knowledge of clinical or IVUS data. All segments within 10 mm from the distal ULMCA bifurcation were analyzed with the cardiovascular measurement system (CMS, Medis, Leiden, the Netherlands). The diameter of the proximal for the LMT and distal for the LAD and LCx angiographically normal segments was used as reference. Minimum lumen diameter (MLD) was measured in multiple projections with results recorded from the view that demonstrated the smallest diameter. ULMCA bifurcation lesion was defined as >50% DS of the LMT proximal to the bifurcation site with or without involvement of the first 5 mm from the ostium of the LAD. Qualitative analysis of the ULMCA bifurcation was assessed according to the system proposed by Medina et al.; 1 indicates the presence of stenosis and 0, the absence of stenosis in 3 segments separated by commas (LMT, LAD, and LCx) [11]. Bifurcation angle between the LAD and LCx at the angiographic projection at which it was the widest. The evaluation by angiography was performed by identifying the view displaying the widest opening and demonstrating the side branch (LCx) most clearly. QCA analysis was performed by more than two cardiovascular physicians who were blinded to the study results.

2.2. Intravascular ultrasound imaging

IVUS imaging (40-MHz IVUS catheter, Boston Scientific Corp, Natick, Mass; 43-MHz IVUS catheter, Terumo, VISIWAVE, Tokyo, Japan) was performed before all interventions and after intracoronary administration of 0.2 mg nitroglycerin. The probe was advanced into the distal reference segment and an imaging run was performed back to coronary ostium using a motorized transducer pullback (0.5 mm/s) system. IVUS images were recorded continuously onto digital media for offline analysis. Pre-procedural LAD-pull back IVUS was obtained from all patients although pre-procedural LCx-pull back IVUS was not possible in 17 patients (17/77 [22.0%]) due to either severe tortuosity or a highly acute bifurcation angle that did not allow this. Qualitative and quantitative analyses were performed by independent observers according to the criteria of the American College of Cardiology Clinical Expert Consensus Document on standards for acquisition, measurement, and reporting of IVUS studies [12]. An IVUS lesion was defined as plaque burden ≥ 40%. The carina cross-section was the frame immediately distal to the take-off of the LCx within 5 mm from the bifurcation point in which both ostia of the LAD and LCx could be visualized as a figure-of-eight shape [13,14]. The distal LMT was the frame immediately proximal to the carina in which the vessel had a circular or oval shape. Cross-sectional images were quantified for lumen cross-sectional area (LCSA), external elastic membrane (EEM) cross-sectional area (CSA), and plaque (P) + media (M) cross-sectional area (P + M CSA = EEM CSA−LCSA), and plaque burden (P + M CSA/EEM CSA). The MLA site either on the LAD ostium or distal LMT was defined as the slice with the smallest lumen area and with the largest plaque area (Fig. 1-B, 1-C). Calcium was brighter than the adventitia with acoustic shadowing of the underlying tissue. The atherosclerotic plaque as identified by IVUS was located on the contra-lateral side of the bifurcation where involvement of the flow divider (bifurcation side) was absent. Calcium arc was measured in degrees at each end of the calcified plaque at the MLA site by pre-procedural LAD-pull back IVUS. The length of the calcified lesion was defined as the distance between the LMT and LAD reference segments [12]. Reference segments were defined as the most normal-looking cross sections proximal and distal to the lesion [14]. The plaque morphology at the MLA site during pre-procedural LAD-pull back IVUS was divided into 3 groups (soft plaque, fibrous plaque and calcified plaque) according to the plaque echogenicity as previously described. Qualitative analysis of the longitudinal IVUS reconstruction identified a singular anatomic pattern of the carina characterized by a spiky morphology known as the "eyebrow" sign. This sign represents the initial parallel course of the LCx origin and the LAD, sharing the flow divider until the LCx undergoes a change of direction [15].

2.3. Statistical analysis

All values are expressed as mean ± standard deviation (continuous variables) or as absolute numbers and percentages (categorical variables). Continuous variables were compared with the unpaired *t*- test. Categorical variables were compared with the chi-square statistic or Fisher's exact test. Receiver-operating curve (ROC) was analyzed to assess the best cut-off values of the calcium arc at the carina to determine predictors of PSN-LCx. The optimal cut-off was calculated using the Youden index. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were obtained. Multivariate logistic regression analysis was performed to determine the independent predictor of PSN-LCx after main branch stenting in ULMCA bifurcation, using predictors associated with PSN-LCx in univariate analysis (p-value <0.10) and those judged to be of clinical importance from previous published literature. All p values are 2-sided, and p values <0.05 were considered statistically significant. All statistical analyses were performed using Statview 5.0 (SAS Institute, Cary, North Carolina).

3. Results

Clinical and procedural characteristics are shown in Table 1. A total of 77 patients (40 males, mean age 70.0 ± 9.5 years) with 77 ULMCA bifurcations lesions were analyzed. Twenty-seven patients (35.0%) were assigned to the PSN-LCx group and 50 (65.0%) patients to the non-PSN-LCx group. Patient characteristics did not significantly differ between the 2 groups. There were no differences in stent type between the 2 groups. Stent size and stent length were also similar between the 2 groups.