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Relation between poststenting peristent plaque components and late stent malapposition after drug-eluting stent implantation: Virtual histology-intravascular ultrasound analysis

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ABSTRACT

Background: Impact of plaque composition on late stent malapposition (LSM) after drug-eluting stent (DES) implantation has not been evaluated.
Methods: We evaluated the relation between plaque components at poststenting peristent area (between external elastic membrane and stent areas) and LSM after DES implantation in 266 patients (314 native lesions; paclitaxel-eluting stent in 205 lesions, sirolimus-eluting stent in 66 lesions, zotarolimus-eluting stent in 32 lesions and everolimus-eluting stent in 11 lesions) in whom virtual-histology intravascular ultrasound was performed at index (poststenting) and follow-up (mean: 11.7 ± 4.8 months).
Results: LSM occurred in 24 patients with 30 lesions (9.6%) and there were no significant differences in the incidences of LSM among 4 DES groups [21/205 (10.2%) in paclitaxel-eluting stent, 6/66 (9.1%) in sirolimus-eluting stent, 2/32 (6.3%) in zotarolimus-eluting stent and 1/11 (9.1%) in everolimus-eluting stent, $p = 0.5$)]. Patients with LSM were presented with more acute myocardial infarction (50% vs. 28%, $p = 0.026$) and were more diabetics (50% vs. 30%, $p = 0.030$) compared with those without LSM. Lesions with LSM had more poststenting peristent %necrotic core (NC) volume compared with those without LSM (25.8 ± 11.1% vs. 21.0 ± 5.7%, $p < 0.001$). Independent predictors of LSM were poststenting peristent %NC volume [odds ratio (OR); 1.216, 95% CI; 1.053–1.405, $p = 0.008$], acute myocardial infarction (OR; 2.897, 95% CI; 1.675–4.118, $p = 0.029$), and diabetes mellitus (OR; 2.413, 95% CI; 1.543–3.996, $p = 0.038$).
Conclusions: Poststenting peristent NC component especially in patients with acute myocardial infarction and in those with diabetes mellitus is associated with the development of LSM after DES implantation.

1. Introduction

Several studies have reported late stent malapposition (LSM) in 4% to 5% of patients after bare-metal stent implantation [1–3]. Although drug-eluting stents (DESs) dramatically reduce the in-stent restenosis, there is an increased frequency of LSM on follow-up intravascular ultrasound (IVUS) examination ranged from 8 to 31% after DES implantation [4–11]. LSM after DES implantation may lead to late stent thrombosis and other adverse clinical outcomes [12,13].

Several postulated mechanisms of LSM after DES implantation have been suggested including positive vessel remodeling, thrombus resolution behind the stent struts, and severe localized inflammatory reaction or excessive fibrin deposition [3–17]. However, so far the association between underlying plaque characteristics and LSM were not fully assessed. Therefore, the purpose of the present study was to evaluate the relation between plaque components at poststenting peristent area and LSM after DES implantation using virtual-histology (VH)-IVUS.

2. Methods

2.1. Patient population

We enrolled 266 consecutive patients who underwent DES implantation [314 native coronary lesions; paclitaxel-eluting stent (PES) in 205 lesions, sirolimus-eluting stent (SES) in 66 lesions, zotarolimus-eluting stent (ZES) in 32 lesions and everolimus-eluting stent (EES) in 11 lesions] in whom VH-IVUS was performed at index and follow-up (mean: 11.7 ± 4.8 months) between January 2008 and December 2009. We excluded patients with stent thrombosis, restenotic lesion, coronary artery bypass graft failure, severe heart failure or cardiogenic shock, important systemic disease, serum creatinine ≥2.5 mg/dl, and poststenting acute stent malapposition, and

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patients in whom adequate IVUS images could not be obtained. The protocol was approved by the institutional review board. Hospital records of all patients were reviewed to obtain clinical demographics and medical history. Written informed consent was obtained from all patients before cardiac catheterization.

2.2. Quantitative coronary angiography (QCA) analysis

Coronary angiogram was analyzed with validated quantitative coronary angiography (QCA) system (Phillips H5000 or Allura DCI program, Philips Medical Systems, the Netherlands). With the outer diameter of the contrast-filled catheter as the calibration standard, the reference diameter and minimal lumen diameter were measured in diastolic frames from orthogonal projections. Perfusion was evaluated according to Thrombolysis In Myocardial Infarction (TIMI) criteria [18].

2.3. IVUS analysis

All gray-scale and VH-IVUS examinations were performed after intracoronary administration of 300 μg nitroglycerin. A 20-MHz, 2.9 F IVUS imaging catheter (Eagle Eye, Volcano Corp, Rancho Cordova, CA) was advanced >10 mm beyond the lesion; and automated pullback was performed to a point >10 mm proximal to the lesion at a speed of 0.5 mm/s. All IVUS studies were archived onto CD-ROM and sent to the IVUS core laboratory for offline quantitative and qualitative analyses by individuals blinded to treatment allocation.

Qualitative analysis was performed as follows. First, we reviewed all follow-up IVUS CD-ROMs to identify cases of LSM. Second, poststenting and follow-up IVUS CD-ROMs were reviewed side-by-side to discriminate cases in which incomplete stent apposition existed immediately after stent implantation. This included independent review of index and follow-up IVUS studies by 2 of the authors (H.Y.J and C.Y.H). The levels of reproducibility for external elastic membrane (EEM) and stent volume measurements at poststenting using the Spearman rank-order correlation coefficients were 0.96 and 0.99, respectively. For plaque components by VH-IVUS at peristent plaque area, reproducibility for the fibrous (FT), fibro-fatty (FF), dense calcium (DC), and necrotic core (NC) volume measurements using the Spearman rank-order correlation coefficients were 0.93, 0.94, 0.93, and 0.93, respectively. Conventional quantitative volumetric gray-scale IVUS analysis was performed according to the American College of Cardiology Clinical Expert Consensus Document on Standards for Acquisition, Measurement and Reporting of Intravascular Ultrasound Studies [19]. Quantitative analysis included measurement every 1 mm of the EEM, stent, and lumen cross-sectional areas (CSAs). Poststenting peristent plaque CSA was obtained by measuring areas between EEM and the stent strut. Neointimal hyperplasia CSA was calculated as stent minus lumen CSA at follow-up. Once a complete set of CSA measurements was obtained, EEM, stent, lumen, peristent plaque, and neointimal hyperplasia volumes were calculated with Simpson's rule. At follow-up, percent net volume obstruction was calculated as neointimal hyperplasia volume divided by stent volume.

LSM was defined as separation of at least 1 stent strut from the intimal surface of the arterial wall that was not overlapping a side branch, was not present immediately after stent implantation, and had evidence of blood flow (speckling) behind the strut (Fig. 1). The follow-up study was reviewed to select the image slice with the maximum LSM area; then, the poststenting study was reviewed to identify the corresponding image slice. Once a complete set of LSM area measurements was obtained, LSM volume was calculated with Simpson's rule.

VH-IVUS analysis classified the color-coded tissue into four major components: green (FT); yellow-green (FF); white (DC); and red (NC) [20–23]. Poststenting and follow-up peristent plaque components were obtained by measuring areas between EEM and just outside the stent strut to reduce the stent strut artifact (this can cause the overestimation of DC and NC areas) (Fig. 2). Plaque components at neointimal tissue were obtained by measuring areas between lumen and just inside the stent strut to reduce the stent strut artifact (Fig. 3). VH-IVUS analysis was reported in absolute amounts and as a percentage of plaque volume.

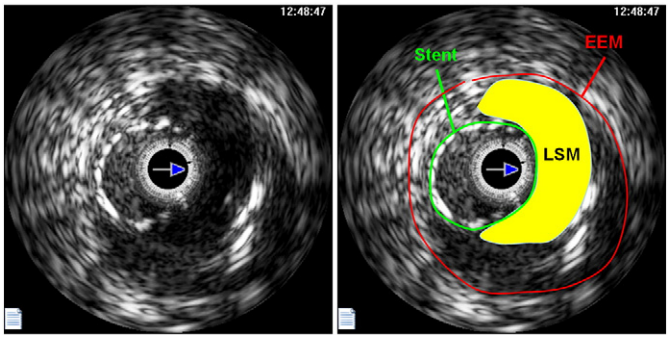

Fig. 1. The gray-scale intravascular ultrasound image of late stent malapposition (LSM) at 12 months after paclitaxel-eluting stent implantation. EEM: external elastic membrane.

2.4. Statistical analysis

The statistical Package for Social Sciences (SPSS) for Windows, version 15.0 (Chicago, Illinois) was used for all analyses. Continuous variables were presented as the mean value ± 1SD; comparisons were conducted by student's t-test or nonparametric Wilcoxon test if normality assumption was violated. Discrete variables were presented as percentages and relative frequencies; comparisons were conducted by chi-square statistics or Fisher's exact test as appropriate. Multivariate analysis was performed to determine the independent predictors of LSM at follow-up. The variables with $p<0.1$ in univariate analysis were entered into multivariate analysis. A p value <0.05 was considered statistically significant.

3. Results

3.1. Patient characteristics

The baseline characteristics are summarized in Table 1. Stenting was performed more frequently for infarct-related arteries in patients with LSM compared with those without LSM (50% vs. 28%, $p=0.026$). Patients with LSM were more diabetics compared with those without LSM. Troponin-I level was tended to be higher in patients with LSM compared with those without LSM. There were no significant differences in the use of anti-platelet agents and statins at follow-up between both groups.

3.2. Coronary angiographic findings and procedural results

Coronary angiographic findings and procedural results are summarized in Table 2. Baseline TIMI flow grade was significantly lower in LSM group compared with non-LSM group. Multiple stents and overlapping stents were used more frequently in LSM group compared with non-LSM group. Stent length was significantly longer in LSM group compared with non-LSM group. There were no significant differences in the incidences of LSM according to the DES types (10.2% in PES, 9.1% in SES, 6.3% in ZES, and 9.1% in EES). There were no significant differences in target vessel, ACC/AHA lesion types, stent diameter, inflation pressure, and prestenting and poststenting minimal lumen diameters between LSM and non-LSM groups.

3.3. Poststenting IVUS findings

Poststenting IVUS findings are summarized in Table 3. EEM, stent, lumen, and peristent plaque volume at poststenting were not different significantly between LSM and non-LSM groups. In poststenting peristent plaque area, absolute and %NC volumes were significantly greater in LSM group compared with non-LSM group, conversely %FT volume was significantly smaller in LSM group compared with non-LSM group.

3.4. Follow-up IVUS findings

Follow-up IVUS findings are summarized in Table 4. Mean follow-up duration was 11.7 ± 4.8 months. EEM volume was significantly enlarged in LSM group from poststenting to follow-up, however this finding was not observed in non-LSM group. Malapposition volume was 51.0 ± 16.6 mm^3 in LSM group. Neointima volume and percent net volume obstruction were not different significantly between LSM and non-LSM groups. In neointima, there were no significant differences in each plaque components between both groups.

3.5. Poststenting and follow-up IVUS findings at LSM site

Poststenting and follow-up IVUS findings at LSM site in patients with LSM are summarized in Table 5. At the follow-up LSM site, EEM CSA was increased significantly, and peristent plaque CSA was tended to be decreased from poststenting to follow-up. Absolute and %peristent NC areas were tended to be increased from poststenting to follow-up,