AsiaIntervention 2017;3:35-40

A modified frequency domain optical coherence tomography procedure for imaging severely stenotic coronary artery lesions

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KEYWORDS

- coronary artery disease
- frequency domain optical coherence tomography
- imaging

Abstract

Aims: This proof-of-concept study aimed to investigate the clinical feasibility of a modified frequency domain optical coherence tomography (FD-OCT) procedure for imaging severely stenotic coronary artery lesions.

Methods and results: In total, 46 patients in whom clear images were unobtainable using conventional FD-OCT examination were consecutively enrolled in this study. Then, they were randomly divided into two groups: group A (FD-OCT examination using the new modified procedure, n=23), and group B (FD-OCT examination using a previously described procedure, the Yamaguchi method, n=23). The procedure success was 100% in group A and 86.96% in group B. Clear images of the proximal segment were obtained by both procedures for all patients. The percentage of clear images for the distal segment was 95.65% in group A and 85% in group B. Clear images of the maximal stenosis segment were 100% in group A and 95% in group B. However, these outcomes were not significantly different between the two groups. The amount of contrast agent used in group A was lower than that used in group B.

Conclusions: The new modified procedure can obtain clear images of severely stenotic coronary artery lesions. The difference in contrast volume is of statistical significance but may be of minimal clinical significance.

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SUBMITTED ON 06/01/2016 - REVISION RECEIVED ON 13/11/2016 - ACCEPTED ON 25/11/2016

DOI: 10.4244/AsiaInterv_V3I1A10

Introduction

Frequency domain optical coherence tomography (FD-OCT) is increasingly used to assess coronary artery lesions in clinical practice. Compared with time domain optical coherence tomography (TD-OCT), FD-OCT has a higher pullback speed without necessitating balloon occlusion of the artery[1,2]. However, the profile diameter of the FD-OCT catheter (approximately 2.7 Fr, 0.9 mm diameter) is larger than that of TD-OCT, which can occlude severely stenotic coronary artery lesions and cause insufficient distal contrast flushing and blood clearance, ultimately leading to poor OCT imaging and examination failure. Therefore, the use of FD-OCT is not recommended for severely stenotic coronary artery lesions with a minimum vessel diameter below 0.9 mm. Yamaguchi et al[3] recently recommended a new FD-OCT imaging procedure that could better characterise severely stenotic coronary artery lesions. Their imaging protocol allowed the acquisition of approximately 5 cm of the coronary segment in 3.5 s, with a contrast medium volume of 14 ml (using a cardiovascular injection pump to deliver the contrast medium through the guide catheter at a rate of 4 ml/s for a total of 14 ml or 3.5 s). The new FD-OCT imaging procedure was an improvement over conventional procedures, and images were obtained for most patients in whom conventional procedures had failed. Using their proposed procedure, the Dragonfly™ imaging catheter (St. Jude Medical, St. Paul, MN, USA) is first passed through the lesion and then retracted to a position proximal to the target lesion. The catheter is then passed through the target lesion again before initiating the pullback. Passing the catheter through severely stenotic coronary artery lesions twice is inconvenient and may damage the Dragonfly catheter. To image severely stenotic coronary artery lesions better, we modified the procedure of Yamaguchi et al. Two important adjustments were made: 1) the Dragonfly catheter was passed through the lesions just once, and pullback was triggered automatically when distal blood was cleared sufficiently, and 2) 5 ml mixed liquid (saline and contrast 1:1) was injected manually to flush the blood before injecting contrast medium into the target coronary artery (flow rate 3 ml/s, volume 9 ml). This proof-of-concept study aimed to analyse the new FD-OCT imaging procedure in patients with severely stenotic coronary artery lesions.

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Methods

STUDY POPULATION AND PROTOCOL

In total, 46 patients with acute coronary syndrome (ACS) who had undergone unsuccessful FD-OCT imaging were enrolled consecutively between December 2013 and December 2014. Examination failure occurred due to severely stenotic coronary artery lesions which resulted in insufficient distal contrast flushing and blood clearance. Patients were randomly divided into two groups, group A (n=23) and group B (n=23), as shown in **Figure 1**. Patients in group A underwent FD-OCT examination using the new modified procedure, and patients in group B underwent FD-OCT examination using the Yamaguchi et al procedure[3]. All patients provided written informed consent prior to coronary angiography and FD-OCT examination. The study protocol was approved by the local research ethics committee.

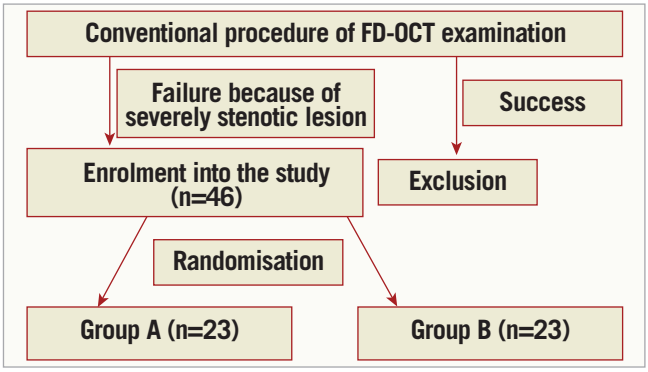

Figure 1. *Flow chart. Flow chart of the study protocol, showing the enrolment procedure. FD-OCT: frequency domain optical coherence tomography; Group A: FD-OCT examination using our modified procedure; Group B: FD-OCT examination using the procedure of Yamaguchi et al[3].*

CORONARY ANGIOGRAPHY AND ANALYSIS

Coronary angiography was performed using a 6 Fr guiding catheter through the femoral or radial artery, and images were acquired after 200 µg of nitroglycerine had been administered into the coronary artery. All results were analysed at an independent core laboratory. The quantitative coronary angiography (QCA) software package QCA-CMS (Medis medical imaging systems, Leiden, The Netherlands) was used for imaging analysis **(Figure 2)**. The minimal lumen diameter, proximal and distal reference lumen diameters, diameter stenosis percentages, the total lesion length, and the length of maximal stenosis were measured.

OCT IMAGE ACQUISTION

The C7-XR™ FD-OCT™ system (St. Jude Medical) using an automatic pullback speed of 20 mm/s was used in this study. A 2.7 Fr Dragonfly catheter (St. Jude Medical) was used to acquire the images. The procedure was attempted using a 6 Fr guiding catheter through the radial artery, and the guiding catheter was placed coaxial to the left or right coronary artery, before passing a 0.014-inch guidewire through the target lesion to deliver the Dragonfly catheter.

In group A, the modified FD-OCT imaging procedure was performed as follows: 1) a cardiovascular pump with a guide catheter was connected, 2) 5 ml of mixed liquid (1:1 saline and contrast) was placed into the injector (volume 5 ml) connected to the flush port of the Dragonfly catheter, air was ejected out of the Dragonfly catheter, then the catheter was connected to the pullback device, 3) the Dragonfly catheter was passed through the target lesion, 4) the pullback trigger of the FD-OCT system was set to automatic and the system mode switched to live view, 5) the 5 ml of liquid was injected manually (flow rate ~1 ml/s), before injecting

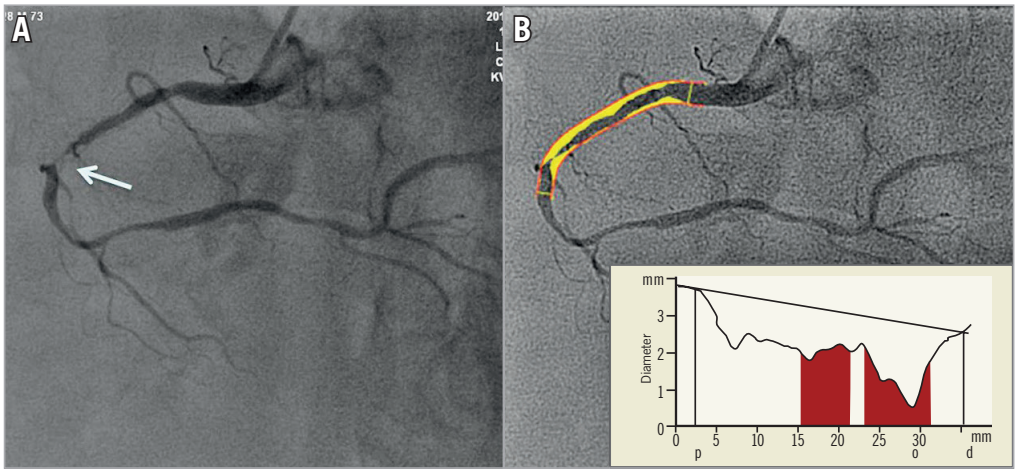

Figure 2. *Quantitative coronary angiography (QCA) analysis. A) Severely stenotic lesions in the right coronary artery (white arrow). B) QCA-CMS software from Medis for imaging analysis of the severely stenotic lesions in the right coronary artery.*

the contrast medium into the coronary artery (flow rate 3 ml/s, volume 9 ml), 6) the catheter was automatically pulled back when the distal blood was cleared sufficiently, 7) when pullback was complete, contrast flush was discontinued, and the Dragonfly catheter was retracted into the guide catheter.

In group B, the procedure proposed by Yamaguchi et al was performed as follows: 1) a cardiovascular injection pump was connected to the guide catheter, 2) an injector (volume 2 ml contrast) was connected with the flush port of the Dragonfly catheter, air was ejected out of the Dragonfly catheter, then the catheter was connected to the pullback device, 3) the lesion size and the ability of the catheter to pass through were confirmed before retracting the catheter to a proximal position, 4) the pullback trigger of the FD-OCT system was set to manual, the system mode switched to live view, and pullback enabled, 5) the contrast medium was injected into the target coronary artery (left coronary artery: flow rate 4 ml/s, volume 14 ml; right coronary artery: flow rate 3 ml/s, volume 12 ml), 6) the Dragonfly catheter was passed through the target lesion and, as soon as positioning was complete, pullback was initiated, 7) when pullback was complete, contrast flush was discontinued, and the Dragonfly catheter was retracted into the guide catheter.

ENDPOINT AND PARAMETERS

The primary endpoint was the proportion of patients in the two groups for whom clear images had been obtained. Clear images were defined as having a clear vessel lumen profile and target lesion segment **(Figure 3)**. The images were assessed by two independent investigators, and the length of the target lesion was divided into three segments (maximum stenosis, distal and proximal); OCT imaging at the three segments was then analysed. The safety endpoint was complications associated with the FD-OCT examination, such as acute vessel occlusion, angina pectoris, dissection, significant arrhythmias and vasospasm. The amount of contrast medium was also recorded.

STATISTICAL ANALYSIS

Continuous variables are expressed as mean±standard deviation and categorical variables as absolute numbers and percentages. Differences between groups were assessed using Pearson's χ^2 test or the Student's t-test. A p-value <0.05 was considered statistically significant. Statistical evaluation was performed using dedicated software (SPSS 11.5 for Windows; SPSS Inc., Chicago, IL, USA).

Results

BASELINE CHARACTERISTICS

FD-OCT examination was performed in 46 patients who exhibited ACS between December 2013 and December 2014. The demographic baseline, serological indicators, current treatments, and angiographic characteristics were not significantly different between the groups **(Table 1)**.

OCT EXAMINATION AND RESULTS

The results of the OCT examinations are shown in **Table 2**. The OCT examination procedure was successful on the first attempt, and clear images were acquired in group A **(Figure 3)**; however, clear images could not be acquired in three patients of group B due to insufficient distal contrast flushing and blood clearance. Therefore, the procedure success rate was higher in group A compared with group B, but the results were not significantly different (100 vs. 86.96%, p=0.233). There were no complications associated with FD-OCT examination in group A. However, one patient in group B experienced angina pectoris which stopped after the examination ended. The OCT images were assessed from the maximal stenosis, distal, and proximal segments. Clear images of the proximal segment were obtained for all patients. The percent of clear images obtained from the distal segment (95.65 vs. 85%, p=0.465) and maximal stenosis segment (100 vs. 95%, p=0.465) in group A was higher than that in group B; however, the differences

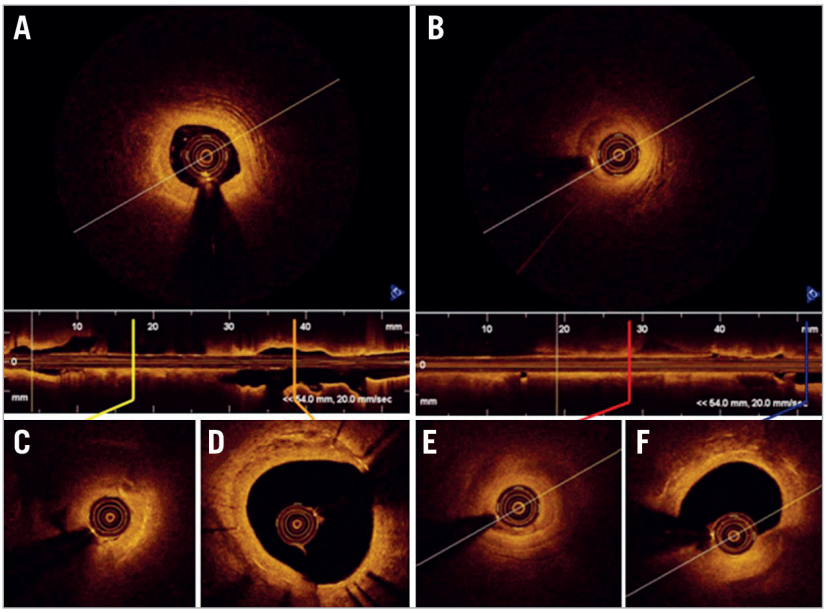

Figure 3. *Optical coherence tomography imaging achieved using the new procedure and the Yamaguchi et al procedure. OCT image of the new procedure: clear image segments show the distal side of the lesion (A), the stenotic lesion (C), and the proximal side of the lesion (D). OCT image of the Yamaguchi et al procedure: image segments show the distal side of the lesion (B), the stenotic lesion (E), and the proximal side of the lesion (F).*

Table 1. Baseline clinical and angiographic characteristics.

	Group A (n=23)	Group B (n=23)	*p*-value
Age (years)	54.8±11.4	58.6±10.9	0.258
Proportion of males, n (%)	16 (69.6)	15 (65.2)	0.753
Hypertension history, n (%)	12 (52.2)	14 (60.9)	0.552
Hypercholesterolaemia, n (%)	8 (34.8)	10 (43.5)	0.546
Current smoker, n (%)	13 (56.5)	11 (47.8)	0.555
Diabetes mellitus, n (%)	9 (39.1)	7 (30.4)	0.536
Systolic blood pressure, mmHg	117.2±20.6	123.1±17.1	0.304
Diastolic blood pressure, mmHg	72.1±15.4	73.7±13.9	0.724
Blood glucose, mmol/L	6.3±1.9	6.1±1.9	0.608
CHO, mmol/L	4.5±0.8	4.3±0.9	0.626
LDL-C, mmol/L	2.8±0.7	2.4±0.9	0.125
Medical treatment			
Aspirin, n (%)	23 (100)	23 (100)	–
Statin, n (%)	23 (100)	23 (100)	–
ACEI/ARB, n (%)	9 (39.1)	10 (43.5)	0.765
ß-blocker, n (%)	9 (39.1)	9 (39.1)	–
Coronary angiography			
Minimum vessel diameter, mm	0.66±0.15	0.68±0.13	0.736
Maximal diameter stenosis (%)	81.06±3.87	79.69±4.44	0.27
Total length of lesion, mm	29.70±6.38	31.96±7.02	0.259
Length of maximal stenosis, mm	7.62±1.35	7.71±1.45	0.784
Proximal reference diameter, mm	3.51±0.28	3.34±0.35	0.156
Distal reference diameter, mm	3.11±0.25	2.98±0.28	0.104

ACEI/ARB: angiotensin-converting enzyme inhibitors/angiotensin receptor blocker; CHO: total cholesterol; LDL-C: low-density lipoprotein cholesterol; Medical treatment: the in-hospital treatment

Table 2. Results of the FD-OCT examinations.

	Group A (n=23)	Group B (n=23)	*p*-value
Procedure success, n (%)	23 (100)	20 (86.96)	0.233
Clear images			
Proximal segment, n (%)	23 (100)	20 (100)	–
Maximal stenosis segment, n (%)	23 (100)	19 (95)	0.465
Distal segment, n (%)	22 (95.65)	17 (85)	0.323
Contrast medium, ml	7.87±1.01	9.74±1.57	<0.001
Complications, n (%)	0 (0)	1 (5)	0.465

were not significant. The amount of contrast agent used in group A was significantly less than that in group B (7.87±1.01 vs. 9.74±1.57 ml, p<0.001).

Discussion

OCT is useful for elucidating the morphologic characteristics of coronary plaques, with high sensitivity and specificity[4-8]. First-generation OCT, TD-OCT, requires a balloon to block the coronary lumen to acquire clear images. This disadvantage limits its clinical application. The second-generation OCT, FD-OCT, can achieve a rapid pullback speed of up to 25 mm/s with no need for balloon occlusion[1,2]. This advantage has expanded its clinical application. However, the catheter used in FD-OCT is larger than that in TD-OCT and may block the coronary lumen and cause blurring of the distal segment in severely stenotic coronary artery lesions. Severely stenotic coronary artery lesions are frequently

overestimated by coronary angiography due to the severe narrowing of the lumen and may result in longer than necessary stent implantation. Therefore, FD-OCT is sometimes necessary to determine the appropriate stent length[9]. Conventional procedures fail to acquire clear images because the catheter occludes the coronary artery when traversing a severe stenosis. This prevents the contrast medium from flushing out the blood for clear imaging. Yamaguchi et al[3] reported that their method could effectively and safely obtain clear images in severely stenotic coronary artery lesions for which conventional procedures failed. However, their proposed procedure requires the catheter to be passed through the lesion at least twice, which is inconvenient and may damage the catheter. For this reason, the FD-OCT procedure was modified for the imaging of severely stenotic coronary artery lesions. Two important modifications were: 1) the Dragonfly catheter was passed through the severely stenotic coronary artery lesion just once, and pullback was triggered automatically when distal blood was cleared sufficiently, and 2) 5 ml mixed liquid (saline and contrast 1:1) was first injected manually to flush out the blood before injecting contrast medium into the coronary artery (flow rate 3 ml/s, volume 9 ml). In this study, we compared our newly modified procedure with that of Yamaguchi. The results of this proof-of-concept study showed that the modified procedure provided clear images without failure, whereas the method by Yamaguchi et al resulted in unclear images due to insufficient distal contrast flushing and blood clearance. The procedure success rate was 86.96% using the Yamaguchi method and 100% using the modified method. The procedure success rate was numerically, although not significantly, lower when using the Yamaguchi method compared with the modified method. Both procedures can acquire clear images from proximal segments; however, imaging the maximal stenosis and distal segments is more challenging due to contrast flushing and blood clearance. The percentage of clear images obtained from the distal (95.65 vs. 85%, p=0.465) and maximal stenosis segments (100 vs. 95%, p=0.465) was higher when using the modified procedure compared with the Yamaguchi procedure. The modified procedure was successful on the first attempt and without complications; however, one patient (5%) experienced angina pectoris when undergoing the Yamaguchi et al procedure. In the study by Yamaguchi et al, clear images were obtained from the 20 patients enrolled. In the three remaining patients, OCT signal attenuation due to blood flow was observed due to inadequate blood clearance distal to the lesion. The main reason for the success of the modified procedure was the use of a mixed liquid (saline and contrast, 1:1) to flush away blood in the maximal and distal segments before the injection of contrast medium. Although the results showed no statistically significant differences, the modified procedure is more convenient than both Yamaguchi's and conventional procedures and may reduce the risk of damaging the Dragonfly catheter. Successful imaging of the lesion ultimately leads to better guidance for stent implantation.

Another advantage of the modified procedure is the reduced use of contrast medium. Conventional procedures require repeated contrast injections, which can enlarge the coronary dissection and result in contrast-induced nephropathy[10,11]. The mean amount of contrast medium used for OCT in Yamaguchi et al's study was 35 ml, with a maximum of 56 ml. These contrast medium volumes were not sufficient for patients with longer lesions or those who required repeat interventional treatment. For the modified method, 5 ml mixed liquid (saline and contrast, ratio 1:1) was injected (flow rate 1 ml/s) before the contrast medium was injected into the target coronary artery (flow rate 3 ml/s, volume 9 ml). The advanced flushing of blood distal to the lesion allowed precise timing for the contrast medium, and the automatic pullback trigger also assured further contrast medium reduction. In this study, the modified method resulted in reduced contrast medium use compared with the method of Yamaguchi et al (7.87±1.01 vs. 9.74±1.57 ml, p<0.001). The difference of approximately 2 ml contrast volume is of statistical significance but has minimal clinical significance. We still hope that patients with severely stenotic coronary artery lesions that are much longer and often require repeat imaging, and patients who may have multivessel coronary stenosis, both of which lead to increased use of contrast medium, could benefit from this. In these cases, the modified FD-OCT procedure may be even more valuable.

Limitations

There are several limitations for this proof-of-concept study. First, the absence of any statistical differences may be due to the small sample size, so further studies are needed to verify the results. Second, the newly modified procedure is unsuitable for complicated lesions. Third, no follow-up data from these patients were obtained, so additional effects were not discovered.

Conclusions

The newly modified procedure can effectively obtain clear images from severely stenotic coronary artery lesions, is more convenient and requires the use of a lower amount of contrast medium.

Impact on daily practice

Severely stenotic coronary artery lesions are frequently overestimated by coronary angiography due to the severe narrowing of the lumen. This may result in a longer than needed stent implantation. Therefore, FD-OCT is sometimes necessary to determine the appropriate stent length. Conventional FD-OCT procedures fail to acquire clear images because the catheter occludes the coronary artery when traversing a severe stenosis. This prevents the contrast medium from flushing out the blood. The modified procedure developed in this study is clinically feasible, is more convenient, and uses a slightly smaller amount of contrast medium compared with the procedure by Yamaguchi et al[3].

Conflict of interest statement

The authors have no conflicts of interest to declare.

References

1. Tearney GJ, Waxman S, Shishkov M, Vakoc BJ, Suter MJ, Freilich MI, Desjardins AE, Oh WY, Bartlett LA, Rosenberg M, Bouma BE. Three-dimensional coronary artery microscopy by intracoronary optical frequency domain imaging: first-in-human experience. *JACC Cardiovasc Imaging.* 2008;1:752-61.

2. Ferrante G, Presbitero P, Whitbourn R, Barlis P. Current applications of optical coherence tomography for coronary intervention. *Int J Cardiol.* 2013;165:7-16.

3. Yamaguchi Y, Kagawa E, Kato M, Sasaki S, Nakano Y, Ochiumi Y, Takiguchi Y, Arakawa Y, Ishimaru A, Ueda A, Dote K. A novel procedure for imaging acute coronary syndrome lesions using frequency-domain optical coherence tomography. *EuroIntervention.* 2013;9:996-1000.

4. Kubo T, Imanish T, Takarada S, Kuroi A, Ueno S, Yamano T, Tanimoto T, Matsuo Y, Masho T, Kitabata H, Tsuda K, Tomobuchi Y, Akasaka T. 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.

5. Jang IK, Tearney GJ, MacNeill B, Takano M, Moselewski F, Iftima N, Shishkov M, Houser S, Aretz HT, Halpern EF, Bouma BE. In vivo characterization of coronary atherosclerotic plaque by use of optical coherence tomography. *Circulation.* 2005;111:1551-5.

6. Tian J, Ren X, Vergallo R, Xing L, Yu H, Jia H, Soeda T, McNulty I, Hu S, Lee H, Yu B, Jang IK. Distinct morphological features of ruptured culprit plaque for acute coronary events compared to those with silent rupture and thin-cap fibroatheroma: combined optical coherence tomography and intravascular ultrasound study. *J Am Coll Cardiol.* 2014;63:2209-16.

7. Fleg JL, Stone GW, Fayad ZA, Granada JF, Hatsukami TS, Kolodgie FD, Ohayon J, Pettigrew R, Sabatine MS, Tearney GJ, Waxman S, Domanski MJ, Srinivas PR, Narula J. Detection of high-risk atherosclerotic plaque: report of the NHLBI Working Group on current status and future directions. *JACC Cardiovasc Imaging.* 2012;5:941-55.

8. Zafar H, Ullah I, Dinneen K, Matiullah S, Hanley A, Leahy MJ, Sharif F. Evaluation of hemodynamically severe coronary stenosis as determined by fractional flow reserve with frequency domain optical coherence tomography measured anatomical parameters. *J Cardiol.* 2014;64:19-24.

9. Kubo T, Tanaka A, Kitabata H, Ino Y, Tanimoto T, Akasaka T. Application of optical coherence tomography in percutaneous coronary intervention. *Circ J.* 2012;76:2076-83.

10. Rihal CS, Textor SC, Grill DE, Berger PB, Ting HH, Best PJ, Singh M, Bell MR, Barsness GW, Mathew V, Garratt KN, Holmes DR Jr. Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. *Circulation.* 2002;105: 2259-64.

11. Chen Y, Hu S, Liu Y, Zhao R, Wang L, Fu G, He Q, Su X, Zheng Y, Qi X, Liu H, Wang J, Gao W, Wang M, Liu S, Zheng X, He B, Yang P, Zhou S, Gao C, Qiu C. Renal tolerability of iopromide and iodixanol in 562 renally impaired patients undergoing cardiac catheterisation: the DIRECT study. *EuroIntervention.* 2012;8:830-8.