Original Article

Clinical Characteristics and Prognosis of Peri-strut Low-intensity Area Detected by Optical Coherence Tomography

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Abstract

Background: Peri-strut low-intensity area (PLIA) is a typical image pattern of neointima detected by optical coherence tomography (OCT) after stent implantation. However, few studies evaluated the predictors and prognosis of the PLIA; therefore, we aimed to explore the genesis and prognosis of PLIA detected by OCT in this study.

Methods: Patients presenting neointimal hyperplasia documented by OCT reexamination after percutaneous coronary intervention were prospectively included from 2009 to 2011. Peri-strut intensity was analyzed and classified into two patterns: Low-intensity and high-intensity. Clinical characteristics were analyzed to assess their contribution to peri-strut intensity patterns. Follow-up were performed in patients who did not receive revascularization during OCT reexamination, and the prognosis of the patients was evaluated.

Results: There were 128 patients underwent OCT reexamination after stent implantation included in the study. PLIA was detected in 22 (17.2%) patients. The incidence of PLIA was positively correlated with serum triglyceride (odds ratio [*OR*]: 2.11, 95% confidence interval [*CI*]: 1.14–3.90, $P = 0.017$), low-density lipoprotein (*OR*: 2.61, 95% *CI*: 1.22–5.66, $P = 0.015$), history of cerebrovascular disease (*OR*: 101.11, 95% *CI*: 6.54–1562.13, $P < 0.001$), and initial clinical presentation of acute coronary syndrome (ACS, *OR*: 18.77, 95% *CI*: 2.73–128.83, $P = 0.003$) while negatively correlated with stent implantation time (*OR*: 0.57, 95% *CI*: 0.33–0.98, $P = 0.043$). The median follow-up was longer than 3.8 years. Major adverse cardiovascular events (MACEs) occurred in 7 (7.3%) patients while showed no correlation with PLIA. A total of 17 (17.7%) patients experienced unstable angina (UA) and showed significant correlation with PLIA (hazard ratio: 6.16, 95% *CI*: 1.25–30.33, $P = 0.025$).

Conclusions: PLIA detected by OCT was positively correlated with higher serum lipid level, history of cerebrovascular disease and initial presentation of ACS, and negatively correlated with stent implantation time. Patients with PLIA were more likely to have UA than those with high-intensity while no significant difference was found in MACEs.

Key words: Optical Coherence Tomography; Peri-strut Low-intensity Area; Unstable Angina

Introduction

Neointimal genesis could prevent in-stent thrombosis after percutaneous coronary intervention (PCI). However, neointimal hyperplasia (NIH) could lead to in-stent restenosis (ISR). Besides lumen narrowing, unhealthy neointimal genesis may prompt neoatherosclerosis of neointima, which is a risk factor for cardiovascular events.[1] Therefore, it is important to evaluate the neointimal characteristics after PCI.

Optical coherence tomography (OCT) is an intravascular imaging technology with higher resolution than intravascular ultrasound. It is useful in analyzing the genesis and characteristics of neointima after PCI. It is easy to detect ISR, neoatherosclerosis, thin cap neoatheroma (TCNA) and

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plaque rupture. Moreover, recent studies showed typical image patterns in the restenotic tissues:[2-4] High intensity of peri-strut region is dominant in restenosis tissue, whereas some of the peri-strut tissues show low-intensity in OCT images. Previous studies explored the tissue characteristics of peri-strut low-intensity area (PLIA),[5-7] however, the predictors and prognosis of this typical image pattern is still unknown. Therefore, in this study, we compared clinical characteristics of patients with different patterns of peri-strut intensity and analyzed predictors and prognosis of these patients.

Methods

Subjects and study design

We prospectively enrolled patients accepted OCT examination at least 6 months after drug-eluting stents (DES) implantation from March 2009 to March 2011 in Fuwai Hospital. The patients with neointimal thickness of at least 100 μm in 5 consecutive cross-sectional images were included.

The exclusion criteria of our study were as follows: (1) age ≥80 years old or ≤18 years old; (2) untreated left main coronary artery disease; (3) underwent balloon predilatation before OCT examination; (4) poor OCT image; (5) left ventricle eject fraction ≤30%; and (6) serum creatinine ≥2.0 mg/dl (150 μmol/L). This study was approved by the Institutional Ethics Committee of Fuwai Hospital, and written informed consent was obtained from each patient.

We assessed the OCT images and divided the patients into two groups according to peri-strut intensity: low-intensity group and high-intensity group [Figure 1]. Then we compared clinical characteristics of the two groups. We also performed a follow-up to compare prognosis of the two groups.

Definitions

Major adverse cardiac events (MACEs) were defined as all cause of death, nonfatal myocardial infarction, or target vessel revascularization. Clinical events were defined according to the Academic Research Consortium.[8] Myocardial infarction was defined as the presence of clinical symptoms, electrocardiographic changes, or abnormal image findings of myocardial infarction combined with an increase in creatine kinase myocardial band fraction >3 times the upper limit of the normal range or an increase in troponin T/troponin I to more than the 99th percentile of the upper limit of normal, all of which were unrelated to an interventional procedure.[8,9] Target vessel revascularization was defined as a repeat percutaneous intervention or bypass surgery of the target vessels with either of the following findings: Ischemic symptoms or a positive stress test and an angiographic minimal lumen diameter stenosis ≥50% assessed by quantitative coronary angiographic analysis or an angiographic diameter stenosis ≥70% assessed by quantitative coronary angiographic analysis without either ischemic symptoms or a positive stress test.[9] Symptoms including stable and unstable angina (UA) were acquired through questionnaire. Patients who had stable effort angina during follow-up were defined as stable angina, those with the initial issuance of effort angina, deterioration of exertional angina, resting angina, infarction angina, or variant angina were defined as UA.[10]

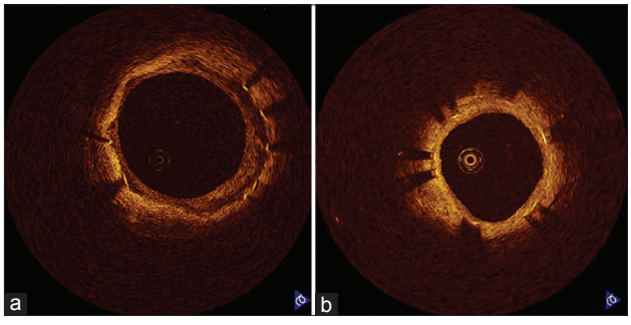

Figure 1: Optical coherence tomography images of peri-strut region. (a) Representative image of peri-strut low-intensity, (b) representative image of peri-strut high-intensity.

Optical coherence tomography image acquisition

OCT was performed according to *the consensus standards for acquisition of OCT*.[11] A 0.016-inch OCT catheter (ImageWire, LightLab Imaging Inc., Westford, MA, USA) was advanced distal to the culprit lesion, using an occlusion balloon catheter (Helios, Goodman Co., Ltd., Nagoya, Japan). To remove blood from the field of view, the occlusion balloon was inflated to a pressure of 0.5 atm (1 atm = 101.325 kPa) at a site proximal to the culprit lesion, and a mixture of dextran and lactate Ringer's solution was infused into the coronary artery from the distal tip of the occlusion balloon catheter at a rate of 0.4–0.7 ml/s. Image acquisition was performed at an automated pull-back speed of 1–2 mm/s. OCT images were recorded and analyzed in LightLab Imaging System (LightLab Imaging Inc., Westford, MA, USA).[3,12]

Optical coherence tomography image analysis

OCT images were analyzed using proprietary off-line software (LightLab Imaging Inc). All of the OCT images were analyzed by two independent investigators who analyze more than 100 cases of OCT images per year, and were blinded to the clinical characteristics. Cross-sectional OCT images were analyzed at 1-mm intervals for qualitative and quantitative measurements. Stent area and luminal cross-sectional area (CSA) were measured. The neointimal area was calculated as the stent area minus luminal CSA. Restenosis ratio was defined as neointimal area divided by stent area. Image patterns were defined as validated criteria.[13] PLIA was defined as homogenous low-intensity around stent struts without significant signal attenuation behind the area on a strut basis [Figure 1a], while peri-strut high intensity was defined as homogenous high intensity around stent struts [Figure 1b]. Patients with one or more cross-sections presented with PLIA were classified into low-intensity group. Macrophage was defined as bright spot reside at the surface of a plaque [Figure 2a];[11,14] TCNA was defined as having an angle of signal-poor lipid pool in <2 quadrants and a fibrous cap thickness ≤65 μm in 3 consecutive images [Figure 2b].[7]

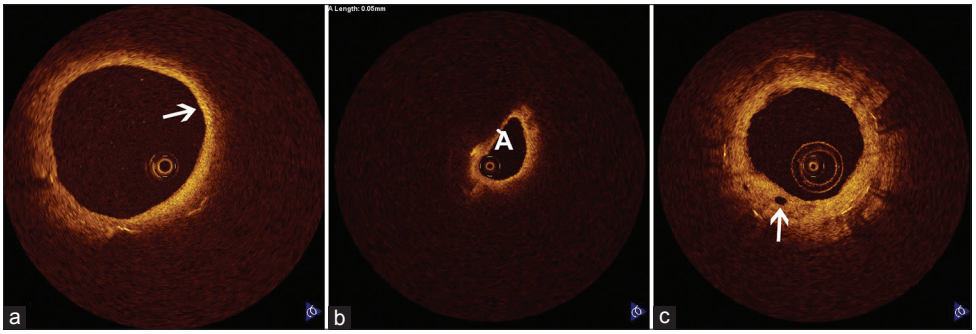

Figure 2: Different image patterns detected by optical coherence tomography. (a) Macrophage showed bright spots at the surface of intima (white arrow). (b) The measurement of neoatheroma cap thickness (label "A" and short white line). Neoatheroma with cap thickness <65 μm was defined as TCNA. (c) Microvessel showed delineated low backscatter structures <200 μm in diameter (white arrow). Cross-sections with one or more positive sites of macrophage, TCNA, or microvessel were defined positive for the specific image pattern. TCNA: Thin cap neoatheroma.

Microvessel was defined as well delineated low backscatter structures <200 μm in diameter that showed a trajectory within the vessel [Figure 2c].[13] Cross-sections with one or more positive sites of macrophage, TCNA, or microvessel were defined positive for the specific image pattern.

Statistical analysis

Statistical analysis was performed with SPSS (version 21.0, SPSS Inc., Chicago, Illinois, USA). Continuous variables were presented as mean ± standard deviation (SD) or median (interquartile range [IQR]) and compared by Student's *t*-test or Mann-Whitney *U*-test. Categorical variables were presented as percentages. Chi-square test was used for comparisons between the groups. To estimate the predictors of PLIA, we performed a binary logistic regression analysis. The initial univariate model included each of the clinical characteristics of the patients. The odds ratio (*OR*) and 95% confidence interval (*CI*) were estimated. The final multivariate model was constructed with the possible factors that were statistically significant in the initial model. The multivariate Cox regression model was used to evaluate the relationship between PLIA and prognosis. Age, gender, and other coronary risk factors (hypertension, diabetes, hyperlipidemia, smoke, total cholesterol, low-density lipoprotein [LDL] and triglyceride) were adjusted. A $P < 0.05$ was considered statistically significant.

Results

Population characteristics

A total of 149 patients accepted OCT examination after DES implantation. Among them, 128 patients were included in this study. There were 2202 cross-sections of OCT images analyzed, and 22 (17.3%) patients presented with PLIA. Baseline characteristics of the patients are listed in Table 1.

There was no significant difference in age, gender, and traditional risk factors for coronary artery disease between the two groups. The median interval from stent implantation to OCT examination is shorter in low-intensity group compared with high-intensity group (0.37 years, IQR: 0.30–1.11 years vs. 1.07 years, IQR: 0.45–4.05 years, $P = 0.004$). While an initial clinical presentation of acute coronary syndrome (ACS) at the time of stent implantation was more frequently observed in low-intensity group than that of high-intensity group (22.7% vs. 6.6%, $P = 0.033$). Total cholesterol (5.46 ± 1.09 vs. 4.71 ± 0.97 mmol/L, $P = 0.002$), LDL (2.39 ± 0.98 vs. 1.91 ± 0.62 mmol/L, $P = 0.041$), and triglyceride (2.42 ± 1.03 vs. 1.87 ± 0.84 mmol/L, $P = 0.010$) were also higher in low-intensity group compared with high-intensity group. Simultaneously, more patients experienced cerebrovascular disease in the low-intensity group than in the high-intensity group (22.7% vs. 1.9%, $P = 0.002$).

Optical coherence tomography assessment of neointima

We analyzed 2202 cross-sections of the OCT image. There was no difference in average intimal thickness and restenosis ratio between the low- and high-intensity groups. Image patterns were qualitatively analyzed. Cross-sections with the presence of macrophage were similar in the two groups. Microvessel was more frequently detected in high-intensity group (4.8% vs. 23.8%, $P < 0.001$), while TCNA was more frequently observed in low-intensity group compared with high-intensity group (7.1% vs. 4.7%, $P = 0.039$) [Table 2].

Factors related to peri-strut low-intensity area

Through the initial univariate binary logistic regression model which included each of the possible coronary risk factors, we found that stent implantation time, history of ACS, cerebrovascular disease, triglyceride, total cholesterol, and LDL were potentially correlated with PLIA. Then using a multivariate binary logistic regression model, we found that factors related to PLIA were stent implantation time (*OR*: 0.57, 95% *CI*: 0.33–0.98), history of ACS (ACS, *OR*: 18.77, 95% *CI*: 2.73–128.83), cerebrovascular disease (*OR*: 101.11 95% *CI*: 6.54–1562.13), LDL (*OR*: 2.61, 95% *CI*: 1.22–5.66), and triglyceride (*OR*: 2.11, 95% *CI*: 1.14–3.90) [Table 3].

Prognosis of the patients

A total of 28 patients accepted PCI treatment once after OCT examination because of other target vessels, and they were excluded from the prospective study. Follow-up was completed in 96 patients. The median follow-up time was more than 3.8 years. No death or myocardial infarction

Table 1: Baseline characteristics of patients with neointimal hyperplasia assessed by OCT

Items	Low-intensity (n = 22)	High-intensity (n = 106)	Statistical values	P
Stent implantation time (years)	0.37 (0.30–1.11)	1.07 (0.45–4.05)	704*	0.004
Follow-up time (years)	3.68 (3.30–3.86)	3.88 (3.43–4.08)	510*	0.208
Clinical variables				
Age (years)	66.1 ± 6.8	62.7 ± 9.5	1.57†	0.119
Male	17 (77.3)	95 (89.6)	2.54‡	0.111
ACS	5 (22.7)	7 (6.6)	5.58‡	0.033
Smoke	7 (31.8)	50 (38.1)	0.59‡	0.303
Hypertension	14 (63.6)	64 (60.4)	0.08‡	0.487
Diabetes	9 (40.9)	31 (29.2)	1.15‡	0.204
Hyperlipidemia	16 (72.7)	64 (60.4)	1.19‡	0.200
Cerebrovascular disease	5 (22.7)	2 (1.9)	15.31‡	0.002
Peripheral vascular disease	0 (0)	1 (0.9)	0.21‡	0.828
Prior MI	11 (50.0)	48 (45.3)	0.16‡	0.432
Prior PCI	4 (18.2)	19 (18.1)	0.00‡	0.600
Prior CABG	1 (4.5)	2 (1.9)	0.55‡	0.438
Laboratory tests				
PLT (×10^9/L)	189 (171–231)	183 (156–221)	982*	0.244
HbA1c (%)	6.10 (5.70–7.18)	6.10 (5.70–6.60)	990*	0.833
Scr (μmol/L)	79.01 ± 18.21	78.93 ± 15.30	0.02†	0.981
Triglyceride (mmol/L)	2.42 ± 1.03	1.87 ± 0.84	2.58†	0.010
TC (mmol/L)	5.46 ± 1.09	4.71 ± 0.97	3.16†	0.002
LDL (mmol/L)	2.39 ± 0.98	1.91 ± 0.62	2.14†	0.041
HDL (mmol/L)	1.12 ± 0.27	1.06 ± 0.26	0.87†	0.385
hsCRP (mg/L)	1.82 (1.78–3.50)	1.64 (0.86–3.46)	961*	0.422
Usage of medication				
Aspirin	22 (100.0)	106 (100.0)	–	–
Clopidogrel	22 (100.0)	97 (94.2)	1.35‡	0.305
β-block	21 (95.5)	94 (91.3)	0.43‡	0.444
ACEI/ARB	15 (68.2)	68 (66.0)	0.04‡	0.529
Statin	21 (95.5)	101 (98.1)	0.53‡	0.443

Values are median (IQR), mean ± SD or n (%); *: U values, †: t values, ‡: χ^2 values, IQR: Interquartile range; SD: Standard deviation; ACS: Acute coronary syndrome; MI: Myocardial infarction; PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass grafting; PLT: Platelet; HbA1c: Hemoglobin A1c; Scr: Serum creatinine; TC: Total cholesterol; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; hsCRP: Hypersensitivity C-reaction protein; ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; OCT: Optical coherence tomography.

Table 2: OCT assessment of neointima between low- and high-intensity groups

Items	Low-intensity (n = 22)	High-intensity (n = 106)	Statistical values	P
Cross-sections (n)	396	1806		
Restenosis ratio (%)	26.59 ± 5.50	27.60 ± 6.92	−1.87†	0.062
Average intimal thickness (mm)	0.12 ± 0.09	0.13 ± 0.05	−1.03†	0.240
Microvessels*	19 (4.8)	429 (23.8)	72.01‡	<0.001
Macrophage*	107 (27.0)	437 (24.2)	1.39‡	0.133
TCNA*	28 (7.1)	85 (4.7)	3.73‡	0.039

Values are mean ± SD or n (%); *With one or more in each cross-section, †: t values, ‡: χ^2 values; SD: Standard deviation; OCT: Optical coherence tomography; TCNA: Thin cap neoatheroma.

happened. A total of seven patients experienced target vessel revascularization (one with PLIA and six without PLIA). Cox regression analysis showed that there was no significant difference between the two groups in MACEs or rehospitalization. While we found that patients in low-intensity group were more likely to have UA during follow-up than in high-intensity group (38.9% vs. 12.8%, hazard ratio: 6.16, 95% *CI*: 1.25–30.33, P = 0.025) [Table 4].

Discussion

PLIA was detected in 17.2% of the patients. It was positively correlated with the initial presentation of ACS, history of cerebrovascular disease, high serum LDL, and triglyceride while negatively correlated with stent implantation time. TCNA was more frequent in low-intensity OCT images while microvessel was less detected in low-intensity group. Patients with PLIA experienced more frequency of UA than that of high-intensity group while no significant difference was found in MACEs between the two groups.

OCT could provide a large amount of information during follow-up after stent implantation. Neointima shows different patterns in OCT images. Peri-strut intensity is one of the distinguishing features among the patterns. The

incidence of PLIA ranges from 6% to 40%,[7,15] which is in consistence with our data. However, few studies researched the genesis and prognosis of PLIA.

We noticed that lipid plaque also showed low-intensity in OCT images. Given that, we hypothesized that PLIA was perhaps correlated with high serum lipid. Therefore, we compared the levels of serum total cholesterol, LDL, and triglyceride of patients with low or high intensity and proved the hypothesis. Considering that previous histological studies did not prove the presence of adipose tissue in swine models,[5,6] we still need a pathological examination of human vessels to confirm the tissue components of neointima.

We also noticed that initial clinical presentation of ACS and shorter stent implantation history were independent risk factors of PLIA. Since inflammation is a key contributor to ACS, it could also provide a reasonable explanation for the detection of more peri-strut inflammation in PLIA pattern.[6] These findings suggest that PLIA may be an immature pattern of neointimal which is associated with ACS or inflammation and appear more frequently in early phases after PCI. Besides, our data showed that patients with PLIA were more likely to be complicated with cerebrovascular disease. It suggests that PLIA may be correlated with vascular disease.

We analyzed the relationship between PLIA and other tissue characteristics. TCNA was found in more cross-sections of patients with PLIA. It suggests that PLIA may be associated with more lipid plaque, and it may be an unstable factor of neointima. The correlation of PLIA and microvessel we found in this study should be interpreted with caution for the reason that the image pattern of microvessel showed low-intensity in OCT images, and it might be hard to distinguish the microvessel patterns from low-intensity neointima. We did not find a correlation between PLIA and NIH, which was different from other studies.[5,16]

Few studies explored the prognosis of patients with PLIA. We compared MACEs and rehospitalization between the two groups. However, no death or MI happened during the follow-up. Therefore, we found no significant difference in MACEs or rehospitalization. As a compromise, we compared the incidence of UA of the patients and found it was positively correlated with PLIA. It suggested that PLIA might lead to poor prognosis.

A possible explanation for PLIA is that patients with ACS or hyperlipidemia are in high inflammation state, after stent implantation, intima healing progression might be different, which would contain more lipid plaques or inflammation cells and with a tendency of more neoatherosclerosis, this type of intima might show low-intensity in OCT images and lead to poor prognosis. We call this phenomenon intimal unhealthy healing. However, further studies are needed to verify this hypothesis in the future.

There are several limitations in this study. First, the limited sample size lead to low incidence of MACEs, hence we had to use UA as end points, which was not a strong enough evidence. Second, we did not quantitatively analyze the intensity of the OCT images which may lead to bias in the classification of intensity. Third, we did not perform serial OCT examinations for a single patient so that we could not explore the natural history of PLIA. Then, stent pressure and length play critical roles in the formation of PLIA, however, we were unable to collect detailed information of stents as most of the patients underwent PCI in other centers. Finally, we did not have a chance to perform pathological examinations of the target vessels so that we could not know the definite tissue components of PLIA tissue.

In conclusion, different types of OCT image patterns may provide meaningful information. PLIA was positively correlated with higher serum lipid level, history of

Table 3: Factors related to peri-strut low-intensity detected by OCT

Factors	*OR*	95% *CI*	*P*
ACS	18.77	2.73–128.83	0.003
Stent implantation time	0.57	0.33–0.98	0.043
LDL	2.61	1.22–5.66	0.015
Triglyceride	2.11	1.14–3.90	0.017
Cerebrovascular disease	101.11	6.54–1562.13	<0.001

ACS: Acute coronary syndrome; LDL: Low-density lipoprotein; OCT: Optical coherence tomography; *OR*: Odds ratio; *CI*: Confidence interval.

Table 4: Major adverse cardiac events and angina pectoris during follow-up after OCT reexamination

Endpoints	Low-intensity (*n* = 18)	High-intensity (*n* = 78)	*HR*	95% *CI*	*P*
MACEs	1 (5.6)	6 (7.7)	1.63	0–138,424.6	0.932
Cardiac death	0 (0)	0 (0)			
MI	0 (0)	0 (0)			
TLR	1 (5.6)	6 (7.7)	1.63	0–138,424.6	0.932
All angina	9 (50.0)	36 (46.2)	1.14	0.39–3.37	0.811
SAP	5 (27.8)	29 (37.2)	0.32	0.07–1.50	0.149
UA	7 (38.9)	10 (12.8)	6.16	1.25–30.33	0.025
Rehospitalization	7 (38.9)	26 (33.3)	0.96	0.23–4.01	0.955

Values are *n* (%); After adjusted for age, gender, hypertension, diabetes, hyperlipidemia, smoke, history of cerebrovascular disease, initial presentation of ACS, TC, LDL, and triglyceride; MACEs: Major adverse cardiovascular events; MI: Myocardial infarction; TLR: Target lesion revascularization; SAP: Stable angina pectoris; UA: Unstable angina; ACS: Acute coronary syndrome; TC: Total cholesterol; LDL: Low-density lipoprotein; OCT: Optical coherence tomography; *CI*: Confidence interval; *HR*: Hazard ratio.

cerebrovascular disease and initial presentation of ACS, and negatively correlated with stent implantation time. Patients with PLIA were more likely to have UA than those with high intensity while no significant difference was found in MACEs between the two groups. Further large, randomized studies are needed to confirm these findings.

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Conflicts of interest

There are no conflicts of interest.

References

1. Park SJ, Kang SJ, Virmani R, Nakano M, Ueda Y. In-stent neoatherosclerosis: A final common pathway of late stent failure. J Am Coll Cardiol 2012;59:2051-7.
2. Ishibashi K, Tanaka A, Kitabata H, Kubo T, Kashiwagi M, Komukai K, *et al.* Clinical significance of low signal intensity area surrounding stent struts identified by optical coherence tomography. Int Heart J 2013;54:7-10.
3. Maejima N, Hibi K, Saka K, Nakayama N, Matsuzawa Y, Endo M, *et al.* Morphological features of non-culprit plaques on optical coherence tomography and integrated backscatter intravascular ultrasound in patients with acute coronary syndromes. Eur Heart J Cardiovasc Imaging 2015;16:190-7.
4. Shibuya M, Fujii K, Fukunaga M, Imanaka T, Miki K, Tamaru H, *et al.* Natural history of low-intensity neointimal tissue after an everolimus-eluting stent implantation: A serial observation with optical coherence tomography. Heart Vessels 2015;30:136-9.
5. Tellez A, Afari ME, Buszman PP, Seifert P, Cheng Y, Milewski K, *et al.* Peri-strut low-intensity areas in optical coherence tomography correlate with peri-strut inflammation and neointimal proliferation: An *in-vivo* correlation study in the familial hypercholesterolemic coronary swine model of in-stent restenosis. Coron Artery Dis 2014;25:595-601.
6. Teramoto T, Ikeno F, Otake H, Lyons JK, van Beusekom HM, Fearon WF, *et al.* Intriguing peri-strut low-intensity area detected by optical coherence tomography after coronary stent deployment. Circ J 2010;74:1257-9.
7. Choi JH, Granada JF, Kim JS, Song YB, Hahn JY, Choi SH, *et al.* OCT-verified peri-strut low-intensity areas and the extent of neointimal formation after 3 years following stent implantation. JACC Cardiovasc Imaging 2012;5:1156-60.
8. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, *et al.* Clinical end points in coronary stent trials: A case for standardized definitions. Circulation 2007;115:2344-51.
9. Kim JS, Lee JH, Shin DH, Kim BK, Ko YG, Choi D, *et al.* Long-term outcomes of neointimal hyperplasia without neoatherosclerosis after drug-eluting stent implantation. JACC Cardiovasc Imaging 2014;7:788-95.
10. Deckers JW. Classification of myocardial infarction and unstable angina: A re-assessment. Int J Cardiol 2013;167:2387-90.
11. Tearney GJ, Regar E, Akasaka T, Adriaenssens T, Barlis P, Bezerra HG, *et al.* Consensus standards for acquisition, measurement, and reporting of intravascular optical coherence tomography studies: A report from the International Working Group for Intravascular Optical Coherence Tomography Standardization and Validation. J Am Coll Cardiol 2012;59:1058-72.
12. Kubo T, Imanishi T, Takarada S, Kuroi A, Ueno S, Yamano T, *et al.* Assessment of culprit lesion morphology in acute myocardial infarction: Ability of optical coherence tomography compared with intravascular ultrasound and coronary angioscopy. J Am Coll Cardiol 2007;50:933-9.
13. Gonzalo N, Serruys PW, Okamura T, van Beusekom HM, Garcia-Garcia HM, van Soest G, *et al.* Optical coherence tomography patterns of stent restenosis. Am Heart J 2009;158:284-93.
14. Tahara S, Morooka T, Wang Z, Bezerra HG, Rollins AM, Simon DI, *et al.* Intravascular optical coherence tomography detection of atherosclerosis and inflammation in murine aorta. Arterioscler Thromb Vasc Biol 2012;32:1150-7.
15. Tada T, Kastrati A, Byrne RA, Schuster T, Cuni R, King LA, *et al.* Randomized comparison of biolimus-eluting stents with biodegradable polymer versus everolimus-eluting stents with permanent polymer coatings assessed by optical coherence tomography. Int J Cardiovasc Imaging 2014;30:495-504.
16. Sato K, Costopoulos C, Takebayashi H, Naganuma T, Miyazaki T, Goto K, *et al.* The role of integrated backscatter intravascular ultrasound in characterizing bare metal and drug-eluting stent restenotic neointima as compared to optical coherence tomography. J Cardiol 2014;64:488-95.