Clinical Research

Evaluation of coronary plaque and stent deployment by intravascular optical coherence tomography in elderly patients with unstable angina and non-ST-elevation myocardial infarction

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Objective To evaluate the feasibility and efficacy of intravascular optical coherence tomography (OCT) in the assessment of plaque characteristics and drug eluting stent deployment quality in the elderly patients with unstable angina (UA) and non-ST segment elevation myocardial infarction (NSTEMI). Methods OCT was used in elderly patients undergoing percutaneous coronary interventions. Fifteen patients, 9 males and 6 females with mean age of 72.6±5.3 years (range 67-92 years) were enrolled in the study. Images were obtained before initial balloon dilatation and following stent deployment. The plaque characteristics before dilatation, vessel dissection, tissue prolapse, stent apposition and strut distribution after stent implantation were evaluated. Results Fifteen lesions were selected from 32 angiographic lesions as study lesions for OCT imaging after diagnostic coronary angiography. There were 7 lesions in the left anterior descending artery, 5 lesions in the right coronary artery and 3 lesions in the left circumflex coronary artery. Among them, 12 (80.0%) were lipid-rich plaques, and 10 (66.7%) were vulnerable plaques with fibrous cap thickness 54.2±7.3 μm. Seven ruptured culprit plaques (46.7%) were found; 4 in UA patients and 3 in NSTEMI patients. Tissue prolapse was observed in 11 lesions (73.3%). Irregular stent strut distribution was detected in 8 lesions (53.3%). Vessel dissections were found in 5 lesions (33.3%). Incomplete stent apposition was observed in 3 stents (20%) with mean spacing between the struts and the vessel wall 172±96 mm (range 117-436 mm).

Conclusions 1) It is safe and feasible to perform intravascular OCT to differentiate vulnerable coronary plaque and monitor stent deployment in elderly patients with UA and USTEMI. 2) Coronary plaques in elderly patients with UA and USTEMI could be divided into acute ruptured plaque, vulnerable plaque, lipid-rich plaque, and stable plaque. 3) Minor or critical plaque rupture is one of the mechanisms of UA in elderly patients. 4) Present drug eluting stent implantation is complicated with multiple tissue prolapses which are associated with irregular strut distributions. 5) The action and significance of tissue prolapse on acute vessel flow and in-stent thrombus and restenosis need to be further studied. (J Geriatr Cardiol 2007;4:3-9.)

Key Words optical coherence tomography; acute coronary syndrome; percutaneous coronary intervention; stent; elderly

Recently, interventional cardiology was dramatically changed by the advancements in stent design, manufacture and implantation, by the improvement in anti-platelet therapy, and by the use of intravascular ultrasound (IVUS) imaging technique. Based in part on the success of these innovations, the use of drug eluting stents (DES), especially coated by the anti-proliferation agent sirolimus, has increased significantly in recent years. In the area of quality control of stent implantation, IVUS was a cornerstone in identifying the significance of stent complete expansion and apposition and in understanding the role of negative remodeling in the late lumen loss due to in-stent restenosis. However, due to the low resolution (100-150 μm) of IVUS imaging and the strong echogenicity of stent struts, this technique is relatively difficult to evaluate the more detailed implantation quality of DES.

Optical coherence tomography (OCT) is a novel imaging modality that uses light in a manner similar to IVUS, but the high resolution (10 to 15 μm) makes it superior for visualizing microscopic structures of the coronary arteries. In in vitro study, OCT has demonstrated an excellent correlation between coronary artery anatomy and plaque characterization. Previous in vivo studies have demonstrated that intravascular OCT could obtain both qualitative and quantitative information about human coronary stenting. The purpose of this study is to explore the feasibility and efficacy of intravascular OCT in the evaluation of coronary plaque and DES deployment in elderly patients with UA and USTEMI.
Patient population

Fifteen patients, 9 males and 6 females with mean age of 72.6±5.3 years (range 67-92 years), were enrolled in the study. Percutaneous coronary intervention (PCI) was indicated for UA in 12 patients and NSTEMI in 3 patients. Altogether 87 angiographic lesions were diagnosed by standard coronary artery angiography.

The culprit lesion was identified according to the following criteria: 1) defined clinical lesion, 2) culprit vessel corresponded with the ischemic surface electrocardiography changes, transthoracic echocardiography and/or nuclear myocardial imaging, 3) lesion characters such as plaque rupture, thrombus formation and vessel wall dissection.

The culprit lesions were then selected for OCT study according to the following criteria: 1) location at the middle part of culprit coronary artery, 2) less than 25 mm in length, 3) stenosis between 70%-90% in lumen diameter, and 4) TIMI flow 3 in distal vessel bed. These lesions were studied by OCT before and after Cypher stent (Cordis, Miami Lakes, Florida, USA) implantation. Other lesions found significantly diseased by coronary angiography and needed to be investigated will be stented by DES in the same session.

This study was approved by the institutional review board of PLA General Hospital and all patients provided formal consent before participation.

Drug eluting stent implantation

Percutaneous coronary artery angiography and interventions were undertaken in a standard manner. Briefly, after informed consent, the right femoral artery was accessed and the whole coronary artery tree was imaged and evaluated with regular projections. Through a 6 or 7 French guiding catheter, a 0.014 inch (0.36 mm) guide wire was snaked through the culprit lesion and arrived at the distal part of the target vessel. The pre-dilatation balloon and stent size were selected by visual estimation with the guiding catheter for calibration. After the stent was successfully deployed, OCT imaging was repeated at the end of the procedure.

Intravascular OCT imaging

The OCT system (model M2) used in our study was manufactured by LightLab Imaging, Inc. (Westford, MA, USA). The imaging technique has been described previously. Briefly, after administration of intracoronary nitroglycerin (200 µg), a 3.2F OCT catheter was advanced through a 7F catheter under fluoroscopic guidance to the culprit site. Images were obtained by automatically pulling back the imaging probe and during constant saline flush through a micro-catheter to transiently displace blood. The images were displayed in real time and stored digitally for subsequent quantitative analysis.

Image processing software provided by the OCT manufacturer was used to evaluate the presence of dissection, thrombus, endothelial tissue prolapse, incomplete apposition of the stent to the vessel wall, and irregular stent strut distribution. The imaging reviewers were blinded to clinical and interventional results.

Definition of OCT image data

For OCT determined lesion with lipid pool, the fibrous cap thickness was measured at its thinnest part. Cap thickness for each image was measured at 3 times, and the average value was computed. Lipid was semi-quantified as the number of involved quadrants on the cross-sectional OCT image. Lipid-rich plaque was defined as lipid being present in ≥ 2 quadrants in any of the images within a plaque. Vulnerable plaque was defined as thin-cap fibro-atheromas, a plaque with lipid content in ≥ 2 quadrants and the thinnest part of the fibrous cap measuring ≤ 65 µm (Fig. 1). Coronary dissection was defined as a vessel wall disruption within or adjacent to the stent where a flap of tissue could be clearly differentiated from the underlying plaque. Intravascular thrombus was defined as an irregular mass protruding into the lumen that had a measured dimension ≥ 50µm. Tissue prolapse was defined as protrusion of endothelial or lesion tissue between stent struts extending inside a circular arc connecting adjacent struts. The distance from the arc to the greatest extent of protrusion was taken as a quantitative measure. Incomplete apposition was defined as clear separation between at least one stent strut and the vessel wall. Irregular stent strut distribution was defined as a variation in inter-strut separation ≥ 200%.

Statistical analysis

Data are expressed as mean ± SD or median with range. Baseline characteristics were analyzed by χ² test or student t test. Fisher’s exact test was applied to analyze an association between dissection, prolapse, incomplete apposition, and irregular strut distribution. All analysis was performed using SPSS version 6.0. A P<0.05 was required for statistical significance.

Results

Altogether 15 patients, 9 males and 6 females with mean age of 72.6±5.3 years (range 67-92 years), were enrolled in the study. Thirty-two culprit lesions were identified after diagnostic coronary angiography. Fifteen were selected for OCT study. They included 7 lesions in the left anterior descending artery, 5 lesions in the right coronary artery and 3 lesions in the left circumflex coronary artery. The baseline clinical characteristics of the patients were listed in Table 1. The OCT image probes were successfully passed through all culprit lesions before pre-dilatation. After stenting, OCT studies were repeated with no complications. The image scan time averaged 7.8±2.4 seconds (range 5.7-9.6 seconds). Saline flush effect was influenced by the distance between the lesion and the temporary occluding catheter, the degree of stenosis at the lesion, and the prominent side branches proximal to the lesion. Figure 1 presented the typical OCT findings of a
Fig. 1. A. Four quadrants were divided on the cross-sectional OCT image for lipid semi-quantification. Tick marks represent 1.0 mm. B and C. Lipid-rich plaque was defined as lipid being present in ≥ 2 quadrants in any of the images within a plaque. The thickness of fibrous cap of the lipid-rich plaques in Fig. C and D was less than 65 μm. So it is a vulnerable plaque. D. Magnification presentation of two lipid pools in Fig. A.

Table 1. Baseline characteristics of the patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>UA (n=12)</th>
<th>NSTEMI (n=3)</th>
<th>Total (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>71.4±5.8</td>
<td>73.2±6.1</td>
<td>72.6±5.3</td>
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<tr>
<td>Male, n (%)</td>
<td>6 (50.0)</td>
<td>3 (100.0)</td>
<td>9 (60.0)</td>
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<td>Family history of CAD, n (%)</td>
<td>4 (33.3)</td>
<td>2 (66.7)</td>
<td>6 (40.0)</td>
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<tr>
<td>Diabetes mellitus, n (%)</td>
<td>5 (41.7)</td>
<td>1 (33.3)</td>
<td>6 (40.0)</td>
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<tr>
<td>Hypertension, n (%)</td>
<td>7 (58.3)</td>
<td>3 (100)</td>
<td>10 (66.7)</td>
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<td>Hyperlipidemia, n (%)</td>
<td>6 (50.0)</td>
<td>3 (100)</td>
<td>9 (60.0)</td>
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<td>Multivessel disease, n (%)</td>
<td>12 (100)</td>
<td>3 (100)</td>
<td>15 (100)</td>
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<td>Interested lesions</td>
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<tr>
<td>LAD, n (%)</td>
<td>5 (41.7)</td>
<td>2 (66.7)</td>
<td>7 (46.7)</td>
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<tr>
<td>LCX, n (%)</td>
<td>3 (25.0)</td>
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<td>3 (20.0)</td>
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<tr>
<td>RCA, n (%)</td>
<td>4 (33.3)</td>
<td>1 (33.3)</td>
<td>5 (33.3)</td>
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</tbody>
</table>

UA, unstable angina; NSTEMI, non-ST elevation myocardial infarction; CAD, coronary artery disease; LAD, left anterior descending coronary artery; LCX, left circumflex artery; RCA, right coronary artery.
culprit lesion in an elderly patient with NSTEMI.

The 15 studied lesions were successfully stented by 15 Cypher stents. The other seventeen non-studied lesions were also successfully treated by implanting 26 cypher stents. There were no major or minor procedure complications. All patients were free of symptoms until discharge.

The OCT findings in fifteen studied culprit lesions are summarized in Table 2. Among them, 12 (80.0%) lesions were lipid-rich plaques, 10 (66.7%) lesions were vulnerable plaques with fibrous cap thickness 54.2±7.3 μm. There were 7 (46.7%) ruptured culprit plaque with 4 being in the UA group and 3 in the NSTEMI group. Tissue prolapse between stent struts was observed in 73.3% lesions (n=11, Fig. 2). The magnitude of prolapse averaged 253±137 mm (range 56-574 mm). Irregular stent strut distribution was detected in 60.0% lesions (n=9, Fig. 3). Vessel dissections were found in 33.3% lesions following stent deployment (n=5, Fig. 4). Incomplete stent apposition was observed in 20% stents (n=3, Fig. 5). The mean spacing between the struts and the vessel wall was 172±96 mm (range 117-436 mm). Acute instant thrombus was found in 26.7% lesions but was not complicated with any clinical symptoms and events (n=4, three in the UA group and one in the NSTEMI group, Fig. 6).

It suggested that tissue prolapse was significantly associated with irregular struts (P<0.05). The correlation

<table>
<thead>
<tr>
<th>Finding</th>
<th>UA (n=12)</th>
<th>NSTEMI (n=3)</th>
<th>Total (n=15)</th>
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<tr>
<td>Lipid-rich plaque (≥ 2 quadrants), n (%)</td>
<td>9 (75.0)</td>
<td>3 (100)</td>
<td>12 (80.0)</td>
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<tr>
<td>Fibrous cap thickness, μm</td>
<td>56.3±6.5</td>
<td>51.0±5.4</td>
<td>54.2±7.3</td>
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<td>Vulnerable plaque, n (%)</td>
<td>7 (58.3)</td>
<td>3 (100)</td>
<td>10 (66.7)</td>
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<tr>
<td>Plaque calcification</td>
<td>5 (41.7)</td>
<td>1 (33.3)</td>
<td>6 (40.0)</td>
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<tr>
<td>Ruptured plaque, n (%)</td>
<td>4 (33.3)</td>
<td>3 (100)</td>
<td>7 (46.7)</td>
</tr>
<tr>
<td>Tissue prolapse, n (%)</td>
<td>8 (66.7)</td>
<td>3 (100)</td>
<td>11 (73.3)</td>
</tr>
<tr>
<td>Irregular strut distribution, n (%)</td>
<td>7 (58.3)</td>
<td>2 (66.7)</td>
<td>9 (60.0)</td>
</tr>
<tr>
<td>Vessel dissection, n (%)</td>
<td>4 (33.3)</td>
<td>1 (33.3)</td>
<td>5 (33.3)</td>
</tr>
<tr>
<td>In-stent thrombus, n (%)</td>
<td>3 (25.0)</td>
<td>1 (33.3)</td>
<td>4 (26.7)</td>
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<tr>
<td>Incomplete stent apposition, n (%)</td>
<td>3 (25.0)</td>
<td>0</td>
<td>3 (20.0)</td>
</tr>
</tbody>
</table>

Values are presented as n (%) or mean±SD. UA, unstable angina; NSTEMI, non-ST segment elevation myocardial infarction. Vulnerable plaque was defined as lipid content in ≥ 2 quadrants and the thinnest part of the fibrous cap measuring ≤ 65 μm.

Fig. 2. OCT image shows tissue prolapse after stent deployment. A. A small piece of tissue was prolapsed at the fourth quadrant and in the position of 5 o'clock, measuring 460 μm from its base to the tip. B. Irregular tissue prolapse was presented at 3 o'clock, measuring 570 μm from the vessel wall.
Fig. 3. Irregular stent strut distribution. A. Irregular spacing between adjacent struts was 2.3–9.6 mm. B. The space between adjacent struts varied from 2.8–7.9 mm.

Fig. 4. Dissection observed with OCT following balloon dilatation. A. The major dissection at about 9 o'clock suggested involvement of the adventitia. B. The minor dissection (~270 μm in depth) existed between stent struts at 9 o'clock.

Fig. 5. OCT imaging showed incomplete apposition after stent deployment. A. Stent struts were more than 200 μm away from the vessel endocardium at one and two quadrants. B. Stent struts apposition was located between 1 and 6 o'clock. The maximum distance from the free strut to the vessel wall was 260 μm (marked in arrows).
between prolapse and other pairs was not significant ($P>0.05$).

**Discussion**

The OCT results in this group of elderly patients with UA and USTEMI supported our current understanding of the pathophysiology of coronary artery disease in elderly patients. Although a limited patient sample was enrolled, it was clear that both the culprit lesion and the non-culprit lesion in the elderly patients had similar characteristics compared with those reported in the adult group.\(^9\)\(^{10}\) According to the OCT study, coronary plaques in elderly patients could be also divided into the following categories: 1) Acute ruptured plaque, obviously the causes of the majority of acute myocardial infarction and minority of UA. 2) Vulnerable plaque, having both larger lipid core and very thin fibrous cap, acting as the number one potential cause of clinically acute cardiac ischemic events. It is also the main cause of UA in its acute phase or growing state. 3) Lipid-rich plaque, having larger lipid core but relatively thicker fibrous cap. It might be the early phrase of vulnerable plaque. 4) Stable plaque, having small lipid core and very thick fibrous cap. It could be either a silent lesion or the common cause of stable angina.

Conversely, some differences were found in this study: 1) More than 30% of vulnerable plaques ruptured in the elderly patients with unstable agina. This suggested that minor or critical plaque rupture could be one of the mechanisms of UA. 2) Intraluminal thrombus was found in less than 27% patients. This unexpected finding may have resulted from two factors. Firstly, there was a time delay between the onset of acute cardiac event and the study procedure. OCT imaging and PCI therapy were conducted selectively in the recovery stage of acute coronary syndrome. Secondly, all the patients received potent antiplatelet or antithrombotic therapy. The combination of pharmacological intervention and an activated endogenous thrombolytic system could have dissolved some thrombi, especially in NSTEMI patients. 3) Tissue prolapse rate after stent implantation was a little higher (73% vs. 69%) than in the adult group.\(^{11}\)\(^{12}\) This might be due to the complexity of vessel structure and lesion physiology in old patients.

Our study suggested that tissue prolapse was associated with irregular struts. In the era of bare metal stent, the metal surface and mass of coronary stent were considered as very important causes of long-term in-stent restenosis. So the stent mesh, strut diameter, total length and configuration were strictly controlled in its design and manufacture stages. This would lose stent supportability. Additionally, larger stent mesh was designed for the protection of larger side branches. All of these will lead to the increase of tissue prolapse. However, in an era of DES, we do not need to care much about the metal surface and mass of the stent. The novel design and manufacture art might be helpful to the decrease of tissue prolapse.

The clinical relevance of the tissue prolapse is still controversial. It is postulated that tissue prolapse is related to the following phenomena: 1) slow reflow or non reflow during emergency PCI, 2) acute, subacute or chronic in-stent thrombus, and 3) long-term in-stent restenosis. These hypotheses still need to be confirmed. However, a recent primary study did not identify association between tissue prolapse and late angiographic in-stent restenosis.\(^{12}\)

This study supports the concept that OCT guidance during PCI procedure is very useful in the identification of some important features, including plaque stratification, vessel dissection, intra-luminal thrombus, tissue prolapse,
DPS tapposition, and irregular stent struts. The high resolution and contrast of OCT could provide clear and detailed morphological information about native plaques and stent delivery. However, the significance of these OCT findings needs further evaluation.

There are still limitations in this study. First, the OCT imaging system used in this study is constructed with a scanning optical fiber, an occluding balloon catheter with a central flushing lumen, and a computer system to obtain, display and analyze images. Limited by the diameter, location and time of the occlusion balloon, the present OCT system could not be used in left main stem coronary and the ostium of main coronary branches such as left anterior descending artery, left circumflex and right coronary arteries. The study processing is a little more complex compared with traditional intravascular ultrasound study. Second, due to the small patient sample, vulnerable plaque was not systematically evaluated in elderly patients with ACS. Third, the constitution, development, and detailed mechanism of tissue prolapse need further evaluation. The influence of various tissue prolapses and their debris on acute distal vessel flow and micro-embolus is also one of the important study fields in the future. Finally, the significance of various tissue prolapses in the action of long-term in-stent restenosis needs to be further explained.

In conclusion, our study showed: 1) It is safe and feasible using high resolution and contrast intravascular OCT to diagnose vulnerable or risk coronary plaque and monitor stent deployment in elderly patients with UA and USTEMI; 2) Coronary plaques in elderly patients could be divided into acute ruptured plaque, vulnerable plaque, lipid-rich plaque, and stable plaque; 3) Minor or critical plaque rupture is one of the mechanisms of UA in elderly patients; 4) Present DES implantation is complicated with multiple tissue prolapses which are significantly associated with irregular strut distributions; 5) The action and significance of tissue prolapse on acute vessel slow flow or noflow, in-stent thrombus and chronic instent restenosis need to be further investigated.

Acknowledgement
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References